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Electrochemistry I

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Preface to the Series on Electrochemistry

The scope of electrochemistry having broadened tremendously within the last ten years has become a remarkably diverse science. In the field of electroorganic synthesis, for example, selectivity has been improved by use of electrogenerated reagents, energy uptake lowered and space-time yields have been improved by using mediated reactions. In addition, electroorganic chemistry has been efficiently applied to the synthesis of key building blocks for complex molecules and has established its role as a new tool in organic synthesis. However electrochemistry has also found new and interesting applications in quite different fields of chemistry. Photoelectrochemistry, as one example, is not only valuable for transformations of organic molecules but also for the very important goal of energy conversion. More insight has been gained in the processes occurring on illuminated semiconductor electrodes and micro particles. Designing the composition of electrode surfaces can lead to the selective activation of electrodes. Electrochemical sensors and techniques present new opportunities for the analysis of biological compounds in medicine and biology. Research in the field of conducting polymers is very intensive because of interesting potential applications.

Therefore I am very happy that Springer-Verlag has decided to account for these important developments by introducing a series of volumes on new trends in electrochemistry within its series Topics in Current Chemistry. The volumes will cover the important trends in electrochemistry as outlined above in the following manner:

Electroorganic Synthesis by Indirect Electrochemical Methods;
New Applications of Electrochemical Techniques;
Recent Developments in Electroorganic Synthesis.

The guest editor is very happy and thankful that well-known experts who are actively engaged in research in these fields have agreed to contribute to the volumes. It is hoped that this collection of reviews is not only valuable to investigators in the respective fields but also to many chemists who are not so familiar with electrochemistry.

Bonn, Mai 1987 Eberhard Steckhan

Preface to Volume I

Volume I of the electrochemistry series in Topics in Current Chemistry is dedicated to indirect electrochemical processes using electrogenerated reagents, homogeneous and heterogeneous redox-catalysts, and light induced electron transfer reactions for the selective synthesis of organic compounds. Selectivity is the main focus of all five contributions to this volume. In the first chapter, selectivity is obtained by using electrochemically regenerable homogeneous redox-reagents. However electrochemical regeneration not only allows for selectivity but also for energy savings and prevention of environmental hazards. The second chapter deals with the selectivity of chemical transformations at illuminated semiconductor electrodes and particles. In this way light may be stored in the form of valuable organic compounds, an important aspect in the search for energy saving processes. In the third chapter the in-situ generation and regeneration of the heterogeneous redox-catalyst NiOOH at the electrode surface is presented in its application for selective transformations. Usually the chemistry of acids and bases would not be expected to be part of electrochemistry. However, electrochemistry provides a means of generating acids and bases not only by a very simple procedure but, moreover, it allows to purposely adjust the reactivity and selectivity of the reagents to the needs of the desired chemical reaction. These are the topics of chapters four and five.

It is hoped that many of the readers will find stimulation and excitement in the contributions of this volume.

Bonn, March 1987 Eberhard Steckhan

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Organic Syntheses with Electrochemically Regenerable Redox Systems

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1 Introduction

Electrochemical reduction and oxidation processes offer several advantages over conventional methods in their application to organic synthesis. For example, selective transformations can be carried out on specific groups in a multifunctional, valuable compound under the usually mild reaction conditions. Independence of a reagent will result in drastically diminished environmental problems by spent reagents. Electrochemistry also allows the application of alternative feedstocks and better use of raw materials. Product isolation and continuous processing are simplified.

An inherent problem with electrochemistry is that at least one heterogeneous step is always involved. The rate of this step is fast for a simple electron transfer. But in many electrochemical processes this step is hindered and that results in the necessity to apply large overpotentials to obtain reasonable current densities. In such a case a redox-catalyst (mediator) can considerably speed up the reaction and lower the overpotential. Such *indirect electrosynthesis*, though it has almost fallen into oblivion, has a long tradition [1] which recently finds fast increasing interest and numerous applications. One of the very early technical applications [2,3] is the oxidation of glucose or lactose to calcium gluconate or lactobionate, respectively, using bromide as redox-catalyst (Eq. (1)). The bromide is anodically oxidized to bromine which with $CaCO_3$ forms calcium hypobromite as oxidizing agent. Bromine is electrochemically regenerated from the resulting bromide after the oxidation step [2,4].

$$2\,C_6H_{12}O_6 + CaCO_3 + H_2O \xrightarrow[\text{anode}]{Br^{\ominus}} Ca(C_6H_{11}O_7)_2 + CO_2 + 2H_2 \qquad (1)$$

As schematically demonstrated in Fig. 1, the indirect electrolysis combines a heterogeneous step, that is the formation and regeneration of the redox-catalyst (Med = mediator) in its active form, with the homogeneous redox reaction of the substrate involving the active mediator.

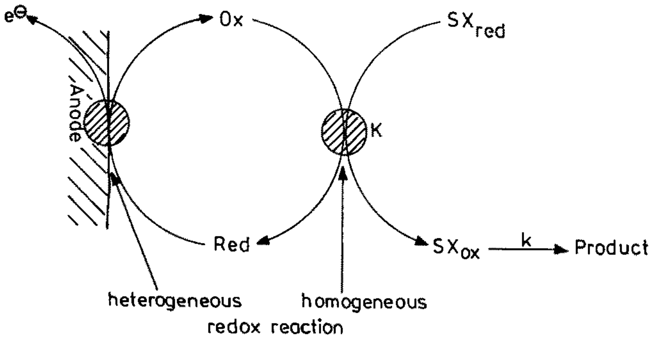


Fig. 1. Principle of the indirect electrolysis examplified by an oxidation

Recently this electrochemical method is being widely accepted [5-11]. One reason for the increasing importance, in the light of environmental considerations, is the possibility for the regeneration of redox reagents *in situ*, so that large amounts of product can be produced from small inventories of reagent with small losses to the surroundings. In addition, the energy consumption can be lowered and otherwise unknown, mostly very high, selectivities can be obtained.

2 Basic Concepts

2.1 The Principle of Indirect Electrolysis

Indirect electrochemical processes are hybrids in a certain sense: they combine an electrochemical and therefore heterogeneous electron transfer reaction with a homogeneous redox process. The redox reagent undergoes a homogeneous reaction with the substrate and is subsequently regenerated in its active form at the electrode (see Fig. 1).

The electrochemical regeneration can be performed in three different ways [3,7,12]. The oldest one, the so-called "ex-cell" method, is long known [13]. It consist of two steps. In the first one, the redox agent reacts with the substrate and is subsequently separated from the products. In the second step, it is electrochemically regenerated externally in the electrolysis cell [3,7] (see Fig. 2). This method possesses the following advantages [8,14]: chemical and electrochemical steps can be optimized independently of each other and neither substrates and products can adversely affect the electrode reaction nor can the electrode interfere with the homogeneous reaction. Though this method is technically more complex, as two independent steps have to be combined, most of the technically applied processes, such as the external regeneration of chromic acid, belong to this group. Despite their need for a two-step reaction procedure, continuous processes can usually be developed without problems.

The second possibility for electrochemical regeneration of a redox catalyst consist in its continuous *internal* retransformation into its active form without isolation, i.e., within the reaction vessel ("in-cell" method, see Fig. 3) [3,7].

The electron transfer agent, often also called mediator, which is inserted between electrode and substrate performs a homogeneous chemical reaction with the

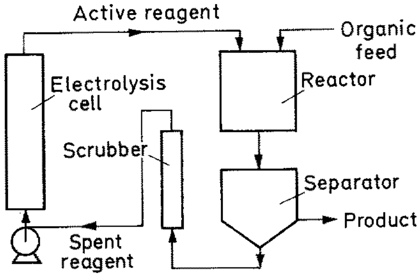


Fig. 2. Flow diagram of an indirect electrochemical process with external regeneration of the redox catalyst (ex-cell process)

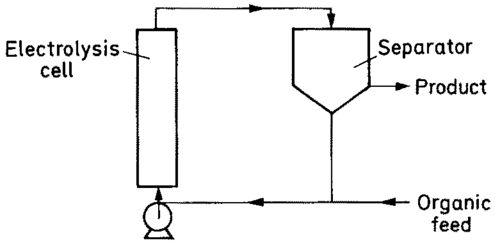


Fig. 3. Flow diagram of an indirect electrochemical process with internal regeneration of the redox catalyst (in-cell process)

substrate and is subsequently regenerated at the electrode. Thus, the electron transfer agent serves as a catalyst for the electron transfer between electrode and substrate. Because of the intimate connection between two very different reactions in one reactor, the one-step process cannot be realized as easily as the two-step method. The reason is the necessity to find conditions under which the organic substrates, reactive intermediates, and products do not hinder the electrochemical regeneration of the reagent or they themselves are not attacked electrochemically. This is the reason why this method has only recently been applied more often. Beside the advantage of lower investment, it is of great importance for the technical application of this method that a continuous reaction processing is facilitated as the separation of the products from catalytic amounts of the redox agent is easier as compared with the isolation out of a reagent excess. It is, however, most advantageous, if possible, to use a two-phase system in which the product concentrates in that phase which does not contain the redox catalyst[15,16,17].

A third way of indirect electrolysis is given, if the redox agent which is activated electrochemically, is fixed at the electrode surface and is regenerated there continuously after reaction with the substrate. In this case a separation step is unnecessary (see Fig. 4).

Such an activation of the electrode surface can, on the one hand, take place *in situ* by the continuous formation of the active redox agent on the electrode surface during the electrolysis. This is valid, for example, for the nickel(III)oxide hydroxide electrode which is spontaneously formed during anodic polarization of a

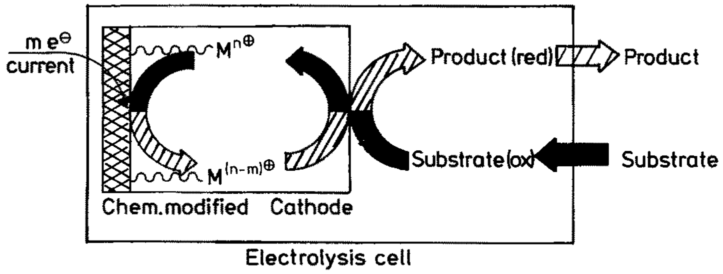


Fig. 4. Principle of an indirect electrochemical synthesis under application of chemically modified electrodes exemplified by a reduction

nickel electrode in alkaline media. This modified electrode is especially qualified for oxidation of primary alcohols to carboxylic acids and of primary amines to nitriles [18a]. This holds also for the amalgam electrode, which is formed through reduction of sodium or tetraalkyl ammonium salts at mercury cathodes and can, for example, be employed for the hydrodimerization of activated olefins and the regioselective synthesis of dihydroaromatic products [6, 18b].

On the other hand, the activation of the electrode can take place by its chemical modification. In this case the redox catalyst is fixed to the electrode surface either by adsorption, polymer coating, or covalent binding. This aspect has been treated in several reviews [19-23] and will be covered separately within this series [24].

2.2 The Potentiality of Indirect Electrochemical Syntheses as Compared with Alternative Methods

In the following, the potentiality and advantages of indirect electrochemical processes are compared with available alternatives [3, 13, 25, 26]. Naturally, exact estimations are only possible using concrete examples:

1. The indirect electrolysis is bound to a redox agent. Therefore, a broad collection of mediators has to be available for a large spectrum of substrates. In this aspect homogeneous redox reactions without regeneration of the reagent correspond with indirect electrolyses, while direct electrochemical transformations have the advantage to be independent of a reagent.
2. In direct electrochemical processes, however, one frequently encounters the problem of electrode passivation or fouling which will lead to a drastic decrease in current density during electrolysis and will rule out the large-scale application of many processes. In indirect electrochemical processes, passivation effects are usually excluded. They are sometimes observed in "in-cell" regenerations, if organic side-products or intermediates are electroactive at the applied potential, or in "ex-cell" regenerations, if organic material is not completely separated [25].
3. In addition, electrode reactions are frequently characterized by an irreversible, i.e., slow, electron transfer. Therefore, overpotentials have to be applied in preparative-scale electrolyses to a smaller or larger extent. This means not only a higher energy consumption but also a loss in selectivity as other functions within the molecule can already be attacked. In the case of indirect electrolyses, no overpotentials are encountered as long as reversible redox systems are used as mediators. It is very exciting that not only overpotentials can be eliminated but frequently redox catalysts can be applied with potentials which are 600 mV or in some cases even up to 1 Volt lower than the electrode potentials of the substrates. These so-called redox reactions "opposite to the standard potential gradient" [27, 28] can take place in two different ways. In the first place, a thermodynamically unfavorable electron-transfer equilibrium (Eq. (3)) may be followed by a fast and irreversible step (Eq. (4)) which will shift the electron-transfer equilibrium to the product side. In this case the reaction rate (Eq. (5)) is not only controlled by the equilibrium constant K, i.e., by the standard potential difference be-

tween the mediator and the substrate (Eq. (6)), but also by the rate constant k, of the chemical follow-up reaction (Eq. (5)).

$$\text{Med} \overset{-e^{\ominus}}{\rightleftarrows} \text{Med}^{\cdot\oplus} \ \text{(anode)} \tag{2}$$

$$\text{Med}^{\cdot\oplus} + \text{SH} \underset{\text{ET}}{\overset{K}{\rightleftarrows}} \text{Med} + \text{SH}^{\cdot\oplus} \tag{3}$$

$$\text{SH}^{\cdot\oplus} \xrightarrow[-\text{H}^{\oplus}]{k} \text{S}^{\cdot} \longrightarrow\longrightarrow \text{products} \tag{4}$$

ET = electrontransfer ; SH = substrate

$$-d[\text{SH}]/dt = k \cdot K[\text{Med}^{\cdot\oplus}][\text{SH}]/[\text{Med}] \tag{5}$$

$$\lg K = \tfrac{1}{58}(E^{o}_{\text{Med}} - E^{o}_{\text{SH}})\,[\text{mV}] \tag{6}$$

Secondly, instead of a pure and simple electron transfer, the redox reaction can be coupled to a chemical reaction in such a way that the electron transfer takes place either after incorporation of the substrate or an intermediate into the inner coordination sphere of a metal ion ("inner-sphere" electron transfer), by formation of a charge transfer complex, or in form of a hydrogen or hydride atom abstraction, respectively. In these cases the reaction between redox catalyst and substrate does not directly depend on the difference of the two standard potentials (see Sect. 2.3).

4. The selectivity and reactivity in indirect electrochemical syntheses can be enhanced by coordination of the substrate or an intermediate to the redox catalyst, for example through metal centers. In direct electrolyses, however, the selectivity and reactivity is mainly controlled by the difference between the electrode potential and the redox potentials of the different functions within the substrate.
5. In direct as well as in indirect electrolyses the burden for the environment by spent reagent is very small. In homogeneous redox reactions with stoichiometric quantities of the reagent, it is intolerably high in most cases. For example, it is unthinkable nowadays to dump spent manganese(II) or chromium(III).
6. The separation of the products is simplified in indirect and direct electrolyses while it is difficult, costly, and uneffective in reactions using stoichiometric amounts of the reagent.
7. A special disadvantage is connected with homogeneous redox reactions without regeneration: The concentration ratios are changing drastically during the reaction. In indirect electrolyses it is, however, easy to maintain the optimum concentrations. In direct electrolyses the steep concentration gradients in front of the electrode surface can adversely affect some types of reactions.

2.3 The Redox Catalyst

In indirect electrolyses the redox catalyst occupies a key position, as it takes part in the heterogeneous as well as in the homogeneous redox reaction. To be suitable for both reactions, the mediators have to fulfill the following conditions:

1. Both redox states must be chemically stable. Even slight side reactions to unregenerable compounds will lead to a fast decay in catalytic activity.
2. Electron exchange with the electrode as well as the redox reaction with the substrate have to be rapid and reversible. Inhibition of the electrode reaction or slow homogeneous redox reactions will prolong the time for turnover drastically and thus will afford larger electrode surfaces and thereby larger investments. Besides that, side reactions will often be favored.
3. Redox reactions with other compounds like the solvent or the product must not take place or must be suppressed.
4. Both redox states must have high enough solubility in the electrolyte (exception: two-phase systems).

Organic compounds are less often employed as redox catalysts than inorganic ions and complexes. One reason is that inorganic ions, metal salts, or metal complexes usually fulfill the requirement of chemical stability easier than organic mediators. However, with inorganic catalysts the redox step quite often is slow. This is due to the fact that in many cases the electron transfer is connected with a change in the complex structure (inner-sphere electron transfer). On the other hand, metal ions or complexes have the advantage that very often the reactive intermediates formed by the electron-transfer step are moderated in their reactivity by coordination and complexation. In this way, high selectivities and specificities can be obtained. Moreover, transition-metal complexes can advantageously be used as mediators, as their redox potentials can be tuned to the requirements of a special substrate by choice of the central atom or the ligand.

Organic redox catalysts in their active forms, mostly radical ions, quite often are not sufficiently stable in many media. The number of stable organic mediators is therefore somewhat limited. However, recently, especially in this field, considerable advances could be made showing that also organic compounds have good prospèctives in their application as redox catalysts.

The redox catalysts can principally be divided into two groups according to the reaction mechanism they undergo:

Mechanism A: The redox step is a pure homogeneous electron transfer

Using *Savéant's* [29] terminology, such a process is called "redox catalysis" in its proper meaning, while *Shono* [9] formed the expression "homomediatory system". This type of mechanism was already schematically presented in the case of an oxidation in Eqs. (2) to (4). To this category of redox catalysts belong, for example, the radical anions and cations of aromatic and heteroaromatic compounds and some reactions of triaryl amine radical cations.

The reductive or oxidative power of electron transfer agents which are generated at relatively low potentials can be increased drastically by photochemical excitation during their electrochemical generation [30,31], as higher molecular orbitals are occupied or holes are generated in lower ones. Mostly the excitation can be performed with visible light, because most of the electro-generated radical ions or ions are intensively colored. The principle is exemplified by an oxidation in the following equations:

$$\mathrm{Med} \xrightarrow[-e^{\ominus}]{\text{anode}} \mathrm{Med}^{\cdot\oplus} \tag{2}$$

$$\mathrm{Med}^{\cdot\oplus} \xrightarrow{h\nu} [\mathrm{Med}^{\cdot\oplus}]^{*} \tag{7}$$

$$[\mathrm{Med}^{\cdot\oplus}]^{*} + \mathrm{SH} \overset{\text{ET}}{\rightleftharpoons} \mathrm{Med} + \mathrm{SH}^{\cdot\oplus} \tag{8}$$

$$\mathrm{SH}^{\cdot\oplus} \xrightarrow[-\mathrm{H}^{\oplus}]{} \mathrm{S}^{\cdot} \rightarrow\rightarrow \text{products} \tag{4}$$

ET = electrontransfer ; SH = substrate

Mechanism B: The redox reaction is intimately connected to a chemical reaction, for instance a hydrogen or hydride abstraction.

In *Savéant's* terminology[29] this process is called "chemical catalysis with electrochemical regeneration" while *Shono*[9] uses the expression "heteromediatory system". In the following equations the principle is exemplified in the simple case, in which the redox step is connected with a hydrogen atom abstraction (oxidation):

$$\mathrm{Med} \xrightarrow[-e^{\ominus}]{\text{anode}} \mathrm{Med}^{\cdot\oplus} \tag{2}$$

$$\mathrm{Med}^{\cdot\oplus} + \mathrm{SH} \longrightarrow \mathrm{MedH}^{\oplus} + \mathrm{S}^{\cdot} \tag{9}$$

$$\mathrm{MedH}^{\oplus} + \mathrm{B} \longrightarrow \mathrm{Med} + \mathrm{HB}^{\oplus} \tag{10}$$

$$\mathrm{S}^{\cdot} \rightarrow\rightarrow \text{products} \tag{11}$$

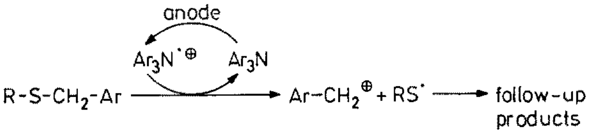
If metal complexes are used as redox catalysts, mechanism A will be an outer-sphere electron transfer, while mechanism B represents an inner-sphere electron transfer.

If in indirect electrolyses the homogeneous chemical step is a pure electron transfer (mechanism A), the following advantages can be used as compared with direct electrolysis:

1. Passivation of electrode surfaces can be suppressed.
2. Overpotentials are eliminated as the reaction rate is high even if the potential of the mediator is of the same order as the standard potential of the substrate.
3. If the electron transfer step (Eq. (3)) is followed by a fast and irreversible chemical reaction (Eq. 4)), the potential of the mediator can even be up to 600 mV lower than the standard potential of the substrate.

4. The number of electrons which are exchanged can be controlled by the choice of the redox catalyst.

Thus, as compared with direct electrolysis, not only a gain in energy can be obtained but also the selectivities can be enhanced. The selectivity of the reaction in this case is determined by the potential differences between the different functional groups of the substrate and the mediator in combination with the rate of the respective follow-up reaction. A typical example of this type is the cleavage of a carbon-sulfur bond using tris(4-bromophenyl)amine as organic mediator*) (Eq. (12)).

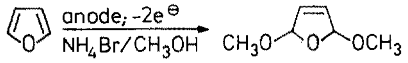


(12)

If, in indirect electrolyses, the homogeneous reaction step is a chemical step combined with a redox reaction (mechanism B), some more advantages are obtained:

1. The selectivity of the process is determined by the chemical step (Eq. (9)).
2. Even potential differences of more than 600 mV can be overcome as the chemical step (Eq. (9)) is not directly potential-dependent.

The problem, however, arises that a chemical follow-up reaction must be found which renders the mediator in such a form that it can be regenerated electrochemically (Eq. (10)). Therefore, expecially in the case of organometallic redox agents, difficulties are often observed, as metal complexes mostly must undergo a ligand exchange after an inner-sphere electron transfer to be electrochemically regenerable [32,33]. Besides transition metal ions, positively charged halogen species, hypohalite ions, and molecular halogen, obtained by anodic oxidation of halide ions, belong to the most frequently used redox catalysts in this category [9]. One of the earliest reactions of this type is the technically applied anodic methoxylation of furan in the presence of bromide ions [34-37] (Eq. (13)).



(13)

3 Indirect Electrochemical Syntheses Using Inorganic and Organometallic Redox Catalysts

The largest group of inorganic redox catalysts consists of metal, especially transition metal ions and complexes. In a large number of cases these reagents are able to undergo selective redox reactions with a multitude of substrates. By variation of the reaction conditions a diversity of products can be obtained. This is based on the fact that these reagents mostly react in an inner-sphere electron transfer (mechanism B: Sect. 2.3) thus moderating the reactivity of the intermediates by complexation, coordination, or even bond formation.

The employment of these reagents, however, mostly is economically and ecologically feasible only in those cases in which the redox catalysts are regenerable. The regeneration using chemical reducing or oxidizing agents is only useful if hydrogen or oxygen are employed as regenerating agents. Otherwise the problem is only shifted to another level. Therefore, from the very beginning, the possibilities for electrochemical regeneration have been taken into consideration. Principally, the indirect electrochemical method should be able to replace the application of redox agents in stoichiometric amounts. It is, however, required that oxygen is employed as regenerating agent. Otherwise the problem is only shifted to another level. Also, the turnover number of the catalyst must be high and the current yield for the formation of the active reagent must stay high over a long period of time [14,25]. But also in cases in which the indirect electrolysis requires higher investments than the comparable non-electrochemical process, the electrochemical regeneration can be economically favorable. This may be the case, if for ecological reasons the spent reagent can not be deposited without environmental hazards [14,38]. A waste treatment may, however, be quite costly giving advantages to the electrochemical

Table 1. Standard redox potentials of some inorganic redox agents [40]

Redox process		Standard potential (V vs. NHE)
$Co^{3+} + e^-$	$\rightarrow Co^{2+}$	1.83
$Ce^{4+} + e^-$	$\rightarrow Ce^{3+}$	1.61
$Mn^{3+} + e^-$	$\rightarrow Mn^{2+}$	1.54
$MnO_4^- + 8\,H^+ + 5\,e^-$	$\rightarrow Mn^{2+} + 4\,H_2O$	1.51
$RuO_4 + 4\,H^+ + 4\,e^-$	$\rightarrow RuO_2 + 2\,H_2O$	1.39
$Cr_2O_7^{2-} + 12\,H^+ + 6\,e^-$	$\rightarrow 2\,Cr(OH)^{2+} + 5\,H_2O$	1.26
$MnO_2 + 4\,H^+ + 2\,e^-$	$\rightarrow Mn^{2+} + 2\,H_2O$	1.22
$Tl(OH)_3 + 3\,H^+ + 2\,e^-$	$\rightarrow Tl^+ + 3\,H_2O$	1.19
$Fe^{3+} + e^-$	$\rightarrow Fe^{2+}$	0.77
$OsO_4 + 2\,e^-$	$\rightarrow OsO_4^{2-}$	0.43
$Fe(CN)_6^{3-} + e^-$	$\rightarrow Fe(CN)_6^{4-}$	0.36
$Sn^{4+} + e^-$	$\rightarrow Sn^{2+}$	0.15
$Ti^{3+} + e^-$	$\rightarrow Ti^{2+}$	—0.37
$V^{3+} + e^-$	$\rightarrow V^{2+}$	—0.26
$Cr^{3+} + e^-$	$\rightarrow Cr^{2+}$	—0.41
$Cl_2(Sol.) + 2\,e^-$	$\rightarrow 2\,Cl^-$	1.40
$ClO^- + 2\,H^+ + 2\,e^-$	$\rightarrow Cl^- + H_2O$	1.70
$ClO_2 + 4\,H^+ + 5\,e^-$	$\rightarrow Cl^- + 2\,H_2O$	1.51
$HClO + H^+ + 2\,e^-$	$\rightarrow Cl^- + H_2O$	1.48
$ClO^- + H_2O + 2\,e^-$	$\rightarrow Cl^- + 2\,OH^-$	0.84
$Br_2(Sol.) + 2\,e^-$	$\rightarrow 2\,Br^-$	1.09
$BrO^- + 2\,H^+ + 2\,e^-$	$\rightarrow Br^- + H_2O$	1.59
$HBrO + H^+ + 2\,e^-$	$\rightarrow Br^- + H_2O$	1.33
$BrO^- + H_2O + 2\,e^-$	$\rightarrow Br^- + 2\,OH^-$	0.761
$I_2 + 2\,e^-$	$\rightarrow 2\,I^-$	0.62
$I^+ + 2\,e^-$	$\rightarrow I^-$	0.95
$IO^- + 2\,H^+ + 2e^-$	$\rightarrow I^- + H_2O$	1.31
$3\,HIO + 3\,H^+ + 4\,e^-$	$\rightarrow I_3^- + 3\,H_2O$	1.21
$IO^- + H_2O + 2\,e^-$	$\rightarrow I^- + 2\,OH^-$	0.49

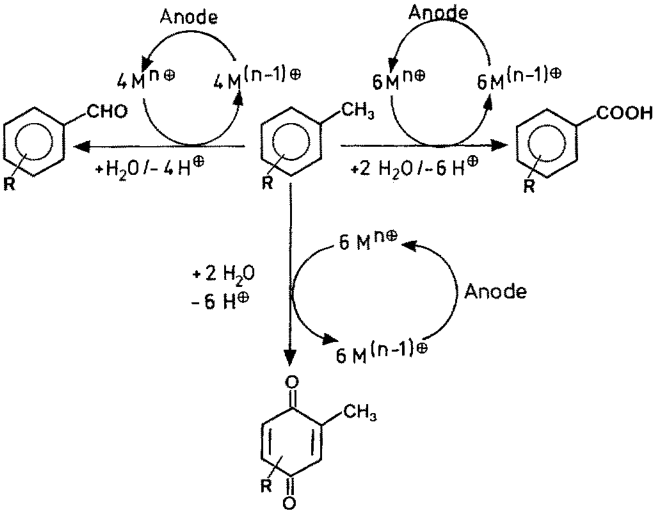
regeneration which, for example, is demonstrated by the electrochemical recycling of chromium(VI) [39].

The electrochemical regeneration of the following inorganic oxidizing agents has been reported: Cr(VI), Ce(IV), Mn(III), V(V), Fe(III), Hg(II), Pd(II), Tl(III), Ag(II), Os(VIII), $Fe(CN)_6^{3-}$, Ru(IV)-complexes, RuO_4, and, in addition, the non-metallic ions NO_3^-, BrO^-, ClO^-, IO_4^-, I^+, Br^+, Cl^+, and the halogens I_2, Br_2, and Cl_2. The electrochemical regeneration of the following reducing agents has been studied: Fe(II), Ti(II), Sn(III), Sn(II), V(III), Cr(II), Pd(O)-, Sn(O)-, Ni(O)-, Ni(I)-, Co(I)-, Rh(I)-, and Fe(O)-complexes. This category is completed by the electrogenerated agents $O_2^{\cdot -}$, metal and tetraalkylammonium amalgams [6, 18b], and solvated electrons. To give an impression of the oxidizing or reducing power of some redox agents, Table 1 lists their standard potentials.

3.1 Oxidation Processes by Metal Salts as Redox Catalysts

3.1.1 Oxidation of Aromatic Compounds

Tremendous effects have been made in studying the possibilities for the electrochemical generation and regeneration of inorganic redox agents like Cr(VI) [73], V(V), Mn(III) [43], Ce(IV) [44], and Co(III) [69], and their application in the oxidation of aromatics. These studies are mainly performed by means of three types of reactions: side-chain oxidations to form benzaldehydes, side-chain oxidations to generate benzoic acids, and nuclear oxidations for the synthesis of quinones (Scheme 1).



Scheme 1. Pathways for the indirect electrochemical oxidation of aromatic compounds by metal salts

Already very early it was proposed to apply electrochemically generated and regenerated Mn(III) and Ce(IV) as "oxygen carriers" for the synthesis of benzal-

Table 2. Indirect electrochemical oxidation of alkyl aromatics to form benzaldehydes using metal salts as redox catalysts

Substrate	Redox catalyst (oxidized form)	Electrolyte	Anode	Product	Ref.
toluene	$Mn_2(SO_4)_3$	H_2SO_4	PbO_2	benzaldehyde	43, 45, 46, 48–51)
toluene	$Mn_2(SO_4)_3/Ce(SO_4)_2$	H_2SO_4	PbO_2	benzaldehyde	52)
toluene	$(NH_4)_2Ce(NO_3)_6$	HNO_3	Pt	benzaldehyde	53)
toluene	$Ce^{4+}/Ag^{2+}/(NH_4)_2S_2O_8$	H_2SO_4	Pt	benzaldehyde	54)
toluene	$Ce(ClO_4)_4$	$HClO_4$	Ti/Pt	benzaldehyde	8, 55)
toluene	$Co_2(SO_4)_3$	H_2SO_4	PbO_2	benzaldehyde	8)
toluene	$Ag(NO_3)_2$	HNO_3	Pt/pyrol. graphite	benzaldehyde	59)
p-xylene[a]	$Mn(SO_4)_3$	H_2SO_4	PbO_2	*p*-tolualdehyde	47, 56, 66)
p-xylene[a]	$(NH_4)_2Ce(NO_3)_6$	NHO_3	Pt	*p*-tolualdehyde	53)
p-xylene[a]	$Ce(SO_4)_2$	H_2SO_4	PbO_2	*p*-tolualdehyde	57)
p-xylene[a]	$Ag(NO_3)_2$	HNO_3	Pt/Pyrol. graphite	*p*-tolualdehyde	59)
o-chlorotoluene	$Ce(ClO_4)_4$	$HClO_4$	Ti/Pt	*o*-chlorobenzaldehyde	55)
m-chlorotoluene	$Mn_2(SO_4)_3$	H_2SO_4	PbO_2	*m*-chlorobenzaldehyde	58)
p-*tert*-butyltoluene	$(NH_4)_2Ce(NO_3)_6$	$AcOH/H_2O$	Pt, C, or PbO_2	*p*-*tert*-butylbenzaldehyde	61, 63)
p-*tert*-butyltoluene	$Mn_2(SO_4)_3$	H_2SO_4	Pt	*p*-*tert*-butylbenzaldehyde	64, 72b)
o-nitrotoluene	$Co_2(SO_4)_3/(AgSO_4)$	H_2SO_4	PbO_2	*o*-nitrobenzaldehyde[b]	69)
p-methoxytoluene	$(NH_4)_2Ce(NO_3)_6$	CH_3OH	Pt or C	*p*-methoxybenzaldehyde	61, 62)
p-methoxytoluene	$Mn_2(SO_4)_3$	H_2SO_4	PbO_2	*p*-methoxybenzaldehyde	71, 64c)
p-methoxytoluene	$Mn_2(SO_4)_3$	H_2SO_4	Pt	*p*-methoxybenzaldehyde	64c)
p-methoxytoluene	$Ce(SO_4)_2$	H_2SO_4	Ti/Pt	*p*-methoxybenzaldehyde	71)
p-phenoxytoluene	$Ce(CF_3OO)_2O$	CF_3COOH	Pt	*p*-phenoxybenzaldehyde	70)
m-phenoxytoluene	$Ce(CF_3OO)_2O$	CF_3COOH	Pt	*m*-phenoxybenzaldehyde	70)
ethylbenzene	$Mn_2(SO_4)_3$	H_2SO_4	Pt	benzaldehyde, acetophenone	67)
ethylbenzene	MnO_2	H_2SO_4	MnO_2	acetophenone	65)
tetralin	MnO_2	H_2SO_4	MnO_2	α-tetralone	65)
tetralin	$KMnO_4$	$CH_2Cl_2/H_2O/H_2SO_4/$ aliquot 336	Pt	α-tetralone	65)
cumene	$Mn_2(SO_4)_3$	H_2SO_4	Pt	*p*-tolualdehyde, *p*-methylacetophenone, cumylaldehyde	68)

[a] similar results with *o*- and *m*-sylene; [b] *o*-nitrobenzoic acid as side-product; [c] similar results with *p*-ethoxytoluene

dehydes from alkyl aromatics [1]. If Mn(III) [43], Ce(IV) [44], or Co(III) [69] redox agents are used, in-cell regenerations are mostly not effective, as high enough current densities can not be maintained for longer periods of time [8,41,42]. Ex-cell processes, however, have been intensively studied [72a] and successfully applied; they are summarized in Table 2. Especially interesting is the formation of *o*-nitrobenzaldehyde from the very-difficult-to-oxidize *o*-nitrotoluene by electrochemically generated Co(III) under the catalysis of silver ions yielding about 80% of the aldehyde [69]. However, the optimum reaction conditions of the chemical and the electrochemical step don't match well. The use of electrogenerated Ag(II) for side-chain oxidations is only effective in an in-cell process, as high conversions of Ag(I) to Ag(II) result in a drastic decrease of the current yield [59].

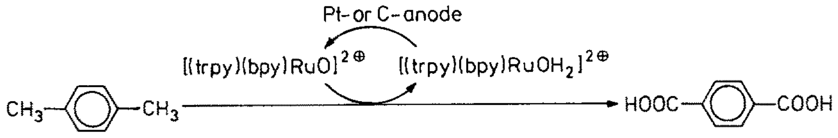
Side-chain oxidations of alkyl aromatic compounds to aromatic carboxylic acids by electrogenerated and regenerated chromic acid [73] have been studied extensively in the case of saccharin formation from *o*-toluene sulfonamide [25,74–78]. This reaction is performed in an ex-cell process using sulfuric acid as electrolyte and PbO_2 as anode material. The yields reach about 80%. The most important problem is the incomplete separation of organic material before the electrochemical regeneration of the oxidizing agent. As the PbO_2-anode is very sensitive to contaminations, this slowly leads to an increase of oxygen formation and a decrease in the current efficiency [25,73c,74]. This is a general problem in most of the ex-cell processes using inorganic redox agents together with PbO_2-anodes. To solve this problem is was proposed to catalyze the electrochemical generation of chromic acid by silver ions according to the following equations:

$$\mathrm{Ag}^{\oplus} - e^{\ominus} \rightleftharpoons \mathrm{Ag}^{2\oplus}\ \text{(anode)} \tag{14}$$

$$6\,\mathrm{Ag}^{2\oplus} + 2\,\mathrm{Cr}^{3\oplus} + 7\,\mathrm{H_2O} \rightleftharpoons \mathrm{Cr_2O_7}^{2\ominus} + 6\,\mathrm{Ag}^{\oplus} + 14\,\mathrm{H}^{\oplus} \tag{15}$$

In this case a platinum anode wich is not sensitive to organic contamination can be used giving a current yield for Cr(VI) of 94%. Electrolyses can be performed in a two-phase medium making an in-cell process possible [73c]. This method has been applied to the synthesis of benzaldehyde from benzylic alcohol giving 100% current yields at 10% conversion while the current yield drops to 60% at high conversions.

In addition to the synthesis of saccharin, also a number of other side-chain oxidations have been studied leading to aromatic carboxylic acids by indirect electrochemical oxidation using chromic acid as oxidizing agent. They include the oxidation of *p*-nitrotoluene [79–82], 2,4-dinitrotoluene [83], toluene, *p*-xylene, and *p*-tolualdehyde [84–87]. Recently, interesting results have been obtained using the electrochemically generated ruthenium(IV) complex $[(\mathrm{trpy})(\mathrm{bpy})\mathrm{RuO}]^{2+}$ in the oxidation of *p*-xylene and *p*-toluic acid to terephthalic acid and of toluene to benzoic acid [88]. The current yield is practically quantitative. After 100 turnovers about 75% of the redox catalyst can be recovered giving a turnover number of about 400 (Eq. (16)).



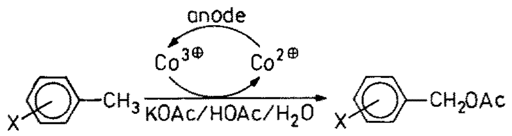
(16)

Table 3. Indirect electrochemical oxidation of aromatic compounds to quinones using metal salts as redox catalysts

Substrate	Redox catalyst (oxidized form)	Electrolyte	Anode	Product	Type of regeneration	Ref.
Anthracene	$Na_2Cr_2O_7$	H_2SO_4	?[a]	anthraquinone	in-cell	2, 3, 92–94, 101)
Anthracene	$K_2Cr_2O_7$	H_2SO_4	Pt	anthraquinone	in-cell	95)
Anthracene	Cr^{6+}/Ag^+	H_2SO_4	Pt	anthraquinone	in-cell	73c)
Anthracene	$Ce(SO_4)_2$	H_2SO_4	Pt	anthraquinone	in-cell	99, 100)
Anthracene	$Ce(SO_4)_2$ or $(NH_4)_2Ce(NO_3)_6$	HNO_3	Pt	anthraquinone	ex-cell	3, 96, 102)
Anthracene	$(NH_4)_2S_2O_8/Ce^{3+}/Ag^+$	H_2SO_4	Pt	anthraquinone	ex-cell	54)
Anthracene	$Mn_2(SO_4)_3$	H_2SO_4	Pb	anthraquinone	ex-cell	45)
Naphthalene	$Ce(SO_4)_2$ or $(NH_4)_2Ce(NO_3)_6$	HNO_3	Pt	naphthoquinone	ex-cell	96)
Naphthalene	$(NH_4)_2S_2O_8/Ce^{3+}/Ag^+$	H_2SO_4	Pt	naphthoquinone	ex-cell	54)
Naphthalene	$Mn_2(SO_4)_3$	H_2SO_4	Pb	naphthoquinone	ex-cell	45)
Naphthalene	$Ce(SO_4)_2$	H_2SO_4	PbO_2	naphthoquinone	ex-cell	103b)
β-Methylnaphthalene	$H_2Cr_2O_7$	H_2SO_4	Pb	β-Methylnaphthoquinone	ex-cell	98)
Benzene	$Mn_2(SO_4)_3$	H_2SO_4	Pb	benzoquinone	ex-cell	45)
Benzene	$Ag(NO_3)_2$	HNO_3	Pt	benzoquinone	in-cell	59, 97)
Aniline	$Mn_2(SO_4)_3$	H_2SO_4	PbO_2	Benzoquinone	in-cell	103a)
Biphenyl	$Ce(SO_4)_2$ or $(NH_4)_2Ce(NO_3)_6$	HNO_3	Pt	*o*-Phenylbenzoquinone	ex-cell	96)
Biphenyl	$(NH_4)_2S_2O_8/Ce^{3+}/Ag^+$	H_2SO_4	Pt	*o*-Phenylbenzoquinone	ex-cell	54)
Pyrene	$Ce(SO_4)_2$ or $(NH_4)_2Ce(NO_3)_6$	HNO_3	Pt	Pyrene-1,6-quinone	ex-cell	96)
Pyrene	$(NH_4)_2S_2O_8/Ce^{3+}/Ag^+$	H_2SO_4	Pt	Pyrene-1,6-quinone	ex-cell	54)

[a] anode material not given

Side-chain acetoxylations of alkyl aromatic compounds can be performed selectively by use of internally electrogenerated cobalt(III) acetate (Eq. (17)) [89–91].



(17)

Nuclear oxidations of aromatic compounds to form quinones (Table 3) have been performed technically in the case of anthraquinone using electrochemically regenerated Ce(IV) or Cr(VI) as redox catalysts [2,3,96]. This technique has, however, become less important since the development of catalytic processes. Technically interesting would be the oxidation of benzene to benzoquinone with regard to a hydroquinone synthesis. The indirect electrochemical processes developed thus far [59,97], however, can not compete with the established ones. Mn(III)- and Ag(II)-salts have also been studied as redox catalysts [103a].

A principally different approach for the indirect electrochemical oxidation of aromatic compounds goes via the formation of hydroxyl radicals from cathodically generated hydrogen peroxide and from reductively formed iron(II) ions. The thus *in situ* formed *Fenton* reagent can lead to side-chain as well as nuclear oxidations of aromatic compounds. Side-chain oxidations to form benzaldehydes [104] according to Eqs. (18)–(24) can also be initiated by the redox pairs $V^{4+/3+}$ and $Cu^{2+/+}$ instead of $Fe^{3+/2+}$.

$$\text{Cathode: } Fe^{3\oplus} + e^{\ominus} \longrightarrow Fe^{2\oplus} \tag{18}$$

$$\text{Cathode: } O_2 + 2e^{\ominus} + 2H^{\oplus} \longrightarrow H_2O_2 \tag{19}$$

$$Fe^{2\oplus} + H_2O_2 \longrightarrow Fe^{3\oplus} + HO^{\bullet} + HO^{\ominus} \tag{20}$$

$$Ph\text{-}CH_3 + HO^{\bullet} \longrightarrow Ph\text{-}CH_2^{\bullet} + H_2O \tag{21}$$

$$Ph\text{-}CH_2^{\bullet} + O_2 \longrightarrow Ph\text{-}CH_2\text{-}O\text{-}O^{\bullet} \tag{22}$$

$$Ph\text{-}CH_2\text{-}O\text{-}O^{\bullet} \longrightarrow Ph\text{-}\underset{\bullet}{C}H\text{-}O\text{-}OH \tag{23}$$

$$Ph\text{-}\underset{\bullet}{C}H\text{-}O\text{-}OH + Fe^{2\oplus} \longrightarrow Ph\text{-}CHO + Fe^{3\oplus} + HO^{\ominus} \tag{24}$$

Nuclear oxidation of benzene and substituted benzenes by this system leads to the selective formation of phenol and substituted phenols. In this case hydrogen peroxide was either generated electrochemically [107–109] or it was added while the iron(II) concentration was cathodically controlled [105,106]. The addition of copper(II) salts makes the reaction more effective, as Cu^{2+} ions are better oxidizing agents than Fe^{3+}. Equations (18)–(28) show the reaction sequence.

$$\text{Cathode: } Fe^{3\oplus} + e^{\ominus} \longrightarrow Fe^{2\oplus} \tag{18}$$

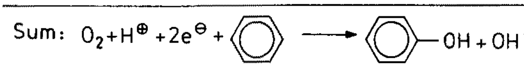
$$\text{Cathode: } O_2 + 2e^{\ominus} + 2H^{\oplus} \longrightarrow H_2O_2 \tag{19}$$

$$Fe^{2\oplus} + H_2O_2 \longrightarrow Fe^{3\oplus} + HO^{\bullet} + HO^{\ominus} \qquad (20)$$

(25)

(26)

$$Cu^{\oplus} + Fe^{3\oplus} \longrightarrow Cu^{2\oplus} + Fe^{2\oplus} \qquad (27)$$



(28)

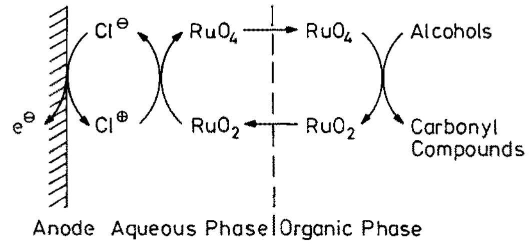
The current yield in phenol reaches 60%[107] while the yield with respect to the hydrogen peroxide consumption is 64%[105,106]. Fluorophenol is generated in 80% yield with respect to the hydrogen peroxide consumption from fluorobenzene in an *ortho* to *para* ratio of 85:15[106]. A similar reaction sequence can also be obtained by the Cu^+/Cu^{2+}-redox pair alone[110,111].

In a similar way it is possible to perform the amination of aromatics by indirect electrochemical reduction of hydroxylamine using a combination of the Cu^{2+}/Cu^+ and V^{4+}/V^{3+} redox pairs[112]. Thus, aniline and toluidine are formed from benzene or toluene in 70% and 50% current yield, respectively.

3.1.2 Oxidation of Alcohols and Ethers

Metal salts and complexes have also often been used as redox catalysts for the indirect electrochemical oxidation of alcohols. Particularly, the transformation of benzylic alcohols to benzaldehydes has been studies. For this purpose oxoruthenium(IV)[88,113] and oxoruthenium(V)[114] complexes have been applied as redox catalysts. In a similar way, certain benzyl ethers can be cleaved to yield benzaldehydes and the corresponding alcohols using a di-oxo-bridged binuclear manganese complex[115]. Electrogenerated $Co_2(SO_4)_3$ was used to generated 1-naphthaldehyde from 1-naphthylmethanol[116].

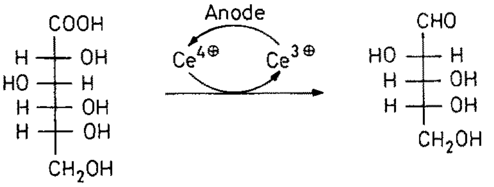
Aliphatic alcohols can be oxidized to ketones, aldehydes, or carboxylic acids using oxoruthenium(IV)complexes[88] as redox catalyst or electrogenerated ruthenium tetroxide[117]. In the latter case, a double mediator system is used in which an electrochemically generated active chlorine species (Cl_2 or "Cl^+") oxidizes RuO_2 to RuO_4 (Eq. (29)).



(29)

The reaction takes place in a two-phase medium. Secondary alcohols form ketones (90%), primary alcohols and aldehydes are oxidized to carboxylic acids (60–77%), 1,2-diols are cleaved to carboxylic acids (75%), 1,4- and 1,5-diols are transformed to lactones and keto acids (75%).

Electrogenerated cerium(IV) sulfate is used to generate D-arabinose from D-gluconic acid (Eq. (30))[118].



(30)

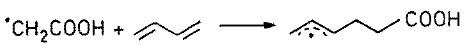
The oxidation of the primary hydroxyl groups in 3-phenyl-2-*N*-acetylamino propanol[119] and propargylic alcohol[120] by electrogenerated chromic acid has been reported. *N*-Acetylphenylalanin and propargylic acid are both formed in 90% current yield.

3.1.3 Generation of Carboxymethyl and Nitromethyl Radicals by Use of Manganese Acetate as Redox Catalyst

Synthetically especially valuable is the oxidation of carbonyl compounds[121] and nitroalkanes[122] by manganese(III) salts to form carboxymethyl and nitromethyl radicals, respectively. These radicals can be trapped by olefins like 1,3-butadiene or aromatic compounds to yield synthetically interesting products. In this case it is very advantageous to generate and regenerate the oxidizing species *in situ* by indirect electrolysis. This was the basis for the development of a process for the synthesis of sorbic acid via γ-vinyl-γ-butyrolactone[123, 124]. Equations (31)–(35) summarize the important steps.

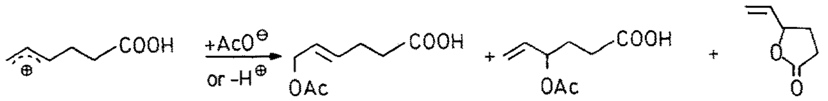
$$\text{Anode: } HOAc + Mn(OAc)_2 \longrightarrow Mn(OAc)_3 + H^{\oplus} + e^{\ominus} \qquad (31)$$

$$Mn(OAc)_3 + HOAc \longrightarrow Mn(OAc)_2 + HOAc + {}^{\bullet}CH_2COOH \qquad (32)$$



(33)

(34)



(35)

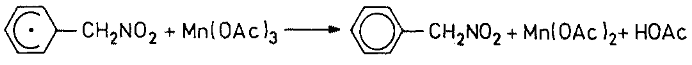
The addition of copper(II) ions favors the formation of the acetoxy hexenoic acids (current yield 78%) while cathodically generated copper(I) catalyzes the transformation of the acetoxy hexenoic acids to the lactone.

Similarly, the nitromethylation of benzene can be performed[125] (current yield 78%; Eqs. (36)–(39).

$$\text{Anode: } Mn(OAc)_2 + HOAc \longrightarrow Mn(OAc)_3 + H^{\oplus} + e^{\ominus} \qquad (36)$$

$$CH_3NO_2 + Mn(OAc)_3 \longrightarrow Mn(OAc)_2 + HOAc + {}^{\bullet}CH_2NO_2 \qquad (37)$$

(38)

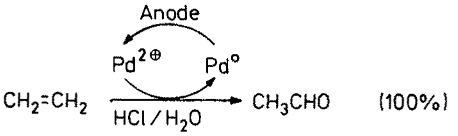


(39)

3.1.4 Olefin Oxidations

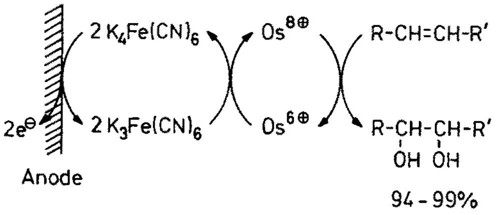
Electrochemically generated and recycled Tl(III), Pd(II), Hg(II), and Os(VIII) species are expecially suitable for the indirect electrochemical oxidation of olefins. Products are carbonyl compounds (Tl^{3+} [126–129], Pd^{2+} [130–132], Hg^{2+} [133, 134]), diols (Tl^{3+}, Os^{8+} [135]), or carboxylic acids (Hg^{2+} [133, 134], Os^{8+} [136–138]).

Ethylene can be oxidized to acetaldehyde in high yields similar to the *Wacker*-process if electrogenerated palladium(II) is used as catalyst. In this way the copper(II) catalyzed air oxidation of palladium(0) is replaced by the electro-oxidation according to Eq. (40).



(40)

Osmium tetroxide can be regenerated electrochemically most favorably by a double mediator system (Eq. (41))[135].



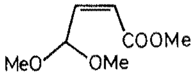
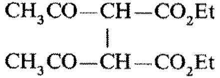
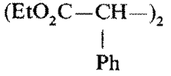
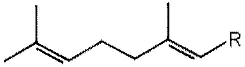
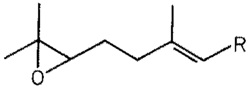
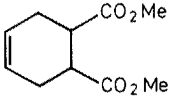
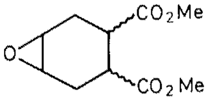
(41)

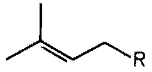
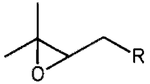
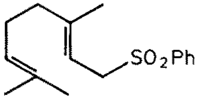
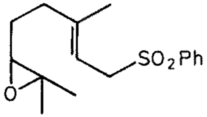
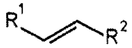
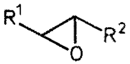
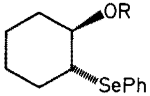
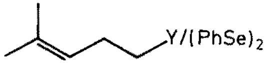
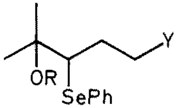
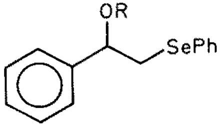
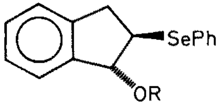
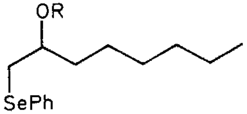
The redox catalyst $[(trpy)(bpy)RuO]^{2+}$ is able to oxidize allylic methylene groups to keto groups while allylic methyl groups are transformed into carboxylic groups[88].

3.2 Oxidations Using Inorganic Anions as Redox Catalysts

Among the numerous mediator systems, halide ions show the broadest applicability. The internal electrochemical generation of the active species, i.e., molecular halogen, hypohalite ions, and halonium ions, is always possible by the in-cell method without

Table 4. Indirect electrochemical oxidations using inorganic anions as redox catalysts

No.	Substrate	Redox catalyst (reduced form)	Electrolyte	Anode	Product	Ref.
1	furan	Cl^- or Br^-	$HOAc/CH_3CN$	Pt	2,5-diacetoxy-2,5-dihydrofuran	139)
2	furan	Br^-	CH_3OH	C	2,5-dimethoxy-2,5-dihydrofuran	34–37)
3	furan-2-carboxylic-acid	NH_4Br/Et_3N	CH_3OH	C		140)
4	$CH_2(COOCH_3)_2$	I^-	CH_3OH	C	$(CH_3O_2C)_2CH-CH(CO_2CH_3)_2$	145–148)
5	$CH_3CO-CH_2-CO_2Et$	I^-	CH_3CN	C	 $\begin{array}{c} CH_3CO-CH-CO_2Et \\ \vert \\ CH_3CO-CH-CO_2Et \end{array}$	146)
6	$Ph-CH_2-CO_2Et$	I^-	CH_3CN	C	 $(EtO_2C-\underset{\underset{Ph}{\vert}}{CH}-)_2$	146)
7	$CH_2(CO_2Et)_2$[a]	I^-	CH_3CN	C	$(EtO_2C)_2CHCH(CO_2Et)_2$	149–151)
8	glucose[b]	$CaBr_2$	$H_2O/CaCO_3$	C	Ca-gluconate	2, 4, 141, 142)
9	lactose	$CaBr_2$	$H_2O/CaCO_3$	C	Ca-lactobionate	141, 143)
10	other aldoses	$CaBr_2$	$H_2O/CaCO_3$	C	aldonic acids	141)
11	glucitol, mannitol	CaI_2	H_2O	Pt	different aldoses and ketohexoses	144)
12	propene	NaCl	H_2O	C	propylene oxide	152, 153)
13	propene	NaCl	H_2O	C	propylene oxide	154, 155)
14	propene	NaBr	H_2O	C	propylene oxide	156, 157)
15	propene	NaBr	H_2O	Pt	propylene oxide	158)
16		NaBr	$CH_3CN/THF/H_2O$	Pt		159, 162)
17		NaBr	CH_3CN/H_2O (1:4)	Pt		160)

18		NaBr	CH_3CN/H_2O (7:2)	Pt		160)
19		NaBr	CH_3CN/H_2O (7:2)	Pt		161)
20		Amberlite IRA-900(Br)	DMF/benzene/H_2O	Pt		163)
21	cyclohexene/$(PhSe)_2$	Et_4NBr	ROH/H_2SO_4	Pt		164)
22		Et_4NBr	ROH/H_2SO_4	Pt		164)
23	styrene/$(PhSe)_2$	Et_4NBr	ROH/H_2SO_4	Pt		164)
24	indene/$(PhSe)_2$	Et_4NBr	ROH/H_2SO_4	Pt		164)
25	1-octene/$(PhSe)_2$	Et_4NBr	ROH/H_2SO_4	Pt		164)

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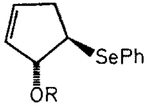
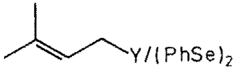
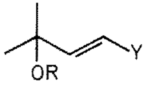
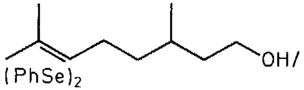
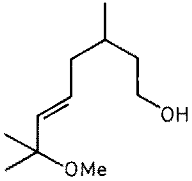
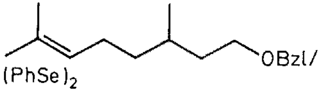
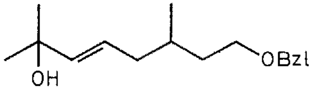
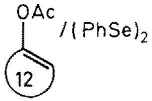
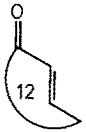
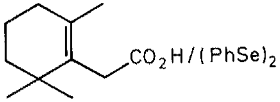
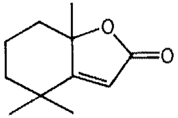
[a] coupled with the cathodic reduction of acrylic ester; [b] sometimes coupled with the cathodic reduction of glucose
[c] coupled with the cathodic reduction of the acetoin to 2-butanone

Table 4. (continued)

No.	Substrate	Redox catalyst (reduced form)	Electrolyte	Anode	Product	Ref.
26	cyclopentadiene/$(PhSe)_2$	Et_4NBr	ROH/H_2SO_4	Pt		164)
27		Et_4NBr	$MgSO_4/CH_3CN/ROH$	Pt		165, 166)
28		Et_4NBr	$MgSO_4/CH_3CN/CH_3OH$	Pt		165, 167)
29		Et_4NBr	CH_3CN/H_2O	Pt		168)
30		Et_4NBr	$MgSO_4/CH_3CN/H_2O$	Pt		166)
31		Et_4NBr	$MgSO_4/CH_3CN/H_2O$	Pt		166)

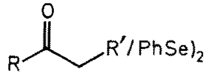
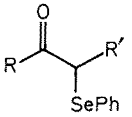
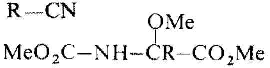
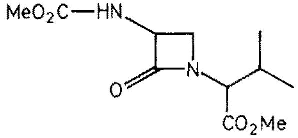
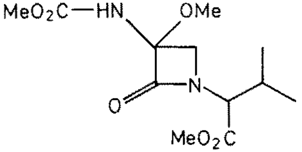
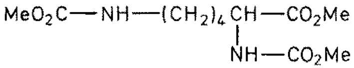
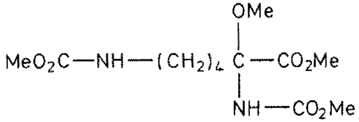
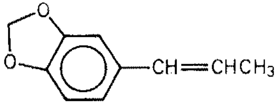
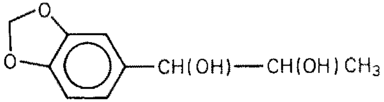
32		Et_4NBr	AcOH or $AcOH/H_2SO_4$ CH_3OH/H_2SO_4 or CH_3CN	Pt		169)
33	phthalimide/RSSR	NaBr	CH_3CN/Et_4NClO_4	Pt	N-thioalkyl(aryl)phthalimide	170)
	succinimide/RSSR	NaBr	CH_3CN/Et_4NClO_4	Pt	N-thioalkyl(aryl)succinimide	170)
34	$H_2N-CHR^1-CO_2R^2/RSSR$	$MgBr_2$	CH_2Cl_2/H_2O	Pt	$RS-N=CR^1-CO_2R^2$	171)
35	$(RO)_2P(O)H/R'SSR'$	$MgBr_2$	CH_3CN/Et_4NClO_4	Pt	$(RO)_2P(O)SR'$	172)
36	$(RO)_2P(O)H/NHR'R''$	NaI	CH_3CN/Et_4NClO_4		$(RO)_2P(O)NR'R''$	173)
37	$R-Ph-CHR'-OH$	NaBr	$H_2O/NaHCO_3/$ Bu_4NHSO_4/amylacetate	Pt	$R-Ph-CO-R'$	174)
38	benzylalcohol	KI	t-$BuOH/H_2O$	C	benzyl benzoate	175)
39	$Ph-CH(OH)-CH_3$	KI	t-$BuOH/H_2O$	C	acetophenone	175)
40	R^1-CHR^2-OH	poly-4-vinyl-pyridine hydrobromide	CH_3CN	Pt	R^1-CO-R^2	176)
41	1-octanol	poly-4-vinyl-pyridine hydrobromide	CH_3CN	Pt	octanoic acid	176)
42	1,3-butanediol	poly-4-vinyl-pyridine hydrobromide	CH_3CN	Pt	4-hydroxy-2-butanone	176)
43	R^1-CHR^2-OH	KI	H_2O or H_2O/t-butanol or H_2O/t-BuOH/hexane	Pt	R^1-CO-R^2	177)
44	R^1-CH_2-OH	KI	H_2O or H_2O/t-butanol or H_2O/t-BuOH/hexane	Pt	$R^1-CO_2CH_2R^1$	177)
45	R^1-CHR^2-OH	$NaCl/RuO_2$	H_2O/CCl_4 or H_2O/acetone	Pt	R^1-CO-R^2	117)
46	R^1-CHR^2-OH	$Et_4NBr/$ n-$C_8H_{17}SCH_3$	PhCN/lutidine	Pt	R^1-CO-R^2	179)
47	R^1-CHO	KI or KBr	$CH_3OH(n$-$BuOH)$	Pt	$R^1-CO_2Me(n$-$Bu)$	178)
48	$R^1R^2CH-CO-R^3$	KI	MeOH/KOH		$R^1R^2\underset{HO}{C}-\underset{R}{C}(OMe)_2$	180)
49	$HCHO/HNR_2$	KI	H_2O	Pt	$H-CO-NR_2$	182)

Table 4. (continued)

No.	Substrate	Redox catalyst (reduced form)	Electrolyte	Anode	Product	Ref.
50	R^1CH_2CHO/HNR_2	KI	$H_2O/t\text{-}BuOH$	Pt	$R^1{-}CO{-}CH_2{-}NR_2$	182)
51	$R^1CH_2{-}NR{-}OH$	NaI	MeOH	Pt	$R^1CH{=}NR{\rightarrow}O$	183)
52	RCH_2NH_2	NaBr	MeOH	Pt	$R{-}CN$	181)
53	$MeO_2C{-}NH{-}CHR{-}CO_2Me$	NaCl	MeOH	Pt	 $MeO_2C{-}NH{-}\overset{OMe}{C}R{-}CO_2Me$	184)
54		NaCl	MeOH	Pt		184)
55	 $MeO_2C{-}NH{-}(CH_2)_4\underset{NH{-}CO_2Me}{CH}{-}CO_2Me$	NaCl	MeOH	Pt	 $MeO_2C{-}NH{-}(CH_2)_4\overset{OMe}{\underset{NH{-}CO_2Me}{C}}{-}CO_2Me$	184, 185)
56	$R{-}CO{-}NH_2$	KBr	MeOH	Pt	$R{-}NH{-}CO_2Me$ or $R{-}NCO$	186)
57		NaBr	CH_3CN/H_2O	Pt		187)
58	2,3-butanediol[c]	NaBr	H_2O	C	3-hydroxy-2-butanone	188)
59	$Ar{-}CH_2{-}R$	poly-4-vinyl-pyridine hydrobromide	$CH_3CN/HOAc/H_2O$	Pt	$Ar{-}CO{-}R$	195)
60	$R^1{-}S{-}R^2$	poly-4-vinyl-pyridine hydrobromide	CH_3CN	Pt	$R^1{-}SO{-}R^2$	189)
61	$R{-}CO{-}S{-}t\text{-}Bu$	Bu_4NBr or LiBr	CH_3CN/H_2O	Pt	$R{-}CO_2H$	190)

62	R^1—CHR^2—OH	NO_3^-	CH_3CN/H_2O	Pt	R^1—CO—R^2	191)
63	*p*-xylene	NO_3^-	CH_3CN	Pt or C	Me—Ph—CH_2—ONO_2 or Me—Ph—CHO	192)
64	starch	IO_3^-	H_2SO_4	PbO_2	dialdehyde starch	193)
65	2,3-butanediol	IO_3^-	H_2O		acetaldehyde	194)

problems. As the redox reation of these mediator systems is usually coupled with a chemical reaction (mechanism B, Sect. 2.3) very high potential differences between the redox catalysts and the substrates of up to 2.0 V can be overcome.

3.2.1 Oxidation of Furans and Aldoses

Technically important is the dimethoxylation of furan and its derivatives to form 2,5-dimethoxy-2,5-dihydrofuran (Eq. (13))[34-37,139,140] and the oxidation of aldoses to aldonic acids (Eq. (1))[2,4,141-144]. The Sandoz company is producing calcium gluconate and lactobionate commercially since 1930 by this type of indirect electrochemical oxidation.

3.2.2 Coupling of Active Methylene Components

Activated methylene components like malonic esters and β-ketoesters can be coupled anodically using small amounts of potassium iodide as redox catalyst (Table 4, No. 4–7)[145-151]. The cathodically formed metallic potassium is used to deprotonate the methylene component generating the oxidizable carbanion. The combination of this reaction with the cathodic hydrodimerization of acrylic esters has been studied several times (Table 4, No. 7)[149-151]. Thus both electrode reactions can be used to produce valuable chemicals.

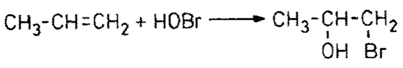
3.2.3 Epoxidation of Olefins

The indirect electrochemical generation of propylene oxide via propylene chloro- or bromohydrin using anodically generated hypochlorite or hypobromite has been studied very intensively. The reason is the lack of a technically useful process for the synthesis of propylene oxide by way of heterogeneous catalysis. The propylene halohydrins are saponified using the cathodically generated sodium hydroxide (Eqs. (42)–(47)) (Table 4, No. 12–15)[152-158].

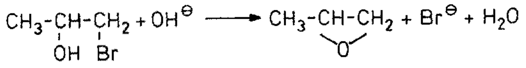
$$\text{Anode: } 2\,Br^{\ominus} \longrightarrow Br_2 + 2\,e^{\ominus} \tag{42}$$

$$\text{Cathode: } 2\,H_2O + 2\,e^{\ominus} \longrightarrow H_2 + 2\,OH^{\ominus} \tag{43}$$

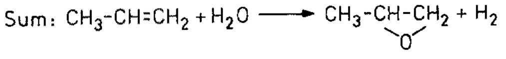
$$\text{Solution: } Br_2 + H_2O \longrightarrow HOBr + HBr \tag{44}$$



$$CH_3\text{-}CH{=}CH_2 + HOBr \longrightarrow CH_3\text{-}\underset{OH}{CH}\text{-}\underset{Br}{CH_2} \tag{45}$$



$$CH_3\text{-}\underset{OH}{CH}\text{-}\underset{Br}{CH_2} + OH^{\ominus} \longrightarrow CH_3\text{-}CH\text{-}CH_2\,(\text{-}O\text{-}) + Br^{\ominus} + H_2O \tag{46}$$

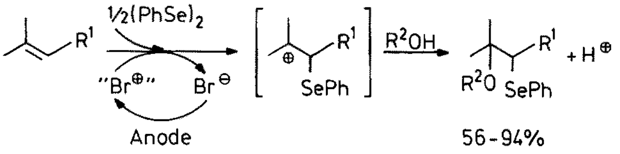


$$\text{Sum: } CH_3\text{-}CH{=}CH_2 + H_2O \longrightarrow CH_3\text{-}CH\text{-}CH_2\,(\text{-}O\text{-}) + H_2 \tag{47}$$

This process has, however, not yet found industrial application. Similarly, polyisoprenoids can be epoxidized regioselectively in ω-position to functional groups (Table 4, No. 16–19)[159-161]. Polymer-bound mediators can also be used in this case. Thus, an anion exchange resin in its bromide form is applied for the generation of epoxides after its electrochemical transformation into the hypobromite (Table 4, No. 29)[163].

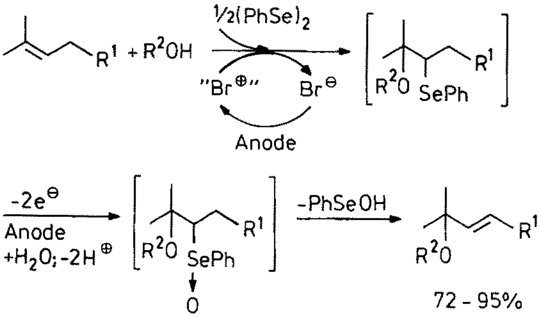
3.2.4 Selenation Reactions

Positively polarized selenation reagents for oxyselenation reactions can be substituted by an indirect electrochemical procedure in which the bromide ion acts as the redox catalyst. The active bromine species generates the phenylselenyl cation from the added diphenyl diselenide (Eq. (48); Table 4, No. 21–26)[164].



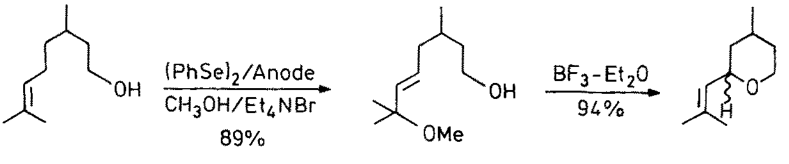
(48)

In many cases even the oxyselenation-deselenation sequence can be performed electrochemically in one step (Eq. (49), Table 4, No. 27–31)[163–168].

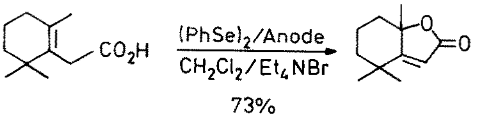


(49)

This allyloxylation was used to produce d,l-rose oxide from citronellol (Eq. 50)[165,167]. Similarly d,l-dihydroactinidiolide was formed in one step by the intramolecular oxyselenation-deselenation sequence (Eq. (51))[166].

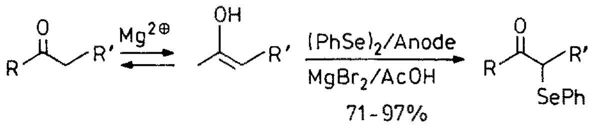


(50)



(51)

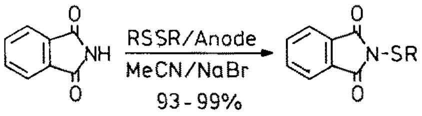
α-Phenylselenyl carbonyl compounds are accessible by indirect electrooxidation of carbonyl compounds in the presence of diphenyl diselenide and bromide as redox catalyst[169]. Magnesium ions seem to promote the enolization of the carbonyl compounds (Eq. (52); Table 4, No. 32).



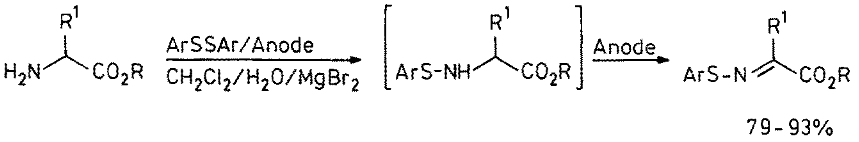
(52)

3.2.5 Formation of Hetero-Hetero Atom Bonds

Bromide and iodide ions are not only effective as redox catalyst in the indirect electrochemical formation of carbon-hetero atom bonds but also of hetero-hetero atom bonds. Thus, the nitrogen-sulfur bond in sulfenimides (Eq. (53); Table 4, No. 33)[170] and sulfenimines (Eq. (54); Table 4, No. 34)[171] can be generated. The electrogenerated active bromine species forms a positively polarized sulfenyl intermediate from disulfides.

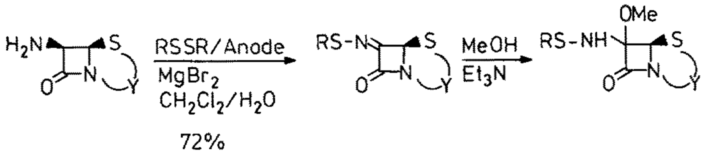


(53)



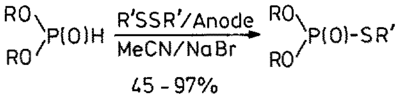
(54)

The last procedure is important as it can be used for the synthesis of 6- and 7-methoxy penicillins or cephalosporins which are potent antibiotics against Gram-negative bacteria (Eq. (55))[171].



(55)

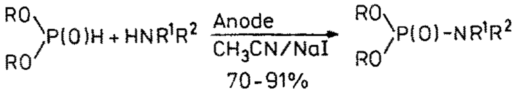
Similarly, the phosphorus-sulfur bond can be generated starting from dialkyl or diaryl phosphites (Eq. (56); Table 4, No. 35)[172].



$$(RO)_2P(O)H \xrightarrow[\text{MeCN/NaBr}]{\text{R'SSR'/Anode}} (RO)_2P(O)\text{-}SR' \qquad 45\text{-}97\%$$

(56)

Iodide is used as catalyst for the indirect anodic formation of the P—N bond to generate *N*-substituted dialkylphosphoramidates from phosphites (Eq. (57); Table 4, No. 36)[173].

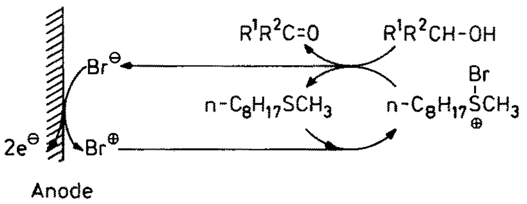


$$(RO)_2P(O)H + HNR^1R^2 \xrightarrow[\text{CH}_3\text{CN/NaI}]{\text{Anode}} (RO)_2P(O)\text{-}NR^1R^2 \qquad 70\text{-}91\%$$

(57)

3.2.6 Oxidation of Alcohols

The direct electrochemical oxidation of aliphatic alcohols occurs at potentials which are much more positive than 2.0 V *vs.* SCE. Therefore, the indirect electrolysis plays a very important role in this case. Using KI or NaBr as redox catalysts those oxidations can be performed already at 0.6 V *vs.* SCE. Primary alcohols are transformed to esters while secondary alcohols yield ketones [174-179]. In the case of KI, the iodo cation is supposed to be the active species. Using the polymer bound mediator poly-4-vinyl-pyridine hydrobromide, it is possible to oxidize secondary hydroxyl groups selectively in the presence of primary ones (Table 4, No. 40) [176]. The double mediator system RuO_4/Cl^-, already mentioned above (Eq. (29)), can also be used effectively [117]. Another double mediator system uses bromide ions in the presence of an organic sulfide (Eq. (58); Table 4, No. 46) [179].



(58)

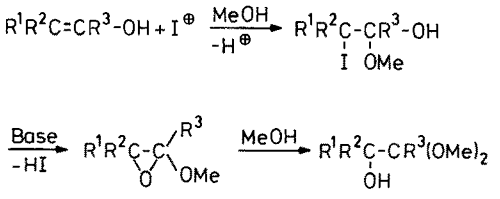
3.2.7 Oxidation of Carbonyl Compounds

Examples for the oxidation of carbonyl compounds using halide ions as redox catalyst are listed in Table 4. No. 47–50. Thus, in the presence of alcohols, aldehydes are transformed to esters (No. 47) [178].

α-Hydroxylated acetals are formed in one step from ketones if KI is used as mediator in the presence of potassium hydroxide (No. 48) [180]. The proposed mechanism is shown in Eqs. (59)–(61).

$$\text{Anode: } I^{\ominus} \longrightarrow I^{\oplus} + 2e^{\ominus} \quad (59)$$

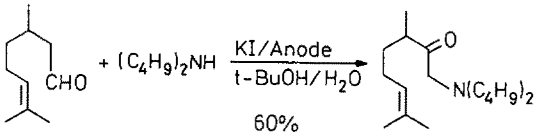
$$R^1R^2CH\text{-}CO\text{-}R^3 \rightleftharpoons R^1R^2C{=}CR^3\text{-}OH \quad (60)$$



$$R^1R^2C{=}CR^3\text{-}OH + I^{\oplus} \xrightarrow[-H^{\oplus}]{MeOH} R^1R^2\underset{I}{C}\text{-}\underset{OMe}{C}R^3\text{-}OH$$
$$\xrightarrow[-HI]{Base} R^1R^2C\overset{O}{-}C(R^3)(OMe) \xrightarrow{MeOH} R^1R^2\underset{OH}{C}\text{-}CR^3(OMe)_2$$

(61)

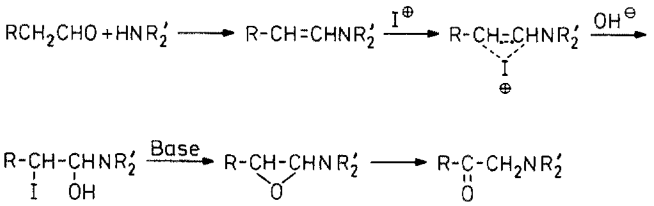
Quite unique is the formation of α-*N*,*N*-dialkylamino ketones from aldehydes and dialkylamines (Eq. (62); Table 4, No. 50) [182].



(62)

The following mechanism is proposed (Eq. 63):

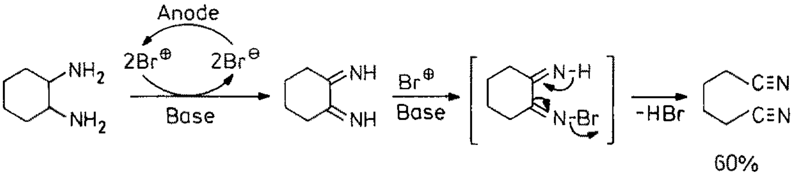
$$\text{Anode: } I^{\ominus} \longrightarrow I^{\oplus} + 2e^{\ominus} \qquad (59)$$



(63)

3.2.8 Oxidation of Nitrogen-Containing Compounds

Examples for the oxidation of nitrogen-containing compounds via halide ions as redox catalysts are listed in Table 4, No. 51–56. In this way, primary amines are transformed to nitriles using the system NaBr/MeOH (Table 4, No. 52) [181]. Thus, 1,2-diaminocyclohexane is cleaved to yield adiponitrile (Eq. (64)) [181].



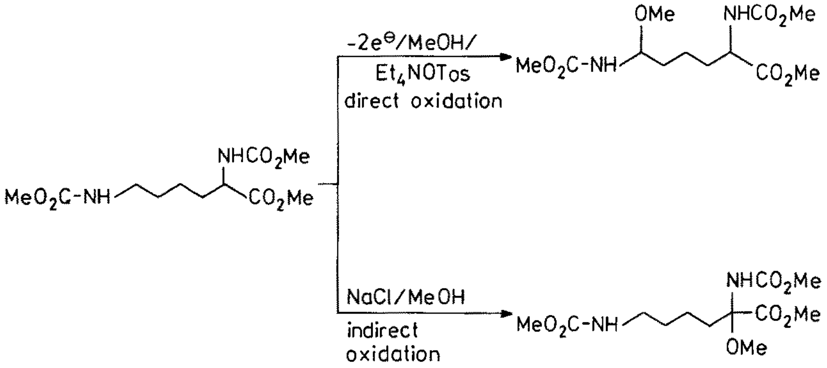
(64)

Quite important is also the α-methoxylation of *N*-carbomethoxylated α-amino acid esters and α-amino-β-lactams (Table 4, No. 53–55) [184, 185]. α-Methoxylation was even possible with β-lactam systems without cleavage of the ring [184] (No. 54). Very interesting is the regioselectivity in the indirect electrochemical α-methoxylation of lysine methyl ester derivatives as compared with the direct electrolysis. Direct anodic methoxylation takes place in the α position to the ω-amino group, while the indirect process using chloride as redox catalyst gave selectively the α-methoxylated α-amino acid derivative (Eq. (65)) [184, 185].

3.2.9 Oxidations Using Nitrate and Periodate as Redox Catalysts

Indirect electrochemical oxidations using the nitrate ion as redox catalyst proceed via the electro-generated NO_3 radical. They are useful for the oxidation of secondary alcohols [191] and of alkyl aromatic compounds in the side-chain [191].

Periodate regeneration was technically applied for the synthesis of dialdehyde starch from starch (Table 4, No. 64) [193] and recently for the generation of acetaldehyde from 2,3-butanediol (Table 4, No. 65) [194].



(65)

3.3 Reductions with Metal Salts and Metal Complexes as Redox Catalysts

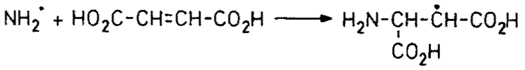
3.3.1 Reductions by Electrochemically Generated Low-Valent Metal Salts and Base Metals

Low-valent metal ions take Ti^{3+}, V^{3+}, Sn^{2+}, and Cr^{2+} are common reducing agents with a wide applicability in organic synthesis [196,197]. Their use in stoichiometric amounts, however, gives rise to problems especially in processes of industrial scale. The most important one is the protection of the environment from the spent metal salts. But also the chemical preparation of the low-valent ions imposes problems, as the chemical reducing agents have to be separated, thus making continuous processes impossible. Therefore, the electrochemical generation and regeneration of the active species *in situ* could be the method of choice in these cases. Numerous publications in this field prove the large interest in the indirect electrochemical process.

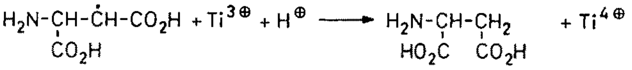
The reductive cleavage of hydroxylamine and its derivatives by electro-generated Ti^{3+} and V^{3+} forming aminyl radicals and the hydroxide ions has been studied intensively. The aminyl radicals are preferably trapped with alkenes and aromatic compounds. Thus, the reaction of hydroxylamine with electro-generated Ti^{3+} in the presence of maleic acid yields aspartic acid (Eqs. (66)–(69)) [198].

$$\text{Cathode: } Ti^{4\oplus} + e^{\ominus} \longrightarrow Ti^{3\oplus} \quad (66)$$

$$Ti^{3\oplus} + NH_2OH \longrightarrow Ti^{4\oplus} + NH_2^{\bullet} + HO^{\ominus} \quad (67)$$

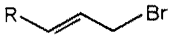
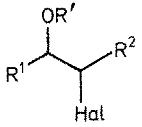
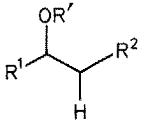
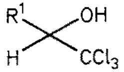
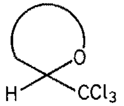
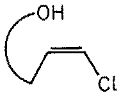
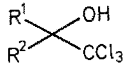
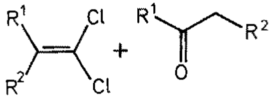
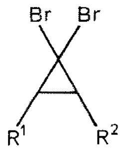


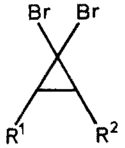
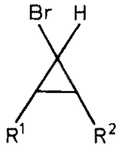
$$NH_2^{\bullet} + HO_2C\text{-}CH{=}CH\text{-}CO_2H \longrightarrow H_2N\text{-}\underset{\displaystyle CO_2H}{\underset{|}{C}H}\text{-}\dot{C}H\text{-}CO_2H \quad (68)$$



$$H_2N\text{-}\underset{\displaystyle CO_2H}{\underset{|}{C}H}\text{-}\dot{C}H\text{-}CO_2H + Ti^{3\oplus} + H^{\oplus} \longrightarrow H_2N\text{-}\underset{\displaystyle HO_2C}{\underset{|}{C}H}\text{-}\underset{\displaystyle CO_2H}{\underset{|}{C}H_2} + Ti^{4\oplus} \quad (69)$$

Table 5. Reductions by electrogenerated chromium(II) reagents

No.	Substrate	Redox catalyst (reduced form)	Product	Yield[a] [%]	Type of regeneration	Ref.
1		$CrCl_2$		my = 77–81 cy = 62–79	in-cell	215)
2	benzyl bromide	$CrCl_2$	bibenzyl	my = 60 cy = 48	in-cell	215)
3	benzal bromide	$CrCl_2$	stilbene	my = cy = 51	in-cell	215)
4	benzotrichloride	$CrCl_2^-$	diphenylacetylene	my = 30	in-cell	215)
5		$Cr(en)_2(ClO_4)_2$		cy = 15 my = 60–98	in-cell	216)
6		$CrCl_2$		cy = 32–48 my = 90	in-cell or ex-cell	217)
7		$CrCl_2$		my = 40–70	in-cell or ex-cell	217)
8		$CrCl_2$		my = 45–80[b] my = 25–50	in-cell or excell	217)
9		$CrCl_2$	$R^1CH{=}C{=}CHR^2$	my = 60–90	ex-cell	218)

10		$CrCl_2$		my = 50–70	in-cell	[218]
11	1,4-butynediol	$CrCl_2$ or $Cr(ClO_4)_2$	trans-1,4-butendiol 2,3-butadienol 3-butenol	my = 60 my = 5 my = 17	ex-cell	[219]
12	3-phenyl-3-hydroxy-propyne	$CrCl_2$ or $Cr(ClO_4)_2$	3-phenyl-propyne phenylallene	my = 20–70 my = 40–10	ex-cell	[219]
13	R^1—CO—R^2	$CrCl_2$	R^1R^2—C(OH)—C(OH)R^1R^2	my = 25–84	in-cell	[220, 221]

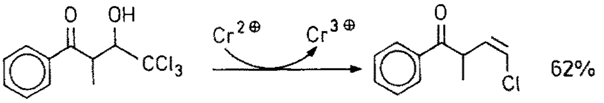
[a] my = material yield; cy = current yield; [b] can be influenced by the reaction conditions

In the presence of 1,3-butadiene, diamino octodienes and dodecatrienes are formed [199]. Amination of aromatic compounds has been mentioned above (Sect. 3.3.3) [112]. Sensitive substituted hydroxylamines may be reduced to the amines in oxylic acid using electro-generated titanium(III) [200].

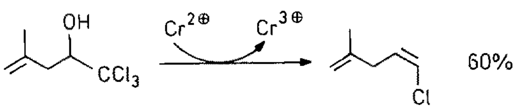
The reduction of aromatic nitro groups by use of electro-generated titanium(III) has also been investigated very intensively, especially in India. Thus, aniline derivatives are generated in high yield [201–212]. Evidently this method has some advantages over the otherwise common catalytic hydrogenation because of the structure of the chemical industry in India. The formation of a substituted benzidine from a substituted azoxybenzene by use of electro-generated Ti^{3+} has also been patented [213]. Electrochemically generated tin(II) can also be used for the reduction of nitro groups. Contrary to the titanium system, the reduction of nitrobenzene can be stoppes at the phenylhydroxylamine stage, which rearranges to *p*-aminophenol [214].

Chromium(II) salts are selective reducing agents with wide applicability in organic synthesis [196, 197]. Because of the sensitivity of chromium(II) reagents towards oxygen, the *in situ* electrochemical generation is favorable. Table 5 lists several examples for the application of electro-generated chromium(II) reagents. Thus, allylic and benzylic halides can be coupled in anhydrous dimethylformamide in yields comparable with those of other coupling methods (Table 5, No. 1–5) [215]. Similarly, the dehalogenation of α-hydroxyhalides and their ethers can be performed if the ethylenediamine complex of chromium(II) perchlorate is electro-generated in moist DMF. Butanethiol acts as hydrogen donor (Table 5, No. 5) [216]. This method is useful as an alternative to the tributyltin hydride method in the formation of deoxynucleotides.

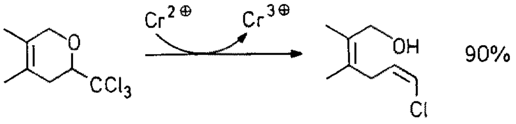
Recently it was found that α-trichloromethyl carbinols and their ethers, a class of compounds which is easily obtainable in large structural variety, can be reduced by chromium(II) chloride in water or aqueous DMF to synthetically very interesting products (Table 5, No. 6–8) [217]. Thus, trichloromethyl-substituted secondary alcohols and ethers give (*Z*)-configurated vinyl chlorides in one step (Eqs. (70)–(72)).



(70)



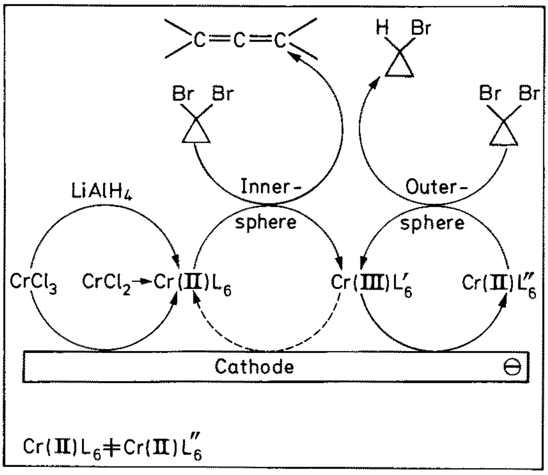
(71)



(72)

From α-trichloromethyl carbinols with the hydroxy group at a tertiary carbon, either dichlorovinyl compounds or, after rearrangement, carbonyl compounds are formed predominantly. The pathway of the reaction can be influenced by the choice of the reaction conditions. As the reduction potentials of some of the substrates are more positive than necessary for the chromium(II) generation, the electro-generation of the active reagent has to be performed separately from the chemical reaction (ex-cell process). An in-cell process is possible if the reaction takes place in a two-phase system. In this way the aqueous phase containing the chromium reagent is predominantly in contact with the cathode.

Geminal dibromocyclopropanes can be reduced to allenes in anhydrous DMF by externally electro-generated and regenerated chromium(II) via an inner-sphere electron transfer mechanism (Table 5, No. 9). If the reaction is performed with internal regeneration, however, after the first regenerative cycle only monobromo cyclopropanes are generated (Table 5, No. 10)[218]. The reason for this behavior must be that the chromium(III) complex which is formed after the first conversion must be different from the originally employed chromium(III)-halogen-DMF complex, for example, through insertion of another ligand. The ligand exchange in those complexes usually is slow. Scheme 2 depicts this proposal.



Scheme 2. Proposed reaction pathways in the indirect electrochemical reduction of geminal dibromocyclopropanes by chromium (II)

Such problems are frequently encountered if metal complexes are used as redox catalysts for inner-sphere electron transfer reactions (Sect. 2.3; mechanism B).

Electro-generated chromium(II) is also very effective in the pinacolization of otherwise unsatisfactory dimerizing carbonyl compounds (Table 5, No. 13)[220–222]. In this case the chromium(II) ion does not act as redox agent but catalyzes the formation of a chromium(III) complex of the carbonyl compound which subsequently is reduced to the pinacol directly at the cathode (Eqs. (73)–(77)).

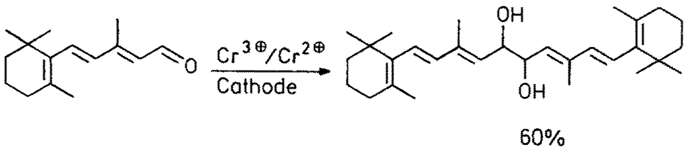
$$\text{Cathode: } [\mathrm{Cr(III)L_6}] + e^{\ominus} \longrightarrow [\mathrm{Cr(II)L_6}] \tag{73}$$

$$[\mathrm{Cr(II)L_6}] + n\mathrm{R_2CO} \rightleftharpoons [\mathrm{Cr(II)(R_2CO)_n L_{6-n}}] \tag{74}$$

$$[\mathrm{Cr(II)(R_2CO)_nL_{6-n}}] + [\mathrm{Cr(III)L_6}] \rightleftharpoons [\mathrm{Cr(III)(R_2CO)_nL_{6-n}}] + [\mathrm{Cr(II)L_6}] \tag{75}$$

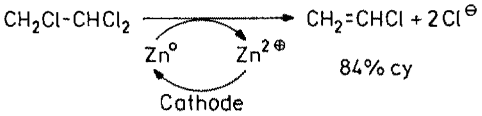
$$\text{Cathode: } [\mathrm{Cr(III)}(\mathrm{R_2CO})_n\mathrm{L}_{6-n}] + n\mathrm{e}^{\ominus} \longrightarrow [\mathrm{Cr(III)}(\mathrm{R_2CO}^{\cdot\ominus})_n\mathrm{L}_{6-n}] \qquad (76)$$

$$[\mathrm{Cr(III)}(\mathrm{R_2CO}^{\cdot\ominus})_n\mathrm{L}_{6-n}] \xrightarrow[+2\mathrm{H}^{\oplus}\ +2\mathrm{L}]{n=2} \mathrm{R_2C(OH)C(OH)R_2} + [\mathrm{Cr(III)L_6}] \qquad (77)$$



(78)

Suspensions of base metals can be generated at the cathode at high current densities ($\geq 0.5\ \mathrm{A\ cm^{-2}}$) in two-phase systems. Since very small particles with oxygen-free surfaces are generated, the reactivity of these metal suspensions clearly surpasses that of commonly employed metals[223, 224]. In this way zinc, copper, iron, and tin powders have been generated in high current yields and used for the reduction of nitro compounds and halogenated hydrocarbons (Eq. (79)).



$$\mathrm{CH_2Cl{-}CHCl_2} \xrightarrow[\mathrm{Zn^0}\ \ \mathrm{Zn^{2\oplus}}\ (\text{Cathode})]{} \mathrm{CH_2{=}CHCl} + 2\mathrm{Cl}^{\ominus} \quad 84\%\ \text{cy} \qquad (79)$$

3.3.2 Indirect Electrochemical Reductions with Transition Metal Complexes

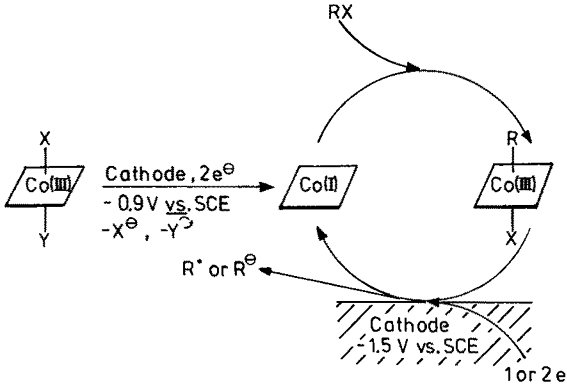
Transition metal complexes are increasingly being applied as redox catalysts, especially for reductions. Mostly Ni(O)-, Ni(I)-, Co(I)-, Sn(O)-, Pd(O)-, or Rh(I)-complexes are used as cathodically generated active forms. The advantage of transition metal complexes as redox catalysts is their broad reactivity spectrum together with the possibility to tune their redox potentials and selectivities to the requirements of a substrate by choice of the central atom or the ligand. Very often the active forms of the complexes undergo an oxidative addition with alkylating reagents like halides which is followed by an electrochemically induced reductive elimination of the thus formed alkyl complex.

3.3.2.1 Co(I)-Complexes as Redox Catalysts

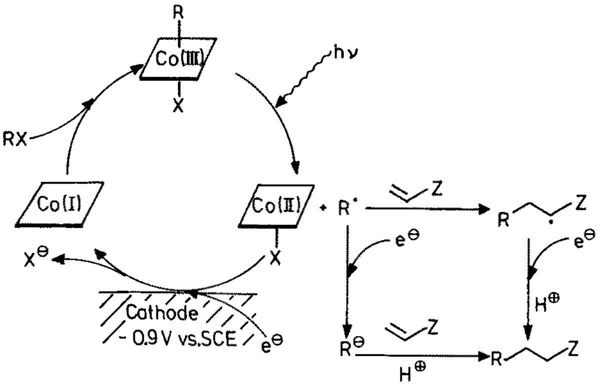
A typical catalytic cycle for cobalt complexes is shown in Scheme 3[225]. The starting Co(III)-complex, in this case the particularly suitable Vitamin B_{12}, is cathodically reduced at —0.9 V (*vs.* SCE) to the Co(I)-complex which reacts with an alkyl halide to give the alkylcobalt(III) complex. This complex then undergoes reductive elimination of an alkyl radical or carbanion at the more negative potential of —1.5 V (*vs.* SCE) regenerating the Co(I) system.

The reduction potential for the reductive elimination can be lowered to —0.9 V (*vs.* SCE) if the alkylcobalt(III) complex is photochemically activated by visible light[225–227, 228] (PEC = Photo-Electro-Catalysis; see Scheme 4).

Very effective and selective syntheses have been performed in this way (see Table 6). Especially valuable is the alkylation[225–228, 230–232] and acylation[225–228]



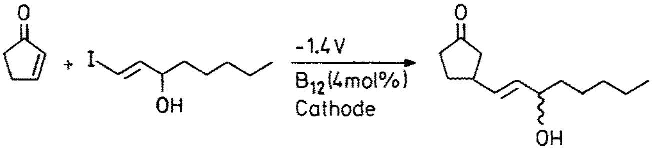
Scheme 3. Catalytic reductive activation of R—X by Vitamin B_{12} in the dark



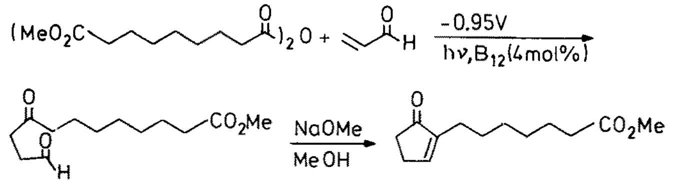
Scheme 4. Catalytic reductive and photochemical activation of R—X by Vitamin B_{12}

of Michael acceptors. The nucleophilic acylation usually runs via the photochemically supported cleavage of the intermediate acylcobalt(III) complex (Scheme 4) [225–228].

This technique can be used for the synthesis of natural products like pheromones, 3-substituted steroids, cyclopentanoids, sugars, etc. Some examples are given in Eqs. (80)–(82).

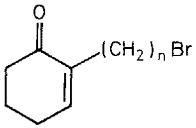
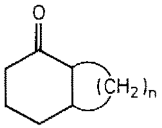
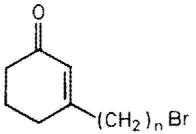
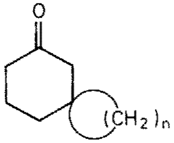
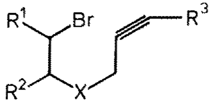
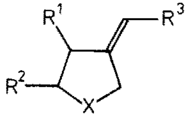


(80)



(81)

Table 6. Reduction with electrogenerated cobalt(I) complexes

No.	Substrate	Redox catalyst (oxidized form)	Product	Yield (%)	Ref.
1	R—X	Vit. B_{12}	R—H	93–97	225, 231)
2	*n*-BuBr	Vit. B_{12}	*n*-BuH	a	234)
3	allyl chloride	$Co(bpy)_3^{3+}$	1,5-hexadiene	53	233)
4	$R—X + CH{\equiv}C—Z$ or $CH_2{=}CH—Z$ (Z = COR, CN, CO_2R)	Vit. B_{12} (1–10 mol %)	$R—CH{=}CH—Z$ or $R—CH_2CH_2—Z$	51–98	225–227)
5	$R^1CH{=}CH—I + R^2CH{=}CH—CO—R^3$	Vit. B_{12} (1–10 mol %)	$R^1CH{=}CH—CHR^2CH_2—CO—R^3$	a	227)
6		Vit. B_{12} (1–10 mol %)		70–95	225–227, 230)
7		Vit. B_{12} (1–10 mol %)		45–95	225–227, 230)
8	$Ph—CH_2—Cl$ or $R—CH{=}CH—CH_2Cl$ $+ CO_2$ $+ CO_2$	Co(salen)	$Ph—CH_2CO_2H$ or $R—CH{=}CH—CH_2—CO_2H$	50–97	235)
9	 X = CH_2; O	Vit. B_{12} (1–10 mol %) or chloro pyridine cobaloxime(III)		44–87 35–87	227) 232)
10	$(RCO)_2O$ or $CH_3COX + CH_2{=}CH—Z$ (Z = COR, CN, CHO, CO_2R)	Vit. B_{12}/light (4 mol %)	$R—CO—CH_2CH_2—Z$	40–80	225–228)
11	$RO—CHR^1CH_2—X + CH{\equiv}C—Z$ or $CH_2{=}CH—Z$	Vit. B_{12}/light (4 mol %)	$RO—CHR^1CH_2CH{=}CH—Z$ or $RO—CHR^1CH_2CH_2CH_2—Z$	80	227)

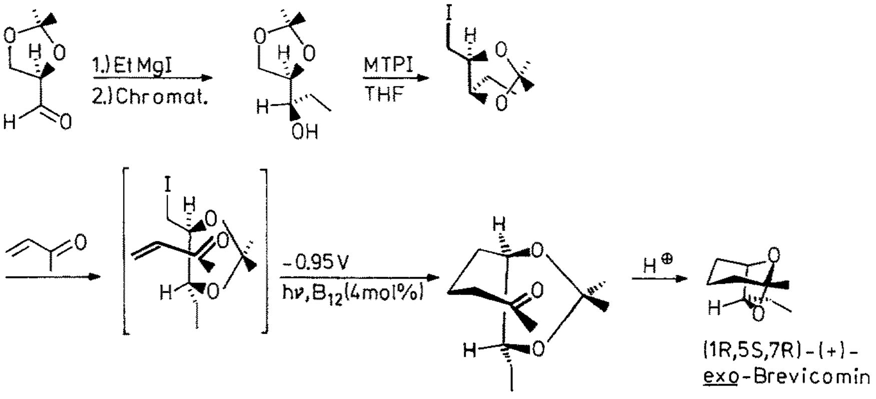
12	R—CO_2—CH_2CH_2X	Vit. B_{12} (4 mol %)	RCO_2H + $CH_2{=}CH_2$		225, 229)
13	R—NH—$CO_2CH_2CH_2X$	Vit. B_{12} (4 mol %)	RNH_2 + CO_2 + $CH_2{=}CH_2$		225, 229)

[a] yield not given

Table 7. Reductions with electrogenerated Ni(O)-, Ni(I)-, Sn(O)-, and Pd(O)-complexes

No.	Substrate	Redox catalyst (oxidized form)	Product	Yield (%)	Ref.
1	Ar—X	$NiCl_2/PPh_3$ or $NiCl_2/Bu_3P$	Ar—H	[a]	238)
2	Ar—X	$NiCl_2/Ph_3P$	Ar—Ar	22–86	32, 236, 237)
3	1,4-dibromobenzene	$NiCl_2$/diphos	poly(1,4-phenylene)	60	242)
4	4,4′-dibromobiphenyl	$NiCl_2$/diphos	poly(1,4-phenylene)	85	243)
5	Ar—X/CO_2	$NiCl_2/Ph_3P$ or $NiCl_2$/diphos	Ar—CO_2H	40–90	239a)
6	$ArCH(CH_3)X/CO_2$	$NiCl_2/Ph_2P(CH_2)_3PPh_2$	$ArCH(CH_3)CO_2H$	76–81	239b)
7	Ar—X/RCH$=CH_2$	NiI_2/Ph_3P	Ar—RC$=CH_2$ + Ar—CH$=$CH—R	50–80	240)
8	Ar—X/$CH_2{=}CH_2$	$NiBr_2$	$(Ar)_2CH$—CH_3	60–65	241)
9	R—I	$Ni(Ph_3P)_2^{2+}$	R—R	75–92	237)
10	RI/RBr	Ni(salen)[b] or $Ni(teta)^{2+}$ [c]	R—R, R—H, R(—H)	40–77	244–247)
11	RBr/$CH_2{=}$CHZ Z$=$CN, CO_2Et, COR	Ni(salen)[b] or $Ni(teta)^{2+}$ [c]	R—CH_2CH_2—Z	11–94	245, 248)
12	$CH_2{=}$CH—CH_2—Br + R^1—CO—R^2	Sn^{2+}	$R^1R^2C(OH)CH_2CH{=}CH_2$	70–90	249)
13	ArI/ArBr	$PdCl_2/Ph_3P$	Ar—Ar	50–99	250)
14	ArI/ArBr + R—CH$=CH_2$ or R—C$\equiv$CH	$PdCl_2/Ph_3P$	Ar—CH_2CH_2—R or Ar—CH$=$CH—R	66–85	251)
15	R—CH$=$CH—CH_2—OAc/E^+ E^+ = H^+, TMSCl	Pd^{2+}/Ph_3P	R—CH$=$CH—CH_2—E E = H, TMS	58–82	252)

[a] yield not given; [b] Ni(salen) = N,N′-ethylene-bis(salicylidene)iminato nickel(II); [c] $Ni(teta)^{2+}$ = 5,5,7,12,12,14-hexamethyl-1,4,8,11-tetraazacyclotetradecane nickel(II)

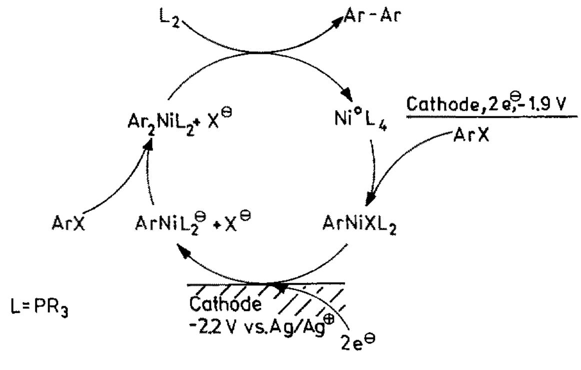


(82)

Recently it was found that similarly benzylic and allylic chlorides can be carboxylated using a cobalt-bis-salicylidene iminato complex (Co(salen)) (Table 6, No. 8)[235].

3.3.2.2 *Ni(O)-Complexes as Redox Catalysts*

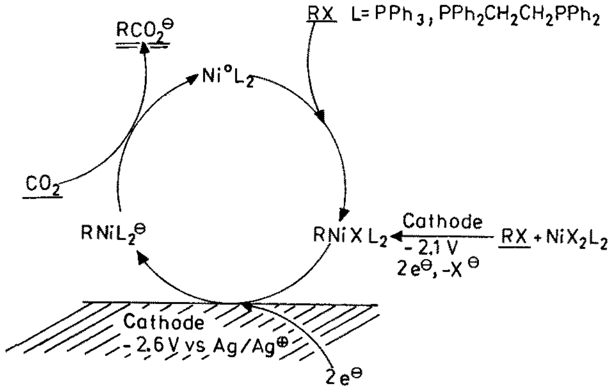
Very similar to the Co(I)-complexes, Ni(O)-complexes can be used as redox catalysts. Thus, the formation of bisaryls and poly(1,4-phenylene) from aryl halides has been studied intensively (Scheme 5).



Scheme 5. Bisaryl formation via electro-generated Ni(O) phosphane complexes

As ligands, phosphanes have proven to be useful[32,236,237,242,243] (Table 7, No. 2–4). Poly(1,4-paraphenylene) is obtained on a preparative scale starting from aromatic dihalides[242,243] (Table 7, No. 3, 4). The electrochemical generation and reduction of the ArNiXL$_2$-complex in the presence of carbon dioxide leads to the formation of benzoic acids (Table 7, No. 5)[239a]. Similarly, 1-arylethyl halides can be carboxylated to yield the pharmaceutically effective 2-arylpropionic acids (Table 7, No. 6)[239b]. The proposed mechanism is given in Scheme 6.

Ethene and mono-substituted alkenes can be arylated by aryl halides in presence of electro-generated Ni(O) phosphane complexes (Table 7, No. 7) [240]. In the absence of phosphanes, ethene is diarylated to give 1,1-diaryl ethane (Table 7, No. 8) [241].



Scheme 6. Carboxylation of halides via electro-generated Ni(O) phosphane complexes

3.3.2.3 *Ni(I)-Complexes as Redox Catalysts*

The indirect electrochemical reduction of alkyl halides is also possible by use of nickel(I) complexes which may be obtained by cathodic reduction of square planar Ni(II)-complexes of macrocyclic tetradentate ligands (Table 7, No. 10, 11) [244-248]. Comparable to the Co(I)- and Ni(O)-complexes, the Ni(I)-species reacts with the alkyl halide unter oxidative addition to form an organo nickel(III) compound. The stability of the new nickel-carbon bond dominates the overall behavior of the system. If the stability is low, the alkyl group is lost in form of the radical and the original Ni(II)-complex is regenerated. A large number of regenerative cycles is the result.

This is the case for secondary and tertiary alkyl bromides. If the stability is high, however, as, for example, with primary alkyl bromides, the organo nickel(III) complex is further reduced to an alkyl nickel(II) complex which loses the alkyl group in form of the alkyl anion. An electroinactive Ni(II) species remains. The number of regenerative cycles is consequently low. The structure of the ligand also influences the lifetime of the alkyl nickel(III) complex; thus, a less stable complex is formed in the case of [*N*,*N*′-ethylene-bis(salicylidene-iminato)]nickel(II) ([Ni(salen)]) as compared with (5,5,7,12,12,14-hexamethyl-1,4,8,11-tetraazacyclotetradecane)nickel(II) ($[\mathrm{Ni(teta)}]^{2\oplus}$), and hence the former complex favors the radical pathway even with primary alkyl halides.

With primary halides, dimers (R—R) are formed predominantly, while with tertiary halides, the disproportionation products (RH, R(—H)) prevail. Both alkyl nickel(III) complexes, formed by electrochemical reduction of the nickel(II) complex in presence of alkyl halides, are able to undergo insertion reactions with added activated olefins. Thus, Michael adducts are the final products. The Ni(salen)-complex yields the Michael products via the radical pathway regenerating the original Ni(II)-complex and hence the reaction is catalytic. In contrast to that, the Ni(III)-complex formed after insertion of the activated olefin into the alkyl-nickel bond of the $[\mathrm{RNi^{III}X(teta)}]^{\oplus}$-complex is relatively stable. Thus, further reduction leads to the Michael products and an electroinactive $\mathrm{Ni^{II}}$(teta)-species.

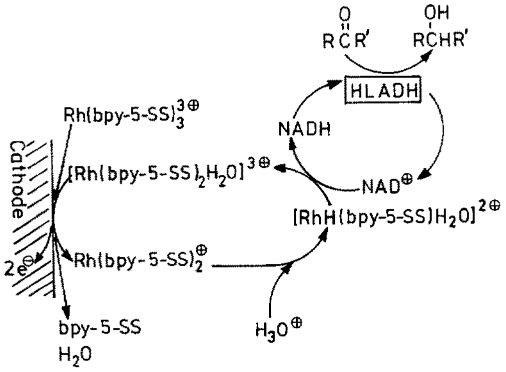
3.3.2.4 Other Low-Valent Transition Metal Complexes as Redox Catalysts

The electrochemical allylation of carbonyl compounds by electroreductive regeneration of a diallyltin reagent from allyl bromide and a Sn^0 species leads to formation of homoallylic alcohols in yields of 70–90% even in methanol or methanol/water (Table 7, No. 12)[249]. Bisaryl formation is possible also from aryl iodides or bromides in the presence of electro-generated Pd^0 phosphane complexes (Table 7, No. 13)[250]. In the presence of styrenes, 1,3-butadienes, or phenyl acetylene the products of ArH addition are formed in this way (Table 7, No. 14)[251]. The electroreductive cleavage of allylic acetates is also possible by catalysis of an Pd^0-complex (Table 7, No. 15)[252].

A copper(O) complex, electro-generated from $Cu(acac)_2$, is able to undergo an oxidative addition with benzyl and allyl bromides. Further reduction leads to the coupling products bibenzyl and 1,5-hexadienes[253]. Methyl-3-hexene-1,6-dicarboxylate can be prepared from butadiene and CO_2 by electroreduction if di-Fe dicyclopentadienyl tetracarbonyl is used as redox catalyst[254]. Electro-generated low-valent tungsten species are able to reductively dimerize benzaldehyde to stilbene according to Eq. 83. The reduction potential was controlled at the third wave of the WCl_6 catalyst ($V \leq -1900$ mV/SCE)[255].

$$2\,\mathrm{Ph{-}CHO} \xrightarrow[\substack{\text{Pt-cathode}\\ -1.9\,\text{V vs. SCE}}]{[\mathrm{WCl_6}]} \underset{97\%}{\mathrm{PhCH{=}CHPh}} \tag{83}$$

Electro-generated and regenerated bis(bipyridine)rhodium(I) complexes were able to catalyze the selective non-enzymatically coupled electrochemical generation of NADH from $NAD^{\oplus}$. The direct cathodic reduction even at very negative working potentials leads to the formation of large amounts of enzymatically inactive NAD dimers, while the indirect electrochemical reduction via the rhodium complex acting as



bpy-5-SS = 2,2'-bipyridine-5-sulfonic acid

HLADH = horse-liver alcohol dehydrogenase

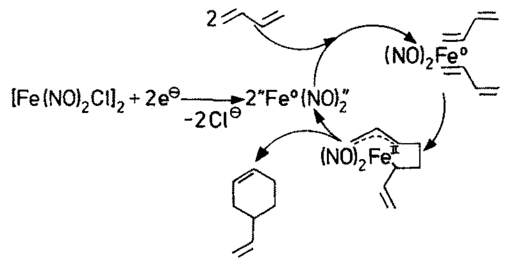
Scheme 7. Indirect electrochemical regeneration of NADH from $NAD^{\oplus}$ using $[Rh(bpy\text{-}5\text{-}SS)_3]^{3\oplus}$ as redox catalysts two-electron transfer agent provides exclusively the enzymatically active NADH. If the indirect electrolysis is performed in presence of alcohol dehydrogenase, carbonyl compounds are transformed into the respective alcohols *in situ* (Scheme 7)[256, 257]. The most effective ligand at the moment is 2,2'-bipyridine-5-sulfonic acid, as it prevents electrode covering because of the higher solubility of the complex in the buffer system as compared with 2,2'-bipyridine as ligand[257].

In addition, the reduction potential of —720 mV *vs.* Ag/AgCl-reference for the complex with the bipyridine sulfonic acid ligand is about 200 mV more positive as compared with the unsubstituted 2,2'-bipyridine ligand. As a consequence, NAD dimer formation is totally suppressed[257].

3.3.2.5 Electrochemical Generation of Transition Metal Catalysts

A very active field of research is the *in situ* generation of transition metal catalysts. After the fundamental work by Lehmkuhl et al.[258], there have been very interesting new results[263].

For example, the dinitrosyliron(O) complex can be formed cathodically. This complex is able to catalyze the cyclodimerization of conjugated dienes (Scheme 8)[259, 260]. Thus, in case of 1,3-butadiene, 20000 turnovers are obtained per hour with complete selectivity towards 4-vinyl-cyclohexene.



Scheme 8. Electro-generated dinitrosyliron(O) complex as catalyst for the cyclodimerization of conjugated dienes

Hydroformylation reactions can be catalyzed by electro-generated $HCo(CO)_4$ and $HCo(CO_3)PBu_3$ species[261]. Similarly, highly active catalysts for olefin metathesis can be obtained from WCl_6 or $MoCl_5$[262]. Aluminum is used as anode material as it forms $AlCl_3$ as the required Lewis acid.

4 Application of Organic Redox Catalysts for Indirect Electrochemical Syntheses

The most important condition for the suitability of a compound to act as a mediator (redox catalyst) is its stability in all oxidation states which are involved in the reaction. Otherwise a fast loss of catalytic activity will be encountered. This prerequisite is difficult to fulfill by organic molecules because their active forms mostly are radical ions which are irreversably attacked in many media. Only recently the number of known stable organic mediators has considerably increased.

Reductions have been performed with radical anions and dianions of mostly aromatic compounds. It is clear that these mediators can not be used in protic media, while viologens can act as electron transfer agents in protic solvents. Their application, however, is limited to potentials of up to about —1.0 V.

For oxidations, the cation radicals of aromatic compounds like 9,10-diphenylantracene, thiantrene, phenoxathiine, or dibenzodioxine are likely candidates. Their reactivity towards nucleophiles, however, limits their application to media of low nucleophilicity. Sometimes the stability of such cation radicals can be enhanced through blocking the reactive positions by substituents. For example, *para*-substituted triarylamines deliver cation radicals with often excellent stability even in methanol. The stability is further increased by incorporation of *ortho*-substituents. Other mediators which have been applied in indirect electrosyntheses are those which are able to abstract hydrogen atoms or hydride atoms.

4.1 Indirect Electrochemical Reductions Using Radical Anions or Dianions of Organic Compounds as Mediators

Radical anions and dianions of a large number of compounds, mostly aromatics, have been tested as mediators for reductions. Table 8 lists the potentials of frequently used mediator systems.

Table 8. Reduction potentials of organic mediators for indirect electroreductions

Compound	$-E_{1/2}V$ (*vs.* SCE)	Ref.	Compound	$-E_{1/2}V$ (*vs.* SCE)	Ref.
perylene	1.67	264)	2,2'-binaphthyl	2.21	264)
phthalonitrile	1.69	265b)	benzonitrile	2.24	265a)
4-methoxybenzophenone	1.75	265b)	chrysene	2.25	264)
9,10-diphenylanthracene	1.85	264)	*m*-tolunitrile	2.27	265a)
anthracene	1.96	264)	*p*-tolunitrile	2.34	265a)
phenanthridine	2.00	265a)	2-methylnaphthalene	2.46	264)
benzo[*f*]quinoline	2.08	265a)	phenanthrene	2.45	264)
pyrene	2.09	264)	1,1-binaphthyl	2.45	264)
benzo[*h*]quinoline	2.12	265a)	naphthalene	2.50	264)
methylbenzoate	2.17	265a)	biphenyl	2.70	264)

The homogeneous electron transfer between the mediator anion radical or dianion and the substrate usually is followed by a bond cleavage. Thus, alkyl and aryl halides, sulfonates, sulfonamides, sulfones, sulfides, onium compounds, and epoxides can be cleaved by indirect electrochemical reduction using organic mediators 5b). According to mechanism A (Sect. 2.3), the redox potentials of the electron transfer agents are considerably lower than those of the substrates (reaction opposite to the standard potential gradient). The driving force for the reaction is in most cases the fast and irreversible cleavage of a carbon-hetero atom bond. The most important reaction steps for such reactions are shown in Eqs. (84)–(95).

$$\text{Cathode}: \quad e^{\ominus} + M \rightleftharpoons M^{\cdot\ominus} \tag{84}$$

$$M^{\cdot\ominus} + RX \xrightleftharpoons{ET} M + RX^{\cdot\ominus} \tag{85}$$

$$RX^{\cdot\ominus} \xrightarrow{k} R^{\cdot} + X^{\ominus} \tag{86}$$

$$M^{\cdot\ominus} + R^{\cdot} \xrightleftharpoons{ET} M + R^{\ominus} \tag{87}$$

$$\text{and/or} \quad R^{\cdot} + e^{\ominus} \rightleftharpoons R^{\ominus} \tag{88}$$

$$R^{\cdot} + SH(\text{solvent}) \longrightarrow RH + S^{\cdot} \tag{89}$$

$$R^{\ominus} + SH(\text{solvent}) \longrightarrow RH + S^{\ominus} \tag{90}$$

$$2R^{\cdot} \longrightarrow RR\,;RH + R(-H) \tag{91}$$

$$R^{\ominus} + RX \longrightarrow RR + X^{\ominus} \tag{92}$$

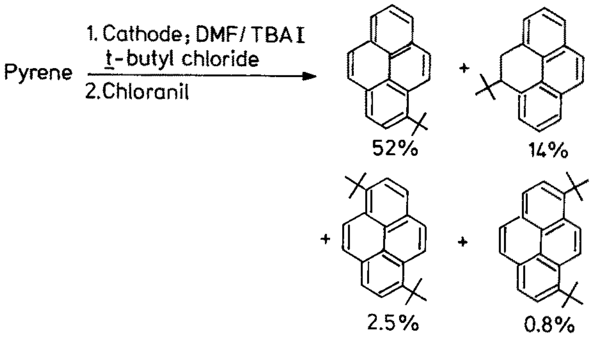
$$M^{\cdot\ominus} + R^{\cdot} \longrightarrow MR^{\ominus} \tag{93}$$

$$MR^{\ominus} + SH(\text{solvent}) \longrightarrow MRH + S^{\ominus} \tag{94}$$

$$MR^{\ominus} + RX \longrightarrow MR_2 + X^{\ominus} \tag{95}$$

M = mediator (aromatic hydrocarbon)
HMR = monoalkylation product of the mediator
MR_2 = dialkylation product of the mediator
ET = homogeneous electron transfer

Hydrogenated products, RH, are formed via the intermediate radicals or anions according to Eqs. (89) and (90). Similarly, elimination and ring-opening products can be observed. Second order reactions of the radicals $R^{\cdot}$, like dimerizations of disproportionations (Eq. (91)), are unfavored, as under the conditions of an indirect electrolysis their stationary concentrations are low. Coupling products, RR, are more likely formed via nucleophilic attack of the anion on the substrate RX (Eq. (92)). A competitive reaction of the radical $R^{\cdot}$ consists of its coupling with the mediator anion radical to form the alkylation product RM^- (Eq. (93)) which is either protonated (Eq. (94)) or undergoes a second alkylation (Eq. (95)). Thus, monalkylated and dialkylated mediator products are formed. An electrochemical regeneration of the



Scheme 9. Products of perturbed redox catalysis with pyrene as mediator

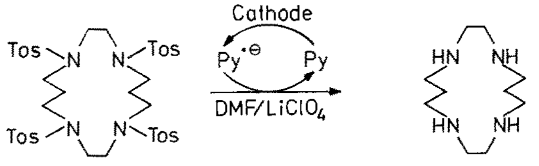
mediator anion radical is therefore not possible. As a consequence, the catalytic current which is otherwise observed by cyclic voltammetry is suppressed. Therefore, the reaction sequence which is described by Eqs. (84)–(86) and (93)–(95) is called "perturbed redox catalysis" by Simonet [5b]. Typical products are shown for pyrene as the mediator (Scheme 9) [288].

The indirect electrochemical cleavage of halides has been studied in detail by Lund and Simonet et al. [266–272]. The course of the reaction is strongly influenced by the structure of the substrates. Thus, aryl and benzyl halides do not form alkylation products of the mediators. The products of the perturbed redox catalysis are, however, favored in the case of aliphatic halides. Primary halides give predominantly monoalkylation products, while tertiary halides favor the formation of dialkylation products.

The methods for the theoretical treatment of the homogeneous redox catalysis have been mainly developed by Savéant et al. [273]. These methods allow to calculate the lifetimes of short-lived anion radicals and the standard potentials of the substrates from redox-catalytic experiments which are directly not accessible [265].

In several examples the reductive halide-hydrogen exchange has been studied on a preparative scale. For example, the indirect electroreduction of 2-chloropyridine in DMF using anthracene as mediator gives pyridine in 83–86% yield [269]. For the dehalogenation of 1-chlorohexane (80% yield), naphthalene is applied as redox catalyst. Similarly, 6-chloro-hexene yields 1-hexene (60%) and methylcyclopentane (25%), which is the product of the radical cyclization [266,267]. The indirect electrochemical reduction of β- and γ-bromocarboxylic esters forms coupling and elimination products besides the dehalogenated products [274].

The reductive deblocking of tosylamide, tosylester, benzyloxycarbonyl, *p*-nitrobenzyloxycarbonyl, benzylester, and benzylether protecting groups is also a field of intensive studies [27, 265d, 275–277]. Because of their mildness and selectivity, indirect electrochemical procedures are especially suitable for application in protective-group chemistry. Thus, Simonet et al. [275] used pyrene as mediator for the release of poly-aza-macrocycles from poly-*p*-toluenesulfonamides (Eq. (96)).

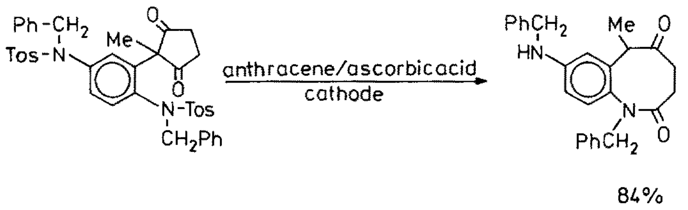


Py = pyrene

Tos = p-toluenesulfonyl

(96)

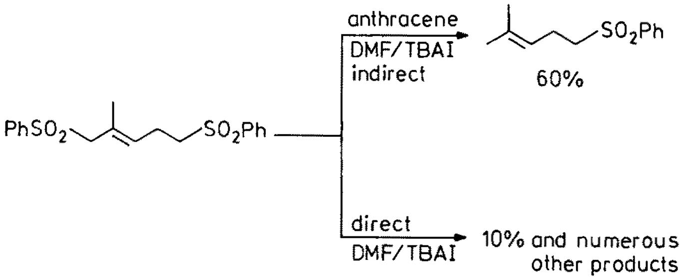
A very effective tosylamide cleavage seems to be possible by the cooperative action of the electro-generated anthracene anion radical as electron transfer agent and of ascorbic acid as proton donor and additional reducing agent (Eq. (97)) [276].



(97)

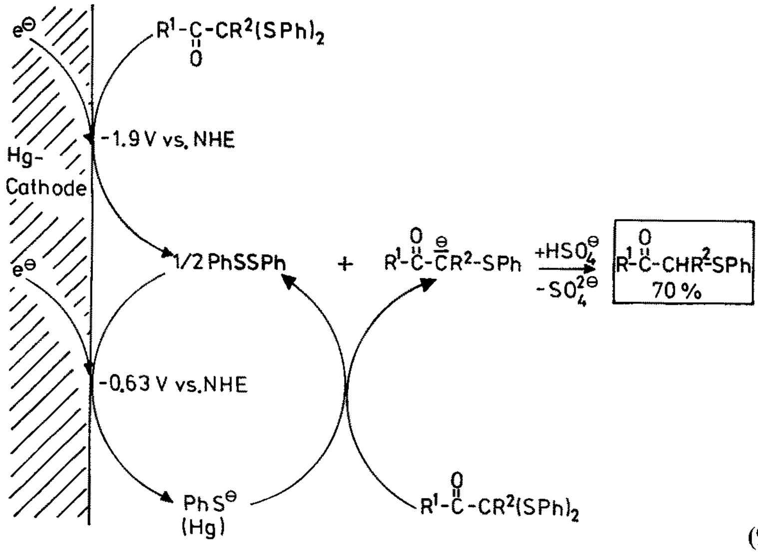
A benzoyl benzoate substituent in 6-position of β-cyclodextrine can act as redox catalyst for the cathodic cleavage of a benzylester-cyclodextrine inclusion compound. Thus, a simple redox enzyme model was formed 277).

The indirect electrochemical cleavage of sulfones demonstrates the increased selectivity of this method as compared with direct electrolysis (Eq. (98)) 278).



(98)

Other applications of this method concern the cleavage of sulfides 279) and disulfides 280) under formation of thiols. An interesting variation of the cathodic elimination is the autocatalytic formation of *trans*-stilbene from 1,2-diphenyl-1-thiophenyl-2-acetoxyethane. In this case the reaction starts with the direct elimination of the acetoxy and the thiophenyl anions. The thus formed stilbene with its more positive reduction potential is reduced to the corresponding anion radical which subsequently acts as the mediator for the reductive elimination of the substrate 279b). Consequently, the working potential drifts to more positive values during the course of the electrolysis. Similarly, an autocatalytic process is observed in the electroreductive cleavage of a carbon-sulfur bond in α-carbonyldithiophenyl acetals yielding α-thiophenyl ketones 281). In this case the diphenyldisulfide which is formed in a first direct electrochemical step acts as the mediator, and the working potential can be changed form —1.9 to —0.63 V (Eq. (99)).

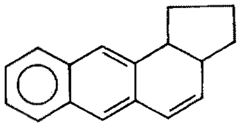
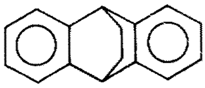


(99)

If small amounts of PhSSPh were deliberately added from the beginning, the more positive reduction potential could be applied from the start. Indirect electrochemical eliminations were also performed in the case of 1,2-dihalides [282]. Ring-opening reactions by the redox catalytic method were possible in the case of methylene cyclopropanes [283] and epoxides [284].

Preparative use could be made also from the perturbed redox catalysis [5b] (Eqs. (84)–(86), (93)–(95). For example, alkylated aromatic hydrocarbons that are difficult to obtain by Friedel-Crafts alkylation could be synthesized in this way. The most suitable alkylating agent is *tert*-butyl chloride or bromide [270, 285–288]. The alkylation can not only be performed by alkyl halides but also by sulfonium or ammonium ions [269, 189]; examples are given in Table 9. Nitroso compounds can similarly act in a double fashion: their anion radicals can act as electron transfer agents to alkyl halides and the thus formed radicals can be trapped by the nitroso compound to give the stable nitroxide radical [294].

Table 9. Examples for the alkylation by perturbed redox catalysis

Organic mediator	Substrate[a]	Product	Ref.
fluorenone	MeCl	9-methyl-9-methoxyfluorene	290)
aryl ketones	*t*-BuCl	*tert*-butyl carbinols and *tert*-butylation in the aromatic ring	291)
pyrene	*t*-BuCl	1-*tert*-butyl-pyrene	288)
naphthalene	*t*-BuCl	isomeric 1- and 2-*tert*-butyl dihydro and tetrahydro naphthalenes	270)
quinolines and isoquinolines	*t*-BuCl	*tert*-butylated dihydro and tetrahydro quinolines and isoquinolines	286)
pyridine carboxamides	*t*-BuCl	*tert*-butylated pyridine carboxamides	287)
1-ethyl-4-methoxy-carbonylpyridinium ion	*t*-BuBr	4-*t*-butyl-1,4-dihydro-1-ethyl-4-methoxy-carbonylpyridine	285)
1-ethyl-4-methoxy-carbonylpyridinium ion	2-bromooctane	4-*sec*-octyl-1,4-dihydro-1-ethyl-4-methoxy-carbonylpyridine	285)
1-ethyl-4-methoxy-carbonylpyridinium ion	CO$_2$	4,4-bis(methoxycarbonyl)-1,4-dihydro-1-ethylpyridine (after methylation)	285)
stilbene	*t*-BuCl	1,2-diphenyl-1-*t*-butylethane and 1-(4-*t*-butylphenyl)-2-phenylethane	270)
anthracene	Cl(CH$_2$)$_3$Br		292)
anthracene	Cl(CH$_2$)$_2$Cl		293)
anthracene	Me$_3$S$^+$	2- and 9-methyl-dihydroanthracenes	289)
acenaphthylene	*t*-BuSMe$_2^+$	1-*t*-butyl-1,2-dihydroacenaphthylene	289)
naphthalene	*t*-BuNMe$_3^+$	1- and 2-*t*-butyltetralin	269, 289)

[a] substrate to be reduced by homogeneous electron transfer

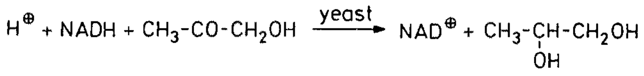
As mentioned earlier, the reductive power of an anion radical can be increased considerably by photoexcitation in the visible part of the spectrum. This type of reaction has been demonstrated in the case of the photo-assisted reductive cleavage of alkyl halides in presence of anthraquinone as mediator [30]. Further work is necessary to evaluate the scope of this potentially important process.

4.2 Indirect Electrochemical Reductions Using Viologen Cation Radicals as Redox Catalysts

Viologens, i.e., *N,N*-dialkyl-2,2'- or 4,4'-bipyridinium salts, have frequently been used as electron transfer agents in the coulometric titration of redox enzymes [295]. Therefore it was obvious to use the same principle for preparative-scale reductions. An especially interesting problem is the electrochemical reduction of $NAD^{\oplus}$ to NADH (see also Sect. 3.3.2.4, Scheme 7). As the direct electrochemical reduction of $NAD^{\oplus}$ never affords NADH exclusively, several authors overcame this problem by using an enzymatically coupled indirect electrolysis. In this case methyl viologen ($MV^{2\oplus}$ = *N,N'*-dimethyl-4,4'-bipyridinium dichloride) acts as an electrochemically regenerable one-electron transfer agent. The intercalated redox enzyme must be able to accept two electrons successively from the electro-generated $MV^{\cdot\oplus}$ before it transfers both of them at the same time to $NAD^{\oplus}$. This principle could be used successfully with the following enzyme systems: ferredoxin reductase [296], lipoamide dehydrogenase [297], 2-oxocarboxylate reductase [296], and enoate reductase [298]. With enoate reductase, enoates can also be hydrogenated stereospecifically by $MV^{\cdot\oplus}$ in the absence of a coenzyme. Simon et al. [298] were even able to generate (R)-1,1-propanediol "electromicrobially" from hydroxyacetone via indirect electrochemical formation of NADH using whole yeast cells (Eqs. (100)–(102)).

$$\text{Cathode:}\ 2\,MV^{2\oplus} + 2\,e^{\ominus} \longrightarrow 2\,MV^{\cdot\oplus} \tag{100}$$

$$2\,MV^{\cdot\oplus} + H^{\oplus} + NAD^{\oplus} \xrightarrow{\text{yeast}} NADH + 2\,MV^{2\oplus} \tag{101}$$



$$H^{\oplus} + NADH + CH_3\text{-}CO\text{-}CH_2OH \xrightarrow{\text{yeast}} NAD^{\oplus} + CH_3\text{-}\underset{\displaystyle OH}{\underset{|}{C}H}\text{-}CH_2OH \tag{102}$$

4.3 Indirect Electrochemical Oxidations Using Triarylamines as Redox Catalysts

As mentioned above, it is difficult to find organic compounds which are suitable as redox catalysts for oxidations. This is the case because organic cation radicals, which are mostly the active forms in indirect electrochemical oxidations, are usually easily attacked by nucleophiles, thus eliminating them from the regenerative cycle. Therefore, the cation radicals must be stabilized towards the reaction with nucleophiles. Nelson et al. demonstrated [299,300] that the cation radicals of triaryl amines and related compounds are very stable if the *para* positions of the aryl

Table 10. Standard potentials of triarylamines and related compounds

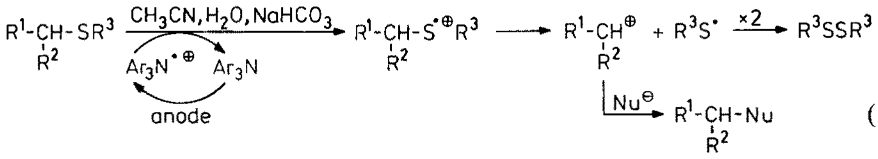
Compound No.	Name	E^0 (V vs. NHE)[a]
4a	Tetraphenyl-*p*-phenylenediamine	0.75
1a	Tris(*p*-methoxyphenyl)amine	0.76
4b	Tetrakis(*p*-bromophenyl)*p*-phenylenediamine	0.93
1b	Tris(*p*-tolyl)amine	1.00
1c	Tris(*p*-trimethylsilylphenyl)amine	1.08
1d	Tris(*p*-iodophenyl)amine	1.27
1e	*p*-(1-trifluoromethyl-vinyl)phenyl-bis(*p*-bromophenyl)amine	1.28
1f	Tris(*p*-bromophenyl)amine	1.30
1g	*N*,*N*-Bis(*p*-bromophenyl)-2-amino-5-bromobenzoic acid	1.41
1h	*N*,*N*-Bis(*p*-bromophenyl)-2-amino-5-bromomethylbenzoate	1.42
1i	Bis(*p*-bromophenyl)(2,4-dibromophenyl)amine	1.42
1k	Bis(*p*-bromophenyl)(*p*-trifluoroacetylphenyl)amine	1.45
1l	Tris(*p*-acetylphenyl)amine	1.50
1m	(*p*-Bromophenyl)bis(2,4-dibromophenyl)amine	1.56
1n	Tris(*p*-trifluoromethylphenyl)amine	1.60
1o	(*p*-Bromophenyl)bis(*p*-nitrophenyl)amine	1.64
1p	Tris(*p*-pentafluoroethylphenyl)amine	1.64
1q	Tris(*p*-cyanophenyl)amine	1.68
1r	Tris(*p*-trifluoroacetylphenyl)amine	1.68
1s	*o*-Bromo-*p*-(1-trifluoromethyl-vinyl)phenyl-bis(2,4-dibromophenyl)amine	1.72
2a	3,6-Dibromo-9-(*p*-bromophenyl)carbazole	1.72
1t	Tris(2,4-dibromophenyl)amine	1.74
1u	Tris(*p*-nitrophenyl)amine	1.80
2b	9-(*p*-Bromophenyl)-1,3,6,8-tetrabromocarbazole	1.83
3	9-(*p*-Bromophenyl)-2,6-dibromoacridone	1.85
1v	Bis(2,4-dibromophenyl)(2-bromo-4-trifluoroacetylphenyl)-amine	1.86
1w	Tris(2,4,6-tribromophenyl)amine	1.96

[a] reported is always the first oxidation potential

rings are substituted. The applicability of triarylamines as redox catalysts was first demonstrated in the oxidation of cyanide ions by electro-generated trianisylamine cation radicals [301]. The advantage of triarylamines as mediators is the possibility to adjust their oxidation potential by the selection of the *ortho* and *para* substituents. We [302] and others [299, 303] have developed a large spectrum of substituted triarylamines, and electrochemically studied their suitability as redox catalysts [302]. The compounds cover a potential range from 0.8 to about 2.0 V *vs*. NHE (Table 10). It should be pointed out that the stability of the triarylamine cation radicals strongly depends on their substitution pattern and the reaction medium. For example, tris(2,4-dibromophenyl)amine has proven to be extremely stable even in methanolic solution. Thus, 2500 turnovers of the mediator could be performed without noticeable consumption [304].

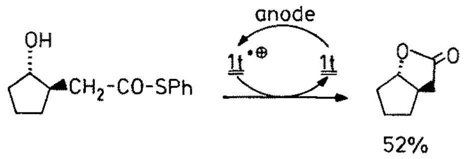
Triarylamine cation radicals seem to be able to react in two different ways: 1 — as simple one-electron transfer agents (mechanism A, Sect. 2.3); 2 — as chemical catalysts (mechanism B, Sect. 2.3) for oxidations in which the redox step is combined with an intermediate complex formation (called "bonded" mechanism by Eberson [305]). Thus, substrates can be oxidized by triarylamine cation radicals with potentials which are up to more than 1 Volt more negative than those of the substrates. The driving force for both types of reactions usually are fast with irreversible bond cleavages which follow the redox step. Especially favorable follow-up reactions are deprotonations in benzyl- or allyl-position or in α-position to hetero atoms and the irreversible cleavage of carbon-sulfur bonds.

Thus, oxidation reactions are possible under very mild conditions and with high selectivities. Therefore, this method is especially useful for oxidative deprotections. For example, the oxidative cleavage of the carbon-sulfur bond is easily possible according to Eq. (103). In this way, disulfides and follow-up products of carbenium ions are formed. This reaction could be exploited for the deprotection of 1,3-dithianes and 1,3-dithiolanes using as mediators tritolylamine (1.0 V *vs.* NHE) and tris(*p*-bromophenyl)amine (1.3 V *vs.* NHE), respectively, in moist acetonitrile in the presence of $NaHCO_3$ or Na_2CO_3 (Table 11, No. 1, 2) [306]. The cleavage conditions are so mild that hydroxy groups and double bonds are totally uneffected.



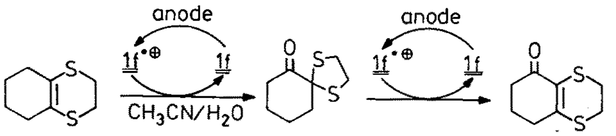
(103)

The cleavage of the carbon-sulfur bond in *p*-methoxybenzyl thioethers under generation of disulfides and follow-up products of the *p*-methoxybenzyl cation was exploited for the directed synthesis of disulfide bridges in *poly*-cystinyl peptides via *S*-(4-methoxybenzyl)cystein units in combination with *S*-tritylcystein groups [307] (Table 11, No. 3, 4). The carbon-sulfur bond in thiol esters can be cleaved oxidatively by indirect electrolysis using tris(2,4-dibromophenyl)amine (1.74 V *vs.* NHE) as mediator yielding the unprotected carboxylic acids in high yield (Table 11, No. 5) [309]. This reaction is useful for the synthesis of otherwise hardly accessible cyclopentano-γ-lactones with *trans*-configuration starting from *S*-phenyl-*trans*-2-hydroxy-cyclopentyl thioacetate (Eq. (104)) [310].



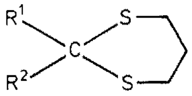
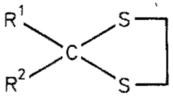
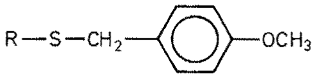
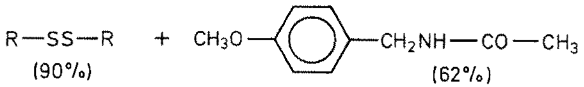
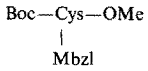
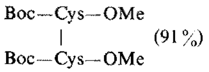
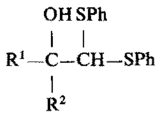
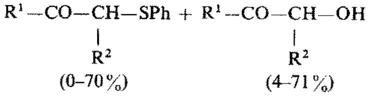
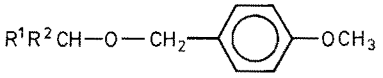
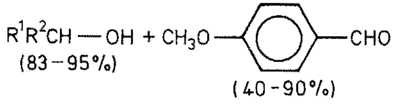
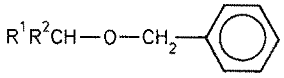
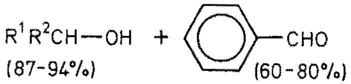
(104)

By indirect anodic cleavage of carbon-sulfur bonds it is also possible to initiate rearrangements (Eqs. (105)–(106)) [311] (Table 11, No. 6).



(105)

Table 11. Indirect electrochemical oxidations using triarylamines as mediators

No.	Substrate	Mediator	Electrolyte	Products	Ref.
1		**1b, 1f**	CH_3CN (0.3% H_2O) $NaHCO_3/LiClO_4$	$R^1R^2C{=}O$ (70–97%)	306, 308)
2		**1f, 1l**	CH_3CN (0.3% H_2O) $NaHCO_3/LiClO_4$	$R^1R^2C{=}O$ (74–100%)	306)
3		**1f**	CH_3CN (0.3% H_2O) $NaHCO_3/LiClO_4$	 R—SS—R (90%) + CH_3O—C_6H_4—CH_2NH—CO—CH_3 (62%)	307)
4	 $\text{Boc—}\underset{\text{Mbzl}}{\text{Cys}}\text{—OMe}$	**1f**	CH_3CN (0.3% H_2O) $NaHCO_3/LiClO_4$	 $\begin{array}{c}\text{Boc—Cys—OMe}\\ \vert\\ \text{Boc—Cys—OMe}\end{array}$ (91%)	307)
5	R—CO—SR' R' = Ph; $PhCH_2$; n-C_8H_{17}; 2-MeO—C_6H_4	**1t**	CH_3CN (0.3% H_2O) $NaHCO_3/LiClO_4$	R—COOH (75–93%)	309)
6	 $R^1\text{—}\overset{\text{OH}}{\underset{R^2}{C}}\text{—}\overset{\text{SPh}}{\text{CH}}\text{—SPh}$	**1f**	CH_3CN (0.3% H_2O) $Li_2CO_3/LiClO_4$	 $R^1\text{—CO—}\underset{R^2}{\text{CH}}\text{—SPh}$ (0–70%) + $R^1\text{—CO—}\underset{R^2}{\text{CH}}\text{—OH}$ (4–71%)	310)
7		**1f**	$CH_3CN/CH_2Cl_2/LiClO_4$ + 2,6-lutidine	 R^1R^2CH—OH (83–95%) + CH_3O—C_6H_4—CHO (40–90%)	312a)
8		**1t**	$CH_3CN/CH_2Cl_2/LiClO_4$ $NaHCO_3$	 R^1R^2CH—OH (87–94%) + C_6H_5—CHO (60–80%)	312b, 312c)

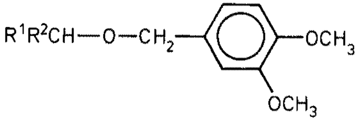
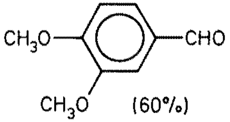
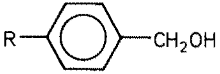
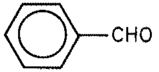
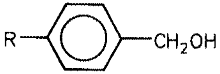
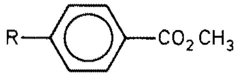
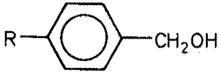
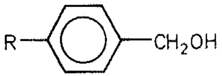
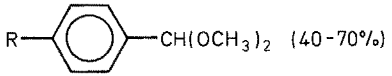
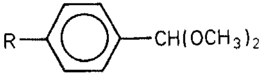
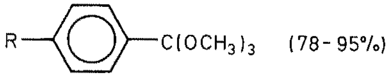
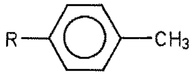
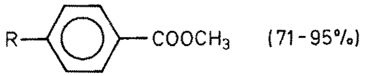
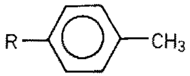
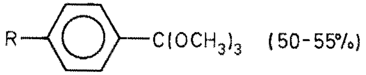
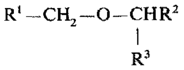
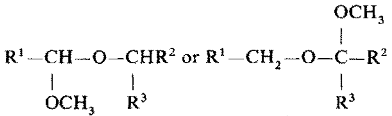
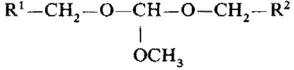
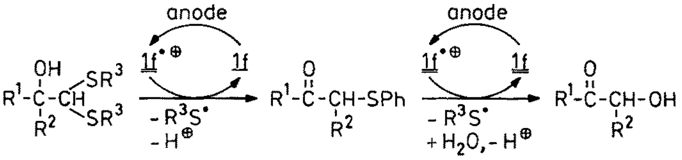
9		**1f** or **4b**	$CH_3CN/CH_2Cl_2/LiClO_4$ + 2,6-lutidine	R^1R^2CH-OH +  (75-85%) (60%)	312e)
10	$R-CO-O-CH_2Ar$ Ar = Ph; 4-MeO—C_6H_4; 2,4-$(MeO)_2C_6H_3$; 4-Br—C_6H_4 R = n-C_7H_{15}; n-C_9H_{19}; Ph; Ar—CO—$(CH_2)_2$	**1f, 1t, 1o**	$CH_3CN/LiClO_4$ + 2,6-lutidine or $NaHCO_3$, Na_2CO_3	R—COOH (45–93%)	309, 313)
11	n-C_9H_{19}—$COOCH(Ph)_2$	**1t, 1o**	$CH_3CN/LiClO_4$ $NaHCO_3$ or Na_2CO_3	n-C_9H_{19}—COOH (84–90%)	309, 313)
12	Z— or Boc—Phe—OCH_2Ar Ar = 4-MeO—C_6H_4; 3,4-$(MeO)_2C_6H_3$	**1f, 1t**	$CH_3CN/LiClO_4$ $NaHCO_3$ or Na_2CO_3	Z— or Boc—Phe—OH (60–90%)	309, 313)
13	Moz—Phe—OH Moz = 4-methoxybenzyloxycarbonyl	**1t**	$CH_3CN/LiClO_4$ $NaHCO_3$ or Na_2CO_3	NH_2—Phe—OH (70%)	309)
14	$R^1-\underset{R^2}{\underset{\mid}{CH}}-NH-S-Ar$ Ar = 2-NO_2—C_6H_4 R^1 = H; $PhCH_2$; R^2 = Me; t-Bu; Ph; n-C_7H_{15}; Ph—CH=CH; RO_2C-CH_2NH-CO; MeO_2C	**1f, 4b**	$CH_2Cl_2/MeOH/TBA^+ClO_4^-$ 2,6-lutidine	$R^1-\underset{R^2}{\underset{\mid}{C}}=N-S-Ar$	309, 327)
15		**1f, 1t, 2a**	$CH_3CN/CH_2Cl_2/Na_2CO_3/$ $LiClO_4$ (divided cell)	 (80-100%)	314, 315)
16		**1f, 1t, 2a**	$CH_3OH/CH_2Cl_2/Na_2CO_3/$ $NaClO_4$ (divided cell)	 +  (55-85%) (4-15%)	314, 315)
17		**1t**	$CH_3OH/CH_2Cl_2/Na_2CO_3/$ $NaClO_4$ (undivided cell)	// // (40-70%) (10-32%)	314, 315)

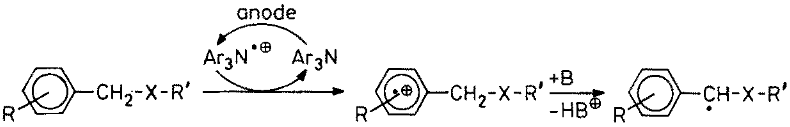
Table 11. (continued)

No.	Substrate	Mediator	Electrolyte	Products	Ref.
18	 R = H; 4-OCH$_3$; 4-Br; 4-Cl; 4-CH$_2$OH; 2,4-Cl$_2$; 3,4-Cl$_2$	**1t**	CH$_3$OH/CH$_2$Cl$_2$/Na$_2$CO$_3$/ (undivided cell)		314, 315)
19		**1t**	CH$_3$OH/NaOCH$_3$/LiClO$_4$ (undivided cell)		315)
20		**1t**	CH$_3$OH/CH$_2$Cl$_2$/LiClO$_4$		315)
21		**1t**	CH$_3$OH/NaOCH$_3$/LiClO$_4$		315)
22	 $R^1-CH_2-O-\underset{R^3}{CHR^2}$	**1t**	CH$_3$OH/NaOMe/LiClO$_4$	 $R^1-\underset{OCH_3}{CH}-O-\underset{R^3}{CHR^2}$ or $R^1-CH_2-O-\overset{OCH_3}{\underset{R^3}{C}}-R^2$	316)
23	$R^1-CH_2-O-CH_2-O-CH_2-R^2$	**1t**	CH$_3$OH/NaOMe/LiClO$_4$	 $R^1-CH_2-O-\underset{OCH_3}{CH}-O-CH_2-R^2$	316)
24	2-cyclohexen-1-ol	**1t**	CH$_3$CN (0.3% H$_2$O)/ CH$_2$Cl$_2$/NaHCO$_3$/LiClO$_4$	2-cyclohexen-1-on (75%)	312d)
25	3-octen-1-ol	**1t**	CH$_3$CN (0.3% H$_2$O)/ CH$_2$Cl$_2$/NaHCO$_3$/LiClO$_4$	2-octen-1-on (84%)	312d)
26	cinnamic alcohol	**1t**	CH$_3$CN/CH$_2$Cl$_2$/LiClO$_4$ + 2,6-lutidine	cinnamic aldehyde (96%)	312d)

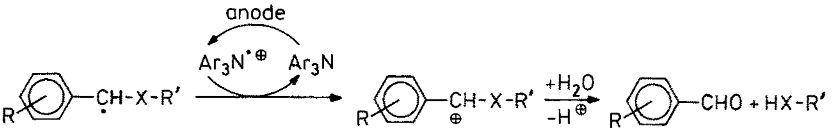


(106)

The indirect anodic cleavage of carbon-hydrogen bonds in the benzyl position using triarylamine mediators was also used for mild and selective deblocking of hydroxy, carboxyl, and amino groups. The primarily formed cation radical of the protective group is readily deprotonated in the benzyl position by an added base (Eq. (107)). This benzylic radical is easily further oxidized to the benzyl cation which subsequently is cleaved by attack of a nucleophile, such as water (Eq. (108)).

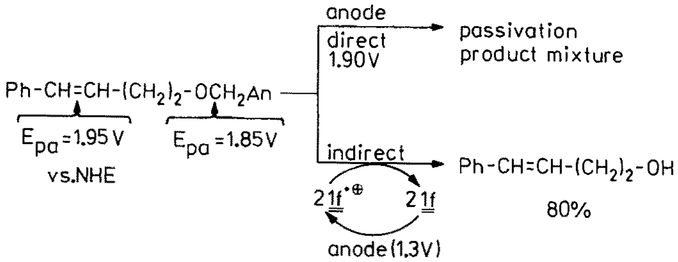


(107)



(108)

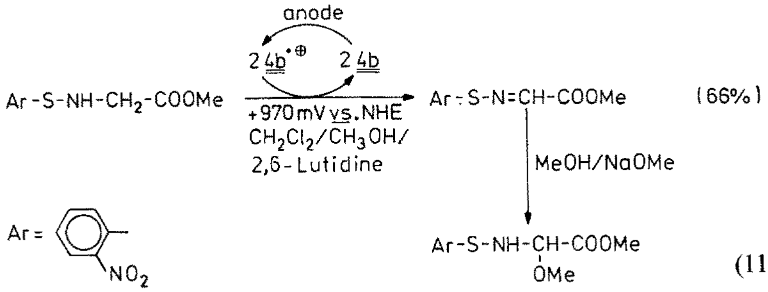
Thus, differently substituted benzyl ethers [312)] (Table 11, No. 7–9) and benzyl esters [309, 313)] (Table 11, No. 10–12) can be deblocked with formation of alcohols and carboxylic acids, respectively. This can be done in such a way that in multifunctional compounds with several benzylic protecting groups, one group after the other can be deblocked selectively according to their substitution pattern by proper selection of the mediator. In this way selectivities can be obtained which otherwise are accessible only under difficulties or even not at all. This principle was exploited for the directed protection and selective deblocking of primary and secondary alcohol functions in polyhydroxy compounds using the combination of benzyl and *p*-methoxybenzyl ether groups [312c)]. Even substantially milder reaction conditions are possible if the anisyl ether function acts as permanent protective group and the 3,4-dimethoxybenzyl ether function as intermediate protective group [312e)]. The selectivity of this reaction can also be demonstrated in case of the anisylether of 4-phenyl-3-butenol [312d)] (Eq. (109)). The substrate contains two electrophores whose potentials differ only by 100 mV. However, the indirect electrolysis shows total selectivity.



(109)

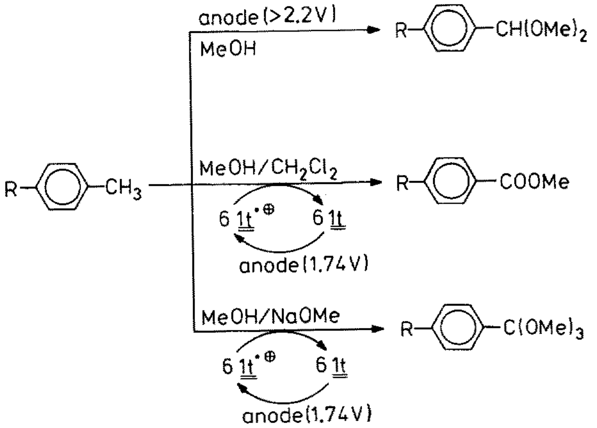
The indirect electrochemical deblocking of benzylic esters by triarylamine cation radicals differentiates not only between unsubstituted benzyl esters and 4-methoxybenzyl, 2,4-dimethoxybenzyl, or benzhydryl esters, but, contrary to common methods, also between the acid-labile 2,4-dimethoxybenzyl esters and the likewise acid-labile 4-methoxybenzyl and benzhydryl esters [309, 313]. The *N*-(*t*-butoxycarbonyl) (Boc) and *N*-(benzyloxycarbonyl) (Z) protective groups are stable under these conditions. In contrast to that, the *N*-(4-methoxybenzyloxycarbonyl) (Moz) protecting group can readily be cleaved by the cation radical of tris(2,4-dibromophenyl)amine (Table 11, No. 13) [309].

The interesting class of *o*-nitrophenylsulfenimines can be generated electrochemically starting from *o*-nitrophenylsulfenamides. In this case tetrakis(4-bromophenyl)-*p*-phenylendiamine acts as mediator (Table 11, No. 14) [309, 327]. This reaction also works for amino acid derivatives (Eq. (110)).



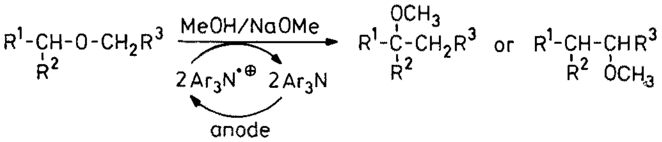
(110)

Technically interesting are the indirect electrochemical oxidations of benzylic alcohols (Table 11, No. 15–18) [314], benzaldehyde dimethylacetals (Table 11, No. 19) [315], and alkyl aromatic compounds (Table 11, No. 20, 21) [315]. It could be proven that benzylic alcohols are oxidizable using tris(2,4-dibromophenyl)amine as mediator not only in acetonitrile in a divided cell but also in methanol in an undivided cell yielding benzaldehydes or benzaldehyde dimethylacetals with high selectivity [315]. Similarly, alkyl aromatics can be oxidized to form methyl benzoates (neutral or acidic conditions) or trimethylorthobenzoates (basic conditions) [315], while direct

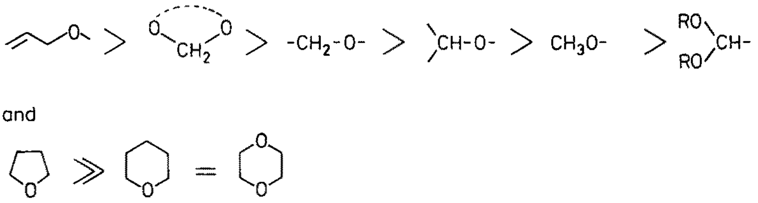


(111)

anodic oxidation only leads to benzaldehyde dimethylacetals (Eq. (111)). Even toluene with an oxidation potential of 2.64 V *vs.* NHE thus is oxidized smoothly to methyl benzoate in 95% material yield. Starting from benzaldehyde dimethylacetals, the orthoesters are formed with more than 90% selectivity if small amounts of NaOMe are present. The current yields can be improved if the substrate is used as a co-solvent. The mediator undergoes over 2000 turnovers without noticeable loss.
Aliphatic ethers can be oxidized in α-position to oxygen in MeOH/NaOMe in the presence of tris(2,4-dibromophenyl)amine as mediator to yield the corresponding acetals or aldehydes (Eq. (112)) (Table 11, No. 22) [316]. Similarly, cyclic acetals can be oxidized to give the corresponding orthoesters (Table 11, No. 23) [316]. The reactivity increases as shown in Scheme 10.



$$R^1\text{-}\underset{R^2}{CH}\text{-O-}CH_2R^3 \xrightarrow[2Ar_3N^{\cdot\oplus}\quad 2Ar_3N]{MeOH/NaOMe} R^1\text{-}\overset{OCH_3}{\underset{R^2}{C}}\text{-}CH_2R^3 \text{ or } R^1\text{-}\underset{R^2}{CH}\text{-}\underset{OCH_3}{CH}R^3 \qquad (112)$$

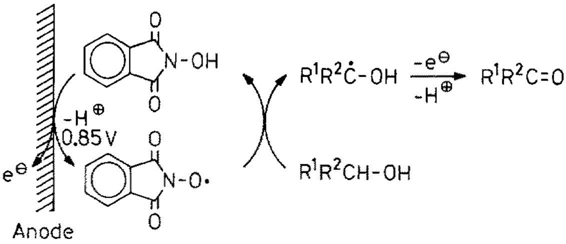


Scheme 10. Reactivity pattern for the methoxylation in α-position to oxygen by indirect electrochemical oxidation in MeOH/NaOMe with tris(2,4-dibromophenyl)amine as mediator

Thus, a secondary carbon in α-position to oxygen is selectively attacked in the presence of a primary or a tertiary one. An allylic carbon in α-position to oxygen is methoxylated with total selectivity in the presence of a secondary carbon. Multiple methoxylation usually is not observed. Because of their low reactivity, primary and tertiary carbons as well as open-chain acetals are methoxylated with low current yields but often with high material yields.

4.4 Indirect Electrochemical Oxidations Using Other Types of Organic Mediators

In several cases *N*-hydroxyphthalimide has been used as an organic mediator for the oxidation of alcohols [317] to ketones, of benzyl ethers to benzoates [318], of alkyl aromatics to aryl ketones [318], and of 4-phenyl-1,3-dioxolanes to unprotected ketones [319]. The *N*-hydroxyphthalimide is anodically oxidized to the phthalimide *N*-oxyl radical which subsequently performs a hydrogen atom abstraction from the substrate. Regeneration of the active radical takes place at the anode in the presence of a base like pyridine or 2,6-lutidine (mechanism B, Sect. 2.3) (Eq. (113)). The turnover numbers are, however, not yet satisfactory. This reaction is similar to the use of electro-generated $NO_3^{\cdot}$-radicals as regenerable mediators [191].



(113)

Other organic mediators act as hydride atom-abstracting agents. This is true, for example, with 2,2-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) and the oxoammonium ion which is anodically accessible from 2,2,6,6-tetramethylpiperidyl oxide (TEMPO). DDQ has been electrochemically regenerated either externally [320] or internally [321]. The *in situ* electrochemical oxidation of TEMPO to the active oxoammonium ion is performed in lutidine-containing acetonitrile. Thus, primary alcohols can be oxidized to the aldehydes, while secondary ones are stable [322]. Primary amines are transformed to nitriles. If water is present, the amines are cleaved via the Schiff bases to the corresponding carbonyl compounds [323].

The half-wave potential for the electrochemical oxidation of NADH to $NAD^{\oplus}$ is ca. +0.6 V *vs.* SCE at pH 7. The formal potential for the $NADH/NAD^{\oplus}$ couple, however, is only −0.56 V. The overpotential therefore is about 1.2 V. As $NAD^{\oplus}$ acts as coenzyme in many enzyme-catalyzed oxidations of practical importance, it would be of interest to regenerate $NAD^{\oplus}$ electrochemically. For this purpose it is necessary to find a mediator system which is able to lower the overpotential. Mediator systems accepting two electrons or a hydride atom are most effective. Therefore, dopaquinone electro-generated from dopamine [324] and quinone diimines derived from diaminobenzenes [325, 326] have been applied successfully.

5 Concluding Remarks

This article demonstrates that the principle of electrochemical regeneration of redox systems finds wide application in organic synthesis. The large number of very recent publications shows that this field is expanding at a tremendous rate. This is the case because the indirect electrolyses offer the advantage of low energy consumption because of the acceleration of the electrode reactions, of high selectivity, and of a low burden for the environment. Especially the last point will become even more important in the near future. Therefore, the field of indirect electrolysis will continue to expand even further. Another reason for future developments is the demand for more selective reactions which will lead to the application of new redox catalysts. Interesting new reactions are expected from the photochemical excitation of electrochemically generated and regenerated mediators. These developments will be important for the photoelectrochemical conversion of light into electrical or chemical energy.

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Selective Formation of Organic Compounds by Photoelectrosynthesis at Semiconductor Particles

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Table of Contents

As the importance of electrosynthesis as a reliable synthetic tool is being increasing recognized, a parallel interest has developed in applying the techniques of photoelectrochemistry to problems of interest to the organic chemist. Although most photoelectrochemical investigations have been concerned with inducing redox reactivity in simple inorganic molecules (e.g., in water splitting or carbon dioxide or nitrogen reduction), the principles developed in these studies are equally applicable to organic transformations. This review will illustrate recent advances toward the objective of using the illuminated surfaces of semiconductors as sites for initiating and controlling organic reactivity. Because this area is inherently interdisciplinary, it is nearly impossible to provide a comprehensive compilation of all work relevant to the photoinduced reactions of concern. The illustrative examples cited here should serve, however, to introduce the interested reader to mechanistic features which must be dealt with in investigating photoelectrochemical transformations.

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1 Introduction

Organic photoelectrochemistry is that field of investigation in which redox reactions of carbon-based compounds are initiated or assisted by the absorption of a photon at or near the surface of an electrode [1]. The principles of photoelectrochemistry have been well described elsewhere [2-11] and only a very brief discussion of their salient features is given here.

In a conventional photoelectrochemical cell, the organic substrate of interest is not converted to an excited state, the photon having been absorbed instead by the electrode. Since metals, by definition, comprise a near continuum of states between which electrons can freely move, electronic excitation energy at the surface of a metal electrode will be degraded by nonradiative decay pathways much more rapidly than it can initiate electron exchange with an adsorbed organic substrate. With semiconductor surfaces, however, photochemical excitation induces a band-to-band transition, causing an electron to move from the filled valence band to the vacant conduction band, Fig. 1. Relaxation of the high energy electron is inhibited by the absence of intra-gap states to assist with energy dissipation, so that we can think of the excited semiconductor as an electron-hole pair localized respectively in the conduction and valence bands. The lifetime of this photogenerated electron-hole pair is sufficiently long, then, to allow the conduction band electron to be captured by interfacial electron transfer to an appropriate adsorbed acceptor and the valence band hole to be filled by interfacial electron transfer from an adsorbed organic donor, in competition with spontaneous back-electron transfer from the charge separated pair, Scheme 1.

If a semiconductor electrode is dipped into an electrolyte containing a redox couple, interfacial electron transfer will occur to equilibrate the solution phase potential and the Fermi level of the bulk semiconductor. In an intrinsic (undoped) semiconductor, the Fermi level will lie at a potential exactly halfway between the bands, whereas with an n-type (negatively doped) material the Fermi level will lie just below the conduction band edge and in a p-type (positively doped) material the Fermi level will be poised just above the valence band edge. As equilibration with the solution occurs and the bulk Fermi level moves to its equilibrium position, the band edge positions at the surface remain fixed. Thus, in moving inward from the semiconductor-electrolyte interface, the bands bend. Charge injection in this region of bent bands will impel electrons to move in the opposite direction from holes: in a n-doped material, electrons will move toward the bulk and holes will move toward the surface. Thus, band bending assists in improving the efficiency of photoinduced charge separation and provides another rationale for the much greater photosensitivity of semiconductor electrodes than is observed for metals.

$$\mathrm{SC} \overset{h\nu}{\rightleftarrows} h^{+} + e^{-}$$

$$h^{+} + \mathrm{D} \longrightarrow \mathrm{D}^{\overset{+}{\cdot}}$$

$$e^{-} + \mathrm{A} \longrightarrow \mathrm{A}^{\overset{-}{\cdot}}$$

Scheme 1.

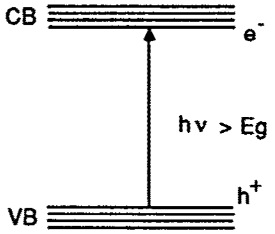


Fig. 1. Electron-Hole Generation upon Photoexcitation of a Semiconductor Electrode

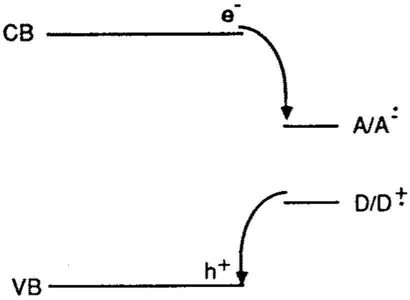


Fig. 2. Thermodynamic Constraints for Interfacial Electron Transfer at an Illuminated Semiconductor Surface

The energetic ordering of the edges of these bands, which can be established independently by any of a number of physical or electrochemical methods [12], provides a reasonable starting point for evaluating the thermicity of the requisite electron transfers. These band edge positions define the limit of attainable photopotential on the irradiated surface. So long as the donor oxidation potential lies less positive than the valence band edge and the acceptor reduction potential lies less negative than the conduction band edge, electron transfer at the illuminated interface will be thermodynamically permissible, Fig. 2. A brief perusal of typical redox potentials for common organic functional groups and of typical band positions for easily accessible semiconductors will quickly reveal that a wide variety of organic species can function as donors toward excited semiconductors [13].

If both electron exchanges occur, an oxidized and reduced species will be formed on the same surface. If these adsorbed intermediates can move together or can diffuse away from the surface before back electron transfer occurs, novel chemistry is likely to ensue. The ability to generate both oxidized and reduced species on the same surface differentiates photoelectrochemical redox reactions from conventional electrochemical transformations where the electrode surface is rendered either oxidizing or reducing by virtue of an imposed potential. In the latter cell, the oxidizing and reducing sites are physically separated appreciably, often even occurring in separate half cells divided by membranes.

The use of semiconductors for photoinduced charge separation is limited by the instability of some irradiated semiconductor surfaces. Although metal oxides withstand decomposition under typical photoelectrochemical conditions, many other semiconductors, especially those with narrow band gaps which are thus responsive to visible light, degrade upon exposure to light. Often this decrease in activity is caused by redox reactivity of the semiconductor itself, such that light causes the formation of an insulating (blocking) layer or the corrosion of the electrode. Although this problem can be significantly reduced by attaching catalysts or inert coverages, by chemically altering the surface composition of the semiconductor (e.g., by silicide formation), by changing the composition of the electrolyte, or by imbedding the semiconductor in a protective layer or film, most photoelectrochemical studies involving selective organic transformations have used the robust, highly stable metal oxides. These materials are unfortunately less useful for solar energy conversion than are their highly colored cousins, since they possess large band gaps.

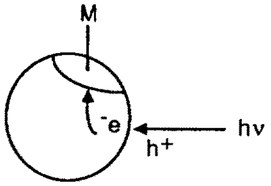


Fig. 3. Redox Exchange on an Irradiated Metallized Semiconductor Powder

This description of the photoelectrochemical event was originally based on the use of an illuminated semiconductor electrode in a standard three electrode cell configuration. The theory can easily be extended, however, for practical applications to "short-circuited" cells prepared by deposition of inert metal with low overvoltage characteristics on a powdered semiconductor [2,14–16]. Such a metallized powder is shown in Fig. 3. Like a photoelectrochemical cell, such a powder includes sites for photoinduced oxidation and reduction, but no external current flow accompanies these transformations. Photoactivity is also maintained as the size of the particle decreases to the colloidal range [17,18], although the absorption characteristics, the quantum efficiency of charge separation, and the kinetics of interfacial electron transfer may be influenced by the particle size. On sufficiently small particles, for example, the calculated space-charge width necessary for effective band bending may exceed the dimensions of the particle.

Even without deposition of a metal island, such powders often maintain photoactivity. The requirement for effective photoelectrochemical conversion on untreated surfaces is that either the oxidation or reduction half reaction occur readily on the dark material upon application of an appropriate potential, so that one of the photogenerated charge carries can be efficiently scavenged. Thus, for some photoinduced redox reactions, metallization of the semiconductor photocatalyst will be essential, whereas for others platinization will have nearly no effect.

Overall, inducing redox reactivity on the surface of an irradiated semiconductor particle offers the electrochemist many of the advantages which are often cited as rationales for enzyme function [19]. Like enzymes, adsorption of both redox partners on the photocatalyst's surface accomplishes approximation of the reagents which will ultimately participate in the oxidative and reductive half reactions. This same preassociation achieves as well favorable entropic interactions as the redox participants approach an interactive transition state. The semiconductor particle can also effect conformational changes at the adsorption site, can exert electrostatic forces to stretch bonds in the adsorbed molecule when compared with the free solvated species, and can direct the relative rates of intra- vs. intermolecular redox reactivity. As with multi-functional enzymes, the irradiated semiconductor particle can simultaneously attain both oxidation and reduction reactions in a well defined environment. The challenge to the photoelectrochemist lies in identifying and demonstrating reactions which illustrate these capabilities.

2 Chemical Control by Photoelectrochemical Methods

Like all electrochemical reactions initiated by the transfer of an electron across an electrode-electrolyte interface, photoelectrochemical transformations are more easily controlled than are reactions taking place in homogeneous solution. The additional control derives from three features of the electrochemical event: an electrochemist can define the applied potential and hence activate a specific functional group in a multi-functional molecule; he can alter the electrode surface and hence the adsorption characteristics of a specific molecule so that the chemical environment in the double layer can be changed; and finally, he can control the current flow and hence constrain the number of electron passed per adsorbed reactant.

2.1 Potential

Since attainable redox potentials for adsorbates at the surface of an illuminated semiconductor particle are governed by the band positions of the semiconductor chosen, selectivity in activating a specific functional group in a multifunctional molecule or in activating one species from a mixture of adsorbates can be attained by judicious choice of the semiconductor. A great deal is known about the band positions of common semiconductors [12,20,21] and how they shift with changes in electrolyte. Band positions for some common semiconductor photocatalysts are listed in Table 1. These positions are known to shift with pH and with solvent. The bands of TiO_2, for example, shift negative by about 0.7 V upon shifting the solvent from water (pH = 1) to acetonitrile [22]. This shift is of great importance for oxidative organic photoelectrochemistry, for the reduction potential of oxygen in acetonitrile is —0.78 V [23], nearly isoenergetic with the conduction band position of TiO_2. This in turn implies that oxygen can assume the role of the acceptor in the photoinduced reduction half reaction, generating superoxide on illuminated titania particles, Eq. (1).

Table 1. Band Positions[a] for Some Common Semiconductor Photocatalysts [12,13,21]

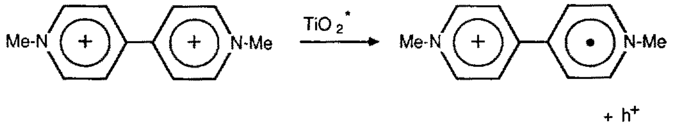
Semiconductor	Valence band (V vs. SCE ± 0.1 V)	Conduction band (V vs. SCE ± 0.1 V)
TiO_2	+3.1	−0.1
SnO_2	+4.1	+0.3
ZnO	+3.0	−0.2
WO_3	+3.0	+0.2
CdS	+2.1	−0.4
CdSe	+1.6	−0.1
GaAs	+1.0	−0.4
GaP	+2.2	−1.0
SiC	+1.6	−1.4

[a] Band positions in water at pH 1

$$\begin{tikzcd} TiO_2 \arrow[r, "h\nu"] & h^+ \arrow[dr, "D"'] & + \; e^- \arrow[r, "O_2"] & O_2^{\cdot -} \\ & & D^{\cdot +} & \end{tikzcd} \qquad (1)$$

Furthermore, photoelectrochemical activation of rutile or anatase can thus be envisioned as a means for oxygen activation.

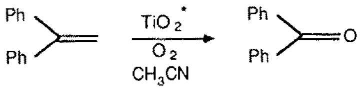
Other acceptors which have reduction potentials below the conduction band edge of the illuminated semiconductor can also function in this role. The single electron reduction product derived from methyl viologen, for example, can be detected spectroscopically when a colloidal suspension of titanium dioxide is flashed in the presence of this electron acceptor, Eq. (2) [24].



(2)

If oxygen can serve the role as acceptor, the role of the organic adsorbate as donor can be tested by choosing a substrate whose oxidation potential lies positive of the valence band edge of the chosen semiconductor and by seeking evidence for formation of the oxidized radical cation. The photoelectrochemical oxidation of many substrates can be rationalized on this basis [13]. We cite only a few illustrative examples here and discuss the observed chemistry in more detail in the following section.

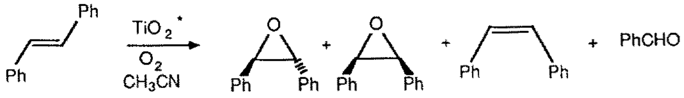
Since the oxidation potential of 1,1-diphenylethylene is +1.8 V in acetonitrile [23, 25], formation of its radical cation should be thermodynamically permissible on illuminated titanium dioxide. The observation of high chemical yields of oxidative cleavage product when a titanium dioxide suspension is irradiated in its presence argues for efficient interception of such an intermediate, Eq. (3).



(3)

A Hammett plot of substituted derivatives indeed was linear with a negative slope, consistent with the localization of positive charge in the transition state for the oxidation reaction observed [26].

Spectroscopic evidence for the transient formation of the trans-stilbene radical cation could be obtained when colloidal TiO_2 suspended in an acetonitrile solution containing trans-stilbene (a species which should also be exothermically oxidized by a TiO_2 valence band hole) was excited with a laser pulse [24]. The observed transient was identical in spectroscopic features and in lifetime with an authentic sample of the stilbene cation radical generated in the same medium via pulse radiolytic techniques. That the surface influences the subsequent chemistry of this species can be seen in the distribution of products observed under steady state illumination, Eq. (4) [25].



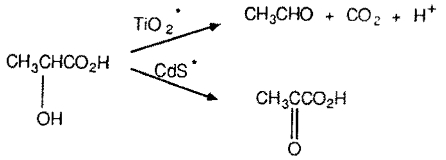
(4)

Although oxygenation products of both the starting material and its cis geometric isomer could be isolated, no evidence for cyclization of the cis-stilbene cation radical could be found, despite the well-known occurrence of the cyclization upon generating the cis-radical cation in homogeneous solution [27]. In fact, oxygenation and isomerization dominated the chemistry, the same distribution of products having been obtained upon starting with either the cis or trans isomer [25].

Chemoselectivity could potentially be achieved if the oxidation potential of a desired donor adsorbate lies between the valence band edges of two possible semiconductor photocatalysts. Since TiO_2 has a more positive valence band edge than does CdS, it should be the more active photocatalyst. Consistent with this idea, decarboxylation of organic acids, Eq. (5), is much more efficient on irradiated suspensions of rutile than of CdS [28].

$$RCO_2H \xrightarrow[H_2O]{TiO_2^{*}} RH + CO_2 \qquad (5)$$

A recent report on the regioselective oxidation of lactic acid also seemed consistent with this idea. Photocatalytic oxidation on platinized TiO_2 led to decarboxylation, while that on platinized CdS led to pyruvic acid by oxidation of the alcohol group, Eq. (6) [29]. However, when potentiostatic oxidation of lactic acid was conducted in the dark on glassy carbon at +1.3, +1.5, or +1.6 V respectively, (potentials less positive, nearly equivalent to, and more positive than the valence band edge of CdS under the reaction conditions), only decarboxylation product could be isolated. Furthermore, nearly equivalent current doubling was observed both on TiO_2 and on CdS, suggesting no evident difference in mechanism on either of the two materials. It was then tentatively suggested that the observed chemoselectivity might instead be caused by adsorption differences on the semiconductor surface [30].



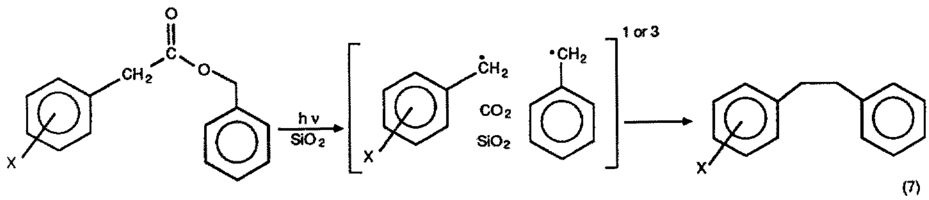
$$CH_3CH(OH)CO_2H \xrightarrow{TiO_2^{*}} CH_3CHO + CO_2 + H^+ ; \quad CH_3CH(OH)CO_2H \xrightarrow{CdS^{*}} CH_3C(=O)CO_2H \qquad (6)$$

We can infer that the band positions of the irradiated semiconductor are greatly influential in controlling the observed redox chemistry and that formation of radical ions produced by photocatalyzed single electron transfer across the semiconductor-electrolyte interface should be a primary mechanistic step in most such photocatalyzed reactions. Whether oxygenation, rearrangement, isomerization, or other consequences follow the initial electron transfer seem to be controlled, however, by surface effects.

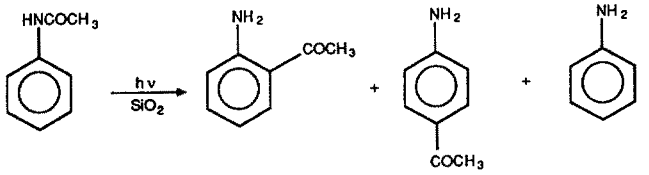
2.2 Surface Effects

All reactions which occur on surfaces are complicated by mass transfer processes and by the factors which govern adsorption equilibrium. These very complications, of course, allow an additional dimension of control in electrochemical or photoelectrochemical events which cannot be routinely achieved in homogeneous solution. The surface cannot only bring together reagents in an anisotropic arrangement, but it can also perturb modes of reaction, kinetically and thermodynamically, so that entirely different reaction courses can sometimes be observed. Such effects are particularly apparent with photoactivated surfaces: lifetimes of excited states and photogenerated transients are particularly sensitive to the special environment afforded by a solid surface. Since selectivity in photoelectrochemical systems will often be determined by selective adsorption of reactants, by adsorptive distortion of surface-bound reagents, and/or by competitive product desorption, a brief description of surface effects is mandatory if we are to understand photoelectrochemical preference.

We consider first how surfaces which are themselves not photosensitive can perturb chemical reactivity. First, the surface can influence diffusional motion of adsorbed substrates, intermediates or products. With preadsorbed substrates, one can probe the nature of motion of intermediates generated on the surface and search for differences in reactivity caused by surface confinement [31]. When several photochemical precursors to benzyl radicals, e.g., benzyl phenylacetate, a dibenzyl ketone, or a dibenzyl sulfone, are irradiated as adsorbates on dry silica gel, singlet and triplet radical pairs are generated, Eq. (7). The extent of radical recombination observed requires that translational motion of the photogenerated radicals must occur on the silica gel surface. This motion was affected by the radical pair multiplicity and photolysis temperature, but was relatively insensitive to the state of hydration of the silica gel and the presence of coadsorbates. The formation of rearranged products not observed in homogeneous solution from the same substrates illustrates chemical consequence of this restricted motion [32]. In other cases, as for example in the photo-Fries rearrangement of amides on silica gel, rearrangement proceeds cleanly and intramolecularly, giving more of the para-isomer than is obtained in methanolic solution, Eq. (8) [33].



(7)



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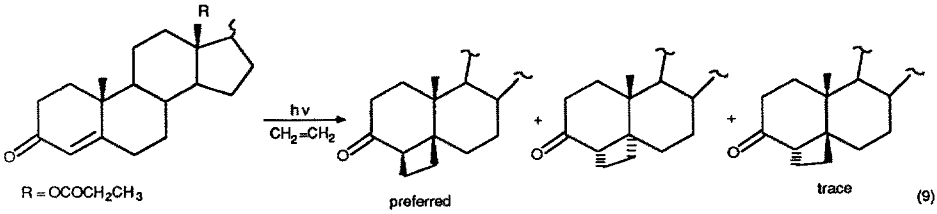


(9)

Surface adsorption can also influence observed stereochemistry in a profound way. In enone photocycloadditions on silica gel and on alumina, the reaction which normally occurs from the less hindered alpha face is shifted toward the more hindered beta face, Eq. (9) [34]. Adsorption thus apparently disfavors conformational inversion in the intermediate biradical, as is required for formation of trans-fused products. The magnitude of the effect is sufficient to be synthetically useful: the above reaction represents a complete reversal of stereochemistry from that observed in methanolic solution [35].

Surface polarity effects can dramatically influence the course of chemical reactions. In the photosensitized evolution of hydrogen from basic aqueous triethanolamine sensitized by $Ru(bpy)_3^{2+}$ and mediated by N,N′-bis-(3-sulfonatopropyl)-2,2′-bipyridine, SiO_2 colloids affect the formation and stabilization of the intermediate charged photoproducts by electrostatic interactions, no hydrogen evolution having been observed in homogeneous aqueous solution under similar conditions [36]. The electrical potential of the particles assists in the separation of the charge transfer within the initial encounter cage complex and results in the repulsion of the reduced bipyridinium product from the colloidal interface, thus retarding the recombination rate. Observed shifts in reaction rate upon alteration of the ionic strength and pH of the colloid solution imply the importance of the electrostatic charge of the colloidal surface in this transformation. Similar effects have been noted on other metal oxide colloids [37, 38] and when the colloids are entrapped within other organized media (micelles, vesicles, etc.) [39–43].

Surface polarity can also be independently evaluated by physical means. deMayo and coworkers have assigned surface polarity of silica gel particles by observing shifts in the absorption spectra of absorbed spiropyrans which are sensitive to solvent polarity [44]. Darwent and coworkers have shown that kinetic salt effects follow surface charge on colloidal titanium dioxide and, with zeta potential measurements, that surface area and charge could be separately evaluated [45].

In considering photoactivity on metal oxide and metal chalcogenide semiconductor surfaces, we must be aware that multiple sites for adsorption are accessible. On titanium dioxide, for example, there exist acidic, basic, and surface defect sites for adsorption. Adsorption isotherms will differ at each site, so that selective activation on a particular material may indeed depend on photocatalyst preparation, since this may in turn influence the relative fraction of each type of adsorption site. The number of basic sites can be determined by titration [46, 47], but the total number of acidic sites is difficult to establish because of competitive water adsorption. A rough ratio of acidic to basic binding sites on several commercially available titania samples has been shown by combined surface ir and chemical titration methods to be about 2.4, with a combined acid/base site concentration of about 0.5 mmol/g [48].

For many photoelectrochemical events, Langmuirian kinetics govern substrate adsorption. That is, the observed photochemically induced reaction rate is found to be proportional to the concentration (or pressure) of the reactant, which in turn can be related to the surface coverage θ by the Langmuir expression, Eq. (10),

$$\Theta = \frac{KC}{(1+KC)} \tag{10}$$

where K = the adsorption coefficient and C = the initial concentration of the reactant.

Deviations from this simple expression have been attributed to mechanistic complexity [49]. For example, detailed kinetic studies have evaluated the relative importance of the Langmuir-Hinshelwood mechanism in which the reaction is proposed to occur entirely on the surface with adsorbed species and the Eley-Rideal route in which the reaction proceeds via collision of a dissolved reactant with surface-bound intermediates [50]. Such kinetic descriptions allow for the delineation of the nature of the adsorption sites. For example, trichloroethylene is thought to adsorb at Ti sites by a pi interaction, whereas dichloroacetaldehyde, an intermediate proposed in the photocatalyzed decomposition of trichloroethylene, has been suggested to be dissociatively chemisorbed by attachment of the alpha-hydrogen to a surface O^{2-} site [51].

Adsorption of substrates may also be altered by photoexcitation or by the presence of other adsorbates. That adsorption and photoadsorption are influenced by thermal removal of water and surface hydroxyl groups has been shown in detailed studies [52-56]. On tin oxide, preadsorption of other reagents can produce a substantial increase in oxygen photoadsorption under sub-band gap irradiation and can shift the photosensitivity threshold to longer wavelengths [57].

Surface effects and adsorption equilibria thus will significantly influence the course of photoelectrochemical transformations since they will effectively control the movement of reagents from the electrolyte to the photoactivated surface as well as the desorption of products (avoiding overreaction or complete mineralization). The stability and accessibility toward intermolecular reaction of photogenerated intermediates will also be controlled by the photocatalyst surface. Since diffusion and mass transfer to and from the photocatalyst surface will also depend on the solvent and catalyst pretreatment, detailed quantitative descriptions will be difficult to transfer from one experiment to another, although qualitative principles governing these events can be easily recognized.

2.3 Current Control

A significant advantage afforded by photoelectrochemical activation of semiconductors compared with applied potentials at conventional dark electrodes lies in the ability to alter light flux to control current flow. Semiconductor particles become strong redox centers upon irradiation, but their ability to accommodate electron transfer is switched off as soon as the charge carrier passes across the illuminated interface. At low light flux, it may be possible to restrict the number of electrons available to each adsorbate compared with those attainable at poised metal electrodes. Furthermore, wavelength sensitivity, crystallite morphology, doping densities, or surface treatments may influence the kinetics for charge transfer across the interface and hence influence the identity of the chemical transformation induced by photoexcitation.

Upon illumination, semiconductor particles become charged, allowing even for electrophoretic mobility under an applied electrical field [58, 59]. When appropriately prepared, colloidal TiO_2 can apparently accumulate charge to effect directly multiple quanta redox reactions [60]. The efficiency of such charge accumulation is surely related to doping level [61], for the doping level can alter band positions and may improve the efficiency of photoinduced electron transfer. For example, the dispersal of Fe_2O_3

into doped TiO_2 produced a material with greatly improved properties for nitrogen reduction [62].

The rate of flow of electrons from such a charged particle depends on the availability of an accessible site for this transfer. Although it is known that lattice defects provide such sites [63] and that conduction band electrons can "trickle down" through solid dislocation levels [64], reduction sites for electron accumulation are usually provided by metallization of the semiconductor particle. This can be achieved through photoplatinization [65] or by a number of vapor transfer techniques [66], and the principles relevant to hydrogen evolution on such platinized surfaces have been delineated by Heller [67]. The existence of such sites will thus control whether single or multiple electron transfer events can actually take place under steady state illumination.

It has recently been recognized that crystal structure and particle size can also influence photoelectrochemical activity. For example, titanium dioxide crystals exist in the anatase phase in samples which have been calcined at temperatures below 500 °C, as rutile at calcination temperatures above 600 °C, and as a mixture of the two phases at intermediate temperature ranges. When a range of such samples were examined for photocatalytic oxidation of 2-propanol and reduction of silver sulfate, anatase samples were found to be active for both systems, with increased efficiency observed with crystal growth. The activity for alcohol oxidation, but not silver ion reduction, was observed when the catalyst was partially covered with platinum black. On rutile, comparable activity was observed for Ag^+, but the activity towards alcohol oxidation was negligibly small [68]. Photoinduced activity could also be correlated with particle size.

In fact, with small particles or clusters, a range of excited state lifetimes could be observed by spectroscopic methods [69]. The observed non-Arrhenius dependence indicated the importance of multiphonon electron tunnelling, probably to preexistent traps. The shorter lifetimes observed at shorter emission wavelenths indicated significant coulombic interaction between traps.

Semiconductors display macroscopic properties by virtue of strong bonding between the individual repeating molecules of the crystal or crystallite. In large crystals, electron delocalization is so extensive that the crystal properties are collective and bear no necessarily close resemblance to the electronic states of the components. The buildup of such strongly interactive crystals involves profound changes in structure, bonding, and reactivity so that a moderate size cluster of the individual molecules must be formed before full solid state properties will be observable. It is reasonable to expect, then, that reducing the size of the semiconductor particle will eventually achieve a disruption of the macroscopic characteristics of the large particle and will significantly affect the course of photoinduced electron transfer reactions.

Recent developments in attaining chemical control in the arrested precipitation of semiconductor particles from solution have made it possible to prepare colloidal clusters of narrow size distribution [70-73]. It is now known that the electronic spectra exhibit dramatic blue shifts as the colloidal cluster size is diminished, a consequence of the kinetic energy requirement to spatially localize the electron-hole pair at proximate sites in a small particle. ZnS crystallites with an average diameter of 20 Å, for example, exhibit an apparent band gap blue-shifted by about 0.6 V from that observed in bulk crystals [74]. With HgSe and PbSe semiconductors with diameter sizes less than 50 Å, the optical edge is shifted by about 2.8 V [75].

Although chemical consequences of these electronic changes are only now being investigated, such quantum size effects are bound to influence photocatalytic activity. It is now established, for example, that the flat band potentials become slightly more negative and that the surface charge shifts as the average colloid size is decreased [71, 75].

Particle size control can also be afforded by constraining the colloid to vesicles [76], membranes [77], or zeolites [78, 79]. An intriguing recent report achieves size limitation of semiconductor electrodes by preparing them by photolithography techniques [80].

The use of specially designed particles with controlled size, morphology, surface catalysts, and dopants can surely influence the selectivity which can ultimately be attained in photoelectrochemical conversions. Judicious control of light flux will also influence the course of photostimulated redox reactions. Only very few tests of these effects in organic systems have yet been reported, however.

3 Selective Photoelectrochemical Transformations

The relevant principles influencing chemical selectivity in photoelectrochemical reactions having been discussed, we can now survey the use of such techniques in organic chemistry.

3.1 Oxidations

Since the valence band edges of most common metal oxide and metal chalcogenide semiconductors lie positive of the oxidation potentials of many common organic functional groups, capture of a photogenerated hole by an adsorbed organic molecule is thermodynamically feasible for many substrates. Not only can pure compounds serve as oxidizable substrates, but so also can nearly any organic substance: one notable paper uses, for example, polyvinyl chloride, algae, protein, dead insects and animal excrement as electron sources [81]. Chemical selectivity is attained only if this broad range of reactivity is controlled. Alcohols were among the first organic species to be investigated as photoelectrochemically oxidizable substrates. Upon excitation of semiconductor suspensions in the presence of alcohols, dehydrogenation ensued, sometimes producing an isolable carbonyl compound, Eq. (11). The superior photoactivity of anatase compared with rutile in the liquid phase photooxidation of 2-propanol [82] compared well with the photoinduced activity of gaseous alcohol on platinized titania [83]. Since most such studies focused on employing the alcohol as a sacrificial reagent for the photochemical production of hydrogen [84–87], less concern was addressed toward organic product analysis or toward selective activation of alcohols in the presence of other functional groups. In the oxidation of carbohydrates, for example, complete oxidative conversion to hydrogen and carbon dioxide was a primary goal [85]. It was noted, however, that alcohol structure affected the quantum efficiency of hydrogen production, methanol and ethanol being more efficiently

$$\mathrm{RR'CHOH} \xrightarrow[O_2]{TiO_2^*} \mathrm{RR'C{=}O} \tag{11}$$

oxidized than other primary alcohols, and water being oxidized as least four times less efficiently than methanol [86].

Such studies also allowed for photocatalyst optimization. For liquid phase alcohol photooxidations, an optimum platinum loading of TiO_2 of 0.1 to 1 weight per cent was observed, with the most effective platinum islands having diameters of approximately 2 nm [87,88]. Other noble and transition metals could also catalyze the reductive half reaction, with activity decreasing in the order Pt > Rh > Pd > Ru > Ir. A preliminary heat treatment enhanced hydrogen evolution [89]. Transition metal oxide dopants influenced photoactivity, sometimes in the reverse direction from thermal catalytic oxidations. Surface-bound vanadium and molybdenum oxides, for example, increased the rate, and decreased the selectivity, of thermal oxidation of methanol on titanium dioxide [90], but decreased photochemical activity. The addition of alkali metal salts similarly shifted the selectivity in the photooxidation of aqueous methanol toward water, and caused further oxidation of partially oxidized products derived from methanol [91]. When metallic nickel was used as a support, the photooxidation of 2-propanol on $SrTiO_3$, CdS, or TiO_2 did not proceed without water, and no hydrogen was evolved in the presence of oxygen [92]. When oxygen uptake was monitored kinetically, a mechanism implicating surface binding by a non-associated hydroxy group was implicated [93]. With fiber optic monitoring, it could be established that the sites responsible for reaction were acidic Ti^{4+} sites [94]. Parallel photodehydrogenation could also be attained on irradiated ZnS particles, with alcohols or amines as electron sources [95-97].

A few studies did address chemical selectivity in these oxidations. Pattenden and coworkers, for example, showed that primary alcohols could be selectively oxidized to the corresponding aldehydes, without appreciable overoxidation, when the platinized TiO_2 photocatalyst was suspended in benzene, Eq. (11). Poor yields were obtained

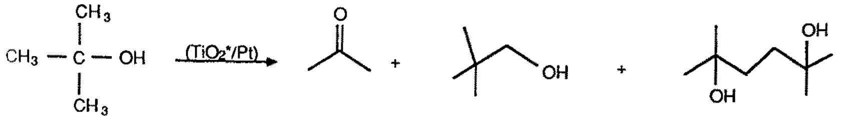
$$C_7H_{15}CH_2OH \xrightarrow[PhH \atop N2]{TiO_2^*/Pt} C_7H_{15}CHO \qquad (12)$$

with secondary aliphatic or aromatic alcohols [98]. In a competition for photodehydrogenation sites between ethanol and D_2O, D_2 was found to be the major gaseous product (88 %) [99]. The ratio of hydrogen to methane evolved was about 14, implying that Eq. (13) proceeded about four times faster than did Eq. (14). In the photooxida-

$$CH_3CH_2OH + 3H_2O \xrightarrow{(TiO_2^*/Pt)} 2CO_2 + 6H_2 \qquad (13)$$

$$CH_3CH_2OH + H_2O \xrightarrow{(TiO_2^*/Pt)} CO_2 + CH_4 + 2H_2 \qquad (14)$$

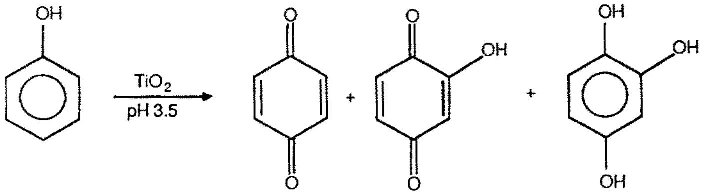
tion of polyols, e.g., sorbitol, photocurrents produced on illuminated TiO_2 were dependent on molecular structure (chain length and the number of OH groups). The reactions were pH dependent and the effects were ascribed to the high concentrations of OH groups at the photoactivated surface when long chain polyols were adsorbed [100].



(15)

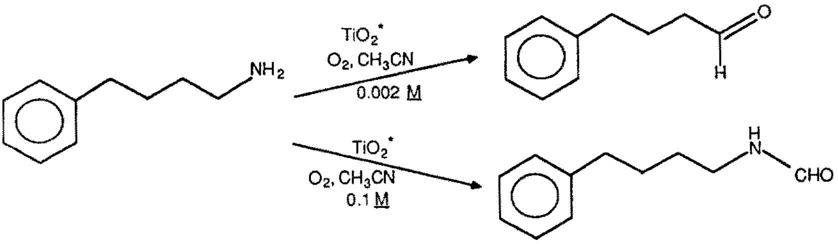
Photoelectrochemical oxidation of primary or secondary tertiary alcohols was much more difficult than that of primary or secondary alcohols, and carbon-carbon bond cleavage products can ultimately be isolated, along with products of radical coupling, Eq. (15) [102]. Low activity was observed without platinization of the TiO_2 photocatalyst, the observed yield increasing linearly with platinum coverage to 10 weight per cent. The formation of acetone as the major product in the presence of air or silver ion was similar to results obtained upon gamma irradiation or in the Fenton reaction, suggestive of hydroxy radical-mediated chemistry.

In the photooxidation of phenol induced by excited titanium dioxide, the hydroxy radical was directly implicated as the reactive species, the observed organic products having incorporated oxygen, Eq. (16) [103]. On further photolysis, aldehydes, acids, and CO_2 could be obtained.



(16)

Other heteroatom-containing compounds exhibit similar chemistry. Primary amines, for example, can be oxidized on irradiated semiconductor suspensions to form Schiff bases [104, 105], which undergo coupling with the starting amine. In fact, two different pathways can be observed depending on the initial concentration of the amine and on the nature of the semiconductor catalyst, Eq. (17) [104]. Primary amines



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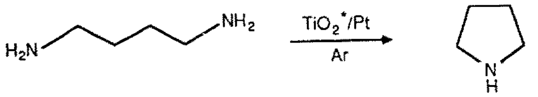
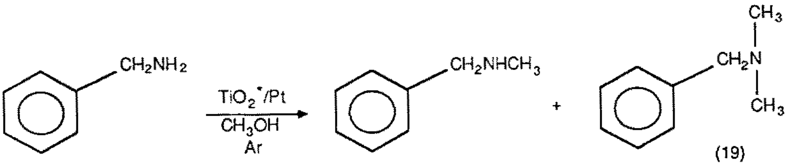


(18)

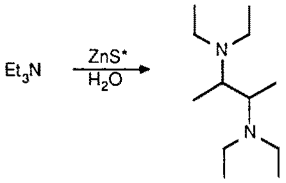
can be converted to secondary amines in a parallel process, and diamines can be cyclized photoelectrochemically, Eq. (18) [106–108]. N-alkylation could also be induced when the irradiation was conducted in the presence of alcohol, Eq. (19) [109, 110].



(19)

In the photocatalytic production of amines from alcohols and ammonia, the efficiency varied with alcohol structure: ethanol > methanol > 2-propanol > t-butanol. A hydrogen atmosphere enhanced the formation of amines, a process which was inhibited by oxygen [110].

Single electron oxidation of amines bearing alpha hydrogens can also effect carbon-carbon coupling. On colloidal ZnS, for example, alpha coupling, presumably through a radical produced by deprotonation of the photogenerated radical cation, is observed with amines, Eq. (20) [95], as well as with ethers and alcohols. Cleavage adjacent to nitrogen was also observed in the photoelectrochemical demethylation of methyl orange [111]. Here cleavage of an N-methyl group was competitive with C—N cleavage adjacent to the azo linkage.



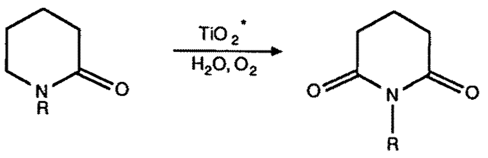
(20)

Coupling at nitrogen could also be observed in the photoelectrochemical activation of aryl amines. With toluidines, for example, azo products are formed, Eq. (21) [112].

$$\text{PhNH}_2 \xrightarrow[\text{Me}_2\text{CHOH},\ \text{O}_2]{\text{ZnO}^*} \text{Ph-N=N-Ph} \qquad (21)$$

N—H deprotonation to form a nitrogen radical is obviously more important than alpha-deprotonation of the pendant alkyl group. Such reactions are reminiscent of the photocatalyzed oxidation of ammonia reported by Pichat and coworkers [113].

The controlled photoelectrochemical oxidation of imides presents an interesting example of chemoselectivity. The photoinduced oxidation of lactams to imides, Eq. (22) [114], and of N-acylamides to imides, Eq. (23) [114], introduces oxygen into the organic substrate, but if the reaction is conducted in the presence of Cu(I), unsaturation is induced instead, Eq. (24) [114].



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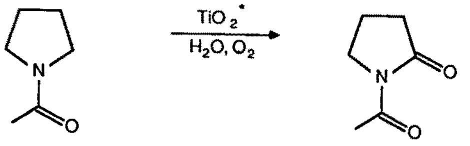
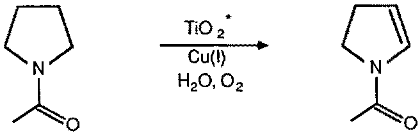


(23)

Photoelectrochemical oxidation products can be obtained from organosulfur compounds. Thioethers can be cleanly converted to the corresponding sulfoxides, Eq. (25)[115]. Various products have been reported in the photocatalyzed oxidation of dimethyl sulfide depending on the initial concentration of thioether. On TiO_2, CdS, or ZnSe, a Stevens rearrangement occurs, Eq. (26)[116]. The key intermediate appears to be a dimethylsulfide dimer cation radical, and the reaction is only efficient in protic solvents.



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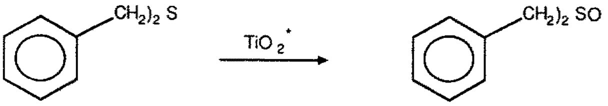


(25)

$$CH_3SCH_3 \xrightarrow{TiO_2^*} CH_3CH_2SSCH_3 + CH_3CH_2SSCH_2CH_3 \qquad (26)$$

Thiols can also be converted to disulfides, as in the CdS-photocatalyzed conversion of cysteine to cystine[117]. In the latter reaction, the uptake of oxygen was pH dependent. Since the reaction rate was not increased in deuterium oxide and was not decreased by added azide, the authors conclude that singlet oxygen is not involved. Since superoxide dismutase inhibited the conversion, a photoinduced electron transfer is probably responsible for the observed transformations. Such organosulfide oxidations may be environmentally important since naturally occurring hematite suffers a photoassisted dissolution in the presence of thiols[118].

Amino acids which lack thioether groups are also oxidized by photoelectrochemical methods, although the efficiency is somewhat reduced. Oligopeptides have been reported to be isolable upon irradiation of semiconductor suspensions in the presence of amino acids with quantum efficiencies ranging from 0.6 to 1.1 %[119]. The molecular weight distribution of the peptides could be partially controlled by choice of the sensitizer: diglycine was formed twice as efficiently on platinized titanium dioxide as on platinized cadmium sulfide, while the yield of pentaglycine was four times higher on CdS/Pt than on TiO_2/Pt.

The photoelectrochemical synthesis of amino acids from simple molecules has also been reported. Low efficiencies were observed in the conversion of mixtures of methane, ammonia and water to several amino acids on platinized TiO_2[120,121]. Amino acids and peptides were reported when glucose replaced methane as the carbon source in a parallel experiment[122]. Higher quantum efficiencies (20–40%) were observed in the conversion of alpha-keto acids or alpha-hydroxy acids to the corresponding alpha-amino acids[123]. Moderate levels of enantiomeric selectivity (optical yields of about 50%) were reported when chiral starting materials were employed. Photoinduced Michael-like reactions were observed when alpha, beta unsaturated acids were used as substrates for the amino acid synthesis[123].

Simple carboxylic acids suffer photo-Kolbe decarboxylation under the usual photoelectrochemical conditions. In fact, this reaction type was one of the first characterized examples of oxidative cleavage of an organic molecule induced by long wavelength irradiation of a semiconductor. In the decarboxylation of acetic acid at the surface of an irradiated n-TiO_2 single crystal or polycrystalline electrode, formation of ethane could be observed, whereas methane formation became dominant on irradiated powders [124–128]. (Since the overall reaction is thermodynamically downhill, this transformation is photocatalytic rather than photosynthetic as are many of the reactions discussed above.) Depending on the identity of the semiconductor, the extent and identity of the adsorbed metal, and the pH of the solution, the extent of alkyl coupling vs. reduction could be closely controlled [128].

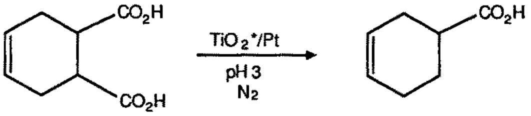
The critical difference between the electrode and powders probably centers on the different operative space-charge thickness developed on each surface. On a powder, a newly formed radical will remain isolated, persisting until back electron transfer generates an anion, protonation of which allows for surface desorption, Eq. (27).

$$RCO_2^{\ominus} \xrightarrow{TiO_2^{*}} \underset{+e^-}{RCO_2^{\cdot}} \longrightarrow \underset{+e^-}{R\cdot \quad CO_2} \xrightarrow{e^-} R^{\ominus} \xrightarrow{H^+} RH \qquad (27)$$

The critical involvement of alkyl radicals has been established in spin-trapping experiments [129], although deuterium incorporation seems to implicate the eventual protonation of an anionic intermediate [125].

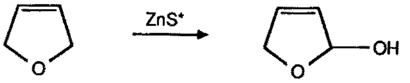
In a series of transition metal oxide semiconductor powders, photochemical activity in the decarboxylation of oxalic acid was controlled by surface properties and the presence of recombination centers, which in turn depended on the preparation method [130]. Similar effects have also been noted in the photodecarboxylation of pyruvic acid [131] and formic acid [132].

With vicinal diacids, the occurrence of mono- or bis-decarboxylation could be controlled by light flux. At low light flux, the primary product is monodecarboxylation, as is consistent with ideas described earlier for photoelectrochemical current control, Eq. (28) [133].



(28)

Carbon-carbon coupling of radicals observed in the photo-Kolbe reaction could also be observed with other surface generated radicals. Kisch and coworkers have shown, for example, that cyclic allylic ethers undergo alpha deprotonation under photoelectrochemical activation, producing radicals that can be oxygenated [134], Eq. (29). On colloidal zinc sulfide, hydrogen evolution accompanies the photocatalytic



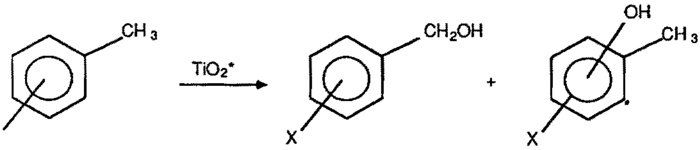
(29)

carbon-carbon bond formation [95,135,136]. With saturated ethers, which can also be dehydrodimerized, appreciable chemoselectivity is observed in competition experiments. For example, 2,5-dihydrofuran (an allylic ether) is much more active than the 2,3-dihydrofuran (a vinyl ether) [136]. With the former substrate, all three diastereomeric coupling products are observed.

Since water is required for the reaction, the primary photochemical product is thought to be a surface bound hydroxy radical. The observed chemoselectivity for radical formation from the adsorbed ether, however, is thought to be governed by adsorption phenomena since a free hydroxyl radical in homogeneous solution is much less selective than the photoirradiated catalyst system.

The photocatalyst used for these conversions can be generated in situ, by photolysis of a zinc dithiolene salt [136], by preformed catalysts [135], or by particles supported within surfactant vesicles [137]. The idea of employing semiconductor surfaces as environments for the enhanced coupling of radicals had previous support in the photochemical coupling of cyclopentadienyl radicals formed by excitation of the corresponding anions at single crystal electrodes [138].

Radical intermediates formed via hydrogen abstraction by photogenerated hydroxy or hydroperoxy may also be important in the photoelectrochemically induced oxidation of hydrocarbons. In the TiO_2-sensitized photooxidation of toluene to cresols, Eq. (30), e.g., a photo-Fenton (radical) type mechanism has been suggested [139,140]. Whether the active radical derives from the reduction of oxygen [139] or from the oxidation of water [141] has recently been tested by an ^{18}O tracer study [142]. With $^{18}O_2$, incorporation of ^{18}O into the photogenerated phenol was pH dependent, suggesting that OH derives from O_2 at high pH and from water at low pH [142].



(30)

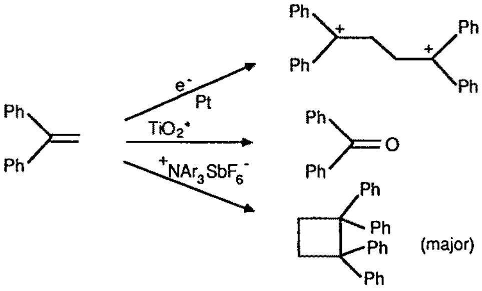
Competitive trapping of the photogenerated conduction band electron by adsorbed protons is thought to be responsible for the reduced contribution of oxygen at lower pH. Water oxidation cannot be solely responsible for the observed chemistry, however, since toluene can be oxidized to benzyl alcohol as a neat liquid [143]. Here the intervention of the hydrocarbon radical cation seems possible.

That products of intermediate oxidation level can be detected in the photocatalytic reactions of hydrocarbons and fossil fuels is also consistent with a surface bound radical intermediate [144]. Photocatalytic isotope exchange between cyclopentane and deuterium on bifunctional platinum/titanium dioxide catalysts indicates the importance of weakly adsorbed pentane at oxide sites. The platinum serves to attract free electrons, decreasing the efficiency of electron-hole recombination, and to regenerate the surface oxide after exchange. Much better control of the exchange is afforded with photoelectrochemical than thermal catalysis [145,146]. As before, hydrocarbon oxidations can also be conducted at the gas-solid interface [147].

The course of hydrocarbon photocatalyzed oxidations seems to depend significantly on the relative positions of the valence band edge of the active photocatalyst and the oxidation potential of the substrate. For example, in contrast to the clean oxidation of toluene described above, lower activity was observed in neat benzene, a substrate whose oxidation potential lies at or slightly below the valence band edge [143]. This observation implies the importance of radical cation formation (via photoinduced electron transfer across the irradiated interface) as a preliminary step to hydrocarbon radical formation. If benzene-saturated aqueous semiconductor suspensions are irradiated, however, complete mineralization of the hydrocarbon is attained[148, 149]. Thus, in order to observe selective photoelectrochemistry, it is necessary to avoid primary formation of the highly reactive, unselective hydroxy radical (formed via water oxidation) by employing an unreactive, but polar, organic solvent.

Evidence for the involvement of radical cations in the photooxidation of olefins has been cited earlier[13, 22–26]. A variety of oxidizable arenes[150] and dienes[151] similarly exhibit oxidative cleavage or rearrangement chemistry consistent with initial formation of a radical cation. The observed oxidative cleavage derives presumably from interception of the surface bound radical cation with superoxide or adsorbed oxygen. With alkanes or simply substituted alkenes, however, the capture of a photogenerated hole is often thermodynamically forbidden. Thus, instead of radical cations, radicals formed by activated oxygen species dominate the observed chemistry. With alkanes, oxygenation at sites controlled by radical stability, rather than oxidative cleavage, is observed[25, 143, 152, 153]. The relative ratio of oxygenation to complete mineralization can be controlled, at least to some extent, by careful choice of the metal oxide photocatalyst[153].

In fact, the surface may mediate the requisite chemistry of the initially formed radical cation so that different products can be observed from the same intermediate when generated photoelectrochemically or by other means. The radical cation of diphenylethylene, for example, gives completely different products upon photoelectrochemical activation[23, 25] than upon electrochemical oxidation at a metal electrode or by single electron transfer in homogeneous solution, Eq. (31)[133]. Surface control of the competition between deprotonation and oxidative cleavage of a photoelectrochemically generated radical cation can be seen in the divergent chemistry attained from the 1-methylnaphthalene cation radical formed on irradiated TiO_2 powders



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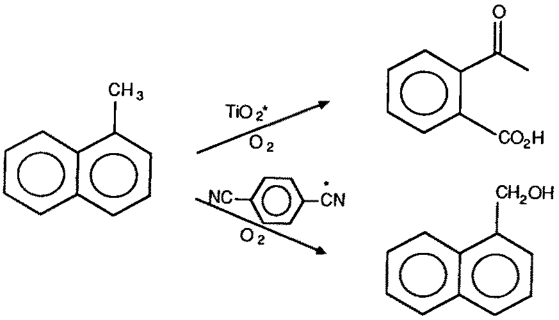
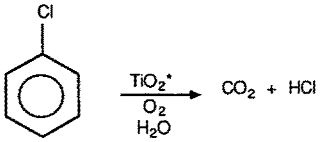


(32)

and by homogeneously dispersed single electron oxidants, Eq. (32) [150]. Here the semiconductor surface delivers the coadsorbed oxygen or superoxide more rapidly than C—H deprotonation can ensue.

The photogenerated hydroxy radical is probably the significant intermediate in the complete mineralization of alkyl [154-160], vinyl [161], and aryl [162-164] halides, e.g., Eq. (33). Such reactions are of great environmental importance, for they allow for an interesting means of water purification.



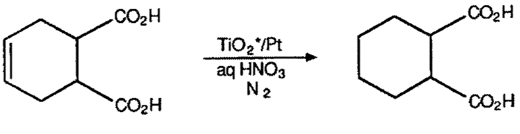
(33)

We conclude that oxidative transformations of organic substrates can be readily understood as emanating from either photogenerated surface adsorbed radical cations or from radicals formed by activated oxygen radicals (surface oxides or adsorbed hydroxy, hydroperoxy or peroxy radicals). Photoelectrochemical methods not only generate the reactive species by interfacial electron transfer, but also control the subsequent activity of the surface adsorbed intermediate.

3.2 Reductions

Few organic reductions induced by photoelectrochemical methods have been reported. Undoubtedly, this derives from the ease with which oxygen assumes the principle role in the reductive half reaction. Nonetheless, when oxygen is specifically removed, other reagents can accept the photogenerated conduction band electron. Because of the only modestly negative potential of electrons at the conduction band edge of conveniently accessible semiconductors, few organic substrates can fill this role. Cationic organic reagents do indeed fill this role, as we saw earlier in the photoinduced reduction of methyl viologen and comparable derivatives (Eq. 2), and indeed many such reagents have been used as photoelectrochemical relays [17]. A brief report on the photoelectrochemical reduction of $NADP^+$ on irradiated CdS has also appeared [165].

Protons present in aqueous acid also act as reasonably efficient electron acceptors. If the reduced hydrogen atoms are formed on metallized suspensions, catalytic hydrogenation can result. For example, in contrast to the oxidative chemistry reported earlier for cyclohexene-4,5-bis-dicarboxylic acid (Eq. 28), if the reaction is conducted in the absence of oxygen in aqueous nitric acid, catalytic hydrogenation of the double bond becomes a major pathway, Eq. (34) [133].



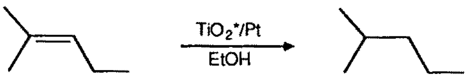
(34)

Photoelectrochemical hydrogenation of double and triple bonds has been reported with sulfide anion acting as a sacrificial donor, Eq. (35) [166]. With CdS metallized with platinum or rhodium as the photocatalyst, hydrogenation was found to be about

$$\mathrm{H{-}C{\equiv}C{-}H} \xrightarrow[S^{2-}\ H_2O]{CdS^*/Pt} \mathrm{H{-}CH_2CH_2{-}H} \qquad (35)$$

four times as efficient as hydrogen evolution, with the efficiency depending on the solution phase pH and the identity of the metal catalyst.

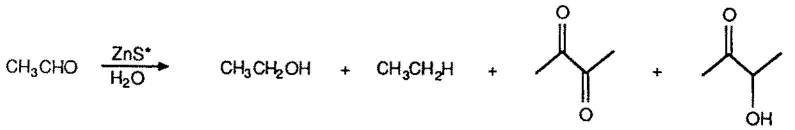
Olefins, vinyl ethers, and the double bond of alpha, beta unsaturated enones could be photoelectrochemically hydrogenated on TiO_2 with ethanol acting as the electron source. With 2-methyl-2-pentene, hydrogenation occurred in 63% yield without side products, Eq. (36)[167].



(36)

The photoelectrochemical reduction of the N=N double bond of the diaryl azo dye methyl orange can be similarly sensitized by colloidal titanium dioxide[168,169]. The reaction was sensitive to pH and the identity of the organic redox reaction could be shifted by conducting the photoreaction in the presence of surfactants. Cationic surfactants increased the efficiency of oxidative cleavage[111], by inhibiting charge recombination. Polyvinyl alcohol instead favored reduction. The ambident photoactivity of methyl orange thus makes it an attractive probe for activity of irradiated semiconductor suspensions.

Carbonyl double bonds can also be photoelectrochemically reduced: ZnS sols prepared from cold oxygen-free aqueous solutions of $ZnSO_4$ and Na_2S induce efficient photodisproportionation of aldehydes, i.e., a photo-Canizzaro reaction[170]. Thus, acetaldehyde produces ethanol and acetic acid, together with smaller quantities of biacetyl and acetoin, Eq. (37).

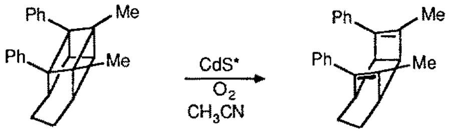


(37)

The relative paucity of photoelectrochemically induced reductions makes this an interesting area for further investigation.

3.3 Cycloadditions and Retrocycloadditions

Reactions which formally can be classified as cycloadditions or retrocycloadditions have been observed in homogeneous solution with single electron oxidative initiation, so the observation of parallel activity on irradiated semiconductor suspensions is certainly reasonable. The first example of such a reaction involved the photocatalysis by ZnO or CdS of the ring-opening of a strained hydrocarbon which could also be opened in the dark by a single electron oxidant, ceric ammonium nitrate, Eq. (38)[171]. In a mechanistic investigation of the valence isomerization of hexamethyldewarbenzene to hexamethylbenzene, Eq. (39), a surface-bound cation radical chain mech-



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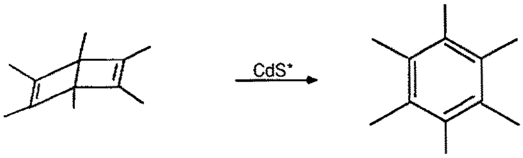
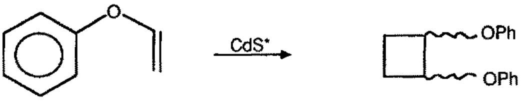


(39)

anism is involved, since quantum yields greater than unity could be obtained [171, 172]. With CdS of different origins, rates varied only by factors of about 2. Different surface areas, impurities, and surface structures did not play the dominant role in determining the rate of reaction. Anthracene [173] and quinolone [171] dimers could also be opened in similar fashion.

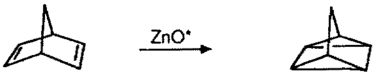
In contrast to these ring openings, only ring closure could be observed in the photodimerization of phenyl vinyl ether, Eq. (40), which proceeded only in one direction [173].



(40)

Both stereoisomers were formed, implying a loss of stereochemical integrity during the formation of the second carbon-carbon bond. When the reaction was conducted on ZnO, surface-related processes affected both the rate and stereochemistry. The effect of various quenchers could be explained as competitive adsorption at active sites, with or without interference with electron transfer. A reaction scheme involving formation of dimer, both in the adsorbed state and in solution, was proposed, the former route being the more important [174]. On CdS, the reaction could sometimes be induced in the dark as well because of the presence of acceptor-like surface states. Neither particle size, surface area, nor crystal structure appeared to significantly influence the dimerization [175], observations parallel to those found in the CdS photoinduced dimerization of N-vinylcarbazole [176].

Intramolecular cycloaddition can also be induced on semiconductors. Norbornandiene, for example, can be cyclized upon irradiation of ZnO, ZnS, CdS, or Ge semiconductors, Eq. (41) [177].

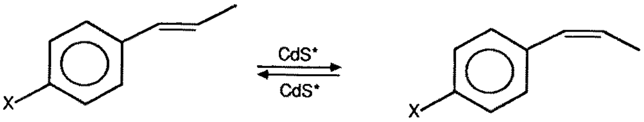


(41)

3.4 Geometric Isomerizations

Several examples have already been cited in which stereochemistry about carbon-carbon double bonds is lost, e.g., Eqs. (4) and (40). We now consider this photoinduced geometric isomerization as an area worthy of independent investigation.

Substituted styrenes have been shown to achieve thermodynamic equilibrium via a radical ion mechanism when exposed to CdS excited with light of energy greater than its bandgap, Eq. (42) [178]. The reaction was quenched by electron donors (methoxybenzenes or pyrenes) and is affected by the ratio of substrate to catalyst, by light intensity and by temperature. Oxygen inhibited the reaction [179]. When a Hammett plot was constructed with donor and acceptor substituents, a sharp break at sigma$^+$ = 0.19 occurred indicating a change in the rate determining step with a change of the electron donating ability of the substituent [180]. Two regions constituting exergonic and endergonic electron transfer are proposed, with a rho value (—0.74) reminiscent of that previously observed for the oxidative cleavage of diphenylethylenes [26]. Although a more positive value might have been expected if the formation of a radical cation were the rate determining step, surface precomplexation would diminish the expected value [181].



(42)

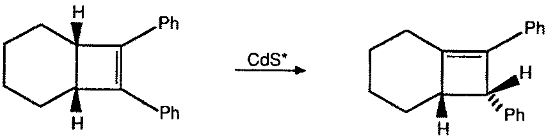
A Stern-Volmer plot obtained in the presence of donors for the stilbene isomerization has both curved and linear components. Two minimal mechanistic schemes were proposed to explain this unforeseen complexity: they differ as to whether the adsorption of the quencher on the surface competes with that of the reactant or whether each species has a preferred site and is adsorbed independently. In either mechanism, quenching of a surface adsorbed radical cation by a quencher in solution is required [182]. In an analogous study on ZnS with simple alkenes, high turnover numbers were observed at active sites where trapped holes derived from surface states (sulfur radicals from zinc vacancies or interstitial sulfur) play a decisive role [183].

Thus, as with the oxidative cleavages, a clear role for surface-adsorbed radical cations is implicated in the observed geometrical isomerizations.

3.5 Miscellaneous Reactions

This section refers briefly to several notable organic transformation types which do not fit conveniently into one of the previous categories. Their inclusion is intended to emphasize the fact that photoelectrochemical methods are useful in a number of applications outside the areas most extensively investigated so far.

For example, CdS can mediate a symmetry forbidden [1,3] sigmatropic shift of hydrogen, Eq. (43) [186]. In the absence of oxygen, these cyclic derivatives of diphenylcyclobutene underwent a reversible double bond migration. Since the reaction was



(43)

at least partially intramolecular, it constitutes a radical cation-mediated hydrogen shift which would have been forbidden in the ground state closed shell system.

Applications of photoelectrochemistry in problems related to environmental issues are manifold. The conversion of acetic acid to methane, the oxidative decomposition of biomass, and the photodegradation of organochlorine contaminants 187, 188) which were discussed earlier represent societally important uses of solar energy. That such reactions can occur under natural conditions 189) to dissolve minerals 190) or to generate biologically active oxidants 191) or metabolites 192) should be of great interest to biologists. It has been estimated, for example, that at least 10% of biological nitrogen fixation derives from photoelectrochemical reduction of chemisorbed nitrogen on titania-rich desert sands 193).

Since this review has focused on photoelectrochemical conversions of organic compounds, it has neglected the redox reactions of simple inorganic materials like nitrogen, water, and carbon dioxide, species which have a rich photoelectrochemical history. Recent progress made with photoelectrochemical CO_2 reduction 194) signals the possibility that in the future organic feedstocks may derive from aldehydes and alcohols produced by photoelectrochemical reductions.

4 Conclusions

A wide array of chemical conversions can be induced by photoelectrochemical activation of light sensitive semiconductor surfaces. This photochemical activation creates an electron-hole pair, which can initiate interfacial electron transfer. The oxidized and reduced species thus produced undergo dark secondary reactions which are greatly influenced by the surface on which they are produced. The observed chemistry is thus controlled by band edge positions, by adsorption effects, and by light-influenced current density. The surface can bring together coadsorbates and can control the local polarity of photogenerated intermediates. Oxidations, reductions, formal cycloadditions and retrocycloadditions, as well as geometric isomerizations, can be rationally conducted on these photocatalytic surfaces.

As with all such transformations, the utility of such new chemical processes lies in the chemist's ability to specify stereochemistry and regiochemistry or to activate a specific functional group in a complex molecule or to choose a particular substrate from a mixture. It is here that substantial challenge remains.

5 Acknowledgements

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Oxidation of Organic Compounds at the Nickel Hydroxide Electrode

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1 Introduction

Organic molecules are synthesized by C—C bond forming reactions (C—C) and functional group interconversions (FGI). Electrolysis can contribute to polar and radical C—C bond forming processes [1]. In functional group interconversions electrolysis can be a method of choice, whenever oxidation numbers are changed. Frequently used FGI's at the cathode are hydrogenation of C=C [2] or C=X [3] double bonds, the replacement of heteroatoms by hydrogen [4], and especially the cleavage of protecting groups [5]. At the anode the mirror image reactions of the cathode can be accomplished. Some of the possible FGI's are dehydrogenation of HC—XH bonds [6], substitution of hydrogen by functional groups [7] or addition of nucleophiles to C=C double bonds [8].

Anodic oxidation can occur either direct by electron-transfer from the substrate to the electrode or indirect *via* a mediator. The same holds in reverse for the cathode. The mediator, which is applied in catalytic amounts and is continuously regenerated at the electrode can either take up electrons (electron-transfer) or abstract hydrogen from the substrate (atom-transfer). Atom- or electron-transfer can happen homogeneously to a mediator dissolved in the electrolyte or heterogeneously to a mediator bound to the electrode surface.

Oxidation at the nickel hydroxide electrode is most probably an indirect, heterogeneous anodic dehydrogenation. The electrocatalyst is presumably a nickel oxide hydroxide, that is continuously reformed at the electrode surface. The reactivity of the nickel hydroxide electrode resembles, as far as known, that of the chemical oxidant nickel peroxide. Therefore suggestions on the preparative use of the nickel hydroxide electrode can be obtained from applications of nickel peroxide [9] in organic synthesis. In this review oxidations at the nickel hydroxide electrode are arranged according to starting materials. Mechanisms, experimental procedures and comparisons with other chemical methods are treated under these headings.

2 Oxidation of Alcohols

2.1 Saturated Primary Alcohols

The oxidation of primary alcohol leads in good to excellent yields to carboxylic acids (Eq. (1), Table 1).

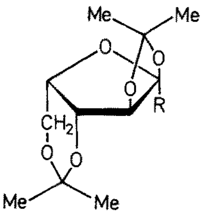
$$RCH_2OH \xrightarrow{NiOOH,\ -e} RCO_2H \qquad (1)$$

Early contributions to the oxidation of n-alcanols at nickel hydroxide electrodes have been described elsewhere [10]. More recent work is summarized in Table 1. Newer applications of the electrode, especially to the oxidation of 2,3:4,6-di-0-isopropylidene-L-sorbose (*1*) to L-gulonic acid (*2*), a step in a commercial vitamin C synthesis, were started by Vertes [13]. The development of the latter conversion to an industrial scale process was achieved by Robertson and Seiler [11]. The mechanism of the alcohol oxidation at the nickel hydroxide electrode was studied most intensively by Fleischmann and Pletcher [12].

Table 1. Selected oxidations of saturated primary alcohols to carboxylic acids at the nickel hydroxide electrode

Alcohol	Electrolyte[a]	Temperature (°C)	Yield (%)	Ref. [b]
Ethanol	A	25	46	13)
1-Butanol	B	25	92	15(14a))
2-Butanol	—	—	90	14b)
1-Hexanol	B	25	91	15)
1-Heptanol	A	25	84	15)
1-Nonanol	A	70	89	15)
1-Dodecanol	A	70	80	15)
1-Octadecanol	A	75	77	15)
2-Methyl-1-butanol	A	25	67	15)
2-Ethyl-1-butanol	A	70	73	15)
2-Ethyl-1-hexanol	A	70	76	15 (17))
3-Methyl-1-butanol	—	64	99.5	16)
2,3:4,6-Di-0-isopropylidene-L-sorbose (Dis, *1*)	A	60	93	11 (18, 19, 21))

[a] A: Aqueous NaOH, B: t-Butanol-water-potassium hydroxide.
[b] In parentheses references reporting different yields



	R
1	CH_2OH
2	CO_2H

If the alkyl chain of the alcohol is longer than six carbon atoms a reaction temperature above 60 °C is necessary to achieve a good conversion (Table 2).

Table 2. Oxidation of alcohols to carboxylic acids at the nickel hydroxide electrode: Influence of the temperature on the yield [15b]

Alcohol	Temperature (°C)	Yield of carboxylic acid (%)
1-Octanol	25	65
1-Octanol	70	89
1-Decanol	25	27
1-Decanol	70	87
2-Ethyl-1-hexanol	25	31
2-Ethyl-1-hexanol	70	76

Only small amounts of side products are formed. The purity of the acid is mostly greater than 98%, the major side product (up to 2%) is the lower homologous carboxylic acid.

For the less reactive, longer n-alcanols the activation of the nickel hydroxide electrode is necessary (Table 3). For that purpose several layers of black nickel oxide hydroxide are deposited on the electrode surface from a buffered nickel sulfate solution by changing the electrode polarity every 5–10 sec [11, 15b, 20, 21].

Table 3. Oxidation of alcohols to carboxylic acids at the nickel hydroxide electrode: Influence of electrode activation on the yield at 25 °C [39]

Alcohol	Electrolyte	Current density (mA/cm^2)	Yield carboxylic acid (%)
Benzylalcohol			
without activation	1 M NaOH	2.4	70
with activation[a]	1 M NaOH	16	85
1-Octanol			
without activation	1 M NaOH	16	3
with activation	1 M NaOH	16	65

[a] Electrolysis prior to substrate addition with 1 mA/cm^2 by changing the polarity of the nickel net from anode to cathode (period 5–10 sec) in a 0.1 N nickel sulfate, 0.1 N sodium acetate, 0.005 N sodium hydroxide solution until 0.5 Cb/cm^2 are consumed.

In the scale up of the L-sorbose *1* oxidation special efforts have been made to maintain the activity of the anode for a longer period of electrolysis. The decrease of activity could be retarded by addition of small amounts of a nickel salt to the electrolyte [21, 22]. The passivation is also influenced by the cation of the supporting electrolyte. Increasing deactivation is found in the order $K^+ < Li^+ < Na^+ < (CH_3)_4N^+$ [21]. Mineral salts in tap water, that is used to make up the electrolyte, can cause deactivation, too [23].

The limiting current density is proportional to the alcohol concentration and up to 0.2 M OH^- also dependent on the $[OH^-]$-concentration.

The preparation of nickel oxide deposits with high surface area on steel, nickel, copper, graphite or titanium electrodes [24] partly for anodic oxidation of organic compounds and the preparation of pressed nickel oxide powder electrodes mainly for application in storage batteries [25a] is described. The performance of nickel oxide anodes for batteries is improved by addition of cobalt(II)hydroxide [25b].

For laboratory scale conversions a simple beaker-type cell (Fig. 1) is convenient [15a]. When lower current densities have to be applied or in big scale operations [11, 21, 26] the "Swiss-roll" cell is of advantage. The latter cell (Fig. 2) contains a rolled-up sandwich, consisting of an anode and cathode sheet and a separator net. This allows a high electrode area applied in a small cell volume, which results in the low current densities necessary for efficient electrolyses at the nickel hydroxide electrode.

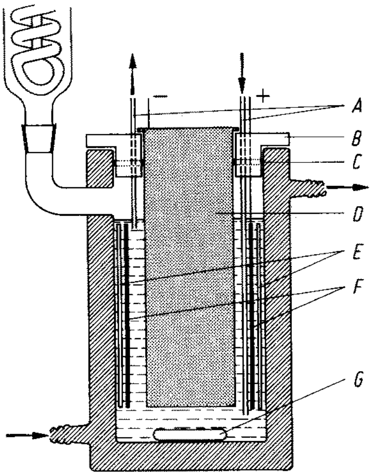


Fig. 1 [15a]. Beaker-type cell for oxidations with the nickel hydroxide electrode. *A*: Inlet and outlet for circulation (pumping) of the electrolyte; *B*: Teflon-stopper (d = 80 mm); *C*: Silicon seal; *D*: Stainless steel cathode; *E*: Glass rods; *F*: Nickel net anode; *G*: Magnetic stirrer

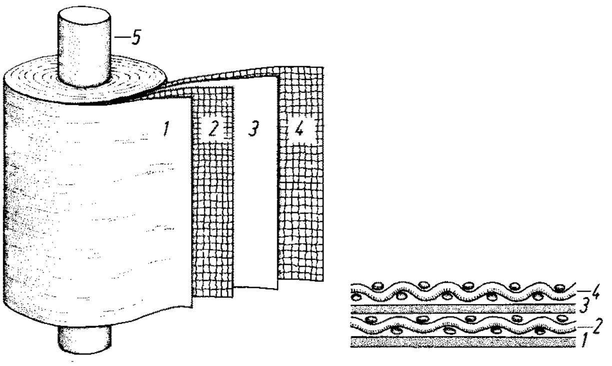


Fig. 2 [11]. "Swiss-roll"-cell, arrangement of the electrodes; *1*: Steel net cathode; *2, 4*: Polypropylene net as insulating separator; *3*: Nickel net anode; *5*: Current feeder

The nickel hydroxide electrode is used since decades in the nickel-iron(Edison)- or nickel-cadmium(Jungner)-storage battery [27]. Here the anodes consist mainly of nickel oxide powder pressed into a support and current feeder, whilst for electroorganic oxidations and electroanalytical measurements a thin nickel oxide hydroxide layer on a nickel support is used.

A nickel surface in contact with an alkaline solution is spontaneously covered with nickel hydroxide [28]. Hereby α-nickel hydroxide is formed which on aging is converted to the β-form [29]. At about 0.63 V (NHE) α-nickel hydroxide is oxidized to γ-nickel oxide hydroxide. At a 80 mV more positive potential the β-form is transformed to β-nickel oxide hydroxide [30]. In the cathodic scan nickel oxide hydroxide is reversibly reduced to nickel hydroxide at about 0.54 V. In multiple scan cyclovoltammetry the current increases with each scan indicating an increase of the active electrode surface.

The electrochemistry and cristallography of the nickel oxides have been extensively investigated in connection with the improvement of storage batteries [31]. In-situ UV/visible reflectance spectroscopy [32a] and laser raman spectroscopy [32b] of the nickel hydroxide and nickel oxide hydroxide layers indicate that nickel oxide hydroxide has more an oxide structure and therefore should be better written as $Ni_2O_3 \cdot xH_2O$. The easy mutual conversion of nickel hydroxide to nickel oxide hydroxide is probably due to the same brucite-type structure for both oxides [33].

The electrochemical kinetics for the oxidation of alcohols and amines at the nickel hydroxide electrode has been studied by Fleischmann and coworkers [12, 34], Robertson [35] and Vertes and coworkers [36]. In the oxidation of ethanol a kinetically controlled plateau current is found, which depends at high OH^--concentrations on the ethanol concentration. The oxidation peak for the nickel hydroxide oxidation is separated from that for the organic species [35, 36b]. The reduction peak for nickel oxide hydroxide is found also in presence of an oxidizable organic species [35, 36b]. In 50% t-butanol:50% water the relative oxidation currents were determined for the alcohols ethanol: 1,6-hexanediol: 2-propanol: 1-propanol: 1-butanol: 1-hexanol to be 32:19:16:4.5:1 [37]. This demonstrates the decreasing reactivity of the alcohol with increasing chain length. As can be seen from 1,6-hexanediol, the diol is faster oxidized than the corresponding monoalcohol, indicating that the ratio of carbon atoms to OH-groups determines the reactivity of the alcohol. The isotope effect for the oxidation has been found to be $k(CH_3OH)/k(CD_3OH) = 7.0$ [34].

Cyclovoltammetry at the nickel electrode is also possible in electrolytes with a high portion of organic cosolvent, e.g. up to 67% t-BuOH/33% water [38] or 30% dioxan/70% water or 50% tetrahydrofuran/50% water [39]. In the first electrolyte the currents for the oxidation of different para-substituted benzylalcohols have been measured. Here $\lg i_L/n$ vs. σ (i_L = limiting current, σ = Hammett substituent constant) shows that the rate is independent of the electron donating ability of the para-substituent. This indicates an uncharged transition state for the chemical step [38]. Also the higher rates for benzyl- and furfurylalcohol compared to ethanol point to a radical pathway [40]. Furthermore for the oxidation with nickel peroxide, which is a chemically prepared nickel oxide hydroxide, a radical pathway has been secured [41].

Thus the essential steps of a mechanism (Eq. (2)), proposed by Fleischmann and coworkers [12, 34], are generally accepted although some mechanistic details are controversially discussed [35, 36b].

$$
\begin{array}{rcll}
OH^- + Ni(OH)_2 & \xrightarrow{\text{fast}} & NiOOH + H_2O + e^- & (a) \\
RCH_2OH_{sol} & \longrightarrow & RCH_2OH_{ads} & (b) \\
RCH_2OH_{ads} + NiOOH & \xrightarrow{\text{rds}} & R\dot{C}HOH + Ni(OH)_2 & (c) \\
R\dot{C}HOH + H_2O & \longrightarrow & RCO_2H + 3\,e^- + 3\,H^+ & (d) \\
R\dot{C}HOH + 3\,NiOOH + H_2O & \longrightarrow & RCO_2H + 3\,Ni(OH)_2 & (d')
\end{array}
\qquad (2)
$$

The individual steps are: (a) fast electrochemical conversion of nickel hydroxide to nickel oxide hydroxide, (b) adsorption of the alcohol at the nickel oxide hydroxide surface, whereby a decreasing adsorption with increasing chain length causes a decrease in the rate of oxidation. In the rate determining step (c) hydrogen is abstracted from the adsorbed alcohol by nickel oxide hydroxide to form a α-hydroxymethyl radical, which is either directly (d) or indirectly (d') oxidized to the carboxylic acid.

This is the mechanism of an indirect electrolysis, where the nickel oxide hydroxide acts as an electrocatalyst that is continuously renewed. Some observations, however, are not consistent with this mechanism. The addition of an oxidizable alcohol should lead to an increase of the current for the nickel hydroxide oxidation and a decrease for its reduction [42)]. This is not the case. The currents for nickel hydroxide and nickel oxide hydroxide remain unchanged, whilst at more anodic potential a new peak for the alcohol oxidation appears. This problem has also been addressed by Vertes [36b)].

As aldehydes are not detected in aqueous sodium hydroxide, they must be rapidly further oxidized. Possibly they form diolates, which should be strongly adsorbed at the electrode and have been identified as intermediates in the anodic oxidation of aldehydes [43)]. On the other hand it is questioned wether aldehydes are intermediates at all in the further oxidation of the α-hydroxymethyl-radical to the carboxylic acid [36a, 44)].

For reactive and short chain alcohols the nickel hydroxide electrode and nickel peroxide exhibit the same reactivity (Table 4).,The oxidation of long chain alcohols, which is possible in good yields at the electrode has not been reported for nickel peroxide. The close similarity in yield and products indicates that in both oxidations the same reagent is effective.

Table 4. Comparison of yields in the chemical (nickel peroxide) and anodic oxidation (nickel hydroxide electrode) of primary alcohols

Alcohol	Yield (%) with	
	Nickel peroxide [9)] (30 °C)	Nickel hydroxide electrode (25 °C)
Benzylalcohol	93	86
Furfurylalcohol	90	79
1-Butanol	85	64 (85, 70 °C)
1-Octanol	59	65 (89, 70 °C)

For ethanol and 1-propanol the oxidation at copper oxide electrodes gives similar yields as at the nickel hydroxide electrode [12)]. However, for 1-butanol the yields are already less satisfactory (copper oxide 77%, 25 °C; silver oxide 26%, 25 °C) [39)]. Copper and silver anodes tend to corrode in alkaline medium, which, however, may be limited by the use of a divided cell [39)].

Besides in electrosynthesis the nickel hydroxide electrode has also been applied in trace analysis. So in the determination of ethanol down to the 10^{-7} g [45a)] or of amines and amino acids in the ng-scale [45b)].

2.2 Unsaturated Primary Alcohols

The oxidation of benzylic type alcohols and alkenols with the double bond more than three carbon atoms distant from the hydroxyl group leads to unsaturated carboxylic acids in good yields (Table 5). 2- and 3-alkenols gave poor to moderate yields due to a partial oxidative splitting at the double bond. 3-Octyn-1-ol is considerably cleaved between C1 and C2, whilst 2-propynol forms propynoic acid in satisfactory yields.

Table 5. Oxidation of unsaturated alcohols at the nickel hydroxide electrode to carboxylic acids [15]

Alcohol	Electrolyte[a]	T (°C)	Yield (%)
Benzylalcohol	A	25	86
Furfurylalcohol	A	25	79
E-4-Methyl-2-penten-1-ol	A	5	10[b]
Z-3-Hexen-1-ol	B	25	34
E-4-Hepten-1-ol	A	25	82
E-4-Nonen-1-ol	A	70	68
2-Propynol	A	5	51[c]
3-Octyn-1-ol	A	25	28[d]

[a] A: 1 M aqueous NaOH; B: 0.18 M KOH in 50% t-BuOH: 50% H_2O.

[b] Together with 2-methylpropanoic acid.

[c] Divided cell.

[d] Mixture of 3-octynoic acid and 2-heptynoic acid.

In mixed organic solvents or in an emulsion electrolysis benzylic type alcohols can be converted to aldehydes as main product (Table 6). In emulsion electrolysis it seems reasonable that the intermediate aldehyde is extracted into the organic layer and thus prevented from further oxidation. In mixed organic solvents the desorption of species with intermediate degree of oxidation is assumed. A more neutral electrolyte improves the aldehyde yield too [38].

Table 6. Oxidation of unsaturated primary alcohols to aldehydes at the nickel hydroxide electrode

Alcohol	Electrolyte[a]	Yield (%)		
		Aldehyde	Carboxylic acid	Ref.
Benzylalcohol	A	45	21	[38]
Benzylalcohol	B	81[b] (85)[c]	4	[46]
Benzylalcohol	C	91	—	[38]
4-Methoxybenzylalcohol	A	83	9	[38]
4-Methoxybenzylalcohol	B	79[b] (83)[c]	6	[46]
2-(4-Methoxyphenyl)-ethanol	A	—	90	[38]
Cinnamylalcohol	A	60	40	[38]
3-Phenylpropan-1-ol	A	—	70	[38]
Furfurylalcohol	B	73[b] (78)[c]	11	[46]

[a] A: 0.1 M KOH in 67% t-BuOH: 33% H_2O; B: 14g K_2CO_3, 225 ml H_2O, 225 ml petrolether; C: 0.1 M aqueous $NaClO_4$.

[b] Determined as 2,4-dinitrophenylhydrazone.

[c] Determined by glc.

2.3 Secondary Alcohols

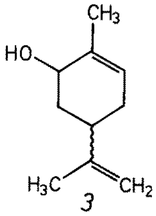
The oxidation of various secondary alcohols, including the allylic alcohols carveol (*3*) and β-ionol (*4*), leads to the corresponding ketones in 70–80% yield (Eq. (3), Table 7). Oxidation of (—)-carveol (*3*) with nickel peroxide (2.5 eq., 50 °C, benzene) yielded only 33% ketone.

$$R^1R^2CHOH \xrightarrow{NiOOH,\ -e} R^1R^2C{=}O \qquad (3)$$

Table 7. Oxidation of secondary alcohols to ketones at the nickel hydroxide electrode

Alcohol	Electrolyte[a]	T (°C)	Yield (%)	Ref.
2-Propanol	—	—	90	12)
1-Methoxy-2-propanol	A	—	57	47)
2-Pentanol	A	25	72	48)
2-Hexanol	A	25	73	48)
3-Hexanol	B	25	70	15b)
3-Heptanol	A	25	69	48)
3-Octanol	C	60	54	48)
Cyclohexanol	B	25	80	15b)
2-Ethylcyclohexanol	B	25	72	15b)
Borneol	B	25	72	15b)
Isoborneol	B	25	81	15b)
(—)-Carveol(*3*)	B	25	75	15b)
β-Ionol(*4*)	B	25	59	15b)
β-Damascol(*5*)	B	25	9	15b)
1-Phenylpropyn-1-ol(*6*)	B	5	4	15b)

[a] A: 30 mmol KOH, 280 ml H_2O; B: 0.1 M KOH, 50% t-butanol: 50% H_2O; C: 20 mmol Na_2CO_3, 450 ml H_2O, 100 ml t-Butanol.



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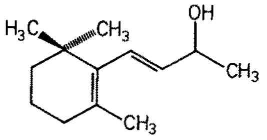

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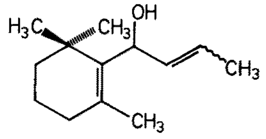

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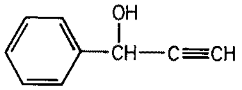

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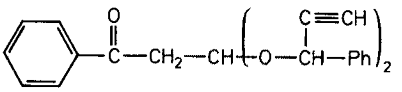

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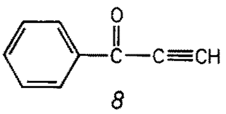

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In a side-reaction 10–15% carboxylic acids are produced by oxidative cleavage of the ketone enolates. The cleavage is favoured by higher temperatures; e.g. cyclohexanol leads to 80% cyclohexanone and 16% adipic acid at 25 °C, whilst at 80 °C 5% ketone and 42% diacid are found. These acidic by-products are easily separated, since they remain in the alkaline solution during workup. The oxidation of *6* gave the acetal *7* as main product (28%) together with 4% of the ketone *8* and 56% of unchanged *6*. The acetal *7* is probably formed by nucleophilic addition of the alcohol *6* at the activated triple bond of ketone *8*.

The oxidation rate of the ketones decreases with increasing steric hindrance. Whilst β-ionol (*4*) is easily oxidized, β-damascol (*5*), where the hydroxy group is shielded by three adjacent methyl groups yields only 9% ketone. In co-electrolyses 2-ethylcyclohexanol was ten times and borneol five times less reactive than cyclohexanol. Small differences in reactivity were observed between *cis*- and *trans*-2-ethylcyclohexanol (rel. rates 1.6:1) and between borneol and isoborneol (1.2:1). These results indicate that for a satisfactory oxidation both the OH-group and the adjacent CH-bond should be readily accessible. Secondary alcohols are only slightly less reactive than primary alcohols. In the co-electrolysis of 3-hexanol with 1-hexanol the primary alcohol is 1.5 times faster oxidized 39).

2.4 Oxidation of 1,ω-Diols and Vicinal Diols

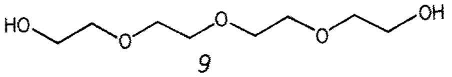
From 1,ω-diols the corresponding dicarboxylic acids are obtained in good yields (Eq. (4), Table 8).

$$HOCH_2{-}(CH_2)_n{-}CH_2OH \xrightarrow{NiOOH,\ -e} HO_2C{-}(CH_2)_n{-}CO_2H \qquad (4)$$

Table 8. Oxidation of 1,ω-diols to dicarboxylic acids at the nickel hydroxide electrode

Diol	Electrolyte[a]	T (°C)	Yield (%) of dicarboxylic acid	Ref.
1,6-Hexanediol	A	25	84	15b)
1,10-Decanediol	A	80	85	15b)
Z-4-Octene-1,8-diol	A	80	80	15b)
2-Butyne-1,4-diol[b]	A	20	55	15b)
2-Ethyl-1,6-hexanediol	A	80	78	15b)
Diethylene glycol	C	—	78–88	49a)
3-Methylpentane-1,3,5-triol	—	—	70–85	50)
3,5,6-Trichloro-2-(2-hydroxyethoxy)-pyridine	C	—	—	49b)
Tetraethylene glycol (*9*)[c]	A	5	50	15b)

[a] A: 1 M aqueous NaOH; B: 0.3 M KOH in 50% t-BuOH: 50% H_2O; C: Aqueous NaOH.
[b] Divided cell.
[c] Controlled potential electrolysis at +0.6 V vs. Hg/HgO 1 M NaOH.



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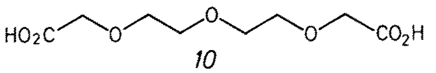
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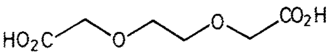
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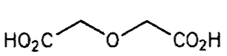
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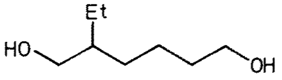
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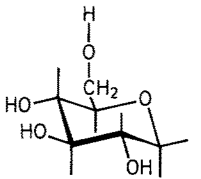
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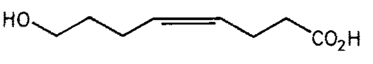
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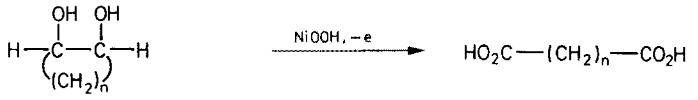
Oxidation of tetraethylene glycol (*9*) results in a 50% yield of the trioxa acid *10*. Additionally 16% of the dioxa acid *11* and 3% of diglycolic acid (*12*) are formed by probably an oxidative ether cleavage.

Diols are faster oxidized than the corresponding monoalcohols as the voltammetrically determined relative rates have already indicated. In preparative electrolysis 1,10-decane diol is about five times faster oxidized than 1-decanol.

In 2-ethyl-1,6-hexanediol (*13*) the less hindered 6-hydroxy group (19%) is oxidized three times faster than the 1-hydroxy group (6%). The selectivity resembles that one found for monoalcohols, e.g. 1-octanol:2-ethyl-hexanol = 3:1. However, in case of the diol additionally 37% 2-ethyl-hexane diacid are formed and 37% *13* recovered. Obviously adsorption after oxidation of the first hydroxy group of the diol facilitates the oxidation of the second in a cooperative manner. Similarly 1,6-hexanediol is converted with 4 Faraday/mol to 26% 6-hydroxyhexanoic acid, 34% adipic acid and 35% diol[51]. In the emulsion electrolysis (cyclohexane as organic cosolvent) of 1,10-decanediol at low conversion mainly 10-hydroxydecanal is obtained[48]. Remarkable results with polyols like α-methyl-D-(+)-glucose (*14*), glucose and sucrose indicate that in these carbohydrates the primary OH-group can be selectively oxidized in presence of the secondary OH-group to yield predominantly the aldehyde[52].

Compared to the anodic oxidation of Z-4-octene-1,8-diol (80%, Table 8) its oxidation with pyridinium dichromate[53] in dimethyl formamide gave as the best chemical alternative only 65% diacid[15b]. Nickel peroxide oxidation under mild conditions (1.3 eq. peroxide, 25 °C, 1 M NaOH) led to 45% hydroxy acid *15*, whereas under more vigorous conditions (3 eq. peroxide, 80 °C, 1 M NaOH) maleic acid was formed[15b].

Vicinal diols are cleaved with high yields to carboxylic acids (Eq. 5, Table 9). Thereby *cis*- and *trans*-1,2-cyclooctanediol react at about the same rate. In the cleavage of 1,2:5,6-di-O-isopropylidene-D-mannitol (*16*) to 2,3-O-isopropylidene-R-glyceric acid (*17*) 98% of the optical purity is retained.

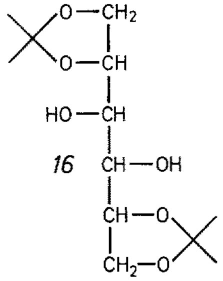


$$\text{H}-\underset{\frown(\text{CH}_2)_n\frown}{\overset{\text{OH}}{\text{C}}-\overset{\text{OH}}{\text{C}}}-\text{H} \xrightarrow{\text{NiOOH}, -e} \text{HO}_2\text{C}-(\text{CH}_2)_n-\text{CO}_2\text{H} \qquad (5)$$

Table 9. Cleavage of vicinal diols to carboxylic acids at the nickel hydroxide electrode [54]

Vicinal diol	Electrolyte[a]	T (°C)	Yield (%) of dicarboxylic acid
cis-1,2-Cyclooctanediol	A	25	80
trans-1,2-Cyclooctanediol	A	25	77
cis-1,2-Cycloheptanediol	A	25	81
1-Methyl-*trans*-1,2-cyclohexanediol	A	25	72[b]
exo,exo-2,3-norbornanediol	A	25	72
1,2:5,6-Di-O-isopropylidene-D-mannitol (*16*)	B	30	70[c]

[a] A: 0.1 M aqueous potassium carbonate; B: 0.1 M aqueous potassium hydroxide.
[b] 6-Ketoheptanoic acid.
[c] Isolated as potassium salt with 98% optical purity.



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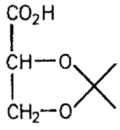

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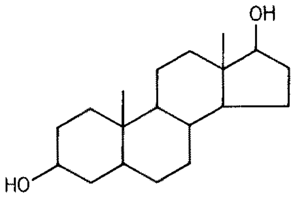
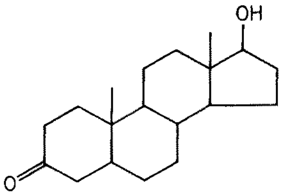
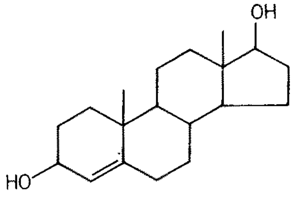
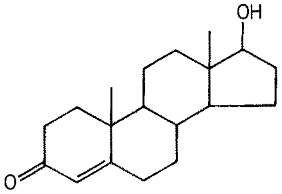
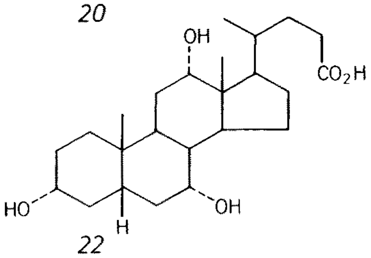
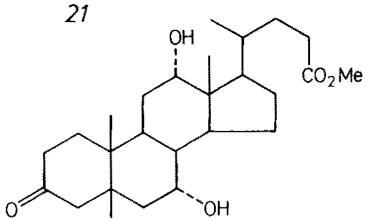
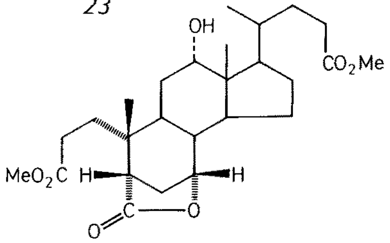
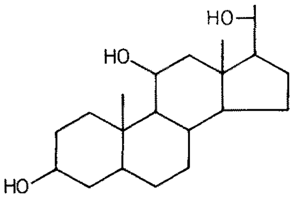
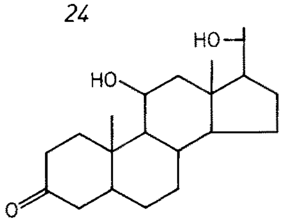
2.5 Oxidation of Steroidal Alcohols

In steroidal alcohols the 3α- or 3β-hydroxy group (*18*, Table 10) is selectively oxidized in the presence of the 17β-hydroxy group. The yield obtained corresponds to that of the Oppenauer-oxidation [55], which is the most selective oxidation method for the 3-OH group.

Additional activation of the 3-OH group by an allylic double bond increases the selectivity and leads to 50% testosterone (*21*). Cholic acid is oxidized exclusively at the 3α-position without any attack at the 7α- and 12α-hydroxy groups. Comparable selectivities have been reported for oxidations by silver carbonate on celite [56] and by molecular oxygen with a platinum catalyst [57]. The yield of *23* is however lowered by a competing reaction to the lactone *24*; this is formed by oxidative cleavage of the C3—C4 bond, followed by lactonization during work-up.

The selective oxidation of the 3β-hydroxy group in the presence of 11β- and 20β-hydroxy groups in the triol *25* is unprecedented. In the Oppenauer-oxidation of similar compounds the 3β-OH group is oxidized in only 30% yield [55]. The remarkable selectivity obtained may be due to the fact that the 20β-hydroxy group is placed on the β-side of the steroid, remote from the electrode, which probably attacks from the less hindered α-side.

Table 10. Selective oxidation of hydroxy steroids at the nickel hydroxide electrode [15b)]

Hydroxy steroid[a]	Product	Yield (%)
 [b] 18	 19	28
 20	 21	50
 22	 23	38
	 24	22
 25	 26	78

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[a] Elektrolyte: 0.01 M KOH in 50% t-BuOH: 50% H_2O.

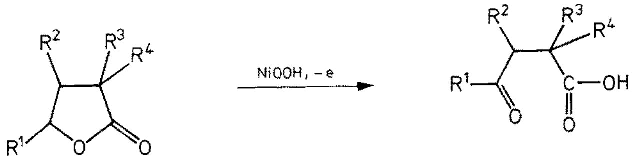
[b] 5α-Androstane-3α,17β-diol gave similar results.

At the nickel hydroxide electrode the reactivity of the different hydroxy groups in steroids, which have been examined up to now, follows the order: 3β-OH ≈ 3α-OH > 17β-OH ≫ 20β-OH > 11β-OH.

2.6 Oxidation of Lactones

γ-Hydroxy acids are usually oxidized under basic conditions by potassium permanganate [58] or after formation of the alkali hydroxycarboxylate by ruthenium tetroxide [59]. These oxidations, however, have disadvantages. Ruthenium tetroxide is toxic and expensive, potassium permanganate gives only poor to fair yields.

Furthermore these reagents can attack ethers, double bonds and aromatic rings in more functionalized compounds. The nickel hydroxide electrode is a suitable reagent to overcome these difficulties [60]. The necessary alkaline electrolyte opens the lactone ring to the oxidizable hydroxycarboxylate. The nickel hydroxide electrode tolerates double bonds, ethers and aromatic rings and leads in good to excellent yields to ketocarboxylic acids (Eq. (6), Table 11).



(6)

Table 11. Oxidation of lactones to ketocarboxylic acids at the nickel hydroxide electrode [60]

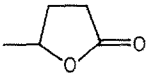
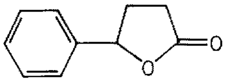
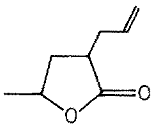
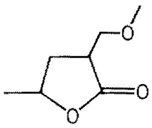
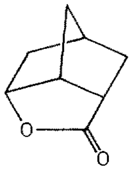
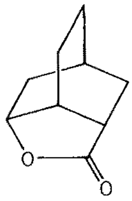
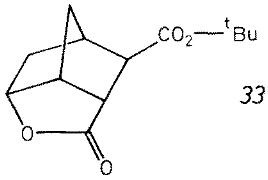
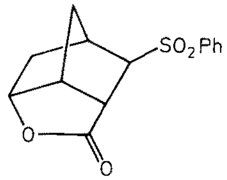
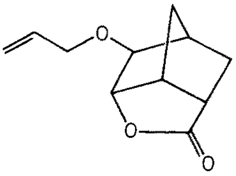
Lactone		Electrolyte[a]	Yield (%) Ketocarboxylic acid
	27	A	94
	28	B	93
	29	B	97
	30	A	92
	31	A	91

Table 11 (continued)

	*32*	A	96
	*33*	C	93
	*34*	D	95
	*35*	C	71

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[a] T = 30 °C; A: 01 N aqueous potassium hydroxide; B: 0.1 N aqueous potassium hydroxide: t-butanol,1:1; C: 0.1 N aqueous potassium carbonate; D: 0.5 N aqueous sodium bicarbonate: t-butanol, 1:1.

2.7 Oxidation of Aldehydes

Aromatic and aliphatic aldehydes can be oxidized after careful and individual optimization of the reaction conditions to carboxylic acids (Eq. (7), Table 12). With aromatic aldehydes yields are excellent, with aliphatic aldehydes good to satisfactory. The electrolyte has to be less alkaline than normal to suppress the aldol condensation. 2-Phenylpropanol is best oxidized at low temperatures to render the cleavage to benzoic acid more difficult, at 70 °C benzoic acid becomes main product (47%). Double bonds in γ,δ- or even α,β-position are not touched in the oxidation.

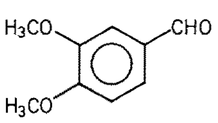
$$RCH{=}O \xrightarrow{\text{NiOOH, }-e} RCO_2H \tag{7}$$

Table 12. Oxidation of aldehydes to carboxylic acids at the nickel hydroxide electrode [48]

Aldehyde	Electrolyte[a]	T (°C)	Yield (%) of carboxylic acid
3,4-Dimethoxybenzaldehyde (*36*)	A	25	85
2,6-Dichlorobenzaldehyde (*37*)	B	60	98
2-Furancarbaldehyde (*38*)	C	−2	62(84)[b]
Hexanal	D	40	78
2-Phenylpropanal	E	0	47(80)[b]
Z-4-Heptenal (*39*)	F	25	68
3-Cyclohexene-1-carbaldehyde (*40*)	E	2	76
(S)-4-Isopropenylcyclohex-1-ene-1-carbaldehyde (*41*)	D	0	57

[a] A: 400 ml H_2O, 50 ml t-BuOH, 50 mmol KOH; B: 450 ml H_2O, 60 ml t-BuOH, 100 mmol KOH; C: 500 ml H_2O, 21 g K_2CO_3; D: 450 ml H_2O, 5 g K_2CO_3, 3 g $NaH_2PO_4 \cdot 2\,H_2O$; E: 450 ml H_2O, 7 g K_2CO_3; F: 300 ml H_2O, 230 ml t-BuOH, 4 g K_2CO_3.

[b] Yield calculated on converted starting compound.



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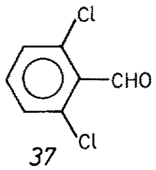

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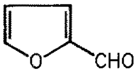

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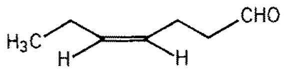

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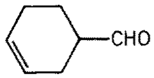

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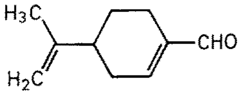

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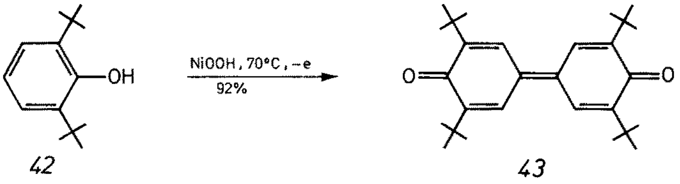
2.8 Oxidation of Carboxylic Acids

Unsubstituted aliphatic carboxylic acids are only very slowly further oxidized to the lower homologous acid; in the oxidation of primary alkanols less than 2% of this acid are found. However, with substituted carboxylic acids the cleavage can become the main reaction. Thus anodic oxidation of phenylacetic acid at the nickel hydroxide electrode leads to 87% benzoic acid [48]. Cleavages of similar to a lesser extent are observed with amino acids (Chapter 3.1) or β-alkoxy substituted acids (Chapter 2.4).

2.9 Oxidation of Aromatic Phenols

For the oxidation of 2,6-di-t-butylphenol (*42*) to diphenoquinone (*43*) nickel peroxide has proved to be the most suitable reagent [61]. At the nickel hydroxide electrode *42* can be oxidized in 92% yield to *43* (Eq. (8)). For this conversion a temperature of 50–70 °C is necessary, at 25 °C the oxidation is very slow.

p-Cresol and 4-t-butylphenol are oxidized slowly at 70 °C to numerous, not yet characterized compounds [37].



(8)

3 Oxidation of Nitrogen-containing Compounds

3.1 Oxidation of Primary Amines

Primary amines can be dehydrogenated under mild conditions and in high yields to nitriles at the nickel hydroxide electrode (Eq. (9)). Short chain and reactive amines are already oxidized at 5 °C, whilst long chain amines need somewhat higher temperatures. Diamines are converted smoothly to dinitriles (Table 13).

$$RCH_2NH_2 \xrightarrow{NiOOH,\ -e} RC{\equiv}N \tag{9}$$

Table 13. Oxidation of primary α-unbranched amines to nitriles at the nickel hydroxide electrode

Amine	Electrolyte[a]	T (°C)	Yield (%) of nitrile or dinitrile	Ref.
Ethylamine	—	—	68	63)
1-Propylamine	—	—	84	12)
1-Butylamine	A	30	85	64 (12))
1-Hexylamine	B	5	72	64)
1-Octylamine	C	40	95	64)
1-Decylamine	C	60	91	64)
Benzylamine	C	40	90	64)
Furfurylamine	A	5	86	64)
1,6-Diaminohexane	C	40	93	64)
1,10-Diaminodecane	C	40	90	64)
1,12-Diaminododecane	C	40	88	64)
6-Aminohexanoic acid	D	40	97	64)

[a] A: 0.1 N aqueous potassium hydroxide; B: 0.1 N potassium hydroxide in acetonitrile:water, 1:1; C: 0.1 N potassium hydroxide in t-butanol:water, 1:1; D: 0.3 N potassium hydroxide in t-butanol: water, 1:1.

The lower amines have been oxidized in similar yields to nitriles at silver oxide and copper oxide anodes [12]. Activation of the electrode by deposition of a nickel hydroxide oxide layer is less essential than with alcohols due to the higher reactivity of the amines. Only for amines with longer chain length activation prior to electrolysis increases the yield.

As can be seen from current-voltage curves the lower amines are about 10 times faster oxidized than the corresponsing alcohols [12,37]. In a competitive preparative electrolysis (0.3 M potassium hydroxide in 50% t-butanol:50% water, 40 °C) 1-decylamine is 5.3 times faster oxidized than 1-decanol [62]. The electrochemical kinetics have been investigated [12,35,63,65] and the following mechanism proposed (Eq. (10)).

$$\begin{array}{ll} CH_3CH_2{-}NH_2 \xrightarrow{NiOOH,\,-e} CH_3CH{=}NH & (a) \\ CH_3CH{=}NH \xrightarrow{NiOOH,\,-e} CH_3C{\equiv}N & (b) \\ CH_3CH{=}NH \xrightarrow{H_2O} CH_3CHO \xrightarrow{-e} CH_3CO_2H & (c) \\ CH_3CH{=}NH \xrightarrow{CH_3CH_2NH_2} CH_3CH{=}NCH_2CH_3 & (d) \end{array} \qquad (10)$$

The individual steps are: (a) the anodically formed nickel oxide hydroxide dehydrogenates the amine to an imine; (b) the imine is further dehydrogenated to the nitrile; (c) competing with the second dehydrogenation are the hydrolysis of the imine to an aldehyde and its further oxidation to an acid or (d) the condensation with the starting amine to form an azomethine.

The yields with the nickel hydroxide electrode and nickel peroxide are comparable (Table 14), which again demonstrates the similarity of the two reagents. Remarkable is however, that at the nickel hydroxide electrode the conversion occurs at much lower temperatures and that the diamine is anodically oxidized in much better yield. With lead tetraacetate as oxidant the yields are lower and side products are found in major amounts [66].

Table 14. Comparison of the oxidation of primary amines with the nickel hydroxide electrode and nickel peroxide

Amine	Yield, %, (°C) in the oxidation with	
	Nickel peroxide	Nickel hydroxide electrode
1-Hexylamine	73(80)	72(5)
1-Octylamine	96(80)	70(5), 95(40)
1,6-Diaminohexane	23(80)	93(40)
Furfurylamine	63(5)	86(5)
Benzylamine	79(60)	85(5), 90(40)

$$R^1R^2CH{-}NH_2 \xrightarrow{NiOOH,\,-e} R^1R^2C{=}O \qquad (11)$$

α-Branched primary amines are oxidized to ketones (Eq. (11), Table 15). Intermediates appear to be imines, which are hydrolyzed to the ketone. In the case of the slowly hydrolysing benzophenoneimine (*45*) from (diphenylmethyl)amine (*44*)

Table 15. Oxidation of α-branched primary amines at the nickel hydroxide electrode

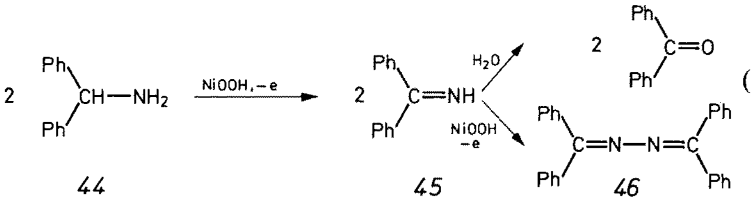
Amine	Electrolyte[a]	T (°C)	Yield (%) of ketone	Ref.
2-Propylamine	—	—	80	[12,67]
Cyclohexylamine	A	20	68(75)[b]	[68]
2-Aminooctane	B	30	66(75)[b]	[68]
α-Phenethylamine	B	30	62(68)[b]	[68]
(Diphenylmethyl)amine (*44*)	B	60	66[c]	[68]

[a] A: 0.1 M aqueous potassium hydroxide; B: 0.1 M potassium hydroxide in 50% water: 50% t-butanol.

[b] In parenthesis gaschromatographic yield.

[c] Additionally 17% benzophenoneazine (*46*).

an indirect evidence of the intermediate is found by its dimerization product benzophenoneazine (*46*) that is isolated in 17% yield (Eq. (12))[68].

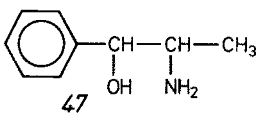


(12)

44 45 46

The yields in these oxidations are comparable to those with potassium permanganate[69] or the more exotic reagent di-t-butylquinone[70].

The vicinal aminoalcohol D,L-norephedrine (*47*) is cleaved to benzoic acid (67%) and benzaldehyde (25%) in 0.1 M potassium hydroxide (10 °C). Under less alkaline conditions (pH 7.5) the cleavage reaction is suppressed, but now a greater number of products with an azomethine, probably *48*, as major component (37%) is obtained.



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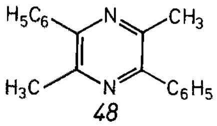


48

The α-amino acid alanine is cleaved to acetonitrile[71], whilst the ε-amino acid 6-aminohexanoic acid is dehydrogenated in excellent yield to the cyanocarboxylic acid.

3.2 Oxidation of Secondary and Tertiary Amines

Secondary amines are less selectively converted than primary amines. With diethylamine 46% acetonitrile, 3% acetaldehyde and 36% acetic acid are obtained; with pyrrolidine 50% of the trimer of 3,4-dihydro-2 H-pyrrole are formed[12]. In our hands[68] controlled potential electrolysis (0.39 V vs. SCE) of pyrrolidine formed moderate yields of 3-cyanopropionic acid, succinic acid and the lactam of 4-aminobutyric acid. With piperidine a remarkable dependence of the product distribution on the reaction conditions can be seen. A current controlled electrolysis (0.3 M aqueous potassium hydroxide, 30 °C) leads to 22% 4-cyanobutanoic acid and 41% glutaric acid, whilst in a potential controlled electrolysis (0.39 V vs. SCE) 63% of the cyano acid and only 7% of glutaric acid are formed[68]. Controlled current electrolysis converts 2-methylpiperidine to at least eight products in low yields, 5-ketohexanoic acid, 4-cyanopropanoic acid and 6-cyano-2-hexanone are the major components. Controlled potential electrolysis only slightly increases the selectivity in favor of the 5-ketohexanoic acid[68]. 2,6-Dimethylpiperidine leads to five products in low yields with 1-methyl-1-cyclohexen-3-one, the aldol product of 2,6-heptanedione as major component[68].

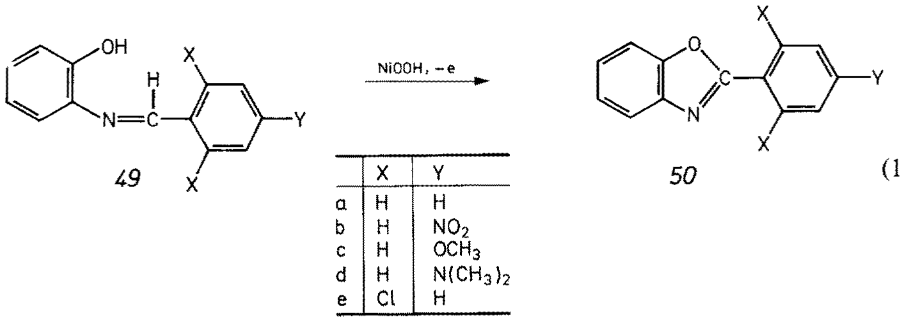
Diphenylamine is only slowly converted even at higher temperatures (50% water: 50% t-butanol, 0.1 M KOH, 50 °C) and there it yields thermal decomposition products, that possibly originate from tetraphenylhydrazine[68].

The tertiary amine tribenzylamine is inert to oxidation even at 85 °C (0.1 M KOH, 50% t-butanol: 50% water)[62].

3.3 Miscellaneous Nitrogen-Compounds

3.3.1 Oxidation of 2-(Benzylideneamino)-phenols

2-(Benzylideneamino)-phenols (*49*) can be oxidatively cyclized to form 2-phenyloxazols (*50*) (Eq. (13)) by direct anodic oxidation[72], by $Pb(OAc)_4$[73], Ag_2O[74] and nickel peroxide[75]. The oxidation of *49* proceeded disappointingly in t-butanol: water at the nickel hydroxide electrode. *50* was isolated only in traces, benzaldehyde was the major product, which indicated that *49* hydrolysed under the reaction conditions. The hydrolysis could effectively be suppressed by electrolysis in an emulsion of water and cyclohexane, where the portion of water was kept low. The temperature was around 70 °C to secure a fast oxidation. With these reaction conditions good yields of *50* were obtained (Table 16).



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50

(13)

	X	Y
a	H	H
b	H	NO_2
c	H	OCH_3
d	H	$N(CH_3)_2$
e	Cl	H

Only the electrolysis of *49d* caused problems. The hydrolysis of *49d* is apparently so fast, that it could not be retarded even by emulsion electrolysis. With a phosphate buffer in a nearly neutral electrolyte the cleavage can be restricted but then the oxidation is too slow.

Table 16. Oxidation of 2-(Benzylideneamino)-phenols (*49*) to 2-Phenyloxazols (*50*) at the nickel hydroxide electrode

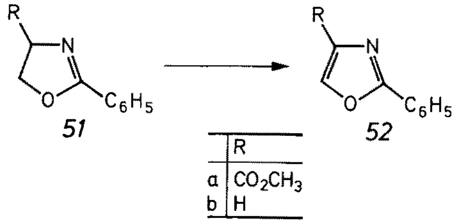
49	Yield of *50* by oxidation with						
	Nickel hydroxide electrode			Pt-Anode in CH_3CN	$Pb(OAc)_4$	Ag_2O	Nickel peroxide
	Electrolyte[a]	T (°C)	%	%[72]	%[73]	%[74]	%[75]
a	A	70	80	—	70	76	72
a	B	73	81	—	—	—	—
b[b]	C	65	70	80	80	80	73
c	D	75	70	85	75	92	72
d	E	35	9	84	40	—	66
e	F	25	73	—	—	—	—

[a] A: 70 mmol K_2CO_3, 50 ml H_2O, 450 ml cyclohexane; B: 70 mmol Na_2CO_3, 50 ml H_2O, 450 ml cyclohexane; C: 70 mmol K_2CO_3, 25 ml H_2O, 100 ml toluene, 200 ml cyclohexane; D: 20 mmol K_2CO_3, 25 ml H_2O, 450 ml cyclohexane; E: 30 mmol K_2CO_3, 20 ml H_2O, 450 ml cyclohexane; F: 20 mmol Na_2CO_3, 50 ml H_2O, 450 ml cyclohexane.

[b] Divided cell.

For the preparation of 2-phenyloxazols the nickel hydroxide electrode is an attractive alternative to other oxidation reagents (Table 16) especially with regard to the cost of reagents and simplicity of work-up.

2-Phenyloxazoline *51a* can be oxidized in 69% yield to 2-phenyloxazol *52a* (Eq. (14)) with nickel peroxide in cyclohexane[76]. At the nickel hydroxide electrode in 0.1 M aqueous NaOH, the conversion of *51b* to *52b* is only very low (6%).



	R
a	CO_2CH_3
b	H

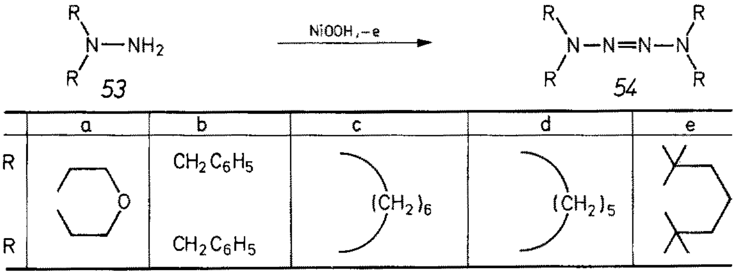
(14)

3.3.2 Oxidation of Hydrazine and its Derivatives

Hydrazine is already oxidized at a very cathodic potential[77]. With nickel peroxide hydrazine has been removed from waste water[78], which could be a possible application for the nickel hydroxide electrode.

Nickel peroxide in benzene converts phenylhydrazine mainly to biphenyl[79]. In the oxidation of phenylhydrazine at the nickel hydroxide electrode (0.1 M aqueous NaOH, 20% t-butanol) only low yields of biphenyl together with phenol, azobenzene and 4-aminodiphenyl are obtained.

The 1,1-disubstituted hydrazine *53a* is rapidly oxidized in high yield to *54a* at the nickel hydroxide electrode (Eq. (15), Table 17). The high reactivity of *53a* can be seen from the dissolution of the black nickel oxide hydroxide deposit at the anode, which indicates that *53a* is faster oxidized than the nickel oxide hydroxide layer is formed. This behaviour was found so far only with benzylamine or benzylalcohol. *53b* forms the tetrazine *54b* only in traces, main product is bibenzyl, also by electrolysis at —1 °C the portion of *54b* can not be increased. Possible intermediate in these oxidations is a nitrene, which has been identified in the dehydrogenative dimerization of *53e* with nickel peroxide [82]. Phenylselenic acid [80] and MnO_2 [81] are chemical oxidants, which convert *53* in similar yields to *54* as the nickel hydroxide electrode. Interestingly phenylselenic acid turns *53b* into the tetrazene *54b*, contrary to the nickel hydroxide electrode.



(15)

Table 17. Oxidation of 1,1-disubstitued hydrazines at the nickel hydroxide electrode and with other oxidants

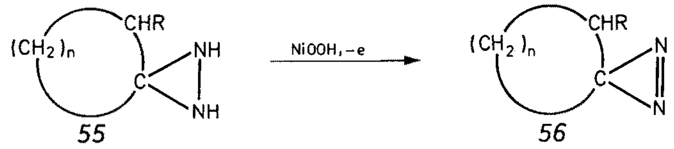
1,1-disubstituted hydrazine *53*	Dehydrodimer *54*, yield (%)					
	$Ni(OH)_2$-electrode [48]			Phenylselenic acid [80]	Selenium dioxide [80]	Manganese dioxide [81]
	Electrolyte[a]	T (°C)	%			
a	A	25	80	78	32	80
b	B	3	91[b]	75	39	49[b]
c	C	0	54	—	—	86
d	—	—	—	74	73	76

[a] A: 15 mmol K_2CO_3, 150 ml t-BuOH, 200 ml H_2O; B: 15 mmol K_2CO_3, 10 ml t-BuOH, 150 ml H_2O; C: 15 mmol K_2CO_3, 550 ml H_2O.

[b] Yield of bibenzyl.

The nickel hydroxide electrode is well suited for the oxidation of diaziridines (*55*) to diazirines (*56*) (Eq. (16), Table 18). The low isolated yield for *56b* compared to its high glc-yield is due to the volatility of the diazirine. The yields compare favorably with those found with silver oxide, the best chemical oxidant reported [83] for this conversion.

The benzoylhydrazone of benzaldehyde (*57*) is oxidatively cyclized at the nickel hydroxide electrode (0.1 M NaOH, 30% t-butanol: 70% water) to the oxadiazole *58*, however in only moderate yield (22%). Main product is benzoic acid (*59*) (60%); additionally a nickel complex (14%) with the probable structure *60* is found (Eq. (17)) [37]. With nickel peroxide in chloroform 30% *58* and 47% *60* are obtained [84].



(16)

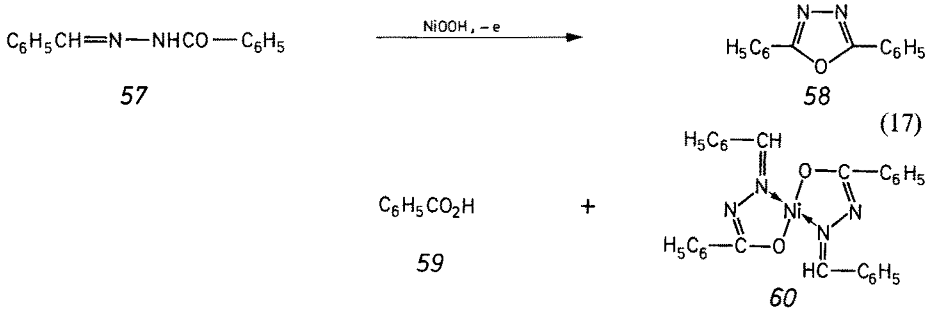
	a	b	c	d	e
R	H	CH_3	H	H	H
n	4	4	5	6	10

Table 18. Oxidation of diaziridines (*55*) to diazirines (*56*) at the nickel hydroxide electrode

Diaziridine *55*	Yield of diazirine (*56*)			
	$Ni(OH)_2$-electrode			Ag_2O
	Electrolyte[a]	T (°C)	%	%
a	A	0	72	75–85
b	B	5	58 (93)[b]	—
c	B	0	79	60–70
d	C	−5	65	80
e	D	25	27	9

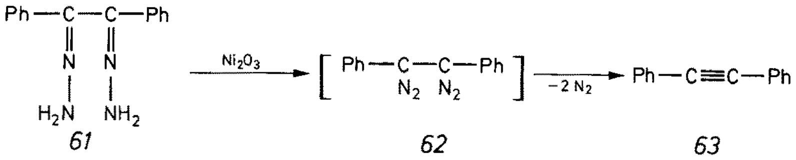
[a] A: 19 mmol Na_2CO_3, 150 ml H_2O, 50 ml t-BuOH; B: 15 mmol K_2CO_3, 250 ml H_2O; C: 87 mmol K_2CO_3, 250 ml H_2O; D: 15 mmol K_2CO_3, 200 ml H_2O, 180 ml t-BuOH.

[b] Yield by glc.

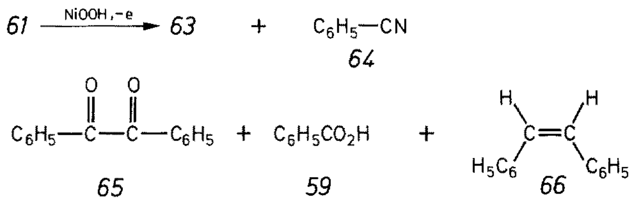


(17)

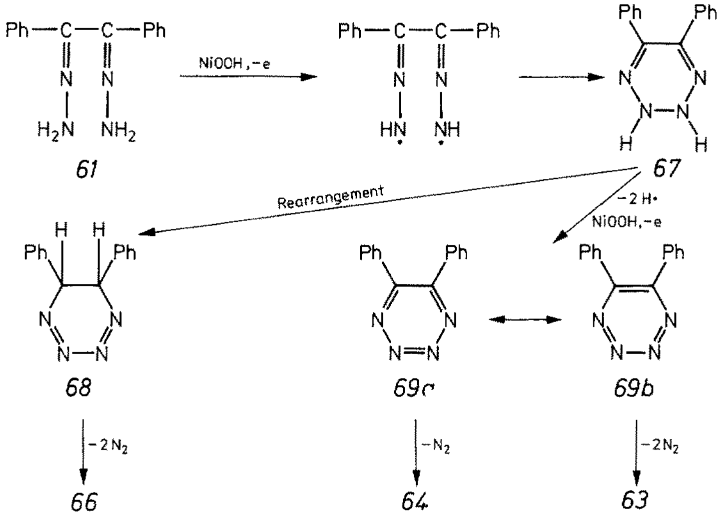
Benzilbishydrazone (*61*) is converted in 61 % yield to tolane (*63*) [85], as intermediate the 1,2-bisdiazo compound *62* is assumed (Eq. (18)) [86]. At the nickel hydroxide electrode tolane is only a minor (11 %), benzonitrile (*64*) the major product (44 %). Additionally 13 % benzil (*65*), 7 % benzoic acid (*59*) and 6 % *Z*-stilbene (*66*) are obtained (Eq. (19)) [68]. The products can be explained by the following hypothetical mechanism (Eq. (20)):



(18)



(19)



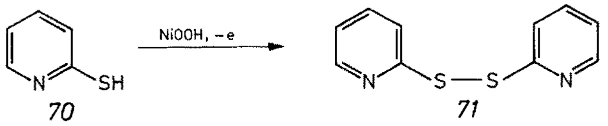
(20)

In the first step *61* is dehydrocyclized to *67*. This intermediate rearranges to *68*, that yields *66* by nitrogen elimination. Further oxidation dehydrogenates *67* to *69*, which decomposes to *63* and *64*. Benzil (*65*) is produced by hydrolysis, *59* by oxidative cleavage of *61*.

Under the same conditions the 6,7-dodecanedione bishydrazone is converted to 36% 6-dodecyne and 19% 6-dodecene (35% Z, 65% E)[68]. Remarkably no hexanonitrile is found in this case. In the oxidation of 1,2-bishydrazones to alkynes so far the chemical oxidants: copper(II)salts[87], mercuric oxide[88] or nickel peroxide[85] are superior to the nickel hydroxide electrode.

4 Oxidation of Thiols

2-Pyridinethiol (*70*) can be coupled at the nickelhydroxide electrode (75 °C, K_2CO_3 in water) in 91% yield to 2,2′-dithiodipyridine (*71*) (Eq. (21))[48]. An oxidation temperature above 70 °C is of advantage, at 65 °C the yield of *71* drops to 64%. The dimerization at the nickel hydroxide electrode leads to higher yield than the direct oxidation at the platinum electrode in methanol (78% *71*)[89]. *71* is used as condensation reagent for the preparation of peptides[90] and macrolides[91].



(21)

5 Comparison of the Nickel Hydroxide Electrode with Nickel Peroxide

Nickel peroxide and the nickel hydroxide electrode have both advantages and disadvantages, these have to be considered carefully, when the two oxidants are applied. The advantages of nickel peroxide are:

1) The chemical oxidation needs less equipment. For the electrolysis some accessories are necessary, that are not found in each laboratory.
2) Oxidation with nickel peroxide can be executed in protic and in aprotic solvents. With the nickel hydroxide electrode water has to be in the electrolyte, because otherwise the regeneration of nickel oxide hydroxide fails. This limits the choice of solvents.
3) Some substrates without a OH- or NH-group are not or only slowly oxidized at the nickel hydroxide electrode, whilst they are converted without problems with nickel peroxide. This is probably due to an insufficient adsorption of these substrates in the presence of the strongly adsorbing water.

Against that the oxidation at the nickel hydroxide electrode has the following advantages:

1) Apart from the activation of the anode no reagent has to be produced. Nickel peroxide, however, has to be prepared by oxidation of nickel(II)sulfate with sodium hypochlorite. Subsequently the reagent has to be carefully dried and the amount of active oxygen determined by iodometric titration. This must be kept in mind, because small amounts of alcohol need already a relative large amount of nickel peroxide, e.g. 100 mmol alcohol more than 75 g nickel peroxide. For that reason the use of the relative expensive, commercial nickel peroxide is restricted.
2) The voluminous nickel hydroxide, that is produced from the oxidant, tends to adsorb organic compounds. This renders the isolation of the product sometimes difficult. In the electrolysis, however, the oxidant forms only a thin layer at the anode surface, which causes no problems in the work-up.
3) The greatest advantage is the electrocatalytic mode of oxidation. In chemical oxidations the reduced form of the oxidant is obtained as by-product. This needs a careful waste treatment to prevent pollutional problems or it has to be regenerated in an additional reaction. At the nickel hydroxide electrode, however, nickel oxide hydroxide is continuously reformed from the hydroxide, so that only electric current is used as reagent. This makes this oxidation also of interest for technical applications.
4) Compared to other electrosyntheses oxidations with the nickel hydroxide electrode are especially simple. The electrolysis can be conducted without potential control and normally in an undivided cell. The high conductivity of the electrolyte allows high currents at low cell voltages.

6 Conclusions

The nickel hydroxide electrode has proved to be a versatile, inexpensive and facile applicable reagent, that allows an easy scale-up of the oxidation. It furthermore exhibits a remarkable selectivity to oxidize the sterically less shielded functional group. It is to be expected, that further applications of the electrode will be developed, which are partly guided by experiences with nickel peroxide oxidations. Furthermore additional chemoselectivities may be found by the use of other transition metal oxide electrodes, e.g. copper-, silver- and cobalt oxide electrodes.

7 Acknowledgement

The author wants to thank enthusiastic and skilled coworkers, that did part of the reviewed reactions, namely H. Kaulen, U. Feldhues, H. Ruholl, Z. Mester and R. Schneider. Furthermore support of the authors work by the Arbeitsgemeinschaft Industrieller Forschungsvereinigungen is gratefully acknowledged.

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Electrogenerated Bases

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Table of Contents

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James H. P. Utley

Cathodically generated anion-radicals and dianions often have useful basic properties. Such electrogenerated bases (EGB's) have been applied to organic synthesis and are either generated stoichiometrically *in situ* or *ex situ*, or, in some cases, in catalytic amounts. Especially useful are bases derived from azobenzenes, ethenetetracarboxylates, dioxygen, and fluoren-9-ylidenemethane derivatives. The method has been successful for a range of base-promoted alkylation reactions, ylid generation, carboxylations, and oxygenations (through carbanion-oxygen reactions).

Recent developments include the measurement of the kinetic basicities of EGB's by convenient electroanalytical methods. The establishment of a scale of EGB basicities will in turn facilitate the measurement of kinetic acidities of carbon acids.

1 Introduction.
Electrogenerated Bases — Definitions and Requirements

Electro-organic chemistry at the cathode is essentially that of radicals, radical-anions, carbanions, and polyanions (which range from dianions to hexa-anions [1]) (Scheme 1). The anions may behave as nucleophiles, bases, and as single electron reductants; the factors governing the competition between these roles are not yet fully understood.

$$M \underset{}{\overset{e}{\rightleftharpoons}} M^{\dot{-}} \overset{e}{\rightleftharpoons} M^{2-} \overset{ne}{\rightleftharpoons} M^{(n+2)-}$$

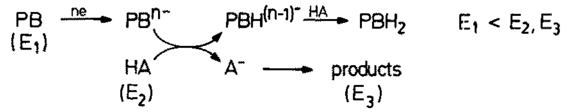
$$M^{+} \overset{e}{\rightleftharpoons} M^{\bullet} \overset{e}{\rightleftharpoons} M^{-} \overset{ne}{\rightleftharpoons} M^{(n+1)-}$$

Scheme 1

For about twenty years there has been a growing realisation that the deliberate cathodic generation of anionic bases, in aprotic solvents, might be preparatively convenient and offer possibilities for control of such factors as base strength and base concentration. The term *probase* (PB) has come into regular use to describe a compound which on reduction is converted into an intermediate which acts predominantly as a base; such bases are described as *electrogenerated bases* (EGB's).

The most important ways of using EGB's in synthesis are: (i) prior generation in aprotic solvent of an otherwise unreactive base; and (ii) *in situ* generation. Most effort has been directed at realising the latter possibility and, with hindsight, the objectives (and constraints) of this approach may be discussed with the aid of Scheme 2. Scheme 2 represents the general case in which an EGB is used to deprotonate a weak acid (usually a carbon acid), the conjugate base of which is involved in reaction with added reagent; i.e. probase, acid, and reagent(s) are present throughout the electrolysis. In this context the properties demanded of good probases and electrogenerated bases are that: (i) the reduction potential of the probase be lower than that of other species present and of the products of subsequent reaction; (ii) the EGB be a poor nucleophile and reducing agent; (iii) that the protonated EGB (PBH^- or PBH_2 in Scheme 2) be capable of conversion into PB; and (iv) that the PB be cheap and readily available. The latter requirement is offset to some extent if regeneration is easy and efficient.

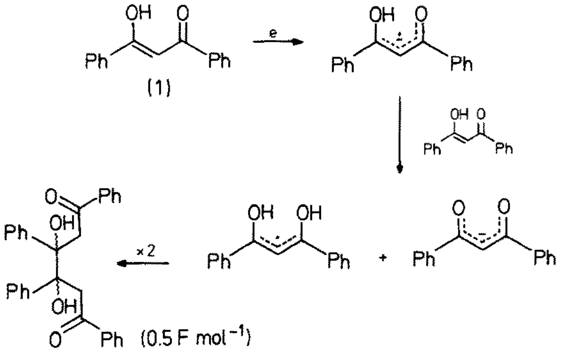
A distinction must also be made between the involvement of EGB's, generated adventitiously, in a reaction pathway, and their premeditated generation for preparative use or for a study of their properties (e.g. basicity). To the extent that the adventitious generation of bases prompted their exploitation it is worth discussing briefly some of the more relevant examples. The bulk of this chapter will, however, be concerned with intentionally generated bases.



Scheme 2

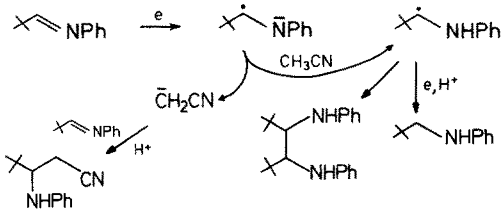
2 The Adventitious Electrogeneration of Bases

The reductive coupling, in dimethylsulphoxide solution, of enolised 1,3-diketones provided an early example where the involvement of acid base reactions of an electrogenerated intermediate could be rigorously established[2]. For instance, cathodic reduction of 1,3-diphenyl-1,3-propanedione (*1*) gave the corresponding pinacol, in high yield, after only 0,5 F mol^{-1}. The mechanism of this reaction was shown to involve neccessary protonation of the initially formed radical-anion by starting material (Scheme 3). Enols are, of course, relatively strongly acidic. Radical-anions of carbonyl compounds may, however, be sufficiently basic to deprotonate acetonitrile (pKa, 31.3)*. As a consequence of this, reduction of aromatic ketones and aldehydes in dry acetonitrile solution leads to the formation of significant amounts of products arising from the addition of $^{-}CH_2CN$ to starting material[3]. More recently it was found that Schiff bases behave similarly upon reduction in acetonitrile[4] (Scheme 4).



Scheme 3

The important role of electrogenerated bases was also recognised by Lund, Simonet et al.[5] when they observed that in dry dimethylformamide solution the two-electron cleavage of alcohols gave, at large cathodic potentials, the corresponding hydrocarbon. This result indicated that the key intermediates, probably the carbanions, rapidly deprotonated the solvent/electrolyte system (DMF-Bu_4NI). Similarly, for reduction of pinacols, in aprotic solvent and at very cathodic potentials, electrogenerated base is involved in the observed carbon—carbon bond cleavage[6]. In this



Scheme 4

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* Unless otherwise stated, pK's of carbon acids will be given on the Bordwell[12] scale, and refer to measurements in DMSO solution at 25 °C.

case, formation in basic solution of radical anions from pinacols, there is good precedent in the work of G. A. Russell et al. 7). In the electrochemical version of this reaction however, there is much uncertainty about the nature of the EGB.

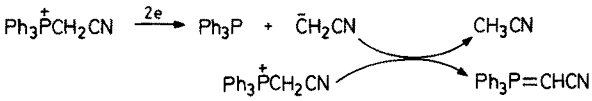
$$\mathrm{PhCOCH_2\overset{+}{P}Ph_3Br^-} \xrightarrow{\text{Hg-cathode}} \mathrm{PhCOCH{=}PPh_3}\ \ (67\%)$$

Scheme 5

The observation that possibly led directly to attempts at using electrogenerated base is summarised in Scheme 5. Horner et al. 8) encountered the formation of a stable ylid during their early studies of the electrolytic cleavage of quaternary phosphonium salts. The particular ylid formed had previously been well characterised 9). Its formation in the electrochemical reaction pointed to the involvement of (unspecified) electrogenerated base. Subsequently, Baizer and Wagenknecht 10), following the work of Ross and Finkelstein 11) on carbon-phosphorus and carbon-nitrogen cleavage, used electrolytic cleavage of phosphonium salts as a possibly useful route to carbanions. For cyanomethyltriphenylphosphonium salts polarography indicated one-electron reduction and, furthermore, a reduction wave extra to that of the starting material and triphenylphosphine was observed. This was interpreted as being due to formation of the ylid according to the mechanism given in Scheme 6. Aqueous work-up after electrolysis gave triphenylphosphine oxide, the expected product of hydrolysis of the ylid. The cyanomethyl anion is therefore probably the first deliberately electrogenerated base!

It was shown later 13) that cyanodimethylsulphonium salts behave similarly upon electro-reduction, although a much more reactive ylid is formed in this case. Formation of relatively unreactive and isolable sulphur ylids has been reported for the electrolysis of 9-fluorenylsulphonium salts 14).

Shono et al. 15) reduced phosphonium halides using carbonyl compounds as solvent; ylids were not only formed but reacted *in situ* to give high yields of the



Scheme 6

Table 1. Electrogenerated ylid in presence of carbonyl compounds 15)

Reaction: $\mathrm{Ph_3P^+CH_2R^1 + R^2R^3CO \xrightarrow[\text{reduction}]{\text{cathodic}^a} R^1CH{=}CR^2R^3}$

		Yield of alkene (%)^b		
R^1	X	$R^2=Ph, R^3=H$	$R^2=C_3H_7, R^3=H$	$R^2, R^3=CH_2(CH_2)_3CH_2$
H	I	84	40	—
C_2H_5	I	95	—	—
$PhCH_2$	Br	72	95	95
MeO_2CCH_2	Cl	75	50	—

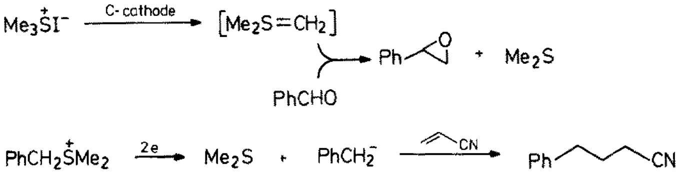
[a] Carbonyl compound as solvent; carbon cathode; divided cell;
[b] By g.l.c.

expected alkenes (Table 1). It is not possible to tell from the reported reaction conditions (carbon cathode, unrecorded potential or current density) whether the phosphonium salt cleaves as in the earlier examples or whether the effective electrogenerated base is the radical-anion of the carbonyl containing solvent. The results did, however, encourage further, preparatively directed, investigations.

3 Electrogenerated Bases Formed by Cathodic Cleavage Reactions

3.1 Onium Salts

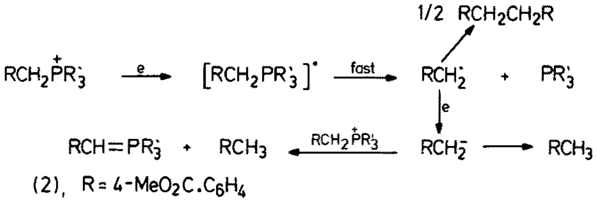
The formation of carbanions, according to Scheme 6, has been much studied but has proved to be of little preparative use. The benzyl anion, generated from benzyldimethylsulphonium tosylate, reacted with acrylonitrile but the addition product was formed in only low yield [16]. Similarly the reactive ylid formed by deprotonation of trimethylsulphonium salts has been cathodically generated [14] and trapped by several aldehydes and ketones as well as ethyl maleate and fumarate; examples are given in Scheme 7. For the best case (benzophenone), the epoxide was formed in 40%



Scheme 7

yield (by g.l.c.); in the presence of benzaldehyde ca. 30% of styrene oxide was obtained. Again, however, the description of the electrolyses does not permit a clear distinction between the two pathways for ylid production, i.e. *via* cleavage to carbanion or *via* carbonyl reduction to radical-anions both species being able to act as EGB's (*cf.* Scheme 6). However, the cleavage route cannot lead to more than a 50% yield of ylid; the low yields of addition products may therefore be an indication of reaction *via* this route.

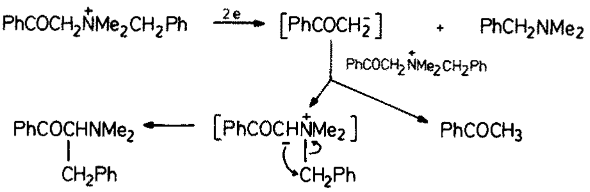
The electroreduction of phosphonium salts, and the way in which ylids are formed, has been studied in some detail [17-20]. Saveant et al. [17] recognised that residual water in aprotic solvents could make difficult the interpretation of the voltammetry of such systems. This came from an investigation of the cathodic reactions of tetraphenylphosphonium perchlorate in acetonitrile and dimethylformamide solution. This salt cannot be converted into an ylid and yet a significant amount of triphenylphosphine oxide was formed which arose from nucleophilic displacement at phosphorus by hydroxide ion. The hydroxide ion was formed by reaction between water and the phenyl carbanion — the product of two-electron cleavage. In an elegant extension of this work [18,19] it was shown that where the phosphonium salt was acidic (e.g. $PhCOCH_2\overset{+}{P}Ph_3$) initial two electron cleavage to the carbanion occured, whereas non-acidic phosphonium salts (e.g. $PhCMe_2\overset{+}{P}Ph_3$) gave one-electron cleavage to the corresponding radical which coupled in high yield. The complete picture for phosphonium salt reduction is, therefore, that given in Scheme 8. Further evidence for this scheme came from examination[20)] of the cathodic reduction of a number of benzylic, allylic, polyenyl, and cinnamyl phosphonium salts. The reduction peaks for the corresponding ylids were identified and in particular the formation and behaviour of the stable ylid (*2*) was observed. Controlled potential coulometry showed that in aprotic conditions the distinctively yellow ylid formed with the consumption of 1 F mol^{-1}; in the presence of an excess of acetic acid 2 F mol^{-1} was consumed and methyl p-toluate was the major product. Finally, in aprotic solvent, exhaustive reduction to 1 F mol^{-1} followed by quenching with acid led to the regeneration of starting material and formation of methyl p-toluate in equal amounts — i.e. the ylid was reprotonated.



Scheme 8

An interesting attempt has been made to use linear sweep voltammetry to estimate the rates at which electrogenerated cyanomethyl anion add to carbonyl compounds present during electrolysis[21)]. One consequence of this approach, however, was that a useful comparison was made between the modes of cathodic cleavage of cyanomethyltriphenylphosphonium and cyanomethyltriphenylarsonium bromides in DMF solution; the electrochemical behaviour of the arsonium salt is closely similar to that of the phosphonium analogue. The conclusion must be drawn, from the sum of the work carried out on production of cyanomethyl anion by cleavage of onium salts; that rapid deprotonation of starting material by that anion will always compete with alternative deprotonations. Even where the onium salt is hindered, (as in cyanomethyltrimesitylphosphonium iodide[21)], ylid formation by the pseudo one-electron route (Scheme 8) is still the favoured reaction.

Essentially the same mechanism is likely to be involved in an electrochemical version[22)] of the Stevens rearrangement. The mechanism of this reaction is not known with certainty; however, it is known to be intramolecular and to involve deprotonation of quaternary ammonium salts to give nitrogen ylids which rapidly rearrange. The scheme set out in Scheme 9 is therefore entirely plausible.

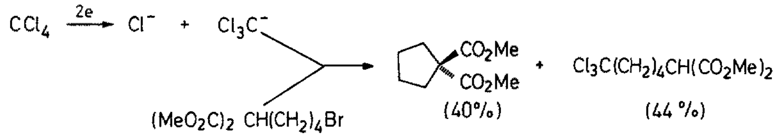


Scheme 9

3.2 Other Probases

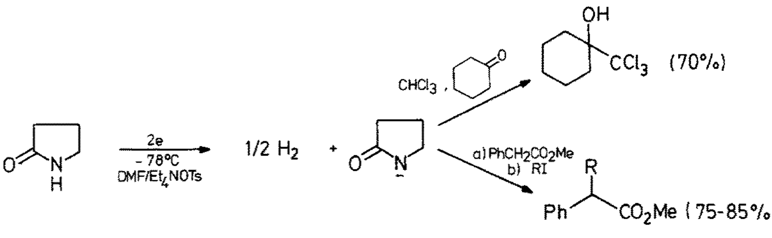
The reported [23] 2 e reductive cleavage of phenylsulphonylacetonitrile ($PhSO_2CH_2CN$) and the observation that in protic media the products were $PhSO_2^-$ and CH_3CN, suggested that this reaction could be a useful source of $^-CH_2CN$. However, careful re-examination [24] showed that in acetonitrile solution the reaction is pseudo one-electron, analogous to the phosphonium and sulphonium salts (Scheme 8), and that phenylsulphonylacetonitrile is sufficiently acidic rapidly to protonate $^-CH_2CN$; assuming additivity of substituent effects an estimate of pK_a 14–16 was made for $PhSO_2CH_2CN$, cf. pK_a 31 for CH_3CN.

Carbon tetrachloride has been employed [25,26] both as a probase and as a chlorinating agent. This is an example where the loss of electrogenerated base is compensated by the higher value of the conjugate acid — i.e. chloroform is marginally more valuable than carbon tetrachloride. This promising approach, outlined in Scheme 10, does not appear to have been pursued further than the examples given. One disadvantage is discernible from the cyclisation reaction described in Scheme 10; the trichloromethyl anion is a good nucleophile as well as a good base and consequently SN2 reaction competes strongly. In this case the problem was avoided by the alternative use of azobenzene probase (Table 2, entries 5 and 6).



Scheme 10

An especially strong nitrogen base may be electrogenerated [27,28] from 2-pyrrolidone, a reaction which formally involves cleavage of an N—H bond to give the corresponding amide anion. The conditions for its generation are severe, involving cathodic potentials in excess of —2.4 V (*vs.* s.c.e.). Consequently it cannot be generated *in situ*: in practise the probase is pre-electrolysed and the base then used, typically in DMF solution at —78 °C. The strength of this base is probably enhanced because it is present as the tetraethylammonium salt in contrast to the strongly ion-paired or chelated lithium salts commonly involved as nitrogen bases. The generation of this base and some examples of applications are given in Scheme 11.



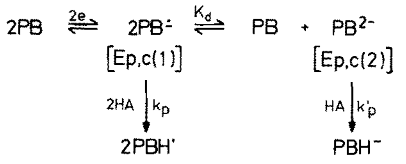
Scheme 11

4 Electrogenerated Bases Formed Without Bond Breaking

Those EGB's formed as a result of bond cleavage must always suffer the disadvantage that it is unlikely that the probases will be easily regenerated. Unless, therefore, the probases are very cheap, or they are converted into more valuable chemicals (as in the CCl_4 to $CHCl_3$ case), the alternative type of probase is to be preferred. These are compounds which may be reduced to radical anions or dianions; ideally such species should have significant lifetimes in the absence of acids or electrophiles, e.g. dimerisation of the radical-anions should be slow.

It may not always be clear from the conditions for electrochemical generation which species is the effective EGB. In some cases a possible complication is fast disproportionation of radical-anion to dianion (Scheme 12). This can mean that for electrogeneration at, say, the first reduction potential $E_{p,c}(1)$ it is possible for either the radical-anion or the dianion to act as base, depending on the relative rates of protonation by acid HA (k_p and k_p'), the value of the disproportionation constant (K_d), and the rate at which equilibrium between radical-anion and dianion is attained. In principle, of course, it is also possible that electrogeneration at $E_{p,c}(2)$ could lead to a situation where radical-anion was the effective base as a consequence of rapid reproportionation causing it to be present in high concentration, thus offsetting its probably much lower kinetic basicity. These points are discussed in more detail on p. 157.

The most useful EGB's in organic synthesis are those generated from azo compounds, activated alkenes, and oxygen; their application and chemistry is most conveniently discussed according to the type of probase.



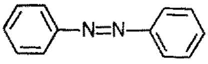
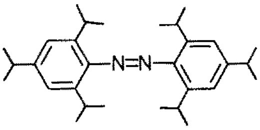
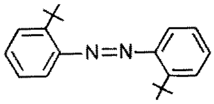
Scheme 12

4.1 Azo Compounds as Probases

Lund and Iversen [29] first showed that azobenzene was an effective probase; it is reduced to radical-anion at a low potential (—0.9 V *vs.* Ag/AgCl) and the reduced form is sufficiently basic to deprotonate benzylphosphonium salts. Its usefulness as an alternative to conventional bases was illustrated by the near quantitative production of stilbene by electrolysis of azobenzene in the presence of benzaldehyde and benzyltriphenylphosphonium bromide (Table 2, entry 1). However, the concomitant formation of the carcinogenic benzidene, by acidic work-up of a product mixture which contains hydrazobenzene, is a severe drawback for this system.

The relative basicity and nucleophilicity of the azobenzene radical-anion has been assessed by comparing the relative effectiveness of methyl iodide and water in quenching the reversibility of the first reduction wave [30]. For HMPA solution it was found that alkylation competed favourably with protonation although inter-

Table 2. Substituted azobenzenes as probases; *in situ* electrolysis

Probase	Entry	Reduction Potential, —E(v)	Solvent Electrolyte
 (entries 1–6)	1.	0.9 (*vs* Ag/AgCl)	DMF, LiCl
	2.	1.65 (*vs* s.c.e.)	MeCN, $Pr^i_4NClO_4$
	3.	1.5 (Ag wire)	DMF, Me_4NClO_4
	4.	1.9 (s.c.e.)	DMF, Et_4NCl
	5.	1.5 (s.c.e.)	DMF, Bu_4NBr
	6.	1.5 (s.c.e.)	DMF, Bu_4NBr
 (entries 7–10)	7.	1.8 (*vs* s.c.e.)	MeCN, Et_4NOTs
	8.	1.8 (*vs* s.c.e.)	MeCN, Et_4NOTs
	9.	2.0 (Ag wire)	MeCN, Et_4NOTs
	10.	1.8 (*vs* s.c.e.)	DMF, Bu_4NBr
 (entries 11–17)	11.	1.7 (Ag wire)	DMF, Bu_4NClO_4
	12.	1.7 (Ag wire)	DMF, Bu_4NClO_4
	13.	1.8 (Ag wire)	MeCN, Me_4NClO_4
	14.	[+1.2 (Ag wire), *anode* potential, see text]	MeCN, Bu_4NCl
	15.	1.5 (Ag wire)	MeCN, Et_4NOTs

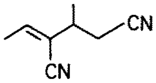
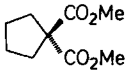
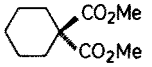
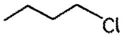
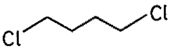
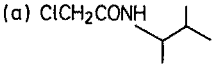
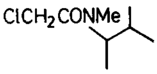
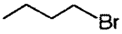
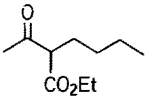
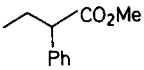
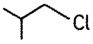
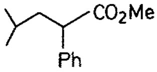
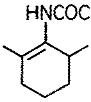
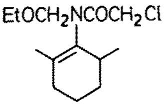
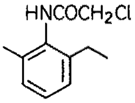
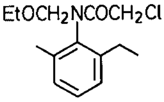
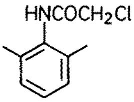
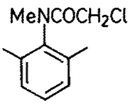
Reactants		Main product(s) [% yield]		Ref.
$PhCH_2\overset{+}{P}Ph_3\overset{-}{Br}$; PhCHO		PhCH=CHPh [98], cis:trans = 3:2		29)
$PhCONMe_2$ (+ $^-CH_2CN$)		$Ph(Me_2N)C{=}CHCN$ [20]		32)
			["major"]	25)
(a) $PhCH_2CO_2Et$, CO_2	(b) EtI	$Ph(CO_2Et)N{-}N(CO_2Et)Ph$		33)
$(MeO_2C)_2CH(CH_2)_4Br$			[80]	26)
$(MeO_2C)_2CH(CH_2)_5Br$			[82]	26)
 (+ $^-CH_2CN$)			[35]	34)
 (+ $^-CH_2CN$)		$NC(CH_2)_6CN$	["major"]	34)
(a) 	(b) Me_2SO_4		["quantitative"]	35)
(a) CH_3CO_2Et	(b) 	 (42 % yield in regeneration mode, see text)	[40, curr. eff.]	36)
(a) $PhCH_2CO_2Me$	(b) EtBr		["quantitative"]	25)
(a) $PhCH_2CO_2Me$	(b) 		[60, curr. eff.]	25)
(a) 	(b) $ClCH_2OEt$		[82, curr. eff.]	35)
(a) 	(b) $ClCH_2OEt$		[60]	35)
(a) 	(b) MeOTs		["quantitative"]	35)

Table 2. (continued)

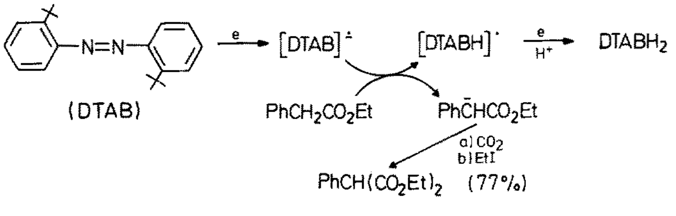
Probase	Entry	Reduction Potential, $-E(v)$	Solvent Electrolyte
	16.	[+1.0 (Ag wire), *anode* potential, see text]	MeCN, Bu_4NCl
	17.	1.1 (s.c.e.)	DMF, Et_4NCl

pretation of the results was complicated by cation effects and by unknown residual water concentrations.

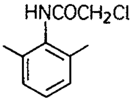
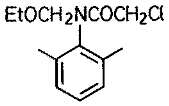
The many advantages of the azobenzene system (low reduction potential, relatively high basicity, ease of work-up) are preserved in two alkylated derivatives which have found much use — i.e. 2,2′-di-*t*-butylazobenzene and 2,2′,4,4′,6,6′-hexa-*i*-propylazobenzene. The radical-anions (or dianions?) of these compounds are slightly more basic than those of azobenzene because the ortho-substituents hinder the planarity necessary for delocalisation of charge; the same effect, of course, raises the reduction potential with respect to azobenzene. The major advantage is that the troublesome benzidene rearrangement is avoided. However, the alkylated azobenzenes are not easily made, although their preparation from the relevant nitrocompounds is well described in the literature [25,31].

A summary of the *in situ* use of the azobenzene probases is given in Table 2. Apart from the generation of ylid, referred to above, the main applications have been for N- and C-alkylation of weak nitrogen and carbon acids, for the promotion of condensation and substitution reactions involving carbanions such as the cyanomethyl anion, for an interesting carboxylation reaction (entries 4 and 17), and for base-promoted cyclisations (entries 5 and 6).

The carboxylation reaction (Scheme 13) nicely illustrates the advantage of using the hindered azobenzenes; azobenzene is itself carboxylated under the reaction conditions used whereas the di-*t*-butyl compound is too hindered and acts only as a probase. Entry 8 is an example of both condensation (of ethyl acetate to ethyl acetoacetate) and subsequent alkylation. Yields are often high and the reaction conditions are usually convenient. The electrogenerated bases are effectively produced in either dimethylformamide or acetonitrile; in the latter case the cyanomethyl anion must also be present but this does not seem to interfere with alkylation reactions.

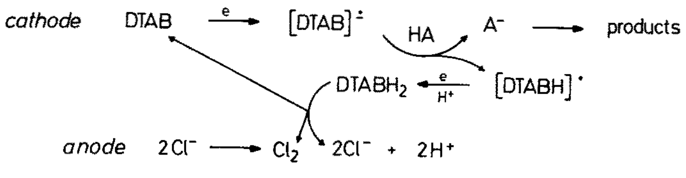


Scheme 13

Reactants		Main product(s) [% yield]		Ref.
(a) 	(b) ClCH$_2$OEt		[84]	[35]
(a) PhCH$_2$CO$_2$Et, CO$_2$	(b) EtI	PhCH(CO$_2$Et)$_2$	[77]	[33]

The base-promoted cyclisations have also been effected by electrogenerated trichloromethyl anion (Scheme 10) but in this case nucleophilic substitution is a significant competing reaction. This complication is avoided by the use of azobenzene as probase.

Several points of practical importance are not evident from Table 2. In most cases divided cells have been used but in two cases (entries 11 and 13) undivided cells have been used combined with the ingenious use of the anode reaction to regenerate the probase. The initial reaction mixture contains the hydrazobenzene with about 10% of the azobenzene (the latter to initiate the production of EGB). The supply of azobenzene is maintained by oxidation of the hydrazobenzene by anodically produced chlorine; the protons thus generated must be scavenged and either 1,2-epoxybutane or an ion exchange resin (e.g. di-isopropylaminomethyl polystyrene) work well. Consequently the reaction is carried out by controlling the *anode* potential and the electricity consumption is 1 F mol^{-1} with respect to the carbon or nitrogen acid. This reaction route is illustrated in Scheme 14. Alternatively in the divided cell mode, anodically generated halogen, e.g. bromine in the case of entry 10, may be used to oxidise an equivalent amount of hydrazocompound — i.e. by batch regeneration of spent probase from a previous reaction.

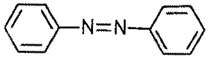
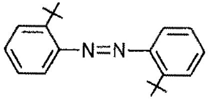
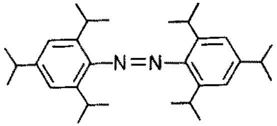
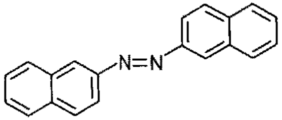
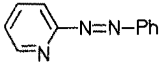
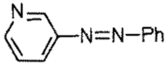
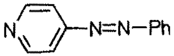
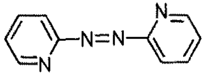


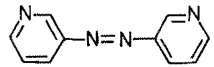
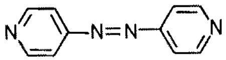
Scheme 14

A confusing feature of the results of the preparative scale experiments summarised in Table 2 is the variety of reference electrodes against which reduction potentials have been controlled. For *in situ* electrolysis it is neccessary to be able to relate the potential at which the EGB is generated to those of other components of the reaction and product mixture. In this context literature values of reduction potentials of relevant aromatic azocompounds are listed in Table 3.

The preparative-scale examples listed in Table 2 all involve the use of stoichiometric amounts of the azobenzene probases. For several Michael addition reactions [39]

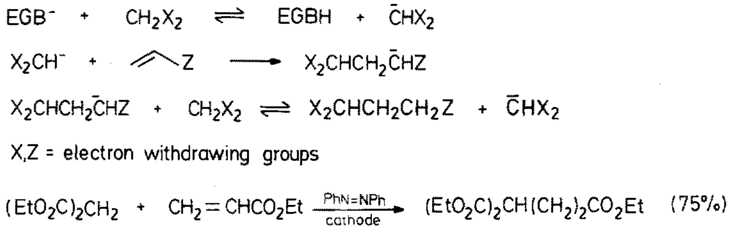
Table 3. Cyclic voltammetric Data[a]: Azocompounds

Compound	Entry	Solvent/Electrolyte/Ref.	$-E_{p,c}(1)$	$-E_{p,a}(1)$	$-E_{p,c}(2)$	$-E_{p,a}(2)$	Ref.
	1.	MeCN, Et_4NBF_4, Ag/Ag^+			2.18		21)
	2.	DMF, Et_4NBF_4, s.c.e.	1.41	[b]	1.85	[b]	33)
	3.	DMF, Me_4NBF_4, s.c.e.	1.34	[b]	1.95	irrev.	30)
	4.	DMF, Et_4NBF_4, s.c.e.	1.52	[b]	1.91	[b]	33)
	5.	MeCN, Bu_4NBF_4/Et_4NBF_4 (Ag wire)	1.77[c]	1.84[c]			37)
	6.	MeCN, Bu_4NBF_4/Et_4NBF_4 (Ag wire)	2.04[c, d]	2.29[c, d]			37)
	7.	DMF, Et_4NBF_4, Ag/Ag^+			2.28		21)
	8.	MeCN, Et_4NBF_4, Ag/Ag^+	1.61	1.51	2.09	1.85	38)
	9.	MeCN, Et_4NBF_4, Ag/Ag^+	1.66	1.58	2.17	2.00	38)
	10.	MeCN, Et_4NBF_4, Ag/Ag^+	1.51	1.42	1.98	1.80	38)
	11.	MeCN, Et_4NBF_4, Ag/Ag^+	1.42	1.35	1.82	1.70	38)

	12.	MeCN, Et_4NBF_4, Ag/Ag^+	1.51	1.44	2.10	1.95	38)
	13.	MeCN, Et_4NBF_4, Ag/Ag^+	1.24	1.17	1.86	1.75	38)

[a] Unless stated otherwise, scan rates in range 0.1–0.3 Vs^{-1}; [b] Reversible, but oxidation potentials not quoted; [c] Not listed in text; read from Figures; [d] Scan rate, 1 Vs^{-1}.

the EGB need only be produced in catalytic amount and reaction proceeds efficiently according to Scheme 15. In most cases the base is generated from the activated alkene itself, (*cf.* Table 4), but in a case where the alkene is reduced at a relatively high potential azobenzene has been successfully used as probase at only 0.0025 equivalents with respect to the alkene (Scheme 16).



Schemes 15 and 16

Although not strictly to be included in this section it is worth comparing the azobenzene-derived EGB's with those generated from azines. The azine-derived bases are of similar strength to the azobenzene radical-anions, as evidenced by their ability to deprotonate phosphonate esters [40] (Table 15, p. 160).

4.2 Activated Alkenes as Probases

4.2.1 Acrylonitrile and Acrylate Esters

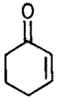
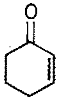
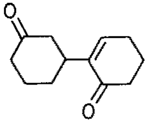
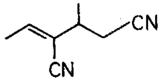
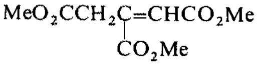
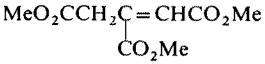
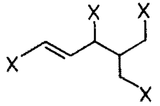
Alkenes may be activated toward electrochemical reduction by electron-withdrawing sucstituents. Thus acrylonitrile and acrylate esters are easily reduced and, depending among other factors on the proton availability of the medium, they undergo either hydrogenation or hydrodimerisation. The basic character of the radical-anions of such substrates has been put to use in EGB promoted Michael additions of the type outlined in Scheme 15; the case where the probase is azobenzene has already been discussed.

The results summarised in Table 4 show clearly that good yields of the 1:1 Michael adducts can be obtained in cathodically initiated reactions. It is not clear, however, why the reaction should fail for acrylonitrile; even if dimerisation of the initially formed radical-anion is much faster than protonation the resulting dimeric dianion should still be sufficiently basic to deprotonate dialkylmalonate esters. A feature of especial significance is the usefulness of esters of ethenetetracarboxylic acid. Apart from their use in EGB catalysed reactions they have been much used in stoichiometric amount.

4.2.2 Ethenetetracarboxylate Esters

These probases, $[(RO_2C)_2C{:}C(CO_2R)_2$, R = Me, Et, $Bu^n]$, give in cyclic voltammetry two reversible reduction peaks [33]. The reduction peak potentials are, respectively, $E_{p,c}(1)$: −0.88 V, −0.95 V, and −0.97 V; and $E_{p,c}(2)$: −1.08 V, −1.15 V, and −1.17 V (vs. s.c.e.). It is the dianion which is the effective base and this EGB

Table 4. EGB promoted Michael reactions (*cf.* Scheme 15)[39]

Probase and Michael acceptor	Entry	Carbon acid and Michael donor	Reduction Potential (−E (V *vs.* s.c.e.)	Charge consumption[a]	Product yield (%)[b]
$CH_2{=}CHCN$	1	$CH_2(CO_2Et)_2$	2.08	0.024	19
$CH_2{=}CHCN$	2	$PhCH(CO_2Et)_2$	2.04	0.016	15
$CH_2{=}CHCO_2Et$	3	$CH_2(CO_2Et)_2$	1.88	0.055	77
$PhN{=}NPh$	4	$CH_2(CO_2Et)_2$	1.65	—	75
$CH_2{=}CHCO_2Et$					
$(EtO_2C)_2C{=}C(CO_2Et)_2$	5	$CH_2(CO_2Et)_2$	1.10	0.10	93
$(MeO_2C)_2C{=}C(CO_2Me)_2$	6	$MeCOCH_2CO_2Me$	1.00	0.039	60[e]
	7		1.90	0.0013	65,  [d]
$CH_2{=}CHCH_2CN$	8	$CH_2{=}CHCH_2CN$	2.16	0.010	35,  [d]
 $MeO_2CCH_2\underset{CO_2Me}{C}{=}CHCO_2Me$	9	 $MeO_2CCH_2\underset{CO_2Me}{C}{=}CHCO_2Me$	1.37	0.015	88, "dimer"[e]
$EtO_2CCH_2CH{=}CHCO_2Et$	10	$EtO_2CCH_2CH{=}CHCO_2Et$	2.10	0.20	50,  [d] $(X = CO_2Et)$

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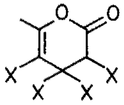
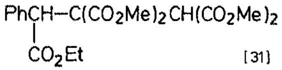
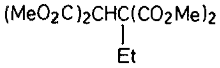
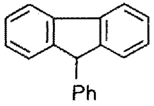
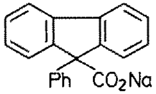
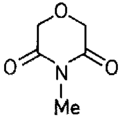
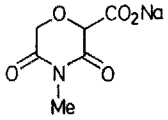
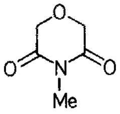
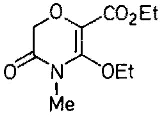
[a] F mol^{-1} based on acceptor; [b] Based on acceptor consumed;

[c] 
(X = CO_2Me)

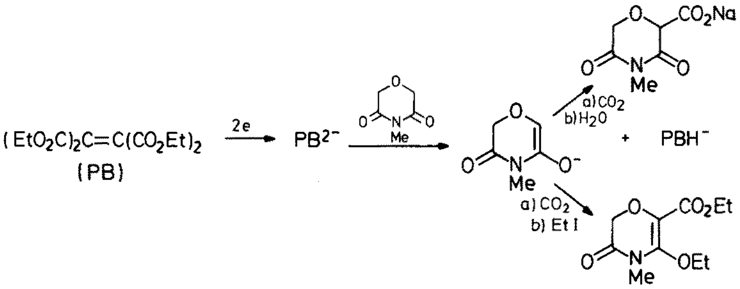
[d] Addition with subsequent base-catalysed isomerisation; [e] Structure of product not given.

Table 5. Ethenetetracarboxylate esters as probases: $(RO_2C)_2C{:}C(CO_2R)_2$

Probase R =	Entry	Reduction Potential, —E(v)	Solvent/Electrolyte	Reactants	Main product(s) [% yield]	Ref.
Me	1	1.1 (*vs.* s.c.e.)	DMF, Et_4NCl	(a) $PhCH_2CO_2Et$, CO_2; (b) EtI	 $PhCH(CO_2Et){-}C(CO_2Me)_2CH(CO_2Me)_2$ [31]  $(MeO_2C)_2CHC(Et)(CO_2Me)_2$ [11]	33)
Bu	2	1.3 (*vs.* s.c.e.)	DMF, Et_4NCl	(a) $PhCH_2CO_2Et$, CO_2; (b) EtI	$PhCH(CO_2Et)_2$ [78]	41)
Et	3	1.2 (*vs.* s.c.e.)	MeCN, Et_4NBr (+ NaBr/18-crown-6)	 , CO_2 (cathode)	 [75]	41)
			(+ Na_2CO_3, anode)	$(EtO_2C)_2CHCH(CO_2Et)_2$ (anode)	$(EtO_2C)_2C{=}C(CO_2Et)_2$ (anode compartment, 100)	
Et	4	1.4 (*vs.* s.c.e.)	MeCN, Et_4NBr (+ NaBr/18-crown-6)	(a)  , CO_2; (b) H_2O	 [79] (probase regeneration in anode compartment)	41)
Et	5	1.4 (*vs.* s.c.e.)	DMF, Et_4NCl	(a)  , CO_2; (b) EtI	 [85]	41)

has been used especially to effect carboxylations of carbon acids. Examples are given in Table 5 and in Scheme 17.

A considerable advantage of these probases is that the hydrogenated form, (i.e. spent probase), is easily re-oxidised by bromine which can be anodically generated. It is worth noting that the ethyl and *n*-butyl esters are to be preferred. The dianion of the tetramethyl ester is apparently significantly nucleophilic, and the probase itself is capable of acting as a Michael acceptor. In contrast the dianion of the tetrabutyl ester acts mainly as a base (*cf.* entries 1 and 2 in Table 5).



Scheme 17

4.2.3 Disubstituted-(fluoren-9-ylidene)methane Derivatives

Derivatives of the general formula (*1*) in Table 6 have been successfully used as probases and their properties in this context are being further explored. In common with the azobenzenes and ethenetetracarboxylate esters, the fluoren-9-ylidene derivatives usually display two reversible one-electron peaks in cyclic voltammetric experiments. Although disproportionation is possible (*cf.* Scheme 12) it is the dianions which are the effective bases. It was shown early on [42] that the radical-anions of such derivatives are long-lived in relatively acidic conditions (e.g. in DMF solution the first reduction peak of $Ph_2C{:}C(CN)_2$ remains reversible in the presence of a 570-fold molar excess of acetic acid, at 0.1 V s^{-1}). Even the dianions are relatively weak bases, useful mainly for ylid formation from phosphonium and sulphonium salts (pK_a's 11–15); they are not sufficiently basic to effect the Wittig-Horner reaction which involves deprotonation of phosphonate esters [40].

This class of probase does, however, offer several advantages as follows:

a) they are easily prepared by Knoevenagel-type condensation of substituted fluorenones with malonates esters or cyanoacetates;

b) the dianions are formed at low reduction potentials, which allows their formation in the presence of a good range of other reactants;

c) the generality of the method of preparation means that a considerable number of fluoren-9-ylidene derivatives have been prepared the dianions of which display different basicites, modifiable further by choice of electrolyte cation. Furthermore the generation of products and intermediates, e.g. ylids, may easily be monitored by cyclic voltammetry in the presence of the probases because of the low potentials at which the dianions are formed. The reduction potentials of the fluoren-9-ylidene probases are given in Table 6 which also illustrates the range of probases available.

Table 6. (Fluoren-9-ylidene)methane derivatives as probases: Reduction potentials

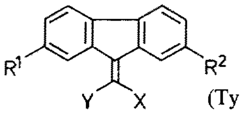
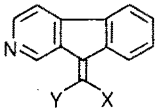
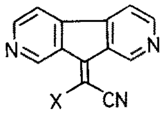
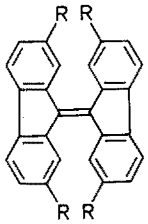
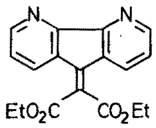
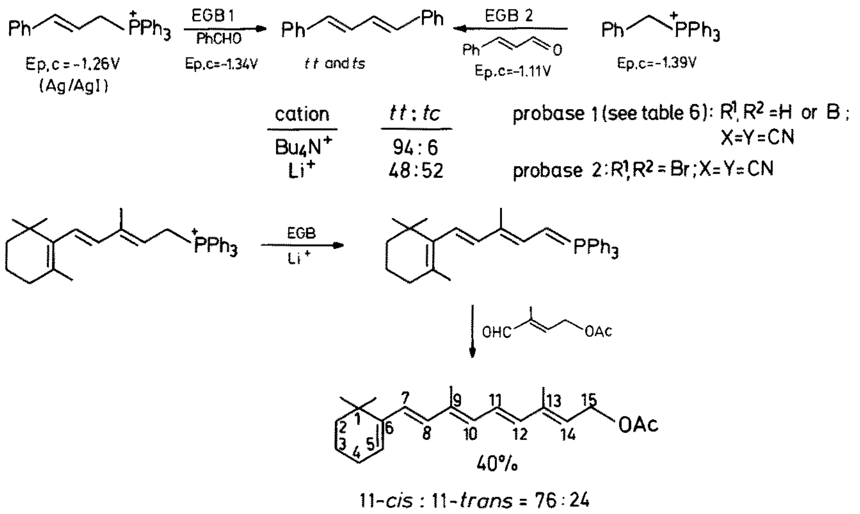
Probase				Entry	$-E_{p,c}(1)$	$-E_{p,c}(2)$	Ref.
 (Type 1)							
R^1	R^2	Y	X				
H	H	CN	CN	1^a	0.23	0.91	43)
				2^b	0.07	0.96	44)
Cl	Cl	CN	CN	3^c	0.06	0.71	43)
Br	Br	CN	CN	4^d	0.13	0.59	43)
H	H	CN	CO_2Et	5^a	0.28	0.86	43)
Cl	Cl	CN	CO_2Et	6^a	0.13	0.66	43)
Br	Br	CN	CO_2Et	7^a	0.08	0.69	43)
Br	Br	CN	$CO_2(CH_2)_5CH_3$	8^c	0.31	0.95	43)
H	H	CO_2Et	CO_2Et	9^a	0.74	0.92	43)
 (Type 2)							
X = CN, Y = CO_2Et				10^a	0.19	0.79	43)
X = CO_2Et, Y = CN				11^a	0.19	0.79	43)
X = CN, Y = CN				12^a	0.05	0.76	43)
 (Type 3)							
X = CN				13^a	0.03	0.75	43)
X = CO_2Et				14^a	0.19	0.80	43)
 (Type 4)							
R = H				15^a	0.44	0.93	43)
R = Cl				16^c	0.32	0.81	43)
R = Br				17^c	0.16	0.70	43)

Table 6. (continued)

Probase	Entry	$-E_{p,c}(1)$	$-E_{p,c}(2)$	Ref.
 (Type 5)	18^c	0.49	0.78	40)
	19^e	0.41^e	—	

Conditions: Scan rate $0.3\ Vs^{-1}$, Ag/AgI reference; ^{a} DMSO-Bu_4NClO_4; ^{b} DMF-Et_4NBF_4; ^{c} DMF-Bu_4NClO_4; ^{d} DMF-Bu_4NI; ^{e} DMF-$LiClO_4$, reversible, 2e.

In practice the low potentials permit a choice of approaches; this is illustrated in Scheme 18 for a Wittig reaction in the presence of EGB wherein the desired product, 1,4-diphenylbutadiene, may be formed either from a reactive aldehyde (cinnamaldehyde) and an ylid from a benzylic phosphonium salt, or from a less reactive aldehyde and the ylid from a more acidic phosphonium salt. The stereochemical course of the Wittig reaction is particularly sensitive to reaction conditions, especially cations which may be present. This point is partly made in Scheme 18 but deserves further elaboration.



Scheme 18

Further examples of preparative use are given in Table 7. Entries 7 and 8 demonstrate that judicious choice of supporting electrolyte can control both the basicity of the EGB and also the stereochemical course of the reaction (see also discussion on p. 159).

Table 7. (Fluoren-9-ylidene)methane derivatives as probases

Reaction[a]: $PhCH_2P^+Ph_3X^- + PhCHO \xrightarrow{EGB} PhCH{:}CHPh$(*cis* + *trans*)

Probase (see Table 6)	Entry	Reduction potential[b]	Cation[c]	Stilbene yield (%)	*trans*/*cis*	Ref.
Type 1: $R^1, R^2 = H; X, Y = CN$	1	−0.9	Li^+	74	1.6	45)
$R^1, R^2 = H; X, Y = CN$	2	−0.9	Bu_4N^+	46	0.7	45)
$R^1, R^2 = Br; X, Y = CN$	3	−0.6	Li^+	21	1.0	45)
$R^1, R^2 = Br; X, Y = CN$	4	−0.6	Bu_4N^+	38	1.0	45)
$R^1, R^2 = H; X = CO_2Et, Y = CN$	5	−0.8	Li^+	94	1.2	45)
$R^1, R^2 = H; X = CO_2Et, Y = CN$	6	−0.8	Bu_4N^+	68	1.0	45)
$R^1, R^2 = H; X, Y = CO_2Et$	7[d]	−1.0	Li^+	60	0.67	40)
$R^1, R^2 = H; X, Y = CO_2Et$	8[d, e]	−1.0	Bu_4N^+	80	9.0	40)
Type 5: $R^1, R^2 = H; X, Y = CO_2Et$	9[d]	−0.5[f]	Li^+	43	1.0	40)
$R^1, R^2 = H; X, Y = CO_2Et$	10[d, e]	−0.9	Bu_4N^+	87	4.0	40)

[a] DMF solution, Hg cathode, $X = NO_3$; [b] V *vs* Ag/AgI(s); [c] As $LiClO_4$ and Bu_4NBF_4; [d] $X = Br^-$; [e] Bu_4NClO_4; [f] No second reduction potential in presence of Li^+; see text p. 30

4.3 Oxygen as a Probase

Cathodic reduction of oxygen is the most convenient method of production of the superoxide radical-anion, $O_2^{\overline{\cdot}}$. The properties of this important species have been well reviewed[46)] and key references to the extensive work on the electrochemistry of oxygen are contained therein. Of immediate significance is the large cathodic shift in E° for the $O_2/O_2^{\overline{\cdot}}$ couple which accompanies a change from aqueous to aprotic solvent (e.g. DMF, DMSO, and MeCN); this is interpreted in terms of relatively weak solvation in aprotic media which enhances the nucleophilicity of the superoxide anion. However, in the presence of acids the chemistry of superoxide is dominated by the disproportionation shown in equation 1.

$$2\,O_2^{\overline{\cdot}} + HA \rightleftharpoons O_2 + HO_2^- + A^- ; \qquad K \sim 10^9 \quad \text{for} \quad HA = H_2O \tag{1}$$

The disproportionation is crucial in determining the action of superoxide anion as a base. According to equation 1, in aqueous solution stoichiometric amounts of the strong bases HO_2^- and HO^- are formed, and the equilibrium constant for this process indicates that superoxide is effective in extracting protons from acids of pK_a up to 24. In contrast $O_2^{\overline{\cdot}}$ itself is a weak base (the pK_a of its conjugate acid, HO_2, is 4.69).

An important development in the use of superoxide as an EGB was the realisation that, if an excess of dioxygen is maintained during electrolysis, many carbanions formed by proton extraction by superoxide will rapidly react with the excess of dioxygen.

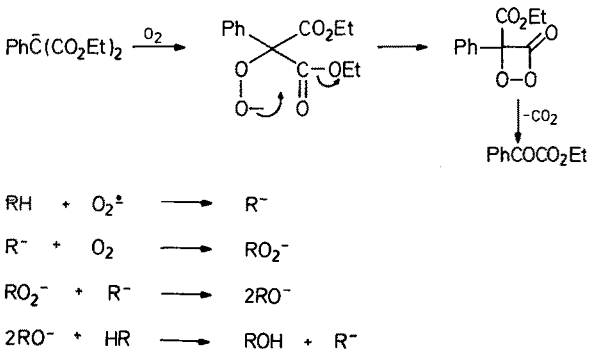
The cathodic generation of superoxide is experimentally simple. The reactions are carried out in a conventional divided cell (H-cell), at a mercury cathode, and, typically, in dry acetonitrile or N,N-dimethylformamide containing tetra-alkylammonium salt. The dioxygen is bubbled through the catholyte using a gas dispersion tube and reduction is carried out at about —1.0 V (*vs.* s.c.e.).

The preparatively useful reactions are of several types, depending on the nature of the carbon acid and the ensuing discussion is so organised.

4.3.1 Reactions of Malonate Esters (gem-diesters) (Table 8) [47)]

Diethylmalonate anion does not apparently react cleanly with dioxygen and in this case a complex mixture of products of self-condensation is obtained. However substituted diethylmalonates are usefully converted into hydroxylated products. In the case of diethyl phenylmalonate conversion into the corresponding carbonyl compound, ethyl phenylglyoxalate, was observed — presumably according to the mechanism given in Scheme 19.

A feature of these reactions is that significantly less than 1 F mol^{-1} is consumed, which points to the operation of a chain reaction, possibly of the type outlined in Scheme 20.



Schemes 19 and 20

Table 8. Electrogenerated superoxide[a]: reaction with malonate esters [47)]

Carbon acid	Product	Yield (%)	Charge ($Fmol^{-1}$)
$(EtO_2C)_2CH_2$	anion inert to O_2[b]	—	—
$(EtO_2C)_2CHMe$	$(EtO_2C)_2C(OH)Me$	95	0.17
$(EtO_2C)_2CHEt$		62	0.52
$(EtO_2C)_2CHPh$	$PhCOCO_2Et$	74	0.23
	$(EtO_2C)_2C(OH)Ph$	7	

[a] Electrolysis conditions given in text; [b] See text.

4.3.2 Reactions of Mono-Esters (Table 9) [48)]

In these cases 1 F mol^{-1} was passed, based on the amount of ester present. As for the *gem*-diesters, *alpha*-hydroxylation was found although it was accompanied by

Table 9. Electrogenerated superoxide[a]: reaction with monoesters [48)]

Carbon acid	Product	Yield (%)
$MeCH_2CO_2Et$	$MeCH(OH)CO_2Et$	15
	$MeCH(OH)CO_2H$	35
Me_2CHCO_2Me	$Me_2C(OH)CO_2H$	40
Ph_2CHCO_2Me	$Ph_2C(OH)CO_2Me$	45
	Ph_2CO	10
Me_2CHCO_2Me	complex mixture	—

[a] 1 F mol^{-1} passed, w.r.t. carbon acid.

hydrolysis. It appears that *alpha*-alkyl or aryl substitution is neccessary for clean reaction, and even so yields are modest.

4.3.3 *Reactions of Amides (Table 10)* [48)]

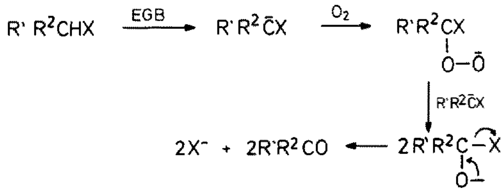
The N,N-diethylamides listed in Table 10 are sufficiently acidic to react with the superoxide/dioxygen reagent. Yields are low and these reactions have limited preparative value. It is noteworthy, however, that N,N-diethyldiphenylacetamide undergoes oxygenation with concomitant cleavage, presumably in a manner analogous to that depicted in Scheme 19.

Table 10. Electrogenerated superoxide: reaction with amides [48)]

Carbon acid	Product(s)	Yield (%)	Charge (Fmol^{-1})
$Ph_2CHCONEt_2$	Ph_2CO	54	1.5
	$Ph_2C(OH)CONEt_2$	40	
$Ph(Me)CHCONEt_2$	$Ph(Me)C(OH)CONEt_2$	53	1.2
$Me_2CHCONEt_2$	no reaction	—	1.5
$PhCH_2CONEt_2$	$PhCO_2H$	5	1.2
	$PhCH(OH)CONEt_2$	30	

4.3.4 *Reactions of Nitriles, Sulphones, and Nitroalkanes*

Compounds of the type R^1R^2CHX, where X = CN, SO_2Ph, and NO_2 are distinguished by the fact that their reaction with the superoxide/dioxygen reagent is accompanied by loss of X, probably as the anion. The mechanism for such reaction has not been completely proven, but there is sufficient evidence to suggest the pathway in Scheme 21 with some confidence.

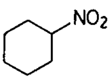
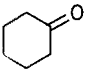
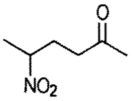
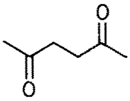
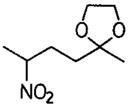
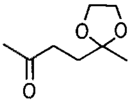
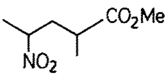
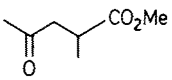
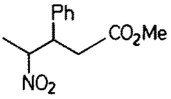
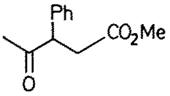


Scheme 21

Table 11. Electrogenerated superoxide: reaction with nitriles [48,49]

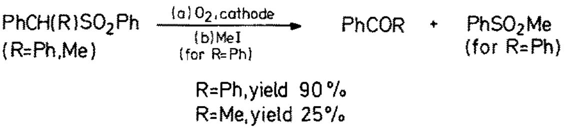
Carbon acid	Product	Yield (%)	Charge ($F mol^{-1}$)
Ph_2CHCN	Ph_2CO	95	0.8
$PhCH(Me)CN$	$PhCOCH_3$	72	1.0
Me_2CHCN	Me_2CO	20	1.0
$PhCH_2CN$	$PhCO_2H$	89	1.8
$PhCH_2CN$ (+ Ac_2O)	$PhCO_2H$	27	1.8
	$PhCH(OAc)_2$	54	
EtO_2CCH_2CN	$EtO_2C{\cdot}CHO$	72	1.3
$(EtO_2C)_2CHCN$	$(EtO_2C)_2CO$	83	1.3

Table 12. Electrogenerated superoxide: reaction with nitroalkanes [50]

Carbon acid	Product	Yield (%)[a]
		70[b]
		82–86
		71
		76[b]
		68

[a] In DMF solution, 1 F mol^{-1}; [b] in MeCN solution.

- *Nitriles* (Table 11) [48,49]: The oxidative decyanation of nitriles can be efficient and experimentally convenient. In particular, good yields of ketones are obtained from secondary nitriles; the reaction is most efficient with the more acidic compounds. Primary nitriles are converted into the corresponding acids, probably *via* the aldehydes. In the presence of acetic anhydride the reaction stops at the aldehyde diacetate stage.
- *Sulphones* (Scheme 22) [48]: The few reactions falling under this heading are including in Scheme 22. The relatively high acidity of the sulphones is reflected in the good yields of oxygenated product. It is also of interest that in this case it has been shown that $PhSO_2^-$ is the leaving group; it is subsequently oxidised to the corresponding sulphonate ion.



$$\underset{(R=Ph,Me)}{PhCH(R)SO_2Ph} \xrightarrow[(b)MeI\ (for\ R=Ph)]{(a)O_2, cathode} PhCOR + \underset{(for\ R=Ph)}{PhSO_2Me}$$

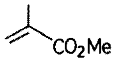
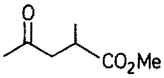
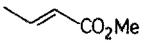
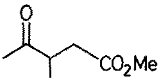
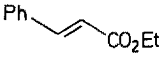
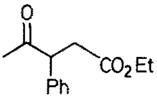
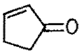
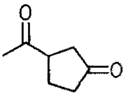
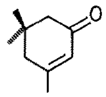
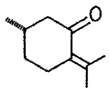
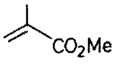
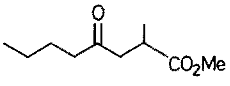
R=Ph, yield 90%
R=Me, yield 25%

Scheme 22

— *Nitroalkanes* (Tables 12 and 13)[50)]: These are possibly among the most useful substrates for reaction with the superoxide/dioxygen reagent, and the loss of nitrite, according to Scheme 21, has been confirmed. Secondary nitroalkanes are efficiently converted into ketones (Table 12), and the reaction may prove to be of especial value for the preparation of 1,4-diketones.

An elegant extension of this approach is the combination of the nitroalkanes to ketone reaction with prior EGB-catalysed Michael condensation involving nitronate anions. Azobenzene works well as the catalyst probase and the condensation and

Table 13. Electrogenerated superoxide: EGB[a] promoted Michael reactions with subsequent autoxidation[50)]

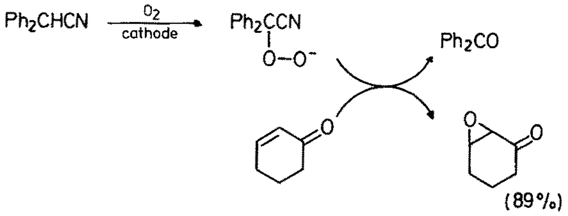
Michael acceptor	Product[b]	Yield (%)
		60
		59
		46
		57
	no reaction	—
	no reaction	—
		62[c]

[a] Azobenzene probase; [b] Carbon acid, $CH_3CH_2NO_2$; [c] $CH_3(CH_2)_4NO_2$

subsequent reaction with superoxide/dioxygen is carried out as a "one-pot" reaction. In dry acetonitrile solution the nitroalkane and azobenzene are briefly electrolysed at −1.4 V (*vs.* s.c.e.), after which the Michael acceptor is gradually added. After completion of the Michael reaction, dioxygen is bubbled through the catholyte during electrolysis at −1.0 V until 1 F mol^{-1} has been consumed. The results of such experiments are summarised in Table 13.

4.3.5 Epoxidation of Enones Using the Superoxide/Dioxygen Reagent (Table 14) [51)]

Yet another strategy for the use of this reagent is outlined in Scheme 23, whereby an "auxilliary" carbon acid is used as an oxygen carrier in epoxidation. Clearly the auxilliary acid must have a pK_a lower than that of the enone; in practice the two auxilliary acids used (Ph_2CHCN and $MeCH(CO_2Et)_2$ are of pK_a (DMSO) 17.5 and 15–16 respectively. For comparison the pK_a of 2-cyclohex-1-one has been estimated at 21–22.



Scheme 23

Table 14. Electrogenerated superoxide: epoxidation of α,β-unsaturated ketones [51)]

Ketone	Charge[a]	Epoxide yield (%)
2-cyclohexen-1-one	1.8	89[b]
4,4-dimethyl-2-cyclohexen-1-one	0.45	31
	1.80	90[c]
4,4,6,6-tetramethyl-2-cyclohexen-1-one	1.80	no reaction[b]
$Me_2C=CHCOMe$	3.70	85[b]
$PhCH=CHCOPh$	3.20	84[b]

[a] F mol^{-1} with respect to ketone; [b] Auxilliary carbon acid, $PhCH_2CN$; [c] Auxilliary carbon acid, $CH_3CH(CO_2Et)_2$

5 Mechanistic Aspects of EGB Chemistry

5.1 The Disproportionation/Reproportionation Problem

The difficulty in judging the nature of the effective EGB has been referred to in the context of azobenzene-derived bases (Scheme 12 and discussion on p. 139). In those cases, in cyclic voltammetric experiments, the reversible first reduction peak becomes irreversible in the presence of weak acids with an approximate doubling of cathodic current [52]. Such enhancement was also observed [53] in early polarographic experiments. The fate of cathodically generated azobenzene radical-anion, in the presence of weak acids, was also followed by u.v. spectroscopy which showed that, eventually, equivalent amounts of azobenzene and hydrazobenzene were formed. The overall reaction is that given in Eq. (2).

$$2[\mathrm{PhN{-}NPh}]^{\cdot -} + 2\,\mathrm{HA} \rightarrow \mathrm{PhN{:}NPh} + \mathrm{PhNHNHPh} \qquad (2)$$

This could be explained in terms of disproportionation of the radical-anion to dianion with subsequent protonation. However, a much more complete explanation followed the realisation [54] that, in most cases, the radical-anion acts not only as a base but also as a single electron-transfer agent (the so-called DISP mechanisms). In particular a comparison of observed cyclic voltammetric behaviour of substituted azobenzenes in the presence of weak acids with that predicted using digital simulation based on various mechanistic possibilities has established the DISP1 route given in Eq. (3) (reactions 1–4).

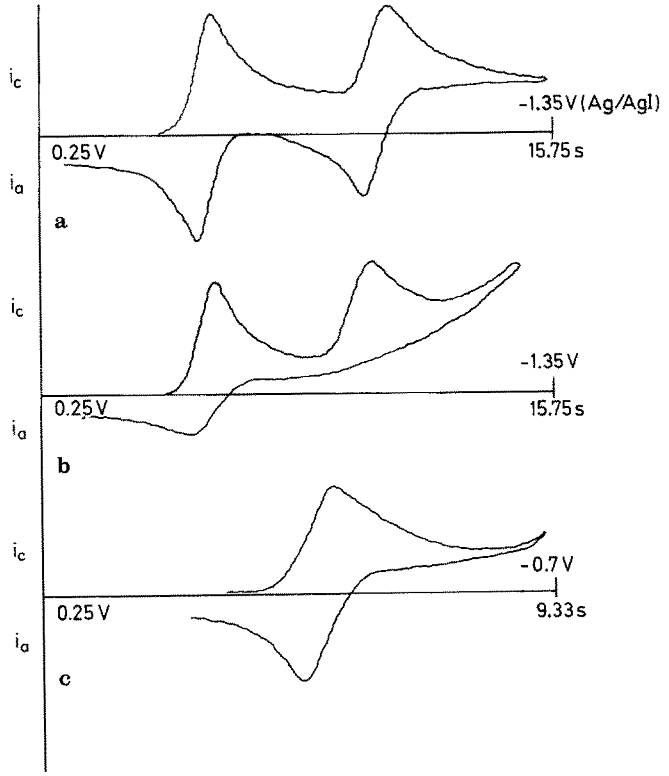


Fig. 1. Cyclic voltammetry of the fluoren-9-ylidenemethane derivative (*5*) with and without $CH_3COCH_2COCH_3$: **a.** DMF/TBAP (O·IM); **b.** plus $CH_3COCH_2COCH_3$; **c.** as **b**, 1st reduction peak only

$$\begin{array}{lllllll} & \mathrm{Az} & \overset{e}{\rightleftharpoons} & \mathrm{Az}^{\cdot-} & & & 1. \\ \mathrm{Az}^{\cdot-} + & \mathrm{HA} & \xrightarrow{k_p} & \mathrm{AzH}^{\cdot} & + & \mathrm{A}^- & 2. \\ \mathrm{AzH}^{\cdot} + & \mathrm{Az}^{\cdot-} & \rightleftharpoons & \mathrm{AzH}^- & + & \mathrm{Az} & 3. \\ \mathrm{AzH}^- + & \mathrm{HA} & \rightleftharpoons & \mathrm{AzH_2} & + & \mathrm{A}^- & 4. \\ \multicolumn{7}{l}{\mathrm{Az = azobenzene}} \end{array} \tag{3}$$

The fluoren-9-ylidenemethane derivatives exhibit different behaviour. Here the radical-anion is very weakly basic[42] and it may clearly be shown by cyclic voltammetry (Fig. 1) that it is the dianion which is the effective base. The reaction scheme in these cases is therefore that given in Eq. (4). It is only with relatively strong acids that reactions 4 and 6 are significant.

$$\begin{array}{lllllll} & \mathrm{Fl} & \overset{e}{\rightleftharpoons} & \mathrm{Fl}^{\cdot-} & & & 1. \\ & \mathrm{Fl}^{\cdot-} & \overset{e}{\rightleftharpoons} & \mathrm{Fl}^{2-} & & & 2. \\ \mathrm{Fl}^{2-} + & \mathrm{HA} & \xrightarrow{k_p} & \mathrm{FlH}^- & + & \mathrm{A}^- & 3. \\ (\mathrm{Fl}^{\cdot-} + & \mathrm{HA} & \longrightarrow & \mathrm{FlH}^{\cdot} & + & \mathrm{A}^-) & 4. \\ \mathrm{Fl}^{2-} + & \mathrm{Fl} & \overset{k_f}{\rightleftharpoons} & 2\mathrm{Fl}^{\cdot-} & & & 5. \\ (\mathrm{FlH}^- + & \mathrm{HA} & \longrightarrow & \mathrm{FlH_2} & + & \mathrm{A}^-) & 6. \\ \multicolumn{7}{l}{\mathrm{Fl = Fluoren\text{-}9\text{-}ylidenemethane\ derivative}} \end{array} \tag{4}$$

There are two reasons for considering the mechanisms in this detail. Firstly, the potential at which preparative experiments are carried out is determined by which is the basic species. Secondly, methods for determining the rate of protonation (k_p) depend on a knowledge of the mechanism. The rate of protonation of an EGB by an acid of known pK_a is the most convenient measure of basicity (kinetic basicity).

5.2 The Effective Basicities of EGB's

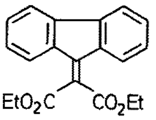
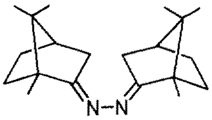
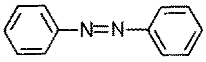
Preparative scale experiments using EGB's provide several indications concerning relative base strengths. Until recently, however, the base strengths of radical-anions and of dianions had not been measured.

The practical basic strength of electrogenerated superoxide ion has already been discussed (p. 152); in this case the effective bases are HO_2^- and HO^-, and in aprotic solvent it appears that they are capable of deprotonating acetonitrile at a significant rate. Furthermore, consideration of the application of EGB's in Wittig and Wittig-Horner reactions allows a rough categorisation of the fluoren-9-ylidenemethane and ethenetetracarboxylate dianions as weakly basic by comparison with the azobenzene and azine radical-anions. The latter will deprotonate phosphonate esters which are less acidic than, say, benzylphosphonium salts (see Table 15).

Another factor which determines basicity is the solvent/electrolyte system. The effect on stereochemistry has been dealt with (Table 7 p. 152); the yields displayed in Table 7 and in Scheme 18 are also revealing. The results have been interpreted[45] in

Table 15. Comparison of EGB basicity: the Wittig-Horner reaction [40]

Reaction[a]: $PhCH_2P(O)(OEt)_2 + PhCHO \xrightarrow{EGB} PhCH:CHPh$(*cis* + *trans*)

Probase	Reduction potential[b]	Stilbene yield	*trans*/*cis*
	−1.0	0% (*cf.* Table 8, entry 8)	—
$(EtO_2C)_2C{=}C(CO_2Et)_2$	−0.65	0%	—
	*ca* −1.1	77%	1.5
	−1.1	89%	mainly *trans*

[a] $DMF\text{-}Bu_4NClO_4$; Hg cathode; [b] V *vs* $Ag/AgI_{(s)}$

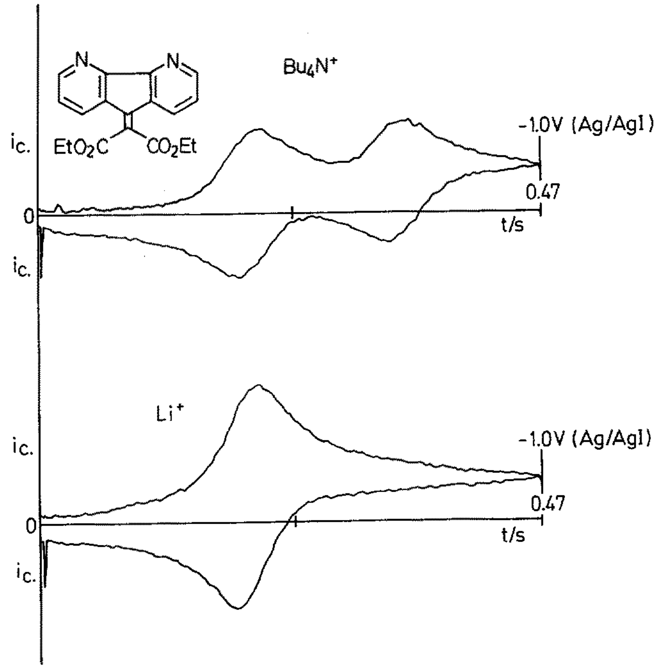


Fig. 2. Stabilisation of dianion by ion-pairing

terms of optimum base strengths for the reactions which arise from particular combinations of dianion and electrolyte cation. For a given dianion it was suggested that Li^+ disperses charge through ion-pairing and is therefore base-weakening in contrast to Bu_4N^+. Consequently a weakly basic dianion combined with Bu_4N^+ might be of equivalent base strength to a more strongly basic dianion paired with Li^+. The dramatic effect of such ion-pairing is well-demonstrated in the cyclic voltammetric behaviour of diethyl-(4,5-diazafluoren-9-ylidene)malonate (Fig. 2). In the presence of Li^+ the dianion is stabilised by ion-pairing to the extent that the first and second reduction peaks merge — i.e. the value of K in reaction 5 in equation 4 is shifted from about 10[11] to near unity. Furthermore the basicity of the dianion is significantly lowered, a fact which is reflected in the relative yields for the preparative experiments listed in Table 7 (entries 9 and 10). A similar merging of the first and second reduction peaks in the presence of Li^+ has been reported for azobenzene reduction[30, 29].

The little quantitative information that is available concerning EGB's is summarised in Table 16. Fortunately a recent development is the application of electroanalytical methods for the determination of basicity, usually as kinetic basicity.

Table 16. Base strengths of some EGB's

Probase	EGB	pK_a (conjugate acid)[a]	Ref.
$R_xM^+CH_2CN$	$^-CH_2CN$	31.3	12)
$R_xM^+CH_2Ph$	$^-CH_2Ph$	*ca.* 44	12)
CCl_4	$^-CCl_3$	15.5 (DMSO/MeOH)[b]	55)
O_2	HO^-/HO_2^-	*ca.* 24[c]	46)
$R_xM^+CH_2COPh$	$^-CH_2COPh$	25	12)
$PhN{=}NPh$	$[PhN{-}NPh]^{2-}$	38 (DMF)[d]	52)
$PhN{=}NPh$	$[PhN{-}NPh]^{\cdot-}$	16.4–22.6 (DMF)[d]	

[a] On Bordwell scale (DMSO) unless otherwise stated; [b] Kinetic acidity determined by $^1H/^2H$ exchange; [c] See text, p. 152; [d] Estimated, in DMF solution, from the pKa's (DMSO) of acids required to remove reversibility of 1st and 2nd reduction waves.

5.3 Measurement of Kinetic Basicities

A major development in the study of EGB's is the recently reported measurements of rates of protonation by acids of known pK_a. The correlation of such rates with pK_a, the Bronsted relationship, also enables bases of determined pK_a to be used in the measurement of kinetic acidities of weak acids. This quantitative approach will eventually lead to the optimisation of reaction conditions for preparative reactions by providing data which can be used to match the acid/base pairs more exactly. In many organic reactions involving bases the base chosen is stronger than is strictly neccessary and consequently such reactions are often complicated by side reactions such as condensation reactions and isomerisations. The advantage of an EGB of moderate strength has been seen in the vitamin A preparation described in Scheme 18, where the facile *cis/trans* isomerisation is avoided.

Both cyclic voltammetry and double potential step chronoamperometry have been used for kinetic measurements of EGB reactions. Provided that the mechanism is known (*vide supra*), application of these techniques is routine [56].

In an important paper Kinlen et al. [37] have reported the results of rate measurements for the protonation in DMF solution of the radical-anions of 2,2′-di-*t*-butylazobenzene (DTAB) and of 2,2′,4,4′,6,6′-hexaisopropylazobenzene (HIAB), using as acids a number of substituted arylacetonitriles, benzylsulphones, and fluorene. In practice, large excesses of the carbon acids are used to ensure pseudo-first order kinetics. This work is distinguished from other studies of rates of protonation of radical-anions in that the bases are ones which have found considerable use in synthesis (*cf.* Tables 2 and 3). As a result of the kinetic measurements on the azobenzene EGB's it has been shown that: (a) acids in the pK_a range 17.5–26 are deprotonated at reasonable rates; (b) the radical-anion of HIAB [$E_{p,c}(1) = -2.04$ V (Ag wire)] is a significantly stronger base than that of DTAB ($E_{p,c}(1) = -1.77$ V]; and good Bronsted correlations hold for this system — i.e. the proton transfer rate is indeed a good measure of basicity.

Where dianions are the effective bases the reproportionation reaction, (reaction 5 in Eq. (4)), is in competition with the protonation step (reaction 3). In this instance the pseudo-first order rates of protonation of dianions cannot be precisely determined using the comparison of experimental current-time relationships with those derived by theory for an EEC reaction (i.e. reactions 1–3 in Eq. (4)) [57].

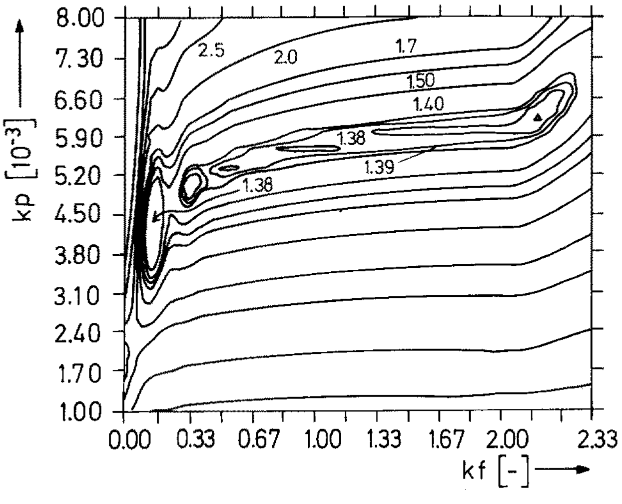
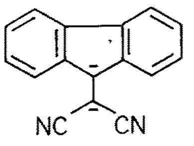


Fig. 3. Protonation rates (k_p) and re-proportionation rates (k_f)



+ $CH_2(CO_2Me)_2$

in DMSO at 25 °C for $\tau = 0.3$ s
The contours correspond to the RMS deviation between the experimental and simulated current-time transients

In a detailed investigation [58] of the kinetic behaviour of bases generated from (fluoren-9-ylidene)methane derivatives the problem has been overcome by computer simulation of current-time transients expected for the extended mechanism (including reaction 5). The program used for the comparison of simulated and experimental curves allows both k_p and k_f to vary independently until the RMS deviation between the two i/t curves is minimised. The equilibrium constant for reproportionation (k_f/k_d) is calculable from values of $E_{p,c}(1)$ and $E_{p,c}(2)$. It is important to realise that there may be any number of pairs of values of k_p and k_f which can give a good fit between experimental and simulated i/t curves.

The quality of the match is expressed as the RMS deviation and it is found that values of RMS < 1.4 correspond to a perfect visual fit. The range of k_p and k_f values which give perfect or near perfect fits may be displayed as computer generated contour plots of the type shown in Fig. 3. The interesting fact which emerges is that whereas k_p may be determined with acceptable precision, a range of k_f values will allow good matching.

Values of k_p emerging from these studies indicate that the (fluoren-9-ylidene)-methane dianions will deprotonate acids in the range pK_a 11–17 at useful rates. Furthermore there is an indication [43] (Fig. 4) that the kinetic basicity of such EGB's may be roughly correlated with the second reduction potential, $E_{p,c}(2)$. This possible correlation needs further rigorous examination as more reliable kinetic information is obtained; the k_p values used in Fig. 4 are not corrected for the competition from reproportionation.

In the near future it is expected that the measurement of kinetic basicity of EGB's will become routine and precise. When available for synthetically useful EGB's the data will be used to optimise the choice of probase and carbon acid and to explore factors (e.g. choice of cation) which influence basicity. Where good Bronsted correlations are observed it will be possible to use data on the basicity of EGB's to

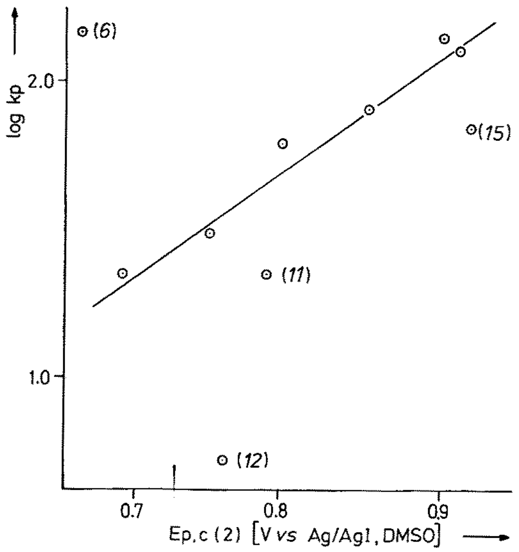


Fig. 4. Plot of log k_p *vs* second reduction potential for fluoren-9-ylidenemethane probases listed in Table 6. (Numbers against aberrant points correspond to entries in Table 6)

devise reliable and convenient methods for the measurement of the acidity of weak acids.

One other prediction may be made. The camphor azine (Table 15) is reduced to give a *chiral* EGB; the tetramenthyl ester of ethenetetracarboxylic acid behaves similarly[40)]. Given that the bases may be generated at low temperature and in the presence of cations which may be chelated it is to be expected that efficient enantioselective deprotonation by EGB's will be realised.

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The Chemistry of Electrogenerated Acids (EGA); How to Generate EGA and How to Utilize it?

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An acid-catalyzed reaction occuring in the vicinity of the anode surface is one of the characteristic electrochemical reactions which are distinguished from any other homogeneous chemical reactions. Even though a total electrochemical reaction system is kept neutral, it is possible to generate a localized quite strong acidic circumstance distinctively in the vicinity of an anode surface. This characteristic phenomenum has long been known but never been recognized as a useful catalytic tool for organic transformations. This review will shed a light on chemistry of electrogenerated acid (EGA). After a brief explanation of a background of EGA, electrolysis conditions in which EGA is efficiently generated and mechanism of EGA generation are discussed. In the following, recent applications of EGA chemistry to organic synthesis are explained so as to understand a scope and limitation of EGA catalysis.

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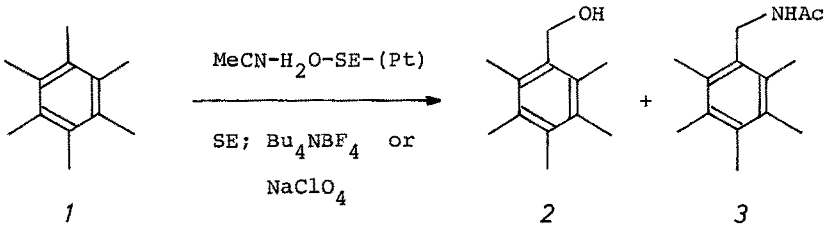
1 Introduction

An electrochemical reaction is distinguished from any other homogeneous chemical reactions by several unique electrode phenomena, one of which, for instance is an acid and base-catalyzed reaction occuring in the vicinity of the electrode surface. On electrolyzing any solutions, one can easily recognize that the vicinity of an anode becomes acidic while that of a cathode becomes basic, respectively. Even though a total reaction system is kept neutral, it is possible to generate a localized quite strong acidic or basic condition distinctively in the vicinity of an anode or cathode. This characteristic phenomenum has long been known but never been utilized as a tool for organic syntheses. Quite recently, the chemistry of the electrogenerated acid (EGA) has become clearer and organic synthetic works by the aid of EGA have just started. Since an only limited number of references in the 1980's is available, we must await future development in this field for full understanding of the EGA chemistry. But this area is a new, unique, and unexplored field among electroorganic chemistry and would attract much attention of synthetic organic chemists. Hopefully, this review may stimulate both electroorganic and synthetic organic chemists to utilize EGA and develop its chemistry.

2 Basic Concept

2.1 Background of EGA

First of all, a historical background of EGA is briefly mentioned. In 1972, Mayeda and Miller [1] had proposed an alternative mechanism to that by Nyberg [2] for the reaction shown in Eq. (1) and suggested the possibility of EGA-catalysis. Acetamide 3



(1)

was predominantly produced on electrolyzing hexamethylbenzene 1 in an MeCN—H$_2$O—NaClO$_4$—(Pt) system, while alcohol 2 was found to be the major product in an MeCN—H$_2$O—Et$_4$NBF$_4$—(Pt) system. Nyberg explained the result based on the hypothesis that Et$_4$NBF$_4$ is solvated by water and thus carrys water to the electric double layer so that the hydrolysis of the benzyl cation generated by the electrooxidation (via ECE mechanism) affords 2. However, Miller pointed out the following facts:

a) alcohol 2 was spontaneously converted to 3 under the same electrolysis conditions employed with LiClO$_4$,

b) change in the counter cation of perchlorate ion from lithium or sodium to the tetrabutyl ammonium ion induced prefered formation of alcohol 2, and

Table 1. Electrooxidative Transformation of Hexamethylbenzene 1 into 2 and 3[a]

Electrolyte	Product ratio	
	2	3
$LiClO_4$	5	95
$NaClO_4$	5	95
Bu_4NClO_4	77	23
$NaBF_4$	60	40
Bu_4NBF_4	82	18
Bu_4NBF_4[b]	5	95

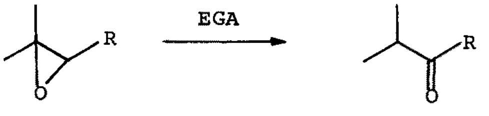
[a] In an undivided cell with $MeCN—H_2O$ (99.6:0.4); [b] In a divided cell

c) Acetamide 3 became a major product if the electrolysis was conducted in a divided cell even if Bu_4NBF_4 was employed as an electrolyte.

On the basis of these facts, it was suggested that the kinetically controlled product 2 would be transformed to the thermodynamically controlled product 3 by EGA generated in the $MeCN—H_2O—NaClO_4$—(Pt) system. Likewise, benzylalcohol was transformed to N-benzylacetamide in the $MeCN—LiClO_4$ system[3,4)]. Indeed, after the electrolysis, the pH of the electrolysis solution was measured to be 2.19 and 3.93 in an $MeCN—LiClO_4$ and $MeCN—Bu_4NBF_4$, respectively, demonstrating that the electrolysis media becomes quite acidic. Although several electrooxidation reactions could be explained in terms of EGA catalysis, no clearcut evidence on EGA had been accumulated before the 1980's, presumably because most of the electrooxidations were conducted in MeCN, MeOH, and DMF, media in which typical acid-catalyzed reactions do not take place. As mentioned later, the nature of EGA is intensively dependent on a combination of electrolytes and solvents which therefore influences the product-selectivity of the electrolysis reaction. In the following, it is examplified how solvents and electrolytes control the reaction rate and the product-selectivity in EGA-catalyzed reactions.

2.2 How to Generate EGA (Electrolysis Conditions)

The conversion of 4 to 5 is a typical example of an EGA catalyzed reaction. The electrolysis is conducted as follows: A mixture of 4 and $LiClO_4$ (1.0 mmol) dissolved in CH_2Cl_2 (7.5 ml) — THF (0.5 ml) is electrolyzed under a constant current (10 mA for 1 min, 0.03 F/mol) at room temperature using platinum foils as electrodes (2×1.5 cm^2)



4 5

(2)

Table 2. Effect of solvents and electrolytes for the EGA catalyzed Transformation of 4 into 5

Electrolyte	Solvent	F/mol	Yield of 5 (%)
$LiClO_4$	THF	0.03	86
	CH_2Cl_2	0.06	91
$NaClO_4$	THF	0.04	83
$Mg(ClO_4)_2$	THF	0.04	79
Et_4NClO_4	CH_2Cl_2	0.5	87
$LiBF_4$	THF	0.9	62
Et_4NOTs	CH_2Cl_2	3.1	12[a]
Et_4NBr	CH_2Cl_2	0.3	0
CF_3CO_2Li	CH_2Cl_2-THF	4.5	0

[a] Allyl alcohol 11 was obtained as a major product (57%)

in an undivided cell. Table 2 shows the effects of solvents and electrolytes for the EGA-catalyzed transformation of oxiranes 4 into ketones 5. The following facts clearly support that this transformation (4 → 5) is one of the typical EGA catalyzed reactions:

a) This transformation is already complete after applying a catalytic amount of electricity (0.01–0.1 F/mol) but never occurs without passing electricity.

b) The reaction occurs only in the anodic compartment and never in the cathodic one when a divided cell is used.

c) On electrolyzing the solvent-electrolyte system first, adding 4 only after disconnecting the electrodes (preelectrolysis conditions) 5 is produced in almost the same yield.

d) One equivalent of pyridine suppresses the reaction.

As shown in Table 2, metal perchlorates are quite effective for the purpose, while both $LiBF_4$ and Et_4NClO_4 induce the oxirane ring opening but require much more current. In contrast to these, both Et_4NBr and CF_3CO_2Li fail to bring about the reaction presumably because the bromide and acetate anions undergo electrooxidation

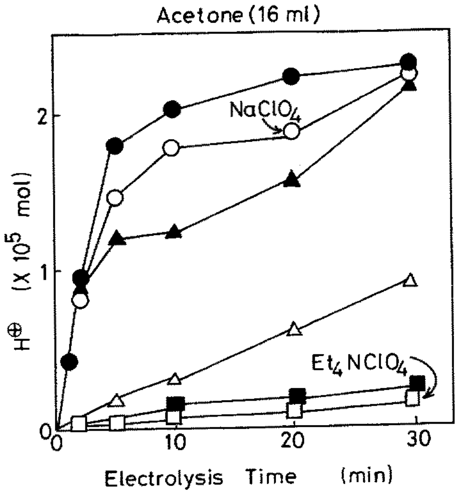


Fig. 1. Electrolyte-dependent EGA Generation in Acetone (16 ml) Containing 2 mmol of Electrolytes

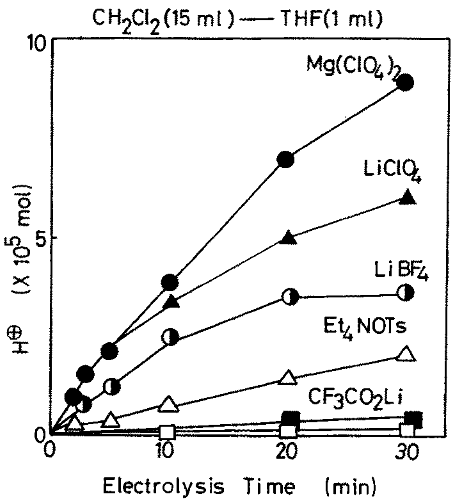


Fig. 2. Electrolyte-dependent EGA Generation in CH_2Cl_2 (15 ml) — THF (1 ml) Containing 2 mmol of Electrolytes

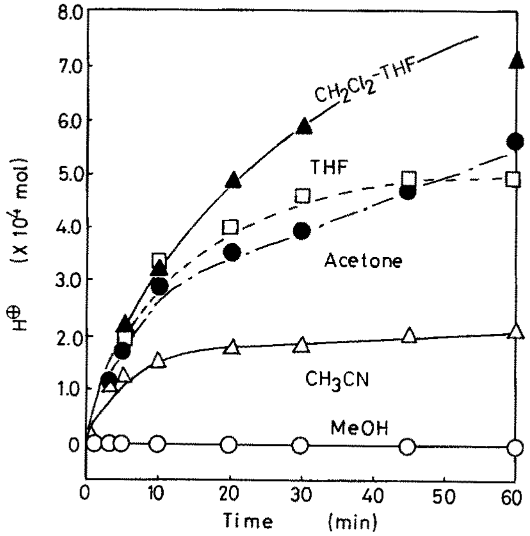


Fig. 3. Effect of Solvents for Generation of EGA Using $LiClO_4$ (200 mg of $LiClO_4$ Dissolved in 16 ml of Solvent Pt-Pt, 3.3 mA/cm^2)

preferentially suppressing the oxidation of water which is essential for EGA generation [6]. Electrolysis with Et_4NOTs initiates the oxirane ring opening after a prolonged passage of current (3.1 F/mol) and promotes the formation of the allylic alcohol 11 instead of the ketone 5. These data clearly indicate that the combination of the metal cation with the perchlorate anion plays the crutial role for the generation of a strong EGA.

The amount of EGA (the current efficiency of EGA generation) is measured in both acetone and methylene chloride-THF. Both Figs. 1 and 2 show that a sharp increase in the concentration of EGA is observed in the electrolysis of lithium, sodium, and magnesium perchlorate solution, being consistent with the result of the oxirane ring opening reaction to ketones (Table 2).

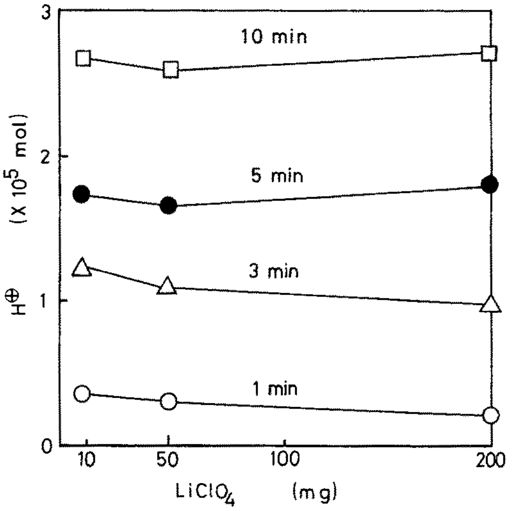


Fig. 4. Relation between the Amount of EGA Generated in CH_2Cl_2 and the Concentration of $LiClO_4$ by Changing Electrolysis Time

Table 3. Effect of Solvent for the Transformation of 4 to 5

Solvent	Yield (%)	
	5	11
$ClCH_2CH_2Cl^a$	91	2
$CH_2Cl_2{}^a$	91	2
$CH_2Cl_2{}^{*a}$	91	7
CH_2Cl_2-THF^b	91	8
THF^b	85	10
CH_3COCH_3	75	2
$AcOEt^b$	76	13
$(CH_3O)_2CO^b$	75	14
CH_3CN^b	0	0
$CHCl_3$—CH_3OH^b	0	0

R = $CH_2CH_2CH(CH_3)CH_2CH_2OBn$;
* Reaction in a pre-electrolyzed solution;
[a] $LiClO_4$; [b] $LiClO_4$—Et_4NClO_4

The effect of solvents is also important and some of the results are listed in Table 3. It is notable that even lithium perchlorate becomes ineffective for this purpose, if the reaction is conducted in MeOH or MeCN. Both CH_2Cl_2 and $ClCH_2CH_2Cl$ are useful, and THF, AcOEt, and methyl carbonate are usable. The effect of the solvent on the EGA generation is illustrated graphically in Fig. 3, supporting the results shown in Table 3 [7]. It is also shown that the amount of EGA generated in CH_2Cl_2 is almost linearly correlated with the time of electrolysis but is kept constant throughout the range of the lithium perchlorate concentration examined [7] (Fig. 4). Fig. 5 illustrates the above mentioned results. It can be used to estimate what kind of combination of electrolytes and solvents can generate EGA of various strength. In general, any combination of electrolytes and solvents appearing in the upper part of Fig. 5

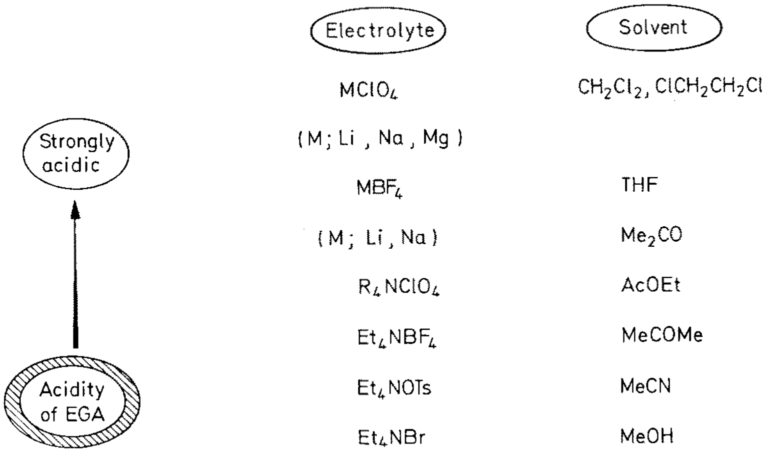
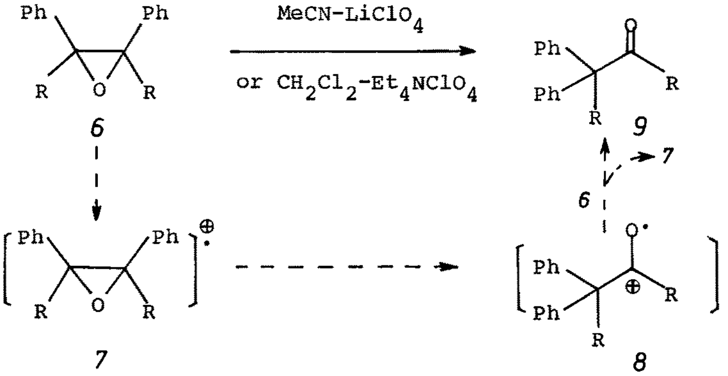


Fig. 5. An Estimated Order of Electrolytes and Solvents, of which Combination Generates a Strong EGA

make it possible to generate a strong acid. However, it is noteworthy to point out that the simple choice of $MClO_4$ and CH_2Cl_2 is not sufficient for the realization of a high product-selectivity in EGA catalyzed reactions. As discussed later, the product-selectivity in EGA-catalyzed reaction is markedly dependent on the nature and the concentration of both cation and anion of electrolytes and solvents.

In connection with the oxirane ring opening, the isomerization of oxirane 6 to ketone 9 in an $MeCN-LiClO_4$—(Pt) and a $CH_2Cl_2-Et_4NClO_4$—(Pt) system has been reported and was explained on the basis of an electron-transfer chain mechanism via 7 and 8 [8]. However, 6 is actually converted to 9 under the preelectrolysis conditions so that the transformation may be explained in terms of an EGA catalyzed reaction [5].



(3)

2.3 Mechanism of the EGA Generation

In this section, the mechanism of the EGA generation will be discussed. The first question is why $LiClO_4$ and Et_4NClO_4 are quite different from other typical electrolytes in terms of efficiency for the EGA generation. Supposing the electrolysis of a CH_2Cl_2—

—$LiClO_4$ system, the lithium cation is reduced to lithium metal at a cathode (In fact, deposit of a black lithium metal on the cathode is observed after a prolonged electrolysis). In the absence of any proton sources, the lithium metal on the cathode can not dissolve into a bulk solution to make a base. On the other hand, a naked perchlorate ion bearing no counter cation (unbuffered perchlorate [1]) is localized in the proximity of the anode surface and is allowed to react with traces of water in the medium affording perchloric acid and hydroxide ion. The latter is subsequently oxidized to produce oxygen or hydrogen peroxide [9] (Eq. (4)). Consequently the total reaction system becomes acidic. Especially, as perchloric acid is markedly concentrated in the proximity of an anode surface, an unusually strong acidic reaction zone can be created where various acid-catalyzed reactions can occur spontaneously (Fig. 6). In contrast, in an MeOH—$LiClO_4$ system, lithium metal, reductively generated on the cathode, instantaneously reacts with methanol to provide a base which neutralizes perchloric acid generated at the anode. Therefore, overall the electrolysis apparently makes no EGA even though an EGA-catalyzed reaction in MeOH can be expected to occur locally in the proximity of an anode surface during electrolysis. Some examples of EGA-catalyzed reaction in an MeOH-$LiClO_4$ system will be shown later.

$$ClO_4^{\ominus} + H_2O \rightleftharpoons HClO_4 + OH^{\ominus} \xrightarrow{-e} O_2 \qquad (4)$$

$$ClO_4^{\ominus} \xrightarrow{-e} ClO_4\cdot \xrightarrow{CH_3CN} HClO_4 + \cdot CH_2CN \qquad (5)$$

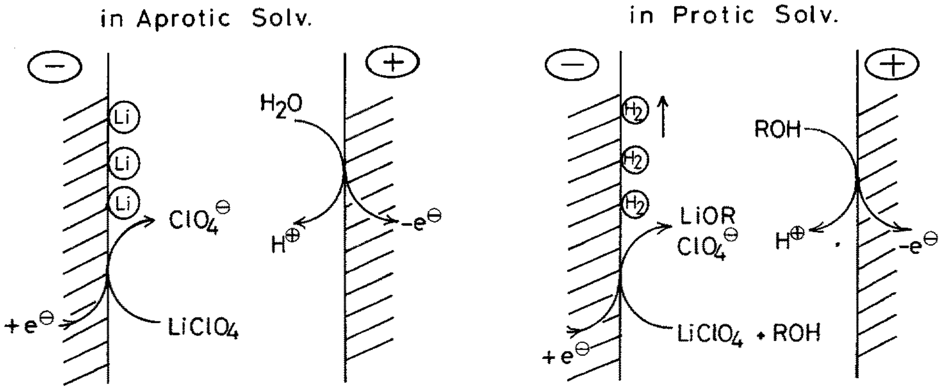


Fig. 6. Illustrations of the Mechanism of EGA Generation

It has been known that the electrolysis in an MeCN—$NaClO_4$ system generates an acid [1]. The hydrogen has to originate from the solvent. A mechanism for hydrogen abstraction from acetonitrile by the electrooxidatively generated radical $ClO_4\cdot$ to produce perchloric acid has been proposed, but no evidence for the succinonitrile formation appeared [10] (Eq. (5)). The detection of the $ClO_4\cdot$ radical by the aid of ESR was tried [11]. But it was found to be difficult to differentiate between the perchlorate radical and the radical from chlorine dioxide [12]. The electrolysis in a CH_2Cl_2—

—R_4NClO_4 system also makes the medium acidic, however the strength of the EGA is much weaker than that of a CH_2Cl_2—$LiClO_4$ system due to neutralization of EGA with trialkyl amine produced by cathodic reduction of the ammonium cation [13]. Therefore, an EGA-catalyzed reaction can be performed even in a CH_2Cl_2—R_4NClO_4 [5] or MeCN—R_4NClO_4 [1] system when a divided cell is employed. Presumably, amines generated in the cathode compartment diffuse slowly into the anode compartment where the EGA reaction occurs.

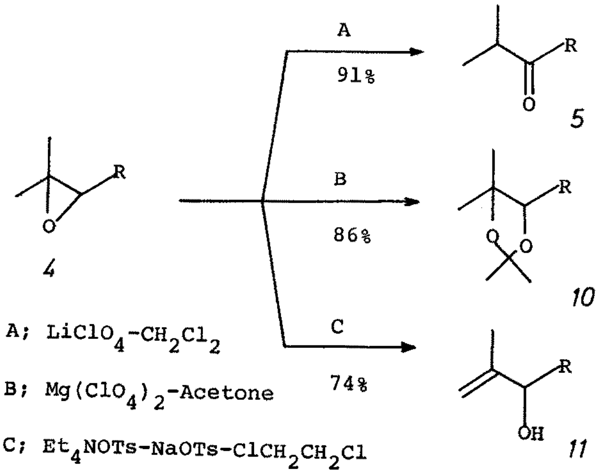
The electrochemical method described here is a useful alternative to the formation of anhydrous $HClO_4$ by chemical methods and can be employed for a variety of acid-catalyzed reactions. Anhydrous $HClO_4$ is not commercially available and must be prepared by the reaction of $AgClO_4$ with dry HCl [14]. This method, however, is not feasible for preparation of a small amount of dry and pure $HClO_4$ without contamination by HCl.

3 What Kind of Chemistry can be Performed by EGA? — Application to Organic Synthesis —

Section 3 surveys the application of EGA to organic synthesis in comparison with other conventional homogeneous acid-catalyzed reactions.

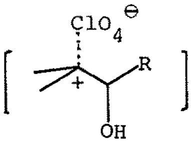
3.1 CH_2Cl_2—$LiClO_4$ and Acetone-$LiClO_4$ System

In the oxirane ring opening reaction (Eq. (2)), it is possible to prepare the ketone 5, the acetonide 10, and the allylic alcohol 11 selectively by controlling the reactivity of the intermediate carbenium ion 12 under some specified reaction conditions. In order to prepare 5 preferentially, a high concentration of perchlorate ion must be employed in CH_2Cl_2, $ClCH_2CH_2Cl$, or THF. In this system, an incipient carbenium ion 12 would be associated with perchlorate ion and stabilized so that the deprotona-



(6)

tion leading to the thermodynamically stable product would be a favored process. The stabilization of 12 with perchlorate ion would be responsible for lowering an activation energy of the process (4 → 5). This means that the acidity of EGA can be measured by the ability of an electrolyte anion to stabilize 12 but not by measuring the concentration of EGA. Several researchers have already reported on the interaction between carbenium ions and perchlorate ions [14, 15] and even some covalently bound perchlorate compounds were isolated [16]. The comparison of the EGA catalyzed transformation of 4 → 5 with those of the conventional homogeneous acid-catalyzed reactions is impressive. The EGA method (91 %) is apparently much more useful than the reaction with CF_3CO_2H (45 %), aq. 60 % $HClO_4$ (77 %), TsOH (47 %), and BF_3—Et_2O (77 %) [5].



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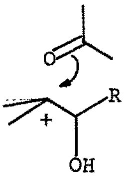

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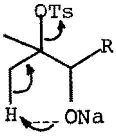

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The EGA method is also usable for the preparation of the acetonide 10 from 4. In this case a trace amount of metal perchlorate is effective, otherwise ketone 5 is produced preferentially [5]. The carbenium ion 12 is trapped by acetone instead of the perchlorate ion leading to 10 as shown in 13. And a minimum amount of metal perchlorate (0.01 eq to 4) serves as a source of EGA and does not work as carbenium ion trapping agent. The yields of 5 and 10 are corelated with the concentration of perchlorate ion in a compensatory manner as shown in Fig. 7.

Electrolysis of 4 in a $ClCH_2CH_2Cl$—Et_4NOTs—NaOTs—(Pt) system provides the allylic alcohol 11 as the major product. The addition and elimination of the tosylate

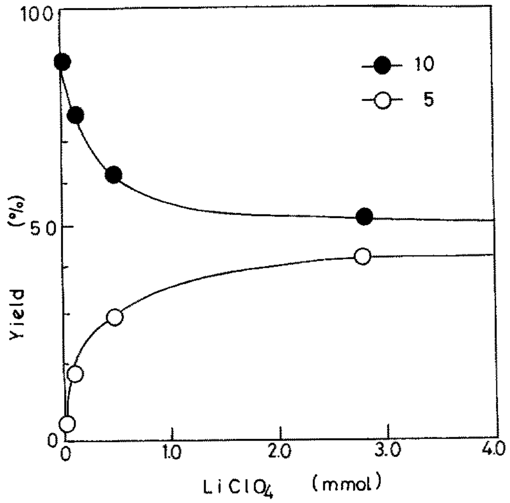
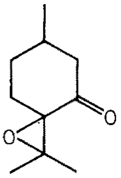
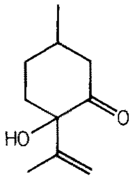
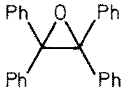
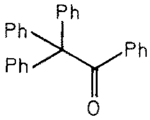


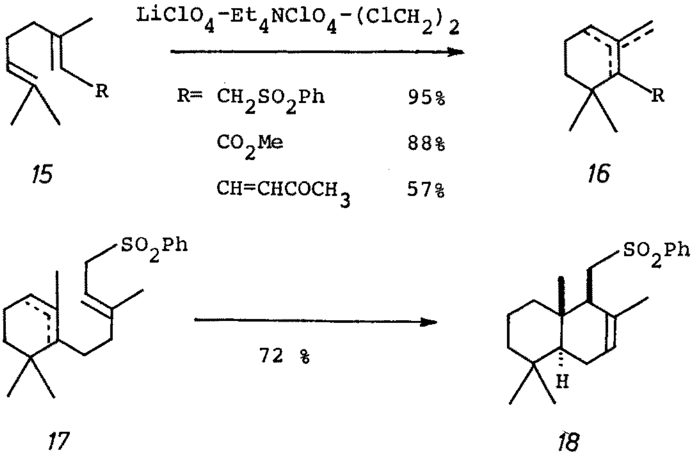
Fig. 7. Relation between Product Ratio (*5* and *10*) and the Concentration of $LiClO_4$ in the Electrolysis of *4* in Acetone

Table 4. EGA-Catalyzed Transformation of 4 into 5, 10, and 11, respectively

Epoxide 4 or R in 4	Yield [%] $5^{b)}$	$10^{c)}$	$11^{d)}$
$(CH_2)_2CH(CH_3)CH_2CH_2OBn$	91	86	74
$(CH_2)_2C(CH_3)=CHCH_2OAc$	87	88	73
$(CH_2)_2C(CH_3)=CHCH_2SO_2Ph$	88	85	81
CH_2OPh	67	83	83
			78
	$97^{a)}$		

a) In pre-electrolysis conditions
b) $LiClO_4$—CH_2Cl_2
c) $Mg(ClO_4)_2$ - Acetone
d) Et_4NOTs-$NaOTs$-$ClCH_2CH_2Cl$

ion is a plausible explanation. An intramolecular hydroxy-assisted elimination (14) is proposed[17]. Although various kinds of strong bases ($LiNR_2$) and Lewis acid-base mixed reagents such as DATMP, 9-BBNOTf, TMSOTf, and $(i\text{-}PrO)_4Ti$ have been employed for the transformation (4 → 11), the EGA method is one of the most

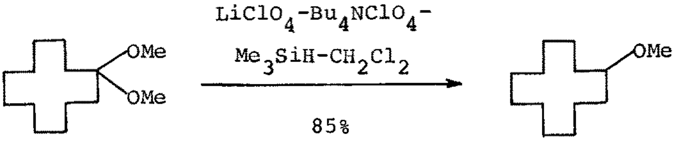


(7)

promising procedures for the purpose. Table 4 is a summary of the solvent and electrolyte-dependent oxirane ring opening reactions.

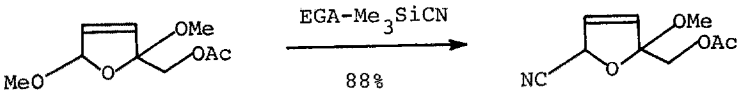
The biomimetic-type cyclization of polyisoprenoids is an important industrial process for terpene synthesis. In most cases, a large excess of concd. H_2SO_4 and $SnCl_4$ has been employed [18]. For example, ionone, a precursor of vitamin A, is prepared by concd. H_2SO_4 catalyzed cyclization of pseudoionone. The disadvantage of this process is undoubtedly the requirement of bases to neutralize the large excess of acid. The EGA method offers a promising alternative for this purpose. Thus, Electrolysis of 15 and 17 in a $ClCH_2CH_2Cl-LiClO_4-Et_4NClO_4-(Pt)$ system provides 16 and 18, respectively in reasonable yields [19] and the neutralization of the reaction solution can be performed simply by addition of a small amount of pyridine [19].

Hydrogenation (19 → 20) [20], cyanation (21 → 22) [21], and allylation (23 → 24) [22]



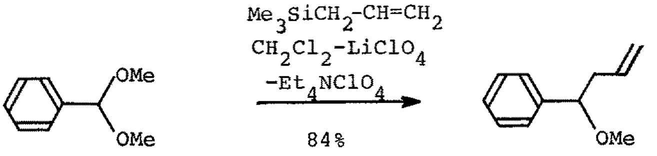
19 20

(8)



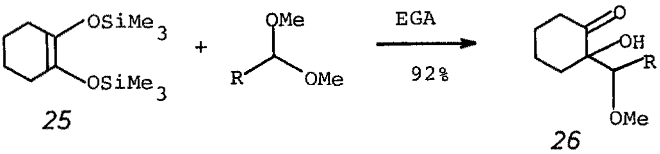
21 22

(9)



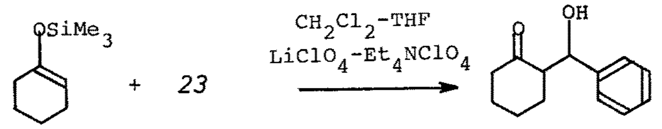
23 24

(10)



25 26

(11)

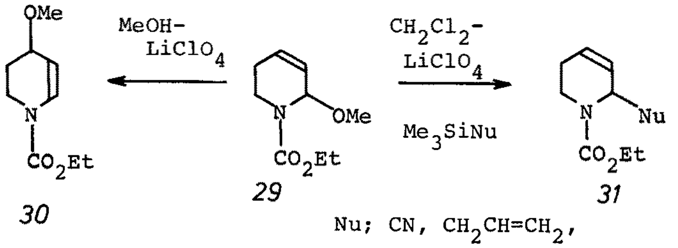


27 28

(12)

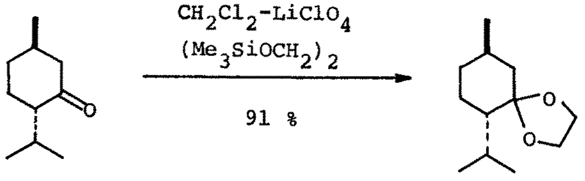
of acetals have been accomplished by the aid of EGA generated in a CH_2Cl_2—$LiClO_4$—Et_4NClO_4—(Pt) system. The corresponding carbenium ions generated in situ by EGA catalysis can be trapped efficiently with nucleophiles such as Me_3SiH, Me_3SiCN, and Me_3SiCH_2—$CH=CH_2$, respectively. Cyanation of 21 takes place regioselectively. Use of $LiBF_4$ or Et_4NOTs results in the recovery of the starting material.

Cross aldol reactions of silyl enol ethers with acetals (25 → 26, and 27 → 28) are also mediated by EGA. The reaction runs smoothly at −78 °C in a CH_2Cl_2—$LiClO_4$—Et_4NClO_4—(Pt) system. At an elevated temperature protonation of both enol ether and acetal occurs competitively to give 28 in a poor yield. Table 5 summarizes yields and diastereoselectivities of 28 obtained by EGA, $TiCl_4$ [23], TMSOTf [24], and $TrtClO_4$ [25]. The EGA method is superior to $TiCl_4$ with regard to the stereocontrol, and comparable with TMSOTf and $TrtClO_4$ in both stereocontrol and yield.



30 29 31

(13)



32 33

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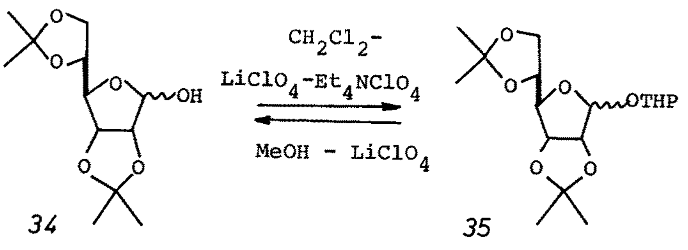


34 35

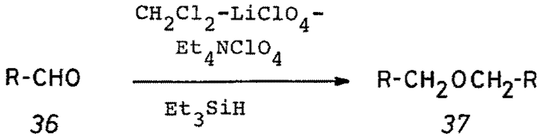
(15)

The regiochemistry observed in the EGA-catalyzed displacement of methoxyl group with nucleophiles is promising [26]. For example, the carbenium ion formed from compound 29 in methanolic solution is trapped to produce the thermodynamically stable compound 30. However, in CH_2Cl_2, a concerted push-pull mechanism ("push" by nucleophile and "pull" by EGA) is operative leading to the exclusive formation of 31. 1-Menthone 32 can be acetalized by EGA catalysis without epimerization at C-2 [27].

Table 5. Yield and Diastereoselectivity of 28 in Comparison of EGA with Other Related Lewis Acid Catalysts

Entry	Acid Catalyst	Yield of 28 (%)	(syn:anti)
1[a]	$TiCl_4$ (1 eq.)	95	50:50
2[b]	Me_3SiOTf (cat)	89	93:7
3[c]	$TrtClO_4$ (cat)	96	88:12
4	EG Acid (cat)	93	86:14

[a] Trt; Triphenylmethyl, Ref. [25]; [b] Ref. [23]; [c] Ref. [24]



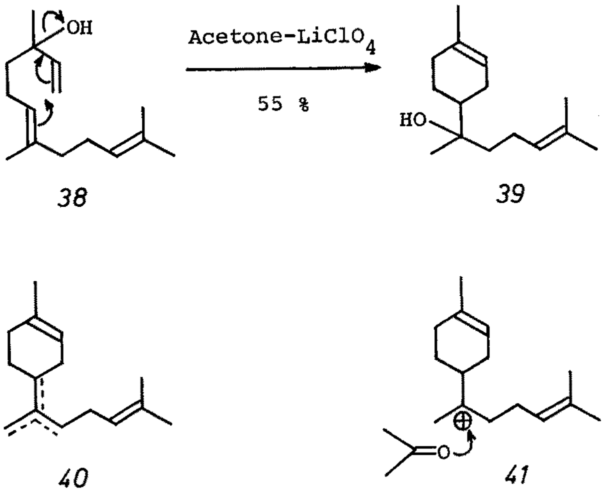
$$\underset{36}{\text{R-CHO}} \xrightarrow[Et_3SiH]{CH_2Cl_2\text{-}LiClO_4\text{-}Et_4NClO_4} \underset{37}{\text{R-}CH_2OCH_2\text{-R}} \qquad (16)$$

Tetrahydropyranilation of alcohols is an important process for the protection of hydroxyl groups. For this purpose pyridinium p-toluenesulfonate and bis(trimethylsilyl) sulfonate have been frequently employed as mild catalysts. The application of EGA catalysis is an effective alternative to protection and deprotection of hydroxyl groups [28]. The combinations, CH_2Cl_2—$LiClO_4$—Et_4NClO_4 and MeOH—$LiClO_4$ are applicable for the protection and deprotection step, respectively (34 $\leftrightarrows$ 35).

Reductive coupling of aldehydes 36 in the presence of triethylsilyl hydride leading to ethers 37 is found to be mediated by EGA [29]. Ethers 37 are obtained in a CH_2Cl_2—$LiClO_4$—Bu_4NClO_4—(Pt) system in 80–90% yield which is comparable to those of the triphenylmethyl perchlorate catalyzed reaction [30].

3.2 Application of EGA to Terpene Syntheses

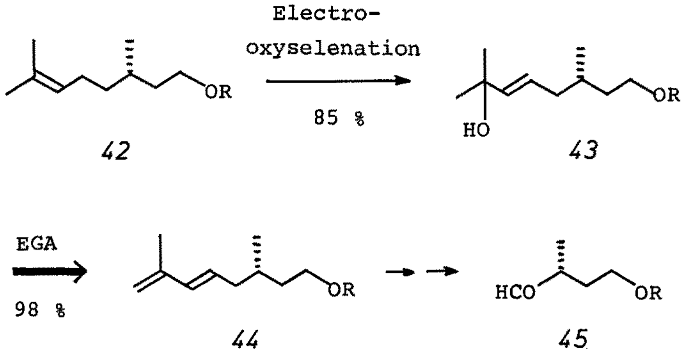
In the following, EGA-catalyzed functionalizations useful for terpene syntheses will be described. The transformation of dl-nerolidol 38 into dl-bisabolol is effectively promoted by electrolysis in acetone-$LiClO_4$ [31]. It is known that the action of either Lewis acids or Brönsted acids to 38 leads to the predominant formation of bisabolenes 40 and cedrenes, and the desired bisabolol 39 was found to be a minor product [32]. It is a highly challenging task to find conditions for the selective transposition of the hydroxyl group from the tertiary carbon of 38 to the thus generated tertiary carbon of 41 in a strong acidic medium. Acetone is an excellent solvent for this purpose forming 39 selectively presumably because it traps the bisabolyl cation as shown in 41. On the other hand, the use of THF (60 °C) and $ClCH_2CH_2Cl$-THF (9:1 at 50 °C) promotes the dehydration exclusively, affording 40 in 72% and 67%, respectively.



38 39 40 41

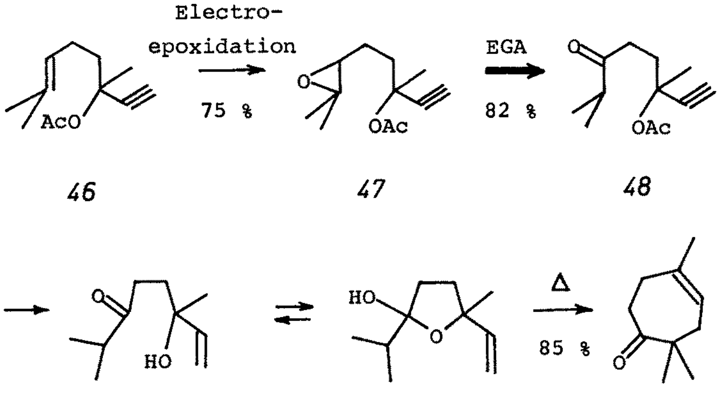
(17)

The chiral C_5 synthetic block 45, the synthetic unit of dolicol, is prepared in the reaction sequence (42 → 45) in which the electrooxidative oxyselenation [33] and the EGA catalysis are effectively employed [34]. Karahanaenone 51, an aroma constituent



42 43 44 45

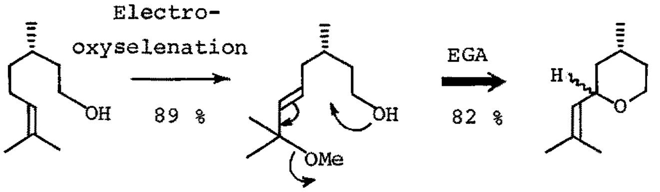
(18)



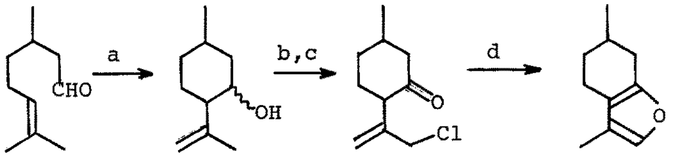
46 47 48 (19)

49 50 51

of hop oil, can be synthesized by a combination of two electrochemical reactions, electrooxidative epoxidation [35] (46 → 47) and EGA-catalysis (47 → 48), followed by a thermal sigmatropic reaction [36]. The application of the same reaction sequence results in the shortest route to optically active rose oxide 54 from (S)-citronellol 52 [37]. Menthofuran 58 can be synthesized by a sequence of electrochemical oxidations (EGA-catalyzed ring closure and electrooxidative ene-type chlorination [38]) as shown in Eq. (21) [7].



52 53 54 (20)



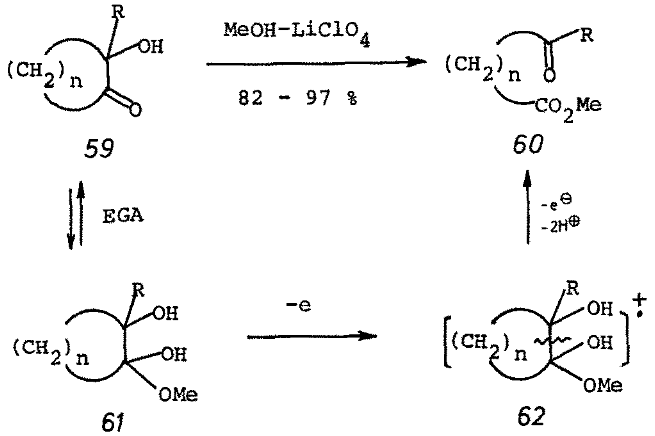
55 56 57 58 (21)

a; THF-CH_2Cl_2-$LiClO_4$-(Pt) 91% b; PCC 95%

c; CH_2Cl_2-H_2O-NaCl-HCl-(Pt) 77% d; 200 °C 72%

3.3 MeOH—$LiClO_4$ System

In contrast to a CH_2Cl_2—$LiClO_4$ system, the concentration of EGA in the bulk solution is negligible in an MeOH—$LiClO_4$ system. However, there remains an ample opportunity for any substrates to suffer an EGA-catalyzed reaction particularly in the proximity of the anode surface on passing current. In this case the EGA reaction can occur parallel to the oxidation of the substrate. The electrooxidative cleavage of α-hydroxycarbonyl compound 59 is a good example. Electrolysis of 59 in MeOH—$LiClO_4$—(Pt) gives ketoester 60 in good yields after passage of 4–7 F/mol of electricity. As shown in Eq. (22), the electrochemically oxidized spieces will be the hemiacetal 61 which is formed from 59 in an EGA-catalyzed equilibrium [39]. In contrast to 1,2-diols the desired bond cleavage of 59 does not occur in MeOH—Et_4NOTs [40], suggesting that $LiClO_4$ is necessary for the generation of a stronger EGA required for hemiacetalization of 59. Similarly, the electrooxidation of epoxyketone 63 in MeOH gives 64. Its yield is markedly dependent on the electrolytes: $LiClO_4$ (90%), $LiBF_4$ (85%), CF_3CO_2Li (16%), and Et_4NOTs (0%). Apparently, the EGA catalyzed oxirane ring opening of 63 leads to the corresponding hydroxyketone. Its EGA-catalyzed hemiacetalization is the rate-determining step. Ketoester 64 is a key intermediate for the synthesis of optically active methyl chrysanthemate 66 from l-carvone [41]. Likewise, ketoester 68, a precursor of the antibiotic dl-Malyngolide 69, is obtained from 67 as shown in Eq. (24) [42].



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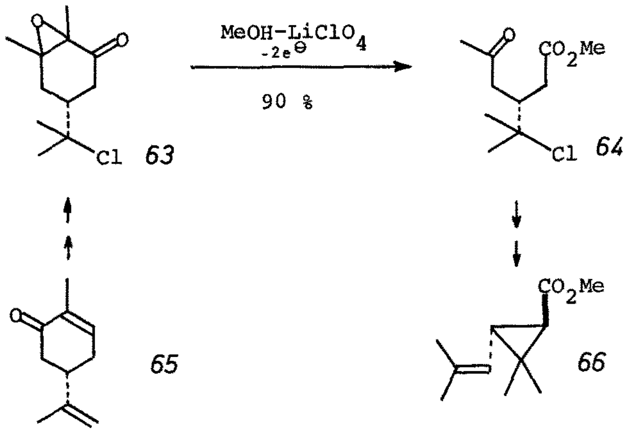

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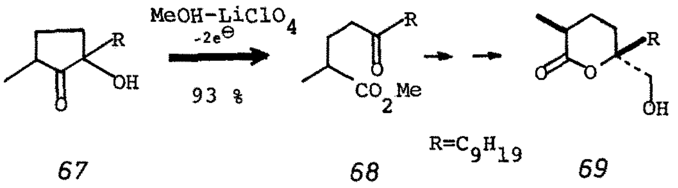
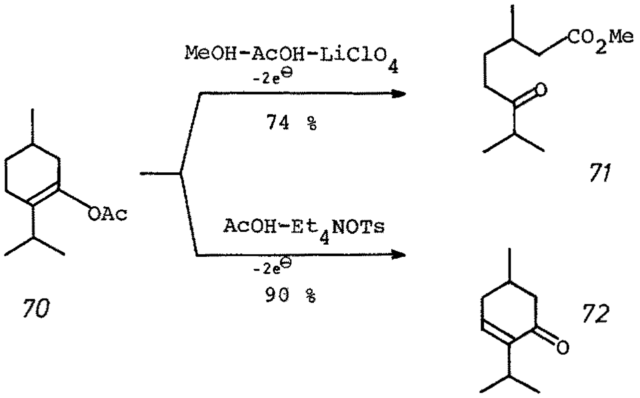


(24)

Electrolysis of 70 shown in Eq. (25) demonstrates the important fact that both electrolyte and solvent are strongly influencing the product selectivity. Electrooxidation of 70 in an MeOH—AcOH—$LiClO_4$—(Pt) system using a divided cell gives 71 in 74% yield [41]. On the other hand electrooxidation in an AcOH—Et_4NOTs—(C) system using an undivided cell gives 72 exclusively [43]. Under both conditions the initial intermediates should be α-methoxy or α-acetoxyketones produced by an ECE mechanism. These intermediates then undergo different reaction pathways. In the former case, a divided cell is employed where the anodic compartment becomes acidic so as to promote the EGA-catalyzed hemiacetalization followed by oxidative carbon-carbon bond cleavage.

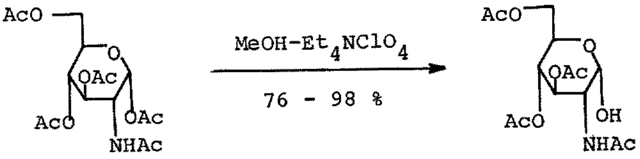


70 71 72

(25)

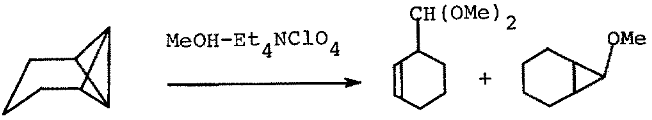
The regioselective ester cleavage of the aminosugar 73 at C-1 [44], the transformation of tricyclo[4.1.0.$0^{2,7}$] heptane 75 into 2-methoxynorcarane 77 [45], and the aromatization of the benzoquinone bisacetal 78 via elimination and rearrangement of a methoxy group [46], are all catalyzed by electrolysis in an MeOH—$LiClO_4$ or Et_4NClO_4—(Pt) system. The transformation (73 → 74) occurs efficiently using both Pt (81 %) or Au (97 %) electrodes, however, graphite electrodes are not effective. This electrolysis is useful for regio- and stereocontrolled deprotection of an anomeric hydroxyl group since the amide group remains intact even after a prolonged electrolysis (6 F/mol) [44]. The action of p-toluene sulfonic acid to 73 results in the nonregioselective hydrolysis. The transesterification of 80 is also possible in ROH—$LiClO_4$ (R = Me, Et and Pr) [28].

The electrooxidation of the carbamate 82 in an MeOH—Et_4NOTs—(C) system leads to the acetal 84 rather than to the methoxycarbamate 83 which presumably undergoes EGA-catalyzed acetalization [47] immediately after its formation.



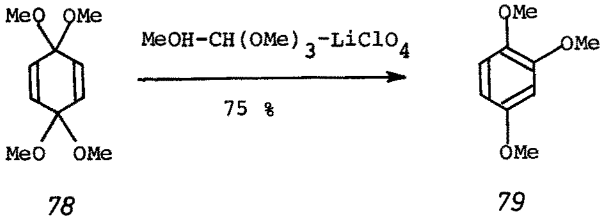
73 74

(26)

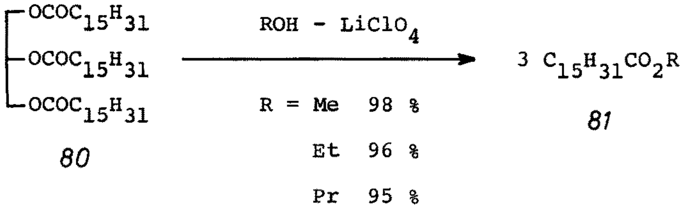


75 76 77

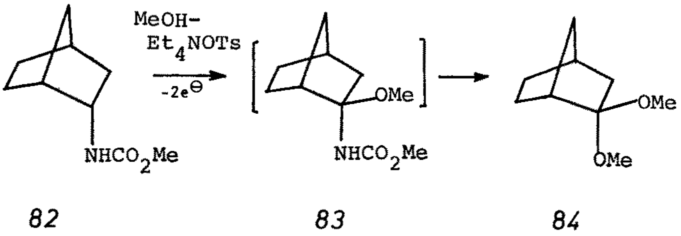
(27)



(28)



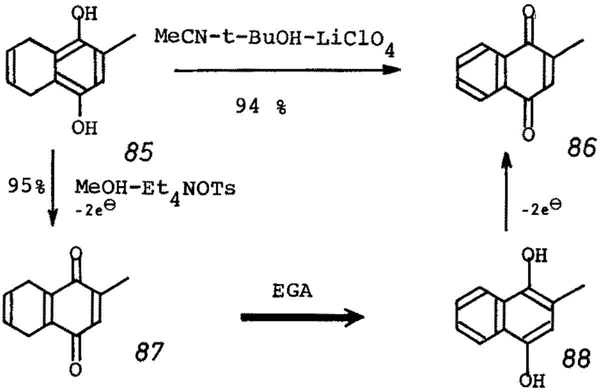
(29)



(30)

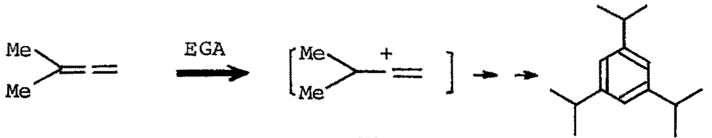
3.4 MeCN—LiClO$_4$ System

The generation of EGA in MeCN—LiClO$_4$ has been reported by Miller [1]. The acidity of EGA in MeCN—LiClO$_4$ seems to be much weaker than that in CH$_2$Cl$_2$—LiClO$_4$. Electrooxidation of 85 in MeCN—LiClO$_4$ and MeCN-t-BuOH (9:1)-LiClO$_4$ gives vitamin K$_3$ 86. Electrolytes such as LiClO$_4$ (94%), Et$_4$NClO$_4$ (87%), LiBF$_4$ (93%), and CF$_3$CO$_2$Li (66%) employed in MeCN are useful. However, Et$_4$NOTs is not effective for the synthesis of 86, giving a mixture of 87 (74%) and 86 (7%). In contrast, electrolysis of 85 in MeOH—Et$_4$NOTs leads to the exclusive formation of 87 (95%)



(31)

and none of 86. In MeCN—$LiClO_4$ electrooxidatively produced dihydronaphthoquinone 87 isomerizes to 88 by EGA catalysis which then suffers further two electron oxidation leading to the final product 86 [48]. The aromatization of allene 89 to 91 [49], and the hydration of carbodiimide 92 [50] can also be explained in terms of EGA catalysis. EGA catalyzed nitration of naphthalene in an MeCN—N_2O_4—$LiBF_4$—Pt system is proposed by Eberson [51].



89 90 91 (32)

$$\underset{92}{t\text{-Bu-N}{=}C{=}N\text{-Bu-t}} \xrightarrow[70\ \%]{MeCN\text{-}LiClO_4} \underset{93}{(t\text{-Bu-NH})_2CO} \qquad (33)$$

4 Conclusion

On electrolyzing any solutions with a platinum electrode, a strong acidic reaction medium is generated in a proximity of an anode surface and can be utilized for EGA-catalyzed functionalization. The nature and acidity of EGA are remarkably dependent on the combination of electrolytes and solvents. As for the acidity of EGA, a combined use of metal perchlorates with aprotic solvents such as CH_2Cl_2 and $ClCH_2CH_2Cl$ generates an extremely strong acidic medium. In addition, the product-selectivity in EGA-catalyzed reactions, is influenced by the following factors, (a) nature of the conjugate bases of EGA (ClO_4^-, OTs^-, BF_4^-, etc.), (b) solvents, (c) concentration of electrolytes, (d) separation of electrolysis compartments or not, (e) degree of driness of electrolytes and solvents, (f) pre-electrolysis, and (g) current density. Among them, (a) and (b) seem to be most important.

It should be kept in mind that on conducting electrooxidation in general, EGA generation does occur in an anode compartment or in a proximity of an anode surface in parallel to the desired oxidation of substrates. So a proper choice of electrolytes and solvents is essential for the successful treatment of any acid-sensitive substrates and products.

Finally it is a great pleasure for the author that this small review may help and encourage both synthetic organic and electroorganic chemists to understand some aspects of EGA chemistry and to apply EGA to various kinds of unexplored fields.

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The author thanks Professor Sigeru Torii, Okayama University, who recently wrote "Electroorganic Synthesis" in which EGA chemistry was also discussed [52], for encouraging him to enter the attractive research area of electroorganic synthesis.

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