Topics in Current Chemistry

148

D. Degner
Organic Electrosyntheses in Industry

E. Kariv-Miller, R. I. Pacut,
and G. K. Lehman
Organic Electroreductions at Very
Negative Potentials

T. Shono
Synthesis of Alkaloidal Compounds
Using an Electrochemical Reaction
as a Key Step

S. Torii, H. Tanaka, and T. Inokuchi
Role of the Electrochemical Method
in the Transformatin of *beta*-Lactam
Antibiotics and Terpenoids

Springer-Verlag

Electrochemistry III

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With 7 Figures and 22 Tables

Springer-Verlag Berlin Heidelberg New York
London Paris Tokyo

This series presents critical reviews of the present position and future trends in modern chemical research. It is addressed to all research and industrial chemists who wish to keep abreast of advances in their subject.

As a rule, contributions are specially commissioned. The editors and publishers will, however, always be pleased to receive suggestions and supplementary information. Papers are accepted for "Topics in Current Chemistry" in English.

ISBN 3-540-19180-1 Springer-Verlag Berlin Heidelberg New York
ISBN 0-387-19180-1 Springer-Verlag New York Heidelberg Berlin

Library of Congress Cataloging-in-Publication Data
Electrochemistry / editor, E. Steckhan ; with contributions by D. Degner . . . [et al.].
p. cm. — (Topics in current chemistry ; 148)
ISBN 0-387-19180-1 (U.S. : v. 3)
1. Electrochemistry. I. Steckhan, E. (Eberhard), 1943– . II. Degner, D. (Dieter)
III. Series.
QD1.F58 vol. 148 [QD555] 541.3'7—dc 19 88-11949 CIP

Printed in GDR

Bookbinding: Lüderitz & Bauer, Berlin
2151/3020-543210

148 Topics in Current Chemistry

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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 Development 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 III

At this rather advanced stage of research and application, I think, it is very appropriate to devote Volume III and part of Volume IV of the electrochemistry series in Topics in Current Chemistry to **recent developments in electroorganic synthesis**. The basis for modern electroorganic synthesis was laid down during the 1960's and 70's by the discovery of the principal reaction mechanisms and by the introduction of a number of industrial processes. Now, electrochemists are in a position in which they can select from an abundance of methodological tools to synthesize complex organic building blocks and target molecules.

This is nicely demonstrated by two contributions to this volume. On one hand, electrochemical strategies for the synthesis of complex bioactive alkaloid structures are developed, and on the other, the electrochemical transformation of readily available bio-molecules (terpenoids and β-lactams) into enantiomerically pure complex synthetic building blocks is demonstrated.

In one paper, a new methodology for the remarkably selective reduction of organic molecules, possessing very negative reduction potentials, is developed. Due to the relatively simple reaction conditions, this method may be an interesting alternative to alkali metal-ammonia reductions.

A tremendous amount of research in the field of electroorganic synthesis has been performed in industrial laboratories. This work usually is only accessible with difficulty because it is hidden in patents. Therefore it is extremely helpful for scientists working in this field that an industrial electrochemist undertook the burden of critically reviewing the patent literature. At the same time the prospects and limitations for future industrial applications of electroorganic syntheses are clearly evolved.

It is hoped that the contributions to this volume will fruitfully influence the further development of electroorganic chemistry and initiate a growing interest in the application of electrosynthetic methods.

Bonn, April 1988 Eberhard Steckhan

ISBN 3-540-19180-1
ISBN 0-387-19180-1

Organic Electrosyntheses in Industry

Dieter Degner

Main Laboratory of BASF Aktiengesellschaft, Ludwigshafen

Table of Contents

Dedicated to Prof. Dr. Dörfel on the occasion of his 60th birthday

Topics in Current Chemistry, Vol. 148

The article gives a survey on research in the field of organic electrochemistry in industry Reference is made to the patent literatur of the last 10 to 15 years. Prospects and problems of electroorganic processes are discussed in detail — also in comparison with proven technologies. Furthermore, some general criteria are presented which can be regarded as preconditions for the realization of electroorganic syntheses in industry. Although there has been considerable progress over the past few years and further electroorganic reactions have been implemented in industry, there is still a need for more highly selective electrosyntheses if this technology is to find broader application in industry.

Table of Contents

Table of Contents of Volume 142

Electrochemistry I

Table of Contents of Volume 143

Electrochemistry II

1 Introduction

Up to the present, electrochemical reactions have not formed an important part of industrial organic chemistry although these syntheses are among the oldest reactions of organic chemistry, the Kolbe reaction being an example [1,2]. This situation is in contrast to that encountered in inorganic chemistry. The electroorganic syntheses of lead-tetraethyl [3] and adipodinitrile [4-5] which were realized industrially in the sixties are to some degree exceptions, although only the adipodinitrile process will continue to be important in the future. At that time, the method was expected by many to become widely established in industry; however, this expectation proved false and industrial activities in this new area were once again restricted. The failure was principally due to the virtually exclusive concentration on finding processes for large-scale products.

The unsuccessful efforts to establish an alternative electrochemical process for the synthesis of propylene oxide [6,7] in industry are an example of this. The consistent application of organic reaction mechanisms to electroorganic syntheses (e.g., [8-9]), and the new indirect electrosyntheses [10] with a preparative basis, have been major factors underlying the industrial chemist's increasing awareness of the neglected preparative potential of organic electrochemistry. Thus, activities in this peripheral area of organic chemistry have once again increased over the past few years, although work at present tends to be concentrated in the area of fine chemicals [11].

The past few years have seen the appearance of a number of excellent monographs [12-17] which give a good overview of the preparative potential of organic electrochemistry. While the scientific literature is generally comprehensively covered, the patent literature receives little or no attention. It is hoped that this article will help to close this gap and furthermore review the projects undertaken in industry over the past few years.

2 Prospects and Risks of Electroorganic Reactions in Industry

The prospects of electrochemical reactions in industry depend primarily on their preparative potential and are much less affected by a lack of know-how in the area of electrochemical process engineering or even by management's lack of interest or unwillingness to take risks, as was frequently claimed in the past [18]. In competing with other technologies, organic electrochemistry has made some progress over the past few years. However, even today there are too few reactions which can be carried out either with high selectivities or particularly advantageously only by an electrochemical route. Examples of industrially important reactions are the anodic substitution reactions, which permit the functionalization of olefins and aromatics; the cathodic hydrodimerization of activated olefins and carbonyl compounds, which provides a simple method for C—C coupling; and finally the electrochemical regeneration of expensive, highly selective redox systems, whose stoichiometric application is ruled out for economic or environmental reasons.

From the point of view of process engineering, electrochemical reactions offer a number of advantages: conversion, reaction rate, and, within certain limits, selectivities can be influenced and easily controlled by means of additional parameters, such as current density and charge. Electrochemical reactions take place under mild reaction conditions (no high temperatures, in general atmospheric pressure) and do not require pressure-tight or corrosion-resistant equipment. This permits comparatively low capital expenditure, at least for the mere synthesis itself. Electrochemical reactions do not in general entail any waste air or wastewater problems. This aspect will become even more important for future investments.

However, these advantages are offset by a number of problems, which may be divided into three groups:

I Electroorganic syntheses require special reactors; the cells used in inorganic electrochemistry are not suitable for electroorganic syntheses in general.

II Electrochemical syntheses are phase boundary reactions. The boundary problems, which are also familiar from heterogeneous catalysis, must be expected especially during continuous operation.

III The necessity of using electrolytes frequently results in expensive separation operations during work up of the electrolysis mixtures. These operations render many electroorganic syntheses uneconomical.

In the past developing an industrial-scale electrosynthesis was directly connected to the construction of an industrial electrolysis cell. Today cells which can be used industrially are commercially available. Examples are the SU cell [19)] and cells from Steetley Engineering [20)] and Reilly Chemical [21)]. Furthermore, the FM 21 cell [22-24)], developed for the chloralkali electrolysis, is now offered by ICI for electroorganic syntheses, too. These cells are based on the construction principle of a plate-and-frame cell and can be used as either divided or undivided cells. They are offered as multipurpose cells and are suitable for small and medium size capacities. For large capacities, it is frequently more economical to use a tailor-made cell. For example, Monsanto and BASF use a specially developed cell [5, 25)] in the adipodinitrile synthesis. For industrial anodic substitution reactions, in which electrolytes with comparatively low conductivities are used, BASF developed an undivided plate-stack cell [26-29)]. The literature describes a number of other cells [30-32)] which have not become industrially important, so far. A good review of cells and cell design is given by Danly in [33)].

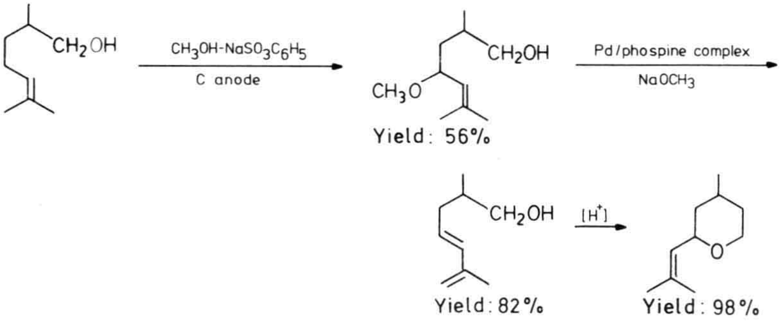
The frequent electrode problems (electrode coatings and deactivation as well as corrosion of electrodes) that occur in continuous operation and the necessity of using auxiliary electrolytes are in many cases the critical problems in the industrial realization of an organic electrosynthesis. Another disadvantage is the very limited possibility of extrapolating experience, gained with one process to the scaling up of new reactions. Therefore, it is generally not possible to dispense with the tedious and hence expensive electrode life tests with simultaneous recycling of the electrolyte. Equally, miniplant technology is only of limited use since long-term tests should as far as possible be carried out on at least one electrode of the planned industrial dimensions. All this has to be considered in advance in order to avoid unpleasant surprises when an industrial plant is commissioned. The problems encountered in scaling up electroorganic reactions are discussed in detail in [34)].

3 Recent Work in the Area of Organic Electrochemistry in Industry

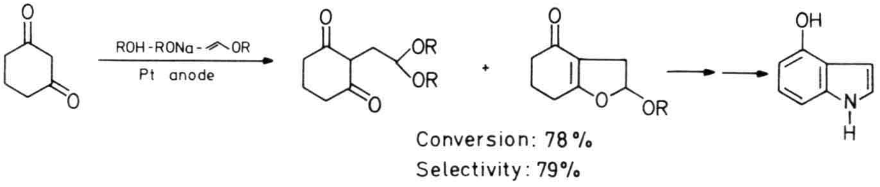
3.1 Anodic Oxidation

3.1.1 Anodic Functionalization of Olefins

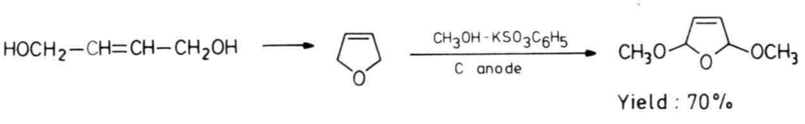
The anodic oxidation of olefins in the presence of nucleophiles, such as CH_3OH or CH_3COOH, is in principle a reaction of very great industrial interest since it permits allyl oxidation as well as C—C coupling. Nevertheless, it is hardly used industrially today. This is essentially due to the fact that the selectivities are frequently poor. Over the past few years, the reaction principle has been used in synthesis problems in the area of fine chemicals. For example, the anodic methoxylation of citronellol is a key step in a new rose oxide synthesis by Sumitomo[35].



Kuraray[36] used the addition of anodically generated radicals of 1,3-dicarbonyl compounds for C—C coupling in the preparation of intermediates for β-blockers.

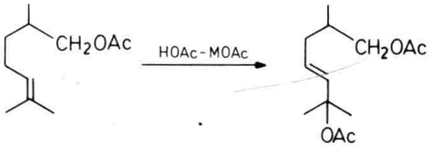


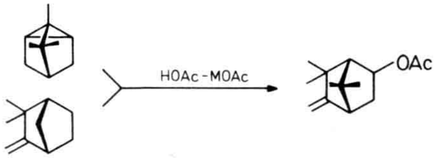
BASF developed a process for the preparation of 2,5-dimethoxy-2,5-dihydrofuran from butene-1,4-diol[37]:



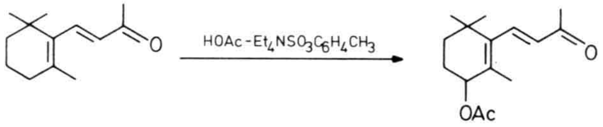
which is an alternative to the anodic methoxylation of furan (cf. 3.1.5).

The anodic acetoxylation of olefinic terpenes was used for the synthesis of new fragrances (Kuraray[38–42])





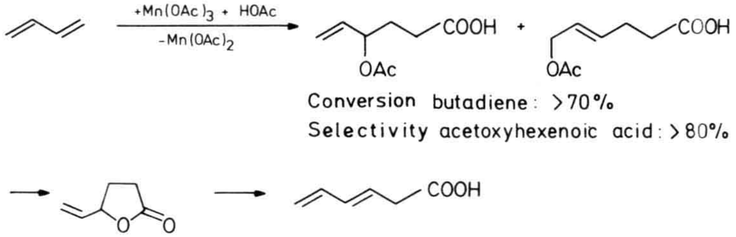
and for the intermediates of canthaxanthin (Hoffmann-La Roche[43]).



Yield : 65%

These reactions — with the exception of[37] — have not progressed beyond the laboratory stage, while a new sorbic acid synthesis based on the addition of carboxymethyl radicals to 1,3-butadiene[44-48] has reached the pilot stage at Monsanto. The core of the new synthesis is the in-cell regeneration of the chemical oxidant $Mn(OAc)_3$ in the presence of catalytic amounts of Cu(II) salts.

$$Mn(OAc)_2 \xrightarrow{\text{anode}} Mn(OAc)_3$$



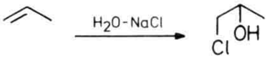
Conversion butadiene : >70%
Selectivity acetoxyhexenoic acid : >80%

The new synthesis is superior to the present process based on ketene and crotonaldehyde in terms of the variable costs (butadiene and acetic acid are inexpensive starting materials). However, high conductive salt concentrations coupled with low concentrations (2–4%) of the desired product in the electrolyte together with considerable corrosion problems make the working up procedure much more expensive. Therefore, the new process so far has not been used industrially.

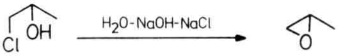
3.1.2 Electrochemical Epoxidation of Olefins

The electrosynthesis of propylene oxide (PO) has already been studied intensively by Bayer[49] in the sixties, and has been scaled up to the pilot scale. The synthesis was carried out in a divided cell at Ti/RuO_2 anodes and steel cathodes.

Anode reaction:

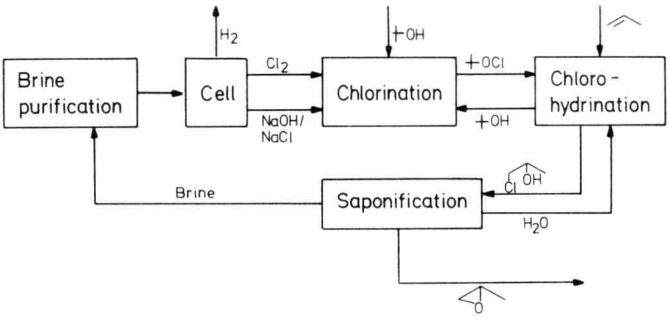


Cathode reaction:



The current efficiencies for propylene oxide were 85 to 90%, and, as in the conventional chlorohydrin process for PO, the principle byproduct was 1,2-dichloropropane (current efficiency up to 10%), which is of no value. Experiments at BASF [50] have shown that the process can also be carried out in undivided cells (anode: Ti/RuO_2 or graphite). The electrolyte was an aqueous NaBr solution. Also in this case, however, it proved impossible to suppress the formation of the 1,2-dibromopropane byproduct. Because of the low concentrations of desired product (2–4% of PO in the electrolyte) and the presence of numerous byproducts, the work-up procedure is complicated rendering the process uneconomical. The addition of carbonates or bicarbonates (UCC [51]) reduces the formation of dibromopropane from about 10 to about 5 mol %, but also in this case the principal problems are not solved. The conventional industrial chlorohydrin process is not very satisfactory as it inevitably produces a large amount of $CaCl_2$. This is why electrochemical alternatives are still searched for. For example, BP has recently proposed a gas diffusion electrode for propylene oxidation [52], and DOW has suggested a special propylene metering system [53].

A more obvious method of avoiding the inevitable production of $CaCl_2$ is the combination of the chloralkali electrolysis with the chlorohydrin process. This is also being pursued intensively [54–55]. A modification proposed by Lummus is shown in the block diagram below [56]:



The electrosynthesis of hypochlorites has been studied in detail by Olin [57–58].

Whereas the electrochemical process of the production of propylene oxide has not advanced beyond the stage of experimental production, the electrosynthesis of hexafluoropropylene oxide [59–62] has been implemented industrially by Hoechst: