6 January 1967, Volume 155, Number 3758 **SCIENCE**

Synthetic Electroorganic Chemistry

Stanley Wawzonek

Recent announcements of commercial developments of electrolytic processes for the preparation of adiponitrile and tetramethyllead have focused attention on a long-known method that has been used only sporadically. Lack of utilization of this technique by chemists and industry has been ascribed to general ignorance of the method, the disorganized condition of the electroorganic literature, and industry's reluctance to undertake long-range studies of the method's potential.

During the last 20 years a reawakening has been stimulated by the appearance of a systematic review of electroorganic preparations (*1*), by polarographic studies in both aqueous and aprotic solvents, by the use of tetraalkylammonium salts as supporting electrolytes, by controlled potentials and rotating cathodes, and by the realization that the cost of electric power has changed very little over the years while the costs of chemicals and labor have mounted considerably. I shall deal with only the more important developments during this period because many reviews have dealt with preparative electroorganic chemistry (*2*).

Electrolytic Reductions

The polarographic method has stimulated the field because it enables very rapid determination of whether a reduction or oxidation will proceed with an organic compound. The resultant polarographic data do not always agree with the results obtained in a large-scale electrolytic preparation, since the former occur under diffusion-controlled conditions while the latter is accompanied by vigorous stirring. An illustration of such a phenomenon is the reduction of benzenediazonium chloride, which polarographically gives two waves in buffered solutions. The first wave is independent of *p*H and represents the following electrode reaction:

$$C_6H_5N_2^+ + e \rightarrow C_6H_5\cdot + N_2$$

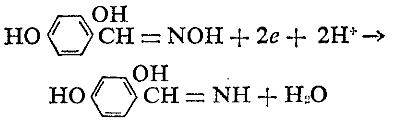
Large-scale electrolysis, with the use of a controlled potential, gave products arising from the phenyl radical, phenylmercuric chloride, and diphenylmercury.

The second wave, which is about four times as high as the first, is *p*H dependent and represents the reduction of the ion to phenylhydrazine:

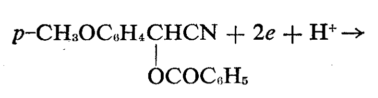
$$C_6H_5N_2^+ + 4e + 3H^+ \rightarrow C_6H_5NHNH_2$$

Large-scale electrolysis, with stirring, however, gave similar products to those obtained by use of the potential of the first wave (*3*). By substitution of a special cell in which the diazonium salt is introduced by gravity through the mercury electrode supported on a permeable disk, phenylhydrazine was obtained in 75-percent yield (*4*).

Conditions for large-scale electrolyses have been based on polarographic data for a number of examples. Reduction of 9-(*o*-iodophenyl)acridine to 9-(*o*-iodophenyl)dihydroacridine (*5*) and reduction of oximes to imines (*6*) required the use of controlled potentials to prevent further reduction to 9-phenyldihydroacridine and benzylamine, respectively—as occurs with chemical reagents.



Reduction of α-benzoxy-*p*-methoxyphenylacetonitrile to *p*-methoxyphenylacetonitrile (*7*),



$$p\text{-}CH_3OC_6H_4\underset{\substack{|\\ OCOC_6H_5}}{CH}CN + 2e + H^+ \rightarrow CH_3OC_6H_4CH_2CN + C_6H_5COO^-$$

required tetraalkylammonium salts as supporting electrolytes. Polarographic waves were obtained in the presence of these salts and not in lithium chloride or ammonium chloride solutions.

Polarographic studies under similar conditions have pointed to a two-electron reduction for saturated ketones and a four- or six-electron reduction for α-hydroxy or dihydroxy ketones in the steroid series. Large-scale reduction of the nonconjugated steroidal nuclear ketones gave the equatorial epimeric alcohol, with a high degree of stereospecificity and in yields comparable to those obtained by reduction with sodium in alcohol (*8*).

Preparations of this type use, in addition to water, organic solvents for solubilization of the organic compounds; high electrical resistances are thus encountered, with subsequent heating of the solution, so that cooling is necessary to prevent loss of the solvent. These factors prohibit scaling-up of such preparations to commercial units, since high current densities are attained only with difficulty.

A technique that circumvents these difficulties and which was ignored until recently is the use of alkali arenesulfonates as solubilizing agents (*9*).

The author is chairman and professor of organic chemistry in the department of chemistry, University of Iowa, Iowa City.

A 200-milliliter saturated solution of potassium sodium xylenesulfonates at 80°C, for example, dissolved 23.7 grams of nitrobenzene and gave, in an electrolytic reduction, a 94-percent yield of azobenzene and hydrazobenzene, with a current efficiency of 93 percent; the current density was 2.4 amperes per square decimeter (*10*). This system is suitable for both reductions and oxidations.

Salts of this type, modified by use of tetraalkylammonium cations, are much more soluble and are the basis for commercial production of adiponitrile from acrylonitrile. The latter compound is reduced polarographically at an $E_{1/2}$ of −1.94 to −2.04 volts versus a standard calomel electrode. Alkali-metal cations are discharged in this range and, when used as electrolytes, lead to the simultaneous formation of propionitrile. The tetraalkylammonium ions are discharged beyond this point and, as electrolytes, give a yield of adiponitrile greater than 95 percent and current densities greater than 10 amperes per square decimeter (*11*).

This hydrodimerization reaction is general for activated olefins and has been applied to derivatives of α,β-unsaturated acids (*12*), α-methyleneglutaronitrile (*13*), α,β-unsaturated ketones, vinyl phosphorus compounds, and methyl vinyl sulfone (*14*). The technique works satisfactorily in mixed couplings of derivatives of α,β-unsaturated acids (*15*), 2- and 4-vinylpyridines (*16*), and arylethylenes (*17*), in intramolecular couplings of activated olefins (*18*), and in the polymerization of acrylonitrile (*19*). Mixed coupling of acrylonitrile and acetone has also been accomplished in aqueous sulfuric acid; it formed γ-hydroxy-γ-methylvaleronitrile and γ,γ-dimethylbutyrolactone (*20*).

The importance of vigorous stirring in attainment of good yields and high current densities has been demonstrated by the use of a rotating cathode in the reduction of nitrobenzene suspensions to hydrazobenzene. A cathode with a rotation of 2000 revolutions per minute gave a yield of 88 percent in contrast with a stationary cathode, with an auxiliary stirrer, that gave 10.7 percent at a current density of 20 amperes per square decimeter (*21*).

The scope of electroorganic chemistry has been extended by polarographic studies in aprotic solvents. This technique has demonstrated the formation of reactive intermediates from various organic compounds and has led to novel electrochemical reactions. Stilbene was found to undergo a stepwise reduction in dimethylformamide to an anion radical and the dianion.

$$\text{first wave}\quad C_6H_5CH=CHC_6H_5+e \rightleftarrows [C_6H_5CHCHC_6H_5]^{\dot{-}}$$

$$\text{second wave}\quad C_6H_5CH=CHC_6H_5+2e \rightarrow (C_6H_5CHCHC_6H_5)^{=}$$

Large-scale reduction gave 1,2,3,4-tetraphenylbutane in a 30-percent yield together with dibenzyl. The same process in the presence of carbon dioxide gave *meso*-diphenylsuccinic acid in 92-percent yield (*22*).

Acids have also been prepared from naphthalene, phenanthrene, and diphenylacetylene by similar reduction of these hydrocarbons in the presence of carbon dioxide; the hydrocarbons formed 1,4-dihydronaphthalene-1,4-dicarboxylic acid, 9,10-dihydrophenanthrene-9,10-dicarboxylic acid, and a mixture of diphenylfumaric acid, diphenylsuccinic acid, and diphenylmaleic anhydride, respectively (*23*).

Reduction of quinones in aprotic solvents proceeds stepwise to the semiquinone anion and the dianion. The large-scale reduction

$$\text{first wave}\quad Q+e \rightleftarrows Q^{\dot{-}}$$

$$\text{second wave}\quad Q^{\dot{-}}+e \rightarrow Q^{=}$$

of anthraquinone in the presence of ethyl bromide produced the diethyl ether of the hydroquinone in 20-percent yield (*24*).

Aromatic ketones and aldehydes show a stepwise reduction in dimethylformamide that points to the following steps:

$$\text{first wave}\quad (C_6H_5)_2C=O+e \rightleftarrows (C_6H_5)_2\dot{C}\text{–}O^-$$

$$\text{second wave}\quad (C_6H_5)_2C=O+2e \rightarrow (C_6H_5)_2C^-\text{–}O^-$$

The stability of the intermediate ketyl varied with the substituents. The product from benzophenone, when produced by large-scale reduction in the presence of ethyl bromide and of carbon dioxide, gave diphenylethylcarbinol and benzilic acid, respectively. Acetophenone and benzaldehyde gave intermediates that dimerized rapidly to pinacols. In the presence of carbon dioxide, reduction of acetophenone gave a 4-percent yield of atrolactic acid; benzaldehyde gave only hydrobenzoin (*25*).

Electron spin resonance studies (*26*) of solutions prepared under controlled potentials have verified the stabilities of these intermediate anion radicals.

α,β-Unsaturated ketones undergo stepwise reduction in dimethylformamide, giving intermediates that have been studied on a large scale for benzalacetophenone (*27*):

$$\text{first wave}\quad C_6H_5CH=CHCOC_6H_5+e \rightarrow (C_6H_5CHCHCOC_6H_5)^{\dot{-}}$$

$$\text{second wave}\quad C_6H_5CH=CHCOC_6H_5+2e \rightarrow (C_6H_5CHCHCOC_6H_5)^{=}$$

Use of potassium iodide as a supporting electrolyte for a large-scale reduction, and consequent restriction of the potential to the formation of the anion radical, gave a trimer from benzalacetophenone. The same electrolysis in the presence of carbon dioxide gave the dipotassium salt of α-phenyl-β-benzoylsuccinic acid and the potassium salt of 1,3,4-triphenyl-1-hydroxy-2-benzoyl-5-carboxycyclopentane (*A*):


A *B*

The former, upon acidification, gave α-phenyl-β-benzoylpropionic acid; the latter, upon heating with base, decarboxylated and formed *dl*-1,3,4,6-tetraphenyl-1,5-hexanedione, which exists as a cyclic tautomer (*B*).

When tetrabutylammonium iodide was used as the electrolyte, the product from a two-electron reduction of benzalacetophenone was obtained and led to a polymer that melted at 426°C; the product probably resulted from a series of Michael-type additions of the dianion to benzalacetophenone. Reduction under the same conditions, but in the presence of carbon dioxide, gave α-phenyl-β-benzoylpropionic acid and a small amount of *meso*-1,3,4,6-tetraphenyl-1,5-hexanedione. Benzalacetone in the same type of reduction gave α-phenyllevulinic acid.

Polarographic studies of organic halogen compounds in aprotic solvents have also led to reactive intermediates. Carbon tetrachloride gave two waves in acetonitrile, which corresponded to the following reactions:

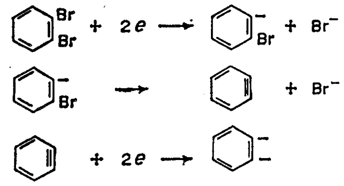
$$CCl_4+2e \rightarrow CCl_3^-+Cl^-$$

$$CCl_3^- \rightleftarrows CCl_2+Cl^-$$

$$CCl_2+2e \rightarrow CCl_2^{=}$$

A large-scale reduction of carbon tetrachloride in the presence of tetramethylethylene in acetonitrile at −20°C gave 1,1-dichloro-2,2,3,3-tetramethylcyclopropane in about 8-percent yield; the potential was not controlled (*28*), so that a portion of the dichlorocarbene was destroyed electrolytically.

Studies of the polarographic reduction of *o*-dibromobenzene in dimethylformamide and acetonitrile gave one four-electron wave, which finding pointed to the formation of benzyne as an intermediate in the reduction.



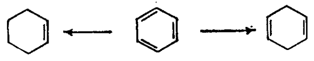
In spite of the fact that benzyne was reduced at the same point as was *o*-dibromobenzene, it was possible to trap this intermediate to the extent of 1 percent in a large-scale reduction in the presence of furan (*29*).

Electrolytic reduction of bromobenzene in dimethylformamide has formed benzaldehyde, and in the presence of carbon dioxide, benzoic acid (*30*). The latter reaction with benzyl chloride gave phenylacetic acid (*31*). These results confirm the formation of carbanions from these compounds.

Phenyl anions are also produced during electrolytic reduction of phosphonium and arsonium salts (*30*). Such electrolytic cleavages, when applied to optically active salts, give the optically active phosphine (*32*) and arsine (*33*) as products.

The technique of controlled-potential electrolysis has been widely used in conjunction with polarographic data to prepare radicals for electron spin resonance studies in aprotic solvents; it has two distinct advantages over oxidation or reduction by chemical reagents in that a variety of potentials is available and the tetraalkylammonium salts, used as the electrolytes, interact with anion radicals to a much smaller extent than do the smaller cations that are formed when alkali metals or similar metallic reductants are used. The method has been applied to electron spin resonance studies of anthracene, benzophenone, anthraquinone (*34*), aromatic nitro compounds (*35*), cyclooctatetraene (*36*), 2-nitro-2-methylpropane (*37*), 5-nitrofuran (*38*), terephthalaldehyde (*39*), aliphatic and aromatic nitriles (*40*), and *p*-benzoquinone-1-C^{13} (*41*).

Aromatic hydrocarbons, such as benzene and the alkylbenzenes, are not reducible electrolytically by direct electron transfer; they are converted electrolytically, however, to the dihydro products in ethylenediamine containing lithium chloride or tetrabutylammonium iodide (*42*), or in methylamine containing lithium chloride (*43*). The mechanism of reduction resembles that of the Birch reduction: the lithium ion is reduced to lithium metal, and the latter causes the reduction, with the solvent acting as the proton donor.

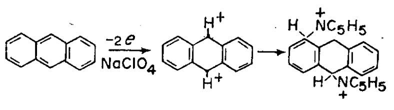


The tetrahydro compound was produced from the reduction of benzene in methylamine in an undivided cell, and the dihydro compound was formed in a divided cell. The latter arrangement prevented the lithium methylamide, generated at the cathode, from interacting with methylamine hydrochloride formed at the anode. The lithium methylamide can cause rapid isomerization of the unconjugated dihydro compound to the conjugated product, which can undergo further reduction.

Electrolytic Oxidation

Electrolytic oxidations, which have received considerable attention during the last 20 years, are the basis for several commercial processes. Oxidations have been carried out in two ways: one involves direct electron transfer; the other generates a reagent electrochemically that reacts with the organic compound in question.

Polarographic studies at a platinum anode in acetonitrile have demonstrated the feasibility of the direct electrochemical oxidation of aromatic hydrocarbons and of cycloheptatriene derivatives. The product from anthracene in the presence of pyridine was the dihydroanthracinium ion, which has been isolated in large-scale oxidation as the dipyridinium salt (*44*):



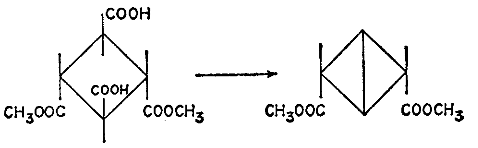
The same oxidation in the absence of pyridine goes stepwise through the cation radical, since oxidation in acetonitrile in the presence of ethanol gave bianthrone (*44*).

The same type of behavior has occurred in the oxidation of aniline at a rotating platinum anode; in the presence of pyridine the anodic wave is twice as high as that observed for the amine in the absence of pyridine. The mechanism of the oxidation, however, is different (*46*).

The corresponding oxidation of cycloheptatriene and bitropyl in acetonitrile gave the tropylium ion (*47*).

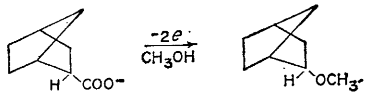
Electrolysis has been used to generate cation radicals for electron spin resonance studies and has been applied to phenothiazine (*48*), dithiohydroquinone dimethyl ether (*49*), 1,2,4,5-tetramethylbenzene (*50*), azoacridine (*51*), and triethylenediamine (*52*).

The Kolbe reaction continues to be useful in the synthesis of hydrocarbons and dicarboxylic acids (*53*). Novel applications of this synthesis were the formation of a bicyclobutane derivative from *trans,trans,trans*-1,3-dicarboxy-2,-4-dicarbomethoxycyclobutane (*54*) and the alteration of poly(methacrylic acid) (*55*):

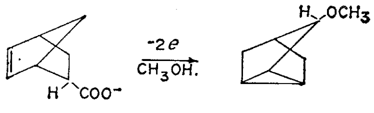


In the production of dicarboxylic acids, the formation of dimethyl sebacate from monomethyl adipate has received the most attention. Maximum yields of 80 to 83 (platinum electrode) and 60 to 65 percent (carbon anode) are reported for this compound (*56*).

A major development in this period was recognition that species could be generated in the Kolbe reaction that behaved like carbonium ions (*57*). The formation of such ionic species becomes more important at higher voltages and seems to be especially favored with structures that give rise to relatively stable carbonium ions; examples that fail to give the normal Kolbe products are usually of this type. Thus *exo*- or *endo*-norbornane-2-carboxylic acid, when electrolyzed in the presence of triethylamine in methanol, produced *exo*-norbornyl methyl ether:



Under similar conditions *exo*- or *endo*-5-norbornene-2-carboxylic acid gave 3-methoxynortricyclene:

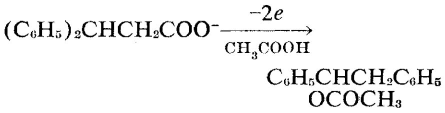


Anodic oxidation of cyclobutane carboxylic acid in water gave mainly cyclobutanol and cyclopropylcarbinol (1 : 1), with a small amount of allylcarbinol, a mixture identical with that resulting from the deamination of cyclobutylamine with nitrous acid (*58*).

Further evidence of the carbonium-ion intermediate is the formation of *N*-*tert*-butylacetamide during electrolysis of pivalic acid in acetonitrile containing a small amount of water (*59*),

$$(CH_3)_3CCOO^- \xrightarrow[CH_3CN]{-2e} (CH_3)_3CNHCOCH_3$$

and the formation of rearranged products in the electrolysis of 3, 3-diphenylpropanoic acid (*60*):

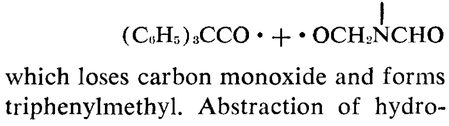


$$(C_6H_5)_2CHCH_2COO^- \xrightarrow[CH_3COOH]{-2e} \underset{OCOCH_3}{C_6H_5CHCH_2C_6H_5}$$

Aryl-substituted acetic acids in this reaction gave products best explained by carbonium-ion intermediates: α-methoxyphenylacetic acid in methanol gave benzaldehyde dimethyl acetal in 61-percent yield and α-methoxydiphenylacetic acid gave benzophenone dimethyl acetal in 74-percent yield (*61*). Diphenylacetic acid (*62*), and the corresponding nitro derivatives (*63*), produced in methanol the benzhydrylmethyl ether and alcohol; when electrolyzed in dimethylformamide, however, the parent acid gave a 24-percent yield of tetraphenylethane (*64*).

Triphenylacetic acid in dimethylformamide gave mainly *N*-methyl-*N*-(triphenylacetoxymethyl)formamide (65 percent) and triphenylmethane (3 percent) (*64*). Products similar to the former were obtained earlier by electrolysis of acetic acid and formic acid in the presence of amides (*65*).

Prolonged electrolysis of triphenylacetic acid gave none of the ester, forming mainly triphenylmethane. It has been suggested that the ester is an intermediate and is cleaved to the triphenylacetyl radical

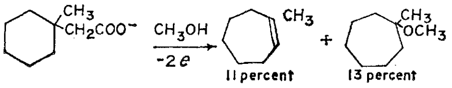


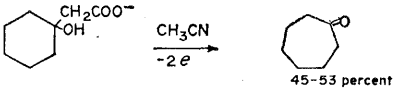
$$(C_6H_5)_3CCOOCH_2\overset{\overset{\textstyle CH_3}{|}}{N}CHO \rightarrow (C_6H_5)_3CCO\cdot + \cdot OCH_2\overset{\overset{\textstyle CH_3}{|}}{N}CHO$$

which loses carbon monoxide and forms triphenylmethyl. Abstraction of hydrogen by this radical would form triphenylmethane. Similar cleavages are proposed as the basis for the formation of dimers in the oxidation of phenylacetic acid and substituted phenylacetic acids (*66*). The possibility was not considered that the carbon monoxide may have come from the dimethylcarbamoyl radical (*67*) that would be formed from the solvent.

Carbonium-ion intermediates are apparently formed even from simple aliphatic acids if a carbon anode is employed. Butyric acid gave propylene and cyclopropane in a 1:2 ratio and *n*-propyl and isopropyl butyrates in a 1:2 ratio (*68*).

The Kolbe reaction is of value in the synthesis of cycloheptane derivatives from cyclohexylacetic acids (*57, 58*):





In the presence of conjugated dienes and aromatic hydrocarbons and their derivatives, the Kolbe reaction has led to introduction of the acyloxy and the related alkyl group into the molecules. Electrolysis of sodium acetate and potassium propionate in the presence of butadiene, isoprene, and cyclohexadienes has given mixtures of monomeric and dimeric products (*69*); in the presence of vinyl chloride, vinyl acetate, and methyl acrylate, it gave polymers (*70*).

Electrolysis of methyl adipate and oxalic acid in the presence of butadiene gave derivatives of 6-dodecene-1,12-dicarboxylic acid, 6,10-hexadecadiene-1,16-dicarboxylic acid (*71*), and 2,6-octadiene-1,8-dicarboxylic acid, respectively (*72*). On the basis of the mechanism proposed for the electrochemical oxidation of oxalic acid (*73*), the formoxy radical is apparently produced from the acid and added to the diene.

Electrochemical oxidation of potassium acetate in acetic acid, in the presence of aromatic hydrocarbons such as benzene, alkylbenzenes, and naphthalene, yields products containing acetoxy and methyl groups in both the ring and side chain (*74*). It has been suggested that, in view of the short lifetime of the acetoxy radical, these reactions involve prior oxidation of the hydrocarbon to a radical ion, which then reacts with the acetate ion (*75*):

$$C_{10}H_8 - e \rightarrow C_{10}H_8^{\pm}$$
$$C_{10}H_8^{\pm} + CH_3COO^- - e \rightarrow$$
$$C_{10}H_7OCOCH_3 + H^+$$

This mechanism is supported by polarographic data (*76*).

A similar ionic mechanism has been suggested for the cyanation of aromatic compounds in the course of electrolysis of methanol-anisole-cyanide mixtures (*77*). The formation of the benzoate of 1-naphthol during the electrolysis of benzoic acid in the presence of naththalene, in acetonitrile (*78*), may proceed by a free-radical mechanism since the benzoyloxy radical is more stable (*76*).

Methoxylation of aromatic compounds in anodic oxidations in methanol may involve prior formation of the methoxyl radical (*79*). The possibility that this radical may play an important role in the Kolbe reactions carried out in methanol containing sodium methoxide (*80*) has not been excluded.

Organometallic Compounds

Growing interest in electrolysis as a method of synthesis of organometallic compounds is evidenced during recent years by the number of patents in a review of the literature (*81*), and the commercial production of tetramethyllead and tetraethyllead by Nalco Chemical Company. This process depends on the electrolysis of alkylmagnesium halides in ether solvents, in which ionization of the alkylmagnesium halide occurs:

$$RMgCl \rightleftarrows R^- + MgCl^+$$

Use of a lead anode and a steel cathode leads to the following reactions at anode and cathode, respectively:

$$4R^- + Pb - 4e \rightarrow R_4Pb$$
$$4MgCl^+ + 4e \rightarrow 2Mg + 2MgCl_2$$

When an appropriate amount of alkyl halide is maintained in solution, magnesium is not desposited on the cathode but is converted to additional alkylmagnesium halide. The alkyl halide must be present in a concentration sufficient for reaction with the magnesium but not high enough to make significant the Wurtz-type side reaction:

$$RCl + RMgCl \rightarrow RR + MgCl_2$$

The process is successful in the preparation of mixed alkyl lead compounds (*82*).

Alkali tetramethylaluminum in tetrahydrofuran or diglyme, a eutectic mixture of sodium tetraethylaluminum and sodium tetramethylaluminum that melts at 83°C, and other aluminum alkyl complexes have reasonably high conductances and have been used as electrolytes for producing organometallic compounds. Electrolysis at a lead anode and a mercury cathode produces the tetraalkyllead compound at the anode and the alkali amalgam at the cathode:

$$NaAl(CH_3)_4 + Hg + Pb \rightarrow Na(Hg)_x + Pb(CH_3)_4 + Al(CH_3)_3$$

The last substance can be used to regenerate the electrolyte (*83*):

$$Na(Hg)_x + CH_3Cl + Al(CH_3)_3 \rightarrow NaAl(CH_3)_4 + NaCl + 2Hg_x$$

Substitution of other metals for the anode in such electrolyses forms the corresponding metal alkyls (*84*).

Organolead compounds have also been prepared by electrolysis of an alkyl halide at a lead cathode in an aprotic solvent such as acetonitrile (*85*); organotin compounds, by electrolysis of acrylonitriles at a tin cathode in aqueous medium (*86*).

Halogenation

Electrochemical fluorination, a commercial operation (*87*) is carried out in an anhydrous hydrogen fluoride solution of an organic substance (*88*). Hydrocarbons, which are only slightly soluble, are fluorinated as suspensions, and the hydrogen fluoride solution is made conductive by the addition of lithium or potassium fluoride. Nitrogen-, oxygen-, and sulfur-containing compounds are electrolyzed alone since they form onium salts that make the solution conductive. This process, first used by Simons and his group, forms hydrogen at a nickel, iron, or steel cathode and the perfluorinated organic compound at a nickel anode. At the potentials used, no fluorine is evolved and fluorination of the organic compound occurs directly.

The electrolysis replaces all the hydrogen atoms by fluorine and may affect a functional group present in the molecule:

$$CH_3COF \rightarrow CF_3COF$$

$$C_8H_{17}SO_2Cl \rightarrow C_8F_{17}SO_2F(25\%) + C_8F_{18}(21\%)$$

Destruction of the functional group leads to the perfluorocarbon and nitrogen trifluoride, sulfur hexafluoride, and oxygen difluoride, respectively, in the fluorination of nitrogen, sulfur, and oxygen compounds. Cleavage of carbon-carbon bonds occurs, but usually to a lesser extent than breakage of bonds between carbon and other elements. Chlorohydrocarbons are an exception, giving chlorofluorocarbons, with a majority of the chlorines being retained in the product although some are eliminated:

$$CH_2Cl_2 \rightarrow CHFCl_2 + CF_2Cl_2$$

The process has the advantage of using relatively cheap anhydrous hydrogen fluoride rather than the more expensive elemental fluorine. Although the yields of some perfluorinated compounds are low, their respective yields are even lower, or nil, by other methods of perfluorination.

Electrochemical bromination, with the use of bromides as electrolytes, has been employed only to a limited extent. A recent example of possible commercial interest is the conversion of hydrogen cyanide to cyanogen bromide in an ammonium bromide solution; the product is an intermediate for the production of melamine (*89*).

Periodate oxidation of starch leads to dialdehyde starch, with cleavage occurring between the C_2 and C_3 carbon atoms of the glucose unit. The reaction has become feasible commercially since one can regenerate the periodate electrolytically *in situ* (*90*).

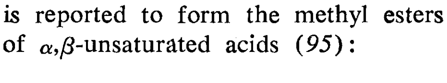
Triphenylphosphine can be electrochemically oxidized to triphenylphosphine oxide by the reduced form of oxygen in aprotic solvents (*30*); oxygen under these conditions forms an anion radical (*97*):

$$O_2 + e \rightarrow O_2^{\dot{-}}$$

Anodic oxidation of the sodium derivatives of ethyl esters of malonic, acetoacetic, and phenylacetic acid leads to the dimeric esters (*92*):

$$2\bar{C}H(COOC_2H_5)_2 - 2e \rightarrow (C_2H_5OOC)_2CHCH(COOC_2H_5)_2$$

Similar couplings have been carried out electrochemically with anions of nitroparaffins (*93*) alone or in the presence of nitrite ion (*94*):



$$\underset{C_2H_5}{CH_3C} = NO_2^- + NO_2^- \xrightarrow{-2e} \underset{C_2H_5}{CH_3C}(NO_2)_2$$

Electrolysis of olefins and carbon monoxide in methanol, in the presence of a platinum carbonyl complex, is reported to form the methyl esters of α,β-unsaturated acids (*95*):

$$C_6H_5CR = CH_2 + CO + CH_3O^- \xrightarrow[Pt_x(CO)_y]{anode} C_6H_5CR = CHCOOCH_3$$

$$R = H,\ CH_3,\ C_6H_5$$

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Facilitation by Carbonic Anhydrase of Carbon Dioxide Transport

T. Enns

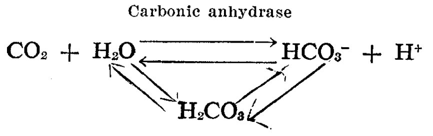
The enzyme carbonic anhydrase greatly increases the rate of conversion of carbon dioxide to bicarbonate ions and the rate of the reverse reaction. In aqueous solution this rapid interchange of carbon dioxide between the form of dissolved gas and the form of bicarbonate ions may be utilized to enhance carbon dioxide transport, the limit of enhancement being the transport of bicarbonate ions. As many biological media contain more than 20 times as many bicarbonate ions as dissolved CO_2 molecules, the enhanced transport can thus become the major CO_2 transport system.

It can also be demonstrated that carbonic anhydrase alone, in the absence of bicarbonate ions, enhances CO_2 transport. While the function of this type of facilitated transport in biological systems has not been established, it may exist in cell membranes.

One can describe three types of transport systems in which carbonic anhydrase facilitates CO_2 transport: (i) flow transport, such as blood flow in pulmonary capillaries, in which the enzyme makes dissolved bicarbonate available for rapid conversion to CO_2 and effectively increases the amount of transported CO_2 by the amount of bicarbonate in the blood, and increases the amount of eliminated CO_2 by the bicarbonate *A-V* difference; (ii) diffusion transport, such as occurs in extravascular space, in which the enzyme mobilizes bicarbonate diffusion for CO_2 transport; and (iii) transport of CO_2 by the enzyme alone. The role of the enzyme in the first type of transport system was demonstrated by tracer experiments in the lungs of intact dogs (*1*). The second and third types of transport facilitation are demonstrated by data that I now present.

Diffusion of CO_2 and Bicarbonate Ions in Aqueous Solutions

The reversible reaction of CO_2 with water to form bicarbonate ions may be expressed in the following form:



The direct reaction of CO_2 with water to give bicarbonate ion in the presence of the enzyme has been suggested by Gibbons and Edsall (*2*) and others. The relation between dissolved CO_2 and bicarbonate concentrations at equilibrium is given by the simplified equation

$$pH = 6.1 + \log [HCO_3^-]/[CO_2] \qquad (1)$$

It follows that in a solution of *p*H greater than 6.1 there is more CO_2 in the form of bicarbonate ions than in the form of dissolved CO_2 at equilibrium: for example, human blood plasma at *p*H 7.4 contains 20 times as many bicarbonate ions as CO_2 molecules.

Diffusion of dissolved CO_2 and bicarbonate ions may be described in terms of the following model. Consider a cylinder of unstirred solution of fixed area and thickness, subject to a difference in CO_2 tension between the flat end faces. Dissolved CO_2 diffuses

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The author is a research physiologist and lecturer in physiology at Scripps Institution of Oceanography, University of California, San Diego, La Jolla.