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The electroreduction of organic compounds in the presence of catalysts causing catalytic evolution of hydrogen and the electrosynthesis of chiral compounds

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ABSTRACT. **A critical examination has been made of the mechanism of catalysts (particularly alkaloids) of the electrochemical catalytic evolution of hydrogen in their effect on the electroreduction of various organic compounds and on the induction of optical activity when prochiral compounds participate. Particular attention has been paid to processes occurring at electrodes modified by chiral compounds and to the preparation of optically active products in media containing asymmetric cosolvents.**

The bibliography contains 98 references.

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I. Introduction

At the end of the sixties it was established by three groups of investigators, independently of one another in different countries, that catalysts causing the appearance on polarograms of currents of the catalytic evolution of hydrogen may also facilitate the electroreduction of certain classes of organic compounds. In addition, if the catalyst is optically active then when prochiral compounds participate in the electrode reaction the formation of enantiomers is possible, i.e. it is possible to effect asymmetric electrosynthesis during electroreduction or electrooxidation in the presence of such catalysts.

In spite of the significant number of studies devoted to such electrode processes their mechanism is still unclear. An attempt is made in the present review to bring together the results of the many investigations in this area and to discuss critically, in chronological order if possible, the development of the ideas of the various schools of investigators on the effect of catalysts on the catalytic evolution of hydrogen when facilitating the electroreduction of several classes of organic compounds and, in the case of prochiral substrates and optically active catalysts, on the mechanism of formation of enantiomeric products.

II. The nature of the electrochemical catalytic evolution of hydrogen

The phenomenon of the catalytic evolution of hydrogen in the polarograph was first revealed in the thirties by the well-known Czechoslovakian scientist Brdicka (for the history and nature of the phenomenon see the review[1]).

Brdicka discovered that the onset of cathodic polarographic waves in solutions of certain compounds is explained not by the reduction of these compounds but by the electrochemical evolution of hydrogen, which is facilitated (catalysed) in their presence. Such substances are organic bases (B), containing heteroatoms with an unshared pair of electrons (nitrogen, phosphorus, oxygen, sulphur, arsenic, etc.) which may add a hydrogen ion (from any proton donor DH^+) and form onium cations.

$$B+DH^+ \rightleftharpoons D+BH^+ . \quad (I)$$

The onion cations BH^+ may decompose on the electrode (transfer of the electron usually occurs reversibly) with the formation of particles having the character of free radicals.

$$BH^+ + e^- \rightleftharpoons BH^\cdot . \quad (II)$$

The bimolecular reaction of these radicals[1] leads to the formation of a hydrogen molecule and regeneration of the catalyst in the base form.

$$2BH^\cdot \rightarrow 2B+H_2 . \quad (III)$$

Base B is once again protonated and the whole cycle is repeated so that the result of the process is discharge of the proton donor by the catalyst with the formation of hydrogen. Cations such as H_3O^+, NH_4^+, uncharged molecules such as H_2O, CH_3COOH, etc. and anions able to give up a proton, such as $H_2PO_3^-$, may act as donors.[1]

III. First observations of the phenomenon

As already mentioned, the catalysts indicated also facilitate the electroreduction of certain classes of organic compounds. Grimshaw and collaborators[2] showed that the waves of the electroreduction of coumarin and 4-methylcoumarin in citrate buffer solution in the presence of alkaloids (narcotine, nicotine, codeine, brucine, sparteine

and yohimbine) became less negative, while under preparative electrolysis conditions the yield of the dimeric pinacol falls in the majority of cases but the yield of the secondary alcohol, dihydrocoumarin, is increased compared with experiments in the absence of alkaloid.[2] On the basis of the scheme outlined above for the catalytic evolution of hydrogen it was proposed[2] that the radical BH· formed by reaction (II) transfers a hydrogen atom to the intermediate reduction product of the ketone, a free radical, which enables the yield of secondary alcohol to be increased as a result of the fall in yield of pinacol. It was shown in the same study[2] that in several cases the alcohol obtained was optically active. The difference in the action of the alkaloids studied was explained by their different adsorbability to the electrode surface.

It was shown by us[3] that the products of electroreduction of aromatic nitroalcohols, viz. the corresponding hydroxylamines and amines, accelerate the electroreduction of the starting material so that the process is autocatalytic. The acceleration of the electroreduction of nitroalcohols by certain amines (pyridine, 2-picoline, 2,6-lutidine), amino acids (cysteine) and alkaloids (ephedrine, quinine) is explained[3] by the fact that the protonated form of the amine facilitates protonation of the depolariser. It was shown[3] in separate experiments by adding tetraalkylammonium salts that the shift in the reduction wave of nitro compounds, observed in the presence of amines, in the direction of less negative potentials in this case, was not linked with a change in the structure of the electric double layer on the electrode surface.

In subsequent work it was shown[4] that pyridine and diethylaniline accelerate the electroreduction of nitroethanol and also increase the first kinetic wave of the reduction of acetophenone which is observed on polarograms in a medium with a sufficiently high proton-donating activity, such as in acetate buffer solutions of pH greater than 5.0.[5] These phenomena were explained[4] by acceleration of the protonation reaction during electroreduction of the compounds indicated by catalysts causing the catalytic evolution of hydrogen. It was established in separate experiments[4] that these catalysts may facilitate the electroreduction of organic compounds by accelerating the protonation reaction occurring both on the electrode surface and in the bulk of the reaction layer.

Horner and collaborators showed[6] that in the electroreduction of acetophenone in methanol solution containing optically active ephedrine hydrochloride (at a concentration of 0.5 M) as electrolyte the corresponding alcohol was obtained with an optical activity of 5%. The pinacol formed (yield 40%) possessed no optical activity.[6] It was proposed that ephedrine adsorbed on the electrode influenced the reduction. On reducing the ephedrine concentration to 0.3 M the optical activity of the alcohol was reduced to 3.1%, but was unchanged on increasing it to 1 M. The effect of changing the temperature from −20 °C to boiling the solution on the optical purity of the resulting alcohol was also studied.[6] This effect proved to be maximal at 25−35 °C.

IV. Effect of various factors on the facilitation of electroreduction and the induction of chirality

After the short communications,[2,6] more detailed papers followed from the same authors[7–9] in which details of the investigations carried out were given, and some new data were presented. In one study[7] the electroreduction of 5-methoxy-4-methylcoumarin in the presence of the same set of alkaloids was also reported.

The reduction of acetophenone N-benzylimine in the presence of tetrasubstituted chiral ammonium salts, of the type of trimethylbenzylammonium iodide or dimethylated (at nitrogen) ephedrine, leads to the amine or to the dihydro dimer depending on the conditions.[8] Amines with an optical purity of 5−7% were obtained on electrolysis. Most investigations have been conducted with aliphatic-aromatic ketones, and the effect of the alkyl chain length of the alkyl aryl ketone on the ratio of the resulting pinacol and alcohol has been studied.[9] In methanol solutions containing tetramethylammonium salt as base electrolyte, the yield of alcohol grew with an increase in alkyl chain length at the expense of a reduction in the yield of pinacol.

The effect has also been studied of the length of the alkyl chain of the alkylammonium salt on the yield of hydrodimer in the electroreduction of cinnamic acid ester.[10] The results of these studies are summarised in a review.[11]

Subsequently Horner and collaborators showed[12] that inversion of the absolute configuration of the catalyst−inducer led to inversion of the configuration of the alcohol obtained. The optical purity and configuration of the alcohol may change depending on the extent of methylation of the ephedrine nitrogen atom (a maximum optical activity of 13.9% was achieved with completely methylated ephedrine). On replacing the hydroxyl group of ephedrine by hydrogen the optical purity of the resulting alcohol was reduced but the configuration was retained. These data are correlated in a review,[13] but a detailed description of these and other experiments is contained in the thorough paper of Horner and Degner.[14] In particular it was recorded that methylation of the ephedrine nitrogen atom permits not only an increase in optical purity but also inversion of the configuration of the resulting carbinol. It is interesting that introduction of a hydroxyl group into the position β to the quaternary nitrogen atom of desoxyephedrine leads to a change in the configuration of the alcohol obtained.[14] It was also shown that the pinacol formed on reduction of acetophenone in the presence of chiral inducers did not possess optical activity. In the presence of tetrasubstituted ammonium salts and ephedrine the *meso*-form of the pinacol is mainly formed while in the presence of ephedrine hydrochloride the DL-form results almost exclusively. The absence of optical activity for the pinacol prompted the authors to consider that the chirality is induced at the transfer of the second electron (and proton) to the ketone molecule.[14]

These studies served as a stimulus for similar investigations in several other laboratories. Particularly major contributions in this direction have been made by the French scientists Jubault, Raoult, Hazard and Tallec and also by Kariv, Miller and Gileadi (Israel) and recently by Wendt (FRG) and Nonaka (Japan).

In the preparative electroreduction of acetophenone in acetate buffer in methanol as base electrolyte in the presence of alkaloids, the yield of alcohol was increased with a concomitant reduction in the yield of pinacol, which may be explained by the inhibition of radical dimerisation by the adsorbed alkaloid.[15] The phenylethyl alcohol formed in the presence of alkaloids possessed optical activity, the maximum optical yield (14.9%) being achieved in the presence of quinine. Comparison of the optical yields achieved in the presence of quinine and quinidine on the one hand and cinchonine and cinchonidine (this pair differs from the first by the absence of a methoxyl group in the quinoline ring) on the other, showed that in the presence of alkaloids having no methoxyl group the yield was significantly less. This was linked[15] with the weaker adsorbability of the latter (although the adsorbability of the alkaloids was not assessed in this study). It was considered[15] that a specific interaction

took place between the adsorbed alkaloid and the reactant on the electrode which caused the appearance of optical activity in the product. The fact that in the presence of alkaloids of the opposite configuration, as in the pairs indicated above, the sign of the rotation of the products is reversed was considered as confirmation of this conclusion. Under the conditions of the experiments,[15] electro-reduction occurred up to potentials of the onset of catalytic evolution of hydrogen consequently the authors[15] doubted the hypothesis of Grimshaw and collaborators[2,7] on the transfer of hydrogen from the catalyst to the free radical of the ketone.

Subsequently the same authors[16] studied the electroreduction of acetophenone in the presence of several alkaloids and particularly in the presence of quinidine in aqueous methanolic acetate buffer solutions (pH 4.8). In these experiments quinidine was first reduced electrochemically to a mixture of products of hydrogenation of the nitrogen-containing quinoline ring, the methoxyl group remaining unaffected. In the presence of hydrogenated cinchonine the polarographic wave of acetophenone was shifted somewhat towards negative potentials while the catalytic wave of hydrogen in the presence of acetophenone became less negative. While criticising the mechanism of action proposed by Grimshaw and collaborators for the catalyst it was indicated[16] that the catalytic evolution of hydrogen sets in at more negative potentials than the electro-reduction of acetophenone itself. However, it follows from Fig. 1[16] that even in the absence of acetophenone at a potential of −1.8 V (at which the greatest optical yield of alcohol is observed) the catalytic current for hydrogen is about 10% of the limiting current of the acetophenone wave, and as already mentioned acetophenone markedly facilitates the catalytic evolution of hydrogen. It was shown[16] that methylation of the quinidine nitrogen atom sharply reduces the optical yield and changes the sign of the rotation of the resulting alcohol. Retention of the inducing ability of methylated quinidine is also considered as an argument against the criticised scheme for the process proposed by Grimshaw and collaborators.[2,7] However it is known[17,18] that on discharge of tetraalkylammonium cations containing different substituents on the nitrogen atom, one of the substituents is removed from the free radical (or is transferred to the substrate) and in this way a trisubstituted amine is formed, which is capable of being protonated and catalysing hydrogen evolution. In our opinion the change in sign of the rotation of the product is probably explained by the formation of such an amine, which may differ in conformation from the initial alkaloid, or by the alkylation of the substrate. In addition the free radical formed on discharge of tetrasubstituted ammonium may serve as the transferer of the electron.[18,19]

The fission of alkyl on discharge of a completely alkylated amine apparently does not always occur. As long as fission of alkyl and protonation of the dealkylated catalyst does not occur then the action shown by the completely alkylated catalyst is caused by the creation of an asymmetric field near the substrate on formation of a hydrophobic adduct between them. The significantly lower optical yield observed in this situation is seemingly achieved on transfer of a hydrogen atom from the discharged protonated amine, within the restrictions of its adduct with the substrate.[16] The completely alkylated inducer may serve only as the transferer of an electron from the electrode to the substrate. The change in sign of the rotation of the product, on reduction of the substrate in the presence of completely alkylated amine,[16] may be explained by the fact that protonation of the substrate anion-radical in its adduct only occurs at the expense of proton donors of the solution, which evidently approach the substrate from the side opposite the inducer. The strength of the asymmetric field generated by the alkylated alkaloid on that part of the adduct opposite to it where proton is being added from the solution is markedly less than when proton is added from the alkaloid itself. Consequently the optical yield on induction by an alkylated alkaloid is significantly less than in the case of a protonated alkaloid.

The absence of a correlation between the ability of various alkaloids to catalyse the evolution of hydrogen and the size of the optical yield was also considered[16] to be an argument against the mechanism proposed.[2,7] However it is relevant to emphasise that only in the case of simple catalysts causing volume catalytic waves of hydrogen was a link successfully established between the structure of the catalyst (more precisely its pK_a) and its ability to catalyse the evolution of hydrogen (see Ref. 1, p. 244). In the case of catalysts of complex structure, such as alkaloids, that link has not yet been successfully established.

The effect of the potential of the mercury cathode during electrolysis on the optical yield of alcohol and the alcohol : pinacol ratio has been studied.[16] The maximum optical yield (up to ~17%) was observed at −1.8 V (relative to a mercury sulphate reference electrode). Maximum adsorption of the acetophenone–catalyst complex was achieved at these same potentials,[16] while maximum yield of alcohol was obtained at the very negative potential of −2.10 V. The optical yield was increased on reducing the temperature which is linked with the increase in adsorbability of the complex indicated.

Study of the electroreduction of acetophenone in the presence of ephedrine showed that in strongly acidic and strongly basic media the optical yield falls and an inversion of its configuration occurs compared with the product obtained at medium pH values. This is explained by the fact that at extreme pH values protonation occurs at the expense of proton donors in solution and in the region of medium pH at the expense of protons from ephedrine (in strongly acidic medium acetophenone itself is protonated and in alkaline ephedrine is in the base form). Other conditions being equal, an increase in optical yield of the carbinol occurs on reducing the dielectric constant of the medium (water–methanol, methanol, methanol–isopropanol), which is linked with the increase in stability of the ephedrine–acetophenone complex in which proton transfer occurs. It was noted that replacement of the mercury cathode by lead did not change the optical yield of alcohol.

Phenylglyoxylic acid was used as a subject for reduction for the first time by Jubault, Raoult and Peltier to study the influence of alkaloids on the induction of optical activity.[21] Unlike acetophenone this acid is reduced over a wide pH range directly to phenylglyoxylic alcohol (with $n = 2$) and the process takes place at less negative potentials. This circumstance and also the absence of dimer significantly facilitate the study of the mechanism of the process. The effect of the nature of the alkaloid (15 different inducers were taken) on the optical yield of the product has been studied in detail.[22] In general the greater the adsorbability of the alkaloid-inducer the greater was the optical yield, other conditions being equal. However a specific effect of the alkaloid also became apparent. Thus the strongly adsorbed narcotine induced practically no optical activity but strychnine acts almost twice as strongly as brucine while showing approximately the same ability to be adsorbed.[22] A detailed study of the effect of various factors on the optical yield led the authors to the conclusion[22] that the process of inducing optical activity occurs with the participation of the inducer adsorbed on the electrode and all the factors aiding its adsorption lead to an increase in the optical yield of product. For example,

with an increase in the temperature of the experiment and on adding an organic solvent to the solution (both reduce adsorption of the alkaloid) the optical yield was reduced. The addition of quinine, which is strongly adsorbed under these conditions but is not an inducer, to the inducer (strychnine) also reduces the optical yield by displacing strychnine from the electrode surface. The dependence of the optical yield of product on the alkaloid concentration is close in shape to the adsorption isotherm of the alkaloid. This also confirms the important role of catalyst adsorption in the induction of optical activity. As already mentioned[22] it is apparently true[15] that the induction of optical activity occurs on forming a complex between the inducer and the substrate itself or an intermediate in its reduction, such as the anion-radical or free radical. The preparation of an optically active product, L-menthyl (*S*)-mandelate, on electroreduction of phenylglyoxylic acid ester with L-menthol in the absence of other inducers points in favour of that hypothesis.[21] In the latter case the induction of optical activity is provided by the asymmetric field of L-menthol.

It must however be noted that the maximum optical yield when reducing phenylglyoxylic acid in the presence of strychnine is observed at a strychnine concentration of 10^{-3} M, at higher concentrations the optical yield falls.[12] A similar phenomenon has been explained[15] by 'association of the alkaloid'. Seemingly this effect is caused either by inhibition of the process due to the formation of a dense film of alkaloid adsorbed on the electrode,[23] or by double-layer adsorption of the alkaloid,[24] which hinders the formation of a complex between the substrate and the alkaloid.

The optical yield depends markedly on the pH of the medium.[22] When reducing phenylglyoxylic acid in the presence of strychnine it is maximal in pH 4.8 acetate buffer solution and gradually falls to zero in strongly acidic and strongly alkaline media. It is claimed that this is linked with hindrance of the formation of a complex between the inducer and one of the forms of the substrate in these media. It must be noted that in the case of the reduction of acetophenone in the presence of ephedrine, passing from a strongly acidic to a strongly alkaline medium leads only to a change in the sign of rotation of the product.[20]

Several valuable recommendations have been made[22] for preparative asymmetric reduction. The benefit of agitating the surface of the mercury cathode (i.e. cleaning it) and of introducing the substrate into the electrolyser in appreciable portions was particularly noted.

Jubault and collaborators[25] have analysed the effect of various alkaloids on the shape of the reduction curve of phenylglyoxylic acid and showed that strongly adsorbed alkaloids such as strychnine at small concentrations (2×10^{-5} M) in weakly acidic media shift the reduction wave to a lower cathode potential, i.e. the electrode process is accelerated, while at large concentrations it is inhibited. On 'instant current–time' curves, taken during the life of the mercury drop, in the presence of low strychnine concentrations the current reaches a maximum value (corresponding seemingly to the achievement of adsorption equilibrium with the inducer), then is reduced somewhat and once again increases but more slowly (evidently due to the increase in the surface of the dropping electrode). The current is markedly greater in the presence of strychnine than in its absence. The authors explain this by the development of the ψ_1 effect, i.e. by a reduction in the potential fall beyond the Helmholtz plane and by the consequent increase in the actual potential difference between the electrode and reacting particles (see for example[26]), as a consequence of the adsorption of protonated forms of strychnine on the electrode. However, as follows from Fig. 1, the rise of the reduction wave current for phenylglyoxylic acid is observed at a potential of −0.63 V relative to a saturated calomel electrode (vs. SCE). On introducing 1.81×10^{-5} M strychnine into the solution the lower part of the wave is shifted to a less negative potential by approximately 30 mV. This wave is located close to the point of zero charge and all the values of the ψ_1 potential are in this case about 20 mV[26] (allowing for the fact that the potentials were given[26] relative to the normal calomel electrode). Seemingly the effects of the double layer, if they develop, play a secondary role in this case. In our opinion the reduction is facilitated by the interaction of the intermediate product with the protonated inducer or even with its uncharged form which transfer a hydrogen atom to the particle being reduced. In the first case the shift of the wave to a lower cathode potential is explained (see Ref. 1, p. 198 or Ref. 27) by linking the reduced form with a reversible redox system (in this case phenylglyoxylic acid, which is reduced reversibly judging by the shape of the polarogram in Fig. 1). An even more weighty argument in favour of the effects of the double layer not playing a decisive role in the acceleration of the electrode process in the present case are the data[25] that the $i-t$ curves of the reduction of phenylglyoxylic acid methyl ester in acetate buffer are increased sharply in the presence of strychnine at a potential even more positive than the point of zero charge, when the ψ_1 potential, although small, is positive. In addition, it is known (for example, Chapter VII, Ref. 28) that transfer of the first electron to the carbonyl-containing compound is reversible in many cases and the structure of the double layer does not affect reversible electrode processes. As already mentioned above, the shape of the reduction wave of phenylglyoxylic acid (Fig. 1) corresponds to a reversible transfer of an electron in the potential-determining step of the process.

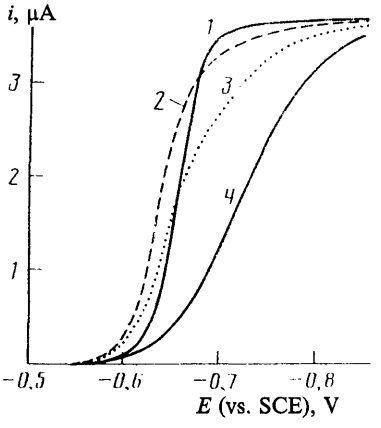


Figure 1. Polarogram of the reduction of phenylglyoxylic acid (5×10^{-4} M) in 0.5 M acetate buffer (pH 4.8) in the presence of strychnine at concentrations (10^{-5} M): *1*, 0; *2*, 1.81; *3*, 2.94; *4*, 16.7.[25]

It is interesting that the addition of alkaloids proved to have no marked effect on the reduction of *p*-nitrobenzoic and picric acids which seemingly indicates some specificity in the reaction of

substrate and inducer. On the other hand strychnine accelerates the reduction of pyruvic acid.[25]

Proceeding from the hypothesis that the formation of an adduct between the substrate and an asymmetric inducer is necessary for the induction of optical activity in an electroreduction product, Jubault and collaborators[29] selected as a model for thorough investigation the phenylglyoxylic acid ester of (−)-menthol in which the asymmetric inducer is one part of the molecule and the prochiral substrate being reduced is the other. In the majority of cases the (*R*)-conformer of mandelic acid menthyl ester predominates in the products of electroreduction of this ester. Its optical yield depends markedly on the pH of the medium,[29] it is maximal (20.6%) in 1 N H_2SO_4 and falls with increasing pH, it passes through a minimum at pH 3−4 and increases once again in neutral and alkaline solution. It is important to note that addition of di-n-butylamine in ammonia buffer solution increases the optical yield from 19.8 to 30%, while a tetrasubstituted ammonium salt reduces the yield under these conditions to 5%. The effect of pH is explained by competition between the reactions of protonation of the intermediate anion-radical and its transformation with inversion of configuration. Naturally the rate of protonation is highest in acid solutions. Protonation also explains the effect of dibutylamine added to the alkaline solution which forms an adduct with the anion-radical in which proton transfer is effected. A similar mechanism, in the opinion of the authors,[29] also takes place in electroreduction in the presence of inducer-alkaloids. The inhibitory action of tetra-alkylammonium cations is explained[29] by displacement of the particle being protonated from the electrode surface. It was established[29] that the maximum optical yield is observed on electrolysis in the vicinity of the zero charge potential. At higher negative potentials the optical yield is reduced which is explained by acceleration of the (*R*)→(*S*) transformation of the anion-radical by the electrode field.[29] The increase in optical yield in acidic medium on increasing the intensity of stirring the solution in the electrolyser is linked with the additional supply of proton donors to the electrode surface where their concentration is reduced as a result of their reaction with the substrate.[29]

Most interesting results were obtained subsequently by Raoult, Jubault and Peltier[30] in a detailed study of the effect of strychnine and *N*-methylstrychnine (which is devoid of proton-donating ability) in the electroreduction of phenylglyoxylic acid, its methyl ester, the two oximes of the acid (*anti* and *syn*), the two isomeric oximes of the methyl ester and the phenylhydrazone of the acid. The introduction of alkaloid into the polarograph solution of the compounds indicated changes the shape of the polarograms, which is a reflection of the change of the kinetics of the individual stages of the process. Reduction of the keto group requires altogether the participation of two electrons and two protons and is accompanied by the formation of a secondary alcohol. The oximes are reduced with the participation of four electrons and protons to primary amines. The preferred configuration of the product, in the authors' opinion,[30] is determined either by stereoselective protonation of the intermediate reduction product, the anion-radical, with an optically active proton donor, the inducer (as also proposed[5,31]), or by the substrate-inducer interaction[14,22,25,29] which, in the authors' opinion,[30] is preserved during many stages of the process. The formation of an adduct with the optically active inducer determines the preferred configuration of the product and the nature of the proton donor plays no role in this case.

In acidic medium (1 N H_2SO_4) addition of increasing quantities of both strychnine and methylstrychnine to the solution leads to a shift of the $E_{1/2}$ of waves of all the compounds studied to a more negative potential. The greatest shift is observed at small concentrations of additive but with its growth the size of $E_{1/2}$ tends to a limit. The displacement of the $E_{1/2}$ of waves for the reduction of the keto group is far greater than for the oxime. It is evident that under these conditions (i.e. at an excess of a strong proton donor) both additives inhibit the electrode process by blocking the electrode surface on which their adsorption depends.

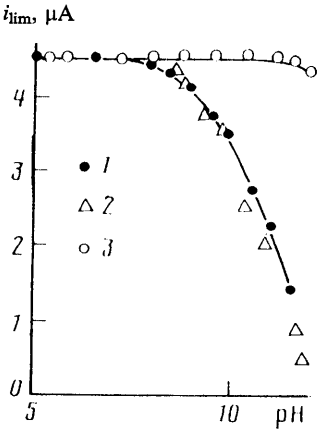


Figure 2. Effect of pH on wave height in the reduction of the oxime of phenylglyoxylic acid ester (5×10^{-4} M) in Britton-Robinson buffer solutions (with 10% ethanol). *1*, Without additions; *2*, in the presence of 9×10^{-5} M methylstrychnine; *3*, in the presence of 9×10^{-5} M strychnine.[30]

In the case of the oxime of phenylglyoxylic acid ester at a solution pH above 7, strychnine and also ammonium ions facilitate reduction while methylstrychnine has almost no effect on the polarograms. It is important to note that in the absence of additives at pH values above 7, a reduction is observed in the wave height for this oxime and it acquires a kinetic character. Methylstrychnine has no effect on the height of the kinetic wave while strychnine increases it to the level of the diffusion current (Fig. 2). The latter effect is caused by the proton-donating properties of protonated strychnine, the strychninium ion. The same properties explain the appreciable displacement of $E_{1/2}$ of the reduction wave of the oxime ester to a lower cathode potential in neutral media on introducing strychnine into the solution. At pH > 10 the $E_{1/2}$ of this wave in the presence of strychnine was almost the same as in the absence of additives or in the presence of methylstrychnine.[30] In weakly acidic medium both strychnine and methylstrychnine inhibit the process, the action of the latter being much stronger. It is interesting that the pK_a of the strychnine cation is 7.4 since with an increase in pH above 7.4 the displacement of $E_{1/2}$ by strychnine is reduced.

In the reduction of the *anti*-oxime of phenylglyoxylic acid in pH 5.4 acetate buffer solution, the addition of strychnine (see Fig. 3) leads to a shift in the lower part of the wave in the direction of greater cathode potentials and simultaneously to the appearance of a more negative wave, which becomes less negative on increasing the

strychnine concentration and blends in with the main reduction wave. The unique wave emerging in the presence of strychnine proved to be far steeper and almost 1.5 times greater than in its absence (see Fig. 3). The authors[30] explain this phenomenon by the suppression of the surface protonation of the oxime on adsorption of strychnine and by the increase of the wave by limited volume overprotonation of the oxime. In our opinion a change occurs in the mechanism of the process in this case. The strychninium cation is discharged and the radical formed transfers its hydrogen atom to the substrate,[2,4] reducing it. The change in the shape of the wave occurring in this way reflects the transition from an irreversible reduction of the oxime to a reversible discharge of the strychninium ion[1] (in this case $E_{1/2}$ of the catalytic hydrogen wave is about −1.1 V). The discharge of the strychninium ion is therefore the rate-determining step of the whole process.

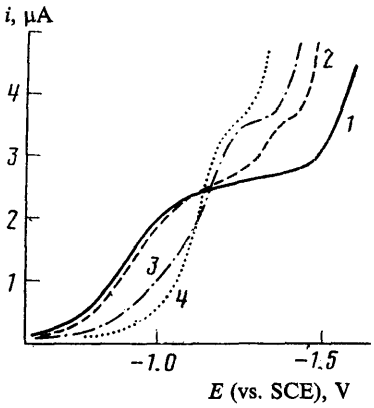


Figure 3. Polarograms of the reduction of the oxime of phenylglyoxylic acid in acetate buffer solution (without ethanol) at pH 5.4. *1*, Without additives; *2*–*4*, in the presence of strychnine (10^{-5} M); *2*, 1.5; *3*, 4.5; *4*, 10.[30]

In several cases facilitation of electroreduction was observed[30] on introducing methylstrychnine into a solution of certain compounds in pH 9.8 buffer containing Li cation (i.e. under conditions when there is no prior protonation) (Fig. 4). This was explained[30] by the formation of hydrophobic ('physical') positively charged complexes (more precisely adducts) between tetrasubstituted ammonium cation and the organic molecule,[32] which increases the substrate concentration close to the electrode.[33] It is however impossible to exclude the possibility that the observed shift is also linked with effects of the double layer since they are displayed in the case of the more cathodic waves on polarograms which may correspond to the reduction of both negatively charged ions, formed on dissociation of the substrate, and of the intermediate anion-radicals. For example, it follows from Fig. 4 that addition of methylstrychnine to a solution of the *anti*-oxime of phenylglyoxylic acid ester in Britton-Robinson buffer (pH 9.8) has practically no effect on the first wave but displaces the second wave appreciably, by almost 200 mV, to a less negative potential and simultaneously removes the fall in current after the first wave (evidently caused by the depolariser). Removal of the fall may be linked with an increase in adsorption of depolariser as a result of the formation by it of an adduct with methylstrychnine and the significant shift of $E_{1/2}$ of the second wave may be linked with the additional effect of a reduction in ψ_1-potential as a result of the adsorption of methylstrychnine cation.

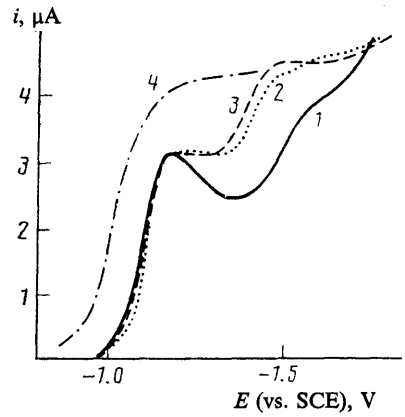


Figure 4. Polarograms of the reduction of the oxime of phenylglyoxylic acid methyl ester (5×10^{-4} M) in pH 9.8 Britton-Robinson buffer solution (with 10% ethanol and 0.01 M Li^+) of pH 9.8. *1*, in the absence and *2*, *3*, in the presence of methylstrychnine (10^{-5} M); *2*, 4.5; *3*, 5.0. *4*, Polarogram of phenylglyoxylic acid ester in 0.5 M ammonia buffer pH 9.8 with 10% ethanol.[30]

In our opinion, the increase in the region of the adsorption potentials of *p*-bromoacetophenone and tetraethylammonium salts when both are present in aqueous medium, described by van Tilborg and collaborators,[34] also indicates the formation of a strongly adsorbing adduct between them, although the authors considered[34] that adducts are not formed and the role of the R_4N^+ cation in facilitating reduction of the ketone is 'polarisation of the C=O bond on collision of R_4N^+ with the carbonyl group'. At very high concentrations of the tetraethylammonium salt, its cations, in the opinion of the authors,[34] displace the ketone from the electrode surface so that the ketone is situated on a layer of ammonium cations adsorbed on the electrode. This also shows the salts own action on the induction of asymmetric reduction on desorption of chiral cations on the electrode.

Subsequently van Tilborg and collaborators[35] studied the effect of tetraalkylammonium salts on the reduction of acetophenone in dry acetonitrile. A very interesting phenomenon was discovered. With LiF as base electrolyte acetophenone was not reduced down to a potential of −3.0 V. On adding a tetraalkylammonium salt to the solution a two-step reduction wave was observed. At a low concentration of R_4NClO_4 the height of the first wave of acetophenone changed with the growth in its concentration according to a curve reminiscent of the shape of the Langmuir isotherm. In the opinion of the authors[35] it therefore follows that reduction occurs only of adsorbed acetophenone. The dependence of the limiting current on the square root of the height of the mercury column implies kinetic limitation of the current. On increasing the

tetraalkylammonium salt concentration the limiting current becomes diffusion in character and changes in proportion to the acetophenone concentration. Judging by one study[35] the dependence of i_{lim} of the acetophenone wave on its concentration becomes nonlinear at values comparable with the concentration of tetraalkylammonium ions. In our opinion only the adduct of acetophenone with the R_4N^+ cation is reduced on the electrode under these conditions.[35] The kinetic character of the current at an excess of acetophenone is caused by R_4N^+ cations on the electrode surface, freed after reduction of acetophenone, combining with other acetophenone molecules diffusing from the solution. The comparatively low rate of formation of such adducts is evidently the reason for the kinetic limitation of the current.

It is also necessary to note the extremely interesting shape of the current intensity–time curves observed in several cases in the process of growth of the mercury drop.[30] When strychnine or methylstrychnine are present in the solution the reduction current of the oxime of phenylglyoxylic acid ester grows from the moment of formation of the mercury drop, reaches a certain limit, falls and then begins to grow once again (Fig. 5). The presence of the first maximum is evidently caused by the inhibition of the electrode process at complete coverage of the surface of the dropping electrode by the adsorbed additive. The subsequent rise in current when methylstrychnine is present is seemingly linked with the formation of hydrophobic adducts and their adsorption on the electrode which may compete successfully with the adsorption of the additive itself. When strychnine has been added to the solution, this rise in current may be explained by the development of a catalytic effect. Numerous examples of such a current increase are given in the studies considered above.

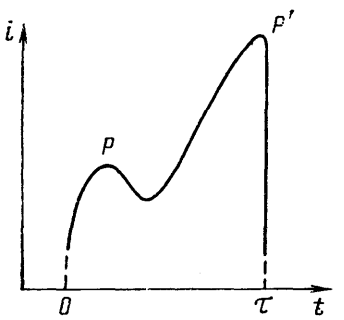


Figure 5. Diagram outlining the shape of $i-t$ curves at the time of the growth of the mercury drop in buffered solutions of phenylglyoxylic acid (and its esters and oximes) in the presence of strychnine and methylstrychnine.[30]

As already mentioned, the optical yield of product on reduction of phenylglyoxylic acid and its oximes in the presence of strychnine depends on the pH of the medium and on the electrode potential.[22,36] For example, on reducing both the *syn* and *anti* isomers of the oxime of phenylglyoxylic acid in acetate buffer in the presence of strychnine at a mercury cathode in the potentiometric mode at a cathode potential of −0.95 V (vs. SCE), the (*R*)-enantiomer of phenylglycine is formed in 17.1% optical yield.[36] On increasing the cathode potential the optical yield of (*R*)-enantiomer falls, reaching zero at −1.14 V, and on increasing the cathode potential further the (*S*)-enantiomer is formed predominantly. The optical yield of the (*S*)-enantiomer increases with the potential and reaches 11.1% at a potential of −1.35 V.[36] As had been shown by Jubault,[37] the optical yield also depends strongly on the strychnine concentration (c_{str}). Using the example of the electroreduction at the mercury cathode of phenylglyoxylic acid and its *anti*-oxime in pH 4.7 acetate buffer solution, it was shown that the optical yield initially rose rapidly with an increase in c_{str} reaching a maximum at $c_{str} = 1 \times 10^{-4}$ M, and then fell slowly, moving towards a fairly constant value. It is interesting that the optical yield reaches its greatest values at an electrode potential of −0.85 V (vs. SCE) for the acid and −0.95 V for the oxime and was reduced to zero on further increasing the cathode potential. Under conditions of high strychnine concentrations ($c_{str} > 2 \times 10^{-3}$ M for the acid and $c_{str} > 2 \times 10^{-4}$ M for the oxime) even the sign of rotation of the resulting mixture of enantiomeric products was changed. At low c_{str} and low cathode potentials (*R*)-(−)-mandelic acid and (*R*)-(−)-phenylglycine respectively predominated and at larger cathode potentials and high c_{str} mainly the (*S*)-(+) enantiomers predominated (Fig. 6). This phenomenon is as yet unexplained. In our opinion, at high concentrations strychnine not only completely covers the electrode surface with a monolayer but is also adsorbed in a second layer, like quinine.[24] The complex of strychnine ion and substrate adsorbed on the electrode surface gives the (*R*)-(−)-enantiomer on reduction but in the second layer a different orientation of strychnine, in comparison with that on the electrode surface, is possible and it may interact differently with the substrate leading to an effect opposite to that on the electrode surface, i.e. to the formation of the (*S*)-(+)-enantiomer. As c_{str} is increased the quantity of strychnine in the second layer grows and its quantity in the first layer (directly on the electrode surface) remains unchanged. Consequently the quantity of (*R*)-form resulting remains unchanged and the proportion of (*S*)-form increases with the growth in c_{str}. This is reflected in the curves given by Jubault.[37] The optical yield approaches zero at not very negative potentials as c_{str} increases.[37] It may be proposed that in this case the formation of (*R*)-form in the first layer is compensated by the formation of approximately the same quantity of (*S*)-form in the second layer. As the cathode potential is increased at high c_{str}, polylayer adsorption occurs due to the electrostatic attraction for strychnine cations and the positively charged adducts of these cations with substrate molecules. This results in the quantity of adducts in the second and subsequent layers becoming greater than in the first layer and the proportion of (*S*)-enantiomer formed exceeds the proportion of (*R*)-form. A change of electrode potential when complex organic molecules, which are inducers, are adsorbed on it frequently causes reorientation of the adsorbed molecules, which may be displayed in the direction of the rotation of the plane of polarisation of the product formed on reduction. This may be an explanation of the extremely interesting observations described.[36,37]

Halogen atoms in organic molecules are apparently particularly prone to interact with tetrasubstituted ammonium cations with the formation of hydrophobic adducts.[38] Consequently on adding 1,1-dibromo-2,2-diphenylcyclopropane to an acid polarograph solution of the alkaloids strychnine, emetine, yohimbine and also methylstrychnine salts an appreciable shift is observed in the reduction wave of this compound to a lower cathode potential.[39] The electroreduction of the compound indicated occurs with the

overall consumption of $2e^-$, by the fission of bromine ion and by protonation of the intermediate anion. The $E_{1/2}$ potential of the reduction wave did not depend on pH and was –1.46 V (vs. SCE), however in the presence of alkaloids it became more positive when reducing the pH. On changing pH from 10 to 4 in the presence of strychnine, $E_{1/2}$ was displaced from –1.45 V (vs. SCE) to –1.25 V. An even larger shift was observed in the presence of emetine, viz. from –1.41 to –1.05 V, for the same change of pH. Methylstrychnine also facilitates the reduction, in its presence $E_{1/2}$ = –1.27 V and did not depend on pH. These phenomena were explained[39] by the interaction of the cationic form of the alkaloid with the depolariser. The fact that strychnine facilitates the reduction to a markedly greater extent than methylstrychninium and in its presence $E_{1/2}$ depends on pH, indicates an effect on the size of $E_{1/2}$ and on the kinetics of protonation of the intermediate. The formation of optically active electroreduction products indicates the important role of protonation when carrying out electrode processes. The (*R*)-enantiomer was formed in the presence of strychnine and emetine and the (*S*)-form in the presence of yohimbine. The optical yield was zero on introducing into the solution methylstrychnine, having no labile hydrogen.[39] In the presence of alkaloid the reduction of dibromide was facilitated both by the electrocatalytic action of the adducts formed with the participation of the alkaloid cation (by transfer of a proton of the inducer or a hydrogen atom from the uncharged alkaloid) and by the change in structure of the double layer, i.e. by a reduction in the absolute value of the ψ_1 potential in the presence of the strongly adsorbed cations (protonated alkaloids or methylstrychninium) which facilitate the irreversible electrochemical fission of the C–Br bond.

Kopilov and co-workers[31,40,41] have studied the electroreduction of the three acetylpyridines in aqueous alcoholic acetate buffer solutions in the presence of alkaloids. Both secondary alcohols and pinacols are formed when reducing acetylpyridines. In the presence of strychnine and brucine, 2- and 4-acetylpyridine give an optically active alcohol.[41] Only the racemate is formed from the 3 isomer. In all cases the pinacols were optically inactive. When reducing 2-acetylpyridine the maximum optical yield (31.2%) was achieved in the presence of brucine. In the presence of quinidine none of the acetylpyridines gave an optically active reduction product. It is interesting that addition of alkaloid to the 2 and 4 isomer markedly increased the yield of alcohol by reducing the quantity of pinacol formed,[31,41] while the yield of alcohol from 3-acetylpyridine was reduced in the presence of alkaloid. In the opinion of the authors[41] the stage determining the optical yield is the protonation of the intermediate by the chiral alkaloid present on the electrode surface in the cationic protonated state. In contrast to the 2 and 4 isomers the 3 isomer gives a stable zwitterion, the intermediate product of which is protonated not by the alkaloid but by the acid of the buffer solution.[41] The increase in the yield of alcohol from the 2 and 4 isomers in the presence of alkaloid also indicates the important role of protonation of the alkaloid in this process. In the case of the 3 isomer, when the alkaloid does not participate in the protonation, the yield of alcohol is markedly reduced in its presence.[41]

The effect of eleven different alkaloids on the electroreduction of the isomeric acetylpyridines has been studied.[31] The highest optical yield of alcohol was achieved in the presence of strychnine, viz. 47.5% for the 2 isomer and 41% for the 4 isomer. In all cases when asymmetric reduction occurred the (+)-enantiomer was formed. Only in the presence of yohimbine was the (–)-isomer obtained with yields for the 2 and 4 isomers for 5 and 4% respectively. The reduction products of the acetyl pyridines possessed no optical activity in the presence of quinine, quinidine, reserpine, eserine and ephedrine,[31] although, as already mentioned, some of these alkaloids are inducers of asymmetry when reducing other compounds. In our opinion, an important factor assisting asymmetric induction is the possibility of forming an associate between the substrate and the inducer which is evidently determined by the specificity of the interaction between them. This specificity is displayed in the varying shift of the $E_{1/2}$ potential of the polarographic wave of the reduction of alkyl bromides in the presence of tetrasubstituted ammonium salts, depending on the nature of the alkyl group.[42] It was also noted[31] that in those cases when asymmetric induction was observed, a marked increase occurs in the yield of alcohol at the expense of a reduction in the yield of pinacol, i.e. the formation of an adduct aids protonation of the intermediate reduction product by hydrogen from the inducer and also facilitates transfer of a second electron.

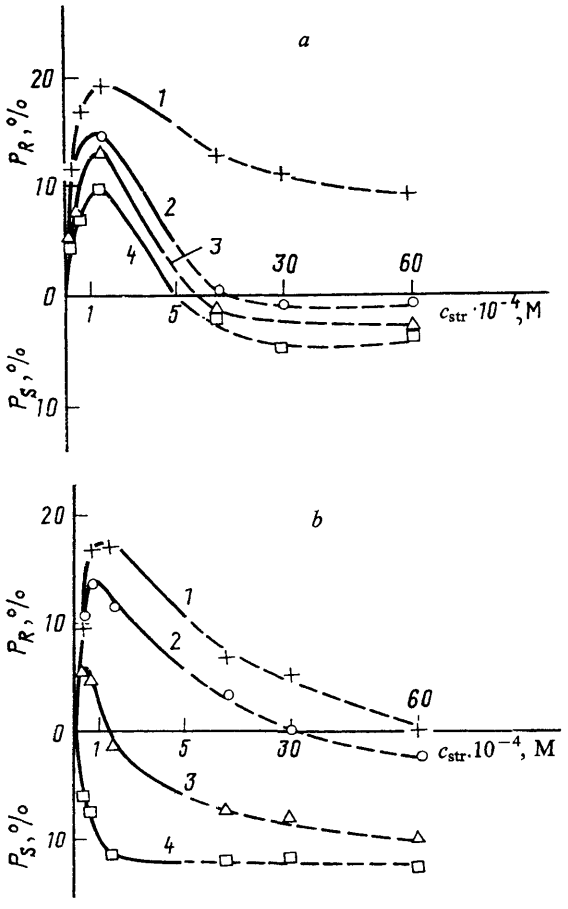


Figure 6. Dependence of enantiomer composition [%(*R*) and (*S*) forms] of the reduction products of (*a*) phenylglyoxylic acid and (*b*) its oxime in pH 4.7 acetate buffer solution on the concentration of strychnine (above c_{str} 0.5 mM the concentration scale is reduced 5-fold) at electrolysis potentials (vs. SCE, V) in (*a*) of *1*, –0.85, *2*, –1.10, *3*, –1.20, *4*, –1.30 and in (*b*) of *1*, –0.958, *2*, –1.05, *3*, –1.15, *4*, –1.30.[37]

A similar phenomenon was repeatedly observed in the reduction of acetophenone in the presence of ephedrine derivatives.[43,44]

A fairly detailed study of the effect of various factors on the optical yield and pinacol: secondary alcohol ratio in the electroreduction of acetophenone, particularly in the presence of methylephedrine[44] showed that the maximum optical yield of alcohol (18%), when carrying out electrolysis under previously selected standard conditions,[43] was achieved at a cathode potential of −1.37 V and falls to 12−13% on increasing the potential to −1.80 V, while the yield of product (alcohol) was increased by this from 14 to 70%. The reduction in optical yield with the growth in cathode potential is explained by the increase in the rate of direct transfer of the second electron to the radical and not to its adduct with the inducer. As proposed previously[14] optical activity is induced on transfer of the second electron. Maximum optical yield is achieved at solution pH 3.0.[44] The nature of the solvent also affects the optical yield of alcohol, the maximum value is observed on carrying out the electrolysis in ethanol. Addition of water to the alcohol or dioxan leads to a reduction in optical yield, the minimum yield occurring in pure aqueous solution. On reducing the temperature the optical yield grew again, the maximum (20%) was reached at −10 to −30 °C, but then was reduced once more.[44]

If the proton-donating ability of the inducer is eliminated, such as by complete methylation of ephedrine, and the electroreduction of acetophenone is carried out in anhydrous acetonitrile in the presence of this inducer, then the pinacol becomes practically the sole reduction product with an enantiomeric excess of 26.3%.[45] This, by the way, is the first case of the asymmetric synthesis of a pinacol. It is curious that in the presence of proton donors, i.e. under conditions when two radicals and not two anion-radicals react, the optical yield of pinacol is reduced to zero.[45] Asymmetric induction arises only on dimerisation of anion-radicals when at least one of them forms a tight ion pair with the inducer cation.[45]

As on reduction of phenylglyoxylic acid and its derivatives,[22,36] the maximum optical yield of pyridylethanol is observed at an electrode potential of −0.7 to −0.8 V and it is reduced at more negative potentials.[31] The optical yield of carbinol when reducing acetophenone in the presence of an inducer, such as substituted ephedrine, reaches a maximum (18%) at a potential of −1.37 V and is reduced somewhat with an increase in the cathode potential, although the overall yield of carbinol grows at the expense of a reduction in yield of the corresponding pinacol.[44] The optical yield also varies with the inducer concentration. In the case of strychnine it reaches a maximum value at $c_{str} = 5 \times 10^{-4}$ M. A reduction in temperature causes an increase in the optical yield,[31] which is seemingly explained both by an increase in adsorption of the components and by facilitation of the formation of an adduct between the intermediate reduction product and strychnine. A change in the alcohol content and replacement of ethanol by methanol and isopropanol in the mixture with aqueous acetate buffer has little effect on the optical yield of pyridylethanol, but addition of acetone sharply reduces the optical yield of the 4 isomer.[31] The relationships of the yield of both the 2 and 4 isomers of pyridylethanol to the solution pH pass through a maximum at pH 4.5, falling in more acidic and more alkaline solutions.[31] On gradually adding quinidine with strychnine to the solution the optical yield of alcohol was reduced continuously.[31] Quinidine itself is not an inducer of optical activity but its strong adsorption on the electrode aids displacment of strychnine and its adducts with the intermediates of acetylpyridine reduction. It was considered[31] that the alcohol becomes optically active at the stage of protonation of the product of the $2e^-$ reduction of the carbonyl group, viz. the enol (if the compound is protonated at the nitrogen atom) or the anion. Protonation proceeds through a hydrogen ion belonging to the strychnine cation which is on the electrode in the adsorbed state. Consequently strychnine methylated at nitrogen does not induce optical activity.[31]

It is important to note that the surface character of the chemical stage of the electrode process responsible for the induction of the optical activity requires specially pure reagents and mercury for the electrode.[40] Careful purification of all the components of the solution and the mercury, reducing the current density by increasing the surface of the mercury cathode, gradual dropwise addition to the electrolyser of the initial acetylpyridine solution[16] and reduction of the duration of electrolysis, i.e. use of all the factors reducing the effect of contaminants adsorbed on the electrode, led to an increase to 50% in the optical yields on electroreduction of 2- and 4-acetylpyridines in the presence of strychnine and to 80% in the total yield of alcohols.[40]

When studying the reduction of acetylpyridines in the presence of alkaloids, Wendt and collaborators[46] found that the reduction wave of 2-acetylpyridine in pH 4.5 acetate buffer solution after addition of 5×10^{-4} M strychnine became appreciably more positive and significantly more steep (Fig. 7). As correctly recorded,[46] this is linked with the proton-donating properties of the strychnine ion, which is adsorbed on the electrode and reacts with the intermediate product, the free radical.

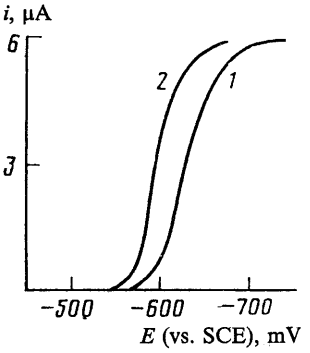


Figure 7. Polarogram of *1*, 2-acetylpyridine (1 mM) in pH 4.5 aqueous acetate buffer solution and *2*, the same in the presence of 0.5 mM strychnine.[46]

In our opinion it is not excluded that, simultaneously with the transfer of an electron (and possibly a proton as well) to acetylpyridine, discharge of the strychninium ion also occurs thereby increasing the steepness of the overall wave due to the reversible discharge of the strychninium ion[47] (see following Chapter).

V. The reversible character of the discharge of the catalyst and the features of the adsorption of organic compounds on the electrode surface

First some additional information is given on the mechanism of the catalytic evolution of hydrogen by organic catalysts and on the rules for the adsorption of organic compounds on electrodes.

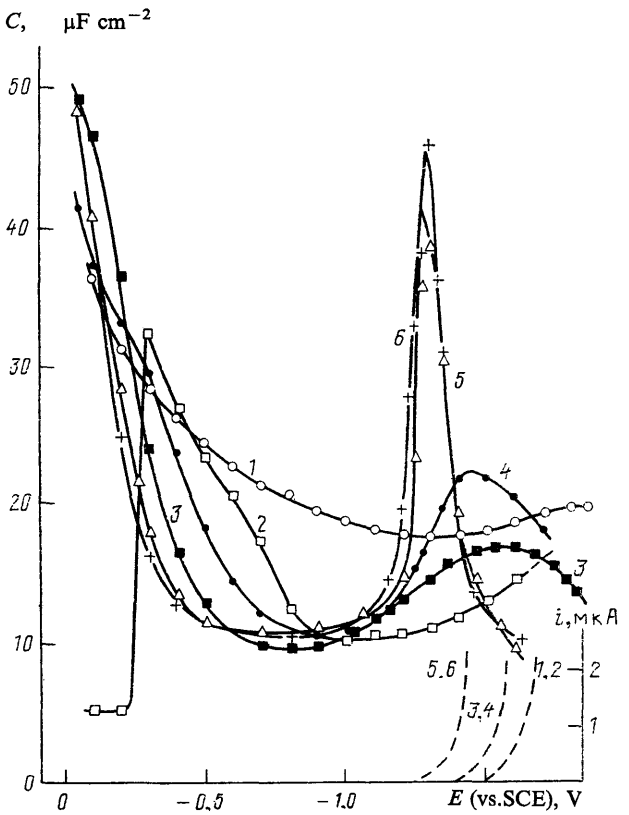


Figure 8. Differential capacity (C) curves (frequency of alternating current 179 Hz) for 0.1 mM alkaloid solutions in 0.5 M acetate buffer: *1*, buffer solution; *2*, *N*-methylstrychnine iodide; *3*, emetine; *4*, codeine; *5*, brucine; *6*, strychnine. Below are the initial portions of classical curves of the catalytic waves of hydrogen and buffer.[47]

As already mentioned at the beginning of this review, the transfer of an electron to the catalyst in the protonated form [i.e. reaction (II)] usually proceeds reversibly. The reversible character of the discharge process for pyridinium ions has been demonstrated.[48] The reversibility of electron transfer to a protonated molecule of the alkaloid pachycarpine on catalytic evolution of hydrogen into its solutions in buffer has also been proved.[49] The reversibility of the electron transfer step on catalytic evolution of hydrogen from buffer solutions of strychnine and brucine is indicated by the pseudocapacity peaks on the differential capacity curves (Fig. 8), which are caused by the discharge–ionisation process of the protonated form of the catalyst when applying an alternating current to the electrode. That the peaks mentioned are peaks of reaction pseudocapacity and not of adsorption–desorption is indicated by the correspondence of their potentials with the potentials at which the rise in current occurs in the catalytic hydrogen waves on classical polarograms obtained in solutions of these catalysts (curves in the lower portion of Fig. 8) and also by the drop in capacity after these peaks.

It is noteworthy that the catalytic hydrogen waves in buffer solutions of strychnine undergo a significant shift, with growth of the catalyst concentration, towards less negative potentials, of approximately 140 mV over a ten-fold increase in strychnine concentration (Fig. 9). There are several reasons for this. An increase in depolariser concentration always causes an earlier discharge of it, i.e. discharge at less negative potentials in the present case. In addition the subsequent bimolecular reaction in the catalytic cycle [reaction (III)] is sharply accelerated on increasing the catalyst concentration, which in its turn also leads to an appreciable shift of the reversible wave in the direction of less negative potentials.[50]

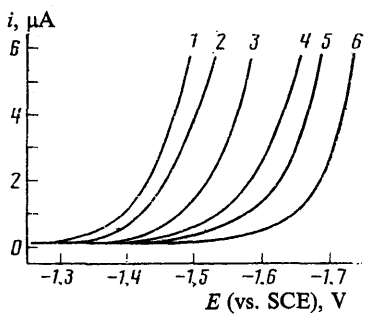


Figure 9. Classical polarographic curves for the catalytic evolution of hydrogen from buffer solutions with different strychnine concentrations (10^{-5} M): *1*, 50; *2*, 14.3; *3*, 6.52; *4*, 4.55; *5*, 2.38; *6*, 0.[47]

According to the theory of A N Frumkin[51] the adsorption of organic molecules on the electrode is maximal at the so-called potential of maximum adsorption (E_M) which is close to the zero charge potential of the electrode or the maximum of the electrocapillary curve. On moving the potential of the electrode both to the positive and to the negative side the adsorbability of compounds β falls according to the equation

$$\beta=\beta_0 \exp(-a\varphi^2), \quad (1)$$

where β_0 is the maximum adsorbability at potential E_M, φ is the potential measured from E_M, i.e. $\varphi = E-E_M$, a is a constant characteristic of each substance. The significant decrease in adsorbability of the catalyst, which depends on the extent of the difference between the electrode potential and E_M, is the reason for the characteristic hump-like shape of the surface catalytic hydrogen waves (see Chapter VI, Ref. 1 and Ref. 52).

The catalytic hydrogen waves become less negative at increased concentrations of strychnine. Under these conditions the adsorbability of strychnine is increased significantly which once again leads to an increase in the catalytic current and a shift in the wave to a less negative potential. The three factors indicated also

determine, in our opinion, the sudden shift mentioned above in the catalytic hydrogen wave in a buffer solution of strychnine on increasing the concentration of the latter, as follows from Fig. 9.

The gradual reduction in the quantity of catalyst adsorbed, which is observed on increasing the cathode potential, is the reason (see chapter VI, Ref. 1) for the fact that the slope of the semilogarithmic plots of the catalytic hydrogen waves is far greater than in the case of the usual reversible waves. The catalytic waves in buffer solutions of strychnine (Fig. 9) are an example. However under conditions of complete occupation of the electrode surface by the adsorbed catalyst, when there is no appreciable desorption, the slope of the semilogarithmic plot (in the absence of subsequent bimolecular reaction as takes place in the case of the catalytic hydrogen waves caused by pachycarpine) is 59 mV at 25 °C,[49] i.e. it corresponds to the value predicted theoretically.

VI. The mechanism of action of asymmetric inducers

Returning to the data on the effect of strychnine on the steepness of the reduction wave of acetylpyridine (Fig. 7) it is noted that discharge of the strychnine ion occurs at appreciably more negative potentials than acetylpyridine reduction. If the product of the reversible discharge of strychnine adsorbed on the electrode reacts rapidly with the product of electron transfer to acetylpyridine (i.e. with its anion–radical or, on protonation, with the radical)

$$StrH^+ + e^- \rightleftharpoons StrH^{\cdot}, \qquad (IV)$$

$$StrH^{\cdot} + AcPy^{-} \text{ (or } AcHPy^{\cdot}) \rightarrow Str + AcHPy^{-} \text{ (or } AcH_2Py)_2 \qquad (V)$$

then these interactions shift the discharge of strychnine to a lower cathode potential. Finally, the electroreduction of strychninium ions may also be facilitated by the formation by them of adducts with acetylpyridine. This was shown in the example of the catalytic hydrogen wave caused by cinchonine which becomes less negative in the presence of acetophenone.[16]

All the above-cited on the possibility of the start of discharge of protonated catalyst ions in the presence of substrate at far less negative potentials than in the case of the catalytic hydrogen wave in a pure catalyst solution, also explains the observation described above (Kariv and collaborators[15]) according to which the effect of the alkaloid on the reduction of the substrate is displayed up to the potential corresponding to the appearance of catalytic hydrogen wave.

It is necessary to note that the corresponding alcohol is formed in 47.5% optical yield in the preparative electrolysis of acetylpyridine in the presence of strychnine at the mercury cathode.[46] On a lead cathode, which is close in properties to mercury, a high optical yield is also achieved, while on a cadmium electrode, to which strychnine is almost not adsorbed, only racemic products were formed.[46] The factors aiding displacement from the electrode of starting materials and intermediates adsorbed onto it, such as the addition of a strongly adsorbing alkaloid or tetrabutylammonium salt, clearly reduce the yield of dimeric pinacol and as a result increase the yield of alcohol.[46] It is possible however to add that the electrolytes introduced into the solution not only displace starting materials and intermediates of their reduction from the electrode surface but often increase their solubility due to the so-called 'salting in' effect (see for example review[53]). The problem of the effect of the adsorption of organic substances on the kinetics and selectivity of their conversions both on a platinum anode and on a mercury cathode was considered even earlier.[54] The action of the inducer clearly grows due to a significant growth in its concentration in the reaction zone as a result of adsorption. The extremely thorough investigation of Koster, Wendt and Lebouc[55] is devoted to the role of the adsorption of components of the chemical reaction of protonation on the electrode in the kinetics of the electroreduction of prochiral compounds in the presence of inducers. The mechanism and kinetics of the electro-reduction of the three isomeric acetylpyridines on electrodes of various metals were studied. The reduction of the acetylpyridines on the dropping mercury electrode and, preparatively, on a large mercury cathode in the presence and absence of strychnine, tetrabutylammonium salts and camphoric acid were examined particularly carefully. The adsorbability of the acetylpyridines, of their reduction products and of strychnine on solid electrodes of various metals was also studied. At pH $\leqslant$ 10 the strychnine cation, which is as well adsorbed on a lead electrode as on mercury (or amalgamated copper), causes an intense catalytic evolution of hydrogen. Strychninium is adsorbed far more strongly than the acetylpyridines and their reduction products. A somewhat weaker adsorption of strychnine and a weaker action on the catalytic evolution of hydrogen was displayed when using bismuth and antimony cathodes. No adsorption of strychnine or catalytic hydrogen evolution was observed on cadmium and zinc electrodes.[55]

The effect of the nature of the cathode metal on optical yield when reducing in the presence of ephedrine methochloride was also studied by Horner and Schneider.[43] The optical yield of alcohol fell in the series Cd > Hg > Pb > Al > Sn, while the overall yield of the secondary alcohol fell along the sequence Pb > Cd > Al > Hg > Sn. The addition of strychnine to the electrolyser when reducing 2-acetylpyridine in acidic medium causes an appreciable shift in the current–potential curve, which has a quasi-reversible character, to a less negative potential on amalgamated copper and lead cathodes. A small shift in the same direction takes place on bismuth and antimony cathodes while strychnine showed no action on the completely irreversible wave for the reduction of 2-acetylpyridine on cadmium and zinc electrodes.[56] On polarography of 2- and 4-acetylpyridines in strongly acidic medium[55] the shape of the first one-electron reduction wave corresponds to a reversible process with subsequent surface dimerisation of the radicals formed, as observed in the reduction of 2-acetylpyridine in acidic medium at not very low concentrations (see final section of Chapter VIII, Ref. 1 and Ref. 56). All the facts given above indicate persuasively that the critical step of the process of inducing optical activity in the presence of an inducer is the interaction in the adsorbed state of the protonated inducer and the intermediate reduction product of the substrate, a ketyl radical in the present case.

It was recorded even in studies[31,40] that 3-acetylpyridine differs electrochemically from the 2 and 4 isomers. In particular the presence of strychnine does not affect the reduction of the 3 isomer and the product of its reduction is the optically inactive pinacol. With a view to clarifying the reason for the special position of the 3 isomer Koster, Wendt and Lebouc[55] studied the polarographic behaviour of all three isomers of acetylpyridine in DMF in the presence and absence of proton donors. The relative basicities of the ketyl radicals of all three isomers were assessed from the values of the half-wave potentials. It turned out that the basicity of the radical of the 2 isomer exceeded by seven orders of magnitude, and that of the 4 isomer by five orders, the basicity of the ketyl radical of the 3 isomer. The relatively low protonation rate of the 3 isomer ketyl radical is also the reason for the particular electrochemical behaviour of the 3 isomer compared with the 2 and 4 isomers. In

view of the low basicity of the 3-acetylpyridine ketyl radical the comparatively strong camphoric acid was very wisely used as inducer and proton donor.[55] In its presence a small shift was observed in the reduction wave of 3-acetylpyridine to a less negative potential which seemingly must lead to the formation of an optically active product in preparative electrolysis. In fact in a subsequent study an optically active product, though in low optical yield (7%), was successfully obtained by the same authors[57] in the preparative electrolysis of 3-acetylpyridine in the presence of camphoric acid. Data are given in the same study on the preparative electrolysis of 2- and 4-acetylpyridines on the mercury and some solid electrodes in the presence of strychnine. Confirmation was obtained of the high optical yields of alcohol, particularly on a lead cathode, which had previously been observed by Kariv and collaborators.[16]

In a detailed review[58] Wendt showed, with numerous examples, the nature of the three main types of electrocatalysis in organic electrochemistry and considered in particular the catalysis with asymmetric inducers – proton donors.

Highly interesting experimental data and extremely valuable correlations and conclusions related to the mechanism of inducing optical activity when reducing organic compounds in the presence of chiral inducers are contained in the study by Hazard and collaborators.[59] The action of several alkaloids, viz. strychnine, strychnine methiodide, brucine, emetine, yohimbine, narcotine and sparteine, on the reduction of 1-mono and 1,1-dibromo derivatives of 2,2-diphenylcyclopropane was studied under various conditions. The highest optical yields of products (up to 44.3% in the reduction of dibromodiphenylcyclopropane) were obtained in the presence of emetine and the lowest in the presence of narcotine and sparteine. It is interesting that in the presence of emetine the optical yield did not depend on the electrode potential nor on the pH of the medium. While noting the importance of the adsorption of the inducer, the authors[59] nevertheless stressed the absence, discovered previously,[22] of a correlation between the optical yield and the adsorbability of the inducer. The main factor determining the development of asymmetry in the reduction product was considered to be the formation of an adduct between the substrate and the inducer,[32,42] which is protonated after receiving an electron. This protonation of the anion-radical in the adduct by the asymmetric inducer (and most frequently with transfer of a proton from it[31]) determines the formation of the enantiomer. As was indicated, the shift of $E_{1/2}$ for the reduction wave of the bromocyclopropanes to a less negative potential, on adding an inducer to the solution being polarographed, points to the formation of an adduct. It must, however, be mentioned that in this case the shift of $E_{1/2}$ for the wave of the irreversible fission of the C–Br bond is determined to a known extent by the change in structure of the double layer on introducing into the solution cationic inducers adsorbing strongly to the electrode. Nevertheless, as follows from the Tables presented in that study,[59] in the presence of strychnine in fairly acid solution (so that strychnine is in the protonated form) the shift of $E_{1/2}$ for the reduction wave of the bromocyclopropanes to a less negative potential was appreciably greater than in the presence of methylstrychnine. This confirms the correctness of the conclusion[59] that an adduct is formed and a proton is transferred to it from the protonated inducer.

The appreciable increase in optical yield on going from a mono to a dibromo derivative of diphenylcyclopropane is extremely interesting.[50] This is seemingly due to the presence of two stereotopic positions in the molecule being reduced.[50] It has also been considered[59] that ion-pairs are generated in addition to the adduct formed by the inducer and the anion-radical (the intermediate reduction product). The preparation in certain cases of an optically active product (though in low optical yield) in the presence of methylstrychnine is explained by this.[59] It is noteworthy that the sign of the rotation of the product is in this case opposite to that of the reduction product in the presence of strychnine, other conditions being equal. This is due to protonation of the anion-radical in the presence of strychnine occurring with a proton from strychnine while in the presence of methylstrychnine the proton donor is in the solution and the proton approaches the anion-radical from the opposite side.[59]

1-Bromo-2,2-diphenylcyclopropane-1-carboxylic acid was one of the subjects of investigation.[59] This compound gives two waves on the polarogram and the second wave, having a kinetic nature in weakly acidic media, increases in the presence of inducers due to acceleration of protonation. It is interesting that in ammonium acetate solution the shift of $E_{1/2}$ for the waves of the bromides studied[59] is reduced on addition of inducers. Evidently this is caused by competition between ammonium and inducer ions both when forming adducts with the substrate and when building up the outer covering of the electrical double layer on the electrode.

The considerable experimental data contained in study[59] confirm the series of observations and conclusions made previously. The relationships of optical yield to the electrode potential and to the solution pH are, as a rule, described by bell-shaped curves (although in the presence of strychnine and brucine the yield grows with an increase in cathode potential). The highest yields were reached at comparatively low inducer concentrations and by reducing the temperature of electrolysis. The inversion occasionally observed of the sign of the rotation of the enantiomer on increasing the cathode potential is linked with the effect of the electric field on the anion-radical.[36]

It is interesting that the electroreduction of 2,2-disubstituted 1,1-dibromocyclopropanes in the absence of inducers in aqueous alcoholic medium on a mercury cathode with a two-electron fission of one C–Br bond occurs stereoselectively with the formation of the *cis* isomer, particularly if one of the substituents at the 2 position is hydrogen and the second $-CO_2H$ (or CO_2Me, CO_2Et). The yield of *cis* isomer exceeds 90% in the presence of tetraalkylammonium salts.[60]

Somewhat earlier Nonaka and collaborators[61] considered in detail the problem of the preferential formation of one diastereoisomer on electroreduction of ketones, having a chiral carbon atom and substituents of various size in the position α to the carbonyl group, in relation to the orientation of the initial ketone on its adsorption on the electrode.

Horner has analysed the mutual disposition of methylephedrine and acetophenone on the electrode in order to explain the induced asymmetric electroreduction. In the opinion of the authors a particular orientation of acetophenone on the electrode causes the formation of a chiral anion-radical on transfer of an electron from the electrode to the acetophenone molecule.[62]

On electroreduction of 4-carbethoxycoumarin in the presence of small quantities of alkaloids the 3,4-dihydro derivative is formed in almost quantitative yield and up to 20% optical yield. However dextrorotatory *o*-hydroxyphenyl monoethyl succinate is formed as a result of the reversible hydrolysis of the obtained laevorotatory lactone,[63] i.e. in time a change occurs in the direction of rotation of the plane of polarised light in the solution after electrolysis.

According to Klabunovskii (see Ref. 64, p. 4), the presence of a disymmetric component, which controls the process stereochemically,

in the transition state is necessary in order to obtain an asymmetric product. Such a component may be an optically active solvent or one of the components of a mixed solvent. Processes have been described for obtaining enantiomeric products when carrying out electrolysis in an optically active solvent. In the studies of Seebach and collaborators (for example Ref. 65) (*S, S*)-1,4-bisdimethylamido-2,3-dimethoxybutane (i.e. the tetramethylamide of dimethoxysuccinic acid) was used mixed with methanol as the optically active component of the solvent. The pinacol, enriched with the (*R,R*)-conformer, was obtained on electroreduction of acetophenone in this medium with lithium bromide as based electrolyte. It was shown[65] by special experiments by photolysis of the solution being electrolysed that the formation of the pinacol occurs at a certain distance from the electrode surface. The shape of the polarographic wave of acetophenone is described, as a rule, by an equation for the reversible transfer of an electron with subsequent dimerisation of the intermediates in the solution.[66] This indicates that the dimerisation of the intermediates of the reduction of acetophenone occurs within a certain volume of the reaction layer. In the opinion of Seebach and collaborators[65] complexes of anion-radicals (or radicals) with dimethoxysuccinic acid tetramethylamide (or its cationic form in acidic media) may emerge as such intermediates. The adsorption of the starting materials or intermediates accelerates the process significantly and aids the increase in optical yield of enantiomers but is not strictly obligatory. This is also indicated by the accelerating effect of pyridine, creating the volume catalytic hydrogen wave, in the electroreduction of aromatic carbonyl-containing compounds.[4]

The enantiomeric alcohol, albeit in very small optical yield (about 2%), was obtained on electroreduction of acetophenone in the presence of the potassium complexes of chiral crown ethers.[67] It is known that a crown ether may give complexes of the 'guest–host' type with organic molecules having an acidic hydrogen atom[68] as a result of the formation of hydrogen bonds between this atom and the oxygen positions of the cavity of the crown ether. However there are no sufficiently acidic hydrogen atoms in acetophenone for it to form a similar complex. The effect of the crown ether in this case may be explained by the fact that it is adsorbed on the electrode surface,[69] creating by its chirality a local asymmetric field near to which the asymmetric reduction of acetophenone occurs. It may also be proposed that the proton donors existing in the solution form a complex with the crown ether and thereby show an asymmetric action on the protonation of the anion-radical or radical. A water molecule, which often enters the cavity of a crown ether, may serve as such a proton donor.[70]

When reducing methyl acetoacetate in the presence of L-cysteine or cystine at a mercury cathode Nonaka and collaborators[71] obtained an enantiomer of 3-hydroxybutyric acid ester with an optical yield of about 1%. From citraconic acid under the same conditions (*R*)-(+)-methylsuccinic acid was successfully obtained with an optical yield of 2.4%. The use of (*R*)-(−)-benzylmethylphenylpropylphosphonium bromide as inducer in the reduction of phenylglyoxylic acid oxime in anhydrous and in aqueous methanol gave (*S*)-(+)- and (*R*)-(−)-phenylglycine respectively in optical yields in each case of about 1.9%.[71]

VII. The use of electrodes with a modified surface

The electroreduction of hexan-2-one on a powdery electrode, Raney nickel, occurs at −1.0 V (vs. SCE) with a yield on current of over 67% (on the mercury cathode reduction begins at a potential greater than −2.0 V).[72] On modifying such an electrode with optically active tartaric acid an enantiomer of hexan-2-ol was obtained in 2–6% optical yield. Heptan-2-one and octan-2-one were also reduced in a similar manner.[72]

The action of the chiral inducer must evidently be significantly enhanced if it is not adsorbed on the electrode surface but is chemically bound to it.[73] This fruitful concept was investigated for the first time by Watkins, Behling, Kariv and Miller.[73] They oxidised graphite rods (by heating in air to 160 °C), so that carboxyl groups were formed on their surface which could be titrated with alkali. By treatment with thionyl chloride in dry benzene these surface carboxyl groups were converted into acid chlorides, which were then converted into substituted amides of carboxylic acids by reaction with chiral phenylalanine ester in dichloromethane. Such electrodes, both in outward appearance and according to current–potential curves taken on them (on polarisation from −0.5 to −1.5 V), did not differ in any respect from unmodified graphite electrodes. Reduction of 4-acetylpyridine in aqueous-alcoholic acetate buffer solution on a modified electrode afforded the corresponding enantiomeric alcohol, albeit in small optical yield. On electrolysis of a solution of phenylalanine in acetate buffer on an unmodified graphite cathode, catalytic evolution of hydrogen was observed which was suppressed on introducing 4-acetylpyridine into the solution. On reducing the latter in this system the preparation of optically active alcohol was unsuccessful. On reducing phenylglyoxylic acid ester on a graphite electrode modified with phenylalanine, a diastereomer of mandelic acid ester was formed in 94% yield and an optical purity of 9.7%.[73] Although reproduction of these results was unsuccessful,[74] after publication of the paper[73] several studies appeared in which electrodes modified with chiral compounds were used for carrying out asymmetric electrosyntheses.

It has been established[75] which of the faces of crystalline graphite (two types of face exist) acquires on treatment the property to induce asymmetry in a product of an electrode reaction. Separate faces were clearly distinguishable in a sample of highly ordered pyrolytic graphite (Union Carbide Corporation, Parma, Ohio). On sealing first one and then the other face with silicone rubber and modifying them with amino acids both on the face of 'edge' atoms and on the face corresponding to the basal layer, the total yield of alcohol was 90% on reduction of 4-acetylpyridine. An enantiomeric excess (2%) was observed only on the 'edge' carbon atoms which, as is known, are readily oxidised with the formation of carboxyl groups.

It was also established[75] that a graphite electrode modified with amino acids may operate at high anode potentials. A graphite electrode modified with phenylalanine methyl ester was used for the oxidation of methyl *p*-tolyl sulphide to the sulphoxide. The yield of sulphoxide reached 90% and the enantiomeric excess of (−)-sulphoxide was 2.5%.

Instead of modifying electrodes with chiral substances, which provide only a comparatively small surface coverage, Abe, Nonaka and Fuchigami[76] proposed the use of electrodes coated with polymeric films obtained from chiral monomers.

An example has already been described of the electrochemical polymerisation of a pyrrole on a platinum electrode and the properties of the electrode modified in this way have been reported.[77] It turned out[78] that on changing the structure of the monomer (*N*-phenyl substituted pyrrolium cations having various substituents in the *para* position of the phenyl ring) used to obtain the polymeric films, the rate constants for electron transfer from a ferrocene molecule in acetonitrile solution to a platinum electrode coated with polymer varied appreciably.

An electrode, coated with a polymeric film obtained from chiral monomers, was used for the first time[76] for the electrochemical preparation of optically active compounds. On reduction of citraconic acid, on a graphite electrode coated with a film of poly-L-valine, in pH 6.0 phosphate buffer solution, an enantiomeric methylsuccinic acid was obtained with an optical yield of 25%, which is approximately 10 times greater than on the usual electrode in the presence of inducers adsorbed on it.[71]

The use has been described of a graphite electrode coated with poly-L-valine for the electroreduction of prochiral ketones, oxides and *gem*-dihalides.[79] The greatest optical yield (16.6%) was obtained on reducing 1,1,-dibromo-2,2-diphenylcyclopropane to the corresponding monobromo derivative.

There are procedures involving the formation of covalent binding of amino acids to graphite which enable the preparation of more stable polymeric films and multiple use of electrodes.[80]

Nonaka, Abe and Fuchigami[81] have used graphite electrodes modified with chiral polyamino acid films for the asymmetric reduction of citraconic acid, its dimethyl ester and of mesaconic acid.[81] The reduction of citraconic acid was carried out on electrodes coated with six different polyamides. The best yield, 26% methylsuccinic acid, was obtained with a poly-L-valine coating. Coating of lead and especially zinc electrodes with the same film did not enable such high optical yields to be reached as on a graphite electrode. This is apparently linked with the lower adhesion of the polymeric film to a metal electrode.[81] The optical yield when reducing dimethyl citraconate under optimum conditions (pH 6.0, 0 °C, $E = -1.0$ V) was far less than when reducing the acid itself (2.3%). This evidently indicates the important role of hydrogen bonds on inducing chirality.[81] The reduction of mesaconic acid occurred with an appreciably lower optical yield (10%) than did the reduction of citraconic acid, but they both gave predominantly enantiomers with the (*S*) configuration. Since the polymeric film is not conducting but is permeable to protons and substrate molecules (the film does not increase the voltage), the process, in the opinion of the authors,[81] proceeds at the graphite/film boundary and induction is effected on transfer of an electron and not a proton.

Komori and Nonaka[82] have described a method of modifying electrode surfaces, by coating the surface of a platinum electrode a polyamide film. It was established that such an electrode is stable to high anode potentials which enables its use for chiral electrooxidation.[82] On a platinum electrode coated with a poly-L-valine film, cyclohexyl phenyl sulphide is oxidised to the sulphoxide in up to 54% yield.[82]

In a subsequent study,[83] the same authors described the oxidation on platinum anodes, coated with films of polymeric chiral compounds, of seven different unsymmetrical alkyl phenyl and cyclohexyl phenyl sulphides to the corresponding sulphoxides. The highest optical yield (93%) was obtained on oxidising t-butyl phenyl sulphide on a platinum electrode coated with a double layer of polypyrrole and poly-L-valine.

It is interesting that such a modified electrode was used by Komori and Nonaka[84] for the enantiomerically differentiating oxidation of racemic 2,2-dimethyl-1-phenylpropan-1-ol to the ketone.[84] After oxidising half of this alcohol on a lead-lead oxide anode, twice coated with polypyrrole and poly-L-valine, 43% of optically pure (*S*)-(−)-enantiomer of the alcohol was in the unreacted state. This is the first example of the kinetic enantiomeric electrochemical resolution of a racemic alcohol.

The high optical yields of products on electrooxidation of sulphides on modified anodes have attracted attention.

There is considerable interest in an electrode coated with a thin film of clay. Certain racemic tris-complexes of metal ions with organic ligands, such as the trisphenanthroline complexes of iron(II), adsorb on the clay surface in such a manner that their enantiomers alternate in a staggered order.[85] An enantiomeric tris-complex occupies only half the area of the electrode, i.e. only its own space. This enabled a tin-tin oxide electrode coated with clay and an enantiomeric tris-complex $Ru(phen)_3^{+}$ to be used for the selective electrooxidation of racemic $Co(phen)_3^{2+}$.[86]

A review[87] has been devoted to the preparation and use of electrodes, the surface of which is modified by films of organic substances and polymers, and to the effect of such electrodes on electrochemical processes.

VIII. Intramolecular induction

The presence in a molecule of an asymmetric atom and a prochiral centre near to it, as already indicated,[61] enable diastereomers to be prepared by electrode processes. Intramolecular induction is observed in the case of prochiral ketones having an asymmetric centre in the positions α or β to the keto group.[88] On reduction of 2,2,3-trimethylindan-1-one on a mercury cathode in aqueous methanolic alkaline solution a diastereomer is formed with an optical yield up to 82%.

An asymmetric centre may be introduced into the molecule of an acid to be reduced by esterification with L-menthol or D-neomenthol.[89] A chiral product was successfully obtained in optical yield up to 5% by the esterification of itaconic, mesaconic, citraconic and phenylmaleic acids and subsequent reduction.

The electroreductive alkylation of phenylacetates of L-menthol and L-borneol in the presence of dimethyl sulphate (and also methylethyl and methylisopropyl sulphate) at −20 to −40 °C on a platinum cathode leads to replacement of the α-hydrogen atom (relative to the carboxyl group) by alkyl in an overall yield of 78% and an optical yield of up to 22%.[90]

On treating the products of deprotonation of the cyclopentadienyl-tetralin-iron cation with menthyl nitrite, a chiral oxime is formed giving a chiral ketone on hydrolysis. On electroreduction in acidic medium the oxime gives an optically active *endo*-amine and the ketone gives an *endo*-alcohol.[91] The small optical yields of products are caused by the very low optical yield on nitrosation (4−7%). On two-electron electroreduction of (*S*)-(+)-1-bromo-1-carboxy-2,2-diphenylcyclopropane and its ester on a mercury electrode in aqueous acetate buffer solution containing ammonium ions, the debromination product retains the initial configuration (up to 70%) for the ester. The configuration is inverted in the presence of tetraalkylammonium, the extent of inversion did not depend on the electrode potential but was increased on increasing the length of the group in the tetraalkylammonium cation.[92] When reducing the ester in the presence of tetrabutylammonium the inversion reached 60%. Similar results were obtained in ammonia buffer but inversion in the presence of tetraalkylammonium salts depended on the potential in this case.[92]

Mandelic acid amide is formed almost quantitatively on electroreduction of aqueous alcoholic buffer solutions of (*S*)-(−)-*N*-(α-methylbenzyl)benzoylformamide on a mercury cathode. In strongly acidic medium the (*R*,*S*) isomer is mainly formed (maximum optical yield 12.5%) and in ammonia buffer the (*S*,*S*)

isomer (optical yield 8.5%).[93] However at a more negative potential the (*R,S*) isomer is formed in the presence of tetrabutylammonium salt.

Some years earlier A Tallec published a fairly detailed review[94] on electrochemical synthesis of chiral compounds, describing the conditions of electrolysis capable of increasing optical yields. The mechanism of inducing optical activity was almost not touched upon, however the author rejected the hypothesis of Grimshaw[2,7] on hydrogen atom transfer from the uncharged form of the protonated inducer to the substrate molecule, within the confines of an adduct between them, as the step at which asymmetry of the product is provided, citing the paper of Kariv and collaborators.[16] The review indicated[94] may serve as a good information manual on work in the area of asymmetric electrosynthesis. There is much factual material in it on the conditions of electrolysis and yields of products.

IX. The use of electrode–catalysts

E I Klabunovskii and collaborators[95] discovered high enantioselectivity when hydrogenating esters on nickel black modified with (*R,R*)-tartaric acid. In subsequent work[96] this catalyst was used for the electrohydrogenation of ethyl acetoacetate. Finely dispersed catalyst was applied in a uniform layer on a horizontal platinum plate (7 cm^2) serving as a cathode. When hydrogenating ethyl acetoacetate in 0.1 M aqueous NaOH solution or 50% aqueous ethanolic 0.3 M KCl both at the potential of the hydrogen region of the electrode (i.e. in the layer of hydrogen adsorbed on the electrode) and in the region of hydrogen overvoltage potentials, ethyl β-hydroxybutyrate was obtained in practically quantitative yield and the optical yield of the (*R*) isomer was in all cases close to 10%.

Slemcu[97] has described the use of the dielectric Electret applied as a 1 mm layer to a metallic foundation as an electrode for the reduction of fumaric acid from aqueous alkaline solution. At 500 V and a current strength of about 1 mA for 150 h at 100 °C, an 18% excess of laevorotatory enantiomer of malic acid was achieved. Electret consists of mica plates and barium titanate, fused in carnauba wax. The latter, evidently, provides chirality to the electrode surface. It remains unclear why malic and not succinic acid was formed. It is possible that the electric current stimulated the hydration of fumaric acid without electroreduction.

Finally it has been shown[98] very recently by a conductiometric method that phenylglyoxylic acid forms an adduct in water with strychnine of composition 1:1 within which optical activity is induced in the mandelic acid formed on electroreduction.

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