Effect of Alkaloid Concentration in Asymmetric Electrosynthesis

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Summary The preferred absolute configurations of mandelic acid and *C*-phenylglycine, obtained from the asymmetric electroreduction of phenylglyoxylic acid and the related oxime in the presence of adsorbed strychnine acting as a chiral inductor, depend on the alkaloid concentration.

THERE are several successful methods for electrochemically reducing prochiral substrates into optically active products.[1,2,3] The most frequently used one involves reduction of the substrate at a mercury pool in the presence of a chiral alkaloid acting as an inductor.[2–8] When the alkaloid is not very strongly adsorbed at the mercury cathode it is introduced in large amounts and used as the supporting electrolyte;[3] when it is very strongly adsorbed, small amounts are sufficient to obtain the maximum optical yield.[5,6]

Recently, we have shown that the electroreduction of phenylglyoxylic acid[5] and the corresponding oximes[8] (*anti*- and *syn*-isomers) in the presence of 10^{-4} mol l^{-1} strychnine gives optically active mandelic acid and *C*-phenylglycine, respectively, with *ca.* 20% maximum optical yield (ρ). We have also established that the preferential configuration of the reduced products and ρ depend on the pH of the solution and on the cathodic potential.[5,8] We report here that increasing the inductor concentration can also reverse the stereochemical course of the electroreduction.

Experiments were performed on the two previously tested substrates: phenylglyoxylic acid (Figure 1) and the *anti*-oxime derivative (Figure 2). Controlled potential electrolyses were carried out at a mercury pool in buffered acetic acid and in the presence of strychnine. We have plotted ρ as a function of the inductor concentration (C_I) for different values of the cathodic potential (E).

Phenylglyoxylic acid and very low C_I values always produce the *R*-(−)-enantiomer in excess and the optical yield (ρ_R) is maximum at C_I *ca.* 10^{-4} mol l^{-1}. When C_I increases, ρ_R decreases slowly; moreover, inversion of the stereochemistry may occur at higher concentrations of the inductor (Figure 1, curves b, c, and d). Also, the spacing between two curves remains nearly the same as C_I is increased. Hence, both the cathodic potential and the inductor concentration influence the decrease in ρ.

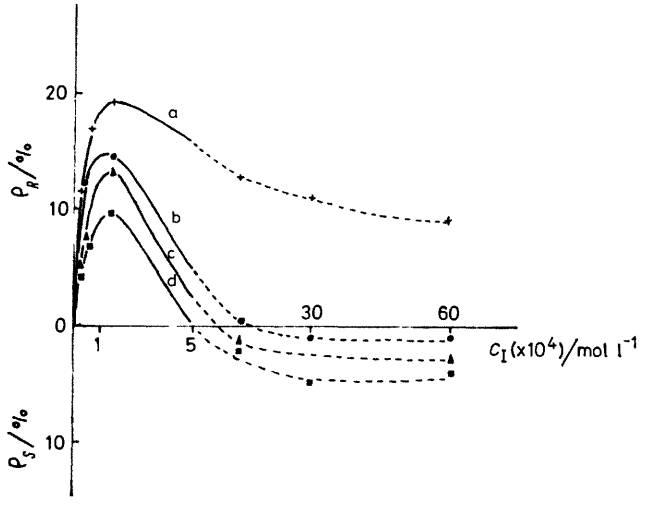

FIGURE 1. Electroreduction of $PhCOCO_2H$ to give $Ph\overset{*}{C}HOHCO_2H$ in buffered acetic acid (pH 4·7); for $C_I > 5 \times 10^{-4}$ mol l^{-1} the C_I scale is divided by 5. E/V (*vs.* saturated calomel electrode, SCE): (a) −0·85, (b) −1·10, (c) −1·20, and (d) −1·30.

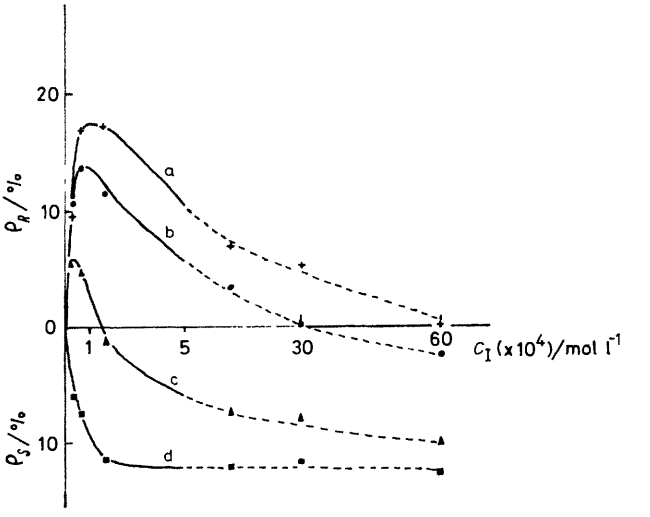

FIGURE 2. Electroreduction of $PhC(:NOH)CO_2H$ to give $Ph\overset{*}{C}H(NH_2)CO_2H$, conditions as for Figure 1. E/V (*vs.* SCE): (a), −0·95, (b) −1·05, (c) −1·15, and (d) −1·30.

In the case of the phenylglyoxylic acid oxime derivative, similar results are obtained when E is not very negative (Figure 2, curves a, b, c). However, at the more negative values of E (curve d), *S*-(+)-phenylglycine is always preferentially obtained and, for $C_I > 10^{-4}$ mol l^{-1}, the optical yield (ρ_S) of the *S*-(+)-configuration no longer depends on C_I.

The effect of alkaloid concentration on ρ has been studied in other cases of asymmetric electrosynthesis;[4,6] only a small decrease in ρ has been observed, but the inversion of stereochemistry has never been pointed out. Our results show that the preferential configuration of the product does not depend only on the intimate relationship between the structure of the alkaloid and the substrate. Some other factors such as the possibility of the intermediate carbanion inverting, before protonation, in the electrical field[9] of the electrode may have a determining influence. Protonation of this intermediate carbanion by

the alkaloid acting as a chiral acid[6] cannot explain the inversion of configuration on increasing the alkaloid concentration. So, as has been shown in the case of cathodic hydrogenation of carbon–carbon double bonds,[10] protonation by a protonated alkaloid does not seem to be the stereochemistry-determining step.[6]

However, more experimental data on the behaviour of the alkaloid at the electrode surface, when the potential is made more negative or when the alkaloid concentration is increased, are needed to explain these results.

(*Received*, 11*th July* 1980, *Com.* 755.)

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