Asymmetric, Cathodic Reduction of Acetylpyridines

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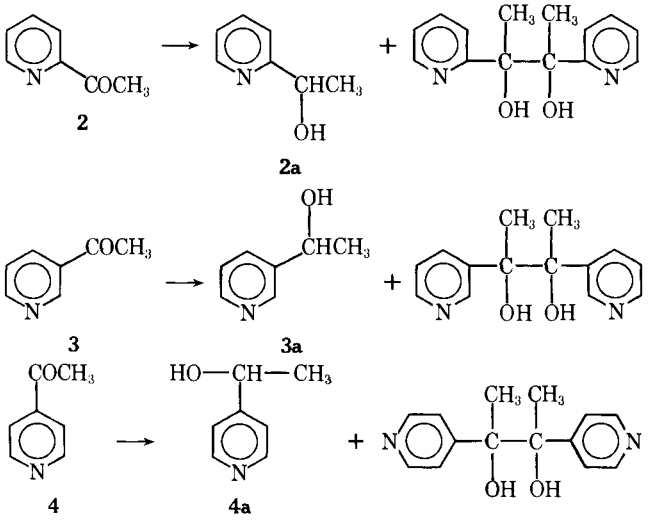
Abstract: Optically active pyridylethanols are produced from the reduction of 2- and 4-acetylpyridine at a mercury electrode if catalytic concentration of certain alkaloids are present. A variety of chiral alkaloids were screened. Brucine and strychnine give the highest optical yield (o.y.). The reduction of 3-acetylpyridine gave optically inactive alcohol under all conditions employed. The pinacols formed competitively in the reductions of these three ketones were optically inactive in all cases. Using strychnine the o.y. of alcohols from the 2 and 4 isomers was measured as a function of temperature, solvent, pH, potential, and alkaloid concentration. Current-potential and drop-time measurements using a dropping mercury electrode are also reported. The o.y. is maximized at pH ≈4.5, strychnine concentration 5×10^{-4}, and $E \approx -0.8$ V (SCE) for the alcohols from either 2- or 4-acetylpyridine. Under these conditions the conjugate acid of strychnine is strongly adsorbed. The correspondence of adsorption and optical yield data as a function of pH and strychnine concentration demonstrates that one mechanism for asymmetric induction involves protonated adsorbed strychnine acting as a chiral acid. This mechanism is also proposed to be viable for the reduction of phenylglyoxylic acid.

The asymmetric reduction of prochiral ketones to alcohols has been observed in many systems, and modest o.y. are obtained with certain reactions, especially those of aryl alkyl ketones. The present paper reports on an electrochemical method. It is of synthetic interest because it is catalytic. The approach used here is the most popular and successful electrolytic one.[2-6] It involves reduction at a mercury electrode in the presence of chiral alkaloids. In the absence of chiral additives a racemic mixture of alcohols is, of course, obtained. Studies of acetophenone[3] (**1**) and phenylglyoxylic acid[4] (**5**) reduction have built a strong case for a mechanism whereby asymmetry is induced via interaction of alkaloid and an intermediate in ketone reduction at the surface of the electrode. Thus, in two cases the alkaloids are known to adsorb under the reduction conditions; the o.y. are a function of electrode potential, very low concentrations, ca. 10^{-4} M, of alkaloid give maximal o.y., and the alkaloid changes the polarogram of the ketone. There are, however, a number of intriguing questions remaining unanswered and these are intimately tied to achieving improved selectivity in electrosynthesis.

The asymmetric reduction of 2-acetylpyridine (**2**), 3-acetylpyridine (**3**), and 4-acetylpyridine (**4**) is the subject of this paper. These compounds were chosen because they reduce



in a convenient potential range[7] where most alkaloids are electroinactive at a mercury electrode and the specific rotations and absolute configurations of the enantiomeric products (**2a, 3a, 4a**) were known. Furthermore, the reactivity of **2, 3,** and **4** was expected to vary. Initial studies, indeed, demonstrated that the o.y. were relatively high for alcohols **2a** and **4a**[5,6] but the 3 isomer gave no asymmetric induction.[5]

Experimental Section

Materials and Purification Methods. Mercury (Merck, "G.R and for polarography") was filtered, distilled, and washed with (a) concentrated H_2SO_4, (b) triple distilled H_2O, and (c) absolute EtOH. The reactants **2, 3,** and **4** (Fluka purum) were freshly distilled before use. Sparteine, reserpine, and ephedrine were Fluka products; all other alkaloids were obtained courtesy of Plantex. Strychnine *N*-methyl iodide was prepared by a reported procedure.[8] All solvents and salts used were of analytical grade, the H_2O was triple distilled, and the N_2 was prepurified.

Electrodes. A polarographic capillary (Sargent Welch, S-29419 2-5 s) was used for measurements. The drops during current potential measurements were knocked off every 0.4 s and thus were of constant surface area. A mercury pool (45 cm^2) was the cathode for preparative electrolysis. In all the experiments a Pt foil was the counter and an SCE (Radiometer K-401) was the reference electrode.

Instruments. Measurements were performed with a Tacussel Model PRG 4. A potentiostat, PAR Model 173, was used for preparative electrolyses. Optical rotations were measured with a JASCO DIP-180 automatic polarimeter. For analytical and preparative VPC a SE-30 (6 ft) column in an F & M Model 720 chromatograph was used, and NMR spectra were recorded with a Varian T-60 spectrometer.

Preparative Electrolyses. The cell was a jacketed 200-mL cylindrical flask, and a thirsty glass (Corning type 7930) tube dipping in it was the anode compartment. The reference electrode was brought to within less than 1 mm from the Hg pool at the bottom of the cell, N_2 was bubbled, and the solution was mechanically stirred.

After completion of electrolysis solid Na_2CO_3 was added adjusting the pH to 9 at which the pinacols precipitated. After filtering, the solution was repeatedly extracted with CH_2Cl_2. The solvent was removed (at 40 °C, reduced pressure) from the combined extracts and the remaining oil was distilled in vacuo. The pure products were identified by comparison with synthetic samples (NMR, VPC).

The o.y. was calculated with reference to the $[\alpha]_D$ reported for the pure enantiomers, $[\alpha]_D$ 49.8° (*c* 0.5, EtOH)[9] for **4a** and $[\alpha]_D$ 62° (*c* 2.5, EtOH)[6] for **2a.**

Results

Preparative Experiments. Electrolysis was carried out in a divided cell on a 45-cm^2 Hg pool at 0 °C with a Pt foil as the counter electrode and a commercial SCE as the reference electrode (all potentials are reported vs. SCE). In the cathode compartment 0.5 mL (0.045 mol) of reactant and 15 mg (5×10^{-5} mol) of alkaloid were dissolved in 100 mL of background (b.g.) solution which consisted of aqueous buffer acetate (pH 4.5)–EtOH (1:1). The anolyte was 20 mL of b.g. solution, and

Table I. Optical Yields for **2a, 3a,** and **4a** Using Different Alkaloids[a]

Alkaloid	**2a**[b] o.y., %	**3a** o.y., %	**4a**[b] o.y., %
None	0	0	0
Strychnine	47.5	0	40
Brucine	27	0	18
Quinine	0	0	0
Quinidine	0	0	0
Chinchonine	2.5	0	0
Chinchonidine	2	0	0
Yohimbine	5[c]	0	4[c]
Sparteine	2	0	0
Reserpine	0	0	0
Eserine	0	0	0
Ephedrine	0	0	0

[a] Alkaloid (5×10^{-4} M) and reactant (0.45 M) in aqueous buffer acetate (pH 4.5)-EtOH (1:1) at 0 °C. Electrolysis potential: −0.8 V for **2**, −1.1 V for **3**, and −0.7 for **4**. [b] The (+) enantiomer was formed in excess unless otherwise indicated. [c] The (−) enantiomer was predominant.

Table II. Effect of Potential on the Asymmetric Reduction of **2** and **4**[a]

Potential, −V (SCE)	**2a** o.y., %	**4a** o.y., %
0.7	45	40
0.75	47.5	41
0.8	47.5	39.5
0.9	44.5	34
1.0	44	33
1.1	41.5	26.5
1.2	33	17.5

[a] Reactant (0.45 M) and strychnine (5×10^{-4} M) in aqueous buffer acetate (pH 4.5)-EtOH (1:1) at 0 °C.

the potentials were −0.8, −1.1, and −0.75 V for 2-, 3- and 4-acetylpyridine, respectively. After 2 Faradays/mol was passed, the products were isolated and identified. In different series of experiments one of the reaction conditions was varied from the standard conditions described above while the rest were kept constant.

In a control experiment, without alkaloid, optically inactive mixtures of the corresponding alcohol and pinacol were obtained. The yields of alcohol under the standard conditions were 50% from **2** and 40% from **3** and **4**.

The effects of electrochemically unreactive alkaloids were investigated and several induced asymmetry in the alcohol products of **2** and **4** (Table I). The pinacol was inactive in all cases. It is of interest to note that when optical induction occurred an increase of the chemical yield (c.y.) of the alcohol was observed. Strychnine induced the highest o.y. and increased the c.y. of **2a** and **4a** by ~20%, and it was shown that the extent of electrolysis had no effect on the o.y. It was, therefore, chosen as the additive for a more detailed study. 3-Acetylpyridine (**3**) did not yield optically active products under any of the conditions investigated; therefore, only the results for **2** and **4** are reported.

Highest o.y. was obtained at −0.7 to −0.8 V and it decreased with increasing negative potential (Table II). The dependence of the o.y. on strychnine concentration showed a maximum around 5×10^{-4} M (Table III) and the asymmetric induction was favored by low temperatures (Table IV). The solvent composition had very little effect on the reaction of **2** and only where acetone was the solvent there was a significant effect on **4** (Table V). A very dramatic effect was, however, found when the pH was varied (Table VI). In this series it was necessary to vary the potential in addition to the pH, as $E_{1/2}$ is pH dependent, and under acidic conditions hydrogen evolution becomes a complicating factor.

Electrolysis of **2** at −0.8 V and **4** at −0.75 V with 5×10^{-4} M strychnine *N*-methyl iodide did not give rise to optically active products.

Table III. Effect of Strychnine Concentration on the Reduction of **2** and **4**[a]

Strychnine, M	**2a** o.y., %	**4a** o.y., %
3×10^{-5}	13.5	11
6×10^{-5}	27.5	19.5
1.2×10^{-4}	33	28.5
2.5×10^{-4}	40.5	33
5×10^{-4}	47.5	41
1×10^{-3}	46	40
2×10^{-3}	43	37
4×10^{-3}	37.5	26.5

[a] Reactant (0.45 M) in aqueous buffer acetate (pH 4.5)-EtOH (1:1) at 0 °C. Electrolysis potential −0.8 V for **2** and −0.75 V for **4**.

Table IV. Effect of Temperature on the Asymmetric Reduction of **2** and **4**[a]

Temp, °C	**2a** o.y., %	**4a** o.y., %
0	47.5	41
16	37	29
40	22.5	19

[a] Reactant (0.45 M) and strychnine (5×10^{-4} M) in aqueous buffer acetate (pH 4.5)-EtOH (1:1). Electrolysis potential −0.8 V for **2** and −0.75 V for **4**.

Table V. Effect of Solvent Composition on the Asymmetric Reduction of **2** and **4**[a]

Solvent	**2a** O/Y/= %	**4a** o.y., %
Aqueous buffer acetate (pH 4.5)	37	37.5
Aqueous buffer acetate-EtOH (3:1)	44	37
Aqueous buffer acetate-EtOH (1:1)	47.5	41
Aqueous buffer acetate-EtOH (1:3)	44.5	29
Aqueous buffer acetate-MeOH (1:1)	40.5	32
Aqueous buffer acetate-*i*-PrOH (1:1)	44	33
Aqueous buffer acetate-acetone (1:1)	40.5	13

[a] Reactant (0.45 M) and strychnine (5×10^{-4} M) electrolyzed at 0 °C. Electrolysis potential: −0.8 V for **2** and −0.75 V for **4**.

Table VI. Effect of pH on the Asymmetric Reduction of **2** and **4**[a]

pH of aq buffer	*E* for **2**, −V (SCE)	**2a** o.y., %	*E* for **4**, −V (SCE)	**4a** o.y., %
0.5 (H_2SO_4)[b]	0.5	23	0.47	18
1.8 (phosphate)[b]	0.57	27	0.55	22
2.8 (chloroacetate)	0.67	30.5	0.65	27
4.5 (acetate)	0.8	47.5	0.75	41
6.6 (phosphate)	0.9	34.5	0.87	32
9.0 (borate)[b]	1.2	24	1.15	22
12 (NaOH)[b]	1.35	3	1.3	3

[a] Reactant (0.45 M) and strychnine (5×10^{-4} M) in aqueous buffer-EtOH (1:1) at 0 °C. [b] The reactant was added dropwise to avoid high pinacol yield.

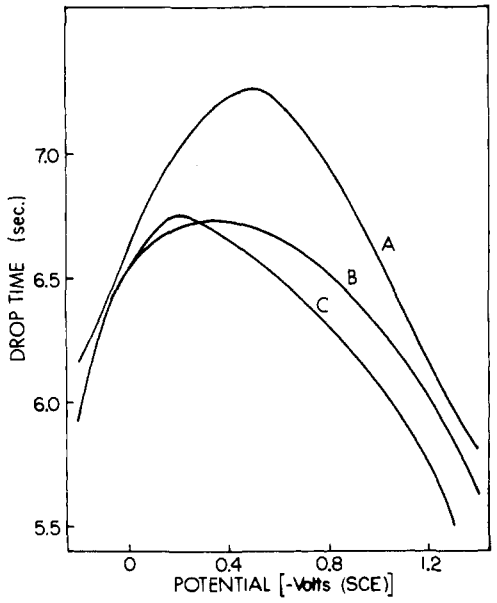


Figure 1. Dependence of Hg drop time on potential. (A) aqueous buffer acetate (pH 4.5); (B) aqueous buffer acetate (pH 4.5)-EtOH (1:1); (C) 5×10^{-4} M strychnine in aqueous buffer acetate (pH 4.5)-EtOH (1:1).

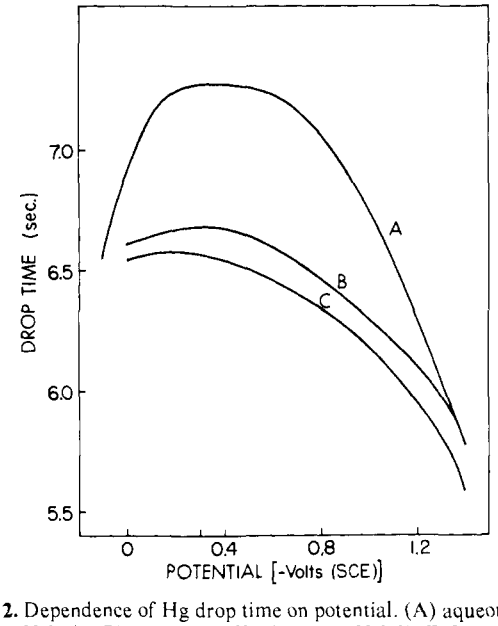


Figure 2. Dependence of Hg drop time on potential. (A) aqueous buffer borate (pH 9.0); (B) aqueous buffer borate (pH 9.0)-EtOH (1:1); (C) 5×10^{-4} M strychnine in aqueous buffer borate (pH 9.0)-EtOH (1:1).

Addition of quinidine, which is adsorbed on the Hg surface but does not induce asymmetry in the investigated reactions, diminishes the effect of strychnine as shown in Table VII.

Electrical Measurements. Current-potential curves on a dropping Hg electrode (of constant surface area) for **2, 3,** and **4** in b.g. solution were recorded. All three exhibited single irreversible reduction waves (most probably $2e^7$). The $E_{1/2}$ for 10^{-3} M (diffusion controlled limiting current) **2** and **4**, of -0.775 and -0.705 V, respectively, became 15 mV more positive with addition of 10^{-4} M strychnine. The curve for **3** and the $E_{1/2}$ -1.045 V were unaffected by the alkaloid.

To clarify the adsorption of strychnine the lifetime of single Hg drops as a function of potential and strychnine concentration was measured. As examples the curves for 5×10^{-4} M strychnine at pH 4.5 and pH 9.0 are shown in Figures 1 and 2, respectively. For some strychnine concentrations drop time measurements above -0.6 V were difficult to reproduce. Therefore, we use data only for the region of interest below -0.6 V to calculate $t/\log C$ plots (Figures 3 and 4) at these two pH values. Coverage was not estimated because no plateau in the concentration dependence (up to 8×10^{-3} M) was observed.

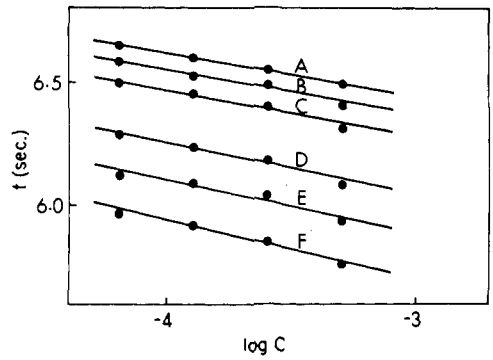


Figure 3. Dependence of Hg drop time on the concentration of strychnine in aqueous buffer acetate (pH 4.5)-EtOH (1:1). (A) -0.6 V; (B) -0.7 V; (C) -0.8 V; (D) -1.0 V; (E) -1.1 V; (F) -1.2 V.

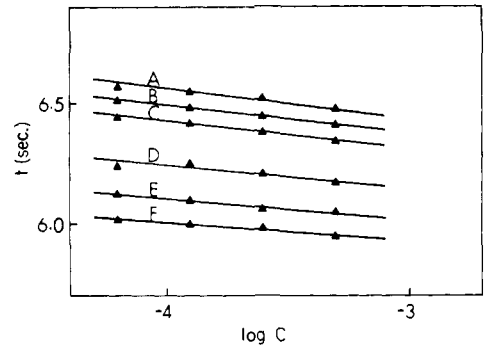


Figure 4. Dependence of Hg drop time on the concentration of strychnine in aqueous buffer borate (pH 9.0)-EtOH (1:1). (A) -0.6 V; (B) -0.7 V; (C) -0.8 V; (D) -1.0 V; (E) -1.1 V; (F) -1.2 V.

Table VII. Effect of Quinidine on the Asymmetric Reduction of **2** and **4**[a]

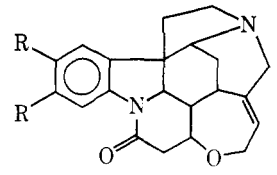
Quinidine, M	Strychnine/ quinidine	**2a** o.y., %	**4a** o.y., %
0	∞	47.5	41
2.5×10^{-4}	2	33	29
5×10^{-4}	1	28.5	23
3×10^{-3}	0.16	15.5	11.5

[a] Reactant (0.45 M) and strychnine (5×10^{-4} M) in aqueous buffer acetate (pH 4.5)-EtOH (1:1) at 0 °C. Electrolysis potential -0.8 V for **2** and -0.75 V for **4**.

Discussion

Strychnine (St) and brucine are electroinactive. They were found to give substantial o.y. in the formation of alcohols **2a** and **4a.** Using St it was shown that the o.y. of **2a** and **4a** depend on the temperature, potential, pH, and St concentration. For the latter three variables this dependence was nonlinear, indicating changes in mechanism with conditions. In spite of this, there is a very close correlation between the o.y. of **2a** and **4a.** Under almost every condition the ratio o.y. **4a**/o.y. **2a** = 0.75 ± 0.15. Furthermore, the absolute configuration of the predominant enantiomer of **2a** and **4a** is always the same. These

results demand that the reduction mechanisms are the same for **2** and **4**. In contrast to the results for **2** and **4** the alcohol from **3** was always optically inactive. Since it is not racemized under the reaction or workup conditions this indicates a fundamental difference in reaction mechanism (see below).



strychnine (St), R = H
brucine, R = OCH_3

The data for **2** and **4** with strychnine are only compatible with mechanisms in which the alcohol products are formed at the surface. Although St is present in very low concentration in solution, it can achieve a high surface concentration. That this adsorbed material is the asymmetric inducer is indicated by the potential dependence of the o.y. since processes occurring away from the electrode should not be affected by changing E. Furthermore, the maximum in the dependence of o.y. on the concentration of alkaloid can only be rationalized in terms of surface chemistry. At these low concentrations it would be improbable that a higher alkaloid concentration would not increase the o.y. of a reaction in solution.

In contrast to this conclusion, which seems general for the limited number of compounds studied to date, pinacol formation does not seem to occur on the surface. The pinacols are always optically inactive and the *dl*/meso yield ratio is not affected by the presence of alkaloid. In agreement with this idea it has been found[11] that pinacol asymmetric induction can be produced by electrochemical reduction of acetophenone (**1**) in a chiral solvent. There is, furthermore, a strong correspondence of photolytic and electrolytic results for **1** which implicate homogeneous coupling mechanisms.

Formation of the new C–H bond is the step which establishes the stereochemistry of the alcohol product. This step in ketone reductions is usually thought to be a protonation, but direct evidence on this point is usually not available. The pH dependence of the o.y. (Table VI) provides a probe of the mechanism of C–H bond formation and indicates that proton transfer is involved. The fact that St gives higher alcohol yields (other variables held constant) strongly reinforces this conclusion.

Two important variables which can be controlled are potential and pH. In order to fully understand the reaction one needs to construct a three-coordinate plot of o.y. vs. pH and E producing a surface which shows the o.y. at a given pH and E. This is experimentally possible over a limited range of pH and E values because of the onset of hydrogen evolution (low pH) and the increasing amounts of pinacol found under less negative E, high pH conditions. Sufficient data can, however, be collected to demonstrate that there is a maximum in the o.y. near pH ≈5 and $E \approx -0.8$ V. The potential dependence using acetate buffer is shown in Table II. Figure 5 shows points for **3**, **4**, and phenylglyoxylic acid (**5**)[4a] run under identical conditions. Note that the curves all have a maximum o.y. using acetate buffer. *This behavior demonstrates that proton transfer is involved in the asymmetric induction for all three compounds.* Since the behavior is qualitatively independent of substrate, it suggests that the pH dependence is due to adsorbed strychnine $(St)_{ads}$ and its conjugate acid $(StH^+)_{ads}$. An explanation which is sufficient is that $(StH^+)_{ads}$ is present below pH ≈6 and reacts as a general acid. Thus, at high pH $(StH^+)_{ads}$ is not present and any asymmetric induction results from the adsorbed base; near the pK of adsorbed strychnine the surface concentration of $(StH^+)_{ads}$ increases and the o.y. goes up; at lower pH the H_3O^+ concentration is so high that protonation by $(StH^+)_{ads}$ is less important and the optical yield again goes down.

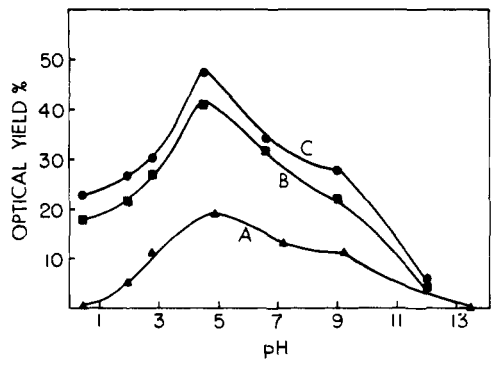
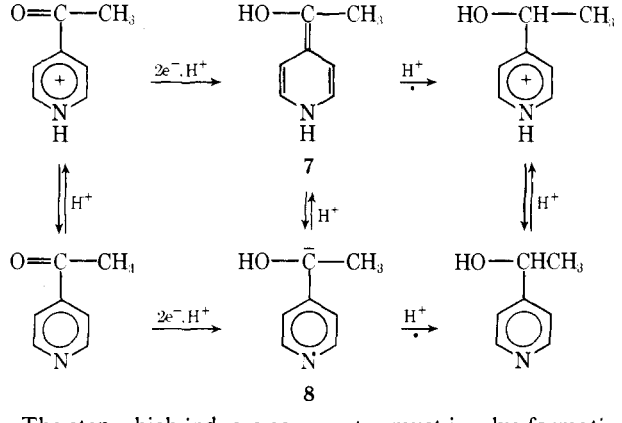


Figure 5. Effect of pH on the o.y. of (A) **5a**; (B) **2a**; (C) **4a**.

This general conclusion based on kinetics can be reinforced by measuring the surface tension of mercury as a function of strychnine concentration and pH. Theory indicates that adsorption decreases the surface tension and results in a shortening of the characteristic drop time (t) of Hg from a DME. From the electrocapillary curves, points for t vs. the log of St concentration (log C) at a constant potential were derived to obtain Figures 3 and 4. Figure 3 shows an increasing average[12] of t/log C with increasing negative potential using acetate buffer. This is only consistent with specific adsorption of a cation. The average[12] slope t/log C using borate buffer decreases with increasing negative potential (Figure 4), which is expected for adsorption of a neutral, polarizable organic. We propose that in acetate buffer $(StH^+)_{ads}$ is present and its adsorption increases at more negative potentials. Contradistinctively in borate buffer $(St)_{ads}$ is present and less strongly adsorbed at more negative potentials.

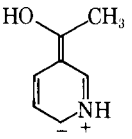
It is quite clear that adsorption of a chiral additive is not a sufficient condition for asymmetric induction. It has been previously shown[4a] that quinidine is strongly adsorbed on mercury, but does not lead to asymmetric induction from **5**. Following Peltier and co-workers[4a] we have run preparative reductions of **2** and **4** in which both quinidine and St were present. The o.y. were substantially lower than those in the presence of St alone (Table VII). This is explained by competitive adsorption where quinidine displaces strychnine.

Having demonstrated that *one* mechanism of asymmetric induction involves adsorbed, protonated strychnine in the case of **2**, **4**, and phenylglyoxylic acid (**5**), we turn to a structural model for this step. At pH ≈5 the predominant species in solution is the pyridinium ion. Its reduction overall will require $2e^-$ and $2H^+$ to produce protonated alcohol. We are concerned with the protonation step and there are two logical possibilities as shown below using the 4 isomer as an example.



The step which induces asymmetry must involve formation of the C–H bond and is noted by an asterisk. This could involve either protonation of enol **7** or carbanion **8** by $(StH^+)_{ads}$.

It is important to understand why **3** has a different mechanism from **2** and **4** and this can be rationalized if **2a** and **4a** are formed via asymmetric protonation of a relatively stable (and therefore selective) enol like **7.** Such an enol is not, however, accessible from **3.** The corresponding intermediate is **9,** a



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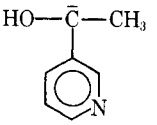

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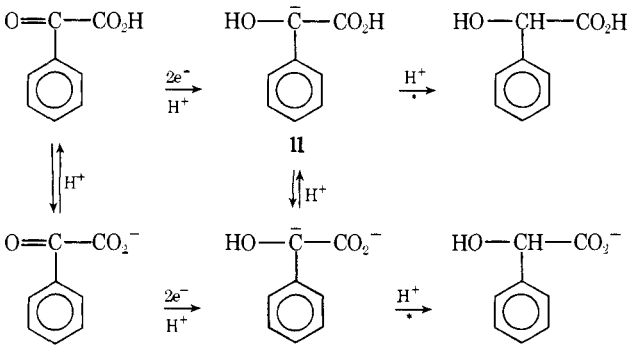
zwitterion which will be much more reactive (and perhaps less selective) than **7.** The carbanions, e.g., **8** and **10,** should, however, have very similar stabilities. In this case there is no obvious rationale for the **2, 4** vs. **3** dichotomy.

Using this same line of reasoning, consider now why phenylglyoxylic acid (**5**) gives asymmetric induction using strychnine at pH ≈5. Again, one is confronted with acid-base equilibria. If, however, the carbanion **11** is involved, one can



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invoke asymmetric protonation of a relatively stable species because the neighboring carbonyl delocalizes the charge. Another similarity between the reductions of **2, 4,** and **5** is the reduction potential.

This discussion pertains primarily to reduction at pH ≈5 where protonated, adsorbed strychnine is involved. At high pH strychnine is adsorbed and, indeed, asymmetric induction still occurs. This might involve protonation by water in an asymmetric environment at the surface. It is of interest that *N*-methylstrychnine iodide gives no asymmetric induction. In this case the proton transfer from protonated strychnine is not possible and interaction of the salt with solvent and substrate at the surface is expected to be much different than that of strychnine itself.

All the above arguments ignore the details of molecular association during C-H bond formation. These details are obviously critical in determining the o.y., but attempting to draw any structural conclusions would be mere speculation. Indeed, it is our opinion that previously proposed, detailed structural models for asymmetric induction rely heavily on imagination. It must be remembered that a 50% o.y. corresponds to only about 1 kcal/mol difference in the activation energies for formation of the two enantiomers. Interpretation of such small differences is difficult in any reaction, but especially in a surface reaction involving an alkaloid. In contrast, we believe that the kinetic concepts invoked here are an important component in determining o.y. and should allow development of a rational approach to maximizing the o.y. in processes such as these.

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References and Notes

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(2) R. N. Gourley, J. Grimshaw, and P. G. Millar, *Chem. Commun.*, 1278 (1967); *J. Chem. Soc. C*, 2318 (1970); L. Horner and D. Degner, *Tetrahedron Lett.*, 5889 (1968); 1245 (1971); *Electrochim. Acta*, **19**, 661 (1974); L. Horner and D. Skaletz, *Tetrahedron Lett.*, 3679 (1970); L. Horner and R. Schneider, *ibid.*, 3133 (1973); L. Horner, D. Degner, and D. Skaletz, *Chem.-Ing.-Tech.*, **44**, 209 (1972); I. A. Titova, I. M. Levinson, V. G. Mairanowski, and A. B. Ershler, *Elektrokhimia*, **9**, 424 (1973).
(3) E. Kariv, H. A. Terni, and E. Gileadi, *J. Electrochem. Soc.*, **120**, 639 (1973); *Electrochim. Acta*, **18**, 433 (1973).
(4) (a) M. Jubault, E. Raoult, and D. Peltier, *Electrochim. Acta*, **19**, 865 (1974); (b) *ibid.*, **21**, 407 (1976).
(5) J. Kopilov, S. Schatzmiller, and E. Kariv, *Electrochim. Acta*, **20**, 535 (1976); Extended Abstracts, 149th Electrochemical Society Meeting, Washington, D.C., 1976, p 725.
(6) J. Hermolin, J. Kopilov, and E. Gileadi, *Electroanal. Chem.*, **71**, 245 (1976).
(7) J. Volke, *Collect. Czech. Chem. Commun.*, **25**, 3397 (1960).
(8) I. M. Hesse, W. Vetter, and M. Schmid, *Helv. Chim. Acta*, **48**, 674 (1965).
(9) G. Gottarelli and B. Samori, *J. Chem. Soc., Perkin Trans. 2,* 1462 (1974). Different $[\alpha]_D$ and absolute configuration for **4a** were reported earlier.[10] We have reproduced the results of Gottarelli and Samori.
(10) O. Cervinka, O. Belovsky, and P. Rejmanova, *Z. Chem.*, **10**, 69 (1970); *Collect. Czech. Chem. Commun.*, **38**, 1358 (1973).
(11) D. Seebach and H. A. Oei, *Angew. Chem.*, **87**, 629 (1975).
(12) The curves *t* vs. log *C* are not straight lines (as can be observed from the points in Figures 3 and 4) and theory demands calculation of the *t*/log *C* slope at each point. In the concentration and potential region of interest, deviation from linearity is small, and since we are only interested in the general change of the slope with potential we have treated *t*/log *C* as a straight line and used the average slope for comparison.