Electrocapillary Curves of Ephedrine and Pseudoephedrine

By LOUIS MALSPEIS, JAMES W. TURNER*, and LEON LACHMAN

Electrocapillary curves at a series of concentrations of the diastereoisomeric ephedrines in 1 N NaOH and of the corresponding salts in 1 N HCl have been determined. The electrocapillary maximum (e.c.m.) was shifted to more positive potentials with an increase in concentration in each instance. Adsorption of the free bases on mercury was greater than that of the cations. The fractional surface coverage of the electrode by the cations was found to be highly dependent upon potential, with maximum coverage occurring at potentials slightly more negative than the e.c.m. Coverage by the free bases was largely independent of potential over a wide range of potentials. The Gibbs surface excess of the isomeric ephedrinium ions was the same from 0.001 M to 0.2 M. At low coverage for a given reduced concentration, the surface excess of (−)-ephedrine was greater than that of (+)-ψ-ephedrine; whereas at high coverage, the surface excess of the diastereoisomers was the same. These results imply that at high surface coverage, orientation of both isomers at the electrode is the same with planar adsorption of the aromatic nucleus on the electrode surface and the side chain in solution; at low surface coverage, the molecules lie flat on the electrode surface. The *extra* electrostatic work for bringing (+)-ψ-ephedrine to the surface, compared with (−)-ephedrine, was interpreted in terms of the conformations of the diastereoisomers in the bulk of the solution and at the surface. Polarograms exhibited no discrete catalytic hydrogen wave; however, the limiting currents at potentials preceding discharge appeared to be catalytic currents. The catalytic current of (−)-ephedrine was greater than that of (+)-ψ-ephedrine in borate buffers. A linear dependence of catalytic current on the concentration of each isomer was observed over a narrow concentration range.

ELECTROCAPILLARY measurements are the classical method for studying the adsorption of ions and molecules at a mercury–solution interface (1, 2). Interpretation of the adsorption of organic molecules and ions is based largely upon the well-known effects of large inorganic anions and quaternary ammonium cations (3). The electrocapillary maximum (e.c.m.) is shifted to more negative potentials by capillary-active anions and to more positive potentials by capillary-active cations, reflecting the respective adsorption on the positive and negative branches of the electrocapillary curve. Analogously, adsorbed organic dipolar molecules orient at the interface, with the electrocapillary maximum shifting to positive or negative potentials, depending upon whether the positive or negative center of the dipole is pointed toward the interface (1).

The purpose of the present investigation is to determine whether the configurational differences of diastereoisomers will affect their electrocapillary characteristics. Diastereoisomers have the same functional groups and approximately the same molecular dimensions. Their dipole moments generally differ. An experimental requirement is that the organic compounds should be electrochemically inert in the potential range studied. The compounds chosen for the initial study are (−)-ephedrine and (+)-pseudoephedrine. These isomers are reported to be electrochemically inactive (4).

EXPERIMENTAL

Materials.—A commercial sample of (−)-ephedrine hydrochloride and a research sample of (+)-pseudoephedrine hydrochloride (Burroughs-Wellcome and Co.) were used in the interfacial tension measurements in 1 N HCl and in the polarographic determinations. The free bases of these amines were used in the interfacial tension measurements in 1 N NaOH.

Reagent grade chemicals were used to prepare the acid, base, and buffer solutions. Deionized water passed through a Darco G-60 column was used to prepare the solutions for the interfacial tension measurements. No differences in the interfacial tensions were noted when using solutions prepared with deionized water, deionized water passed over activated charcoal, or redistilled conductance water.

Interfacial Tensions.—The conditions suggested by Breiter and Delahay (5) were used to determine interfacial tensions. The capillary was standardized with 1 N HCl, in which the mercury–solution interfacial tension is 422.6 dynes/cm. at −0.542 v. *versus* S.C.E. (6). Interfacial tensions were calculated from drop-time values with the equations of Corbusier and Gierst (7). The electrocapillary data for 1 N HCl agreed generally with those reported by Conway *et al.* (6).
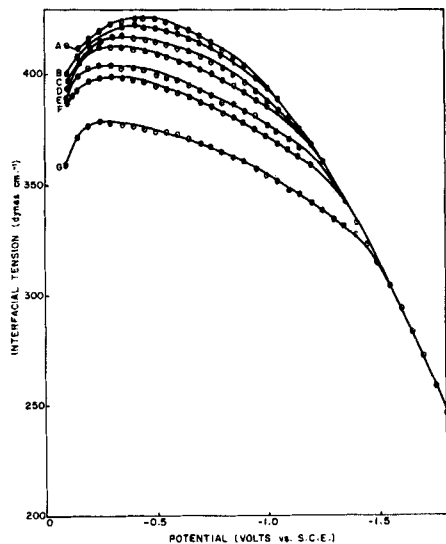
Fig. 1.—Electrocapillary curves for (−)-ephedrine and (+)-ψ-ephedrine at different molar concentrations in 1 *N* NaOH. The curve at 0.1 *M* concentration is for (−)-ephedrine alone. Key: A, 0; B, 0.0005 *N*; C, 0.001 *N*; D, 0.002 *N*; E, 0.005 *N*; F, 0.01 *N*; G, 0.1 *N*.

A jacketed H-type cell containing a saturated calomel reference electrode separated from the solution compartment by a potassium chloride–agar plug and a sintered-glass disk was employed. The cell was thermostated at 25 ± 0.1°. A corrected mercury head of 96.0 cm. was maintained by replacing mercury after each determination. A Rubicon model 2730 potentiometer was used to measure applied voltages. Oxygen was removed from the solution by bubbling nitrogen through it for 20 min. The nitrogen used for deaerating the solutions was bubbled first through 1 *N* HCl in measurements of the acidic solutions. Since traces of oxygen affected the drop-time values, the solutions were deaerated between measurements at different potentials. During measurements, water from the constant-temperature bath was not circulated through the cell jacket to avoid vibrations.

Polarographic Determinations.—The polarographic measurements were made with a Leeds and Northrup Electro Chemograph, type E; the electrolysis vessel was the H-cell described above. The temperature was maintained at 25 ± 0.1°. The dropping mercury electrode had values of $m^{2/3}t^{1/6}$ of 4.990 mg.$^{2/3}$ sec.$^{-1/2}$ open circuit and 3.093 mg.$^{2/3}$ sec.$^{-1/2}$ at −1.95 v. *versus* S.C.E. in borate buffer at a corrected mercury head of 96.0 cm. The initial potential of the polarogram was calibrated with the Rubicon potentiometer.

RESULTS AND DISCUSSION

Electrocapillary Curves.—Representative electrocapillary curves for (−)-ephedrine and (+)-ψ-ephedrine in 1 *N* NaOH are shown in Fig. 1. The concentration range studied was from 0.2 m*M* to 0.1 *M*. The solubility of ψ-ephedrine in 1 *N* NaOH is considerably less than that of ephedrine, and the experimental points at the 0.1 *N* solution refer to

ephedrine only. Experimental values were determined at 50 mv. intervals; each value is the mean of five separate determinations. The precision of the interfacial tension values is ±0.25%. Within the experimental error, the interfacial tension values for solutions of both diastereoisomers at the same molar concentrations were the same at all potentials. As the molar concentration is increased, the electrocapillary maximum of the curves is shifted toward positive potentials. On the positive branch, the curves diverge, adsorption increasing with concentration. On the negative branch, the top part of the curve becomes flatter with increasing concentration, and the curve coincides somewhat sharply at negative potentials with the electrocapillary curve of the base solution. The desorption potential becomes more negative with increasing concentration.

Representative electrocapillary curves for solutions of the hydrochlorides of (−)-ephedrine and (+)-ψ-ephedrine in 1 *N* HCl are shown in Fig. 2. The concentration range studied was from 2 m*M* to 0.2 *M*. Interfacial tension values for both salts were again identical within the experimental error for the same molar concentrations and potentials. The shape of these curves is similar to those observed by Conway *et al.* (6) for the adsorption of quinine on mercury in aqueous HCl solutions.

The e.c.m. is shifted to positive potentials with increasing concentration. On the positive branch, the curves appear to converge with increasing positive potential. Adsorption is substantially greater on the negative branch, where the electrocapillary curves diverge.

The approximate values of the potentials of the electrocapillary maxima relative to the S.C.E. are given in Table I.

Surface Excess.—The methods for characterizing the adsorption of neutral organic molecules on electrodes have been summarized by Breiter and Delahay (5). Application of the Gibbs equation to electrocapillary data affords the surface excess, Γ, of adsorbate; thus, for an uncharged adsorbate at
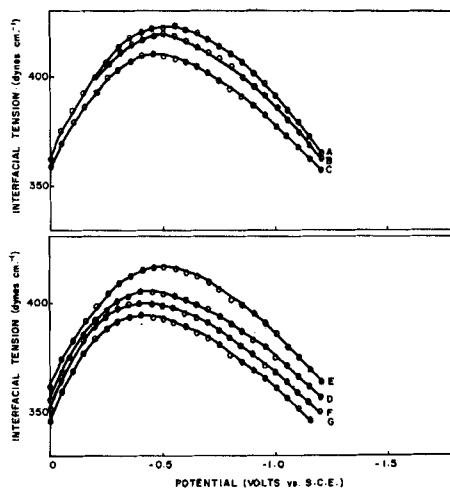

Fig. 2.—Electrocapillary curves for (−)-ephedrinium and (+)-ψ-ephedrinium chlorides at different molar concentrations in 1 *N* HCl. Top: A, 0; B, 0.005 *N*; C, 0.025 *N*. Bottom: D, 0.05 *N*; E, 0.01 *N*; F, 0.1 *N*; G, 0.2 *N*.

TABLE I.—POTENTIALS OF THE ELECTROCAPILLARY MAXIMA OF (−)-EPHEDRINE AND (+)-ψ-EPHEDRINE IN 1 N HCl AND 1 N NaOH RELATIVE TO THE S.C.E.

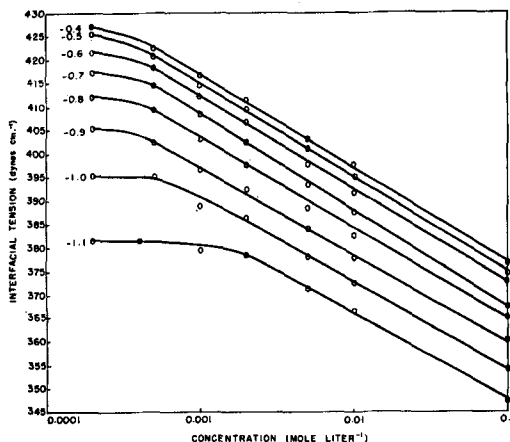| ———1N HCl——— | | ———1N NaOH——— | |
Concn.	− $E_{e.c.m.}$	Concn.	− $E_{e.c.m.}$
0	0.55	0	0.48
0.001	0.53	0.0002	0.40
0.005	0.50	0.0005	0.38
0.01	0.50	0.001	0.33
0.025	0.45	0.002	0.28
0.05	0.45	0.005	0.28
0.1	0.40	0.01	0.30
0.2	0.40	0.1[a]	0.28

[a] Value is for (−)-ephedrine alone.

Fig. 3.—Interfacial tension *vs.* log molar concentration of the diastereoisomeric ephedrines in 1 N NaOH at constant potential. (Potentials stated on figure.)

a given temperature $\Gamma = -[(a/RT)(d\gamma/da)]_{V,T,\mu_b}$ where γ is the interfacial tension at applied potential V, a is the activity of the adsorbate, Γ is the surface excess of adsorbate per unit area, and μ_b is the chemical potential of the base solution.

The dependence of the interfacial tension on the molar concentrations of the alkaloids in alkaline and acidic solutions at various potentials are given in Figs. 3 and 4. Surface excess values were calculated from these curves. The curves of the alkaline solutions are similar to those reported for *n*-amyl alcohol in aqueous acid solutions (5, 8) and various amines in aqueous alkaline solutions (9).

Any inference relating the surface excess of an organic molecule to its structure depends upon the assumption made regarding the activity coefficient of the adsorbate. Conway *et al.* (6) have observed that the activity coefficients of certain alkaloids vary considerably with concentration. They have shown that neglect of the activity coefficients has pronounced effects on the adsorption isotherms of quinine and narcotine in acidic solution, and they have proposed an empirical method for calculating the coefficients. Blomgren and Bockris (10) have interpreted deviations from the Langmuir isotherm for aniline in 0.1 N HCl to be due to coulombic repulsion between adsorbed cations.

Little information is available regarding activity coefficients of neutral molecules. It is sometimes

assumed that the activity coefficient of the neutral molecule in an electrolyte solution of constant chemical potential is unity and invariant over the concentration range (5). More often, it is assumed that Traube's rule is followed, and the adsorption isotherm is considered to be the dependence of Γ on the reduced concentration C/C_0, where C_0 is the solubility of the adsorbate in the base solution (8, 11). Comparisons based upon the latter assumption have been criticized (12). Nevertheless, the preponderance of available data indicates that the latter assumption is appropriate for qualitative comparisons of adsorption behavior for compounds of similar structure having different solubilities in the base solution when values of C/C_0 are less than 0.8.

The present results are interpreted on the assumption that the reduced concentration approximates the adsorbate activity. The order of magnitude of the solubilities of the isomeric ephedrinium chlorides is the same. As a first approximation in the absence of activity coefficients, the activities of the salts in 1 N HCl are considered constant over the concentration range studied. Accordingly, the values of Γ of the isomeric ephedrinium ions are the same at a given concentration and temperature. On the other hand, the solubility of (+)-ψ-ephedrine in 1 N NaOH is substantially less than that of (−)-
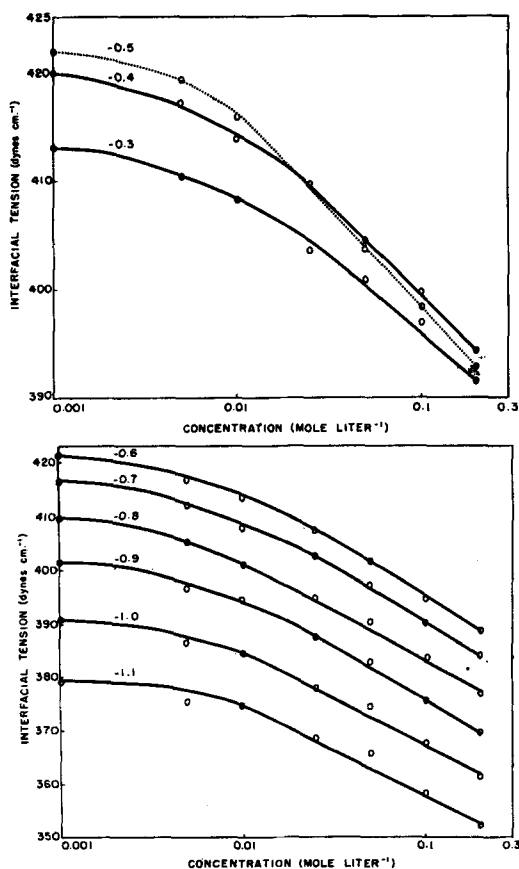

Fig. 4.—Interfacial tension *vs.* log molar concentration of the diastereoisomeric ephedrinium ions in 1 N HCl at constant potential. (Potentials stated on figure.)
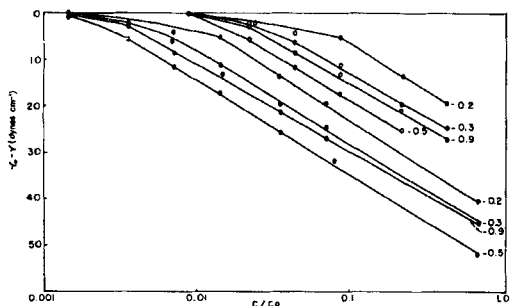
Fig. 5.—Variations of interfacial tension decrease with log reduced concentrations of (−)-ephedrine (●) and (+)-ψ-ephedrine (○) at constant potentials.
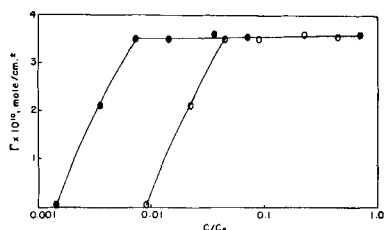

Fig. 6.—Surface excess as a function of the reduced concentrations of (−)-ephedrine (●) and (+)-ψ-ephedrine (○) in 1 N NaOH at e.c.m.

ephedrine, so that the solution activity of the former compound is higher for the same molar concentration.

Since identical values of $(d\gamma/d\ln C)_{V,T,\mu_b}$ were observed for the diastereoisomers, it follows that the dependence of the decrease in interfacial tension, $\gamma_0 - \gamma$, on reduced concentration, C/C_0, at a given potential and temperature is greater for (−)-ephedrine than (+)-ψ-ephedrine. Typical plots at $E_{e.c.m.}$ and at more positive and negative potentials are shown in Fig. 5. The linear dependence of $\gamma_0 - \gamma$ on log C/C_0 above a given value of C/C_0 is evidence that a Gibbs monolayer has formed.

The surface excess-log concentration curves of the isomeric ephedrinium ions in 1 N HCl were found to possess a maximum in the vicinity of the e.c.m. and at more negative and positive potentials, resembling curves reported for aniline in 0.1 N HCl (10). Thus, the assumption that the activity coefficients of the ions is constant over the concentration range studied is incorrect.

In alkaline solution, the dependence of surface excess on the log reduced concentration of the amines at constant potential exhibited saturation characteristics at the e.c.m. (Fig. 6) and over a wide range of potentials. Scattering of points increased with departure of potential from the e.c.m.

Following the suggestions of Breiter and Delahay (5), the dependence of the fractional surface coverage, $\theta = \Gamma/\Gamma_{max.}$ on potential for adsorption of the isomeric ions and amines was determined (Fig. 7). In acidic solution, maximum surface coverage appears to occur on the negative branch of the electrocapillary curve. The coverage is highly dependent on potential with pronounced desorption of the cations occurring with increasing or decreasing potential. Pronounced adsorption of cations occurs on the nega-

tive branch of the electrocapillary curve. In alkaline solution, the surface excess is largely independent of potential over a wide range of potentials. Maximum coverage is in the neighborhood of the e.c.m. The high surface coverage on the positive branch suggests that the aromatic nucleus and probably the amino electrons are involved in the adsorption process. The high surface coverage on the negative branch indicates that the electrode–dipole interaction more than offsets the tendency to desorb the phenyl and amino groups.

Orientation at the Electrode-Solution Interface.— The adsorption isotherms (Fig. 6) based on the reduced concentrations of the isomeric amines indicates that a quasicompact monolayer is formed by (−)-ephedrine at a lower C/C_0 than by (+)-ψ-ephedrine. Once a compact monolayer is formed, the $\Gamma_{max.}$ of the two compounds remains sensibly the same with increasing C/C_0, an indication of a similar orientation of the isomers in the monolayer. Using the projected molecular area from Fisher-Taylor-Hirschfelder models to calculate $\Gamma_{max.}$ for various orientations of the isomers in the monolayer (Table II), the observed $\Gamma_{max.}$ agrees with either the model in which the benzene ring lies flat on the surface and the remainder of the molecule projects into the solution or the similar model in which the flat benzene ring and adjacent carbinol are on the surface and the remainder of side chain is in the solution.
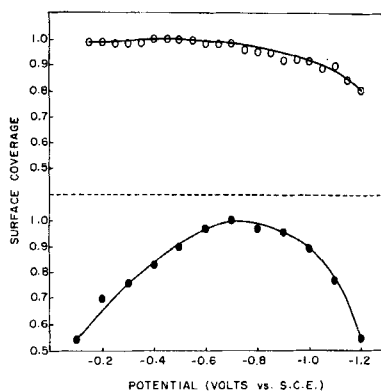

Fig. 7.—Surface coverage as a function of potential for the diastereoisomeric ephedrinium ions 0.2 M in 1 N HCl (●) and for the (−)-ψ-ephedrine 0.1 M and (+)-ψ-ephedrine 0.01 M in 1 N NaOH (○).

TABLE II.—ORIENTATION IN MONOLAYER AT ELECTRODE SURFACE

Orientation	$\Gamma_{max.} \times 10^{10}$, mole cm. $^{-1}$
	Calcd.
Phenyl perpendicular; side chain in solution	8.2
Phenyl flat on surface; side chain in solution	3.8
Phenyl flat + carbinol on surface	3.3
Phenyl flat + side chain on surface	2.2
	Observed
	3.6

Thus, the effects of configurational differences on the adsorbability of diastereoisomers are observable only at C/C_0 values below that needed for quasicompact monolayer formation. In this region of the isotherm, the adsorbability of the molecules is influenced substantially by electrode-molecular dipole interactions. At low concentrations, it is likely that the entire molecule lies flat on the surface, and with increasing concentration, the polar moiety is desorbed as the monolayer is formed.

It is instructive to estimate the *extra* work needed to bring the $(+)$-ψ-ephedrine molecule to the inner double layer at the electrode surface. In 1 N NaOH the diffuse double layer is more narrow than the Helmholtz layer (3), and the concentration of molecules at the Helmholtz layer is expressed by the relation

$$C_s = C' \exp\left(-\frac{W_0 + W_e}{RT}\right)$$

where C' is the reduced concentration in the bulk of the solution, W_0 is the nonelectrostatic work, and W_e is the electrostatic work. If the total work is denoted by $W = W_0 + W_e$, the *extra* work needed to bring $(+)$-ψ-ephedrine to the surface, compared to that of $(-)$-ephedrine, is given by $W_\psi - W_E$. Following the method of Langmuir (13), $C_s = \Gamma/\delta$, where δ is the thickness of the double layer. Thus $W = RT \ln C'/C_s = RT \ln (\delta C'/\mu)$ so that

$$W_\psi - W_E \cong RT \ln (\delta C'_\psi/\Gamma_\psi)/(\delta C'_E/\Gamma_E)$$

and

$$W_\psi - W_E \cong RT \ln 6.2 \cong 1076 \text{ cal./mole}$$

The orientation of the molecules at the electrode surface at low surface coverage must be interpreted in terms of the calculated *extra* work. Vleck (14) has proposed that the electrostatic work needed to bring an ion from the bulk of the solution into an inhomogeneous field is the sum of the charge and dipole interactions. At the electrode surface, the total work is largely electrostatic work because of the high strength of the electrode field. Since the molecules in alkaline solution are uncharged, the *extra* work must be largely the work of orienting the dipoles to minimize the energy of the system. It is necessary, therefore, to consider the probable conformations of the molecules in the bulk of the solution and at the electrode surface. In the bulk of the solution, the probable conformations of the neutral molecules (15) are shown in Fig. 8. The thermodynamically more stable isomer is $(+)$-ψ-ephedrine, due largely to the smaller nonbonded interactions and to a lesser extent due to the intramolecular hydrogen bonding. At the electrode surface, the orientation of the molecules with the phenyl group adsorbed on the surface and the remainder of the molecules in the solution side of the double layer is the model of adsorpton in the monolayer. This model predicts no difference in surface excess between the diastereoisomers at low surface coverage and is considered unlikely when the concentration is less than that required for monolayer formation.

At low surface coverage, two possible conformations at the interface are considered at the electrocapillary maximum and more negative potentials. In the first case, both the C—O and the C—N dipoles are oriented so that the positive ends are
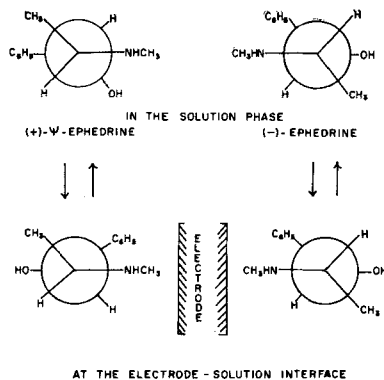

Fig. 8.—Probable conformations of the neutral molecules.

pointed toward the mercury. The energy required in going from the probable conformations in the bulk to these conformations at the surface is greater for $(-)$-ephedrine than it is for $(+)$-ψ-ephedrine, which is contrary to the experimental results. In the second case, the secondary amino group is oriented toward the mercury, and the C—O dipole is oriented with the positive side toward the electrode (Fig. 8). It can be argued that this orientation is not correct on the grounds that the negatively charged electrode should repel the negative end of the C—N dipole, and hydration of the amino group should favor orientation away from the electrode. Both of these arguments were used by Gierst (9) in predicting the orientation of pyridine derivatives at the mercury-solution interface. Similarly, Blomgren *et al.* (16) deduced from electrocapillary characteristics of aliphatic amines that the molecules are oriented at the electrode–solution interface with the hydrocarbon chain perpendicular to the surface and the amino group in solution. On the other hand, the interaction of the amino group of aliphatic amines with a metal interface has been cited often in the literature (17–20). The second surface conformation of the diastereoisomeric ephedrines is in accord with the latter evidence. Moreover, the C—O dipole is larger than the C—N dipole, so that this orientation should cause the observed positive shift of the electrocapillary maximum. These conformations at the surface are consistent with the experimental results for low surface coverage inasmuch as the energy required in going from the probable bulk conformations is greater for $(+)$-ψ-ephedrine. If the net difference in the free energy change, $\delta(\Delta G^\circ)$, is attributed to the electrostatic work of conformer rotation

$$\delta(\Delta G^\circ) = (\bar{\mu}_\psi^{\circ,a} - \bar{\mu}_\psi^{\circ,s}) - (\bar{\mu}_E^{\circ,a} - \bar{\mu}_E^{\circ,s}) \cong 1 \text{ Kcal./mole}$$

where $\bar{\mu}_\psi^{\circ,a}$ and $\bar{\mu}_E^{\circ,a}$ are the respective standard electrochemical potentials of $(+)$-ψ-ephedrine and $(-)$-ephedrine in the adsorbed state, and $\bar{\mu}_\psi^{\circ,s}$ and $\bar{\mu}_E^{\circ,s}$ are the respective standard electrochemical potentials in solution.

This $\delta(\Delta G^\circ)$ value is not consistent with the calculations of Everett and Hyne (21) for free energy changes accompanying the rotation of the isomeric ephedrines. They found that in going from the 0° conformation (OH and CH_3NH groups eclipsed) of

both isomers to the most stable conformations in solution, the most stable conformation of (−)-ephedrine relative to its 0° conformer is more stable by 225 cal./mole than the most stable conformer of (+)-ψ-ephedrine relative to its 0° conformer. The rotations from the eclipsed conformations are 60° for (+)-ψ-ephedrine and 180° for (−)-ephedrine. From this value of $\delta(\Delta G°)$, the predicted energy barrier to internal rotation for either isomer is approximately 500 cal./mole, a value which is less than the equipartition value at ordinary temperature (600 cal./mole), representing a negligible barrier to rotation. The magnitude of the internal rotation barrier in ethane is 2.7–3.0 Kcal./mole (22). Eyring and co-workers (23) have calculated that the non-
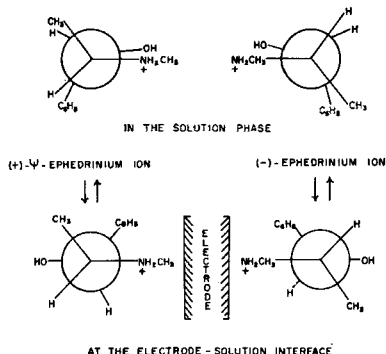

Fig. 9.—Probable conformations of the ions.

bonded H⋯H interaction in ethane affords a barrier of 2.88 Kcal./mole and suggest that this interaction is responsible for the rotation barrier. The isomeric ephedrines may be viewed as substituted ethanes with bulky groups on each carbon; *a priori*, the internal rotation barrier should be at least several kilocalories per mole.

No rotation is predicted (Fig. 8) for the transfer of (−)-ephedrine from the bulk solution to the electrode surface, whereas a 120° rotation is predicted for (+)-ψ-ephedrine. As a first approximation, the internal rotation barriers can be taken to be two or three times the barrier to the 120° rotation. Accordingly, the estimated $\delta(\Delta G°)$ value of 1 Kcal./mole is of a reasonable order of magnitude.

The similar adsorption characteristics of the (−)-ephedrinium and (+)-ψ-ephedrinium ions in 1 *N* HCl can be interpreted in the same general fashion. With both ions, the contribution of the charge interaction to the electrostatic work should be the same. The most probable conformations of both ions in the bulk of the solution are those in which the CH_3-NH_2^+ and OH groups are eclipsed as shown in Fig. 9 (21). At the electrocapillary maximum and at the negatively charged electrode surface, the CH_3-NH_2^+ group will be pointed toward the electrode, and the negative end of the C—O dipole will be repelled (Fig. 9). The work needed for the rotation processes in going from the bulk of the solution to the electrode surface is approximately the same for both isomers. Since the electrostatic work of both ions is approximately the same, there is no difference in surface excess.

Catalytic Hydrogen Evolution.—An extensive study of catalytic hydrogen evolution in solutions of

alkaloids was made by Kirkpatrick. He reported that ephedrine is polarographically inactive (4), and this observation has been cited in the literature (24). However, most nitrogenous compounds which cause catalytic hydrogen waves are adsorbed at the electrode surface (25). Since the adsorption of the diastereoisomeric ephedrines on mercury was found to occur, a renewed search for catalytic hydrogen evolution by these alkaloids was undertaken.

The mechanism proposed by Mairanovskii (25), describing catalytic hydrogen evolution in solutions of organic bases, is represented in outline by

$$B + DH^+ \underset{k_2}{\overset{k_1}{\rightleftarrows}} BH^+ + D$$

$$BH^+ + e^- \rightarrow BH$$

$$2BH \overset{k_d}{\rightarrow} 2B + H$$
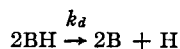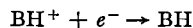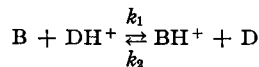
in which B is the catalytic base, DH^+ is a proton donor, and BH is a free radical. It is evident that catalytic hydrogen evolution will only occur in solutions in which the catalytic base, B, and its conjugate acid, BH^+, are in equilibrium. The dissociation constant of a 0.01 *M* (−)-ephedrinium and (+)-ψ-ephedrinium ions in solution of ionic strength 0.10 were reported to be 9.71 and 9.89, respectively, at 20° (21). Accordingly, polarograms of the diastereoisomers in borate buffer solutions were examined.
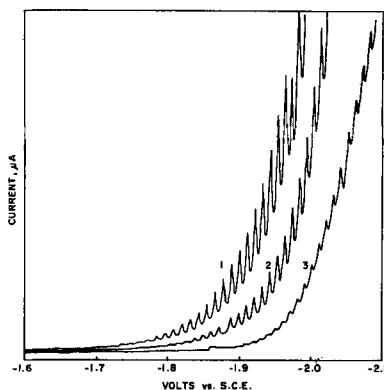

Fig. 10.—Polarograms of (−)-ephedrine (*1*) and (+)-ψ-ephedrine (*2*) in borate buffer (0.05 *M* $NaBO_2$; 0.109 *M* H_3BO_3) (*3*) at pH 8.76 and ionic strength of 0.058. Alkaloid concentration 8 × 10^{-3} *M*.
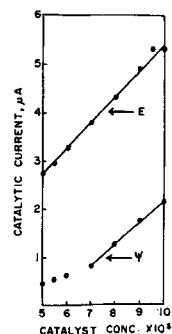

Fig. 11.—Dependence of the limiting catalytic hydrogen current on (−)-ephedrine (E) and (+)-ψ-ephedrine (ψ) concentrations in borate buffer solutions with pH 8.76 and ionic strength 0.058 (−1.95 v. *vs.* S. C. E.).

Typical polarograms are shown in Fig. 10. The polarograms exhibit no discrete hydrogen waves; however, the limiting current at potentials preceding discharge appear to be catalytic currents. The catalytic current of ephedrine is greater than that of ψ-ephedrine.

The catalytic current at a given potential is taken as the difference between the limiting current of the buffer solution of the alkaloid and the limiting current of the buffer solution alone. The dependence of the catalytic current at -1.95 v. *versus* S.C.E. on the total alkaloid concentration was examined at pH 8.76 in borate buffers with $[H_3BO_3]$ $= 0.1\ M$. The catalytic current varied linearly with concentration between $5 \times 10^{-3}\ M$ and $1 \times 10^{-2}\ M$ for ephedrine and between $7 \times 10^{-3}\ M$ and 1×10^{-2} M for ψ-ephedrine (Fig. 11). The leveling of catalytic current with decreasing concentration is a well-known observation (25). The linear dependence of catalytic current on concentration in this concentration range suggests that the third step of Mairanovskii's mechanism is not current limiting. It is probable, therefore, that the catalytic current depends upon the first step, *i.e.*, the rate of protonation of the basic form of the catalyst. From the known dissociation constants (21), it is estimated that the concentration of the free base of ephedrine is approximately 1.5-fold greater than that of ψ-ephedrine at pH 8.76. The observed limiting catalytic current at -1.95 v. *versus* S.C.E. for ephedrine is approximately threefold greater than that of ψ-ephedrine.

If it is assumed that at this extreme negative potential the diastereoisomers are not adsorbed on the electrode surface, the rate of protonation preceding electron transfer of ephedrine is greater than that of ψ-ephedrine. Analogous to the kinetic currents in the reduction of the diastereoisomeric *N*-nitrosoephedrines (15), the rate of protonation is expected to be greater with that isomer in which there is a lesser degree of intramolecular hydrogen bonding. The greater degree of intramolecular hydrogen bonding in $(+)$-ψ-ephedrine is well established (15).

Interpretation of these results depends upon whether the catalytic current has true *bulk* character, with protonation occurring only in the reaction layer near the electrode, or whether it has both *bulk* and *surface* character, with protonation of catalyst adsorbed on the electrode surface causing the surface component of the current (25). Consideration of the desorption potentials of the amines (Figs. 1 and 2) leads to the conclusion that the catalytic current possesses no *surface* character since it is occurring at potentials more negative by about 0.65 v. However, this conclusion is open to serious question. The fractional surface coverage which will give the catalytic current partial surface character is extremely small; certainly it is less than can be determined by electrocapillary or differential capacity measurements. The electrocapillary curves (Fig. 2) show that the desorption occurs at more negative potentials with an increase in concentration. At potentials more negative than the electrocapillary

maximum, a plot of the variation of surface excess with log concentrations shows that the desorption occurs somewhat sharply, an observation which is similar to that made by Gierst (9) for the adsorption of pyridine derivatives on mercury in alkaline medium. Frumkin (26) has attributed both the desorption of neutral organic molecules and large organic cations at negative potentials to the energy gain, a result of the capacitance increase with desorption. He reported that the desorption potential of the tetrabutyl-ammonium ion is sharply defined and becomes more negative with increasing concentration, generally in accord with the present observations. Frumkin (26, 27) calculated that the adsorption isotherm of the tetrabutyl-ammonium ion exhibits an S shape at very negative potentials. Thus, for a given concentration of organic molecule at potentials negative to the desorption peak of the capacitance-polarization curve, extremely low fractional surface coverage may occur. Thus, it is possible that the higher catalytic current for $(-)$-ephedrine may, to some extent, be due to its greater adsorbability.

REFERENCES

(1) Butler, J. A. V., "Electrocapillarity," Chemica Publishing Co., Inc., New York, N. Y., 1940, pp. 80–89.
(2) Kolthoff, I. M., and Lingane, J. J., "Polarography," Vol. I, 2nd ed., Interscience Publishers, Inc., New York, N. Y., 1952, pp. 134–143.
(3) Grahame, D. C., *Chem. Rev.*, 41, 441(1947).
(4) Kirkpatrick, H. F. W., *Quart. J. Pharm. Pharmacol.*, 19, 526(1946).
(5) Breiter, M., and Delahay, P., *J. Am. Chem. Soc.*, 81, 2938(1959).
(6) Conway, B. E., Bockris, J. O., and Lovrecek, B., *C.I.T.C.E. Proc.*, 6, 207(1955).
(7) Corbusier, P., and Gierst, L., *Anal. Chim. Acta*, 15, 254(1956).
(8) Hansen, R. S., Kelsh, D. J., and Grantham, D. H., *J. Phys. Chem.*, 67, 2316(1963).
(9) Gierst, L., "Transactions of the Symposium on Electrode Processes," Yeager, E., ed., John Wiley & Sons, Inc., New York, N. Y., 1961, p. 294.
(10) Blomgren, E., and Bockris, J. O., *J. Phys. Chem.*, 63, 1475(1959).
(11) Adamson, A. W., "Physical Chemistry of Surfaces," Interscience Publishers, Inc., New York, N. Y., 1960, pp. 575–577.
(12) *Ibid.*, pp. 577–580.
(13) Langmuir, I., *J. Am. Chem. Soc.*, 39, 1848(1917).
(14) Vlcek, A. A., "Progress in Inorganic Chemistry," Vol. 5, Cotton, F. A., ed., Interscience Publishers, Inc., New York, N. Y., 1963, p. 252.
(15) Maispeis, L., and Hung, N. G. M., THIS JOURNAL, 53, 506(1963).
(16) Blomgren, E., Bockris, J. O., and Jesch, C., *J. Phys. Chem.*, 65, 2000(1961).
(17) Hoar, T. P., *Proc. Intern. Congr. Surface Activity*, 2nd, London, 3, 81(1957).
(18) Matsen, F. A., Makrides, A. C., and Hackerman, N., *J. Chem. Phys.*, 22, 1800(1954).
(19) Bewig, K. W., and Zisman, W. A., *J. Phys. Chem.*, 67, 130(1963).
(20) Yao, Y. F. Y., *ibid.*, 67, 2055(1963).
(21) Everett, D. H., and Hyne, J. B., *J. Chem. Soc.*, 1958, 1636.
(22) Wilson, E. B., "Advances in Chemical Physics," Vol. II, Prigogine, I., ed., Interscience Publishers, Inc., New York, N. Y., 1959, p. 367.
(23) Eyring, H., Grant, D. M., and Hecht, H., *J. Chem. Educ.*, 39, 466(1962).
(24) Milner, G. W. C., "The Principles and Applications of Polarography," Longmans Green and Co., Inc., New York, N. Y., 1957, p. 591.
(25) Mairanovskii, S. G., *J. Electroanal. Chem.*, 6, 77 (1963).
(26) Frumkin, A., "Transactions of the Symposium on Electrode Processes," Yeager, E., ed., John Wiley & Sons, Inc., New York, N. Y., 1961, p. 1.
(27) Frumkin, A., *Proc. Intern. Congr. Surface Activity*, 2nd, London, 3, 58(1957).