J. Am. Chem. Soc. **1982**, *104*, 6191–6194

Proximate Charge Effects. 2.[1] Enthalpies of Solvent Transfer in the Choline–Anhydrocholine Equilibrium

Paul Haberfield* and Jeffrey Pessin

Contribution from the Department of Chemistry, Brooklyn College of the City University of New York, Brooklyn, New York 11210. *Received February 8, 1982*

Abstract: Equilibrium constants for the choline–anhydrocholine equilibrium, eq 1, $^+(CH_3)_3NCH_2CH_2OH + OH^- \rightarrow {}^+(CH_3)_3NCH_2CH_2O^- + H_2O$, were measured conductometrically in water, aqueous alcohol, and aqueous dimethyl sulfoxide at several temperatures. On going to progressively less H-bonding media, there was a large shift of the equilibrium constant toward anhydrocholine (to the right) accompanied by an even larger exothermic shift of the enthalpy of reaction. Calorimetric measurement of the enthalpies of solvent transfer revealed that, in the case of the aqueous alcohol solvents, the exothermic shift was caused by enhanced solvation of anhydrocholine, $^+(CH_3)_3NCH_2CH_2O^-$, by the less polar media. In the comparison of aqueous ethanol with aqueous Me_2SO, the dominant factor was found to be the very great desolvation of both hydroxide ion and anhydrocholine in the less H-bonding medium.

The customary formulation of choline,[2] $^+(CH_3)_3NCH_2CH_2OH\,OH^-$, is no doubt based on the belief that the choline ion, $^+(CH_3)_3NCH_2CH_2OH$, has a pK_a sufficiently close to that of water so that in dilute aqueous solution reaction 1 can be neglected

$$^+(CH_3)_3NCH_2CH_2OH + OH^- \rightleftarrows {}^+(CH_3)_3NCH_2CH_2O^- + H_2O \quad (1)$$

While following the rate of the base-catalyzed hydrolysis of acetylcholine in water conductometrically, we noticed that the conductance of solutions of choline were substantially lower than would be required by the customary formulation. Furthermore, this discrepancy increased on going to aqueous organic solvents.[1] Using this discrepancy between the expected and the actual conductance of solutions of choline, we were able to determine the concentration of anhydrocholine,[3] $^+(CH_3)_3NCH_2CH_2O^-$, present in solutions of choline.

The susceptibility of the equilibrium constants of eq 1 to change on changing the medium raised the possibility that anhydrocholine might be a viable biomolecule, even in environments where the bulk pH is very much lower than it is in choline solutions.[4] A characteristic of biological systems, such as enzymes, is the existence of microenvironments in which, for example, acidic or basic groups function as if their pK's were very much higher (or lower) than in aqueous solutions.[5] It is likewise possible that some small biomolecules might be particularly susceptible to such changes in acidity, either on an enzyme surface or in some other cellular environment, and that this variability might be an essential part of their function.

An interesting feature of the choline–anhydrocholine system is the possibility of intramolecular charge stabilization of the negatively charged oxygen of anhydrocholine. The choline cation itself is predominantly (88–94%) in the gauche rather than in the less hindered trans conformation.[6] The reason is apparently electrostatic attraction, since carbocholine (3,3-dimethylbutan-1-ol), where the N^+ is replaced by C, is mainly (68%) in the trans conformation.[7] In anhydrocholine, $^+(CH_3)_3NCH_2CH_2O^-$, the driving force stabilizing the cyclic (gauche or even syn) conformation would of course be much greater, particularly in solvents that are less polar or are weaker hydrogen-bond donors.

Choline–Anhydrocholine Equilibrium

Equilibrium constants were determined by measuring the conductances of solutions of choline chloride, sodium chloride, sodium hydroxide, and choline chloride plus sodium hydroxide. Use of eq 3 (see Experimental Section) yielded the equilibrium constants shown in Table I.

To make sure that the equilibrium constants obtained by this conductometric method are not the result of some unfortunate artifact, we tested the method in one case (water solvent) using a completely unrelated technique. We followed the upfield shift of the NMR peak of the α-methylenes as the choline ion is converted to anhydrocholine. This is not a very precise or convenient method, but it gave results in good agreement with the conductometric methods (see Experimental Section).

As can be seen, even in water, the equilibrium constant favors anhydrocholine over choline (78% anhydrocholine in a 1 M solution at 25.0 °C). The 25.0 °C equilibrium constant for the choline–anhydrocholine equilibrium (eq 1) is 16.55, which gives the following values for the ionization constant of choline chloride in water [$^+(CH_3)_3NCH_2CH_2OH \rightarrow {}^+(CH_3)_3NCH_2CH_2O^- + H^+$]: p$K_a$ (25.0 °C) = 12.8, $\Delta H° = 17.73$ kcal/mol, $\Delta S° = 1.6$ cal/(mol K).[8,14]

This compares with the literature values of other hydroxyethyl compounds as follows: CF_3CH_2OH, pK_a = 12.43,[9] $N{\equiv}CCH_2CH_2OH$, pK_a = 14.03.[10]

As one passes from water to less polar solvents, there is a slight shift in equilibrium 1 toward anhydrocholine (see Table I). The equilibrium constant doubled for 60 mol % aqueous ethanol and rose to 10-fold its aqueous value in 85 mol % aqueous ethanol. The largest effect, a 100-fold increase, was observed in 60 mol

---

(1) Part 1: Haberfield, P.; Pessin, J. *J. Org. Chem.* **1976**, *41*, 3773.

(2) For a review of choline, see: Harris, R. S.; Griffith, W. P.; Nyc, J. F.; Hartcroft, W. S.; Porta, E. A. "The Vitamins"; 2nd ed.; Sebrell, W. H., Harris, R. S., Eds., Academic Press: New York, 1971; Vol. III.

(3) Since the salt $^+(CH_3)_3NCH_2CH_2OH\,OH^-$ is called *choline*, the reasonable name for its dehydration product, $^+(CH_3)_3NCH_2CH_2O^-$, is *anhydrocholine*.

(4) Anhydrocholine, being a good nucleophile, may, for example, be a good candidate for the reactive species at the active site of choline acetylase or choline kinase.

(5) E.g., lysozyme, where glutamic acid 35 appears to be protonated (i.e., a weak acid) in the enzyme but then acts as a strong acid in the enzyme–substrate complex [Phillips, D. C., *Proc. Natl. Acad. Sci. U.S.A.* **1967**, *57*, 484. See also: Bender, M. L.; Kezdy, F. J. In "Proton Transfer Reactions"; Caldin, E., Ed.; Wiley: New York, 1975; pp 385–407.

(6) Lichtenberg, D.; Kroon, P. A.; Chan, S. I. *J. Am. Chem. Soc.* **1974**, *96*, 5934.

(7) Partington, P.; Feeney, J.; Burgen, A. S. V. *Mol. Pharmacol.* **1972**, *8*, 269.

(8) An old literature report on the acidity of choline chloride (based on the measurement of the pH of dilute solutions of choline chloride) gives a value of pK_a = 9 (Lewis, C. W.; Price, W. C. M. *Trans. Faraday Soc.* **1933**, *29*, 777.) A value of pK_a = 13.9 is listed in Fasman [Fasman, G. D., Ed. "Handbook of Biochemistry and Molecular Biology", 3rd ed.; CRC Press: Cleveland, OH 1976; p 315]. This value is taken from Dawson et al. [Dawson, R. M. C.; Elliot, W. H.; Elliot, D. C.; Jones, K. M. "Data for Biochemical Research"; Clarendon Press: Oxford, 1959; p 8], which in turn gives no further reference.

(9) Ballinger, P.; Long, F. A. *J. Am. Chem. Soc.* **1959**, *81*, 1050.

(10) Takahaski, S.; Cohen, L. A.; Miller, H. K.; Peake, E. G. *J. Org. Chem.* **1971**, *36*, 1205.

0002-7863/82/1504-6191$01.25/0

Table I. Equilibrium Constants and Thermodynamic Parameters for the Reaction

$(CH_3)_3N^+CH_2CH_2OH + OH^- \rightarrow (CH_3)_3N^+CH_2CH_2O^- + H_2O$

solvent[a]	T, K	K^b	ΔH°, kcal/mol	ΔS°, cal/(mol K)
H_2O	291.15	13.9 ± 0.2	4.39 ± 0.22	20.3 ± 0.8
H_2O	322.90	29.3 ± 1.6		
0.60 aqueous ethanol	273.15	27.5 ± 1.0	2.58 ± 0.02	15.9 ± 0.1
0.60 aqueous ethanol	291.15	33.3 ± 1.3		
0.60 aqueous ethanol	322.90	55.9 ± 2.1		
0.85 aqueous ethanol	291.15	141.7 ± 6.7	−1.47 ± 0.08	4.79 ± 0.18
0.85 aqueous ethanol	322.90	110.4 ± 3.7		
0.60 aqueous Me_2SO	273.15	1766 ± 57	−2.35 ± 0.21	6.27 ± 0.87
0.60 aqueous Me_2SO	291.15	1397 ± 54		
0.60 aqueous Me_2SO	322.90	911.7 ± 84		

[a] Solvent composition indicated as mole fraction of organic solvent. [b] Values are the averages of 3–6 determinations. The uncertainties are given as the standard deviation of the mean.

Table II. Enthalpies of Solvent Transfer, $\delta\Delta H_{S_1\rightarrow S_2}$, of Compounds and Ions, 25.0 °C (kcal/mol)

	solvent transfer[a]	$\delta\Delta H_{S_1\rightarrow S_2}$		solvent transfer[a]	$\delta\Delta H_{S_1\rightarrow S_2}$
$(n\text{-}C_4H_9)_4NB(n\text{-}C_4H_9)_4$	methanol → 0.60 aq ethanol	3.96[b]	choline chloride	H_2O → 0.60 aq ethanol	0.40[b]
$(n\text{-}C_4H_9)_4N^+$	methanol → 0.60 aq ethanol	1.98	choline chloride	H_2O → 0.85 aq ethanol	1.06[b]
$(n\text{-}C_4H_9)_4N^+$	0.60 aq ethanol → 0.85 aq ethanol	−0.22[c]	choline chloride	H_2O → 0.60 aq Me_2SO	0.63[b]
$(n\text{-}C_4H_9)_4N^+$	0.60 aq ethanol → 0.60 aq Me_2SO	−1.51[c]	$HOCH_2CH_2N(CH_3)_3^+$	H_2O → 0.60 aq ethanol	−1.2
$(n\text{-}C_4H_9)_4N^+$	methanol → 0.60 aq ethanol	1.98	$HOCH_2CH_2N(CH_3)_3^+$	H_2O → 0.85 aq ethanol	0.5
$(n\text{-}C_4H_9)_4N^+$	methanol → 0.85 aq ethanol	1.76	$HOCH_2CH_2N(CH_3)_3^+$	H_2O → 0.60 aq Me_2SO	−1.3
$(n\text{-}C_4H_9)_4N^+$	methanol → 0.60 aq Me_2SO	3.49	NaCl	H_2O → 0.60 aq ethanol	0.45[b]
$(n\text{-}C_4H_9)_4NCl$	methanol → 0.60 aq ethanol	1.72[b]	Na^+	H_2O → 0.60 aq ethanol	−1.2
$(n\text{-}C_4H_9)_4NCl$	methanol → 0.85 aq ethanol	0.43[b]	NaOH	H_2O → 0.60 aq ethanol	−1.72[b]
$(n\text{-}C_4H_9)_4NCl$	methanol → 0.60 aq Me_2SO	3.53[b]	OH^-	H_2O → 0.60 aq ethanol	−0.5
Cl^-	methanol → 0.60 aq ethanol	−0.26	OH^-	0.60 aq ethanol → 0.85 aq ethanol	−2.37[c]
Cl^-	methanol → 0.85 aq ethanol	−1.33	OH^-	0.60 aq ethanol → 0.60 aq Me_2SO	14.24[c]
Cl^-	methanol → 0.60 aq Me_2SO	0.04			
Cl^-	H_2O → methanol	1.9[d]	OH^-	H_2O → 0.85 aq ethanol	−2.9
Cl^-	H_2O → 0.60 aq ethanol	1.6	OH^-	H_2O → 0.60 aq Me_2SO	13.7
Cl^-	H_2O → 0.85 aq ethanol	0.6	H_2O	H_2O → 0.60 aq ethanol	−0.23[e]
Cl^-	H_2O → 0.60 aq Me_2SO	1.9	H_2O	H_2O → 0.85 aq ethanol	−0.20[e]
			H_2O	H_2O → 0.60 aq Me_2SO	−1.15[f]

[a] Composition of mixed solvents indicated as mole fraction of organic component. [b] See Table V, Experimental Section. [c] Haberfield, P.; Friedman, J.; Pinkston, M. *J. Am. Chem. Soc.* **1972**; *94*, 71. [d] Choux, G.; Benoit, R. L. *Ibid.* **1969**, *91*, 6221. [e] Lama, R. F.; Lu, B. C. Y. *J. Chem. Eng. Data* **1965**, *10*, 216. [f] Kenttämaa, J.; Lindberg, J. J. *Suom. Kemistil. B* **1960**, 33, 32.

% aqueous dimethyl sulfoxide (Me_2SO), a solvent that is not appreciably less polar than water[11] but one that is a very poor hydrogen-bond donor. Measurement of equilibrium constants at several temperatures yielded the enthalpy and entropy values shown in Table I. The following points can be raised: (1) In water, the greater stability of anhydrocholine over choline is an entropy-driven effect. (2) The increase in the equilibrium constant on going to aqueous ethanol and aqueous Me_2SO is accompanied by an even larger shift to an exothermic enthalpy of reaction (by almost 7 kcal/mol; see Table I). This large increase in $\Delta H°$ is opposed by a concomitant decrease in the $\Delta S°$, thus damping the effect on the equilibrium constant. As this damping entropic effect might be absent in the highly ordered biological environments in which the choline ion functions, the factors favoring anhydrocholine in a water-poor biological environment may be even more pronounced. (3) What causes the dramatic shift of the $\Delta H°$ of reaction 1 on going to water-poor solvents? Is it caused by destabilization of OH^- or the choline ion in the water-poor solvents, or is it caused by enhanced solvation of anhydrocholine, $^+(CH_3)_3NCH_2CH_2O^-$, or perhaps of the H_2O molecule produced in the water-poor solvent?

Enthalpies of Solvent Transfer. The above question can be answered by measuring the enthalpies of transfer of the four species in eq 1 from water to each of the other three media. The enthalpy of transfer of a compound from one solvent to another, $\delta\Delta H_{S1\rightarrow S2}$, is the difference between the heats of solution, ΔH_S, of the compound in the two solvents of interest:

$$\delta\Delta H_{S1\rightarrow S2} = \Delta H_{S2} - \Delta H_{S1}$$

The enthalpy of transfer of H_2O was obtainable by this method in a straightforward manner, using calorimetric measurements. The enthalpies of transfer of OH^- and $^+(CH_3)_3CH_2CH_2OH$ were determined by calorimetry using the $(n\text{-}C_4H_9)_4N^+(n\text{-}C_4H_9)_4B^-$ extrathermodynamic assumption employed in our earlier work.[12] Table II shows the requisite enthalpies of transfer of compounds and ions. They are listed in a rational sequence showing how each

Table III. Enthalpies of Solvent Transfer of Anhydrocholine and of the Reactants and Products in the Reaction $^+(CH_3)_3NCH_2CH_2OH + OH^- \rightarrow {}^+(CH_3)_3NCH_2CH_2O^- + H_2O$ at 25.0 °C (kcal/mol)[a,b]

solvent transfer	reactants	products	anhydrocholine
H_2O → 0.60 aq ethanol	−1.7	−3.5	−3.3
H_2O → 0.85 aq ethanol	−2.4	−8.3	−8.1
0.60 aq ethanol → 0.60 aq Me_2SO	14.1	9.2	10.1

[a] All values ±0.2 kcal/mol standard deviation. [b] Composition of mixed solvents indicated as mole fraction of organic component.

---

(11) The dielectric constants of these solvents are as follows: H_2O, 78; 0.60 mol % aqueous ethanol, 33; 0.85 mol % aqueous ethanol, 27; 0.60 mol % aqueous Me_2SO, 60 [Akerlof, G. *J. Am. Chem. Soc.* **1932**, *54*, 4125. Lindberg, J. J.; Kentamaa, J. *Suom. Kemistil. B* **1960**, *B33*, 104].

(12) Haberfield, P.; Friedman, J.; Pinkston, M. F. *J. Am. Chem. Soc.* **1972**, *94*, 71.

Table IV. Enthalpies of Solvent Transfer of Benzene at 25.0 °C (kcal/mol)[a,b]

solvent transfer	$\delta\Delta H_{S_1 \rightarrow S_2}$
$H_2O \rightarrow$ 0.60 aq ethanol	0.49
$H_2O \rightarrow$ 0.85 aq ethanol	0.78
0.60 aq ethanol $\rightarrow$ 0.60 aq Me_2SO	0.41

[a] All values ±0.1 kcal/mol. [b] Composition of mixed solvents indicated as mole fraction of organic component.

Table V. Heats of Solution[a]

solute	solvent[b]	ΔH_S, kcal/mol
choline chloride	H_2O	3.29[c]
choline chloride	0.60 aq ethanol	3.69
choline chloride	0.85 aq ethanol	4.35
choline chloride	0.60 aq Me_2SO	3.92
$(n\text{-}C_4H_9)_4NCl$	methanol	0.29
$(n\text{-}C_4H_9)_4NCl$	0.60 aq ethanol	2.01
$(n\text{-}C_4H_9)_4NCl$	0.85 aq ethanol	0.72
$(n\text{-}C_4H_9)_4NCl$	0.60 aq Me_2SO	3.82
NaCl	H_2O	0.928[d]
NaCl	0.60 aq ethanol	1.38
NaOH	H_2O	−10.64[d]
NaOH	0.60 aq ethanol	−12.36
$(n\text{-}C_4H_9)_4NB(n\text{-}C_4H_9)_4$	methanol	6.99[e]
$(n\text{-}C_4H_9)_4NB(n\text{-}C_4H_9)_4$	0.60 aq ethanol	10.95[f]
benzene	H_2O	0.11[g]
benzene	0.60 aq ethanol	0.60
benzene	0.85 aq ethanol	0.89
benzene	0.60 aq Me_2SO	1.01

[a] Integral heats of solution, measured at concentrations of 0.001–0.01 M; standard deviations were 0.1 kcal/mol or better; temperature 25.0 °C. [b] Composition of mixed solvents indicated as mole fraction of organic component. [c] Literature value 3.26 [Parker, V. B. *Natl. Stand. Ref. Data Ser. (U.S. Nat. Bur. Stand.)* 1965, 2]. [d] Parker, V. B. *Ibid.* 1965, *2*. [e] Haberfield, P.; Clayman, L.; Cooper, J. S. *J. Am. Chem. Soc.* 1969, *91*, 787. [f] Haberfield, P.; Friedman, J.; Pinkston, M. *Ibid.* 1972, *94*, 71. [g] Krishnan, C. V.; Friedman, H. L. *J. Phys. Chem.* 1969, *73*, 1572.

value was derived from the experimental data. In Table III are shown the desired enthalpies of transfer of reactants and products. Before discussing these, it is necessary to consider to what extent these values reflect solute–solvent interactions. An enthalpy of transfer of a solute from one solvent to another consists of two contributions: (1) the difference between the solute–solvent interactions in the two solvents and (2) the difference between the cavity formation energies in the two solvents. Since only (1) is of interest here, it is necessary to show that (2) does not contribute significantly to the values of Table III. To estimate the differences between the cavity formation energies in our solvents, we use as a model the enthalpies of transfer shown in Table IV. As can be seen while these transfer enthalpies are not negligible, they are about an order of magnitude smaller than those of Table III, and hence, the values of Table III can be reasonably discussed in terms of solute–solvent interactions.[13]

Examination of the enthalpies of transfer shows that the dramatic exothermic shift of the $\Delta H°$ of reaction 1 on going from water to aqueous alcohol was caused by enhanced solvation of anhydrocholine, $^+(CH_3)_3NCH_2CH_2O^-$, by the less polar media (Figure 1). In the comparison of aqueous ethanol with aqueous Me_2SO (Figure 2), it was found that the main factor was the great desolvation of both OH^- and $^+(CH_3)_3NCH_2CH_2O^-$, in the medium that was the worse H-bond donor (aqueous Me_2SO). This desolvation is 4 kcal/mol less for anhydrocholine than for hydroxide ion, and this is the principal cause of the exothermic shift of the enthalpy of reaction between these two solvents.

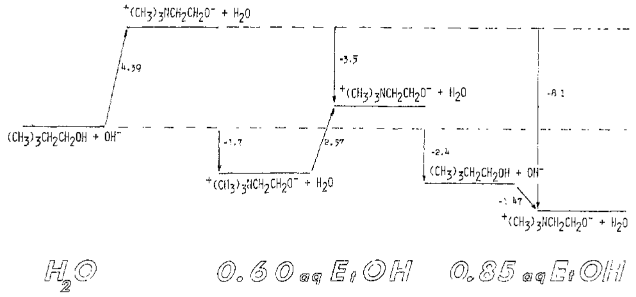

Figure 1. Relative enthalpies of reactants and products in the choline–anhydrocholine equilibrium (eq 1) in water, 0.60 mol fraction aqueous ethanol, and 0.85 mol fraction aqueous ethanol.

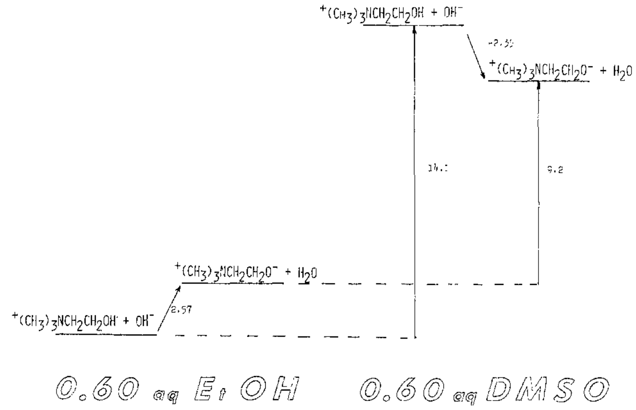

Figure 2. Relative enthalpies of reactants and products in the choline–anhydrocholine equilibrium (eq 1) in 0.60 mol fraction aqueous ethanol and 0.60 mol fraction aqueous dimethyl sulfoxide.

Experimental Section

Materials. Dimethyl sulfoxide (Aldrich Chemical Co.) was allowed to stand over calcium hydride overnight. It was then decanted and fractionally distilled at reduced pressure. Ethanol (Commercial Solvents Corp.) was used without further purification. The following compounds were also used: NaOH (Matheson, Coleman and Bell, Analyzed Reagent, A.C.S.); NaCl (Fisher Scientific, Certified, A.C.S.); benzene (Matheson, Coleman and Bell, Spectroquality), fractionally distilled; choline chloride (Nutritional Biochemicals), recrystallized and titrated with silver nitrate solution; tetra-*n*-butylammonium chloride (Eastman Organic Chemicals), recrystallized and titrated with $AgNO_3$ solution; methanol (Fisher Scientific Spectranalyzed, Certified, A.C.S.).

Solution Preparation. The mixed solvents were prepared from weighed amounts of distilled water and Me_2SO or ethanol. Dissolved carbon dioxide was removed from all solvents by passing purified nitrogen gas through a sintered glass bubbler immersed in the solvent. All subsequent operations were performed under a nitrogen atmosphere. NaCl solutions were prepared by weight, followed by dilution. NaOH and choline chloride solutions were standardized by titration with HCl and $AgNO_3$, respectively, followed by dilution where necessary.

Conductance Measurements. Several all-glass conductance cells, having platinum electrodes with cell constants ranging from 0.1 to 3 cm^{-1}, were used. The conductance values were measured with a Wayne-Kerr Model B224 conductivity bridge at a frequency of 1592 Hz. In each solvent and at each temperature, separate conductance measurements were made for solutions of pure NaCl, pure NaOH, and pure choline chloride at several concentrations. The conductance of an equimolar mixture of NaOH and choline chloride was then compared with the above three conductances (at the same ionic strength as that prevailing in the mixture) to calculate the choline–anhydrocholine equilibrium constant, *K*.

The choline–anhydrocholine equilibrium constant, *K*, was calculated from

$$K = \frac{(\text{Anh})}{[C - (\text{Anh})]^2} \tag{2}$$

and

$$(\text{Anh}) = \frac{C(L_{\text{CholCl+NaOH}} - L_{\text{NaOH}} - L_{\text{CholCl}})}{L_{\text{NaCl}} - L_{\text{NaOH}} - L_{\text{CholCl}}} \tag{3}$$

---

(13) The differences in the cavity formation enthalpies of our four solvents may well be even smaller than the transfer enthalpies of Table IV. This is so because the implicit assumption that there are no solute–solvent interactions between benzene and our solvents is obviously not exactly true.

(14) $\Delta H°$ calculated using 13.3 kcal/mol as the heat of ionization of water (Bertrand, G. L.; Millero, F. J.; Wu, C.; Hepler, L. G. *J. Phys. Chem.* **1966**, *70*, 699).

Table VI

choline chloride, M	NaOD , M	% anhydrocholine	
		calcd	obsd
0.82		0	
0.81	0.34	39	37
0.79	0.66	70	66
0.69	2.33	100	

where *L* is the conductance of the subscript compound or compounds at concentration *C*. The constant, *K*, was determined at a minimum of three concentrations, with *C* ranging from 10^{-4} to 10^{-2} mol/kg. The equilibrium constant, *K*, as defined by the above equations uses a value of unity for the concentration of H_2O in eq 1. Using the actual concentrations of H_2O yields *K* values that are somewhat different and ΔH and ΔS values that are slightly different from those in Table I. In the two ethanolic media, this calculation of *K* does not distinguish the relative contributions of OH^- and $C_2H_5O^-$ to the equilibrium but rather measures the *K* of the equilibrium $(CH_3)_3N^+CH_2CH_2OH + SO^- \rightarrow (CH_3)_3N^+CH_2CH_2O^- + SOH$ (SOH = solvent).

NMR Measurements. The proton NMR spectra of three solutions of choline chloride plus NaOH in D_2O and one of choline chloride alone in D_2O were recorded on a Varian T-60 spectrometer at 42.5 °C. The quaternary methyl peak was observed at δ 3.2 in all four samples, indicating no observable interaction between this group and hydroxide ion and no decomposition. The α-methylene resonances, at about δ 3.4, were found to shift steadily upfield on addition of NaOH. By use of this shift, the percent of anhydrocholine formed was calculated and compared with that calculated from our aqueous ΔH and ΔS values (Table VI).

Considering the very large concentrations that had to be used and the change from H_2O to D_2O, the agreement is quite reasonable. This experiment was repeated in H_2O solvent with similar results.

Calorimetry. Heats of solution were measured with an LKB-8700 reaction and solution calorimeter.

Acknowledgment. This work was supported in part by a grant from the City University of New York Faculty Research Award Program.

Registry No. $(CH_3)_3N^+CH_2CH_2OH$, 62-49-7; $(CH_3)_3N^+CH_2CH_2O^-$, 44519-34-8; $(CH_3)_3N^+CH_2CH_2OH\ Cl^-$, 67-48-1; $(C_4H_9)_4NCl$, 1112-67-0.

On the Use of Ion-Selective Electrodes for Monitoring Oscillating Reactions. 1. Potential Response of the Silver Halide Membrane Electrodes to Hypohalous Acids

Z. Noszticzius,[1] E. Noszticzius,[2] and Z. A. Schelly*

Contribution from the Department of Chemistry, The University of Texas at Arlington, Arlington, Texas 76019. *Received March 15, 1982*

Abstract: The potential response of halide ion selective (AgCl, AgBr, and AgI membrane) electrodes to hypohalous acids (HOCl, HOBr, and H_2OI^+) is investigated under experimental conditions prevailing in oscillating reactions, i.e., at H_2SO_4 concentrations of 0.15 and 1.5 M. Hypohalous acids are known intermediates in these reactions. The two current theories, the kinetic buffer theory (KBT) and the corrosion potential theory (CPT), of the potential response for halide ion concentrations $[X^-]$ below the solubility limit (i.e., where $[X^-] < K_s^{1/2}$) are compared. Experimental results are presented which clearly contradict KBT and confirm CPT. New methods of synthesis for silver-free HOBr and silver-free HOI, and a method of quantitative determination of H_2OI^+ beside IO_3^-, are described.

Introduction

Ion-selective electrodes play an important role in monitoring chemical oscillations. All the well-known and extensively studied oscillating reactions, the Bray–Liebhafsky (BL),[3,4] the Belousov–Zhabotinsky (BZ),[5–7] the Briggs–Rauscher (BR)[8,9] reactions, as well as their modifications,[10,11] and even a recently discovered new family of chemical oscillators,[12] have been followed by iodide- or bromide-sensitive electrodes. Possibly the apparent ease of their monitoring with specific electrodes has contributed to the fact that the iodide and bromide ions were assigned to be important, sometimes even essential, components in the complex mechanisms of these chemical oscillators.[7,10,13–16] Clearly, the understanding of the potential response of ion-selective electrodes under the conditions prevailing in oscillating systems is crucial. Nevertheless, the interpretation of the responses is not unanimous, especially when halide ion concentrations $[X^-]$ are believed to be measured below their solubility limits.[17,18]

In the present paper, we shall discuss the contradicting interpretations and present experimental results that support the de-

---

(1) R. A. Welch Postdoctoral Fellow. On leave of absence from the Technical University of Budapest.

(2) R. A. Welch Predoctoral Fellow. On leave of absence from the Technical University of Budapest.

(3) Bray, W. C.; Liebhafsky, H. A. *J. Am. Chem. Soc.* **1931**, *53*, 38–48.

(4) Woodson, J. H.; Liebhafsky, H. A. *Anal. Chem.* **1969**, *41*, 1894–7.

(5) Belousov, B. P. *Ref. Radiats. Med., 1958, Medgis Moscow* **1959**, 145.

(6) Zhabotinsky, A. M. *Dokl. Akad. Nauk USSR* **1967**, *157*, 392–400.

(7) Field, R. J.; Körös, E.; Noyes, R. M. *J. Am. Chem. Soc.* **1972**, *94*, 8649–64.

(8) Briggs, T. S.; Rauscher, W. C. *J. Chem. Educ.* **1973**, *50*, 469.

(9) Roux, J. C.; Vidal, C. In "Synergetics"; Pacault, A., Vidal, C., Eds.; Springer-Verlag: West Berlin, 1979; pp 47–50.

(10) Noyes, R. M. *J. Am. Chem. Soc.* **1980**, *102*, 4644–9.

(11) Cooke, D. O. *Int. J. Chem. Kinet.* **1980**, *12*, 683–98.

(12) Orbãn, M.; DeKepper, P.; Epstein, I. R. *Nature (London)* **1981**, *292*, 816–8.

(13) Sharma, K. R.; Noyes, R. M. *J. Am. Chem. Soc.* **1976**, *98*, 4345–61.

(14) Liebhafsky, H. A.; McGawck, W. C.; Reyes, R. J.; Roe, G. M.; Wu, L. S. *J. Am. Chem. Soc.* **1978**, *100*, 87–91.

(15) Noyes, R. M.; Furrow, S. D. *J. Am. Chem. Soc.* **1982**, *104*, 45–8.

(16) DeKepper, P.; Epstein, I. R. *J. Am. Chem. Soc.* **1982**, *104*, 49–55.

(17) Ganapathisubramanian, N.; Noyes, R. M. *J. Phys. Chem.*, submitted. We thank Professor Noyes for sending us the preprint.

(18) Noszticzius, Z. *Acta Chim. Acad. Sci. Hung.* **1981**, *106*, 347–57.

0002-7863/82/1504-6194$01.25/0