TABLE I
RATES AND ISOTOPE EFFECTS FOR SOLVOLYSIS AT 25° OF *t*-BUTYL CHLORIDE IN SOLVENTS OF CONSTANT *Y*

Solvent[a]	k_H[b] [$(CH_3)_3CCl$] × 10^5, sec.$^{-1}$	k_D[b,c] [$(CD_3)_3CCl$] × 10^5, sec.$^{-1}$	k_H/k_D
Ethanol–water (54:46)	22.4 ± 0.3	9.52 ± 0.06	2.35 ± 0.03
Acetone–water (49:51)	22.5 ± 0.3	9.40 ± 0.26	2.40 ± 0.08
Acetic acid–water (63:37)	22.7 ± 0.5	9.32 ± 0.25	2.41 ± 0.07
Pyridine–water (51:49)	22.3 ± 0.2	9.08 ± 0.06	2.46 ± 0.03
Isopropyl alcohol–water (48:52)	22.4 ± 0.6	9.28 ± 0.12	2.42 ± 0.07
Acetic acid–formic acid (29:71)[d]	23.3 ± 0.3	10.15 ± 0.16	2.30 ± 0.05

[a] Numbers in parentheses are per cent by volume before mixing. [b] Average rate constant (in most cases for three or four runs), followed by standard deviation from mean. [c] >99% deuterated. [d] The acetic acid used contained 0.02 *M* acetic anhydride to ensure absence of water in the reaction mixture; also, 0.2 *M* anhydrous lithium formate was added to ensure complete reaction.

of fairly high dielectric constant; however, it is probably not energetically feasible.

Second, it may be that the isotope effects *fortuitously* remain similar in spite of widely different transition state structures. The fact that the isotope effect in the nonaqueous solvent is similar to the others appears to eliminate the possibility of "solvent-sorting"[6] as a major factor in making the isotope effects so similar.

Third, it may be that the structure of the transition state for the solvolysis of *t*-butyl chloride is determined largely by the structure of the substrate, the function of the solvent being to allow the molecule to reach this transition state structure by whatever means are available. Assistance by the solvent could be quite specific, but different for each solvent. The structure of the transition state, *e.g.*, the extent of bond breaking, would depend only on the *amount* of solvent assistance and not on the detailed *nature* of the assistance.

The fact that such large isotope effects as those reported here, *ca.* 2.4, should be very sensitive to changes in structure or environment of the transition state has provided a very sensitive tool for elucidating the nature of solvolysis reactions. The constancy of the isotope effects seems to indicate that the activation process is remarkably insensitive to the presence of solvent species of widely variable electrophilic and nucleophilic properties.

(6) See. J. B. Hyne, R. Wills, and R. E. Wonkka, *J. Am. Chem. Soc.*, **84**, 2914 (1962); also E. M. Arnett, P. M. Duggleby, and J. J. Burke, *ibid.*, **85**, 1350 (1963).

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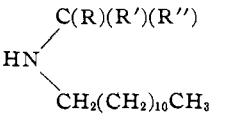
Liquid Ion-Exchange Membranes of Extreme Selectivity and High Permeability for Anions

Sir:

Liquid membranes of extreme degrees either of anionic or cationic selectivity which facilitate the exchange of inorganic ions in readily analyzable quantities across their thickness between two adjacent electrolyte solutions seemingly have not been described. Such membranes can now be made of so-called "liquid ion exchangers."[1] These liquid ion exchangers are solutions, in water-insoluble organic solvents, of substances consisting of an ionogenic group which is attached to an organic molecule of proper size (mol. wt. 250–500) and configuration to make these compounds sparingly soluble in aqueous electrolyte solutions. The best liquid exchangers have only a minimal solubility in aqueous solutions. Generally, these liquid ion exchangers in contact with aqueous electrolyte solutions behave similarly to weak base and weak acid ion-exchange resins. However, many do not absorb measurable quantities of water, nor is there any invasion by "nonexchanger electrolyte."

(1) R. Kunin and A. G. Winger, *Angew. Chem. Intern. Ed. Engl.*, **1**, 149 (1962).

Since liquid anion exchangers are available with a greater variety of structures than cation exchangers, we started with anion exchangers, mainly a secondary amine, lauryl(trialkylmethyl)amine (mol. wt. *ca.* 360), "Amberlite LA-2," Rohm and Haas Co.



R, R′, and R″ being short aliphatic chains having altogether 11 to 14 carbons. Before use this material was brought into a salt form by treatment with acid

The *rates of exchange of anions* and of *leakage of cations*, and thereby the *ionic selectivity of a membrane*, are determined in cells

solution 1		solution 2
A^+L^- c_1	liquid membrane	B^+M^- c_1

the liquid membrane floating on the two solutions which are separated by a glass wall. The membranes were 5–80% solutions of anion-exchange compound in benzene, xylene, or nitrobenzene, which had been equilibrated beforehand with an equimolar mixture of the (strong) electrolytes A^+L^- and B^+M^-. Until a quasi-stationary state is reached under the dynamic conditions of the experiment, the quantities of L^- appearing in solution 2 and of M^- appearing in solution 1 are not necessarily strictly equivalent, and hydrolysis of the functional material in the membrane phase which depends on the concentrations of the adjacent solutions enters as another complication. These secondary factors, however, do not blur the main effect: a fairly fast exchange of L^- and M^- occurs between the two solutions while barely measurable quantities of A^+ and B^+ appear in solutions 2 and 1. The rates of exchange are approximately proportional to the concentration of the ion-exchange compound in the membrane phase.

For instance, with 20% LA-2 in xylene, 1.0 *N* KCl in solution 1, and 1.0 *N* NaSCN in solution 2 (and all three liquids stirred), the rates of exchange of Cl^- and SCN^- were about 95 μequiv./cm.^{2} hr.; the rates for K^+ and Na^+ were less than 1.1×10^{-3} and 4.9×10^{-4} μequiv./cm.^{2} hr. The ionic selectivity of the membrane, that is the ratio of its permeabilities for anions and cations, was thus 80,000:1 for Cl^- *vs.* K^+, and 200,000:1

for SCN^- *vs.* Na^+. Similar ionic selectivities in the range of 50,000 to 400,000 were obtained for various concentrations of ion-exchange compounds and solutions of different alkali salts at solution concentrations up to 4 *N*. These liquid membranes do not show a decrease of ionic selectivity with increasing concentrations of the adjacent solutions, contrary to the situation prevailing with porous permselective membranes. The *absolute rates of exchange* of anions across the liquid anion-exchange membranes are of the same order of magnitude as those across the most permeable anion permselective membranes studied in our laboratory.[2] The *ionic selectivities* of the liquid membranes exceed by one to several orders of magnitude the ionic selectivities of even the most highly ion selective porous permselective membranes[2] at all but the lowest solution concentrations.

Ionic specificity was studied in systems of the type[3]

solution 1		solution 2
c_1 A^+L^- c_1 A^+M^-	liquid membrane	$2c_1$ A^+N^-

L^- and M^- exchanging against N^-. The ratio of the rates of exchange of L^- and of M^-, $\varphi_{L^-}/\varphi_{M^-}$, is a measure of the ionic specificity of the membrane for these two ions. Typical ratios were $\varphi_{SCN^-}/\varphi_{Cl^-} = 20$, $\varphi_{Br^-}/\varphi_{Ac^-} = 25$, $\varphi_{I^-}/\varphi_{Br^-} = 2.2$. The sequence of the ionic specificities corresponds to the Hofmeister series, as with porous permselective membranes.[3]

(2) M. H. Gottlieb, R. Neihof, and K. Sollner, *J. Phys. Chem.*, **61**, 154 (1957); M. Lewis and K. Sollner, *J. Electrochem. Soc.*, **106**, 347 (1959).

The *electrical resistivity* of these membranes is very high. In aromatic hydrocarbons there is a minimum of resistivity with 80–90% of exchange material, about 70 kohms cm.; the resistivity is much higher at lower concentrations, reaching the megohm centimeter range with concentrations of less than 40% of ion-exchange compound in solution.

The *concentration potentials* in cells of the type KCl $2c_1$ | liquid membrane | KCl c_1 reach the calculated thermodynamically possible maximum values within a few tenths of a millivolt in a concentration range of several hundredths to at least several tenths normal.

Biionic potentials[4] in cells of the type 0.1 *N* KCl | membrane | 0.1 *N* KSCN show that the anion which is more readily adsorbed (higher in the Hofmeister series) than the other, here SCN^-, impresses its charge on the other solution, as with porous permselective membranes. The ionic specificities which can be computed[3] from these data agree semiquantitatively with those obtained from rate of exchange studies.

Preliminary experiments with liquid cation exchanger membranes are yielding analogous results.

(3) R. Neihof and K. Sollner, *Discussions Faraday Soc.*, **21**, 108 (1956).
(4) K. Sollner, *J. Phys. Colloid Chem.*, **53**, 1211 and 1226 (1949); S. Dray and K. Sollner, *Biochim. Biophys. Acta*, **18**, 341 (1955).

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BOOK REVIEWS

Enzyme and Metabolic Inhibitors. Volume I. General Principles of Inhibition. By J. LEYDEN WEBB, School of Medicine, University of Southern California, Los Angeles, Calif. Academic Press, Inc., 111 Fifth Ave., New York 3, N. Y. 1963. 949 pp. 16.5 × 23.5 cm. Price, $26.00.

Professor Webb has set himself the task, as he puts it in his preface, "to present concisely the basic principles of inhibition, to describe the actions and mechanisms of the most important and interesting inhibitors, to correlate the actions at the enzyme level with the changes observed in cellular functions, and to provide practical information on the use of these inhibitors." It is clear from this that like all dedicated scientists he is an enthusiast for his chosen field; moreover, as he himself admits a few sentences later, he wants to convert others. This is a formidable task and it takes a scientist of Webb's stature with respect to catholicity of interests and encyclopedic knowledge of his subject matter to even try to make the attempt. In a way, the two aims are self-contradictory and the scope is self-defeating. Any topic which needs four volumes for its presentation, of which the first, dealing with general principles, runs to over 900 pages, overwhelms the reader with its sheer bulk—and price; compendia do not converts make. There are many valuable contributions in this book, and a tremendous amount of work and imagination has gone into its writing; there are ideas and practical suggestions enough to fascinate any enzymologist, chemist, or biologist. But this reviewer fears that the book will remain largely on the reference shelves in the library, rather than on everybody's desk where a thinner, more critical and more selective cousin might claim to belong. One also feels a little uneasy that among this welter of facts, the book has little or nothing to say about inhibition in the most interesting and fruitful area of biosynthesis; interference with and competition in the formation of functional coenzymes, proteins, or nucleic acids are either not discussed at all or barely mentioned.

Related to this criticism there is another, that of timeliness. This book is meant to deal with fundamental principles of inhibitor action; that is, its crucial and central core is to be found in Chapters 6 and 7, which are concerned with the mechanism of interaction of inhibitors with enzymes and enzyme systems. (The chapters preceding deal with kinetics of enzyme-catalyzed reactions in the presence and absence of inhibitors and the determination of inhibition constants from kinetic data, and Chapters 14 and 15 are concerned with the effect of temperature and other variables on these systems. The other chapters have as their titles: "Distribution and Fate of Inhibitors in Living Organisms," "Inhibition in Cells and Tissues," "Effects of More Than One Inhibitor," and "Localization of the Site of Inhibition.") It is here that Prof. Webb has made his most valuable contribution: pp. 204–318 which deal, in a rigorous, quantitative manner with the physico-chemical parameters determining the strength of interaction not just between enzymes and inhibitors, but between all proteins and small solutes, should be required reading for everybody interested in molecular biology. Unfortunately, however, the book's cut-off date as far as literature review is concerned, occurred some time early in 1960, earlier no doubt for some sections. Now, it is a fact that there has been an almost explosive upsurge of important developments in precisely this