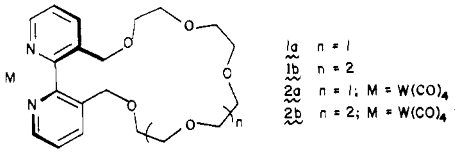
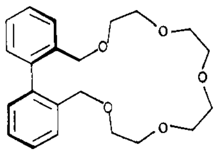
Allosteric Effects. Remote Control of Ion Transport Selectivity

Sir:

We recently introduced the macrocyclic polyethers **1**, and demonstrated the specificity of their binding sites.[1] These structures incorporate two receptors: the polyether which binds alkali metal ions and the 2,2′-bipyridyl function which binds transition metals. Though some distance separates these sites, they are *mechanically coupled* in that binding at one site forces conformational restrictions which alter receptivity at the remote site. Here we give evidence that ion transport selectivity can be regulated through this "mechanism".



1



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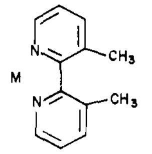

4
a M = —
b M = W(CO)4

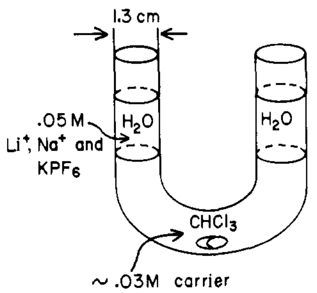

Figure 1.

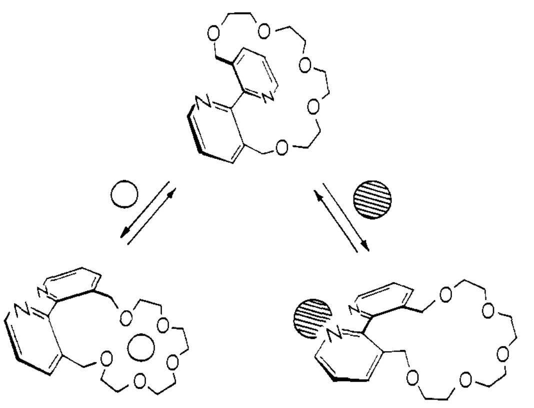

Figure 2. Binding-induced conformational changes.

Table I. Ion Transport Rates Relative to Na^+

	3	1a	1b	2a	2b	dibenzo-18-crown-6			
						PF_6^-	picrates	I^-	Br^-
Li^+	0.012	0.047	0.018	0.037	0.05	<0.01	0.06	0.02	0
Na^+	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
K^+	14	3.8	16	0.80	12	18	16.6	41.5	55
							(ref 5)	(ref 6)	(ref 6)
	1[a] :	3 :	2 :	4 :	1 :	10			

[a] 0.09 M **3** in 10 mL of $CHCl_3$ and 5 mL of each aqueous phase; 5×10^{-6} g-atom of Na^+ was transported after 65 h. Numbers in this row reflect the relative efficiencies of Na^+ transport for the various carriers.

Transport of Li^+, Na^+, and K^+ across a $CHCl_3$ liquid membrane with **1**, **2**, and controls **3** and **4** was examined within a U-tube (Figure 1). The three ions as their PF_6^- salts in the left arm of the tube were placed in direct competition for the carrier and atomic absorption analysis[2] was used to determine the relative rates of transport to the right arm.

The control experiment with the bipicoline **4a** established that neither Li^+ nor K^+ was transported by a nonplanar 2,2′-bipyridyl function, but Na^+ was carried to a small degree (ca. 10% of the value for **1a**). The extent of transition-metal involvement was tested with **4b** and shown to be negligible under these conditions.[3] In addition, transport experiments with the standard dibenzo-18-crown-6 were performed and established that our apparatus gives results which are in fair agreement with those obtained in other laboratories. The absolute rate of transport, given the specifications of Figure 2, was about 10^{-8} M/h; however, variations in the stirring speed (ca. 600 rpm) between two runs (or even during a given run) do not permit rigorous comparisons of the transport efficiency of the various carriers.[4] To the extent that we are willing to make such comparisons, they are recorded in the lowest row of Table I.

The efficiencies of ion transport are functions of distribution constants between the two phases, uptake and release rates,[5] and an optimum association constant[7] between ions and a given carrier. The remarkable inversion of the K^+/Na^+ transport preference in **1a** vs. **2a** demonstrates that these variables are subject to control within a single carrier by remote binding forces. As shown in Figure 2, binding of an alkali metal to **1a** can involve both benzylic oxygens. In complex **2a**, the rapid racemization[1] of the structure forces the benzylic oxygens into conformations in which only one can participate in the formation of an ether cavity. This results, apparently, in the preference of **2a** for transporting smaller ions. The increase in Na^+ and Li^+ transport relative to K^+ in **2b** vs. **1b** is also consistent with this interpretation, although here the effect is less striking.

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(1) Rebek, J., Jr.; Trend, J. E.; Wattley, R. V.; Chakravorti, S. *J. Am. Chem. Soc.* **1979**, *101*, 4333.

(2) Performed on a Perkin-Elmer 603 AA spectrophotometer at Carnegie-Mellon Institute of Research, Pittsburgh, Pa., and reported as the average of two runs. The U-tubes were constructed from borosilicate glass. The PF_6^- counterion was selected because of interactions observed between picrates or halides and the metal in complexes **2**; these interactions preclude determination of binding selectivities by extraction techniques.

(3) The complex **4b** showed Na^+ transport comparable to **4a** (five times that of a blank $CHCl_3$ solution) and Li^+, K^+ transport twice that of the blank solution.

(4) In particular, emulsions formed at the interfaces of experiments involving the complexes **2**; these reduce the overall rate of transport but presumably do not affect the relative rates for the three ions.

(5) Kobuki, Y.; Hanji, K.; Horiguchi, K.; Asada, M.; Nakayama, Y.; Furukawa, J. *J. Am. Chem. Soc.* **1976**, *98*, 7414.

(6) Christensen, J. J.; Lamb, J. D.; Izatt, S. R.; Starr, S. E.; Weed, G. C.; Austin, M. S.; Stitt, B. D.; Izatt, R. M. *J. Am. Chem. Soc.* **1978**, *100*, 3219.

(7) Kirch, M.; Lehn, J.-M. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 555.

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Binding-induced conformational changes lie at the heart of allosteric effects in enzymology and their dynamics are responsible for the regulation of enzymic activity. The system described above presents a simple model for these general effects.[8]

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[8] For other systems which can be interpreted as allosteric effects see: Lehn, J.-M. *Acc. Chem. Res.* **1978**, *11*, 49. Traylor, T. G.; Tatsuno, Y.; Powell, D. W.; Cannon, J. B. *J. Chem. Soc., Chem. Commun.* **1977**, 732

Book Reviews

Introduction to Powder Surface Area. By S. Lowell (Quantachrome Corp.). John Wiley & Sons, New York. 1979. xvi + 199 pp. $19.95.

The theory and experimental methods used to study the surface area and porosity of solids are presented at an introductory level. The first part discusses the theory of surface area from size distributions, gas adsorption and adsorption isotherms, Langmuir and Brunauer, Emmett and Teller adsorption isotherms, as well as the Harkins and Jura methods and permeametry.

The calculation of cross-sectional areas of adsorbates from the liquid molar volume and standard nitrogen areas is described as well as analysis of the pore characteristics from adsorption measurements. The determination of porosity characteristics of solids from mercury porosimetry measurements is also presented.

The second part of the text describes methods for adsorption measurements using volumetric, gravimetric, flow, and dynamic methods, including a comparison of the experimental methods. Methods for determining true, apparent, bulk, and effective densities are described, and finally a brief presentation of factors involved in mercury porosimetry is given.

The text would be useful to those having little or no experience in the characterization of solids with respect to their surface area and/or porosity characteristics.

Robert G. Craig, *The University of Michigan*

Organometallic Chemistry (Specialist Periodical Reports). Volume 7. Senior Reporters: E. W. Abel (University of Exeter) and F. G. A. Stone (University of Bristol). The Chemical Society, London. 1978. xviii + 502 pp. $81.50.

This volume of the Specialist Periodical Reports of "Organometallic Chemistry" contains a review of the literature published in this area of research during 1977. The format of the previous volumes is retained: organo derivatives of the main group metals are surveyed according to element groups, whereas compounds of the transition metals are reviewed by ligands (e.g., metal carbonyls, etc.) as well as by reactions (homogeneous catalysis, etc.). The concluding chapters review aspects of organometallic compounds in biological systems and summarize the X-ray diffraction studies of main group and transition elements which were published in 1977.

The reporters have endeavored to provide a complete account of progress in their respective reporting areas. Most chapters include a bibliography of papers which are not reviewed in the cursive text. In this fashion, the authors manage to cover an enormous volume of literature in a rather concise fashion.

The reports are clearly written accounts of the advances made in the area of organometallic chemistry. They are must-reading for those active in this area of research.

George W. Kabalka, *University of Tennessee—Knoxville*

Organometallic Chemistry Reviews. Volume 7. Edited by D. Seyferth. (Massachusetts Institute of Technology). Elsevier Scientific Publishing Co., Amsterdam–Oxford–and New York. 1979. vii + 521 pp. $95.50.

Volume 7 in this series presents six reviews of rather diverse areas of organometallic chemistry. The first review is concerned with the synthetic application of boron hydrides for the hydrogenation of carbon-carbon multiple bonds (K. Avasthi, D. Devaprabhakara, and A. Suzuki). The next three reviews deal with the organic compounds of the group IV elements: Allyl Derivatives of the Group IVA Metals and Mercury (J. A. Mangravite); Silylmercurials in Organic Synthesis (W. P. Neumann and K. Reuter); Organosiliciumverbindungen des Schwefels, Selens und Tellurs (D. Brandes). The remaining reviews deal with metallocene chemistry: Ferrocenylcarbocations and Related Species (W. E. Watts); the Chemistry of Cobaltocene, Cobalticinium Salts and Other Cobalt Sandwich Compounds (J. E. Sheats).

Each of the reviews is well written and quite comprehensive. Mangravite's review of the allyl derivatives of the group IVA metals is especially noteworthy owing to its scope.

The literature is covered through 1977 except for the review of the use of boron hydrides in hydrogenation and the review of the chemistry of cobaltocene, each of which covers the literature through 1976. The reviews in this volume serve as an effective starting points for those interested in current research in the areas covered.

The book has neither a subject index nor an author index.

George W. Kabalka, *University of Tennessee*

Cell Membrane Permeability and Transport. Edited by G. R. Kepner (The University of Minnesota). Dowden, Hutchinson, and Ross, Inc., Stroudsburg, Pa. 1979. xiii + 410 pp. $35.00.

This book is the 12th volume in the series of Benchmark Papers in Human Physiology. Earlier reviews have discussed pro and con the strategy of collecting and reprinting benchmark papers. The present volume may well avoid some of the objections by limiting itself to really classical papers, none less than 20 years old. The editor, G. R. Kepner, has selected a group of research papers of historical significance with respect to the development of the physical aspects of membrane research between 1855 and 1960. As a result addition of a subtitle, "A Historical Perspective", might have proven useful. The papers included in this volume were chosen by a survey of the editor's colleagues as well as his own judgment. The insight necessary for such an undertaking has developed from the editor's long-standing interest in and teaching of the historical aspects of so-called classical papers in cell membrane research. Overall the choices appear to have been the appropriate ones, including such authors as Overton, Danielli, Widdas, Ussing, Nernst, Donnan, Goldman, Skou, and Post. With the exception of one paper on placental glucose transfer, the subject of organic metabolite transport has been disregarded, even though great strides were made in this area during the 1950s. This omission leaves the book slanted toward water and electrolyte permeability, which may, of course, suit many users.

Following each of the book's two sections (Part I: Water and Nonelectrolyte Permeability and Transport; Part II: Sodium and Potassium Permeability and Transport—these sections contain 11 and 12 papers, respectively), the editor has presented concise summaries discussing the historical impact of the papers presented. These informative overviews provide an excellent means for showing the underlying continuity of the independent articles in this collection. A major contribution of this volume which should not be overlooked is the increased availability in English of several of the older papers which were originally published in German. These publications have in addition been relatively inaccessible to many scientists, who use the principles taught in them although a personal reading of the research has been difficult.

This book is highly recommended for those interested in either the physical aspects of contemporary cell membrane research, or the historical significance of early research on membranes.

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