

- analysis and  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectroscopy.
- (6) The rearrangement was followed by observation of the methyl (doublet) proton resonances at  $\delta$  0.5 and 0.9 for **1** and **2**, respectively.
  - (7) We quote half-lives because, like a number of other reactions of organocobalt, -rhodium, and -iridium complexes which involve radical-chain displacements, the reactions proceed smoothly but show a characteristic dependence on the rate of initiation.
  - (8) We cannot rule out the presence of small quantities of methylcyclopropylcarbinylcobaloximes in the equilibrium mixture.
  - (9) Nitroxyl radicals broaden the  $^1\text{H}$  NMR spectrum, but this is not sufficient to prevent observation of the rearrangement. The addition of diamagnetic traps such as nitrones has no effect on the rate.
  - (10) G. N. Schrauzer, *Inorg. Syn.*, **11**, 61 (1968).
  - (11) The formation of 1-methyl-2-( $\beta,\beta,\beta$ -trichloromethyl)cyclopropane has been the subject of an independent study.<sup>12</sup>
  - (12) A. Bury and M. D. Johnson, unpublished work.
  - (13) Under these conditions the rearrangement is slower, but an accurate estimate of the rate was not made.
  - (14) Pratt has suggested such a unimolecular process for the rearrangement of cyclopropylcarbinylcobalamin to butenylcobalamin: S. Chemaly and J. M. Pratt, *J. Chem. Soc., Chem. Commun.*, 988 (1976).
  - (15) Only after many hours at 53 °C is hydridocobaloxime detected (by its reaction in situ with phenylacetylene<sup>16</sup>).
  - (16) K. N. V. Duong, A. Ahond, C. Merienne, and A. Gaudemer, *J. Organomet. Chem.*, **55**, 375 (1973).
  - (17) Species capable of displacing cobaloxime(II) from butenylcobaloximes include polyhalogenomethyl, alkanesulfonyl, and arenesulfonyl radicals: A. E. Crease, B. D. Gupta, A. Bury, M. R. Ashcroft, H. Morris, and M. D. Johnson, unpublished work.
  - (18) Trichloromethyl and other electrophilic radicals also displace cobaloxime(II) from allyl-, allenyl-, and benzylcobaloxime(III) complexes: T. Funabiki, B. D. Gupta, and M. D. Johnson, *J. Am. Chem. Soc.*, **98**, 6697 (1976); *J. Chem. Soc., Chem. Commun.*, 653 (1977); A. Bury, C. J. Cooksey, B. D. Gupta, and M. D. Johnson, unpublished work.
  - (19) Bimolecular displacement of cobaloxime(II) from alkylcobaloxime(III) complexes by cobaloxime(II) reagents has been described in detail: D. Dodd, M. D. Johnson, and B. L. Lockman, *J. Am. Chem. Soc.*, **99**, 3664 (1977). Bimolecular displacement of cobaloxime(II) from allylcobaloxime(III) complexes by cobaloxime(II) reagents can be sufficiently fast as to be evident on the NMR time scale. This accounts, at least in part, for the dynamic character of allylcobaloximes: C. J. Cooksey, D. Dodd, B. D. Gupta, and M. D. Johnson, unpublished work; D. Dodd and M. D. Johnson, *J. Am. Chem. Soc.*, **96**, 2279 (1974).
  - (20) Trichloromethylcobaloxime is readily formed by the reaction between bromotrichloromethane and cobaloxime(II) by a two-step mechanism involving reactions 7 and 8.
  - (21) Any halogenomethyl radical from a chlorinated solvent can replace  $\text{Cl}_3\text{C}$  in reaction 5, thereby causing the production of cobaloxime(II).
  - (22) Diprotonation of benzylcobaloxime leads to the formation of dibenzyl in good yield.
  - (23) In several rearrangements catalyzed by coenzyme  $\text{B}_{12}$ , it has been shown that the hydrogen atom from the substrate is transferred to the 5' carbon of the adenosyl moiety; one of the three equivalent hydrogens of the 5'-methyl group is then transferred back to the substrate fragment.<sup>1</sup>
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  - (25) Only one conformation of the substrate **7** is shown in reaction 9. Reaction of the other conformation would equally give retention of configuration.

Adrian Bury, Martyn R. Ashcroft, Michael D. Johnson\*

Department of Chemistry, University College  
London WC1 HOAJ, England

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### Effect of Anion Type on Rate of Facilitated Transport of Cations across Liquid Membranes via Neutral Macrocyclic Carriers

Sir:

Transport of cations across a hydrophobic organic layer (liquid membrane) which separates two water phases has attracted recent interest.<sup>1</sup> The carrier is usually a synthetic or naturally derived cyclic multidentate ligand. When such uncharged carrier ligands are employed, the complexed cation carries its anionic counterion(s) with it through the organic phase.<sup>2,3</sup> The nature of the anion should thus be a factor in determining the rate of cation transport.<sup>4</sup> We show here that the rate of transport of a given cation through such a membrane can be varied by several orders of magnitude simply by altering the anion present in the original salt solution.

Two crown ethers, dibenzo-18-crown-6 and *tert*-butylbenzo-15-crown-5, were used as membrane carriers inasmuch

**Table I.** Rate of Transfer of Various Salts through a Chloroform Membrane Containing  $7 \times 10^{-4}$  M Dibenzo-18-crown-6 or *tert*-Butylbenzo-15-crown-5

Salt Type	Concn. mol/L	Transfer rates, <sup>a</sup> (mol/h) $\times 10^7$	
		Dibenzo-18-crown-6 <sup>b</sup>	<i>tert</i> -Butylbenzo-15-crown-5 <sup>c</sup>
LiCl	1.0	0	0
LiBr	1.0	0	0
LiI	1.0	0.33	0
NaCl	1.0	0.31	0
NaBr	1.0	1.6	0
NaI	1.0	15	0
KF	1.0	0.85	
KCl	1.0	6.1	0.17
KBr	1.0	88	1.8
KI	1.0	620	36
KI	0.50	370	
KI	0.10	34	
KI	0.010	0.46	
KNO <sub>3</sub>	1.0	250	1.9
KOH	1.0	2.1	
KClO <sub>4</sub>	0.10	123	2.0
K acetate	1.0	1.4	
K benzoate	1.0	110	
K picrate	0.0020	510	2.1
K <sub>3</sub> PO <sub>4</sub>	1.0	<1	
K <sub>2</sub> HPO <sub>4</sub>	1.0	<1	
KH <sub>2</sub> PO <sub>4</sub>	1.0	290	1.3
KBF <sub>4</sub>	0.020	3.1	0
KPF <sub>6</sub>	0.020	66	0.78
BaCl <sub>2</sub>	1.0	<1	
BaBr <sub>2</sub>	1.0	<1	
BaI <sub>2</sub>	1.0	280	

<sup>a</sup> Each value is the average of two or more independent determinations. The experimental values deviate from the reported values by an average of  $\pm 10\%$ . <sup>b</sup> 2,3,11,12-Dibenzo-1,4,7,10,13,16-hexaoxacyclooctadeca-2,11-diene. <sup>c</sup> 2,3-(4'-*tert*-butyl)-1,4,7,10,13-pentaoxacyclopentadeca-2-ene.

as the cation-binding properties of 18-crown-6 and 15-crown-5 ligands and their derivatives have been studied more extensively than those of other synthetic macrocycles.<sup>5,6</sup> The liquid membrane system used was adapted from the work of Kobuke et al.<sup>7</sup> and is similar in principle to the Schulman Bridge used by Cussler<sup>4</sup> and Smid<sup>2</sup> and their co-workers. A chloroform layer containing  $7.0 \times 10^{-4}$  M carrier sits at the bottom of a deep evaporating dish and is stirred by a magnetic stirrer driven at 200 rpm. Atop this layer are two water phases separated by a glass cylinder. The inner phase (transfer surface area = 36.3 cm<sup>2</sup>, volume = 42 mL) is a concentrated salt solution serving as the cation source and the outer phase (transfer surface area = 76.8 cm<sup>2</sup>, volume = 168 mL) is a receiving solution for transferred salt. Vessels were covered and maintained at  $25 \pm 0.5$  °C in a thermostated room. Experimental runs were conducted over a two-day time period during which 2-mL samples were withdrawn at intervals from the receiving water phase. These samples were analyzed for cation concentration on a Perkin-Elmer Model 603 atomic absorption spectrophotometer.

Salts of four cations,  $\text{Li}^+$ ,  $\text{Na}^+$ ,  $\text{K}^+$ , and  $\text{Ba}^{2+}$ , were used in this study, the latter three of which are known to bind to dibenzo-18-crown-6 in both water and methanol.<sup>5</sup> Reaction has also been reported in these solvents between  $\text{Na}^+$  and  $\text{K}^+$  and benzo-15-crown-5.<sup>5</sup> Molar concentrations of the salt solutions used are listed in Table I. At least three separate units were employed in the determination of cation transport rate for each salt-macrocycle combination. One of these contained a blank membrane having no macrocycle carrier, while the other two or more which contained carrier served to produce the results listed in Table I. In no case was there any detectable movement

of the cation across the chloroform membrane in the blank unit. A plot of moles of cation transported vs. time was made for each system studied, the slope of which indicates rate of transfer. Such plots were invariably linear as in similar experiments by other workers,<sup>2,4</sup> and deviation in slopes between different runs of the same system was <10%.

Table I lists the cation transfer rates in moles of cation which move across the chloroform membrane per hour for the various salts of the four cations studied. These rates of transfer can be compared only by normalizing all initial solution concentrations to the same value. From the transfer rate of KI at various concentrations, we find that transfer rate varies essentially linearly with the concentration of the originating solution over the range of concentrations studied. This relationship was used to adjust transfer rates of  $\text{KBF}_4$ ,  $\text{KPF}_6$ , K picrate, and  $\text{KClO}_4$  to those of 1 M solutions. This method of adjustment is probably conservative as the rates for KI at higher concentrations are actually somewhat higher than a straight-line extrapolation from lower concentrations would predict.

The ordering of anions according to transfer rate is consistent with size-charge considerations which would be expected to determine the ion's affinity for a polar solvent like water and commensurate lack of affinity for chloroform. For instance, among the halides, it is true for every cation-carrier combination that the iodide always transfers most rapidly, followed in order by the bromide, chloride, and fluoride. The large monovalent anions like picrate,  $\text{PF}_6^-$ ,  $\text{ClO}_4^-$ ,  $\text{H}_2\text{PO}_4^-$ ,  $\text{NO}_3^-$ , and  $\text{BF}_4^-$  transfer more rapidly than the smaller ones such as  $\text{OH}^-$  and the smaller halides. In addition, the multiply charged phosphates transfer little if at all. These results suggest that the anion desolvation energy barrier is one of the more important factors in controlling the rate of transfer across the membrane.

No attempt was made to buffer solutions of weak acid salts and undoubtedly hydrolysis was influential in such cases. This may partially account for picrate having a higher transfer rate than benzoate and the anomalously low transfer rate of acetate. This pH effect will also play a significant role in the case of the mono-, di-, and trivalent phosphates.

To check the findings of Kobuke et al.<sup>7</sup> who used mixtures of K picrate and  $\text{KNO}_3$  in experiments similar to ours and who measured  $\text{K}^+$  concentrations via picrate determination only, we measured the transfer rate for  $\text{K}^+$  carried by dibenzo-18-crown-6 with both anions present. Transfer samples were analyzed for  $\text{K}^+$  via atomic absorption and for picrate ion via colorimetry. No measurable difference could be detected between the rate of transfer of  $\text{K}^+$  and that of picrate. Thus it appears that, when more than one anion is available for co-transport, the anion which normally transfers more readily will be preferred over the other.

The barium salts gave lower transfer rates than would be expected from the fact that  $\text{Ba}^{2+}$  normally binds to crown-6 ligands as well as or better than  $\text{K}^+$ .<sup>5</sup> The energy expended in desolvating a divalent ion along with two monovalent anions must be prohibitive.

The magnitude of the effect of anion on the facilitated transport of cations across liquid membranes holds significant implications. Comparisons of transport carrier effectiveness and system design can only be made where a common anion has been employed. Furthermore, the anion effect may be exploited in that transport of cations across membranes can be turned on or off simply by altering the anion present in the source solution. This same anion effect might be useful in separating or detecting anions themselves.

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J. J. Christensen,\* J. D. Lamb, S. R. Izatt  
S. E. Starr, G. C. Weed, M. S. Astin, B. D. Stitt, R. M. Izatt

Contribution No. 138  
Departments of Chemistry and Chemical Engineering  
and the Thermochemical Institute  
Brigham Young University, Provo, Utah 84602

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### Electrochemistry of Vitamin B<sub>12</sub>. 3. One-Electron Intermediates in the Reduction of Methylcobalamin and Methylcobinamide

Sir:

Although redox processes are likely to be involved in the enzymic reactions of methylcobalamin,<sup>1</sup> there have been much less studies on the electrochemistry<sup>2-4</sup> of this biologically important compound, than, e.g., on its photochemical behavior (see ref 5 and references therein). Investigations in the related field of  $\gamma$ -ray radiolysis have concerned cyanocobalamin and 5'-deoxyadenosylcobalamin<sup>6,7</sup> but not methylcobalamin. The previous electrochemical studies have given indications on the number, height, and potential location of the polarographic<sup>2,4</sup> and cyclic voltammetry<sup>3</sup> waves in water<sup>2,3</sup> and DMF<sup>4</sup> of methylcobalamin<sup>2-4</sup> and methylcobinamide.<sup>2,3</sup> However, these data are most probably affected by adsorption on mercury.<sup>3</sup> On the other hand, attempts to detect a one-electron intermediate before cleavage of cobalt-carbon bond have been unsuccessful so far.<sup>4</sup>

We report here on the results of a preliminary investigation of the electrochemical reduction of methylcobalamin and cobinamide showing the existence of such one-electron intermediates. Estimations of the lifetime of the intermediates and of the standard potentials of the electrontransfer processes were also obtained.

In water, reactant adsorption seriously affects the polarization curves of both compounds. Some reversibility is observed upon raising the sweep rate. It could be, however, related to adsorption on mercury. Addition of a salt of a large organic cation such as tetrabutylammonium tends to decrease adsorption as in the case of the B<sub>12r</sub>/B<sub>12s</sub> system,<sup>8</sup> but the reduction wave is then too close to the proton or supporting electrolyte discharge, especially in the case of methylcobalamin, to allow the analysis of the reduction process. Mixtures of DMF with water or, better, with ethanol or 1-propanol were found suitable for our purposes. Separation between the reduction wave and the supporting electrolyte was satisfactory. Adsorption effects on the alkylcobalt reduction waves were practically absent as checked by comparison with results obtained with a gold or vitreous carbon disk electrode. Some interference of adsorption was however still noticeable at the B<sub>12s</sub>/B<sub>12r</sub> wave obtained upon scan reversal at low sweep rates (Figure 1).

**Methylcobinamide** shows a simpler behavior than methylcobalamin owing to the absence of the nucleotide side chain. At -20 °C (Figure 1) a single irreversible cathodic wave was observed at low sweep rates corresponding to the reductive cleavage of the cobalt-carbon bond. A reoxidation wave indeed appears upon scan reversal in the same potential region (-0.75 V vs. SCE) as the oxidation of cob(I)inamide.<sup>9,10</sup> Upon raising the sweep rate the cathodic wave becomes progressively reversible, clearly showing the existence of a one-electron in-