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Metal Cation Transport Studies Comparing Dibenzo-18-crown-6 (DB18C6) with N, N, N', N'-Tetrakis (n-propyl)-2,3-naphthalenedioxydiacetamide (NPr)

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Abstract. The previously synthesized 3,6-dioxa-4,5-disubstitutedoctanedicarboxamides including NPr bind cations in methanol in the order: $Ca^{2+} > Sr^{2+} > Ba^{2+} > Mg^{2+} \gg Na^{+}$, K^{+}. These compounds also extract Group II cations better than Group I cations from water to dichloromethane. In contrast, these diacetamides were found by W. Simon *et al*., to sense $Na^{+} \gg Ca^{2+}$ when they were incorporated into ion-selective electrodes using a low dielectric constant solvent. It was of interest to determine the order of Group I and Group II cation transport rates of these compounds using a three-phase system with a liquid organic phase of low dielectric constant. We now report that NPr transports thiocyanates in such a system using dichloromethane in the order K^{+} (7.2) $> Ca^{2+}$ (6.6) $> Ba^{2+}$ (5.8) $> Na^{+}$ (1). The transport rate for KSCN with DB18C6 is 20.5 times faster than with NPr.

Key words: Cation transport, 3,6-dioxa-4,5-disubstitutedoctanedicarboxamides, DB18C6

1. Introduction

We have synthesized and studied the properties of neutral dioxydiacetamide ionophores such as N, N, N', N'-tetrakis-(n-propyl) 2,3-naphthalenedioxydiacetamide (NPr, **1**) for a number of years [1–5]. Our single phase binding studies in MeOH [2–5] and two-phase extraction studies (water-dichloromethane) [2] all show Group II cations better bound and extracted than Group I cations. The single phase binding selectivity of **1** and related ligands that incorporate cyclohexane or benzene rings in place of the naphthalene ring of **1**, is $Ca^{2+} > Sr^{2+} > Ba^{2+} > Mg^{2+} \gg Na^{+}$, K^{+}. These ligands exhibit complicated binding stoichiometry. There is a tendency for 2 : 1 ligand/cation stoichiometry of coordination in concentrated solution and in isolated complexes [6,7], but 1 : 1 stoichiometry in very dilute solution [2-4]. In contrast, **1**, our other aromatic or alicyclic-ring containing diacetamides, and Simon's ethanedioxydiacetamide **2** exhibit $Na^{+} > Ca^{2+}$ selectivity when incorporated into ion selective electrodes using the low dielectric constant solvent, dibutyl

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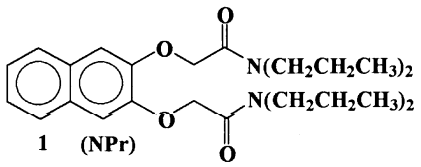

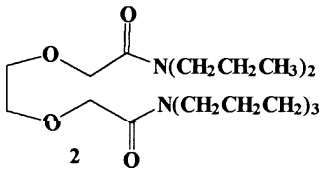

Figure 1.

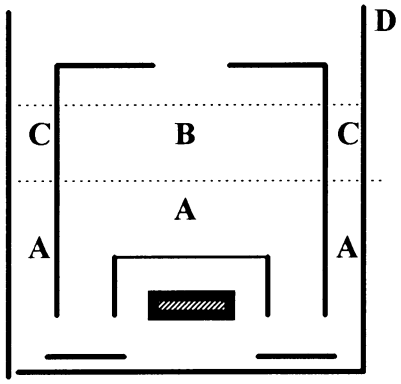

Figure 2. Thoman apparatus. (A) Lower layer, ionophore in CH_2Cl_2. (B) source phase, thiocyanate salts in H_2O. (C) receiving phase, $Fe(NO_3)_3$ in aqueous $HNO_{3;}$. (D) 600 mL beaker.

sebacoate ($\in \approx 4$) [1–3]. In general, $Na^+ > Ca^{2+}$ selectivity is greater for those ligands which incorporate an aromatic-ring. Thus **1** had an ion-selective electrode Na^+/Ca^{2+} selectivity (K^{pot}_{NaM}) of 333 while **2** had a ratio of only 25 [1]. It has been shown by Simon *et al.* that **2** transports Ca^{2+} faster than Na^+ through bulk membranes by a carrier mechanism [8]. Such transport data have not been available for **1** or other aromatic-ring related ligands. We hoped that relevant information would be obtained by finding the relative transport rates for M^{2+} *vs* M^+ for **1** in a three-phase liquid (water-organic-water) bulk membrane system. Would Na^+ be transported faster than Ca^{2+} by **NPr**?

2. Experimental

The thiocyanates were obtained from Fisher Scientific or Aldrich Chemical. $Ca(SCN)_2$ was formerly obtained from ROC/RIC or Alfa Thiokol. More recently it was purchased from Advanced Materials, New Hill, NC, one of the few suppliers left. DB18C6 was purchased from Aldrich Chemical and **1** was prepared by us as previously published [2]. Originally, for the transport apparatus, crystallizing dishes with a glass partition added to separate aqueous layers from a heavier than water organic layer were used. This system sometimes led to leakage of the aqueous layers upon magnetic stirring and was abandoned. Salt solutions of 0.05–0.1 M

were originally used. These concentrations did not give fully reproducible results with our ligands, either with atomic absorption or with the thiocyanate method described as follows. This was probably because the transport rates were too slow, allowing measurement errors to be magnified. The best transport rate results were obtained with copies of a transport apparatus modified by Thoman [9, 10] from an original design by Lamb *et al.* [11] (Figure 2). The apparatus was a "cup" (diameter 5.8 cm, height 6.5 cm, four legs 12 mm wide each) with a 12 mm diameter hole in its top to allow the introduction of the inner aqueous layer. This cup was placed in a 600 mL beaker with a magnetic stirring bar. The method involves the transport of metal thiocyanates (0.3M, 40 mL) from an inner upper aqueous phase ("source") through a lower organic phase containing 7×10^{-4} M ionophore in CH_2Cl_2 (200 mL) to an outer upper aqueous phase ("receiving phase") of 0.1 m $Fe(NO_3)_3$ in 0.2 N HNO_3 (50 mL). The beaker was covered with a glass dish and placed in a styrofoam container which was usually kept at 0–2 °C with ice/water. The mixture was stirred at *ca* 60 rpm. The binding and transport of the thiocyanates were confirmed by the appearance of the red color of $Fe(SCN)^{2+}$. Aliquots (3 mL) of this outer layer were removed, placed in a standard borosilicate cuvette, analyzed by visible spectroscopy at 450 nm using a Fisher Scientific Spectromaster™ Spectrophotometer (Model 41S), and returned. Other procedures involving more dilute solutions of thiocyanates (0.05–0.1 M), smaller sampling involving microcuvettes, transport vessels of other designs, and a Varian Spectroscan UV-VIS spectrophotometer, did not give totally reproducible results. A calibration curve for $FeSCN^{2+}$ generated from 0.1 M $Fe(NO_3)_3$ and 0.3 M NaSCN confirmed the known adherence of this system to Beer's Law. The concentration of $FeSCN^{2+}$ was determined by reference to this graph and also by using literature values of 120 for its equilibrium constant and 5000 for its absorption coefficient [12]. At a concentration of Fe^{3+} of 0.1M, *ca* 92% of available SCN^- is complexed as $FeSCN^{2+}$. Thus $[SCN^-] = [FeSCN^{2+}] \times 1.09. = [M^+] = 2[M^{2+}]$. Various control experiments including ruling out reverse transport of H^+, or various Fe^{3+} species, were previously done by Thoman [9,10] and confirmed, in some cases, by the present work. Most of our runs with **1** started with an induction period which varied from 20 to 60 min depending upon conditions. Similar induction periods were noted by Thoman in his work with Polysorbate 80 [10]. They were attributed to the time needed to attain a steady-state concentration of the cation-ligand complex in the organic phase. The transport rates (in mol hr^{-1}) were obtained by plotting and analyzing the data with Excel™, Cricket Graph™, and most recently, the Kaleidograph™ program. The rates of cation transport (mol hr^{-1}) were divided by the "source" areas to give flux values (mol hr^{-1} cm^{-2}). This is valid since the rate-determining step in these transport runs involves the uptake of cations from the aqueous "source" to the organic phase [9–11].

Table I. Three phase transport of KSCN (0.3 M) with DB18C6 (7×10^{-4} M).

Description	Rate (mol hr^{-1})	Flux (mole hr^{-1} cm^{-2})[a]
Our method, 25 °C[b]	13.1×10^{-5}	7.08×10^{-6}
Izatt *et al.*, 25 °C[c]	1.5×10^{-5}	0.42×10^{-6} [d]
Our method, 0 °C[b]	24.0×10^{-5}	13.0×10^{-6}

[a] Rate values divided by source areas (18.5 cm^2 our apparatus; 36 cm^2 Izatt's apparatus [11]).
[b] CH_2Cl_2 organic phase; $FeSCN^{2+}$ method.
[c] $CHCl_3$ organic phase, atomic absorption method.
[d] Calculated from Izatt's published rate, volume data [11].

3. Results and Discussion

We first tested the thiocyanate method by studying the transport of 0.3 M KSCN with 7×10^{-4} M DB18C6 at room temperature and then at 0 ° C (Table I). The interesting temperature effect previously found by Thoman, wherein cation transport is faster at lower temperatures [10], was confirmed. Thus DB18C6 moves KSCN *ca* 1.8 times faster at 0 °C than at 24 °C in our system. This is in reasonable agreement to the 2.0–2.7 factors found by Thoman for KSCN transport with other ionophores, using the same organic solvent (CH_2Cl_2) and the same transport apparatus. DB18C6 moved KSCN at a rate of 13.7×10^{-5} mol hr^{-1} in our system compared to the reported rate of 1.5×10^{-5} mol hr^{-1} found by Izatt *et al.* [11] in their system. Their somewhat different system involved a less polar solvent ($CHCl_3$), the use of atomic absorption for cation detection, and a larger surface area transport vessel. The flux values, which take into account the source phase areas involved in the rate-determining take-up of cations from the aqueous to the organic phase [11,14], were even more divergent [15]. The rates and fluxes of transport of NPr (**1**) with several thiocyanates are reported in Table II. The rate for KSCN with **1** is 20.5 times slower than with DB18C6. The relative rates of cation thiocyanate transport with **1** are found to be: K^+ (7.2) > Ca^{2+} (6.6) > Ba^{2+} (5.8) > Na^+ (1.0). The rates for $Ca(SCN)_2$ had to be estimated at 0.3 M from rates found at 0.1 M, since the only fresh material available to us could not be prepared at the higher concentration. Using reference [11], concerning variations of transport rates of DB18C6 with salt concentrations, we assumed that the rate is at least 3 times more at 0.3M than at 0.1 M. Thus, the actual rate for $Ca(SCN)_2$ may be higher and possibly greater than for KSCN.

The greater transport flux for Ca^{2+} over Na^+ for **1** is in agreement with the much stronger single-phase binding (log K_{MeOH} = 4.68 [2]) and two-phase extraction of Ca^{2+} *vs* Na^+. It is expected according to the arguments of Lamb *et al.* relating transport rates with *moderate* log K_{MeOH} values [14]. It is not predictable, however, from Simon's ion-selective electrode data wherein **1** and related aromatic-ring

Table II. Three phase transport of MSCN (0.3 M) with 1 (7×10^{-4} M).

Description[a]	Rate (mol hr^{-1})	Flux (mol hr^{-1} cm^{-2})
$Ca(SCN)_2$ [b,c]	9.68×10^{-6}	5.23×10^{-7}
$Ba(SCN)_2$ [b]	8.46×10^{-6}	4.57×10^{-7}
NaSCN	1.46×10^{-6}	7.89×10^{-8}
KSCN	10.5×10^{-6}	5.68×10^{-7}

[a] CH_2Cl_2 organic phase, 0 °C.
[b] Rate of $FeSCN^{2+}$ divided by 2 = $[M^{2+}]$.
[c] Rate determined at 0.1 M $Ca(SCN)_2$ (solubility limitation) times 3.

containing diacetamide ligands sense Na^+ over Ca^{2+} by large factors [1]. Simon *et al.* have discussed how K_{ij}^{pot} values for neutral ligands, such as our dioxydiacetamides, can be predicted from theory [17,18]. However, there are differences in the experimental conditions involved in the performance of a ligand in an electrode *vs* its behavior in bulk membrane transport. These differences include possibly different stoichiometries of complexation at different concentrations of the ligand and different distribution equilibria in the two systems due to differences in the polarities of the organic phases [16]. Our counterions are SCN^- which may interact differently with metal cations than do the sites in the ion-selective electrode (PVC) membranes [16]. Also, as pointed out by Izatt [19], "the prediction of the ordering of three-phase transport of M^{2+} *vs* M^+ from single phase binding and/or two phase extraction is difficult at best. Three phase transport involves two distribution processes and a complexation-decomplexation process. Complexation equilibria also exist in all three phases. Single phase binding does not involve a distribution process but several equilibria usually exist."

Despite all of these *caveats*, it is found that the stronger single phase binder Ca^{2+} is transported faster than the weaker binder Na^+ by **2** and now, in this work, by **1**. The reversal of selectivity to $Na^+ > Ca^{2+}$ in ion-selective electrodes for these ligands remains a striking phenomenon. The slower transport of KSCN by **1** as compared to DB18C6 is probably related to the weaker binding of K^+ by **1** *vs* the binding of K^+ by DB18C6 [2,14].

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