J Incl Phenom Macrocycl Chem (2008) 60:153–161
DOI 10.1007/s10847-007-9365-5

ORIGINAL ARTICLE

Ethylene oxide-bridged bipyridine oligomers that function as selective host molecules for the encapsulation of small alkali cation guests

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Received: 21 May 2007 / Accepted: 7 August 2007 / Published online: 7 September 2007

Abstract Two novel ethylene oxide-bridged bipyridine oligomers were synthesized that contain host pockets with four (**1**) or six (**2**) oxygen donor atoms and a pyridyl nitrogen donor. The alkali picrate extracting ability and selectivity of these free ligands was investigated using a liquid–liquid dichloromethane–water extraction study. Both open-chain oligomer frameworks display unexpectedly high extraction efficiency (EE) values for specific guest ions (EE = 57% Na^+ extracted by **1**, and EE = 39% Cs^+ extracted by **2**). These extraction values are comparable to macrocyclic analogues and their ion selectivities follow the 'same-fit' concept that has been extensively reported for fixed pocket systems. The shorter chain oligomer (**1**) binds ions in the series ($Na^+ > K^+ > Cs^+$), while the larger oligomer (**2**) binds ions in the reverse order ($Cs^+ > K^+ > Na^+$). Formation of the host–guest ligand–ion complexes were verified by ^1H NMR spectroscopy and MALDI-TOF mass spectrometry experiments. A Job's plot analysis based on UV spectral data also supported the 1:1 (oligomer to ion) complexation observed in the MALDI mass spectra.

Keywords Alkali picrate · Binding selectivity · Bipyridine oligomers · Ethylene oxide pocket · Extraction efficiency (EE) · Host–guest · Inclusion complex · Open-chain · 'same-fit' concept

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Introduction

There are numerous examples of functionalized crown ether and aza-crown ether macrocycles that function as efficient and selective host molecules for small cationic guests [1–5]. In some cases, research efforts have focused on derivatizing these macrocycles with pendent arms, producing the corresponding lariat or cryptand systems. Both of these systems produce either partial or fully-formed cage molecules that enhance their ion-binding efficiencies, and in some cases, their binding selectivities [6–10]. However, there are only a few examples of 'open-chain' acyclic ethers or amines that produce host–guest complexes with the efficiency of their macrocyclic analogues and in most of these examples the hosts display little, if any, selectivity for a specific ion [11, 12].

In typical binding studies, long chain acyclic compounds, such as glymes or polyamines, have been used as control molecules during ion-complexation experiments to highlight the necessity of a fixed host cavity to produce measurable complexations [13, 14]. Extraction efficiencies reported for these acyclic controls are usually less than 1% of total ion concentration or are reported as negligible [15]. The enhanced binding affinities generally observed for macrocycles relative to their acyclic analogues has been termed the "macrocyclic effect" [11]. In the few examples where binding efficiencies of acyclic systems are comparable to their cyclic counterparts, these compounds didn't display the same guest-ion selectivity as their cyclic analogues [16]. In addition, it was shown that the unusually high binding efficiencies observed for these acyclic systems were predominately influenced by the chains peripheral functional groups and not by the nature of the host donor pocket [17].

An open-chain host framework presents several synthetic and structural advantages over a macrocyclic or cage

counterpart. In many cases, the preparation of long-chain oligomers does not require the high-dilution conditions or the ion-template approach often necessary to obtain the macrocyclic analogues and these acyclic oligomers are usually obtained in higher yield. Oligomeric-host donor systems are often prepared following a stepwise approach where the oligomer chain length and basicity may be controlled by varying the number, type, and spacing of donor atoms. These compounds should be tunable for specific cationic guests based on matching the steric and electronic preferences of host and guest. The structural advantage afforded by the flexible acyclic molecules is their ability to encapsulate size-variant cationic guests, while still displaying selectivity based upon a 'same-fit' concept of oligomer pocket size to guest ionic radii. There are numerous examples in the literature of fixed-pocket crown ethers and aza-crown ethers selectivity binding ions due to the necessary size compliance of host and guest, however, these systems are much less efficient at binding ions where a significant host-pocket and ionic-radii mismatch occurs [12, 18–21].

During the course of synthesizing mono- and bi-metallic coordination complexes, we discovered the unique ion binding efficiency and selectivity of several uncoordinated ethylene oxide-bridged bipyridine ligands. Herein we report the synthesis and ion-extracting ability of two novel ethylene oxide-bridged bipyridine ligands (**1** and **2**). The extraction efficiencies (EE) of various alkali picrates by these free ligands (non-bipyridine metallated) can be determined by a liquid–liquid (dichloromethane–water) alkali picrate binding study. The resulting host–guest oligomer–ion complexations were confirmed using MALDI-TOF mass spectrometry and ^{1}H NMR spectroscopy measurements.

Experimental

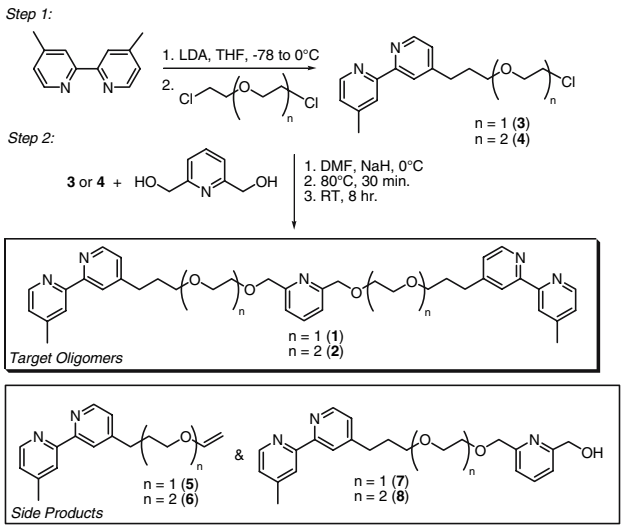
General procedures

NMR spectra were obtained on a 300 MHz FT-NMR spectrometer (Bruker Avance) in $CDCl_3$, *d_6-acetone*, or CD_3CN with TMS as an internal standard. Absorbance measurements were obtained on a diode array UV–vis spectrophotometer (Agilent). Mass spectra were recorded on a MALDI-TOF mass spectrometer (Bruker Daltonics OmniFlex LT) using an α-cyano-4-hydroxycinnamic acid (CHCA) matrix. Chromatography was performed using a binary gradient prep-phase liquid chromatograph system (ISCO CombiFlash) equipped with an Ocean Optics UV spectrophotometer (300 nm). General chemicals were obtained from Aldrich.

4,4′-dimethyl-2,2′-bipyridine (Me_2bpy) was prepared following a modified literature procedure using 4-picoline and a Raney-nickel catalyst [22]. 4-(6-chloro-4-oxahexyl)-4′-methyl-2,2′-bipyridine (**3**) and 4-(9-chloro-4,7-dioxanonyl)-4′-methyl-2,2′-bipyridine (**4**) were prepared by reacting 4,4′-dimethyl-2,2′-bipyridine with bis(2-chloroethyl) ether or 1,2-bis(2-chloroethylene oxide) ethane following a modified literature procedure [23]. The alkali picrates were prepared from picric acid and the corresponding alkali hydroxide following literature procedures [24].

Synthesis of **1** (Scheme 1)

A three-necked flask equipped with an addition funnel and a condenser was flame dried and then charged with NaH (141 mg, 5.90 mmol) and 2,6-pyridinedimethanol (371 mg, 2.67 mmol) under $Ar_{(g)}$. Dry and degassed DMF (200 mL) was added to the flask and the mixture was heated to 90 °C for 30 min. The flask was allowed to cool to room temperature, at which point the bipyridyl chloroether **3** (1.547 g, 5.32 mmol) was added dropwise and the mixture was stirred at 110 °C for 12 h. After cooling to room temperature a few drops of methanol were added, the sodium salts were filtered from solution and the mother liquor reduced under vacuum. The resulting yellow oil was dissolved in dichloromethane, washed with water, dried over magnesium sulfate, and concentrated under vacuum. The crude product was purified by LC using silica (0–40%, acetone/hexane) to remove starting material and side products. Later fractions from the silica column were collected and run through a neutral alumina column (0–25%, dichloromethane/acetone) to afford the target compound **1** (118 mg, 3.4%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ [ppm] 1.95 (m, 4H, 2 × CH_2), 2.48 (s, 6H 2 × CH_3bpy), 2.76 (t, 4H, 2 × CH_2bpy), 3.47 (t, 4H, 2 × CH_2O), 3.60



Scheme 1 Synthesis of bipyridine oligomers **1** and **2**

(t, 4H, 2 × CH_2O), 3.68 (t, 4H, 2 × CH_2O), 4.64 (s, 4H, 2 × CH_2py), 7.09 (m, 4H, bpy), 7.33 (d, 2H, py), 7.65 (t, 1H, py), 8.18 (s, 2H, bpy), 8.21 (s, 2H, bpy), 8.49 (m, 4H, bpy). ^{13}C NMR ($CDCl_3$) δ [ppm] 21.3 (2 × CH_3), 30.3 (2 × CH_2), 32.0 (2 × CH_2bpy), 70.2 (2 × CH_2O), 70.3 (2 × CH_2O), 70.4 (2 × CH_2O), 74.2 (2 × CH_2py), 120.0 (CH-py), 121.4 (2 × CH-bpy), 122.1 (2 × CH-bpy), 124.1 (2 × bpy-*C*-CH_3), 124.8 (2 × bpy-*C*-CH_2), 137.4 (2 × CH-py), 148.2 (2 × CH-bpy), 149.0 (2 × ipso-bpy), 149.2 (2 × ipso-bpy), 152.2 (2 × CH-bpy), 156.1 (2 × N*C*-bpy), 156.3 (2 × N*C*-bpy), 158.1 (2 × ipso-py). MALDI-MS, *m/z* 648.0 (**1+H$^+$**), 670.0 (**1+Na$^+$**), 686.0 (**1+K$^+$**), 780.0 (**1+Cs$^+$**).

Synthesis of **2** (Scheme 1)

Compound **2** (137 mg, 4.69% yield) was obtained as a colorless oil according to a procedure similar to that reported for **1** with only slight modifications to the reaction times. ^{1}H NMR ($CDCl_3$) δ [ppm] 2.03 (m, 4H, 2 × CH_2), 2.44 (s, 6H 2 × CH_3bpy), 2.79 (t, 4H, 2 × CH_2bpy), 3.50 (t, 4H, 2 × CH_2O), 3.61 (m, 4H, 2 × CH_2O), 3.68 (m, 4H, 2 × CH_2O), 3.72 (s, 8H, 4 × CH_2O), 4.66 (s, 4H, 2 × CH_2py), 7.14 (m, 4H, bpy), 7.36 (d, 2H, py), 7.66 (t, 1H, py), 8.22 (s, 2H, bpy), 8.24 (s, 2H, bpy), 8.53 (m, 4H, bpy). ^{13}C NMR ($CDCl_3$) δ [ppm] 21.2 (2 × CH_3), 30.2 (2 × CH_2), 31.9 (2 × CH_2bpy), 70.2 (4 × CH_2O), 70.3 (2 × CH_2O), 70.6 (2 × CH_2O), 70.7 (2 × CH_2O), 74.0 (2 × CH_2py), 119.9 (CH-py), 121.3 (CH-bpy), 122.0 (2 × CH-bpy), 124.0 (2 × bpy-*C*-CH_3), 124.6 (2 × bpy-*C*-CH_2), 137.2 (2 × CH-py), 148.1 (2 × CH-bpy), 148.9 (2 × ipso-bpy), 149.0 (2 × ipso-bpy), 152.1 (2 × CH-bpy), 156.0 (2 × N*C*-bpy), 156.2 (2 × N*C*-bpy), 157.9 (2 × ipso-py). MALDI-MS, *m/z* 736.0 (**2+H$^+$**), 758.0 (**2+Na$^+$**), 774.0 (**2+K$^+$**), 868.0 (**2+Cs$^+$**).

Synthesis of monomers **7** and **8** (byproducts obtained from synthesis of **1** and **2**)

The mono-addition side products **7** and **8** were isolated as the second compounds eluting from the alumina chromatography (25% dichloromethane/acetone) of oligomers **1** and **2**, respectively. Compound **7** (colorless oil)—^{1}H NMR ($CDCl_3$) δ [ppm] 1.95 (m, 2H, CH_2), 2.39 (s, 3H, CH_3bpy), 2.76 (t, 2H, CH_2bpy), 3.47 (t, 2H, CH_2O), 3.60 (m, 2H, CH_2O), 3.68 (m, 2H, CH_2O), 4.28 (bs, 1H, OH), 4.63 (s, 2H, CH_2py), 4.68 (d, 2H, CH_2py), 7.09 (m, 2H, bpy), 7.11 (d, 1H, py), 7.31 (d, 1H, py), 7.61 (t, 1H, py), 8.17 (s, 1H, bpy), 8.19 (s, 1H, bpy), 8.48 (m, 2H, bpy). MALDI-MS, *m/z* 393.5 (**7+H$^+$**). Compound **8** (colorless oil)—^{1}H NMR ($CDCl_3$) δ [ppm] 1.95 (m, 2H, CH_2), 2.44 (s, 3H, CH_3bpy), 2.79 (t, 2H, CH_2bpy), 3.50 (t, 2H, CH_2O), 3.61 (m, 2H, CH_2O), 3.69 (m, 2H, CH_2O), 3.73 (s, 4H, 2 × CH_2O), 3.95 (bs, 1H, OH), 4.69 (s, 2H, CH_2py), 4.72 (d, 2H, CH_2py), 7.12 (m, 2H, bpy), 7.16 (d, 1H, py), 7.37 (d, 1H, py), 7.66 (t, 1H, py), 8.22 (s, 2H, bpy), 8.54 (m, 2H, bpy). MALDI-MS, *m/z* 437.8 (**8+H$^+$**).

Ion extraction studies

The procedures described here are similar to those described in previous papers [3, 5, 13–15]. Freshly distilled dichloromethane and deionized water (18 MΩ) were first saturated with each other to minimize neat ion mobility and volume changes between the two liquid phases. A dichloromethane solution of **1**, **2**, **7**, or **8** (0.050 mM, 25.00 mL) was added to a 125 mL Erlenmeyer flask equipped with a spin vane along with 25.00 mL of a 0.050 mM solution of the corresponding alkali picrate in water. The flask was stoppered and the solution was stirred vigorously (until solution emulsified) at 25.0 ± 2.0 °C for a period of 6–24 h. The stirring was stopped each hour and the flask was allowed to stand for 15 min to complete phase separation. The concentration of the alkali picrate in the aqueous phase was obtained at 355 nm. The aqueous samples were then returned to the extraction flask and stirring continued until there were no measurable changes in the alkali ion concentrations. The extraction efficiencies were reported as a percent of total ion complexation once apparent equilibrium conditions were reached.

^{1}H NMR binding experiments

Stock solutions of the oligomers (**1** and **2**) and of the corresponding alkali ion picrates were prepared in *d_6-acetone*. ^{1}H NMR spectra were first obtained for the neat ligand and the alkali picrate solutions. Spectra were then obtained for the complex ion solutions in a 4:1 molar excess of the corresponding alkali ion picrate to the oligomer. An excess of the picrate salt was used to force the solution equilibrium towards the complexed form. The neat and the complex spectra were then compared and chemical shift differences were recorded.

MALDI-TOF mass spectrometry binding experiments

MALDI mass spectrometry samples were prepared by adding 1.00 μL of a 0.050 mM acetonitrile solution of the oligomer (**1** or **2**) to 10.00 μL of a 0.050 mM acetonitrile solution of the alkali ion picrate(s) and 10 μL of a saturated acetonitrile solution of α-cyano-4-hydroxycinnamic acid (CHCA) matrix in 1% aqueous trifluoracetic acid (TFA)

[25]. The resulting mixture was allowed to stir for 10 min on a vortex mixer prior to spotting and the samples were then allowed to evaporate to dryness. Mass spectra for the oligomers and the alkali picrates were also obtained in an anhydrous environment by spotting the samples in a CHCA-acetonitrile matrix without aqueous TFA. Sodium and potassium contamination in the samples could be controlled by passing an acetonitrile solution of the oligomers through a cation-exchange column (Dowex 50—proton form). The assignment of the major matrix associated species were confirmed by varying the molar ratio of the analyte to matrix the compound. The LD mass spectra (matrix free environment) were also obtained for the ion-pair complexes $\mathbf{1}+\mathbf{M}^+$ or $\mathbf{2}+\mathbf{M}^+$ (where M = Na^+, K^+, or Cs^+) by spotting in neat acetonitrile.

Stoichiometric determination for oligomer 2, Job's plot analysis

Acetonitrile solutions (10.00 or 5.00 mL) containing oligomer **2** and an alkali picrate (Na^+, K^+, or Cs^+) were prepared at seven different mole fractions ($n_{total} = 8.83 \times 10^{-7}$ for Cs species and $n_{total} = 8.83 \times 10^{-8}$ for Na and K species) of ligand vs. picrate (χ_{Ligand} = 0, 0.25, 0.33, 0.50, 0.66, 0.75, and 1). The solutions were shaken for a 24 h period to ensure that equilibrium had been reached and the absorbance values were recorded for each solution at 304 nm. UV spectra of solutions containing complex showed a spectral shoulder at 304 nm, at which wavelength the absorbance of the picrate–oligomer mixture was greater than the sum of the two individual species. Absorbance measurements at this wavelength were used to construct a Job's plot. A corrected absorbance value for the complex was obtained by subtracting the absorbances due to uncomplexed oligomer and picrate. The corrected complex absorbance was then plotted against the oligomer mole fraction and solution-state stoichiometries were determined from the curve's maximum absorbance.

Results and discussion

Ligand synthesis

The target bipyridine host oligomers **1** and **2** were obtained in only two synthetic steps starting from 4,4′-dimethyl-2,2′-bipyridine (Scheme 1). Although overall reaction yields are low (3.4% and 4.7%, respectively for **1** and **2**), the reactions were unoptomized and were successfully scaled to obtain gram quantities for the extraction studies. Bipyridine chloro-ethers **3** and **4** are the key intermediates in the preparation of the long chain oligomers. Both of these monomeric intermediates were prepared in relatively high yields by reacting recrystallized (ethyl acetate) Me_2bpy with the appropriate dichloro ether (Scheme 1). These intermediates were then reacted with the spacer molecule, 2,6-pyridinedimethanol, producing the target oligomer (**1** or **2**) along with a vinyl bipyridine side-product (**5** or **6**) and the mono-addition side-product (**7** or **8**). The high purity of the resulting target oligomers was verified using ^{1}H and ^{13}C NMR spectroscopy as well as MALDI-TOF mass spectrometry.

From a synthetic standpoint these compounds are much easier to prepare than a closed macrocycle and as a result are readily customizable for various guests. The overall pocket volume can be controlled by changing the length and the number and type (typically O, N, or S) of basic donor-atom sites within the chain. Macrocycle preparation typically requires either high dilution conditions or a very slow pump delivery method of reagents and extensive purification steps to remove oligomeric and polymeric side products [26–28]. Comparatively, oligomers **1** and **2** are prepared in modest yields in just two synthetic steps and other analogues may be isolated following the identical procedure using the appropriate polyether or polyamine bipyridyl starting material.

Ion-extraction studies

The ion-binding efficiencies and preferences of the shorter (**1**) and the longer (**2**) bipyridine oligomers were determined by a liquid–liquid two-phase extraction of the aqueous alkali picrate salts (sodium, potassium, or cesium) into dichloromethane. The absorbance changes for all of the aqueous alkali picrates solutions were monitored at 355 nm using UV-visible spectroscopy every hour until there were no appreciable changes in absorbance, which indicated that an equilibrium state was established. Apparent equilibrium was reached in approximately 6 h. By comparing initial (neat aqueous alkali picrate solution) absorbance values with the final values, the extraction efficiency, expressed as a percent change, was calculated for each oligomer/ion-pair complex (Fig. 1). The ion selectivities were determined by comparing the extraction efficiency of the oligomer within the ion set (Na^+, K^+, and Cs^+) or between the two oligomers for a common ion. A control alkali picrate extraction using neat (aqueous washed) dichloromethane was performed for all three alkali ions (Na^+, K^+, and Cs^+) to ensure that there was simply not ion migration between the two liquid phases. In all control experiments there was less than a 0.1% transfer of the alkali picrate into the dichloromethane phase (6, 24, and 48 h data collected). Each extraction measurement reported in Fig. 1 was performed in duplicate.

Both oligomers displayed unexpectedly high extraction efficiencies considering the fact that the host pocket is derived from an open-chain framework. The cation extracting ability of oligomer **1** is modest for the larger cesium and potassium ions at 17% and 18%, respectively. Sodium, a smaller ion, is extracted more efficiently at 57%; overall cation binding ability for oligomer **1** is $Na^+ \gg K^+ > Cs^+$ (Fig. 1a). This binding preference indicates that the shorter four-oxygen and one-nitrogen donor-atom pocket is following a 'same-fit' model that is typically reserved for fixed-pocket systems. The larger oligomer **2**, which contains a six-oxygen and one-nitrogen donor-atom pocket extracts 39%, 28%, and 16% of the cesium, potassium, and sodium ions, respectively (Fig. 1b). The overall binding selectivity for oligomer **2** ($Cs^+ > K^+ > Na^+$) is the exact opposite of that reported for oligomer **1**. The larger cavity size created by oligomer **2** accounts for the enhanced extraction efficiency, relative to oligomer **1**, of the larger potassium and cesium ions, but there is still a clear preference for the largest ion. This reverse trend in ion affinity suggests that the 'same-fit' model is also observed by the longer oligomer. This sterically-controlled 'same-fit' concept seems to be the driving force behind ion preference and not the overall basicity differences between the two host pockets. One might expect that the harder six-oxygen donor-atom pocket of oligomer **2** would preferentially bind the harder sodium ion based upon increasing the number of favorable hard/soft–donor/acceptor interactions, but this is clearly not the case.

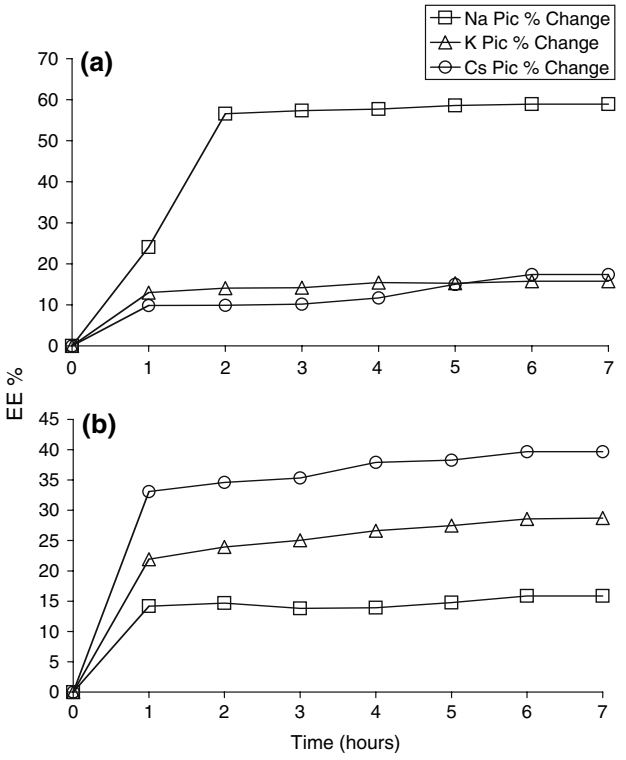


Fig. 1 Extraction efficiency (EE) plots for oligomers **1** (**a**) and **2** (**b**); efficiency data is reported as the percentage of alkali picrate extracted from aqueous solution

The ion-extracting ability of the dimeric compounds (**1** and **2**) were also compared to their corresponding monomeric species (**7** and **8**) in order to see whether the two ethylene oxide chains of the dimers were necessary for ion extraction. Compounds **7** and **8** were byproducts obtained from the synthesis of oligomers **1** and **2** (Scheme 1); these compounds contain either two (**7**) or three (**8**) donor oxygen atoms and a terminal pyridine ring. The maximum extraction values for dimers **1** and **2** and monomers **7** and **8** are reported in Table 1. It is clear from this study that the dimeric compounds are much more efficient ion extractors than their monomeric analogues. Compound **7** extracted only 2.79%, 2.31%, and 0.88% of the Na^+, K^+, and Cs^+ ions, respectively, and compound **8** extracted only 0.54%, 3.40%, and 0.20% of the Na^+, K^+, and Cs^+ ions. Had the monomers produced EE values that were similar to the dimer values, we would have concluded that a closed conformation of the oligomers is not necessary for effective ion binding. Instead, this data argues that both ethylene oxide chains present on the oligomers are required to work together to encapsulate ions. This cooperative effect strongly supports the conclusion that the two chains are needed to form the closed-pocket pseudomacrocyclic conformation necessary to promote effective ion encapsulation.

In addition, this data suggests that the likely stoichiometric ratio of oligomer to ion in the host–guest complex is 1:1. The lack of significant ion extraction by the monomeric species makes it unlikely that the stoichiometry would be 1:2 (oligomer to ion), as the monomeric chains themselves show little evidence of an ion-binding capability. One might suspect that the shorter-chain compounds (**7** and **8**) could effectively bind cationic centers in 2:1 (monomer to ion) ratios, but the low extraction values indicate that such ternary complexes do not form at the concentrations used in these experiments. By analogy, it is therefore unlikely that the dimers would form 2:1 (oligomer to ion) complexes at the reactant concentrations used.

Table 1 Maximum ion extraction values for dimeric oligomers **1** and **2**, for monomers **7** and **8**, and neat dichloromethane (solvent control)

	Host species	Na^+ (%)	K^+ (%)	Cs^+ (%)
Dimer species	Oligomer **1**	57.0	18.0	17.0
	Oligomer **2**	16.0	28.0	39.0
Monomer species	Monomer **7**	2.79	2.31	0.88
	Monomer **8**	0.54	3.40	0.20
Solvent	CH_2Cl_2	0.04	0.01	0.01

Extraction data is reported as the percentage of alkali picrate extracted from aqueous solution

These oligomeric complexes represent a novel example of host–guest complexations where ion-binding efficiency and selectivity properties are comparable with other closed-chain counterparts. Typically, a covalently bound macrocycle with a fixed host pocket is required for effective ion binding; however, these oligomeric compounds display extraction efficiency values that are similar in magnitude to analogous aza-crown ether systems. For example, the mono-aza-15-crown-5 compound, which contains the same number of oxygen (4) and nitrogen (1) donor atoms as oligomer **1** displayed lower extraction efficiencies for sodium and potassium ions compared to **1** and was also less selective for extracting one specific ion [10].

The surprisingly efficient ion-extraction properties observed for compounds **1** and **2** relative to other open-chain compounds such as glymes and polyamines could be explained by the increased lipophilicity of oligomers **1** and **2**. Bako et al. has recently reported that in general the lipophilic nature of a host crown molecule may be as important as the number and type of donor atoms present within the host ring to the formation of ion complexes in a liquid–liquid ion extraction [10]. Bako correlated log p values (provides a lipophilic measure) of various lariat crown ether compounds to their ion-extracting abilities and he found that the more lipophilic the compound, the more efficient it is at ion extraction for all ions, regardless of size. If the number or type of donor atoms is varied or if the size of the crown is varied, the lipophilicity comparisons are harder to make. With oligomers **1** and **2**, it is reasonable to expect that the peripheral bipyridine moieties enhance their lipophilic character relative to simple glymes and polyamines, and subsequently increase the oligomer extraction capabilities.

In addition to possible influences due to solubility, the two bipyridine moieties may serve to preorganize the oligomers into a macrocyclic framework through a π–π ring stacking interaction. If a ring-stacking affect is present in the solution state, then the compound would be expected to behave more like a covalently-linked fixed-pocket macrocycle and may help explain the interesting binding efficiencies of these compounds. It would also be possible for the guest ions to template the macrocyclic conformation where the bipyridine moieties would help to stabilize the host–guest complex through weak π–π stacking. A future area of study for these systems will be to coordinate the bipyridine moieties of oligomers **1** and **2** to a transition metal center producing the monometallic fixed pocket macrocycles. These covalently bound metallomacrocycles may display different binding preferences and efficiencies relative to their non-metallated open-chain analogues.

Investigation of ion binding by ^{1}H NMR spectroscopy

^{1}H NMR spectroscopy was used to investigate the likely position of the guest alkali ion within the host framework of oligomers **1** and **2**. It is feasible that ion binding could include interactions between one or both of the terminal bipyridine moieties. As a result, there are three possible binding sites: the ion could perch or nestle within the ethylene oxide pocket, the peripheral bipyridines could bind the ion producing the metallomacrocycle conformation, or the ion could be cooperatively bound by the ethylene oxide pocket and one of the bipyridine and pyridine units. In order to establish the most likely site of ion binding, the ^{1}H NMR spectra of the neat oligomer solutions were compared to the spectra obtained following ion complexation reactions between sodium picrate and oligomer **1** (Table 2) and sodium picrate and oligomer **2** (Table 3). It was evident that the bipyridine and the pyridine resonances remained unshifted suggesting that the bipyridine residues are not involved in ion binding. The most significant chemical shift differences were observed for the methylene protons on the ethylene oxide backbone. This would suggest that the guest ion is positioned within the ethylene oxide pocket of the oligomer. If the bipyridine units were involved in stabilizing the guest ion, then binding efficiencies may be compromised by subsequent transition metal center coordination reactions. It was not possible, however, to investigate the ion-binding preferences using this NMR technique because similar differences in chemical shifts were observed for all three ions.

Analysis of oligomer/ion complex formation by MALDI-TOF mass spectrometry

The oligomer/ion-pair complex formation was confirmed using MALDI-TOF mass spectroscopy analysis. The mass

Table 2 Selected ^{1}H NMR chemical shift (δ) and the chemical shift difference ($\Delta\delta$) data for oligomer **1** and the sodium picrate complex **1+Na$^+$** in *d_6-acetone*

		Bipyridine			Ethylene oxide pocket				Pyridine	
Oligomer **1**	δ	7.26	8.34	8.53	3.49	3.58	3.71	4.61	7.41	7.80
1+Na$^+$	δ	7.26	8.34	8.53	3.53	3.65	3.74	4.63	7.41	7.80
	$\Delta\delta$	0	0	0	0.04	0.07	0.03	0.02	0	0

Chemical shifts reported in ppm

Table 3 Selected ^{1}H NMR chemical shift (δ) and the chemical shift difference ($\Delta\delta$) data for oligomer **2** and the sodium picrate complex **2+Na$^+$** in *d_6-acetone*

		Bipyridine			Ethylene oxide pocket					Pyridine	
Oligomer **2**	δ	7.23	8.31	8.51	3.49	3.58	3.61	3.68	4.58	7.35	7.73
2+Na$^+$	δ	7.23	8.31	8.51	3.53	3.62	3.66	3.72	4.63	7.35	7.73
	$\Delta\delta$	0	0	0	0.04	0.04	0.05	0.04	0.05	0	0

Chemical shifts reported in ppm

spectra were first recorded for the uncomplexed oligomers (**1+H$^+$** and **2+H$^+$**); these spectra display the expected mass peaks at 648 *m/z* and 736 *m/z*, respectively (Figs. 2a and 3a). The mass spectra were then obtained for the complexes by adding the appropriate alkali picrate (Cs, K, or Na) to an acetonitrile solution containing the host oligomer. The resulting host–guest molecular-ion peaks were observed at 670 *m/z*, 686 *m/z*, and 780 *m/z* for the **1+Na$^+$**, **1+K$^+$**, and **1+Cs$^+$** complexes, respectively, and mass peaks at 758 *m/z*, 774 *m/z*, and 868 *m/z* were observed for the **2+Na$^+$**, **2+K$^+$**, and **2+Cs$^+$** analogues, respectively (Figs. 2b and 3b). The observance of a single host–guest molecular-ion species for all oligomer/ion pairs indicated that the inclusion complexes were present in a 1:1 (oligomer to ion) stoichiometry. In addition, the intensity of the complex ion peak could be controlled by varying the ratio of guest ion to host oligomer, as the ratio was increased from a 1:1 to a 20:1 ratio the resulting host–guest complex became the dominant species observed in the mass spectrum.

Using a mixture of all three ions (Cs^+, K^+, and Na^+) and the corresponding oligomer (**1** or **2**), no apparent ion preference was observed for either oligomer. This is not surprising, however, given the destructive nature of the desorption process. At this molecular weight, these compounds absorb a significant amount of energy before entering the gas phase, so molecular fragmentations and ion-decomplexations are commonly observed. The mass spectra of these complexes always displayed some amount of the decomplexed molecular ion, even when ion to ligand

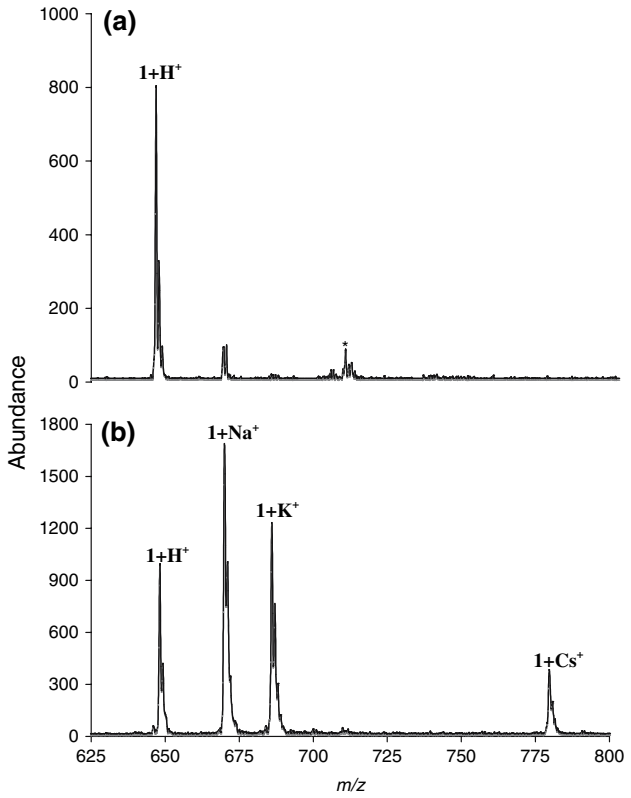


Fig. 2 MALDI-TOF mass spectra of oligomer **1**: (**a**) spectrum of uncomplexed oligomer **1+H$^+$**; (**b**) spectrum of oligomer–ion complexes **1+M$^+$** for all three ions (Na^+, K^+, and Cs^+). *indicates minor matrix species

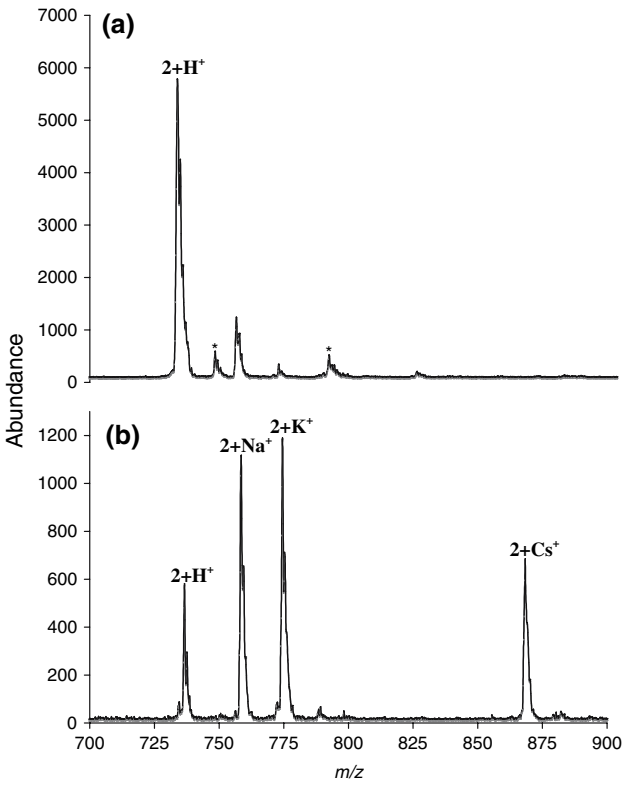


Fig. 3 MALDI-TOF mass spectra of oligomer **2**: (**a**) spectrum of uncomplexed oligomer **2+H$^+$**; (**b**) spectrum of oligomer–ion complexes **2+M$^+$** for all three ions (Na^+, K^+, and Cs^+). *indicates minor matrix species

molar ratios were increased to values in excess of 20:1 (ion to ligand). Further, these complex solutions were only mixed for a period of about 10 min (same conditions as prior mass analysis), so it is likely that these systems had not reached equilibrium.

It is interesting to note that the mass spectra for the **1**+M^+ or **2**+M^+ (where M = Na^+, K^+, or Cs^+) complexes may also be obtained without the aid of the matrix compound or other proton sources. Although this LD-TOF mass analysis does produce a considerable amount of fragmented species, there are still clearly defined complex-ion mass peaks observed. These spectra were obtained by spotting an acetonitrile solution containing an oligomer and an alkali picrate on the target and allowing the sample to completely dry. When these conditions were repeated for the neutral free oligomers, no mass spectra were recorded presumably because these compounds do not become ionized without a matrix ion source. The fact that these complexes survive the conditions of laser desorption intact suggests that the host–guest oligomer–ion complexations are quite robust.

Determination of oligomer **2**/ion stoichiometry using continuous variation methods

In order to establish the solution-state stoichiometry of the host–guest complexes, a Job's plot analysis was performed for the ion pairs of oligomer **2** [29, 30]. The UV-visible absorbance values at 304 nm of the complexes (**2**-Na^+, **2**-K^+, **2**-Cs^+) were corrected for the absorbances of the free host oligomer **2** and guests (alkali picrates) to generate the Job's Plot in Fig. 4. We recognize that there is a considerable amount of noise in this data, which was due to the difficulty in finding a unique absorbance window for the complex that was different from the simple sum of the absorbances due to free oligomer and alkali picrates. We were, however, able to find a small spectral handle at 304 nm for the complexes of oligomer **2**, which showed a slight increase in complex absorbance relative to the free species. Generating the corrected absorbances, therefore, involved the inherently noisy subtraction of similar absorbance values. Nonetheless, all of our oligomer **2** complexes displayed maximal corrected absorbance values at the 0.5 mole fraction of oligomer, which supports our previous conclusions (extraction studies and MALDI experiments) that these complexes are likely formed with 1:1 (oligomer to ion) stoichiometries (Fig. 4).

Unfortunately, the oligomer **1** studies did not provide any unique absorbance wavelengths that were indicative of the host–guest complexes It is likely, however, that the oligomer **1** complexes are also forming 1:1 host–guest complexes based on the similarities to oligomer **2** observed

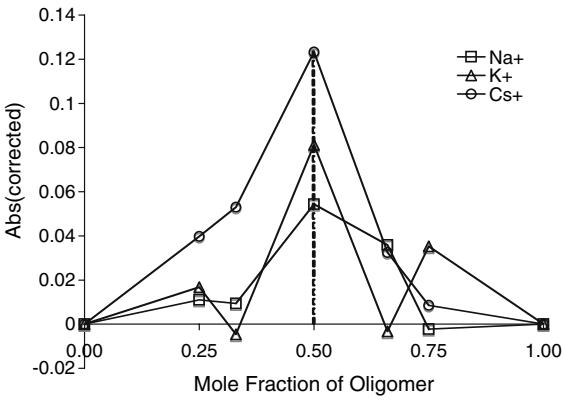


Fig. 4 Job's plot displaying the complexation of oligomer **2** with all three ions (Na^+, K^+, and Cs^+). Corrected complex absorbance was plotted against mole fraction of oligomer

during the ion extraction studies of the oligomers (reverse size trend for ion encapsulation studies), the extraction studies of the monomers (low EE's for both **7** and **8**), and the MALDI-TOF mass spectrometry studies (we only observed 1:1 complexations). A ^{1}H NMR titration study was also attempted, but the changes in chemical shifts were too small to determine complex stoichiometry.

Conclusions

Two novel acyclic bipyridine oligomers were prepared that are capable of extracting alkali picrates from an aqueous phase into an organic solution. The shorter, four-oxygen donor, oligomer (**1**) displayed the highest extraction efficiency for sodium ion (EE = 57%) and the lowest for cesium ion (EE = 17%). The longer, six-oxygen donor, oligomer (**2**) is most efficient for cesium ion (EE = 39%) and is the least efficient for sodium ion (EE = 16%). These preferences mimic the 'same-fit' concept that has been reported for 'closed-chain' macrocyclic analogues, where ionic radii of the guests and pocket volume of the hosts dictate binding preferences. The two monomeric control compounds (**7** and **8**) displayed very low EE values for all ions (EE = 0.20–3.40%). These low extraction values suggested that the hosts form macrocyclic or pseudomacrocyclic complexations through the cooperative effect of the two ethylene glycol chains. The stability and stoichiometry of the resulting host–guest complexes were confirmed by MALDI-TOF mass spectrometry, which displayed intense complex-ion mass peaks even in the absence of a protonating matrix source. A Job's plot analysis suggested that the oligomer **2** complexes exist in a 1:1 (oligomer to ion) stoichiometric conformation in the solution state, which is consistent with the 1:1 complexes that were observed in the gas phase MALDI-TOF mass spectrometry experiments. The ^{1}H NMR spectra of these

complexes indicate that the guest ion is bound within the oligomers ethylene oxide pocket and does not interact with the bipyridine subunits. This is an important feature of these systems as the bipyridine moieties will be later metallated to investigate the ion-binding properties of the resulting metallomacrocyclic complexes.

Acknowledgments We would like to thank the following agencies for their support of this work: National Science Foundation (award #0346623), Merck/AAAS (2003–2005 Undergraduate Science Research Program), and internally from the Neidig Research Fund (Lebanon Valley College).

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