Alkali Metal Cation Selectivity of an Oligo-Ether Substituted Norbornadiene and Quadricyclane Isomer

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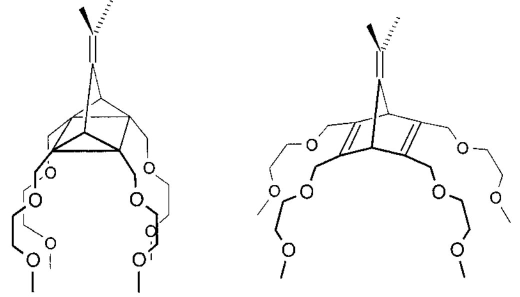
We present investigations aimed at using the norbornadiene/quadricyclane system as a framework for a switchable cation carrier. According to molecular modelling studies a suitably substituted system should perform a pincer-like motion upon isomerisation and reisomerisation, while complexing and decomplexing a host molecule. To this end, we investigated the complexing abilities of a 1,5,6,7-tetrasubstituted quadricyclane polyether and its corresponding norbornadiene isomer. The picrate extraction method was applied to determine the extraction constants K_{ex} and the association constants K_{ass} of these polyethers with alkali metal cations in chloroform. As expected, the complexes of the quadricyclane polyether with Li^+, Na^+, K^+ and Cs^+ are more stable than those of the norbornadiene isomer. This difference reaches a maximum for potassium. The interconversion between the norbornadiene polyether and the corresponding quadricyclane was also examined. The norbornadiene can be converted photochemically to the quadricyclane with 50% conversion while the reverse reaction is catalysed by neutral aluminium oxide in 71% yield. No by-product was detected in either of the isomerization reactions.

Introduction

In the pursuit of our research towards an active ion transport through lipophilic membranes[1] we investigated the complexing properties of ether-substituted norbornadiene and quadricyclane derivatives. The norbornadiene/quadricyclane system was chosen as a molecular framework for a switchable ion carrier[2] because the on/off switching isomerisation can be achieved by an efficient photochemical/catalytic process in a number of substituted systems.[3] For binding alkali metal cations four (2-methoxy)ethoxymethyl groups were introduced and the quadricyclane tetraether **1** and the corresponding norbornadiene tetraether **2** were synthesized as promising targets (Scheme 1).[4] Due to the large energy difference between the highly strained quadricyclane **1** and the thermodynamically more stable norbornadiene **2** the presence of a complexed cation should have little effect on the switching process; the opening of the ligands in the presence of a guest is a problem in a number of known photoswitchable systems.



1 **2**

Scheme 1. Ether-substituted quadricyclane **1** and norbornadiene **2**

Determination of the Association Constant K_{ass}

The picrate extraction method was applied to determine the association constants of the norbornadiene **2** and the quadricyclane **1**. Solutions of the ligands in chloroform were used to extract alkali metal picrates from an aqueous solution. A basic requirement for this method is a very low solubility of the ligands in water, which is the case for compounds **1** and **2**. The concentration of the deeply yellow picrate in the organic phase ($\lambda_{max} = 364$ nm, $\varepsilon = 18600$ L mol^{-1} cm^{-1})[5] was then determined by UV/Vis spectroscopy. Using these data, the molar ratio R of the complexed ion and the free ligand in the organic phase was calculated using Cram's method.[6] Knowing the volume of the aqueous and the organic phase (V_{aq} and V_{org}, respectively), the starting concentration of the salt in the aqueous phase $[M^{+}_{aq}]_{start}$ and of the ligand in the organic phase $[L_{(org)}]_{start}$ and assuming $V_{org} = V_{aq}$, we can calculate the extraction constant K_{ex} according to Equation (1):

$$K_{ex} = \frac{R}{(1-R)\left(\left[M^{+}_{(aq)}\right]_{start} - R\left[L_{(org)}\right]_{start}\right)^{2}} \qquad (1)$$

The association constant K_{ass} of the complex in the organic phase can be calculated from the extraction constant K_{ex} and the extraction constant of the pure metal picrate ($K_{ex_{MA}}$), i.e. the distribution constant of the metal salt between the organic phase and the aqueous phase without

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any ligand [Equation (2)]. The extraction constants of the alkali metal picrates are known (Table 1).[5,7]

Table 1. Extraction constants $K_{ex_{MA}}$ of alkali metal picrates

Picrate salt	$K_{ex_{MA}}$ [10^{-3} L mol^{-1}]
Li^+ Pic^-	1.42
Na^+ Pic^-	1.74
K^+ Pic^-	2.55
Cs^+ Pic^-	6.60

$$K_{ass} = \frac{K_{ex}}{K_{ex_{MA}}} \qquad (2)$$

Results and Discussion

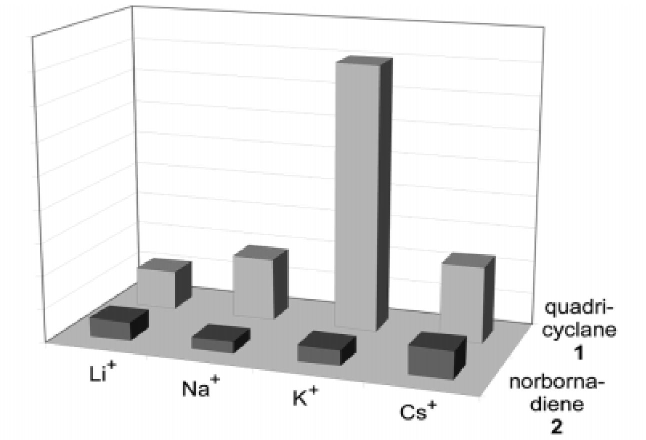
As expected, the association constants of the isolated norbornadiene tetraether **2** are significantly lower than the association constants of the corresponding pure quadricyclane tetraether **1** (Tables 2 and 3 and Schemes 2 and 3). A large difference in complexing abilities is an important prerequisite for the application as a switchable ion carrier. The ratio K_{ass} (quadricyclane)/K_{ass} (norbornadiene) increases continuously from lithium (2.1) to potassium (16.1) and then decreases for caesium (2.7). Obviously the size of the cavity formed by the four ether substituents of the quadricyclane **1** is suitable for binding K^+ while Li^+ and Na^+ are too small and Cs^+ is too large for this cavity. In distinct contrast to quadricyclane **1**, the association constants of the norbornadiene tetraether **2** decrease continuously from lithium to caesium. Although the extraction constant K_{ex} for caesium is higher than that of potassium, this effect is compensated in the calculation of K_{ass} by the fact that the value of $K_{ex_{MA}}$ for caesium is much higher than that of potassium. Both the low association constants of the norbornadiene **2** and the lack of size selectivity indicate that the four ether substituents are not able to form a suitable cavity for complexation. The size selectivity and higher complexation constants of the quadricyclane **1** and the lack of size selectivity and lower complexation constants of the norbornadiene **2** thus confirm our hypothesized grab-like movement of the four ether substituents.

Table 2. Extraction constants K_{ex} of ligands **1** and **2** with alkali metal cations

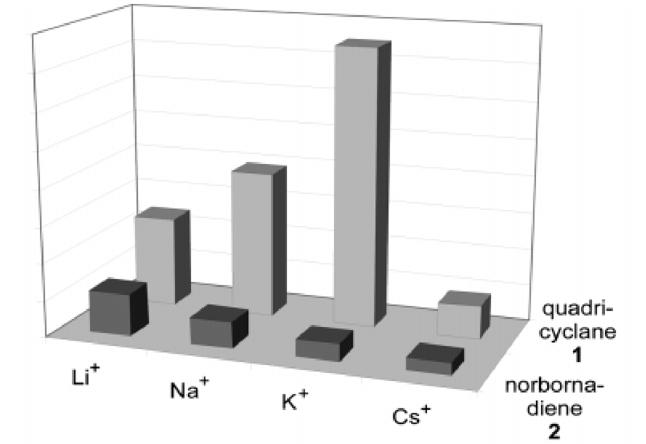
Cation	K_{ex} for quadricyclane **1** [L^2 mol^{-2}]	K_{ex} for norbornadiene **2** [L^2 mol^{-2}]
Li^+	5.81 ± 0.21	2.75 ± 0.04
Na^+	9.48 ± 0.47	1.72 ± 0.10
K^+	40.16 ± 1.12	2.47 ± 0.23
Cs^+	11.55 ± 0.54	4.29 ± 0.35

Table 3. Association constants K_{ass} of ligands **1** and **2** with alkali metal cations in chloroform

Cation	K_{ass} for quadricyclane **1** [L mol^{-1}]	K_{ass} for norbornadiene **2** [L mol^{-1}]
Li^+	4842.93 ± 175.49	2295.36 ± 34.22
Na^+	7900.16 ± 393.19	1431.35 ± 85.23
K^+	15040.99 ± 420.94	931.48 ± 44.82
Cs^+	1769.05 ± 62.97	649.46 ± 40.15



Scheme 2. Extraction constants K_{ex} of the quadricyclane **1** and the norbornadiene **2** with alkali metal cations



Scheme 3. Association constants K_{ass} of the quadricyclane **1** and the norbornadiene **2** with alkali metal cations in chloroform

Molecular Modelling Studies

According to MD studies[8] and structure optimizations using the MMFF94 force field,[9] the most stable structure of the complex of the quadricyclane tetraether **1** with K^+ has C_2 symmetry. The K^+ ion coordinates to each of the eight ether oxygen atoms of the four substituents and forms a "tentacle-like" complex (Figure 1). The corresponding conformations of the free ligands (all ether substituents are directed downward, with the ether oxygen atoms facing the cavity) are local minima also with C_2 symmetry. There are several other slightly more stable conformations with the ether substituents pointing downward and upward in an alternating sequence. The "pincer-principle" or the "breathing" cavity can be visualized by comparing the C_2 symmetrical structures of the free ligands (Figure 2). Upon closer inspection of the K^+ complex of the quadricyclane **1** it becomes evident why smaller cations do not fit properly into the cavity: the steric hindrance of the terminal methyl groups is considerable and puts a lower limit on the size of the cavity. The shortest H···H distance in the K^+ complex is only 1.9 Å (Figure 1). Smaller guest cations should even aggravate this steric problem.

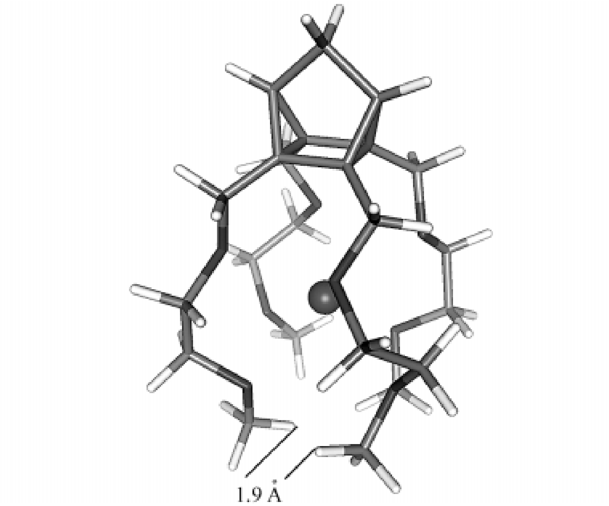


Figure 1. Structure of the K^+ complex of the quadricyclane polyether calculated using the MMFF94 force field; to simplify the system the isopropylidene group in the 3-position is replaced by hydrogen

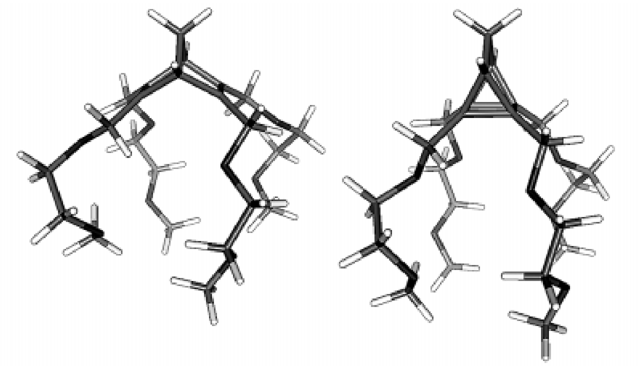
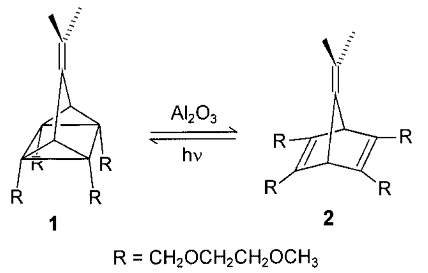


Figure 2. C_2 symmetrical structures of the norbornadiene polyether and the quadricyclane polyether calculated using the MMFF94 force field; the isopropylidene groups in the 7- (**2**) and 3-positions (**1**) are replaced by hydrogen

Norbornadiene−Quadricyclane Interconversion

In addition to sufficiently different complexing abilities, the facile and clean interconversion of the norbornadiene **2** and the quadricyclane **1** is another precondition for an application as a switchable ion-carrier.[10] We have previously reported that the ring opening from the quadricyclane **1** to the norbornadiene was achieved by adsorption on neutral aluminium oxide (Scheme 4).[3] The product is obtained in a yield of 71% by elution. Apart from remaining starting material no other by-products can be detected. The reverse reaction was achieved by irradiation of the norbornadiene tetraether **2** in tetrahydrofuran at −30 °C in a quartz tube with acetophenone as a sensitizer (Scheme 4). A photostationary equilibrium containing 50% of both starting material and product is obtained. Similar to the ring opening reaction no other by-products can be detected by NMR spectroscopy.



Scheme 4

Even though both isomerisation reactions obviously proceed without detectable amounts of by-products, the conversion rates are not sufficient for a light-driven uphill (against concentration gradient) transport in a lipophilic membrane. Further studies are devoted to a structurally very similar system in which the isopropylidene group is epoxidized. We recently found reaction conditions under which the photochemical/catalytic switching of this system is very efficient.[11]

Experimental Section

Preparation of the Solutions for the Extraction: The picrate solutions that were used for the extraction experiments were prepared by dissolving dry picric acid in 0.01 M alkali metal hydroxide solutions. To make sure there is no free picric acid in the solution, the pH-value was adjusted to pH 9.0 ± 0.1 by further addition of hydroxide solution after the picric acid had been completely dissolved. Deionized water that was also adjusted to pH 9.0 ± 0.1 by addition of an alkali metal hydroxide solution was used for blank experiments. The 0.01 M ligand solutions were prepared by dissolving 0.121 g (0.250 mmol) of each ligand in chloroform in a 25 mL volumetric flask.

Extraction Experiments: To prepare the extraction experiments, 4 mL of both the ligand solution and the picrate solution were mixed in a 10 mL vial. The cap was closed tightly and the mixture was shaken for one hour on a vertical mechanical shaker at 20 °C. Each value for the association constants was averaged over four identical samples. After phase separation the organic phase was sucked off the vial with a pipette and then filtered through a filter of glass wool. The filtrate was analysed by UV/Vis spectroscopy using 1 cm quartz cells. For the determination of the background in the UV spectrum an identical sample was prepared which contained deionized water adjusted to pH 9.0 instead of the picrate solution. The extraction and workup of the blank sample was carried out as described above for the picrate samples. The picrate concentration was calculated using the Lambert−Beer law. In almost all cases the standard deviation was less than 5%. The only exception was the value for the norbornadiene **2** with sodium (9%).

Catalytic Isomerisation of 1 to 2: For the ring opening reaction of the quadricyclane tetraether **1**, neutral aluminium oxide (50 g) was added to a solution of **1** (1.00 g, 2.07 mmol) in dichloromethane (150 mL). The solvent was completely evaporated under vacuum on a rotary evaporator. The crude product was then eluted in a glass column with dichloromethane (1.5 L). After removing the solvent the product was separated from unchanged quadricyclane by flash liquid chromatography (silica gel, diethyl ether/ethanol 10:1, $R_f = 0.50$). A slightly yellow oil (0.71 g, 1.47 mmol, 71%) was obtained. The ^{1}H NMR spectroscopic data were identical to those previously published.[4]

Photochemical Isomerisation of 2 to 1: A solution of **2** (0.050 g, 0.100 mmol) in dry tetrahydrofuran (5 mL) containing one drop of acetophenone as a sensitizer was put into a quartz tube. The solution was cooled to −30 °C and irradiated with a high-pressure mercury arc lamp (125 W) while a slight stream of nitrogen was passed through the solution. The reaction progress was monitored by TLC (silica gel, diethyl ether/ethanol 10:1, R_f = **1:** 0.46; **2:** 0.50). After the photostationary equilibrium had been reached the solvent was removed under a high vacuum and the ratio of **1** and **2** was determined by ^{1}H NMR spectroscopy (200 MHz, CDCl$_3$). The mixture contained 50% of both starting material and product.

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