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A new tetrapyrazolic macrocycle. Synthesis and its use in extraction and transport of K^+, Na^+ and Li^+

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Abstract—The synthesis of a new tetrapyrazolic macrocyclic structure with a functionalised arm is described. The complexing properties of this new compound towards alkali metal ions (K^+, Na^+, Li^+) were studied by liquid–liquid extraction and liquid membrane transport processes. The extracted and the transport cation percentage were determined by atomic absorption measurements and UV spectroscopy.

1. Introduction

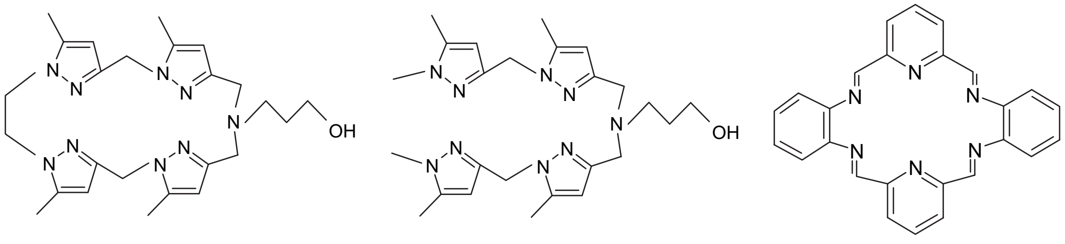
The ability of pyrazole and its derivatives to act as ligands with sp^2 hybrid nitrogen donors is evident from the large number of articles, several of them being reviews.[1,2] In our recent works, a series of acyclic pyrazole compounds containing one, two, three or four pyrazole rings were prepared and demonstrated to extract only transition metal cations[3–6] whereas macrocyclic pyrazolic compounds are expected to also form stable complexes with alkali metals.[7,8]

We now describe the synthesis of a new tetrapyrazolic macrocycle **4** (Fig. 1) containing a mobile chain with a donor heteroatom and its binding ability (extraction and transport) towards alkali metal ions. The presence of a functional mobile chain also provides this structure with the possibility of being immobilised on the surface of a solid material (organic resin or silica gel) by covalent bonding.

2. Results and discussion

Our strategy was to develop a simple and high yielding procedure, in only a few steps, to prepare the desired macrocycle compound. The result of our investigation is given below (Scheme 1). The preparation in good yield of *N*-(3-chloromethyl-5-methylpyrazolyl)-4-methylpyrazolyl methane **2** from 3(5)-carboxymethyl-5(3)-methylpyrazole **1** has been already reported[9] in the literature. The reaction of compound **2** with 3-aminopropanol in THF using sodium bicarbonate as base leads to the tetrapyrazolic structure **3** in a 70% yield. The final cyclisation step was carried out under liquid–liquid phase transfer catalysis conditions and the target macrocycle **4** was formed in a 20% yield.

Structures of all compounds were determined on the basis of the corresponding analytical and spectroscopic data.



4

A[3]

B[10]

Figure 1. New tetrapyrazolic macrocycle **4** and literature compounds **A** and **B**.

Keywords: Macrocycle; Liquid–liquid extraction; Liquid membrane; Transport; Cations.

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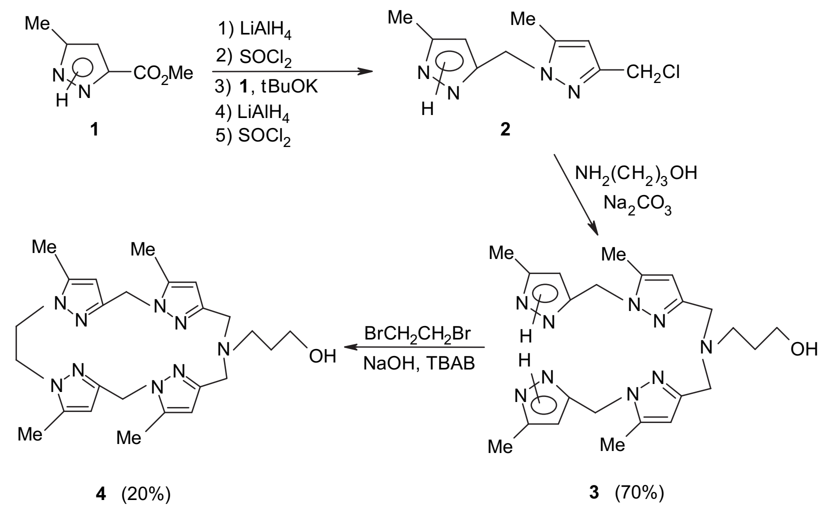

Scheme 1. Preparation steps of compound **4**.

2.1. Liquid–liquid extraction of individual cations

We used this method in order to study the relative capabilities of macrocycle **4** in extracting Li^+, Na^+ and K^+ cations. Metal picrates were extracted into the organic phase by complex formation with the macrocycle; the decrease in absorbance of the picrate in the aqueous phase was followed by UV spectroscopy. The percentage limits of extraction are given in Table 1.

Table 1. Yields of extraction of alkali metal ions

	Potassium (1.33 Å)	Sodium (0.98 Å)	Lithium (0.60 Å)
4	50	38	38
A	0	0	0
B	0	0	0

A: acyclic pyrazolic compound.[3]
B: macrocycle with pyridine-type sp^2 nitrogens.[10]

In order to show that the macrocycle does not simply protonate in the presence of metal picrates, we have determined the extracted cation percentage by atomic absorption measurements and the same results were found.

The results in Table 1 show that in analogy to our previous works[3–8] in which acyclic pyrazolic compound **A** with a weak affinity for alkali cations led to no extraction properties and pyrazolic macrocycles were expected to form stable complexes, again this new macrocycle **4** shows better extraction percentages for alkali cations.

We noticed a high affinity for all alkali metal cations, especially for potassium. This is undoubtedly related to the size of the cavity, which is possibly enlarged at the junctions between pyrazole units. The ionic radii and the flexibility of the macrocycle also enable cation binding with a possible contribution from the side arm.

The complexing power of this pyrazolic macrocycle was attributed to the existence of sp^2 lone pairs forming an electronegative internal cavity. In order to verify this, we compared a known[10] cyclic structure **B**, which possesses pyridine-type sp^2 nitrogens with an internal cavity of a comparable size, with a synthesized macrocycle **4** and it gave negative results regardless of the cation used (Li^+, Na^+ or K^+). This serves to emphasise the novel complexation properties of the macrocycle structures containing linked pyrazole groups, and indicates that the shape of the macrocyclic cavity of **4** must play an important role.

2.2. Transport of individual cations across a membrane

As an extension of the ability of this macrocycle to extract or release (according to the conditions) alkali metal cations, its role as transfer agent across a liquid membrane was studied.

These experiments were performed using the Schulman bridge method.[11] In each case there was no transfer of picrate ion across the membrane in the absence of the macrocycle.

In the presence of macrocycle, the transfer rates were calculated (from the linear part of the curve) and are given in Table 2.

Table 2. Cation transport rates ($\times 10^{-6}$ mol/h) across a liquid membrane

	Potassium (1.33 Å)	Sodium (0.98 Å)	Lithium (0.60 Å)
4	0.23	0.12	0.06

The results in Table 2 show that in analogy to the extraction yield, the potassium cation, which is well extracted (50%), has a higher rate of transport. This means that this cation, which is better extracted also is better transported, one can say that transport is determined by complex lipophilicity.

However, Li^+ and Na^+, which have identical percentage of extraction (38%), have different rates of transport. It is 0.12×10^{-6} mol/h for Na^+ and only half this for Li^+ (0.06×10^{-6} mol/h). This suggests that the stability constant of ligand–cation is higher in the case of lithium than in the case of sodium and consequently the Na^+ is more easily decomplexed in the receiving aqueous phase. We can thus say that the phenomenon of transport for these cations (Li^+ and Na^+) is simply controlled by the decomplexation step.

3. Conclusion

In conclusion, we have prepared a new tetrapyrazolic macrocycle, which has an unusual aptitude for formation of complexes with alkali cations. It has been demonstrated that this macrocycle particularly extracts and transports K^+ ions.

4. Experimental

4.1. General

All solvents and other chemicals, obtained from usual commercial sources, were of analytical grade and used without further purification. The proton NMR spectra were obtained with a Bruker AC 300 spectrometer. Elemental analyses were performed by Microanalysis Central Service (CNRS). Molecular weights were determined on a JEOL JMS DX-300 Mass Spectrometer. Picrate absorbances were measured with a Philips PU 8620 Spectrophotometer. Atomic absorption measurements were performed by Spectra Varian A.A. 400 Spectrophotometer.

4.1.1. Synthesis of 3. A mixture of compound **2**[9] (1.75 g, 7.8×10^{-3} mol), 3-aminopropanol (0.293 g, 3.9×10^{-3} mol) and sodium carbonate (4.96 g, 46.8×10^{-3} mol) in THF (100 mL) was stirred under reflux for 20 h. The mixture was then filtered, evaporated and the residue was separated on alumina using CH_2Cl_2/EtOH (90/10) as eluent to give a 70% yield of **3** as yellow oil. R_f=0.60 CH_2Cl_2/EtOH (9/1); ^1H NMR ($CDCl_3$) δ: 1.82 (m, 2H); 2.22 (s, 6H); 2.26 (s, 6H); 2.74 (t, 2H, J=6.2 Hz); 3.57 (s, 4H); 3.74 (m, 2H); 5.17 (s, 4H); 5.90 (s, 2H); 6.00 (s, 2H). Anal. Calcd for $C_{23}H_{33}N_9O$: C, 61.19; H, 7.31; N, 27.93. Found: C, 61.14; H, 7.40; N, 27.90; m/z: 451 (M^+); IR: ν(OH)=3300 cm^{-1}, ν(NH)=3140 cm^{-1}, ν(tertiary nitrogen)=1120 cm^{-1}.

4.1.2. Synthesis of macrocycle 4. To a mixture of **3** (2.12 g, 4.7×10^{-3} mol) and 1,2-dibromoethane (0.89 g, 4.7×10^{-3} mol) in toluene (500 mL) was added a concentrated solution of NaOH (2 g of NaOH in H_2O (2 mL)). The mixture was stirred under reflux for 20 h in the presence of a catalytic quantity of tetrabutyl ammonium bromide. The resulting mixture was then filtered, evaporated and separated on alumina using CH_2Cl_2/EtOH (95/5) as eluent to give a 20% yield of **4** as yellow oil. R_f=0.40 CH_2Cl_2/EtOH (9.5/0.5); ^1H NMR ($CDCl_3$) δ: 1.79 (m, 2H); 2.24 (s, 12H); 2.66 (t, 2H, J=6.2 Hz); 3.60 (s, 4H); 3.81 (m, 2H); 4.10 (s, 4H); 5.17 (s, 4H); 5.82 (s, 2H); 6.00 (s, 2H). Anal. Calcd for $C_{25}H_{35}N_9O$: C, 62.89; H, 7.33; N, 26.41. Found: C, 62.85; H, 7.35; N, 26.39; m/z: 477 (M^+); IR: ν(OH)=3250 cm^{-1}, ν(C=N)=1615 cm^{-1}, ν(C=C)=1575 cm^{-1}, ν(tertiary nitrogen)=1120 cm^{-1}.

4.2. Extraction experiments

A solution of 7×10^{-5} M of macrocycle in CH_2Cl_2 (50 mL) was stirred for 2 h with an aqueous solution (50 mL) of metal picrates 7×10^{-5} M; the complexation was followed first by measuring the picrate anion concentration in the aqueous phase by UV spectroscopy at 355 nm, second by measuring the concentration of cations in the aqueous phase by atomic absorption. The temperature remained constant during all the experiments at 25 °C and at pH 7 measured by a pH-meter. This was explained by the absence of nitrogen protons in macrocycle and by the low alkalinity and concentration of picrate ions exchanged.

4.3. Transport experiments

The apparatus used in the method of Schulman bridge[11] contains three phases. Phase I: aqueous solution (6 mL) of nitrate (10^{-1} mol/L) and alkali cation picrate (2×10^{-3} mol/L). Phase II: chloroform solution (50 mL) of the product to be studied (7×10^{-4} mol/L). Phase III: distilled water (24 mL).

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