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New tetrapyrazolic macrocycle. Synthesis and preliminary use in metal ion extraction

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Abstract—A new macrocycle containing two bipyrazolic units, with a side-arm bearing an attached donor-group is reported. The complexing properties of this compound towards heavy metal ions (Hg^{2+}, Cd^{2+}, Pb^{2+}) and alkaline metal ions (Ca^{2+}, Cs^{+}, K^{+}, Na^{+}, Li^{+}) was studied by a liquid–liquid extraction process and the extracted cation percentage was determined by atomic absorption measurements and UV spectroscopy.

1. Introduction

For many years, the ability of pyrazole and its derivatives to act as ligands with sp^2 hybrid nitrogen donor have been the research subjects of many coordination chemists. This is evident from the large number of articles, several of them being reviews.[1,2] Moreover, polydentate pyrazolic receptors are well known for their ability to complex not only alkali cations[3–7] but also to form stable complexes with transition metal ions.[8–11] These complexes are so stable that it is often difficult to obtain the free macrocycles from them.

For some time, we have been interested in acyclic pyrazole compounds containing one, two, three or four pyrazole rings, which have the ability to extract only the transition metal cations.[12]

In this paper, we describe the synthesis of a new tetrapyrazolic macrocycle (Fig. 1) containing a mobile chain with a donor heteroatom and its binding ability towards alkali and transition metal ions. It has been found that a donor atom in a side chain of lariat ethers increases the binding ability of the macrocycle.[13–15] Furthermore, structures with side arms attached at a nitrogen (N-pivot lariat ethers) instead of a carbon (C-pivot lariat ethers) have stronger binding properties because of greater flexibility, allowing the donor site to have the best binding position.[16]

Keywords: Tetrapyrazolic macrocycle; Liquid–liquid extraction; Cations.
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2. Results and discussion

Our goal was to find a convenient and high yielding procedure, in few steps, to prepare the desired hydroxy-substituted pyrazole macrocycle. Having inexpensive starting materials was another important requirement. The route used by us to prepare this macrocycle is shown in Scheme 1.

The preparation of 1,3-bis(3-chloromethyl-5-methylpyrazole) propane **2** from 3(5)-carboxymethyl-5(3)-methyl pyrazole[17] **1** has been already reported[18] in our laboratory. The reaction of synthon **2** with 3(5)-carboxymethyl-5(3)-methylpyrazole was carried out under solid-liquid phase transfer catalysis to favour the α-isomer.[17] Thus, one isolated major product **3** in 75% as the αα-isomer was formed. Compound **3** was then converted in the presence of lithium aluminium hydride to give a 80% yield of the hydroxy product **4**. This reaction was followed by the addition of thionyl chloride to compound **4** to give **5** in a 80% yield. In the cyclization step we condensed the chlorinated compound **5** with 3-aminopropanol in acetonitrile under high dilution conditions in order to favour the macrocyclic compound, which was formed in 60% yield.

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

2.1. Liquid–liquid extraction of individual cations

We used this method in order to compare the relative capabilities of macrocycle **6** in extracting Li^{+}, Na^{+}, K^{+}, Cs^{+}, Ca^{2+}, Cd^{2+}, $Pb^{2+}$and Hg^{2+}cations. Metal picrates

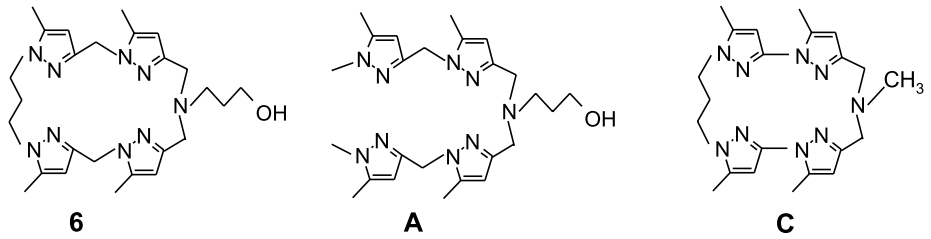


Figure 1. Structures of synthetised tetrapyrazolic macrocycle **6** and of literature compounds **A**[12] and **C**[20].

were extracted into the organic phase by complex formation with the macrocycle, and 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.

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

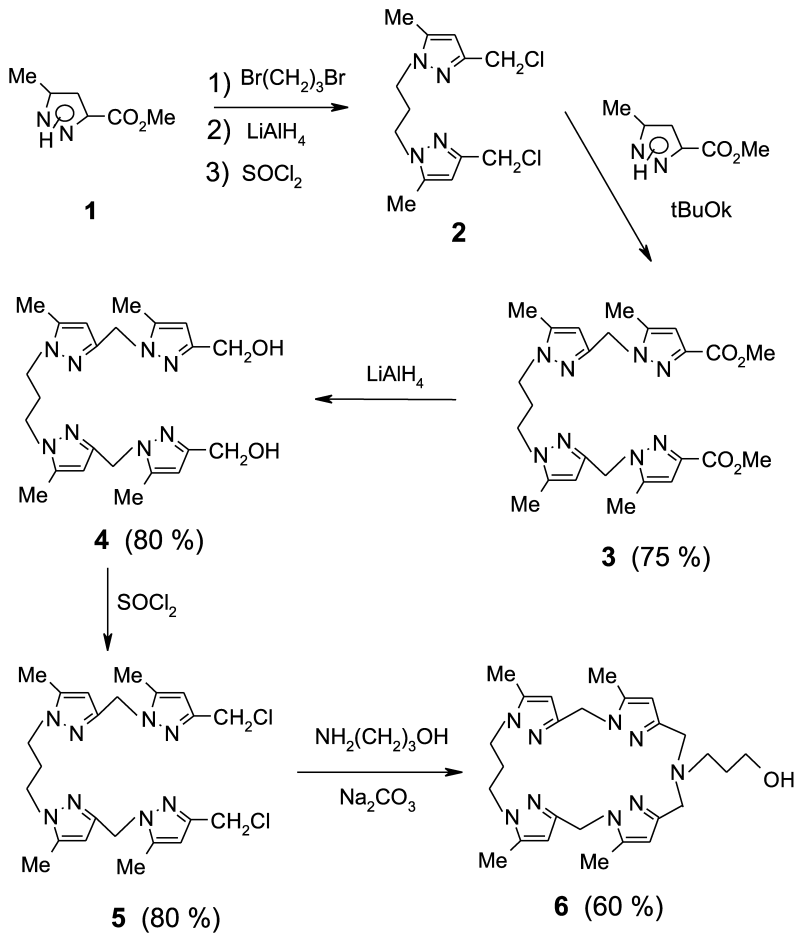
The results in Table 1 show that the comparison with an acyclic pyrazole compound[12] **A** (Fig. 1) which can extract only the transition metal cations and crown-ethers[19] **B** or cryptands which extract only the alkali cations. Macrocycle **6** shows better extraction percentages for alkali cations and for transition metal ions. Only calcium ions are poorly extracted.

We also noticed a high affinity for cesium in the series of alkali cations and a high affinity toward all heavy metal ions. This is undoubtedly related to the size of the cavity possibly enlarged by 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. Moreover, the macrocycle shows high selectivity between Ca^{2+} and other cations.

A possible effect of the lariat arm on the cation binding can be observed by the comparison with a tetrapyrazolic macrocycle[20] **C** (Fig. 1) without donor atoms in the side arm, which shows a different activity.

3. Conclusion

In conclusion, we have prepared a new tetrapyrazolic



Scheme 1.

Table 1. Yields of extraction of various heavy and alkali metal ions

	Mercury (1.10 Å)	Cadmium (0.92 Å)	Lead (1.20 Å)	Calcium (0.99 Å)	Cesium (1.69 Å)	Potassium (1.33 Å)	Sodium (0.98 Å)	Lithium (0.60 Å)
6	60	40	50	6	45	39	39	29
A	55	15	26	0	0	0	0	0
B	0	0	0	0	5	30	2	0
C	—	—	—	—	0	1	25	43

A, acyclic tetra-pyrazole compound[12]; **B**, dibenzo-18-crown-6 ether[19]; **C**, tetrapyrazolic macrocycle compound without donor atoms in the side arm.[20]

macrocycle which has an unusual aptitude for formation of complexes with both alkali and transition metal cations, due to the presence of four donor sp^2 nitrogen atoms in the cavity.

4. Experimental

4.1. General

4.1.1. Syntheses of 3. A mixture of (4.1×10^{-2} mol) of **1** and (4.1×10^{-2} mol) of potassium *tert*-butoxide in 150 ml of THF was stirred under reflux for 30 min. Compound **2** (2×10^{-2} mol) in 100 ml of THF was then added slowly. After stirring under reflux for 6 h, the mixture was filtered, evaporated and the residue was separated on alumina using CH_2Cl_2 as eluant to give a 75% yield of αα-isomer **3** (yellow oil): *Rf*=0.55 (CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ: 2.00 (s, 6H); 2.20 (q, 2H, *J*=7 Hz); 2.30 (s, 6H); 3.83 (s, 6H); 4.00 (t, 4H, *J*=7 Hz); 5.25 (s, 4H); 5.85 (s, 2H); 6.80 (s, 2H). Anal. calcd for $C_{25}H_{32}N_8O_4$: C 59.05, H 6.30, N 22.05. Found: C 59.18, H 6.31, N 22.17; *m/z*: 508 (M^+).

4.1.2. Syntheses of 4. To a solution of $LiAlH_4$ (2.7×10^{-2} mol) in 70 ml of THF was slowly added **3** (1.26×10^{-2} mol) in 100 ml of THF. The mixture was stirred under reflux for 2 h. After cooling, water (1.2 ml), 15% aqueous sodium hydroxide (1.2 ml) and then water (3.6 ml) were added successively to the mixture at 0 °C. The solid material was filtered and the residue was washed with hot THF. The filtrate and THF washings were concentrated under reduced pressure. The residue was passed through a short alumina column (CH_2Cl_2/MeOH, 95:5) to give a 80% yield of **4** (white solid): *Rf*=0.10 (CH_2Cl_2/MeOH, 97:3); mp=69–71 °C (diethyl ether); ^{1}H NMR ($CDCl_3$) δ: 2.10 (s, 6H); 2.25 (bs, 8H); 4.00 (t, 4H, *J*=7 Hz); 4.70 (s, 4H); 5.20 (s, 4H); 5.90 (s, 2H); 6.10 (s, 2H). Anal. calcd for $C_{23}H_{32}N_8O_2$: C 61.06, H 7.08, N 24.78. Found: C 61.08, H 7.11, N 24.77; *m/z*: 452 (M^+).

4.1.3. Syntheses of 5. A solution of thionyl chloride(10 ml) in 15 ml of methylene chloride was slowly added to a compound **4** (3×10^{-2} mol) in 80 ml methylene chloride. This mixture was stirred for 4 h at room temperature. The solvent was removed under reduced pressure and the residue was dissolved in 100 ml of ether. The mixture was then neutralized with about 20 ml of saturated sodium bicarbonate solution and the ether solution was dried over anhydrous sodium sulfate. After evaporating the mixture, the residue was filtred through a short alumina column to give a 80% yield of **5** (yellow oil): *Rf*=0.75 (diethyl ether); ^{1}H NMR ($CDCl_3$) δ: 2.10 (s, 6H); 2.20 (bs, 8H); 4.00 (t, 4H, *J*=7 Hz); 4.50 (s, 4H); 5.20 (s, 4H); 5.90 (s, 2H); 6.10 (s, 2H); *m/z*: 489 (M^+).

4.1.4. Syntheses of macrocycle 6. To a solution of 0.01 mol of sodium carbonate in 1 l of acetonitrile was added slowly and under reflux an equimolar mixture (2×10^{-3} mol) of **5** and 3-aminopropanol in 200 ml of acetonitrile. The mixture was stirred under reflux for 24 h. The solid material was filtered and the filtrate was concentrated under reduced pressure. The residue was purified on alumina using CH_2Cl_2 as eluant to give a 60% yield of **6** (yellow oil): *Rf*=0.42 (CH_2Cl_2/MeOH, 96/4); ^{1}H NMR (DMSO-d_6) δ: 1.65 (m, 2H); 2.10 (m, 4H); 2.15 (s, 6H); 2.20 (s, 6H); 3.20 (s, 4H); 3.35 (m, 2H); 3.85 (t, 4H, *J*=7 Hz); 4.90 (s, 4H); 5.90 (s, 4H). Anal. calcd for $C_{26}H_{37}N_9O$: C 63.54, H 7.53, N 25.66. Found: C 63.58, H 7.51, N 25.67; *m/z*: 520 (MH^+); IR: ν(OH)=3300 cm^{-1}, ν(tertiary nitrogen)=1100 cm^{-1}.

4.2. Extraction experiments

A solution of 7×10^{-5} M of macrocycle in 50 ml of CH_2Cl_2 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 was 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.

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