SHORT PAPER

J. Chem. Research (S),
2003, 712–714

New tetrapyrazolic macrocycle. Synthesis and cation binding properties[†]

Smaail Radi[a*], Abdelkrim Ramdani[a], Yahya Lekchiri[b], Michel Morcellet[c], Grégorio Crini[c] and Ludovic Janus[c]

[a]Laboratoire de Chimie Organique Physique, Département de Chimie, Oujda Maroc

[b]Laboratoire de Biochimie, Département de Biologie, Oujda, Maroc

[c]Laboratoire de Chimie Macromoléculaire, Université des Sciences et Technologies de Lille,
59655 Villeneuve d'Ascq, France

The synthesis of a new tetrapyrazolic macrocyclic structure with a functionalised arm is described. The complexing properties of this new 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. This ligand is able to complex each of these metal ions with yields depending on the nature of the metal.

Keywords: tetrapyrazolic macrocycle, Liquid-liquid extraction, cation

For many years, pyrazole and its derivatives as ligands with an sp^2 hybrid nitrogen donor have been researched, as 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 property to extract only the transition metal cations.[12]

In this paper we describe the synthesis and behaviour of a new hydroxy-substituted macrocycle (Fig. 1) containing two bidentate bipyrazolic entities towards alkali and transition metal ions.

Results and discussion

Our strategy was to develop a simple and convenient method for obtaining the macrocycle compound. The result of our investigation was given below (Scheme 1): The preparation of 1,1-bis(3-chloromethyl-5-methylpyrazole) methane **2** from 3(5)-carboxymethyl-5(3)-methylpyrazole **1**[13] has been already reported[14] in our laboratory. The reaction of synthon **2** with 3(5)-carboxymethyl-5(3)-methylpyrazole using potassium *tert*-butoxide as base yielded after 6 hours one isolated major product **3** in 75 % yield. Compound **3** was then converted in the presence of lithium aluminium hydride to give an 80 % yield of the hydroxy product **4**. This reaction was followed by the addition of **4** in thionyl chloride to give **5** in a 80% yield. In the cyclising step we condensed the chlorinated compound **5** with 3-aminopropanol in acetonitrile under high dilution in order to favour the macrocycle compound which was formed in 50 % yield.

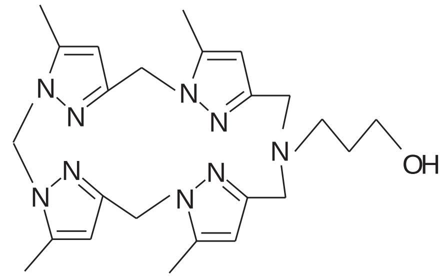


Fig. 1

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

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 were extracted into the organic phase by complex formation with the macrocycle; the decrese 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.

Results in Table 1 show that in contrast to acyclic pyrazole compounds, which have the property to extract only the transition metal cations, and crown-ethers or cryptands, which extract only the alkali cations, our macrocycle show better extraction percentages for alkali cations as well as for transition metal ions except for calcium.

We also notice a high affinity for potassium and sodium 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 formed by (Pz)C–CH_2–N(Pz) junctions, the ionic radii and the flexibility of macrocycle to bind easily the cation with a possible contribution of a side arm. Moreover, the macrocycle shows high selectivity between Ca^{2+} and any of other cations.

In conclusion, we have prepared a new tetrapyrazolic macrocycle which has an unsual aptitude for formation of complexes with alkali and transition metal cations, due to the presence of four donor sp^2 nitrogen atoms in the cavity.

Experimental

Synthesis of **3:** A mixture of (4.1×10^{-2} mole) of **1** and (4.1×10^{-2} mole) of potassium *tert*-butoxide in 150 ml of THF was stirred under reflux for 30 min. Compound **2** (2×10^{-2} mole) 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

---

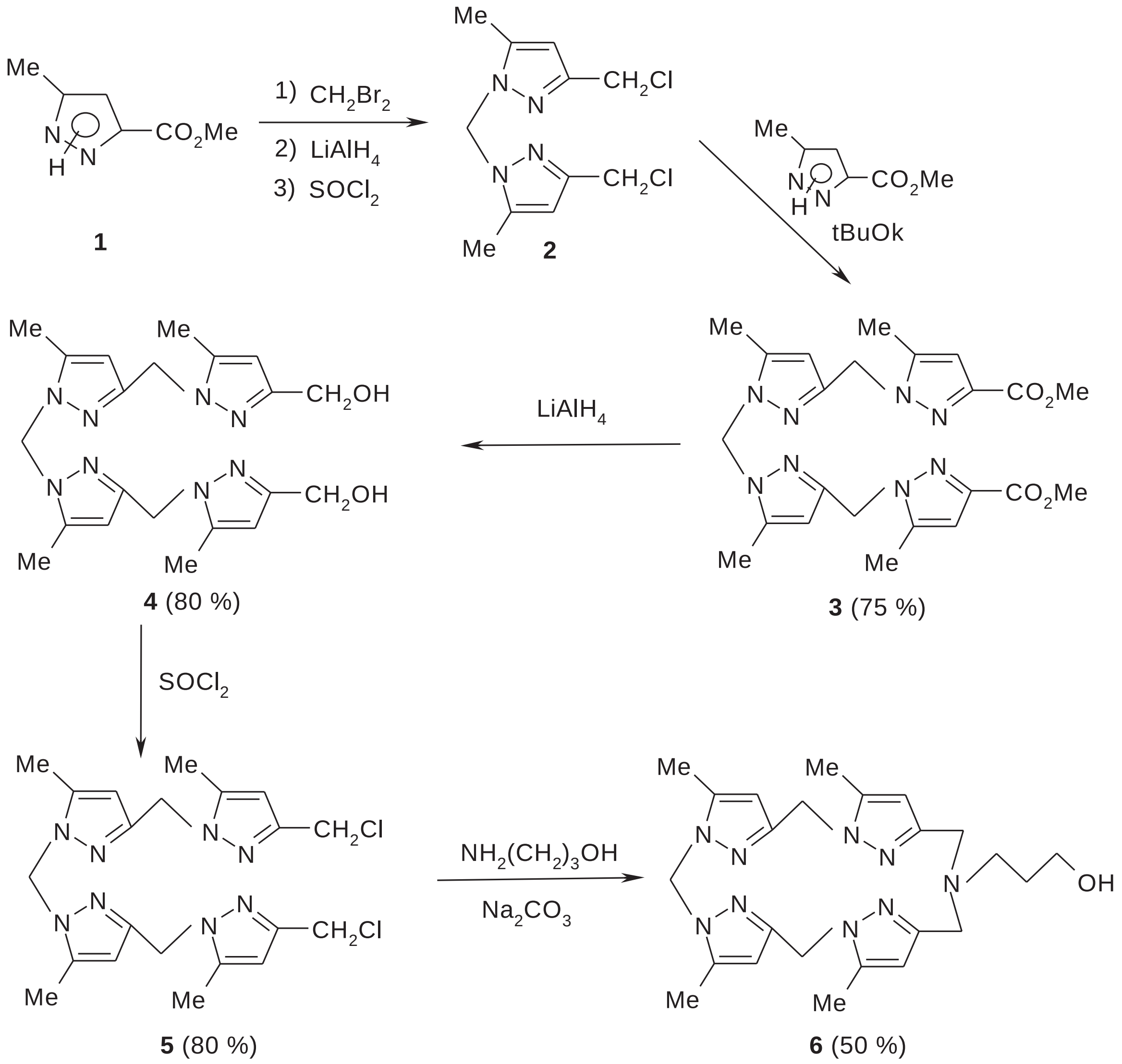
[*] To receive any correspondence. E-mail: radi@sciences.univ-oudja.ac.ma

[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

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

	Mercury	Cadmium	Lead	Calcium	Cesium	Potassium	Sodium	Lithium
	(1.10 Å)	(0.92 Å)	(1.20 Å)	(0.99 Å)	(1.69 Å)	(1.33 Å)	(0.98 Å)	(0.60 Å)
6	59	46	50	5	50	40	36	25
A	55	15	26	0	0	0	0	0

A = acyclic tetra-pyrazole compound.[12]



Scheme 1

CH_2Cl_2 as eluant to give a 75 % yield of the ∝∝-isomer **3**: Rf = 0.40 (CH_2Cl_2); F = 88–90°C (diethyl ether); ^1H NMR ($CDCl_3$) δ: 2.30(s,6H); 2.43(s,6H); 4.00(s,6H); 5.36(s,4H); 6.00(s,2H); 6.20(s,2H); 6.70(s,2H); *m/z*: 480 (M^+).

Synthesis of **4:** To a solution of $LiAlH_4$ ($2.7.10^{-2}$ mole) in 70 ml of THF was slowly added ($1.26.10^{-2}$ mole) of **3** in 100 ml of THF. The mixture was stirred under reflux for 2 h. After cooling, 1.2 ml of water, 1.2 ml of 15% aqueous sodium hydroxide, and then 3.6 ml of water 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**: Rf = 0.10 (CH_2Cl_2/MeOH, 96/4); ^1H NMR ($CDCl_3$) δ: 2.30(s,6H); 2.43(s,6H); 3.47(s,4H); 5.30(s,4H); 5.90(s,2H); 6.15(s,2H); 6.60(s,2H); *m/z*: 424 (M^+).

Synthesis of **5:** A solution of 10 ml of thionyl chloride in 15 ml of methylene chloride was slowly added to a compound **4** (3×10^{-2} mole) 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 neutralised 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**: Rf = 0.70 (diethyl ether); F = 135–139°C (diethyl ether); ^1H NMR ($CDCl_3$) δ: 2.00(s,6H); 2.10(s,6H); 3.70(s,4H); 4.30(s,4H); 5.56(s,2H); 5.83(s,4H); *m/z*: 461 (M^+).

Syntheses of macrocycle **6:** To a solution of 0.01 mole of sodium carbonate in 1 litre of acetonitrile was added slowly and under refluxing an equimolar mixture (2×10^{-3} mole) 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 CH_2Cl_2 using as eluant to give a 50 % yield of **6**: Rf = 0.33 (CH_2Cl_2/MeOH, 96/4); ^1H NMR (DMSO-d_6) δ: 1.80(m,2H); 2.15(m,2H); 2.25(s,6H); 2.40(s,6H); 3.20(s,4H); 3.35(m,2H); 5.00(sl,4H); 5.80(s,2H); 6.00(s,2H); 6.10(s,2H); Anal. Calc. for $C_{24}H_{33}N_9O$: C 62.20, H 7.13, N 27.21, Found: C 62.18, H 7.11, N 27.17; *m/z*: 464 (MH^+) (FAB > 0); IR: ν(OH)=3300cm^{-1}, ν(azote tertiaire)=1100cm^{-1}.

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 maintained constant at 25°C and pH 7 during all the experiments.

Received 23 June 2003; accepted 26 August 2003
Paper 03/1989

References

1 S. Trofimenko, *Chem. Rev*. 1972, **72**, 497.
2 S. Trofimenko, *Progr. Inorg. Chem.*, 1986, **34**, 115.
3 B. Lupo and G. Tarrago, *Bull. Soc. Chim. Fr*., 1984,473.
4 A. Ramdani and G. Tarrago, *Tetrahedron*, 1981, **37**, 987.
5 M. Gal, G. Tarrago, P. Steel and C. Maezin, *New J. Chem*., 1985, **9**, 617.
6 S. Boudouche, C. Coquelet, L. Jacquet, C. Marzin, R. Sandeaux and G. Tarrago, *J. Inclusion Phenom*., 1993, **16**, 69.
7 F. Malek, M. Persin, A. Ramdani, J. Sarrazin and I. Zidane, *New J. Chem.*, 2002, **26**, 876.
8 J. Elguero, M. Espada, A. Ramdani and G. Tarrago, *J. Heterocyc. Chem*., 1980, **17**, 137.
9 C. Marzin, G. Tarrago, G. Gal, I. Zidane, T. Hours, D. Lerner, C. Andrieux, H. Camp and J.M. Saveant, *Inorg. Chem*., 1986, **25**, 420.
10 J.E. Bol, B. Mars, G. Gonesh, W.L. Driessen, K. Goubitz and J. Reedijk, *Heterocycles*, 1997, **45**, 1477.
11 F. Mary, C. Marzin, S. Salhi and G. Tarrago, *Supramol. Chem*., 1993, **3**, 57.
12 S. Radi, A. Ramdani, Y. Lekchiri, M. Morcellet, G. Crini, J. Morcellet and J. Janus, *European Polymer J.*, 2000, **36,** 1885.
13 J. Fifani, A. Ramdani and G. Tarrago, *New J. Chem*., 1977, **1**, 521
14 S. El Kadiri, G. Tarrago, C. Marzin and C. Coquelet, *New J. Chem*., 1991, **15**, 677.