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Preparation of pyrazole compounds for attachment to chelating resins

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Abstract

Several new pyrazole ligands have been prepared for use in the separation of metal ion from aqueous solution. These hydroxy-substituted pyrazole compounds were covalently bonded to a macroreticular styrene-divinylbenzene (1%) copolymer. The structure of the functionalized resins was confirmed by IR spectrophotometry and elemental analysis. The complexation behavior of these pyrazole resins was investigated towards Pb(II), Hg(II), Cd(II), Ca(II), Cs(I), K(I), Li(I) and Na(I) ions in aqueous solution by a batch equilibration technique. Polymers can be regenerated by washing with a solution of hydrochloric acid (6 N).

1. Introduction

There has been considerable interest in the design of heterocyclic compounds for the selective complexation and separation of metal ions. One of the major problems in using the solvent extraction and liquid membrane systems is keeping the ligand in the organic phase.

In recent years there has been an increased interest in the metal complexation behavior of polymer-supported ligands as analytical reagents, catalysts and in pollution control.

Various functional groups such as thiols [1–3], pyridine [4], pyridine derivatives [5–8], cyclame [9–11], 8-hydroxyquinoline [12], dioxime [13], polyamine [14], 2-mercaptobenzothiazole [15], bicine [16], glycol chains [17] have been immobilized, mainly on styrene-divinylbenzene copolymer and also on glycidyl methacrylate-divinylbenzene copolymer, phenol-formaldehyde resins, and cellulosic materials.

The chemistry of the pyrazole compounds polymer has not yet been developed, although there has been a recent work concerning pyrazolone [18] attached to styrene-divinylbenzene copolymer in which some metal ion separation was observed.

This paper reports the synthesis of various hydroxy-substituted pyrazole compounds which are expected, according to literature [19], to exhibit good complexing properties toward both hard and soft metals (see Scheme 1). These pyrazole compounds have been immobilized on a polymer matrix in order to prepare a series of pyrazole bound Merrifield resins. A preliminary study of the separation of some metal ions using these materials is presented.

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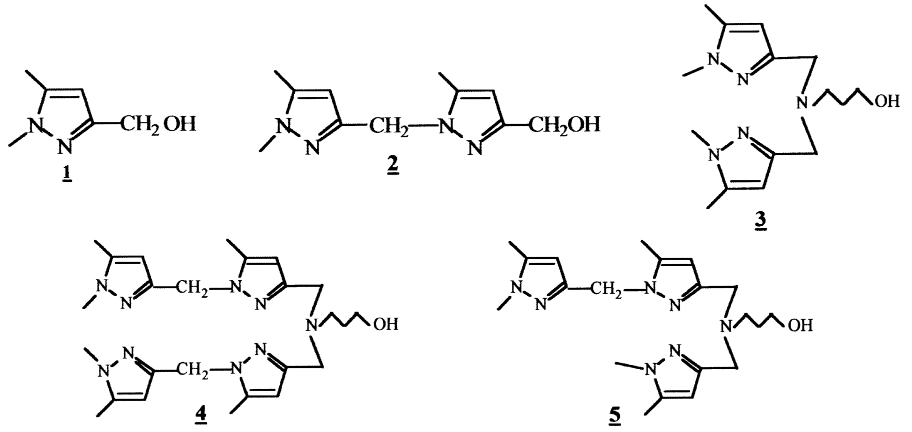


Scheme 1. Pyrazole compounds.

2. Experimental

2.1. Chemicals and apparatus

IR spectra were obtained on a Perkin-Elmer PE 1310 spectrometer. The proton NMR spectra were obtained with a Bruker AC 300 spectrometer. The ^{13}C-NMR spectra were obtained by courtesy of the G. Ronzoni Institute in Milano, Italy. Elemental analysis were performed by Microanalysis Central Service (CNRS). Molecular weights were determined on a JEOL JMS DX-300 Mass Spectrometer. Atomic absorption spectroscopy was performed on a Spectra Varian AA 400 Spectrometer and on a Vision 2000 Spectrometer (CNRS). Starting materials were purchased from commercial sources. 3-hydroxymethyl 1,5-dimethylpyrazole **1**; 3-chloromethyl 1,5-dimethylpyrazole **6** and 3(5)-carboxymethyl 5(3)-methylpyrazole **7** were prepared as reported by Tarrago and co-workers [20].

2.2. Synthesis

2.2.1. N,N-[3-(1,5-dimethylpyrazolyl)methyl] 3-aminopropanol *3*

To a mixture of compound **6** (6.0 g, 4.1×10^{-2} mol) and sodium carbonate (17.0 g, 16×10^{-2} mol) in 150 ml of acetonitrile was added slowly 1.55 g (2.0×10^{-2} mol) of 3-aminopropanol. The mixture was stirred under reflux for 12 h. The solid material was filtered and the filtrate was concentrated under reduced pressure. The residue was purified on alumina using 99/1 CH_2Cl_2/MeOH as eluant to give a 70% yield of **3** as viscous oil: ^{1}H-NMR ($CDCl_3$) δ 1.72 (*m*, 2H), 2.20 (*s*, 6H), 2.68 (*t*, 2H), 3.58 (*s*, 4H), 3.70 (*s*, 6H), 3.72 (*t*, 2H), 6.01 (*s*, 2H); $MH^+ = 292$ (FAB > 0).

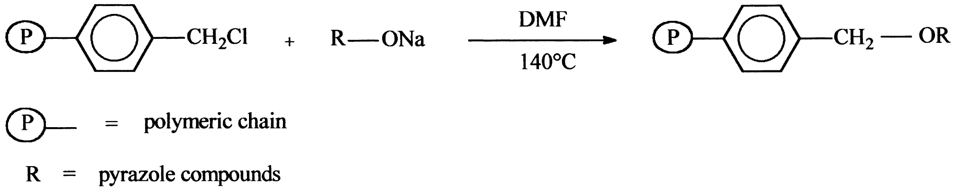
2.2.2. 3-carbomethoxy 1′,5,5′-trimethyl 1,3′-dipyrazolylmethane *8*

A mixture of 8 g (5.2×10^{-2} mol) of **7** and 5.9 g (5.2×10^{-2} mol) of potassium *tert*-butoxide in 150 ml of THF was stirred under reflux for 30 min. Compound **6** (7.5 g, 5.2×10^{-2} mol) in 100 ml of THF was then added slowly. After stirring under reflux for 12 h, the mixture was filtered, evaporated and the residue was separated on alumina using CH_2Cl_2 as eluant to give a 70% yield of α-isomer **8** and a 15% yield of β-isomer. The spectral properties for α-isomer **8** are as follows: ^{1}H-NMR ($CDCl_3$) δ 2.20 (*s*, 3H), 2.30 (*s*, 3H), 3.70 (*s*, 3H), 3.87 (*s*, 3H), 5.30 (*s*, 2H), 5.85 (*s*, 1H), 6.50 (*s*, 1H); $MH^+ = 249$ (FAB > 0).

The spectral properties for β-isomer are as follows: ^{1}H-NMR ($CDCl_3$) δ 2.30 (*s*, 3H), 2.40 (*s*, 3H), 3.68 (*s*, 3H), 4.40 (*s*, 3H), 5.65 (*s*, 2H), 6.00 (*s*, 1H), 6.60 (*s*, 1H); $MH^+ = 249$ (FAB > 0).

2.2.3. 3-hydroxymethyl 1′,5,5′-trimethyl 1,3′-dipyrazolylmethane *2*

A solution of compound **8** (6 g, 2.3×10^{-2} mol) in 100 ml of THF was slowly added to a stirred solution of 1 g of lithium aluminium hydride in 70 ml of THF at 0°C. The mixture was stirred under reflux for 2 h. After cooling, 1 ml of water, 1 ml of 15% aqueous sodium hydroxide, and then 2 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 85% yield of 2: ^{1}H-NMR ($CDCl_3$) δ 2.10 (*s*, 3H), 2.20 (*s*, 3H), 3.60 (*s*, 3H), 4.50 (*s*, 2H), 4.87 (*s*, 2H), 5.05 (*s*, 1H), 5.78 (*s*, 1H), 6.05 (*s*, 1H); $MH^+ =$ 221 (FAB > 0).



Scheme 2. Synthetic pathway for the coupling of the pyrazole derivatives to the polymer matrix.

*2.2.4. 3-chloromethyl 1′,5,5′-trimethyl 1,3′-dipyrazolylmethane **9***

A solution of 5 ml of thionyl chloride in 15 ml of methylene chloride was slowly added to a compound **2** (3 g, 13.6×10^{-3} mol) in 80 ml of 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 filtered through a short alumina column to give a 80% yield of **9**: ^{1}H-NMR ($CDCl_3$) δ 2.20 (*s*, 3H), 2.26 (*s*, 3H), 3.72 (*s*, 3H), 4.65 (*s*, 2H), 5.20 (*s*, 2H), 5.95 (*s*, 1H), 6.10 (*s*, 1H).

*2.2.5. Preparation of **4** from **9***

Compound **4** was prepared as above for **2** to give a 70% yield of an oil: ^{1}H-NMR ($CDCl_3$) δ 1.80 (*m*, 2H), 2.15 (*s*, 6H), 2.25 (*s*, 6H), 2.80 (*t*, 2H), 3.70 (*sl*, 10H), 3.75 (*m*, 2H), 5.15 (*s*, 4H), 5.35 (*s*, 2H), 5.75 (*s*, 2H); MH^+ = 480.3 (FAB > 0).

*2.2.6. Preparation of **10***

A mixture of **9** (13×10^{-3} mol) and 3-aminopropanol in ratio 1:5 in 50 ml of acetonitrile was added to a sodium carbonate (65×10^{-3} mol) in 50 ml of acetonitrile. The resulting mixture was stirred at room temperature for 24 h. After filtering and evaporating, the residue was chromatographed on alumina using 97/3 CH_2Cl_2/MeOH as eluant to give a 75% yield as viscous oil: ^{1}H-NMR ($CDCl_3$) δ 1.75 (*m*, 2H), 2.15 (*s*, 3H), 2.20 (*s*, 3H), 2.75(*t*, 2H), 3.70 (*sl*, 7H), 5.30 (*s*, 2H), 5.75 (*s*, 1H), 5.95 (*s*, 1H); MH^+ = 278 (FAB > 0).

*2.2.7. Preparation of **5***

A mixture of **10** (13×10^{-3} mol) and **6** (13×10^{-3} mol) in 100 ml of acetonitrile in the presence of sodium carbonate (65×10^{-3} mol) as base was refluxed for 6 h. The resulting mixture was filtered, evaporated and purified to give a 65% yield of **5**: ^{1}H-NMR ($CDCl_3$) δ 1.85 (*m*, 2H), 2.15 (*s*, 3H), 2.25 (*s*, 3H), 2.35 (*s*, 3H), 2.70 (*m*, 2H), 3.75 (*sl*, 12H), 5.25 (*s*, 2H), 5.85 (*s*, 1H), 6.15 (*s*, 1H), 6.30 (*s*, 1H); MH^+ = 386 (FAB > 0).

2.3. Binding to Merrifield resins

The chloride content (3.73 wt%) in the starting Merrifield resin was determined by elemental analysis, corresponding to an exchange capacity of 1.05 mmol g^{-1}. Different routes were tried for the coupling of the pyrazole compounds by using: (i) sodium hydride in dimethylformamid [21]; (ii) potassium hydroxide in water using tetrabutylammonium hydrogenosulfat as catalyst [22]; (iii) potassium carbonate in dimethylformamid (Williamson reaction) [23] giving poor yields (see Scheme 2). Thus, the pyrazole compounds (**1**–**5**) were converted into the alcoolate salt derivative using equimolar amounts of sodium metal in tetrahydrofuran. The alcoolates were able to bind to the Merrifield resin by a nucleophilic substitution reaction SN_2.

2.4. Batch experiments

The complexation of pyrazole resins was carried out with Hg(II), Cd(II), Pb(II), Ca(II), Cs(I), K(I), Na(I) and Li(I) ions by batch equilibration method. Pyrazole resins (0.1 g) were shaken with different metal solutions (5 ml) containing 6.48×10^{-3} M of metal ions. Each solution was stirred for 24 h at 25°C. The final solution was filtered and the concentration of metal ions released was determined by Atomic Absorption Spectrometry. Commercially available reagent-grade chemicals and distilled, deionized water were used in all experiments.

3. Results and discussion

3.1. Synthesis of the pyrazole compounds

Our goal was to find a convenient and high yielding procedure, in few steps, to prepare the desired hydroxy-substituted pyrazole compounds. Having inexpensive starting materials was another important requirement. The routes used by us to prepare the pyrazole compounds are shown in Scheme 3.

Compounds **2** was prepared in an 85% yield by reacting 3-chloromethyl 1,5-dimethylpyrazole **6** with 3(5)-carboxymethyl 5(3)-methylpyrazole **7** [20] using potassium *tert*-butoxide as base to give a good yield of α-isomer **8**. Compound **8** was then converted in the presence of lithium aluminium hydride to give a 85% yield of the hydroxy product **2** (Scheme 3).

Compounds **3** was obtained in a 70% yield by reacting the chloro derivative **6** with commercially available 3-aminopropanol in ratio 2:1 under reflux using sodium carbonate as base.

As shown in Scheme 3, we have prepared **4** in a 70% yield in similar procedure as above for **3** from **6**, by reacting 3-aminopropanol with **9**. This latter compound was prepared from **2** using thionyl chloride.

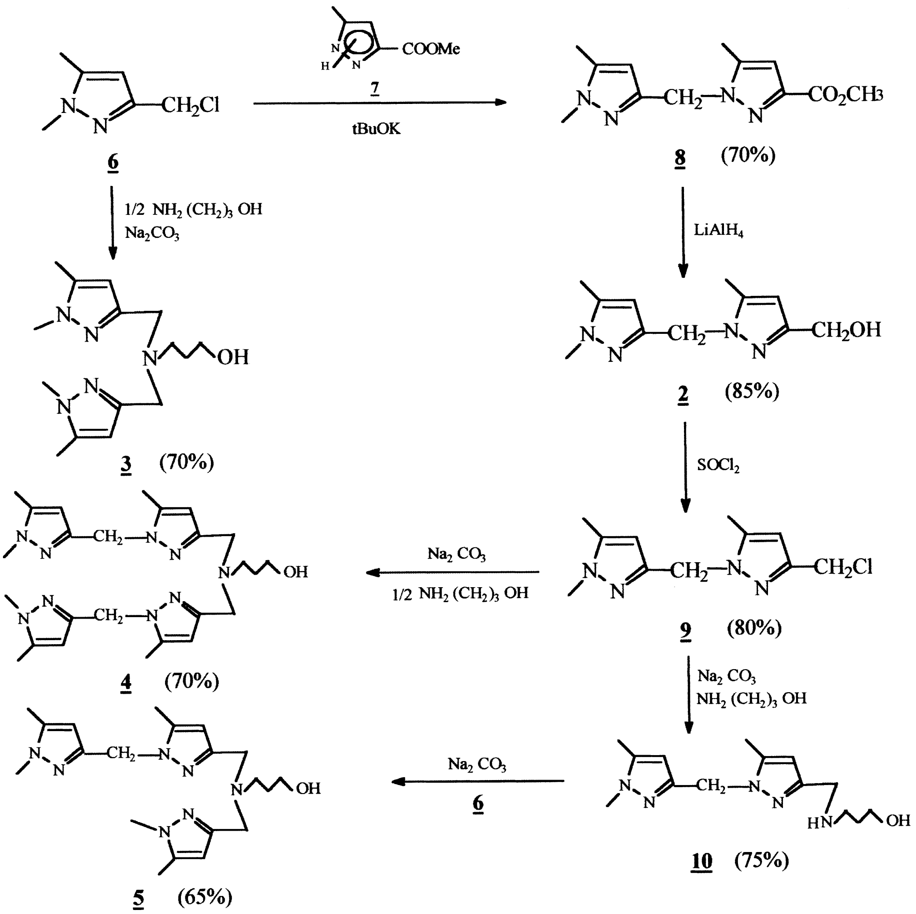
The first step in the preparation of compound **5** was the reaction of **9** with an excess of 3-aminopropanol at room temperature to form a mono-alkylation group **10** in a 75% yield. This reaction was followed by the addition of **6** in sodium carbonate as base to give **5** in a 65% yield.

Samples **1**–**5** were characterized by IR spectroscopy, mass spectra, proton and carbon NMR spectra. Figs. 1–3 show as an example the spectra obtained for compound **4**. The IR spectrum shows a typical C=N band at 1540 cm^{-1}.

3.2. Characterization of resins

IR spectrophotometry and elemental analysis were used to characterize all the resins. The IR spectrum of the native Merrifield resin exhibit a band at 1260 cm^{-1} typical of the C–Cl bond which disappears during substitution of the resin. A strong band at about 1150 cm^{-1} assigned to the ν (C–O–C) appears in all the spectra of P_1–P_5 polymers (see Fig. 4)

From the elemental analysis of nitrogen, the amount of pyrazole grafted and the yield of grafting were obtained. For the P_5 sample, the amount of nitrogen was very low and the figures were based on the carbon percentage giving somewhat approximate results. Nevertheless, it appears clearly that the yield of graft-



Scheme 3. Preparation of pyrazole compounds

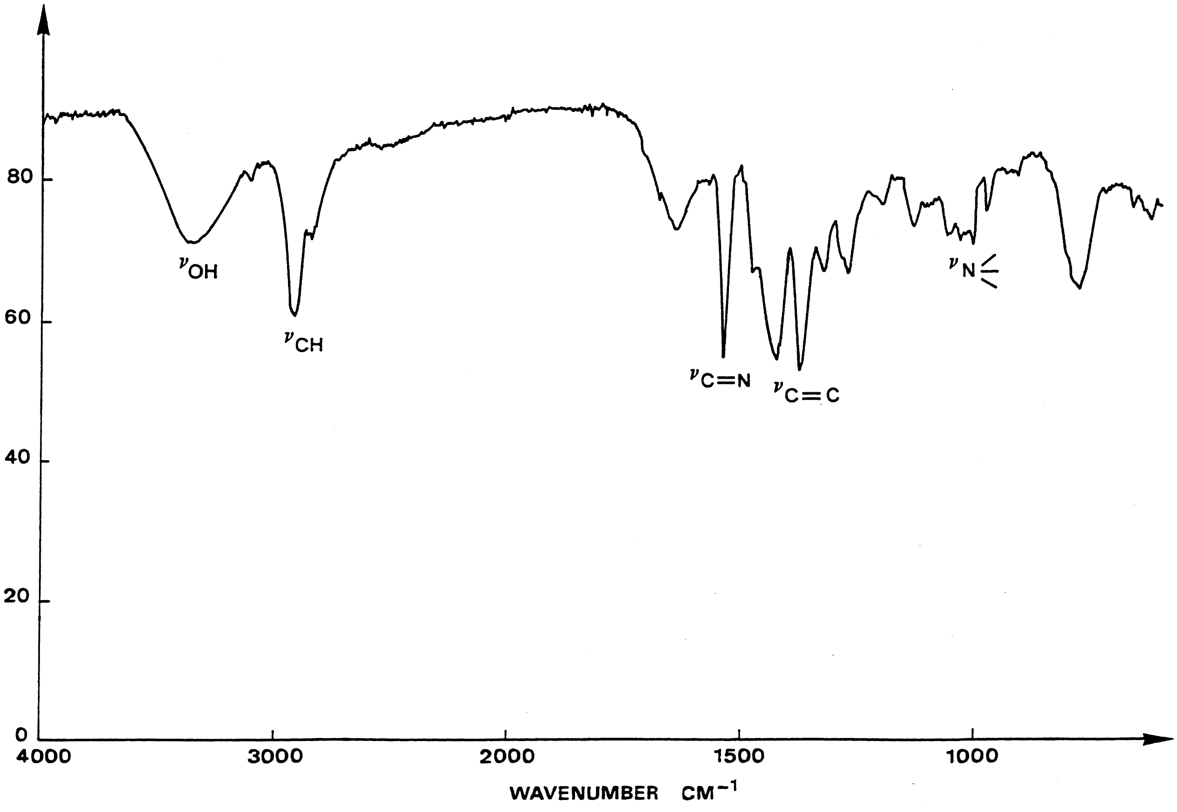


Fig. 1. Infrared spectrum of compound **4**.

ing decreases when increasing the number of pyrazole rings (see Table 1). This is undoubtedly an effect of steric hindrance. In fact, when using a rather long spacer group, the yield of grafting becomes independent on the nature of the pyrazole compound [24].

3.3. Complexation with metal ions

As described in Section 2, the complexing properties of the resins towards different metal ions were evaluated by the batch method. It was checked that the native Merrifield resin was unable to bind the metal ions under study, even by physical sorption (see Table 2). Whatever the metal is, the complexation yield is maximum for the P_4 compound which has the larger amount of nitrogen complexing group and is also the more symmetrical. For a given resin, the ability to complex decreases from mercury to cadmium and lead, when considering the transition metal ions. The affinity of nitrogen for mercury and cadmium is well known. The results for lead are slightly more surprising though polymeric amines were reported to bind it [25]. The symmetry of the complexing unit P_4 seems to be of importance in this case.

Table 1
Elemental analysis

Polymer	P_1	P_2	P_3	P_4	P_5
N (%)	1.15	1.01	1.37	1.38	Very low
C (%)	90.14	90.01	90.50	89.14	89.56
Ligand: µmol/g of support	410	181	196	109	42[a]
Yield of grafting[b]	39	17	18	10	4

[a] Calculated on the basis of the carbon content.

[b] Calculated on the basis of the chloride content of the resin.

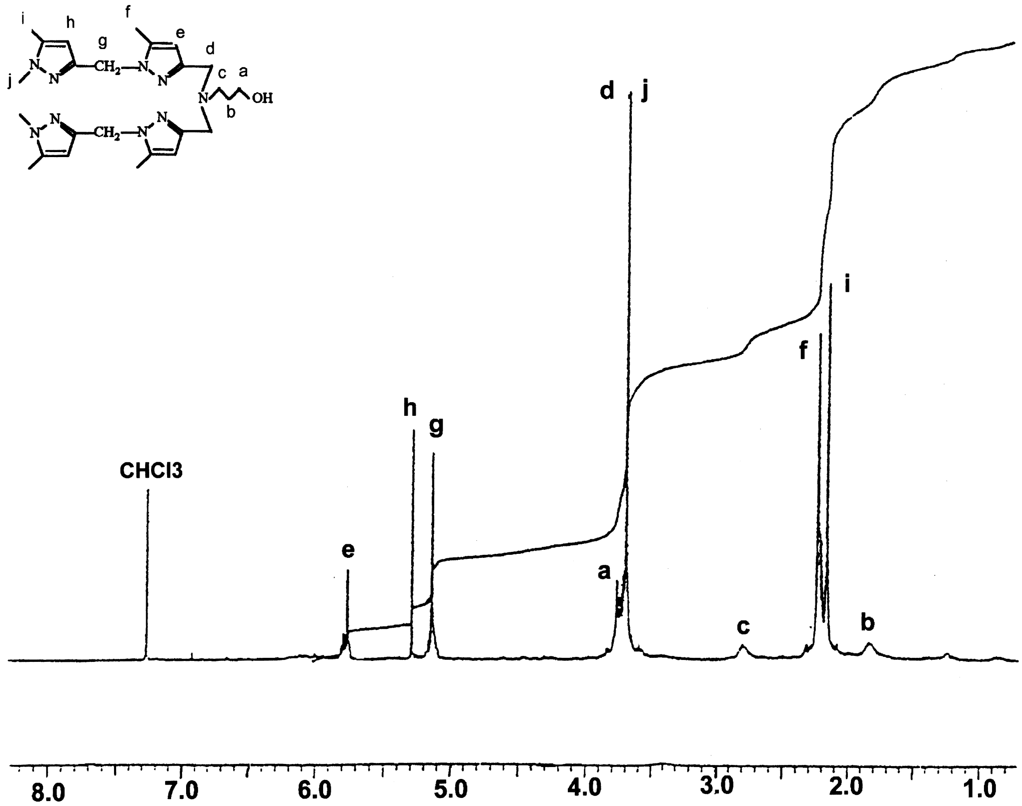


Fig. 2. 250 MHz proton NMR spectrum of compound **4**.

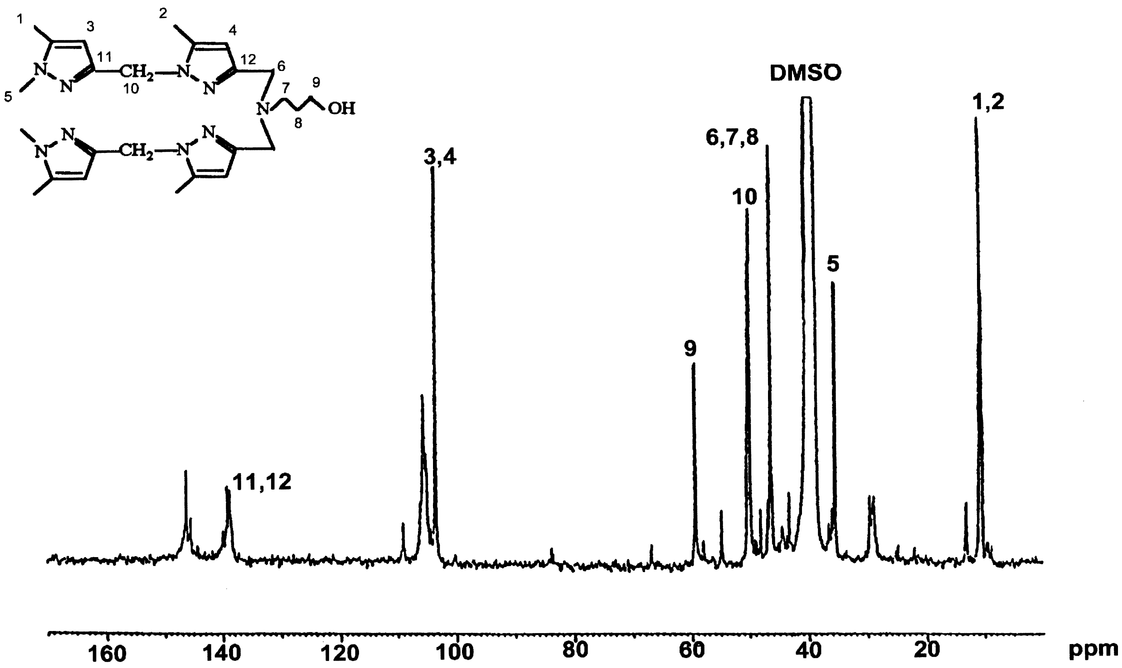


Fig. 3. ^{13}C-NMR spectrum of compound **4**.

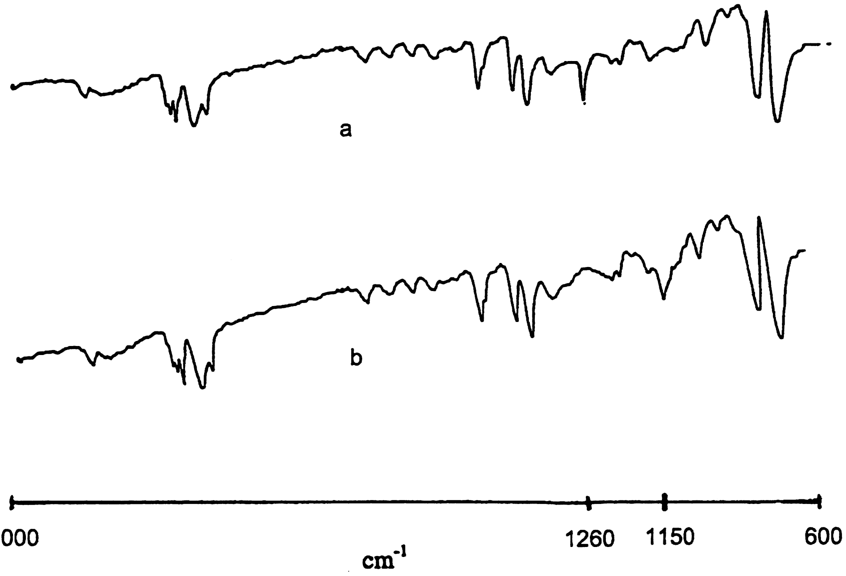


Fig. 4. Infrared spectra of (a) pyrazole free Merrifield resin; (b) P_3 resin.

Among the monovalent alkaline metal ions, sodium to fit the more easily in the cavity of the P_4 derivative. The results reported in Table 2 may be compared to those obtained for analog unbound pyrazole ligands [26] in liquid–liquid extraction process. The order $P_1 < P_2 < P_3 > P_4 > P_5$ was also found in this case and the efficiency also decreased from mercury to cadmium and lead. Thus, the complexing properties of the pyrazole ligands are not affected by the binding to a polymer matrix. This is an interesting result from the practical point of view since filtration is a very simple separation procedure. Concerning the alkali metal ions, the unbound pyrazole ligands revealed unable to bind them. Thus a matrix effect can be suspected.

In conclusion, some of the pyrazole bound systems presented here seem to exhibit some selectivity between different metal ions, for example P_3 towards mercury and lead or P_3 and P_5 towards sodium and potassium. Nevertheless, a more conclusive interpretation needs a more detailed investigation of the binding properties through, for example, the sorption isotherms. Such a study is in progress together with flow sorption experiments.

Table 2
Adsorption activity of pyrazole resins

	Complexation yield (%) (capacity in μmol metal/g resin)							
Resin	Hg(II)	Cd(II)	Pb(II)	Cs(I)	Ca(II)	K(I)	Na(I)	Li(I)
P_0	0	0	0	0	0	0	0	0
P_1	14	6	0	0	0	0	0	0
	57	25						
P_2	30	3	0	0	0	15	20	
	54	5.5				27	36	
P_3	40	20	15	0	0	0	15	0
	78	39	29				29	
P_4	52	20	25	0	0	15	30	0
	57	22	27			16	33	
P_5	35	10	10	0	0	0	25	0
	22	9	9				11	

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