Physico-chemical Behaviour of Newly Synthesized Macrocyclic Compounds

A reality between expectations and experimental evidences

ALINA-GIORGIANA NEGRU[1], **CECILIA ARSENE**[1], **ANA-MARIA ZBANCIOC**[1,2], **IONEL I. MANGALAGIU**[1]*, **ROMEO IULIAN OLARIU**[1]*
[1]"Alexandru Ioan Cuza" University of Iasi, Faculty of Chemistry, 11 Carol I Blvd., 700506, Iasi, Romania
[2] University of Medicine and Pharmacy "Grigore T. Popa", Faculty of Pharmacy, 16 Universitatii Str., 700115, Iasi, Romania

Three newly synthesized macrocyclic amidic compounds have been tested for their potential to act as chelators for various metals. Spectroscopic (Fourier-Transformed-Infrared-Spectroscopy, fluorescence, UV-Vis absorption) and electrometric (conductometry) techniques have been used to characterize the chelating potential of the newly synthesized macrocyclic compounds towards metals such as Ag, Al, Ca, Cd(II), Co(II), Cr(III), Cu(II), Fe(III), Mg, Mn(II), Ni(II), Pb(II) and Zn. Experimental investigations have been undertaken at M:L or L:M ratios of 1:1, 1:2, 1:3 and 1:4. From the interest potential chelators only for one macrocyclic amidic compound some experimental evidences have been obtained for its possible implication in silver ions chelatization both in methanol (MeOH) and methanol-dimethyl sulphoxide (MeOH-DMSO) binary systems.

Keywords: macrocyclic amidic compounds, chemosensors, silver ions, chelators

Nowadays researchers interest to develop new sensitive, selective and rapid methods for the determination and removal of toxic metals from the environment has enhanced [1]. Development and application of chemical sensors for the detection of heavy metal ions, even at trace levels, is a modern research topic [2-3]. Molecular receptors based on crown ethers are well known complexing agents especially for heavy metal cations [4-5]. In addition, macrocyclic compounds containing azo moiety are another important class of molecular receptors [6-7]. Supramolecular chemistry offers wide possibilities for azobenzocrowns functionalization, lipophilic crowns being successfully applied as ionophores in order to obtain miniaturized ion-selective membrane electrodes [8]. Some azoarylcrown ethers may act as chelators with good selectivity for binding metal ions in solution and, usually, the cation-ligand interactions are well illustrated by changes in the UV-Vis spectra [9]. It has been shown that changing the structure of some azobenzocrown ethers may induce favourable processes responsible on the formation of compounds with chromoionophore and fluoroionophore properties [10]. Synthesis of amides-based supramolecular systems has been reported, neutral macrocyclic amides showing anion binding properties [11]. Interactions occurring between electron donors and electron acceptor complementary groups, may lead to the formation of intramolecular charge transfer complexes. Influence of dimensionality and charge on anions binding of macrocyclic amides was reported by Kang et al. [12]. In addition, these macrocyclic amides can form complexes with metal ions, such as Cd(II), Fe(III) and Cu(II), and therefore, they can be used for selective complexation of metal ions. Studies of cyclophane amides complexation of metal ions, Cu(II), Ni(II) and Cd(II) have been reported [13].

In the present work, three newly synthesized macrocyclic amidic compounds (fig. 1a,b,c) have been tested for their potential to act as chelators for various metals.

Experimental part

Materials and methods

Chemicals

The compounds used in the present work as potential chelators, i.e. GZ-I ($C_{16}H_{20}N_2O_5$, M: 320 g/mol), GZ-II ($C_{15}H_{18}N_2O_5$, M: 306 g/mol) and GZ-III ($C_{16}H_{20}N_2O_5$, M: 320 g/mol), have been synthesized in the Organic Chemistry Laboratory. For the investigated compounds stock solutions of 1.0×10^{-3} and 5.0×10^{-3} mol L^{-1} have been prepared by dissolving appropriate amounts into standard flasks of 25 mL. Methanol has been used for compounds dissolution and dilution to the mark. For the GZ-III compound a stock solution of 1.0×10^{-2} mol L^{-1} was prepared in the same way, using as solvents either methanol (MeOH) or methanol-dimethyl sulphoxide (MeOH-DMSO) (1:1, v/v) mixture. Sodium citrate, with addition of suitable amounts of hydrochloric acid, was used to prepare buffer solutions with pH values of 2.8, 3.4, 4.8 and 7.0. Sodium hydroxide solutions in various concentrations, i.e. 10^{-1} mol L^{-1} (*p*H 12.7), 10^{-2} mol L^{-1} (*p*H 11.9), 10^{-3} mol L^{-1} (*p*H 9.4) and 10^{-4}

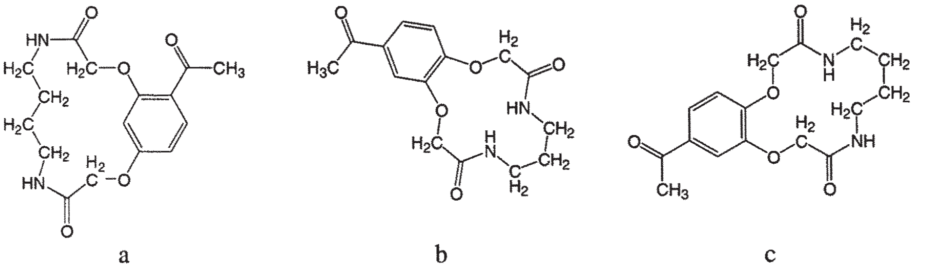

Fig. 1a,b,c: Chemical structures of the newly synthesized macrocyclic compounds, i.e. GZ-I (a), GZ-II (b), and GZ-III (c), used in the present study

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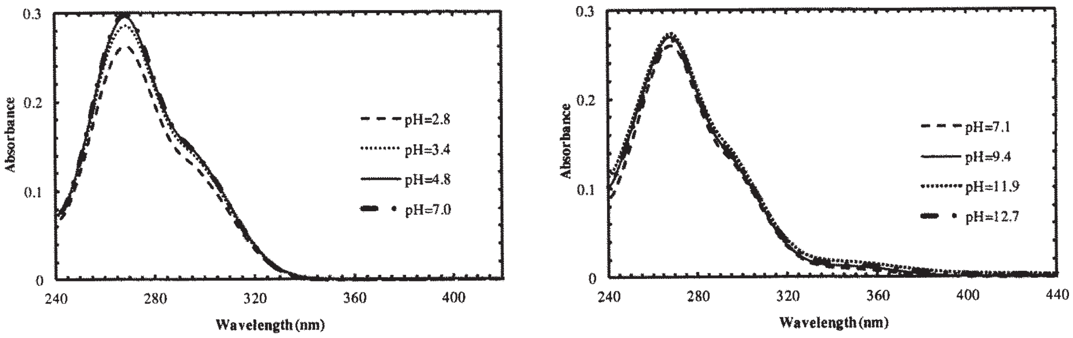
* email: oromeo@uaic.ro; ionelm@uaic.ro



a b

Fig. 2a,b. UV-Vis spectra recorded for GZ-III macrocyclic compound at various *p*H values, i.e. in citrate buffer (a) and sodium hydroxide (b) solutions

mol L^{-1} (*p*H 7.1), were prepared by appropriate dilutions of concentrated NaOH solution (32%). A reference multi-element standard solution (1000 mg L^{-1}, Merck), containing Ag, Al, B, Ba, Bi, Ca, Cd(II), Co(II), Cr(III), Cu(II), Fe(III), Ga, In, K, Li, Mg, Mn(II), Na, Ni(II), Pb(II) Sr, Tl and Zn ions, was used to prepare by appropriate dilution a stock solution of 1.0×10^{-3} mol L^{-1} reported at silver ions. Ultrapure water (18.2 MΩ.cm rezistivity) has been used for appropriate standard dilution into a 25 mL standard flask. All chemicals, of highest available purity, were purchased from commercial sources and used without further purification.

Instrumentation

A double beam UV-Vis spectrophotometer (Specord 210 Plus, ANALYTIC JENA) was used for the absorbance measurements. Fluorescence measurements were performed on a FLS-920s spectrofluorometer (Edinburgh Instruments). *p*H measurements have been undertaken by using a pH meter HANNA HI, Model 4221. The conductivity measurements were performed on a digital HANNA HI conductivity apparatus, Model 4321, at 23.2 °C. IR absorption spectrum, for the crystals formed between GZ-III and Ag$^+$, were recorded at room temperature, in KBr pellets, with a FTIR Vertex 70 spectrophotometer, with ATR and RAMAN II modules. Morphological details for the interest chemical structures (powder, crystals) were obtained by using a **S**canning **E**lectron **M**icroscope (SEM), Model Quanta 250.

Measurement procedures

The influence of *p*H on the behaviour of the interest macrocyclic compounds has been investigated in a 10 mL final volume. Usually, 100 μL of 1.0×10^{-3} mol L^{-1} ligand stock solution were added at 9.9 mL of citrate buffer solutions with various *p*H values. Similar procedure has been undertaken for solutions containing sodium hydroxide at various concentrations. Absorption spectra were recorded after appropriate homogenization. For the GZ-I and GZ-II compounds UV-Vis spectra in aqueous solutions were measured for M:L or L:M ratios of 1:1, 1:2, 1:3 and 1:4. Control samples have been used during the present investigations since methanol, used as solvent in particular situations, possesses specific absorption band in the interest UV-Vis region. Controls samples have been obtained by replacing with methanol in equivalent quantity the existent amount of the interest ligand.

Fluorescence measurements have been undertaken for the 1.0×10^{-2} mol L^{-1} GZ-III solution and for the organic-aqueous mixture between GZ-III and Ag$^+$ ions. Indications about a possible complexation between the GZ-III compound and Ag$^+$ cations have been obtained by following the conductometric profile during titration with fixed titrant volume. The conductance of the interest mixture solution was measured after adding in a titration cell of a specific aliquot of Ag$^+$ solution (1.0×10^{-1} mol L^{-1}) followed by appropriate dilution with 30 mL of ultrapure· water to ensure complete immersion of the electrode. The conductance of the solution in the cell was measured after each addition, of 500μL of GZ-III solution, in a step-by-step procedure.For the GZ-III macrocyclic compound conductivity measurements were performed both in MeOH and MeOH-DMSO binary systems.

Results and discussions

pH influence on the macrocyclic compounds stability

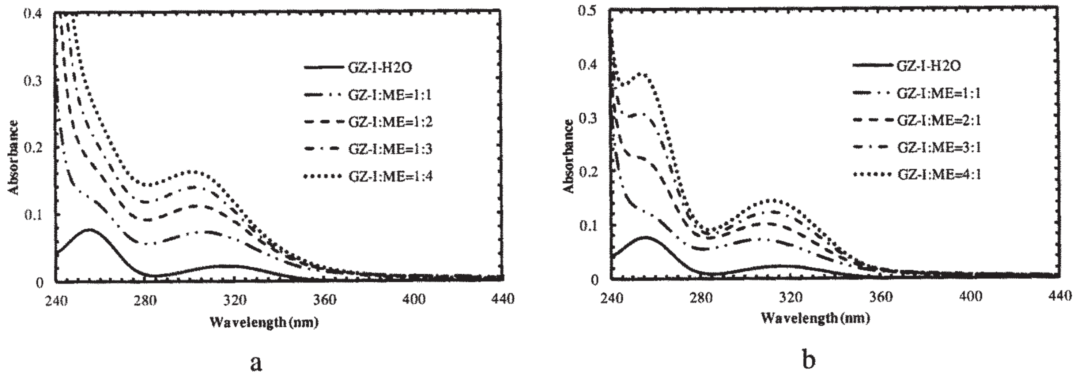
Citrate buffer and sodium hydroxide solutions, with *p*H values between 2 and 13, have been used to study the influence of *p*H on the behaviour of the interest macrocyclic compounds. For the GZ-III macrocyclic compound the results are presented in figure 2a,b.

As can be seen in figure 2a, similar intensity at 268 nm and 295 nm of the absorption bands have been observed in the spectra of GZ-III in citrate buffer at *p*H 4.8 and 7. The absorption band with maximum intensity at 268 nm shows a low hypochromic effect at *p*H 3.4. The absorption band with maximum at 295 nm presents an observable hypochromic effect only for GZ-III spectrum recorded in citrate buffer at *p*H 2.8. As evident from figure 2b, identical absorption spectra have been recorded for GZ-III compound in various sodium hydroxide solutions. Taking into account the recorded experimental evidences, as shown in figure 2a,b, it seems that in the GZ-III macrocyclic amidic compound the atoms do not undertake any reorganization processes which could be responsible for changes in the profile of the absorption bands with maxima at 268 nm and 295 nm.

The GZ-I and GZ-II compounds potential to act as metal chelators

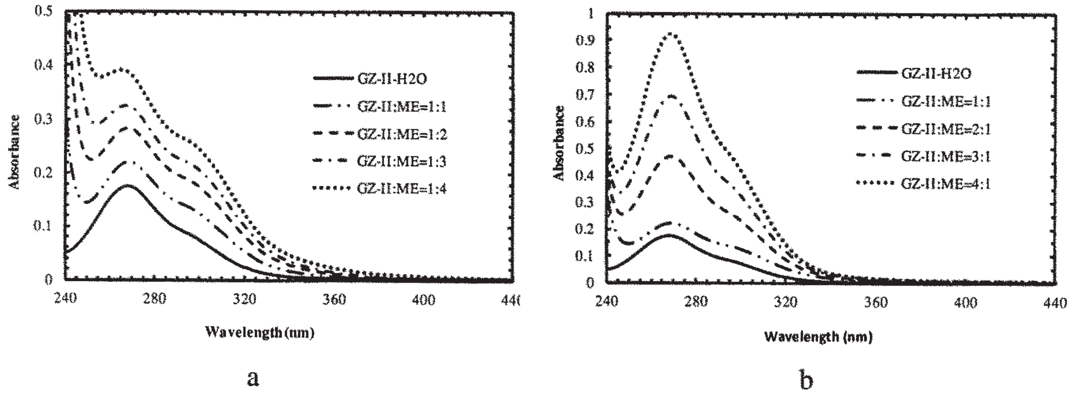
In order to investigate the potential of the GZ-I and GZ-II macrocyclic compounds to act as metal chelators a multi-element (ME) solution containing Ag, Al, Ca, Cd(II), Co(II), Cr(III), Cu(II), Fe(III), Mg, Mn(II), Ni(II), Pb(II) and Zn ions has been used during the present study. Absorbance spectra have been measured at various M:L ratios. Figure 3a,b shows the spectral features for GZ-I compound, while figure 4a,b shows similar experimental evidences for GZ-II compound.

Within these investigations it has observed that under 240 nm the spectra behaviour was strongly affected by the specific band of nitrate ion existent in the standard solution of the multi-element mixture (made in concentrated nitric acid). However, the intensity of the interest absorption bands showed a behaviour reflecting a direct proportionality with the multi-element variable quantity used both for GZ-I (fig. 3a) and GZ-II (fig. 4a) compounds. It has been also observed that increasing GZ-I and GZ-II compounds quantity induced a behaviour reflecting again the proportionality with the existent amount but with similar spectral features (fig. 3b and fig.



a b

Fig. 3a,b The absorption spectra obtained for: (a) constant quantity of GZ-I macrocyclic compound and variable quantity of ME, (b) variable quantity of GZ-I macrocyclic compound and constant quantity of ME



a b

Fig. 4a,b. The absorption spectra obtained for: (a) constant quantity of GZ-II macrocyclic compound and variable quantity of ME, (b) variable quantity of GZ-II macrocyclic compound and constant quantity of ME

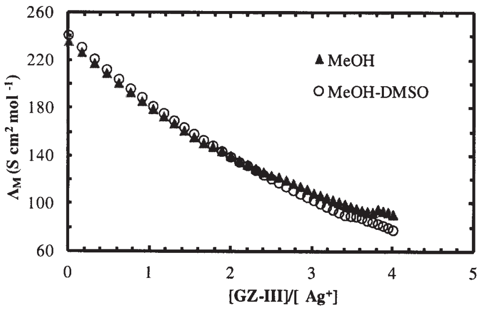


Fig. 5. Molar conductivity *vs.* mole ratio plots for GZ-III with Ag$^+$ complex in MeOH and in MeOH-DMSO binary systems

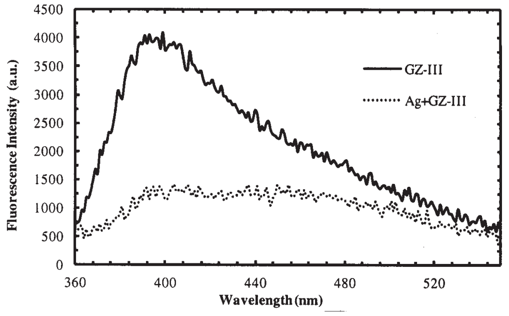


Fig. 6. Changes in the GZ-III macrocyclic compound (10 mM) fluorescence intensity upon addition of Ag$^+$ ions in a MeOH-DMSO binary systems

4b). The absorption spectra of the GZ-I and GZ-II compounds did not showed any observable changes in the spectral features recorded in the presence of the metals existent in the used multi-element reference material. It was concluded that these two macrocyclic compounds do not possess any potential to act as chelators for the existent metal ions.

Chemical behaviour of the GZ-III macrocyclic compound

Spectroscopic (FTIR, fluorescence) and electrometric (conductometry) techniques have been used to obtain experimental evidences for the possible implication of GZ-III macrocyclic compound in silver ions chelatization.

Conductivity measurements

The conductometric profiles induced by a possible complexation between GZ-III macrocyclic compound with Ag$^+$ cations in both MeOH and MeOH-DMSO binary systems have been investigated. Changes of molar conductivity ($\ddot{E}_M$) *versus* the ligand and cation mole ratio, [GZ-III]/[Ag$^+$], have been followed at 5 and 10 mM concentrations in GZ-III. As shown by figure 5, addition of GZ-III to Ag$^+$ cations in both MeOH and MeOH-DMSO binary systems resulted in a decrease in molar conductivity.

Such behaviour might indicate that the complex formed between GZ-III and silver ions is less mobile than the free solvated Ag$^+$ cations. Further experimental investigations revealed that DMSO addition did not induced a significant influence on the species solvation in solution. The details presented in figure 5 show that the slope of each curve changes at the point where the ligand and cation mole ratio is about 3, which should be considered as an evidence for formation of a 1:3 [Ag:GZ-III] complex. Similar assignment procedure for the formation of different complexes has been used in a study performed by Rounaghi et al. [14].

Fluorescence spectra

Fluorescence spectra have been measured in order to extract information about the potential of the interest compound, i.e. GZ-III, to present fluorescence. Details presented in figure 6 reveal that the GZ-III macrocyclic compound solvated in a MeOH-DMSO binary systems presents low intensity fluorescence emission. The presence of Ag$^+$ cations in the above presented system is suppressing fluorescence intensity, which might be a result induced by the formation of the complex with GZ-III compound.

IR Spectrum

For the GZ-III macrocyclic compound and the chemical structure obtained from a mixture between the GZ-III macrocyclic compound and Ag$^+$ ions, the IR spectra in the 1200-400 cm^{-1} wavenumber region are presented in figure 7.

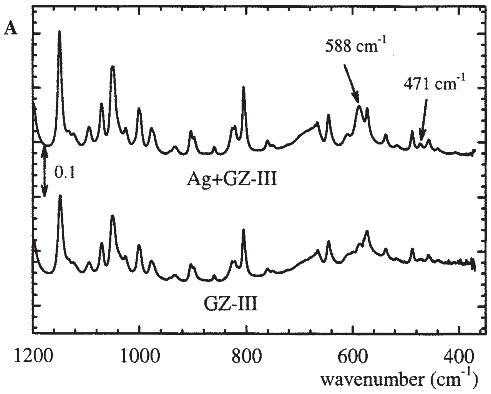


Fig. 7: IR spectrum of GZ-III macrocyclic compound and of the chemical structure resulted from a mixture between GZ-III macrocyclic compound and Ag^+ ions

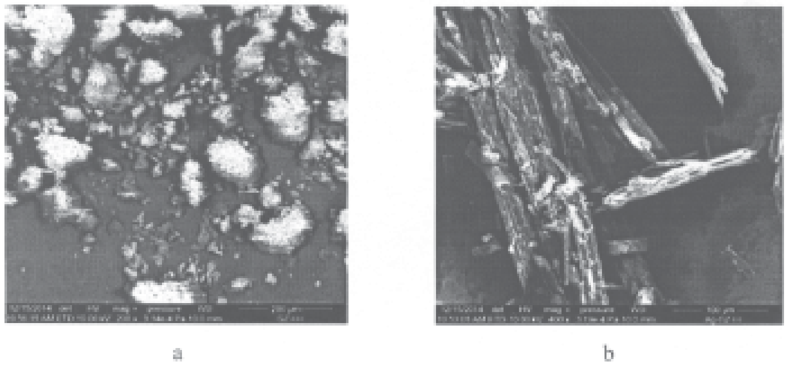


Fig. 8a,b. SEM details for GZ-III macrocyclic compound powder (a) and for the crystals formed between GZ-III and Ag^+ (b)

The details presented in figure 7 reveal in some regions similar spectral characteristics but there are also two absorption bands with different behaviour. In the spectrum specific for the mixture between the GZ-III macrocyclic compound and silver ions the maxima observed at 471 and 588 cm^{-1} can be actually attributed to Ag-O and, respectively, Ag-N bonds vibrations [15-16]. These observations may indicate a possible coordination between the GZ-III compound with silver ions through the N and O atoms of the amidic groups.

SEM technique

Figure 8a shows the morphological details for GZ-III macrocyclic compound powder while figure 8b reveals the existence of some very fine acicular crystals obtained after drying to sec the organic-aqueous mixture between GZ-III and Ag^+. The crystallization of the complex in the form of overlapping acicular crystals is very well illustrates by figure 8b. Unfortunately, at present it was not possible to isolate a single crystal, in order to use X-ray diffraction technique for establishing the structure of the newly formed compound.

Conclusions

The chemical behaviour of three newly synthesized macrocyclic compounds has been investigated in the present work especially due to the fact that their particular three-dimensional shape could provide suitable cavities for selective complexation of heavy metals. Various experimental approaches (spectrophotometry, fluorimetry, conductometry, microscopy) have been used in order to identify the potential of the interest macrocyclic compounds to bind some metal ions. The obtained results revealed that the GZ-I and GZ-II macrocyclic compounds do not have any potential to act as chelators for various metals in a spectacular opposition with the expectations from their chemical structures. Only for the GZ-III macrocyclic compound some experimental evidences have been obtained for its possible implication in chelating silver cations. For the GZ-III macrocyclic compound it has been observed that the *p*H do not influence its chemical behaviour. Further work should be undertaken to confirm the present experimental observations and to investigate if or not the macrocyclic structure GZ-III can be used to develop a specific sensor for Ag^+.

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References

1.FU, F., WANG, Q., J. Environ. Manage. **92**, 2011, p. 407.
2.IBANEZ G.A., ESCANDAR G.M., Fluorescence and phosphorescence chemical sensors applied to water samples, in Real-Time Water Quality Monitoring, MUKHOPADHYAY S.C., MASON A. (eds.), Springer-Verlag Berlin Heidelberg, 2013, p. 45.
3.PUJOL, L., EVRARD, D., GROENEN-SERRANO, K., FREYSSINIER, M., RUFFIEN-CIZSAK A., GROS P., Front. Chem., **2**, 2014, p. 1.
4.ARAGAY ,G., PONS, J., MERKOCI ,A., Chem. Rev., **111**, 2011, p. 3433.
5.MINKIN, V.I., DUBONOSOV, A.D., BREN, V.A., TSUKANOV, A.V., Arkivoc, **4**, 2008, p. 90.
6.DUGAVE, C., DEMANGE, L. Chem. Rev., **103**, 2003, p. 2475.
7.SPATH, A., KONIG, B., Beilstein J. Org. Chem., **6**, 2010, p. 1.
8.WAGNER-WYSIECKA, E., RZYMOWSKI, T., SZARMACH, M., FONARI, M. S., LUBOCH, E., Sensor. Actuat. B, **177**, 2013, p. 913.
9.FLETCHER, N.C., LAGEMAS, M.C., Chromo- and fluorogenic organometallic sensors, in Molecular Organometallic Materials for Optics, LE BOLZEC, H., GUERCHAIS, V. (eds)., Springer-Verlag Berlin Heidelberg, 2010, p. 143.
10.WAGNER-WYSIECKA, E., RZYMOWSKI, T., FONARI, M. S., KULMACZEWSKI, R., LUBOCH, E., Tetrahedron, **67**, 2011, p. 1862.
11.GALE, P.A., BUSSCHAERT, N., HAYNES ,C.J.E., KARAGIANNIDIS, L.E., KIRBY I.L., Chem. Soc. Rev., **43**, 2014, p. 205.
12.KANG, S.O., HOSSAIN, M.A., BOWMAN-JAMES, K., Coord. Chem. Rev., 250, 2006, p. 3038.
13.RAJAKUMAR, P., PADMANABHAN, R., Tetrahedron Lett., **51**, 2010, p. 1059.
14.ROUNAGHI, G.H., RAZAVIPANAH, E., KAVEH, F., J. Incl. Phenom. Macrocycl. Chem., **68**, 2010, p. 245.
15.MORZYK-OCIEPA ,B., MICHALSKA, D., Spectrochim. Acta Part A, **55**, 1999, p. 2671.
16.PUI, A., COZMA, D. G., Lucrari practice de chimia compusilor coordinative, Ed. Universitatii "Al.I. Cuza", Iasi, 2001, p. 57

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