Supramolecular Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gsch20

Chromogenic derivatives of new bis(phenylhydrazono-1H-tetrazol-5-yl-acetonitriles) - synthesis and properties

A. Pazik [a] & A. Skwierawska [a]

[a] Department of Chemical Technology, Gdansk University of Technology, Narutowicza Street 11/12, 80-233, Gdansk, Poland

Version of record first published: 09 Jul 2012.

To cite this article: A. Pazik & A. Skwierawska (2012): Chromogenic derivatives of new bis(phenylhydrazono-1H-tetrazol-5-yl-acetonitriles) - synthesis and properties, Supramolecular Chemistry, 24:10, 726-737

To link to this article: http://dx.doi.org/10.1080/10610278.2012.701303

Supramolecular Chemistry
Vol. 24, No. 10, October 2012, 726–737

Taylor & Francis
Taylor & Francis Group

Chromogenic derivatives of new bis(phenylhydrazono-1*H*-tetrazol-5-yl-acetonitriles) – synthesis and properties

A. Pazik* and A. Skwierawska

Department of Chemical Technology, Gdansk University of Technology, Narutowicza Street 11/12, 80-233 Gdansk, Poland

(*Received 6 May 2012; final version received 1 June 2012*)

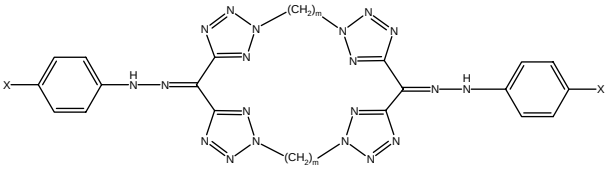
Derivatives of bis(phenylhydrazono-1*H*-tetrazol-5-yl-acetonitriles) with oxygen and sulphur atoms in the structure of aliphatic chains were successfully synthesised. The correlation between the ligand structure and its complexation properties was investigated by absorption spectroscopy. The formation of complexes of presented compounds with metal cations (Cu^{2+}, Ni^{2+}, Zn^{2+}, Co^{2+}, Fe^{2+} and Pb^{2+}) was studied. Ligands **5**–**8** were additionally applied as ion carriers in ion-selective membrane electrodes. Membranes of ion-selective electrodes doped with these ligands are selective to Cu^{2+} and Pb^{2+} cations.

Keywords: UV–vis spectroscopy; chromoionophores; membrane electrodes; bis-tetrazole; synthesis

Introduction

In recent years, the development of supramolecular chemistry in a range of molecular receptors has been related to the high demand for new, miniature tools, biosensors and molecular devices. Different methods of synthesis of molecular receptors allow obtaining highly important receptors. According to Pearson Hard-Soft Acid-Base (HSAB) theory, hard electron donor atoms like oxygen atoms attract preferentially electron acceptors such as alkali or alkaline earth cations (*1*–*3*). Spherical shapes of cations greatly facilitate design of appropriate host molecules (*4*, *5*). Tetrazoles due to their structure and similarity to the carboxylic acids can bind metal ions forming complexes with different molar ratios. They are used to design new bioreceptors, drugs (*6*–*8*) and coordination polymers (*9*). Tetrazoles are also used as materials for photography (*10*), in data recording systems, as ligands for analytical reagents and in explosives (*11*). In biological systems, the tetrazole N—H group occurs mainly in the neutral or anionic form.

Recently, the synthesis of tetrazoles has gained significant interest. The most direct synthetic procedure of 1,5-substituted tetrazoles is cycloaddition of nitriles and azides catalysed by, for example, Brønsted and Lewis acids (e.g. $ZnCl_2$ and $ZnBr_2$) (*12*) in water. New reports describe also use of heterogeneous catalyst (*13*), nanoparticles (*14*) and CoY zeolite (*15*) and microwave irradiation. The first macrocyclic molecule containing tetrazole residue was synthesised in 1992 by Butler (*16*). Its structure is presented below.



This macrocycle is the first example of compound, in which tetrazole and hydrazone residues were involved in complexation of metal cations. The literature data on this type of compounds are quite poor and do not concern complexation and ions transport through membranes or equilibrium studies in solution. Furthermore, according to recent research, some phenylhydrazono-1*H*-tetrazol-5-yl-acetonitrile derivatives with different substituents in the phenyl ring have antimicrobial activities; particularly they show greater activities against Gram-positive than Gram-negative bacteria (*17*).

In our research, we focus on the synthesis of new ionophores for the selective recognition of transition and heavy metal ions. We herein report the synthesis of bis(phenylhydrazono-1*H*-tetrazol-5-yl-acetonitriles) chelating reagents (Figure 1). The binding ability of compounds **5**–**8** with metal ions has been studied using UV–vis spectroscopy. Ligands with different cavity size and heteroatoms in the linkage are described and their selectivity for the metal ions was compared. UV–vis spectroscopic studies show that all compounds are able to complex Cu^{2+} ions only with one exception, i.e. compound **5**, which forms also complexes with Zn^{2+} and Ni^{2+} cations. In addition, all

*Corresponding author. Email: mikaga20@wp.pl

ISSN 1061-0278 print/ISSN 1029-0478 online

http://dx.doi.org/10.1080/10610278.2012.701303
http://www.tandfonline.com

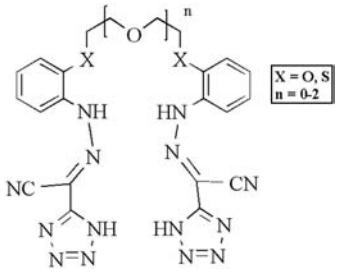


Figure 1. Chemical structures of ligands studied.

compounds have been studied as ion carriers in ion-selective membrane electrodes. Selectivity of these membranes towards various cations and anions was determined.

Results and discussion

Synthesis

The synthetic approach to new bis(phenylhydrazono-1*H*-tetrazol-5-yl-acetonitriles) **5**–**8** is shown in Figure 2. 1,1-Dicyanohydrazone derivatives **1**–**4** were obtained according to the well-known method from malononitrile with diazo salts, which were synthesised from appropriate diamines. The final step of reaction was formation of tetrazole ring in reaction of nitriles with sodium azide and ammonium chloride in N,N-dimethylformamide (DMF). After reaction in order to release the anionic tetrazolate salt mixture is treated with concentrated sulphuric acid. The reaction proceeds via a traditional [2 + 3] mechanism. The mechanism of the addition of azide ion to nitrile involves the activation of nitrile by protonation, proceeding through a previously unsuspected imidoyl azide intermediate. Interestingly, only two tetrazole rings can be introduced into the systems in one reaction step.

Compounds **5**–**8** were obtained in good yield (52–88%) and purified by crystallisation from water. The compounds are brown (**5** and **7**) and yellow (**6** and **8**) solids. The progress of diazo salt coupling reaction was monitored by ^{1}H NMR spectroscopy. The ^{1}H NMR spectra confirmed formation of hydrazones N—H signals at 10.53 ppm (Figure 3, e.g. **3**) and the cyclisation reaction with the wide signal at 4.9 ppm characteristic for tetrazole N—H band. IR spectra show two typical C≡N bands at ca. 2233 and 2200 cm^{-1}. After formation of tetrazole ring, one of the C≡N bands (2233 cm^{-1}) disappears (Figure 4); furthermore, it shows characteristic tetrazole ring deformation vibrations that reflect presence of different groups (e.g. C—N, N—H and N—N bands). Surprisingly, tetrazole ligands **5**–**8** with hydrazone bonds and their spectroscopic properties have never been studied. Accordingly, we have prepared a series of bis-ligands differing in length and

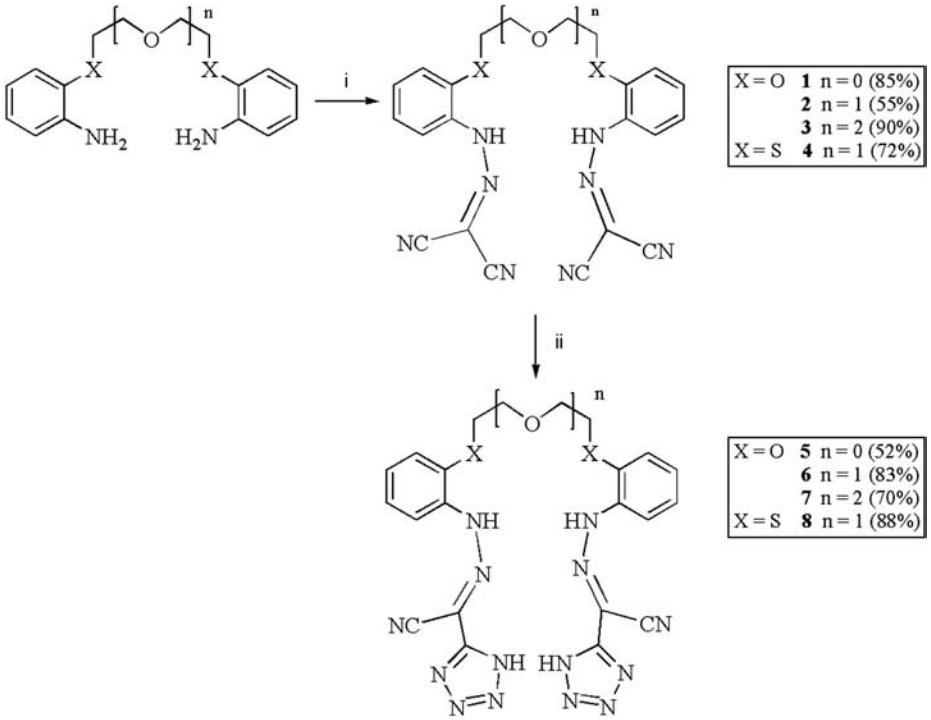


Figure 2. Synthesis of bis(phenylhydrazono-1*H*-tetrazol-5-yl-acetonitriles) derivatives **5**–**8**. Reagents and conditions: (i) $NaNO_2$/HCl, 0–5°C, $C_3H_2N_2$, EtONa/EtOH; (ii) NaN_3, NH_4Cl, DMF, 120°C, 24 h.

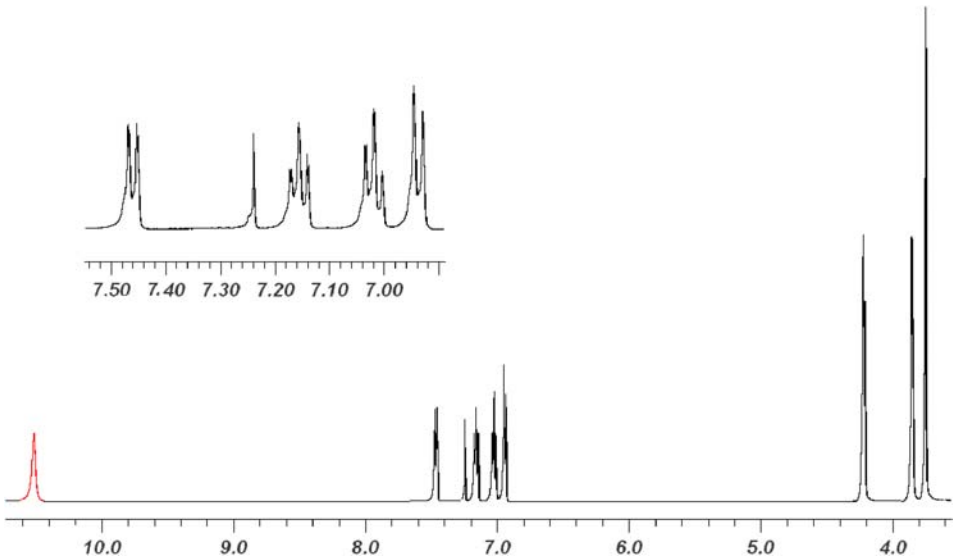


Figure 3. ^{1}H NMR (500 MHz, $CDCl_3$) of 1,8-bis[2-(phenylhydrazonodi-acetonitriles) phenoxy]-3,6-dioxaoctane (**3**).

heteroatoms of linkage. We assume that even small structural changes can modify their complexing properties.

Spectrophotometric studies of metal cation complexation

Design of potential sensing material for transition and heavy metal cations is nowadays very important from medical/clinical point of view because they accumulate in the human body and cause numerous diseases. Tetrazoles, due to their similarity to carboxylic acids (pK_a values) and π-acceptor properties, are able to form metal complexes and coordination polymers with high thermal stability.

The UV–vis absorption maxima (λ_{max}) and molar extinction coefficients of ligands **5**–**8** are summarised in Table 1. In methanol solution, ligands **5**–**7** show absorption bands in the range 200–450 nm with a maximum at about 361–370 nm. Introduction of sulphur atoms into ligand **8** structure caused major changes in values of molar extinction coefficients comparing with compound **6**.

Ligands **5**–**8** represent an interesting chelating system. The frame is based on dibenzo-substituted mixed-donor

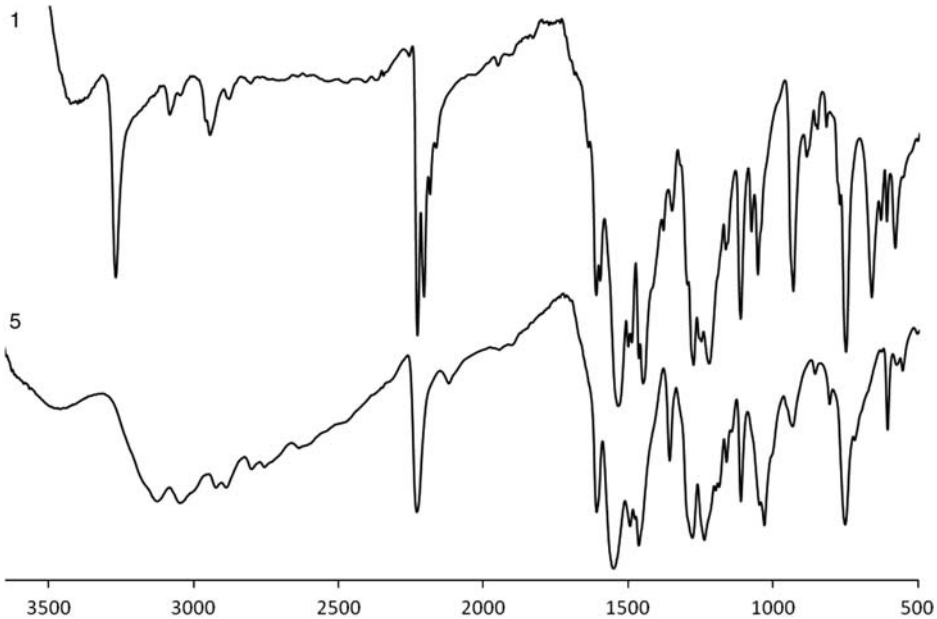


Figure 4. IR spectra of 1,1-dicyanohydrazone derivative **1** and bis-tetrazole derivative **5** in KBr.

Table 1. The absorption maxima (λ_{max}) and corresponding extinction coefficients of new bis-tetrazole **5**–**8** in MeOH at 298 K.

Compounds	λ_{max} (nm)	ε ($M^{-1}\,cm^{-1}$)
5	361	166,000
6	362	74,600
7	363	66,200
8	370	219,000

structure incorporating oxygen, sulphur and nitrogen atoms. Aliphatic chain with heteroatoms is the most flexible part of the molecule which allows to adjust the host to the guest molecules. Conjugated phenylhydrazono-acetonitriles form chromogenic but more rigid system which required accurate guest. In the preliminary studies, spectroscopic titration of compounds **5**–**8** with Li^+, Na^+, K^+, Mg^{2+}, Ca^{2+}, Co^{2+}, Cu^{2+}, Ni^{2+}, Pb^{2+}, Fe^{2+} and Zn^{2+} chlorides in methanol solution was carried out. In case of chlorides of metals of the first and second groups of the periodic table, any changes in absorbance spectra were observed. Absorption spectra of ligands **5**–**8** upon addition of 10-fold excess of transition metal and lead chlorides are shown in Figure 5. Probably, ligands **5** and **6** show the best adjustment to transition metal cations. The most significant changes for compound **5** in absorption spectra were observed in the presence of Cu^{2+}, Zn^{2+}, Co^{2+} and Ni^{2+} chlorides. Bis-tetrazole **6** exhibits increase of maxima upon addition of Fe^{2+} chloride; however, the last ions do not influence absorbance of other ligands. It is worth to note that only ligands **6** and **8** show positive response to Pb^{2+} chloride. Furthermore, spectroscopic titration of compound **6** with Pb^{2+} shows continuous increase of the main band that makes determination of complexation constant impossible (Figure 6). Introduction of two sulphur atoms makes the ligands more sensitive to Ni^{2+} and Co^{2+} ions. All ligands show response to Cu^{2+} ions and form complexes with it of diversified stoichiometry.

UV–vis titrations were carried out to estimate the stability constant values of the respective complexes with Cu^{2+}, Ni^{2+} and Zn^{2+} ions. Changes in UV–vis absorption

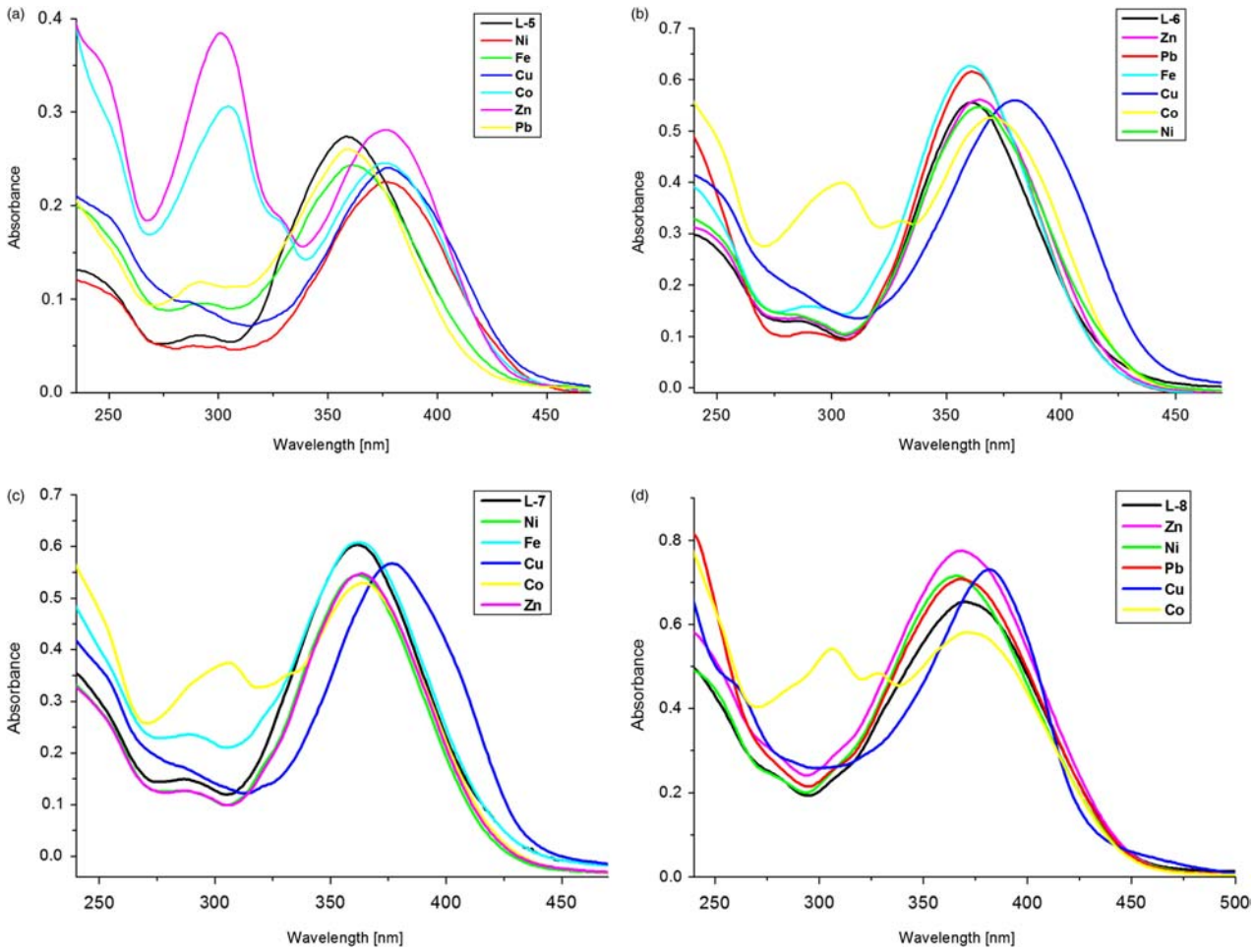


Figure 5. Absorption spectra of bis(phenylhydrazono-1*H*-tetrazol-5-yl-acetonitriles) in the presence of 10-fold excess of metal chlorides in methanol. (a) **5** ($c = 10^{-6}$ M); (b) **6** ($c = 5 \times 10^{-6}$ M); (c) **7** ($c = 10^{-5}$ M); (d) **8** ($c = 3 \times 10^{-6}$ M).

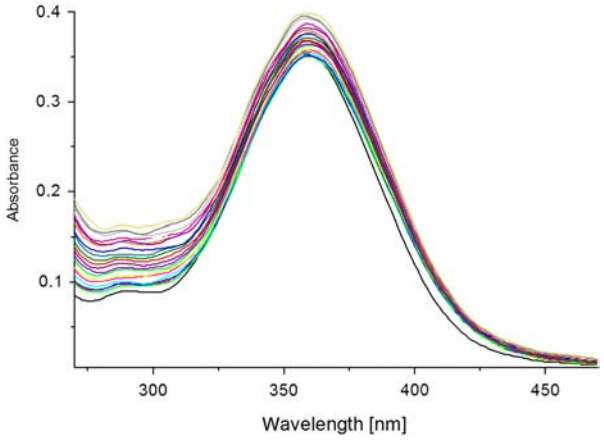


Figure 6. UV–vis titration of compound **6** ($c = 10^{-5}$ mol dm^{-3}) with $Pb(ClO_4)_2$ ($c = 0$–3.5×10^{-5} M) in methanol solution.

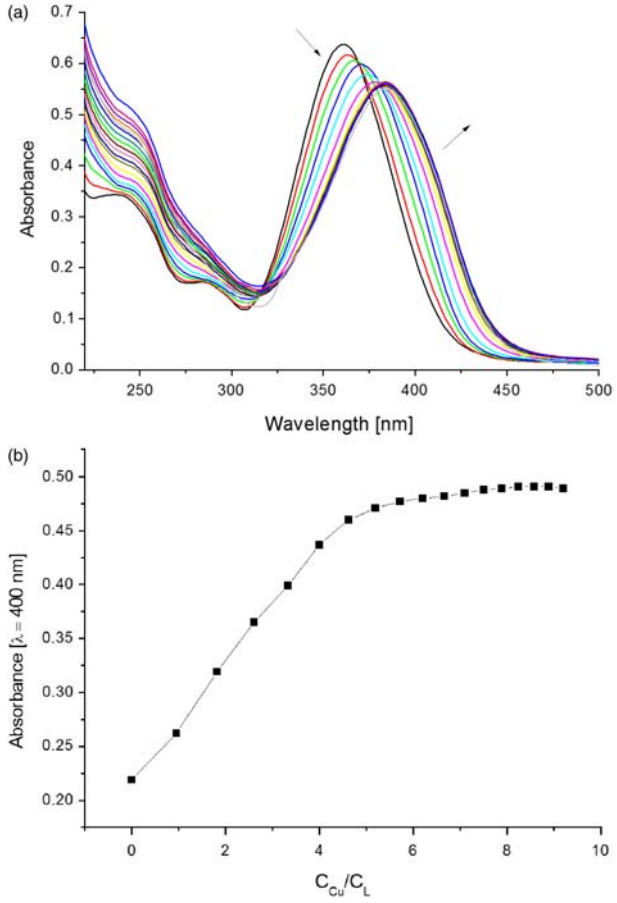


Figure 7. (a) Changes in UV–vis absorption spectrum of ligand **6** ($c = 5 \times 10^{-6}$ M) upon increasing concentration of $Cu(ClO_4)_2$ ($c = 0$–0.47×10^{-4} M) in methanol solution. (b) Titration plot to determine the stability constant of the complex between **6** and Cu^{2+}(1:4) at 400 nm.

spectra of compounds **6** and **7** under various concentrations of Cu^{2+} perchlorate in methanol are shown in Figures 7 and 8. A molar ratio plot revealed that under titration experiments complexes of 1:4 and 1:2 stoichiometry for ligands **6** and **7** were found, respectively. The association constants were determined to be 4.43×10^7 M^{-1} for **6** Cu^{2+} and 2.6×10^7 M^{-1} for **7** Cu^{2+} complexes (Figure 9). As the concentration of Cu^{2+} increased, the absorption maximum of the free ligands **6** and **7** at 362 and 363 nm is shifted to 382 and 378 nm, respectively. In contrast, control compound **3** with 1,1-dicyanohydrazones units showed also batochromic shift that relies on spectral band shift from 371 nm to longer wavelength 381 nm (see titration of compound **3** in Figure 10). The stoichiometry of complex with Cu^{2+} was 1:1.3, and the value of K_a was determined to be 4.2×10^7 M^{-1}. Comparing the results with those obtained for compound **7**, the stability constant value for Cu^{2+} complex is higher than for its tetrazole analogue.

Furthermore, the results from UV–vis titration of ligands **5** and **8** upon titration with various concentrations of Cu^{2+} in methanol are presented in Figure 9. For UV–vis titration ligand **8**, the absorption maximum at 370 nm is shifted to 382 nm, whereas in case of ligand **5** the band at 361 nm is shifted to 379 nm with one isosbestic point at 322 nm. The increase of the main band and major concentration of the salt makes determination of complexation constant impossible for these compounds.

We observed the same problem with stability constants under UV–vis absorption spectra for **5** and **6** with Ni^{2+} and Zn^{2+} ions (Figure 11). The absorption spectra of **5** with Ni^{2+} and Zn^{2+} with various concentrations of the ions show batochromic shift; absorption band at 361 nm is shifted to 386 and 375 nm, respectively. In case of spectroscopic titration of **5** with $Zn(ClO_4)_2$, the formation of a new band at 271 nm was observed (Figure 12). In addition, the formation of the new wide band at 264 nm was also observed in spectrum of **5** with Ni^{2+} ions.

Different patterns of spectroscopic changes in absorption spectra may suggest that the length of the polyether linker is essential in the complexation properties. The smaller is the cavity size, the better is the selectivity towards transition metal cations. Modifications in the polyether chain with the sulphur atom do not improve selectivity of compound. Moreover, we supposed that the cation is implemented inside the ligand cavity between hydrazone bonds and tetrazole rings. However, different patterns of spectroscopic changes in absorption spectra (increase without batochromic shift) in case of Pb^{2+} ions and our earlier studies may confirm that only tetrazole rings are involved in complexation.

To prove our hypothesis on complexation properties, additional experiments were carried out using IR spectroscopy. An IR spectrum of ligand **7** in the presence of Cu^{2+} chloride was recorded within the range of 3500–500 cm^{-1}. The initial stage of the process was to prepare a sample for

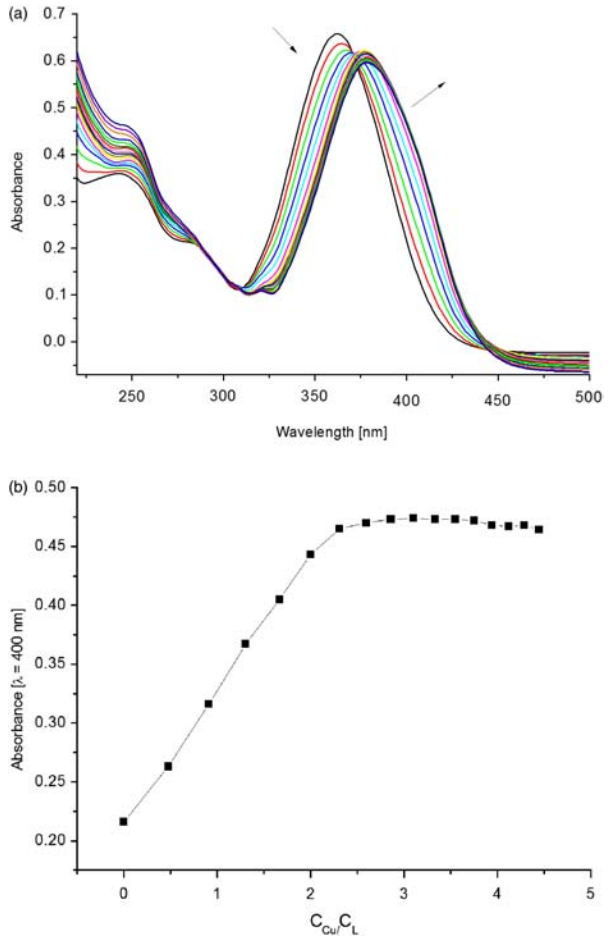


Figure 8. (a) Changes in UV–vis absorption spectrum of ligand **7** ($c = 10^{-5}$ mol dm^{-3}) with $Cu(ClO_4)_2$ ($c = 0$–0.44×10^{-4} M) in methanol solution. (b) Titration plot to determine the stability constant of the complex between **7** and Cu^{2+}(1:2) at 400 nm.

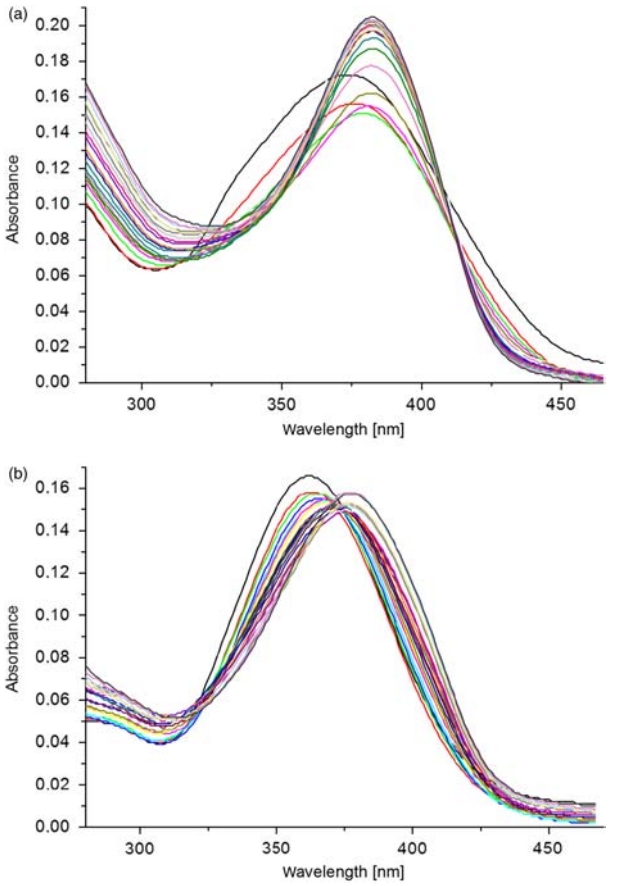


Figure 9. UV–vis titration of compound (a) **8** ($c = 3 \times 10^{-6}$ mol dm^{-3}) with $Cu(ClO_4)_2$ ($c = 0$–2.5×10^{-5} M); (b) **5** ($c = 10^{-6}$ mol dm^{-3}) with $Cu(ClO_4)_2$ ($c = 0$–0.52×10^{-5} M) in methanol solution.

testing. By using a molar excess of salt, we took **7** and $CuCl_2$ separately and dissolved then in small amount of chloroform and methanol, respectively; then the solutions were combined, stirred and the solvents were evaporated to dryness. The residue was dried in vacuum and protected from moisture. The obtained solid and dry KBr was used in the preparation of tablets for IR spectroscopy. Results of our experiments are presented in Figure 13. A reference spectrum was taken from pure ligand **7** in KBr. The changes in ligand **7** spectrum upon complexation are significant. Complexation can be observed in the loss of stretching vibration at 1552 cm^{-1}, and the new signals can be found below 1453 cm^{-1}. The band is characteristic of bond stretching vibration for coordinated tetrazole rings and can be assigned to C═N vibrations.

After complexation, up-shift of 55 cm^{-1} can be observed in the enhanced band at 1239 cm^{-1}, which is also due to stretching vibration of the tetrazole rings. Deformation of the substituted hydrazone bonds in the phenyl ring and its complexation properties can be seen in the absorption at 750 cm^{-1} and the appearance of new signal at 680 cm^{-1}. It was noteworthy that after Cu^{2+} ions complexation by **7**, new strong absorptions bands at 3350 and 3440 cm^{-1} were observed. The symmetry of complex and 1:2 stoichiometry is observed in IR spectroscopy in the two large signals deriving from two tetrazole N—H stretching vibration and N—H hydrazone bonds. No changes in the intensities of absorption characteristic for nitrile groups C≡N suggest that it is not engaged in the complex.

Molecular simulation

To understand the structure of **7** and the nature of bonding interaction with the cations, ground-state optimisation was carried out using Gaussian 03 software with B3LYP and 6-31 + + G(dp) basis set at the density functional theory level. The optimised global minima of receptor **7** show that the N—H hydrazone moieties are not in the same plane (Figure 14). The optimised structure of **7** shows that distances N1···H1 and N2···H2 are 1.063 Å, the same

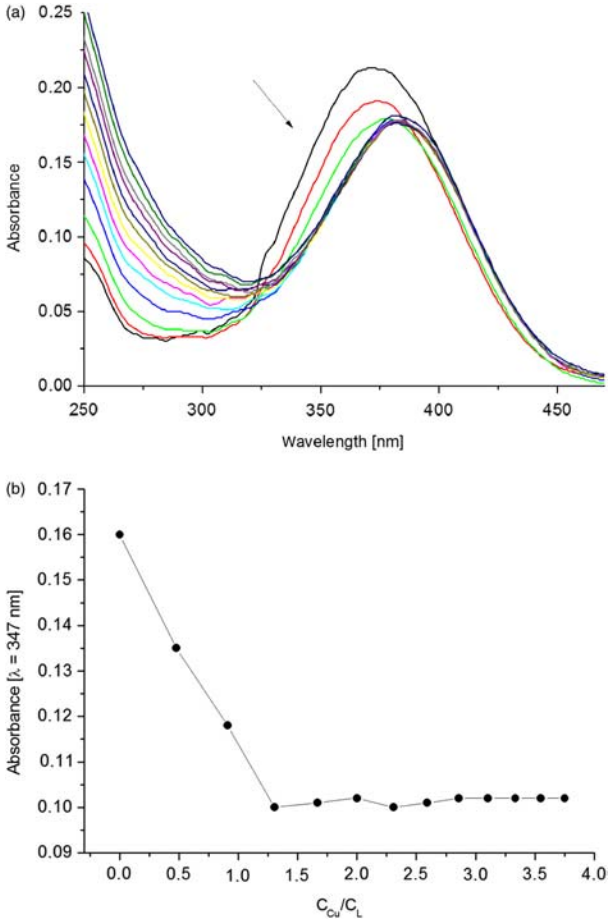


Figure 10. (a) UV–vis titration of compound **3** ($c = 10^{-5}$ mol dm^{-3}) with $Cu(ClO_4)_2$ ($c = 0$–0.37×10^{-4} M) in methanol solution. (b) Titration plot of the complex between **3** and Cu^{2+}(1:1.3) at 347 nm.

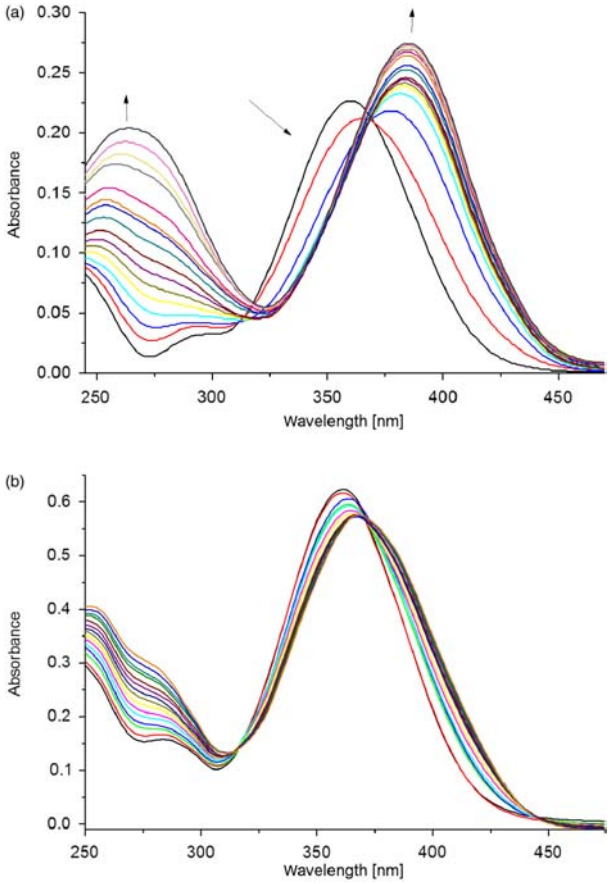


Figure 11. UV–vis titration of compound (a) **5** ($c = 10^{-6}$ mol dm^{-3}) with Ni $(ClO_4)_2$ ($c = 0$–0.44×10^{-4} M); (b) **6** ($c = 5 \times 10^{-6}$ mol dm^{-3}) with Ni $(ClO_4)_2$ ($c = 0$–0.41×10^{-4} M) in methanol solution.

value. In the presence of Cu^{2+} ions, ligand **7** rearranges itself from a flexible conformer to a more rigged system presented in Figure 15 and forms 1:2 complexes with Cu^{2+} ion. The structure of **7** Cu^{2+} complex shows that two Cu^{2+} ions are nitrogen bonded within distances N1$\cdots$$Cu^{2+}$ = 2.0309 Å (N2$\cdots$$Cu^{2+}$ = 2.0395 Å) and N3$\cdots$$Cu^{2+}$ = 2.036 Å (N4$\cdots$$Cu^{2+}$ = 2.026 Å). However, the Pb^{2+} ion can fit between tetrazole rings and forms 1:1 complex (Figure 16) with a small change in the structure of the conformer. The optimised structure of complexes shows that in both cases cations are differently located in the cavity which is formed between hydrazone bonds and tetrazole rings, which confirm our earlier hypothesis (Table 2).

Membrane electrodes and potentiometric measurements

Properties of compounds **5**–**8** as ion carriers have been tested using membrane electrodes. The examined membranes consisted of 1.1% (w/w) ionophore, 0.3% (w/w) potassium tetrakis(4-chlorophenyl) borate (KT*p*ClPB), 65.7% (w/w) 2-nitrophenyl octyl ether (*o*-NPOE) and 32.9% (w/w) poly(vinyl chloride) (PVC). Membrane components, total 182.5 mg, were dissolved in 1.5 ml of

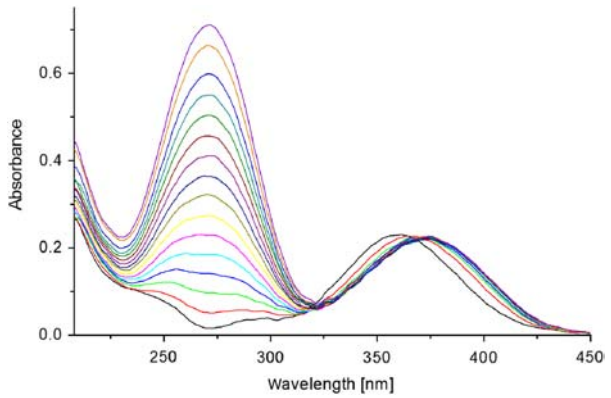


Figure 12. Absorption spectra recorded in methanol solution containing ligand **5** ($c = 10^{-6}$ M) with $Zn(ClO_4)_2$ ($c = 0$–0.43×10^{-4} M).

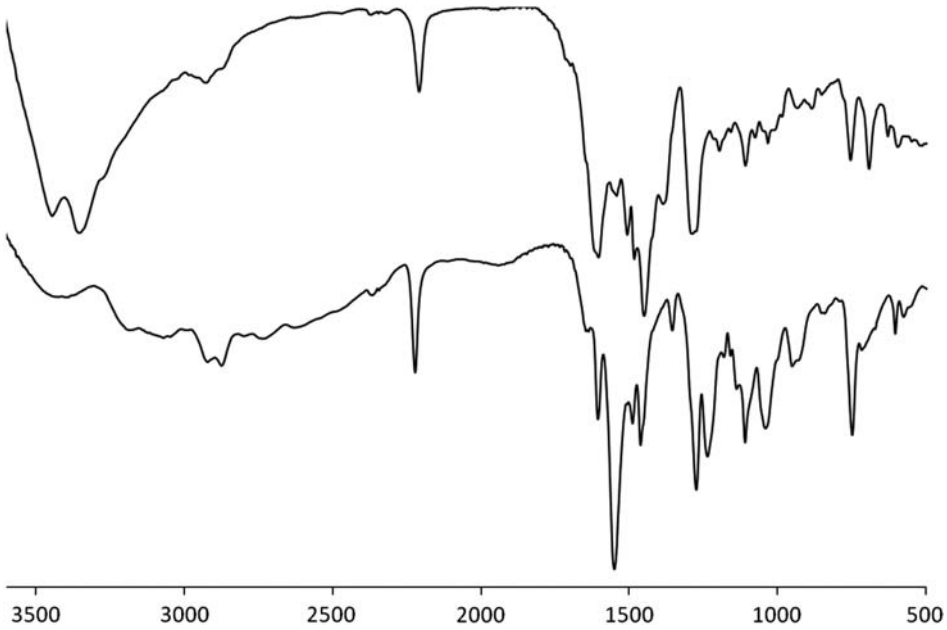


Figure 13. IR spectra of free ligand **7** and its complex with Cu^{2+} chloride recorded in KBr.

freshly distilled tetrahydrofuran (THF). The potentiometric selectivity coefficients were determined by the separate solution method (SSM) according to the procedure described by Bakker et al. (*18*) and were calculated using the EMF values for the highest measured ion activities that belong to the linear response range for a given ion.

In preliminary experiments, we investigated the potentiometric response towards various cations, starting from the most discriminated. The solution of Co^{2+}, Zn^{2+}, Ni^{2+}, Fe^{2+}, Cu^{2+} and Pb^{2+} chlorides was examined ($c_M = 10^{-5}$–10^{-2} M). The ion-selective membrane electrodes doped with compounds **5**–**8** were selective for Pb^{2+} cations. For all membranes, the electrode slopes for Pb^{2+} have been close to the Nernstian value: 28.2 mV dec^{-1} (compound **5**), 29.0 mV dec^{-1} (compound **6**), 26.4 mV dec^{-1} (compound **7**) and 27.8 mV dec^{-1} for compound **8**. Spectroscopic studies revealed that ligands **6** and **7** form complexes with copper(II) perchlorate in methanol solution. Usually compounds which form stable complexes with the cation are weak ionophores for that discriminated one in the ion-selective membrane. Conducted measurements showed worse electrode slopes for Cu^{2+} than for Pb^{2+}: 22.4 mV dec^{-1} (compound **5**), 22.2 mV dec^{-1} (compound **6**), 28.2 mV dec^{-1} (compound

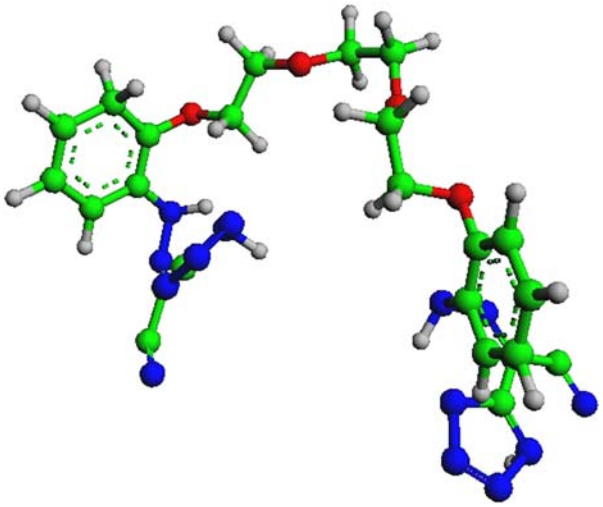


Figure 14. Optimised geometry of **7**.

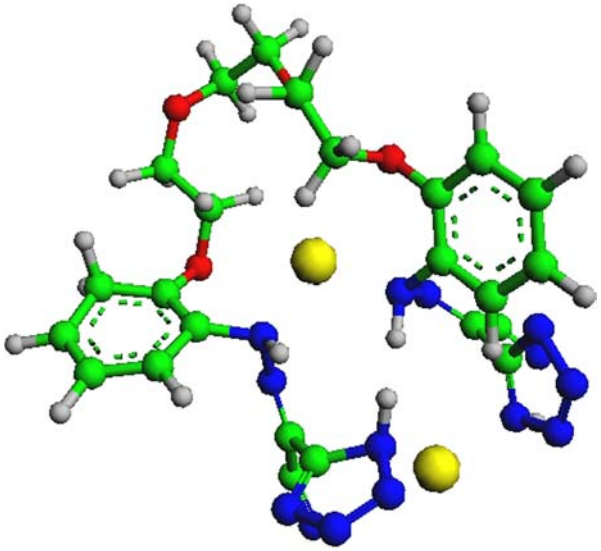


Figure 15. Optimised geometry of **7** Cu^{2+} complex.

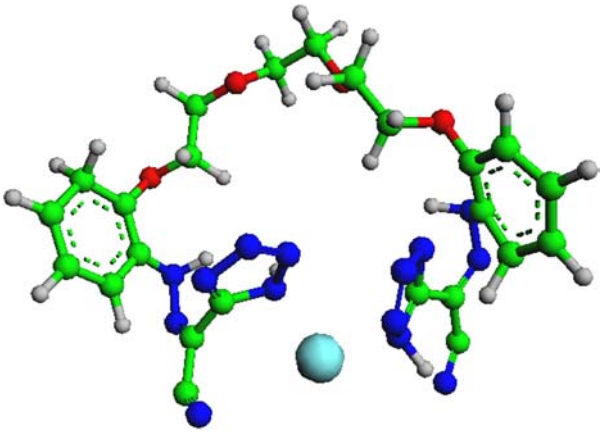


Figure 16. Optimised geometry of **7** Pb^{2+} complex.

7) and 25.1 mV dec^{-1} for compound **8**. In addition, it was found that the examined electrodes responded towards other ions (Zn^{2+}, Ni^{2+} and Fe^{2+}) only in the 10^{-4} to 10^{-2} M concentration range, with slopes being nearer to Nerstian values (22–25 mV dec^{-1}). Because of the high detection limit of electrodes, they were excluded from further studies and only the characteristics of electrodes based on compounds **5**–**8** towards Pb^{2+} and Cu^{2+} are presented in Figure 17.

Table 2. Some theoretical parameters of receptor **7** and after complexation.

Substrates	**7** Cu^{2+}	**7** Pb^{2+}
N1···X	2.0309	5.004
N2···X	2.0395	5.680
N5···X	2.036	2.733
N6···X	2.026	2.744
H1···X	1.467	5.147
H2···X	1.644	4.458
H5···X	2.503	2.178
H6···X	1.637	2.187
N3···X	2.896	4.290
N4···X	2.874	5.229

A comparison of the selectivities of membranes based on bis-(phenylhydrazono-1*H*-tetrazol-5-yl-acetonitriles) derivatives **5**–**8** with different lengths of polyether chains indicates that all compounds are lead selective. Moreover, it can be seen from Table 3 that the incorporation of sulphur atoms improves lead selectivity. Membranes doped with compound **8** show higher affinity towards Pb^{2+} ($\log K_{Pb,Cu} = -2.0$) than membranes with compound **6** ($\log K_{Pb,Cu} = -1.65$). Membrane doped with compounds **5** and **7** is less selective with respect to Cu^{2+}. The temporal changes in potentiometric response of

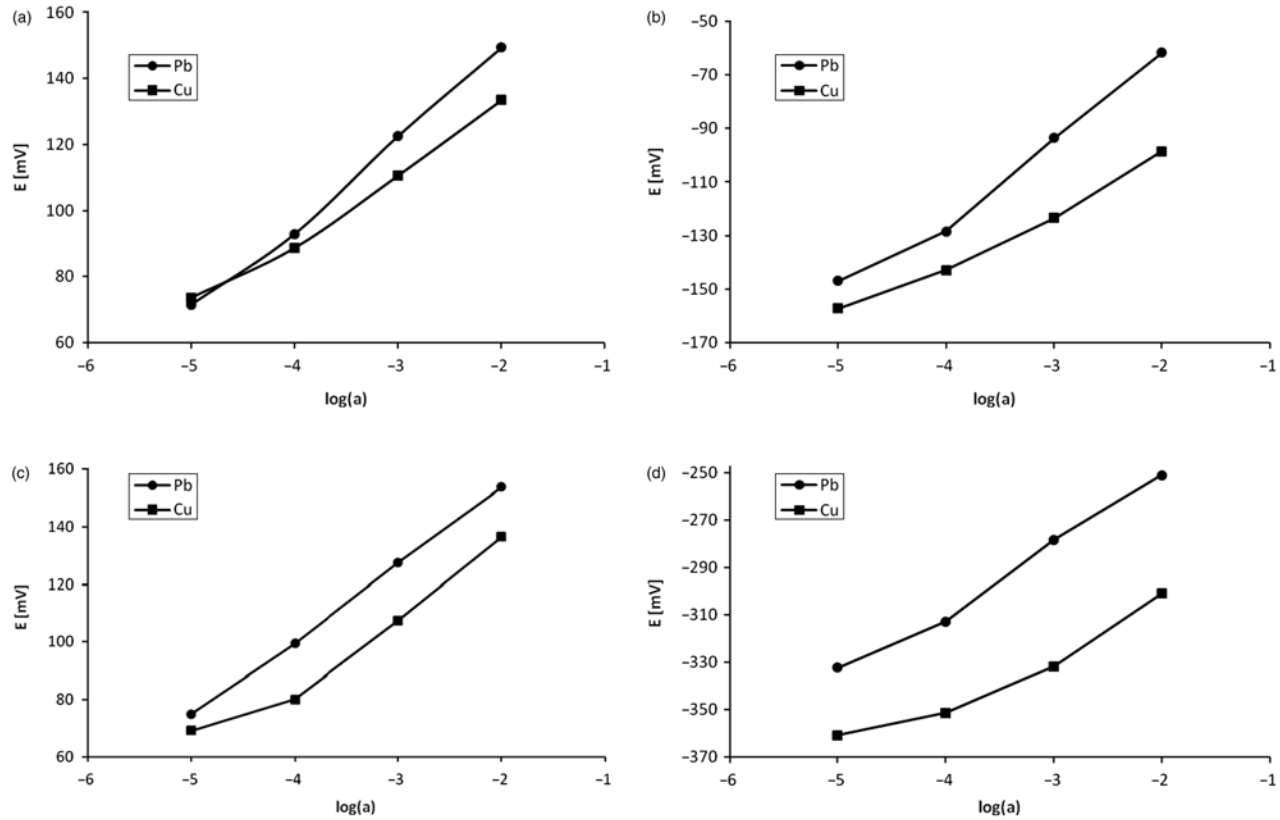


Figure 17. Potentiometric response of membrane ion-selective electrode for Pb^{2+} and Cu^{2+} ions: (a) compound **5**; (b) compound **6**; (c) compound **7**; (d) compound **8**.

Table 3. Selectivity coefficients for various interfering ions.

Interfering ion	5	6	7	8
Zn^{2+}	−2.038	−3.179	−3.068	−2.067
Ni^{2+}	−1.629	−2.72	−2.62	−1.69
Co^{2+}	−1.906	−2.00	−2.382	−0.219
Cu^{2+}	−0.71	−1.65	−0.61	−2.05
Fe^{2+}	−0.811	0.14	−0.168	0.287

electrodes towards Pb^{2+} and Cu^{2+} ions presented in Figure 17 illustrate that electrodes start to show Nerstian response towards metal cation at relatively low concentrations.

For further selectivity studies, the potentiometric measurements were carried out at different pH values (pH 4–6). Nitrate solution of Cu^{2+} and Pb^{2+} was adjusted with HNO_3 to balance the level of pH. The selectivity coefficients for Pb^{2+} and Cu^{2+} in case of ligands **5**–**8** depend on pH values. Only at pH 5, the electrode responded towards Pb^{2+} and values of slopes were nearer to the Nernstian value: 27.4 mV dec^{-1} (compound **5**), 29.5 mV dec^{-1} (compound **6**), 26.6 mV dec^{-1} (compound **7**) and 28.5 mV dec^{-1} for compound **8** (see Figure 18).

The selectivity of electrodes towards various anions, such as bromide, iodide, chloride, fluoride, nitrate, sulphate, phosphate and acetate have also been studied. Unfortunately, the examined electrodes did not respond to the Nernstian slope for those anions.

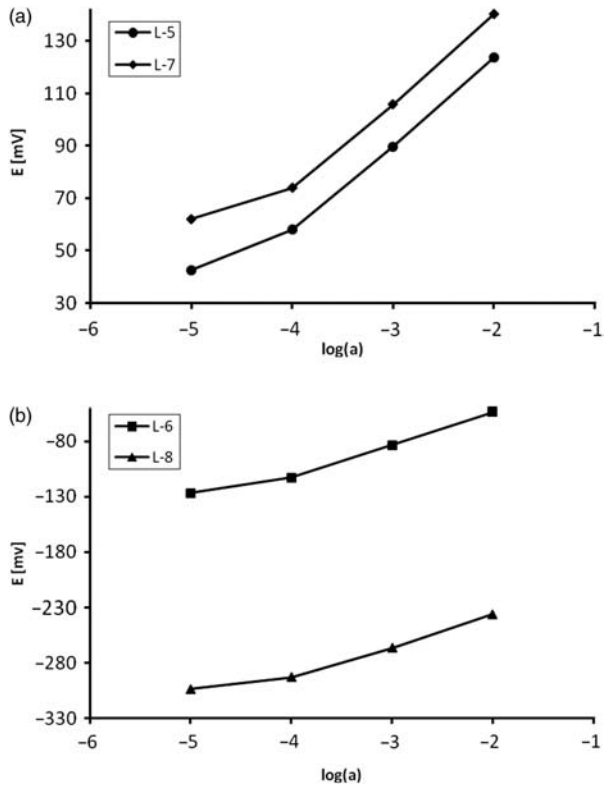


Figure 18. Potential response of membrane ion-selective electrode for Pb^{2+} cation at pH 5: (a) compounds **5** and **7**; (b) compounds **6** and **8**.

Conclusion

A series of new bis-tetrazole compounds **5**–**8** containing aliphatic chains with oxygen and sulphur atoms and with hydrazone bonds have been obtained. The bis(phenylhydrazono-1*H*-tetrazol-5-yl-acetonitriles) were synthesised by cycloaddition using 1,1-dicyanohydrazone derivatives with sodium azide and ammonium chloride. The spectroscopic properties of the resulting bis-tetrazoles have been studied by UV–vis spectroscopy. UV–vis measurements showed very similar chromogenic abilities for all ligands towards Cu^{2+} ions. Furthermore, the compound with shorter polyether linkers (**5** and **6**) showed stronger association constants towards Ni^{2+} and Zn^{2+} ions than **7**. The obtained compounds were used as ionophores in ion-selective electrodes. It was found that they are Pb^{2+}-selective ionophores.

Experimental section

General methods

All materials and solvents were of analytical reagent grade. Thin layer chromatography was done on aluminium plates covered with silica gel 60 F_{254} (Merck), Germany. ^1H NMR spectra were taken on Varian, USA instrument at 200 and/or 500 MHz. IR spectra were recorded on Genesis II FT-IR (Mattson), USA instrument. UV–vis measurements were carried out with the use of UNICAM UV, England 300 Series spectrophotometer. Elemental analyses were done on EAGER 200 apparatus. The melting points are uncorrected. High-molecular weight PVC, KT*p*ClPB, *o*-NPOE and THF were purchased from Fluka, Poland. All aqueous solutions were prepared from salts of analytical grade using deionised water. All measurements were carried out at room temperature. Gaussian 03 software was used for all theoretical calculations (*19*).

Procedure for synthesis of 1,1-dicyanohydrazones derivatives (1–4)

Concentrated hydrochloric acid (8.5 ml) was added to a suspension of respective diamine (7.5 mmol) in water (20 ml). An ice-cooled solution of sodium nitrite (1.035 g, 0.015 mol) in water (2 ml) was treated with cooled suspension of hydrochloride and was stirred at 5°C for 30 min. The mixture was added quickly to a solution of malononitrile (0.99 g, 0.015 mol) in a mixture of ethanol (20 ml) and water (25 ml) containing sodium acetate (13.95 g, 0.17 mol). The yellow precipitate was filtered off and purified by recrystallisation using distilled water.

*1,2-Bis[2-(phenylhydrazonodi-acetonitriles)phenoxy]ethane (**1**)*

Yellow solid; mp 121–123°C; 85% yield. ^{1}H NMR (200 MHz, *d*-DMSO): $\delta = 4.56$ (s, 4H, CH_2O), 6.96–7.10 (m, 4H, H_{Ar}), 7.21–7.25 (m, 2H, H_{Ar}), 7.39–7.44 (m, 2H, H_{Ar}), 10.58 (s, 2H, NH) ppm. IR (KBr): 3270, 3083, 2944, 2227, 2205, 1609, 1596, 1534, 1499, 1448, 1274, 1219, 1162, 1111, 1073, 1051, 929, 747, 658, 577 and 469 cm^{-1}. Anal. calcd for $C_{20}H_{14}N_8O_2$: C 60.30, H 3.53, N 28.13. Found: C 60.39, H 3.62, N 28.22.

*1,5-Bis[2-(phenylhydrazonodi-acetonitriles)phenoxy]-3-oxa-pentane (**2**)*

Yellow solid; mp 134–137°C; 55% yield. ^{1}H NMR (200 MHz, *d*-DMSO): $\delta = 4.07$–4.10 (m, 4H, CH_2O), 4.25–4.29 (m, 4H, CH_2O), 6.89–6.99 (m, 6H, H_{Ar}), 7.37–7.40 (m, 2H, H_{Ar}), 10.61 (s, 2H, NH) ppm. IR (KBr): 3283, 3070, 2936, 2876, 2229, 2211, 1598, 1510, 1480, 1360, 1270, 2257, 1130, 1105, 1042, 915, 753, 651, 604, 571 and 467 cm^{-1}. Anal. calcd for $C_{22}H_{18}N_8O_3$: C 59.72, H 4.11, N 25.33. Found: C 59.80, H 4.22, N 25.39.

*1,8-Bis[2-(phenylhydrazonodi-acetonitriles)phenoxy]-3,6-dioxaoctane (**3**)*

Yellow solid; mp 80–82°C; 90% yield. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 3.77$ (s, 4H, CH_2O), 3.87 (t, $J = 4.30$ Hz, 4H, CH_2O), 4.24 (t, $J = 4.38$ Hz, 4H, CH_2O), 6.96 (d, $J = 8.3$ Hz, 2H, H_{Ar}), 7.04 (t, $J = 7.8$ Hz, 2H, H_{Ar}), 7.18 (t, $J = 7.8$ Hz, 2H, H_{Ar}), 7.48 (d, $J = 7.8$ Hz, 2H, H_{Ar}), 10.53 (s, 2H, NH) ppm. IR (KBr): 3490, 3250, 2900, 2233, 2200, 1637, 1615, 1597, 1550, 1490, 1351, 1290, 1228, 1161, 1114, 1060, 950, 930, 748, 677, 603, 574 and 472 cm^{-1}. Anal. calcd for $C_{24}H_{22}N_8O_4$: C 59.25, H 4.55, N 23.02. Found: C 59.31, H 4.64, N 23.11.

*1,5-Bis[2-(phenylhydrazonodi-acetonitriles)phenyl(thio)]-3-oxapentane (**4**)*

Yellow solid; mp 129–130°C; 72% yield. ^{1}H NMR (200 MHz, *d*-DMSO): $\delta = 3.02$–3.06 (m, 4H, CH_2S), 3.41–3.47 (m, CH_2O), 7.22–7.25 (m, 2H, H_{Ar}), 7.36–7.42 (m, 4H, H_{Ar}), 7.53–7.57 (m, 2H, H_{Ar}), 10.77 (s, 2H, NH) ppm. IR (KBr): 3188, 2923, 2225, 2209, 1580, 1520, 1420, 1314, 1276, 1232, 1191, 1075, 1039, 871, 798, 760, 667, 605, 579, 541, 465 and 414 cm^{-1}. Anal. calcd for $C_{22}H_{18}N_8OS_2$: C 55.68, H 3.82, N 23.60, S 13.52. Found: C 55.74, H 3.89, N 23.71, S 13.49.

Procedure for synthesis of bis(phenylhydrazono-1H-tetrazol-5-yl-acetonitriles) (5–8)

A mixture of 1,1-dicyanohydrazone (1 mmol), sodium azide (0.28 g, 4.4 mmol) and ammonium chloride (0.23 g, 4.4 mmol) in dry DMF (5 ml) was stirred and heated at 120°C for 24 h. It was subsequently cooled to room temperature, the insoluble salts were filtered and the solvent was evaporated under reduced pressure. The resulting solution was poured into 50 ml of water and then was brought to pH 2 using concentrated hydrochloric acid to give a crude product that was purified by recrystallisation using distilled water.

*1,2-Bis[2-(phenylhydrazono-1H-tetrazol-5-yl-acetonitriles)-phenoxy]ethane (**5**)*

Brown solid; mp 203–207°C; 52% yield. ^{1}H NMR (200 MHz, *d*-DMSO): $\delta = 4.62$ (s, 4H, CH_2O), 5.08–5.2 (m, 2H, NH), 6.97–7.04 (m, 4H, H_{Ar}), 7.23–7.27 (m, 2H, H_{Ar}), 7.38–7.43 (m, 2H, H_{Ar}), 12.73 (s, 2H, NH) ppm. IR (KBr): 3500, 3380, 3265, 3050, 2939, 2221, 1611, 1600, 1522, 1489, 1444, 1274, 1219, 1162, 1110, 1108, 1080, 1045, 980, 774, 650, 550 and 440 cm^{-1}. Anal. calcd for $C_{20}H_{16}N_{14}O_2$: C 49.59, H 3.33, N 40.48. Found: C 49.65, H 3.39, N 40.33.

*1,5-Bis[2-(phenylhydrazono-1H-tetrazol-5-yl-acetonitriles)-phenoxy]-3-oxapentane (**6**)*

Yellow solid; mp 177–180°C; 83% yield. ^{1}H NMR (200 MHz, *d*-DMSO): $\delta = 4.05$–4.08 (m, 4H, CH_2O), 4.24–4.28 (m, 4H, CH_2O), 4.98–5.12 (m, 2H, NH), 6.93–7.0 (m, 6H, H_{Ar}), 7.46–7.5 (m, 2H, H_{Ar}), 12.84 (s, 2H, NH) ppm. IR (KBr): 3423, 3296, 3084, 2939, 2865, 2222, 1600, 1550, 1480, 1378, 1268, 1247, 1108, 1100, 1036, 910, 750, 659, 646, 577 and 464 cm^{-1}. Anal. calcd for $C_{22}H_{20}N_{14}O_3$: C 50.00, H 3.81, N 37.10. Found: C 50.09, H 3.88, N 37.28.

*1,8-Bis[2-(phenylhydrazono-1H-tetrazol-5-yl-acetonitriles)-phenoxy]-3,6-dioxaoctane (**7**)*

Brown solid; mp 132–135°C; 70% yield. ^{1}H NMR (200 MHz, *d*-DMSO): $\delta = 3.70$ (s, 4H, CH_2O), 3.85 (s, 4H, CH_2O), 4.18 (s, 4H, CH_2O), 4.90–5.15 (m, 2H, NH), 6.89–7.04 (m, 5H, H_{Ar}), 7.51–7.54 (m, 3H, H_{Ar}), 12.84 (s, 2H, NH). IR (KBr): 3532, 3450, 3200, 2956, 2221, 1645, 1608, 1600, 1549, 1456, 1440, 1389, 1277, 1237, 1181, 1110, 1108, 1060, 967, 783, 667, 578 and 460 cm^{-1}. Anal. calcd for $C_{24}H_{24}N_{14}O_4$: C 50.35, H 4.23, N 34.25. Found: C 50.41, H 4.30, N 34.29.

*1,5-Bis[2-(phenylhydrazono-1H-tetrazol-5-yl-acetonitriles)-phenyl(thio)]-3-oxapentane (**8**)*

Yellow solid; mp 108–110°C; 88% yield. ^{1}H NMR (200 MHz, *d*-DMSO): $\delta = 3.04$ (t, $J = 6.22$ Hz, 4H, CH_2S), 3.47 (t, $J = 6.21$ Hz, 4H, CH_2O), 3.88–4.01

(m, 2H, NH), 7.24 (d, $J = 7.53$ Hz, 2H, H_{Ar}), 7.38–7.47 (m, 4H, H_{Ar}), 7.55 (d, $J = 7.61$ Hz, 2H, H_{Ar}), 12.05 (s, 2H, NH) ppm. IR (KBr): 3407, 3220, 3155, 2923, 2225, 2209, 1600, 1540, 1520, 1440, 1307, 1268, 1222, 1191, 1080, 1045, 870, 788, 755, 667, 579, 543, 457 and 410 cm^{-1}. Anal. calcd for $C_{22}H_{20}N_{14}OS_2$: C 47.13, H 3.60, N 34.98, S 11.44. Found: C 47.22, H 3.64, N 34.85, S 11.49.

Membrane preparation

The membrane components: 2 mg of ionophore (**5**–**8**), 60 mg of PVC, 120 mg of *o*-NPOE and 0.5 mg of KT*p*ClPB were dissolved in 1.5 ml of freshly distilled THF. The solution was placed in a glass ring over a glass plate. After evaporation of the solvent overnight, the resulting membrane was peeled from the glass mould, and discs of 7 mm i.d. were cut out. The membranes were incorporated onto Ag/AgCl electrode bodies of IS 561 type (Moeller S.A., Zurich, Switzerland). Electrode bodies were filled with an internal filling solution – KCl (10^{-3} M). The electrode was conditioned in deionised water for 2 h. A double-junction reference electrode Eurosensor EagClK-312 was used with KNO_3 (1 M) solution in the bridge cell. The measurements were carried out at room temperature using the following cell: Ag/AgCl/internal electrolyte/membrane/sample/KNO_3 (1 M)/KCl (1 M)/AgCl/Ag and 16-channel LAWSON LAB potentiometer (16 EMF, USA). The selectivity coefficients were determined using the SSM at ion activities of 10^{-2} M.

Spectrophotometric studies of metal cation complexation

All reagents and solvents were of the highest commercial quality and were used without further purification. $Zn(ClO_4)_2{\cdot}6H_2O$, $Cu(ClO_4)_2{\cdot}6H_2O$, $Ni(ClO_4)_2{\cdot}6H_2O$, $Pb(ClO_4)_2{\cdot}6H_2O$, $CoCl_2$, $CuCl_2$, $NiCl_2$, $ZnCl_2$, Cl_2-$Fe{\cdot}4H_2O$ and $PbCl_2$ were purchased from Aldrich and dried under vacuum. UV–vis titration was carried out by addition of metal ion to the bis(phenylhydrazono-1*H*-tetrazol-5-yl-acetonitriles) solution. Titrations were carried out in 1-cm path length quartz cuvette keeping the volume of the ligand solution constant (2 ml). Titration step 0.01 ml.

Acknowledgement

Financial support of this work from Gdansk University of Technology, Grant Nos BW 014694/038 and BW 014694/039, is kindly acknowledged.

References

(1) Pedersen, C.J. *J. Am. Chem. Soc.* **1967**, *89* (26), 7017–7036.
(2) Shinkai, S.; Torigoe, K.; Manabe, O.; Kajiyama, T. *J. Am. Chem. Soc.* **1987**, *25*, 4458–4464.
(3) Kozbia, M.; Pietraszkiewicz, M.; Pietraszkiewicz, O. *J. Incl. Phenom. Macrocycl. Chem.* **1998**, *30*, 69–77.
(4) Gokel, G.W.; Korzeniowski, S.H. *Macrocyclic Polyether Synthesis*; Springer-Verlag: Berlin, Heidelberg, New York, 1982.
(5) Pearsons, D.G.; Truter, M.R.; Wingfield, J.N. *Inorg. Chim. Acta* **1975**, *14*, 45–48.
(6) (a) Herr, R. *J. Bioorg. Med. Chem.* **2002**, *10*, 3379–3393. (b) Holland, G.F., Pereira, J.N., *J. Med. Chem.* **1967**, *10*, 149–154.
(7) (a) Mavromoustakos, T., Kolocouris, A., Zervou, M., Roumelioti, P., Matsoukas, J., Weisemann, R. *J. Med. Chem.* **1999**, *42*, 1714–1722. (b) Toney, J.H., Fitzgerald, P.M.D., Grover-Sharma, N., Olson, S.H., May, W.J., Sundelof, J.G., Vanderwall, D.E., Cleary K.A., Grant, S.K., Wu, J.K., Kozarich, J.W., Pompliano, D.L., Hammond, G.G. *Chem. Biol.* **1998**, *5*, 185–196.
(8) (a) Hashimoto, Y., Ohashi, R., Kurosawa, Y., Minami, K., Kaji, H., Hayashida, K., Narita, H., Murata, S. *J. Card. Pharm.* **1998**, *32*, 568–575. (b) Abell, A.D., Foulds, G.J. *J. Chem. Soc. Perkin Trans.* **1997**, *1*, 2475–2482.
(9) Aromi, G.; Barrios, L.A.; Roubeau, O.; Gamez, P. *Coord. Chem. Rev.* **2011**, *255*, 485–546.
(10) Koldobskii, G.I.; Ostrovskii, V.A.; Poplavskii, V.S. *Khim. Get. Soed.* **1981**, *17*, 1299–1326.
(11) Ogihara, W.; Yashizawa, M.; Ohno, H. *Chem. Lett.* **2004**, *33*, 1022–1023.
(12) Shie, J.-J.; Fang, J.-M. *J. Org. Chem.* **2002**, *68*, 1158–1160.
(13) (a) Gang, Q., Wei, L., Zhining, B. *Chin. J. Chem.* **2011**, *29*, 131–134. (b) Teimouri, A., Chermahini, A.T. *Polyhedron* **2011**, *30*, 2606–2610.
(14) Sreedhar, B.; Suresh Kumar, A.; Yada, D. *Tetrahedron Lett.* **2011**, *52*, 3565–3569.
(15) Rama, V.; Kanagaraj, K.; Pitchumani, K. *J. Org. Chem.* **2011**, *76*, 9090–9095.
(16) Butler, N.B.; Quinn, K.F.; Welke, B. *J. Chem. Soc. Chem. Commun.* **1992**, *20*, 1481–1482.
(17) Yavuz, S.; Aydın, O.; Çete, S.; Dişli, A.; Yıldırır, Y. *Med. Chem. Res.* **2010**, *19*, 120–126.
(18) Bakker, E. *Anal. Chem.* **1997**, *69*, 1061–1069.
(19) Frisch, M.J. *Gaussian 03, in Revision B.03*; Gaussian, Inc.: Pittsburgh, PA, 2003.