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Synthesis, IR and NMR characterization and ion extraction properties of tetranonylcalix[4]resorcinol bearing acetylhydrazone groups

Sergey N. Podyachev *, Nadezda E. Burmakina, Viktor V. Syakaev, Svetlana N. Sudakova, Roald R. Shagidullin, Alexander I. Konovalov

A. E. Arbuzov Institute of Organic and Physical Chemistry, Kazan Scientific Center of Russian Academy of Sciences, Arbuzov str. 8, 420088, Kazan, Russia

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ABSTRACT

A series of new calix[4]resorcinarenes (*rccc*-isomer) and resorcinols functionalized by acetylhydrazone binding fragments have been synthesized. The IR and NMR data and stereochemical behaviour of hydrazones are reported and compared with the results of earlier investigations. The barriers of rotation of hydrazone fragments for some octahydrazone derivatives of calix[4]resorcinarenes and their resorcinol analogues have been determined by NMR-measurements. The complexing behaviour of bis- and octahydrazones has been studied by liquid–liquid extraction towards the s-metal ions (Li^+, Na^+, K^+, Cs^+ and Ca^{2+}), p-metal ions (Pb^{2+}), d-metal ions (Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+} and Hg^{2+}) and f-metal ions (La^{3+}, Gd^{3+} and Lu^{3+}). The stoichiometry of complexes and the extraction constants have been determined. It has been established that octahydrazones do not extract alkali metal cations but show excellent selectivity towards transition and soft heavy metal cations (especially Hg^{2+} or Pb^{2+}).

1. Introduction

Chelating systems are widely used in coordination chemistry as a class of ligands forming predominantly five- and six-membered metal rings.[1] In order to enhance the binding efficiency and selectivity of the designed ligands complementary matching between the interacting sites is usually optimized. Another approach of modification of chelating system properties is the synthesis of three-dimensional polydentate ligands with ligating groups fixed on a suitable molecular skeleton. The presence of several such groups in a molecule can be used for creating new architecture compounds with unusual properties. The resulting nanometre-scale structures are normally capable of simultaneously binding two or more metal ions located in defined positions relative to each other. On the other hand, the cooperative effect of closely located binding centres can increase the yield of more kinetically and thermodynamically stable metal complexes than their monomer acyclic analogues.[2–4]

In the last decade, the interest in polychelate compounds has notably increased due to the further development of supramolecular chemistry and especially the chemistry directed to the synthesis of spatially-organized structures, particularly, calixarenes.[5–8] The parent compounds are readily available and can be functionalized both at the phenolic OH groups and at the *para* positions of phenol rings into numerous of derivatives. By variation of the number and type of aromatic fragments (usually phenol, resorcinol and pyrogallol fragments are widely used) the required coordinating capacity of supramolecular receptor can be reached. The use of a template approach in the case of calix[4]phenol, the choice of suitable condensing agent for the calix[4]resorcinol synthesis allows as a rule to fix the desired molecular configuration at the initial stages of their synthesis. In this connection, calixarenes are appealing macrocyclic platforms for the preorganization of chelating groups and can be considered as 'multivalent scaffolds'.[9] Multivalency is the ability of a particle to bind another particle via multiple simultaneous noncovalent interactions. The valency is therefore the number of 'ligating functionalities of the same or similar types connected to each of these entities'.[9]

The calixarenes, as parent compounds, have been transformed into their ethers,[7,8,10] which are suitable precursors for the subsequent synthesis of polydentate ligands. By the hydrazinolysis of these ethers, a series of hydrazide derivatives of calix[4]phenols, calix[4]resorcinols and calix[4]pyrogallols have been synthesized.[11] The high extraction ability and selectivity of calix[4]phenols with acetylhydrazide groups towards a series of transition metal ions have been established.[11,12] By the interaction of calix[4]phenol

* Corresponding author. Fax: +07 843 2731872.
E-mail address: spodyachev@iopc.knc.ru (S.N. Podyachev).

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acetylhydrazides with aldehydes, new hydrazone derivatives possessing interesting conformations and dynamic behaviour have been obtained.[13,14] Hydrazone compounds are attractive not only due to their potential antibacterial, bactericidal, fungicidal and antitumoral properties,[15–17] or the ability to control the release of volatile aldehydes and ketones,[18] but also due to their effective extraction properties towards transition metal ions.[19–21] Acetylhydrazone complexes with metal cations are well studied in coordination chemistry, which is also explained by their unique physico-chemical properties and physiological activity.[19,22] The presence of donor oxygen and nitrogen atoms in hydrazone molecules provides them with the ability to coordinate hard as well as soft transition metal ions. The incorporation of hydrazone groups in calixarenes will help to maintain the corresponding metal derivative's integrity under a variety of conditions. Such types of compound are very promising for liquid extraction procedure with the aim of recovery, separation and concentration of transition metal ions.

In this paper, we present details of the synthesis, IR and NMR characterization of a new family of hydrazones—derivatives of calix[4]resorcinol and their structural units. The investigation of the receptor properties of this family of calixarenes towards alkali, alkali-earth and transition metals has been carried out. Their binding properties have been investigated by the liquid–liquid extraction method by using the aqueous solutions of metal picrates. The extraction efficiency and selectivity, stoichiometry of complexes and extraction constants for transition metals have been established.

2. Results and discussion

2.1. Synthesis

The synthesis of hydrazones **2a–f** and **4b–f** is shown in Figure 1. By the reaction of ethyl bromoacetate with resorcinol or calix[4]pyrogallol, the corresponding esters have been obtained. Then, by the subsequent treatment with an excess of hydrazine hydrate, the esters were transformed into hydrazides **1** and **3** according to a procedure described by us earlier.[11] Condensation of compound **1** or **3** with an excess of appropriate aldehyde (or acetone) has resulted in the conversion of all acetylhydrazide groups to acetylhydrazone. The hydrazones **2a–f** and **4b–f** have been obtained with yields in the range 52–92%. The composition and the structure of synthesized compounds **2a–f** and **4b–f** have been proven by the elemental analysis, HRMS (EI) and MALDI-TOF mass spectrometry, NMR and IR spectroscopy data.

Recently we have also reported the synthesis of tetrathiacalix[4]phenols functionalized by acetylhydrazone fragments.[13,14] However, the desired product of complete substitution has been obtained only by using picolinaldehyde as a reagent. The reaction of tetrathiacalix[4]arene acetylhydrazide with an excess of 4-nitrobenzaldehyde leads to the preferential formation of an unconventional tetrathiacalix[4]arene with two acetylhydrazone fragments and the additional formation of *N,N′*-diacetylhydrazine bridge in the 1,3-positions. Though for the *1,3-alternate* conformer of calix[4]phenol as well as for calix[4]resorcinol and resorcinol derivatives in our case such a phenomenon did not take place. Obviously this is caused by the relative ordering of functional groups.

2.2. IR characterization in solid

IR spectra of **4b–f** in solid state are practically similar to the spectra of **2a–f** and earlier reported data for 4-*tert*-butylphenoxyacetylhydrazones[23] that is caused by the similarity of their structural blocks (Table 1). The absorption band ν(C=N) appeared as a shoulder in the region of ~1640–1660 cm^{-1} and only for compound **2a** registered as a weak single peak with the maximum at 1640 cm^{-1}. At the same time IR spectra of **4b–f** in comparison with their acyclic analogues spectra have broader absorption bands. The

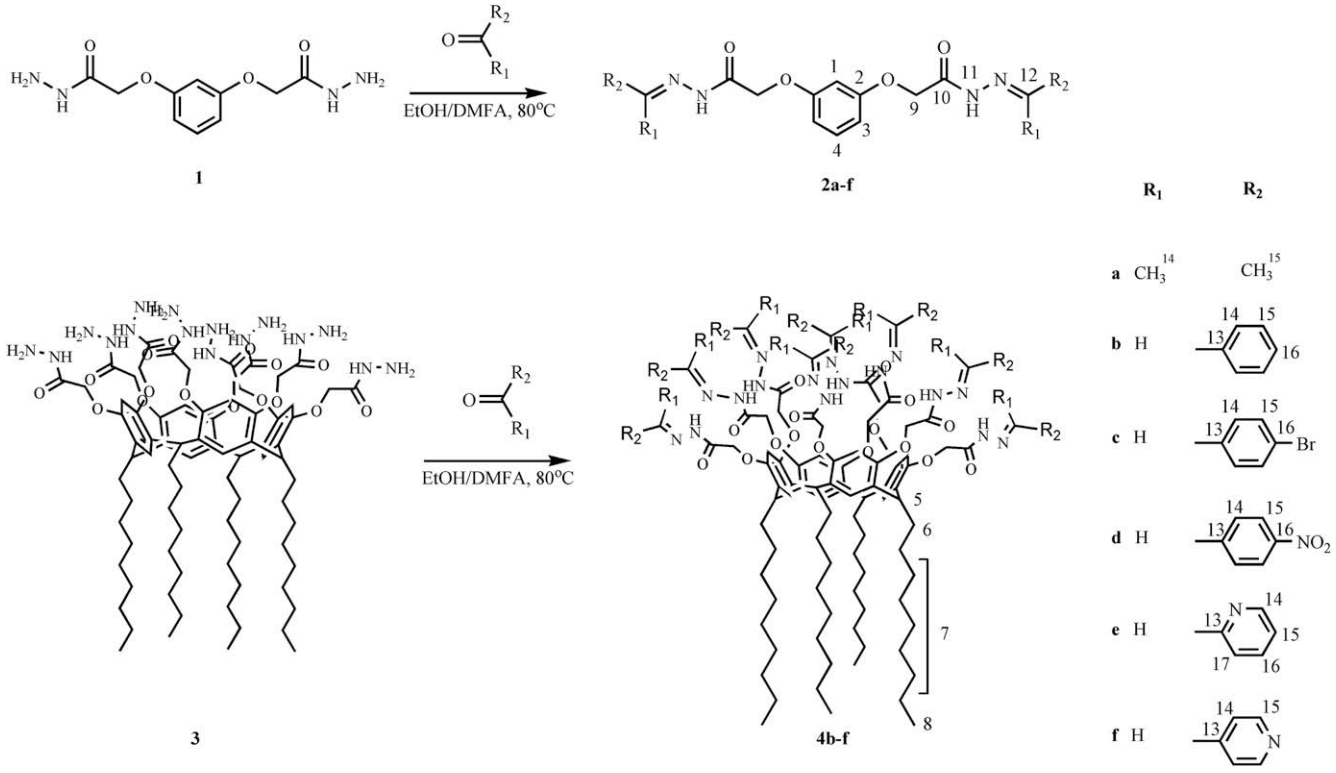


Figure 1. Synthesis of the hydrazones **2a–f** and **4b–f** and atomic numbering scheme.

Table 1
The frequencies of characteristic vibrations (ν, cm^{-1})[a] in IR spectra and cis/trans conformational composition of acetylhydrazones **2a–f** and **4b–f**

Compound	Vibration, assignment (Nujol)			Conformational composition
	ν(NH)	δ(NH)	N(C=O)	
2a	3221br	**1556**	*1683*	*cis/trans*[b]
	3054br			
2b	3237sh	**1556**	*1687*	*cis/trans*
	3215		1675sh	
	3073br			
2c	**3187**	—	*1685*	*cis/—*
	3088		*1675*	
	3067sh			
2d	3191br	**1565**	1696	*cis/trans*
	3062		1667	
2e	3294	1530	1705sh	*cis/trans*[b]
	3090br		*1698*	
	3061			
2f	3311	1546	*1702*	*cis/trans*[b]
	3219br		*1683*	
	3163br			
4b	3218br	**1534**	*1695br*	*cis/trans*[b]
	3062br			
4c	**3214br**	**1533**	*1695br*	*cis/trans*[b]
4d	3250br	(—)[a]	*1698br*	*cis/trans*[b]
4e	3205br	**1531**	*1697br*	*cis/trans*[b]
	3055			
4f	**3331**	**1549**	*1704br*	*cis/trans*[b]
	3213br	**1531**		

[a] Additional characteristics of absorption bands: sh—shoulder; br—broad; vbr—very broad. The maxima of rather intensive bands of signals are italicized. The maxima of weak intensive bands of signals are in bold.
[b] The *trans*-conformer dominated.

occurrence of four resorcinol fragments in compounds **4b–f** leads to a variety of conformational states and the appearance of additional intra- and intermolecular interactions.

The structural characteristics of hydrazones are determined by the presence of *cis/trans* conformers about C(O)–N bond and *E/Z* geometrical isomers respect to the *C=N* double bonds (Fig. 2). The $\boldsymbol{Z}_{N-N}$ conformer is not realized because of steric hindrance. IR, ^1H, ^{13}C NMR and X-ray analysis have shown the *cis/trans*-amide conformers only. The $E_{C=N}/Z_{C=N}$ isomerization is registered only for the 4-*tert*-butylphenoxyacetylhydrazone of picolinaldehyde in special conditions in $CDCl_3$.[24]

According to the literature data[25] the absorption bands of *trans*-amide forms are revealed in the regions: ~3300 cm^{-1} ν(NH); ~3100 cm^{-1} (weak absorption of overtone 2δ(NH)); ~1680–1630 cm^{-1} (high intensive absorption band Amid I ν(C=O)) and ~1550 cm^{-1} (Amid II δ(NH)). The absorbance of δNH is the most characteristic attribute of *trans*-form, because it is not observed for *cis*-amide conformers in the above mentioned region of spectrum. The absorption bands for *cis*-amide form appear in the regions: ~3200 (νNH); ~3100 cm^{-1} (composite tone ν(C=O)+δ(NH)) and ~1650 cm^{-1} ν(C=O); ~1490–1440 cm^{-1} δ(NH). In conformity with this point of view, the spectra of 4-*tert*-butylphenoxyacetylhydrazones have been interpreted earlier.[23] In agreement with these data the specific spectral characteristics for hydrazones **2a–f** and **4b–f** allowed their conformation composition in the solid to be established (Table 1).

The *trans*-amide conformation of hydrazone fragment in the investigated molecules is revealed in a pair of absorption bands νNH>3200 and 2δNH≈3070 cm^{-1}, where the first peak has a higher frequency and intensity. An additional specific criterion of *trans*-amide conformation is the presence of peak δNH≈1540 cm^{-1}. A similar picture is observed in the spectra of compounds **2e**, **2f**.

The *cis*-amide conformation is characterized by the vibrations ν(NH)<3200 cm^{-1} and composite tone ν(C=N)+δ(NH)≈3070 cm^{-1}. Therewith the first component in this pair of bands has the lower than for trans-conformer frequency and the lower intensity of absorption compared to its partner—composite tone. This situation is clearly illustrated by the spectrum of compound **2c** and is rather sophisticated for **2d** due to Fermi resonance, which was observed earlier for the 4-*tert*-butylphenoxyacetylhydrazone analogue.[23]

In the most of cases the picture of spectrum is complicated by the presence of both cis- and trans-conformer simultaneously and by the influence of functional groups. In general the total content of trans-form in solid state of investigated compounds increased under going from mono-[23] to bishydrazones **2a–f** and octahydrazones **4b–f**. Apparently, the fixing of a large number of hydrazone fragments on a molecule prevents the formation of *cis*-H-dimers owing to steric hindrance. Most of the calix[4]resorcinols **4b–f** prefer the *trans*-conformation of amide fragments, obviously, due to the possibility of formation of unhindered *trans*-H-polymer chains.

2.3. NMR characterization in solution

^1H NMR spectra of calix[4]resorcinols **4b–g** in DMSO at 303 K show broad overlapping signals. With increasing temperature, the spectra are simplified and at temperatures above 373 K only single signals corresponding to the aromatic protons of upper (H1) and lower (H4) rim are observed. Compounds **4b–g** have been synthesized from the calixarenes having *rccc*-configuration. The investigation of unsubstituted calix[4]resorcinols and the compounds with functionalized hydroxyl groups has shown that even at high temperatures the *rccc*-isomer does not transform into another isomer.[26,27] Taking these facts into consideration, it may be concluded that at ambient temperature compounds **4b–g** adopt an *rccc*-configuration.

In contrast to 4-*tert*-butylphenoxyacetylhydrazones[24] investigated by us earlier compounds **2a–f** and especially **4b–f** can adopt much more spatial forms. Thus, there are at least two groups of signals in NMR spectra of compounds **2a–f** in DMSO-d_6 at 303 K. This is explained by the presence of three spatial forms of molecules where pairs of acetylhydrazone fragments can exist in *cis/cis*, cis/trans or *trans/trans* conformations. The presence of eight acetylhydrazone fragments in calix[4]resorcinol molecules of **4b–f** leads to an additional multiplicity of spatial forms as compared to model compounds. Moreover, a large number of polar groups (C(O), NH etc.) favourable to intra-and intermolecular hydrogen bonds, which are stable even in such polar solvent as DMSO, result in the broadening of signals and the overlapping of multiplets in the NMR spectra. For this reason it was impossible in most of the cases to

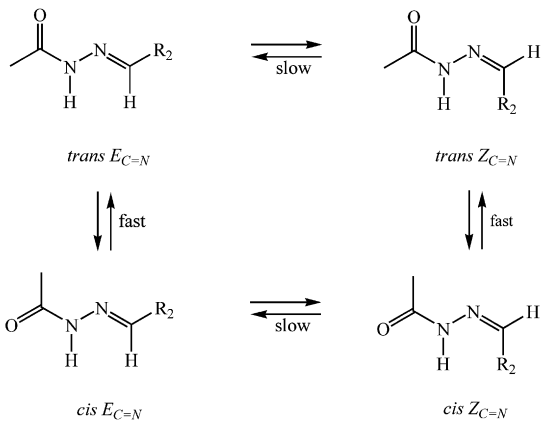


Figure 2. The isomer forms of acetylhydrazone fragment.

determine the coupling constants. The assignment of spatial forms was performed by using mainly the differences in chemical shifts on the basis of criteria described in our previous works.[14,24] In accordance with these criteria, ^{1}H signal of CH_2–C(O) group for *cis*-conformer should be shifted in downfield by ~0.5 ppm as compared with *trans*-conformer. The ^{13}C chemical shift of carbonyl group of the *cis*-conformer should be also downfield shifted by 5–6 ppm relatively to the signal for *trans*-conformer. The results of conformational assignment for investigated compounds **2a**–**f** and **4b**–**f** are represented in Tables 2 and 3. The O–CH_2 group signals are the most sensitive to the conformational change, which allowed the quantitative evaluation of relative population of all spatial forms for bishydrazones **2a**–**f** (Table 4). Whereas, the calix[4]resorcinols **4b**–**f** have essentially more complicated conformational composition, only the relative content of *cis*/*trans*-conformers has been determined.

The percentage of *trans*-amide form for resorcinols **2a**–**b** equals 38–45% and is practically similar to the conformational composition for corresponding 4-*tert*-butylphenoxyacetylhydrazones.[24] Under going to calix[4]resorcinols **4b**–**f** the percentage of *trans*-form increases by 8–18%. A similar phenomenon has been observed under going from 4-*tert*-butylphenoxyacetylhydrazone of picolinaldehyde (40%) to tetrathiacalix[4]arene functionalized by the identical hydrazone fragments (55%).[14] It is in agreement with IR spectroscopy data indicating an increase of *trans*-form percentage for octahydrazones **4b**–**f** as compared with bishydrazones **2a**–**f** in the solid state. The attachment of acetylhydrazone substituents to the calixarene unit obviously prevents their intramolecular interaction, which is observed in cyclic H-dimers and leads to the stabilization of *cis*-conformers.[23,24] Whereas, the formation of hydrogen bonds between NH···C(O) groups of neighbouring acetylhydrazone fragments having *trans*-configuration is less spatially hindered and promotes the generation of *trans*-H-polymer chains.

The *E*/*Z* isomerization relative to the C=N double bonds has not been revealed in most of the investigated cases. Our previous investigations[14,24] have shown that the irradiation of hydrazones in $CDCl_3$ by UV light only in the case of 4-*tert*-butylphenoxyacetylhydrazone of picolinaldehyde resulted in the partial conversion of the $E_{C=N}$ into the $Z_{C=N}$ isomer. A thermally induced isomerization was not found for all hydrazone compounds studied by us earlier.

A similar situation has been also observed for compounds **2** and **4**. The irradiation and keeping of samples at 373 K for 2 h did not lead to the appearance of any new peaks in their NMR spectra, with the exception of compound **2e**. Under heating of a DMSO-d_6 solution of this resorcinol for 2 h the conversion of $E_{C=N}$ into the $Z_{C=N}$ isomer (9%) was observed. When the solution was heated for 12 h the $Z_{C=N}$ isomer content had increased to 21% and practically did not change on further keeping this solution at this temperature (Fig. 3a and b).

The signals attributed to the *trans* $Z_{C=N}$ form (24%) are presented in the spectrum of compound **2e** in $CDCl_3$ immediately after dissolution (Fig. 3c). Irradiating a solution of compound **2e** by UV light (254 nm) for half an hour in a quartz dish increases the amount of the $Z_{C=N}$ isomer to 66% (*trans* $Z_{C=N}$: 64%; *cis* $Z_{C=N}$: 2%) (Fig. 3d). The high percentage of *trans* $Z_{C=N}$ form may be provided by the participation of the amide hydrogen atom of the hydrazone fragment in the formation of bifurcated H-bonds with the ether (–OCH_2) group and nitrogen of the pyridine atom.

The ΔG values depend only slightly on imine group substituents in 4-*tert*-butylphenoxyacetylhydrazones.[24] On going to resorcinols **2b**, **2e** and particularly to calix[4]resorcinols **4b**, **4e** the values of the energy barriers increase by 2.8–5.3 kJ/mol (Table 4). This is probably due to a large number of intra-molecular hydrogen bonds.

Table 2
^{1}H chemical shifts (ppm) of **2a**–**f** and **4b**–**f** in DMSO-d_6

Hydrogen no.	Chemical shift (ppm)										
	2a	**2b**	**2c**	**2d**	**2e**	**2f**	**4b**	**4c**	**4d**	**4e**	**4f**
1	6.34; 6.45; 6.54	6.49	6.49	6.55	6.57	6.56	6.68	6.51; 6.70	6.56; 6.65	6.51; 6.66	6.56; 6.65
3	6.46 d, *J*=7.3 Hz	6.62 d, *J*=8.4 Hz	6.65 d, *J*=8.2 Hz	6.60 d, *J*=8.2 Hz	6.61 d, *J*=7.8 Hz	6.60 d, *J*=8.5 Hz					
4	7.17 t, *J*=7.3 Hz	7.22 t, *J*=8.4 Hz	7.21 t, *J*=8.2 Hz	7.22 t, *J*=8.2 Hz	7.22 t, *J*=7.8 Hz	7.21 t, *J*=8.5 Hz	6.86	6.87	6.7–7.07	7.25–7.33	6.7–7.07
5							4.83	4.77	4.79	4.79	4.52
6							1.88	1.87	1.88	1.88	1.875
7							1.18	1.17	1.18	1.17	1.172
8							0.79	0.79	0.80	0.78	0.784
9	4.59 (4.93)	4.65;[a] 4.66[b] (5.12;[c] 5.14[d])	4.64;[a] 4.66[b] (5.11;[c] 5.12[d])	4.69;[a] 4.71[b] (5.16;[c] 5.18[d])	4.68;[a] 4.70[b] (5.15;[c] 5.17[d])	4.69;[a] 4.68[b] (5.14;[c] 5.16[d])	4.48 (5.05)	4.47 (5.02)	4.48 (5.04)	4.53 (5.03)	4.52 (5.04)
11	10.14 (10.30)	11.52 (11.56)	11.61 (11.60)	11.83 (11.84)	11.78 (11.76)	11.83 (11.82)	10.90 (11.46)	11.46 (10.88)	11.67 (11.31)	11.57 (11.17)	11.7 (11.2)
12		8.35 (8.01;[c] 8.02[d])	8.32 (7.96;[c] 7.98[d])	8.43 (8.07;[c] 8.11[d])	8.37 (8.04;[c] 8.06[d])	8.32 (7.97;[c] 7.99[d])	8.34 (7.86; 7.91)	8.26 (7.82)	8.35 (8.12)	8.29 (7.87)	8.29 (7.79)
14	1.94[e] (1.93[f])	7.71 (7.69)	7.63 (—)[g]	7.95 (—)[g]	8.61 (8.59)	7.63 (—)[g]	7.63 (—)[g]	7.49 (—)[g]	7.70 (—)[g]	8.49 (—)[g]	7.49 (—)[g]
15	1.87[e] (1.86[f])	7.41 (—)[g]	7.64 (—)[g]	8.27 (8.26)	7.4 (—)[g]	8.65 (—)[g]	7.50 (—)[g]	7.49 (—)[g]	7.93 (—)[g]	7.58 (—)[g]	8.49 (—)[g]
16		7.47 (—)[g]			7.87 (7.85)		7.51 (—)[g]			7.70 (—)[g]	
17					7.93 (7.98)					7.84 (—)[g]	

The assignment of signals for *trans*-(*cis*-) amide conformers of acetylhydrazone fragments.
[a] For *trans*-amide conformation of hydrazone fragment when neighbouring group has *cis*-conformation.
[b] For *trans*-amide conformation of hydrazone fragment when neighbouring group has *trans*-conformation.
[c] For *cis*-amide conformation of hydrazone fragment when neighbouring group has *cis*-conformation.
[d] For *cis*-amide conformation of hydrazone fragment when neighbouring group has *trans*-conformation.
[e] Methyl group at *Z* position to N11.
[f] Methyl group at *E* position to N11.
[g] Signal not assigned as it was covered by other signals or due to low concentration of conformer.

Table 3
^{13}C chemical shifts (ppm) of *trans*-(*cis*-) amide conformers of **2a–f** and **4b–f** in DMSO-d_6

Carbon no.	Chemical shift (ppm)										
	2a	**2b**	**2c**	**2d**	**2e**	**2f**	**4b**	**4c**	**4d**	**4e**	**4f**
1	101.37(101.61)	101.66 (101.91)	101.46[a]; 102.03[b] (101.86[c])	101.86[a]; 102.05[b] (101.27[c])	101.97[a]; 101.70[b]	101.65[a]; 102.00[b] (101.95[c])	100.43 (—)[g]	100.5 (—)[g]	100.83 (—)[g]	100.79 (—)[g]	100.83 (—)[g]
2	159.00 (159.30)	158.88[a]; 158.81[b] (159.29;[c] 159.36[d])	158.79[a]; 158.85[b] (159.26;[c] 159.33[d])	158.83[a]; 158.88[b] (159.27;[c] 159.33[d])	158.81[a]; 158.88[b] (159.27;[c] 159.31[d])	158.83[a]; 158.89[b] (159.30;[c] 159.36[d])	154.04 (—)[g]	154.36 (—)[g]	154.06 (—)[g]	154.02 (—)[g]	154.06 (—)[g]
3	107.16 (106.72)	107.44[a]; 107.55[b] (106.84;[c] 106.93[d])	107.44[a]; 107.55[b] (106.84;[c] 106.93[d])	107.63 (107.1)	107.64[a]; 107.55[b] (106.94;[c] 107.02[d])	107.65, 107.58 (107.02)	127.32 (—)[g]	126.50 (—)[g]	127.02 (—)[g]	127.32 (—)[g]	126.62 (—)[g]
4	139.94 (129.71)	130.00 (129.91)	130.05 (129.87)	129.99 (129.84)	129.93 (—)[g]	130.16[b] (129.96)	125.77 (—)[g]	127.21 (—)[g]	127.61 (—)[g]	124.51 (—)[g]	127.38 (—)[g]
5							35.2 (—)[g]	35.2 (—)[g]	34.95 (—)[g]	34.87 (—)[g]	34.77 (—)[g]
6							34.58 (—)[g]	34.23 (—)[g]	34.72 (—)[g]	34.32 (—)[g]	34.36 (—)[g]
7							21.96; 27.58; 28.67; 29.07; 29.82; 31.19	21.98; 27.61; 28.70; 29.13; 29.35; 31.22	22.07; 27.62; 28.78; 29.21; 29.48; 31.32	22.00; 27.67; 28.73; 29.13; 29.36; 31.24	22.05; 27.62; 28.75; 29.17; 29.39; 31.29
8							13.74 (—)[g]	13.75 (—)[g]	13.82 (—)[g]	13.80 (—)[g]	13.83 (—)[g]
9	66.06 (64.83)	66.59 (64.69)	66.56 (64.66 ;[c]64.74 [d])	66.57 (64.82;[c] 64.69[d])	66.60 (64.69)	66.56 (64.75)	68.27 (66.40)	68.4 (67.7)	67.21 (65.03)	68.64 (65.86)	68.39 (66.33)
10	164.07 (168.83)	164.07 (168.83)	164.18 (168.89)	164.69 (169.34)	164.46 (169.09)	164.73 (169.39)	164.26; (169.20)	164.71 (169.5)	166.33 (168.39)	164.82 (169.49)	164.88 (169.70)
12	157.56 (151.36)	147.94 (143.77)	146.68 (142.57)	145.52 (141.48)	148.13 (144.24)	145.63 (141.43)	148.18 (143.31)	146.94 (142.29)	145.52 (141.48)	148 (144.52)	145.78 (141.18)
13	24.89[e] (25.11[f])	134.3 (133.87)	133.33 (133.16)	140.37 (140.18)	152.98 (152.75)	140.29 (141.10)	133.98 (133.87)	133.5 (131.27)	140.37 (140.18)	149.1 (—)[g]	140.87 (—)[g]
14	17.49[e] (16.95[f])	127.03 (126.81)	128.68 (128.88)	128.05 (127.82)	149.45 (149.37)	121.06 (120.88)	127.04 (126.72)	129.06 (128.64)	127.80 (127.40)	149.4 (—)[g]	120.93 (120.58)
15		128.72 (128.69)	131.66 (131.71)	123.97 (123.89;[c]123.94[d])	124.41 (124.22)	150.23 (150.20)	128.49 (—)[g]	132.7 (—)[g]	123.57 (123.54)	126.3 (—)[g]	149.98 (—)[g]
16		130.05 (129.83)	123.30 (123.03)	147.93 (147.70;[c] 147.75[d])	136.79 (136.73)		129.94 (129.52)	123.52 (123.07)	147.93 (147.75)	136.5 (—)[g]	
17					119.93 (119.77)					119.94 (—)[g]	

[a] For *trans*-amide conformation of hydrazone fragment when neighbouring group has *cis*-conformation.
[b] For *trans*-amide conformation of hydrazone fragment when neighbouring group has *trans*-conformation.
[c] For *cis*-amide conformation of hydrazone fragment when neighbouring group has *cis*-conformation.
[d] For *cis*-amide conformation of hydrazone fragment when neighbouring group has *trans*-conformation.
[e] Methyl group at *Z* position to N11.
[f] Methyl group at *E* position to N11.
[g] Signal not assigned as it was covered by other signals or due to low concentration of conformer.

Table 4
The distribution of spatial forms *cis/cis*, *trans/trans* and *cis/trans* of hydrazone fragments, the percentage of *trans*-amide conformers, the coalescence temperatures and the energy barrier values for the conformational conversion of compounds **2a–f** and **4b–f** as determined by NMR data (DMSO-d_6)

Compound	*trans*, %	Distribution of spatial forms, %			T_c, K	ΔG, kJ/mol
		trans/trans	*cis/cis*	*trans/cis*		
2a	45	(—)[a]	(—)[a]	(—)[a]	(—)[b]	(—)[b]
2b	43	18	31	51	385	74.5
2c	41	17	36	47	(—)[b]	(—)[b]
2d	39	15	37	48	(—)[b]	(—)[b]
2e	42	13	37	50	371	71.6
2f	38	14	39	47	(—)[b]	(—)[b]
4b	55				388	75.0
4c	51				(—)[b]	(—)[b]
4d	47				(—)[b]	(—)[b]
4e	64				383	73.4
4f	48				(—)[b]	(—)[b]

[a] Percent was not determined due to overlapping of signals in ^{1}H spectrum.
[b] Value was not determined.

2.4. Extraction studies

Liquid–liquid extraction experiments were performed to examine the efficiency and selectivity of hydrazones **2b**, **2e**, **4b**, **4c**, **4e** and **4f** in transferring s-metal ions (Li^+, Na^+, K^+, Cs^+ and Ca^{2+}), p-metal ions (Pb^{2+}), d-metal ions (Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+} and Hg^{2+}) and f-metal ions (La^{3+}, Gd^{3+} and Lu^{3+}) from aqueous phase into chloroform. Unfortunately, some of the synthesized hydrazones have insufficient solubility in the organic phase. The concentrations of picric acid (HPic) and metal cations in aqueous phase were identical in all experiments.

The presence of the lone electron pair on the nitrogen atom in hydrazone molecules provides their basic properties. The protonation of these compounds in acid conditions leads to the formation of an ion-pair complex with the Pic^- anion and, as a result, to the transfer of picric acid from the aqueous to the organic phase even without metal ion participation (Fig. 4). The nitrogen atom of the pyridine fragment in resorcinol derivatives **2e**, **4e** and **4f** contributes additionally to the efficiency of HPic transfer, obviously, providing the more basic properties of these compounds as compared with **2b**, **4b** and **4c**. It is interesting to notice, when going from bishydrazones **2b** and **2e** to octahydrazone analogues **4b** and **4e** the HPic transfer notably increases, though the effective concentrations of hydrazone groups in these experiments remain equal.

Increasing the pH of the aqueous phase would obviously prevent the protonation process. Therefore for correct comparison of extraction data and simplicity of complex stoichiometry and extraction constant calculations the liquid–liquid extraction experiments were carried out at pH=6.0 with buffer using. Under such conditions, the transfer of picric acid from aqueous to organic phase was only observed for **4f** ($\alpha \sim 0.1$ see Fig. 4). Higher values of pH usually lead to undesirable hydrolysis of metal ions. Under these conditions, the extraction of metal cations accompanied by z picrate anions and n neutral organic ligands (L) can be described by Eq. 1:

$$M^{z+}_{aq} + zPic^-_{aq} + nL_{org} \leftrightarrows [M^{z+}L_nPic^-{}_z]_{org} \quad (1)$$

where M^{z+}, Pic^-, L, $[M^{z+}L_nPic^-{}_z]$ denote the metal ion, picrate anion, ligand, ion-pair metal complex and the subscripts aq and org mean that the species exist in the aqueous or organic phase. Assumptions are made that the partition of the ligand to the aqueous

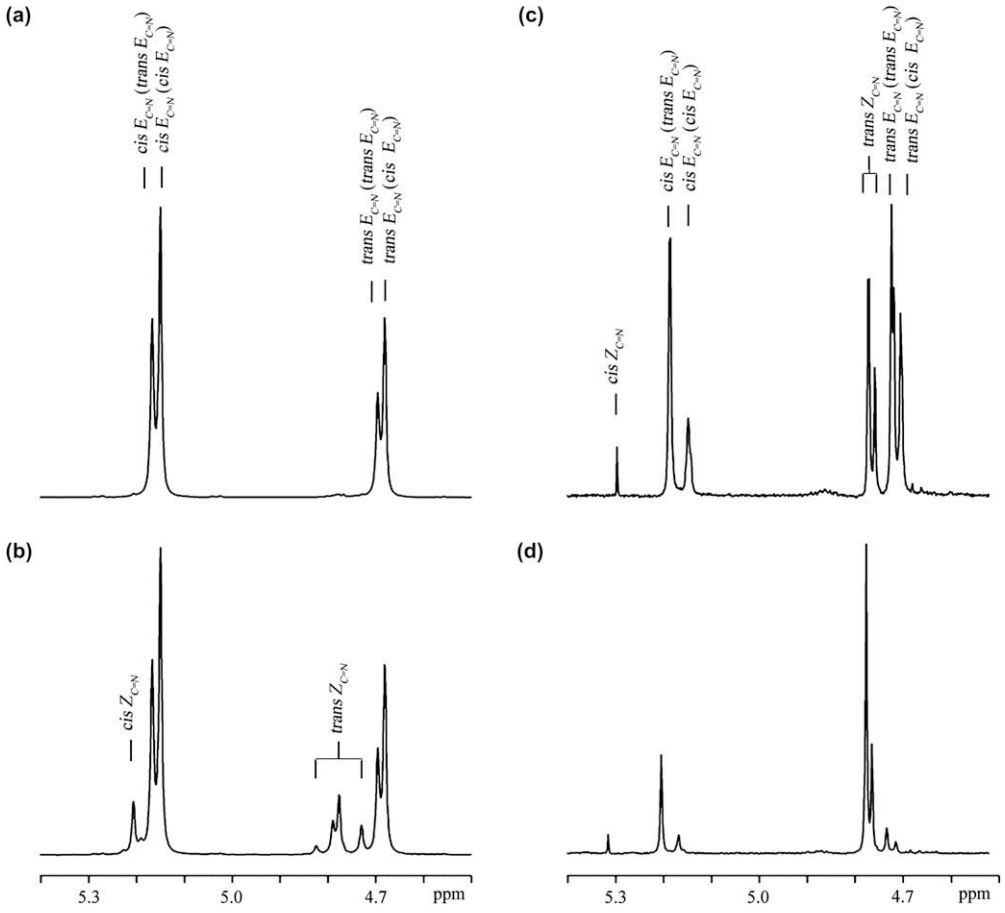


Figure 3. The assignment of –OCH_2C(O)– signals in ^{1}H spectrum of compound **2e** to spatial forms of acetylhydrazone fragments (the spatial form of neighbouring group is shown in parentheses): (a) in DMSO-d_6 at 303 K; (b) sample (a) after keeping at 373 K at 24 h; (c) in $CDCl_3$ at 303 K; (d) sample (c) after irradiating by UV light for half an hour.

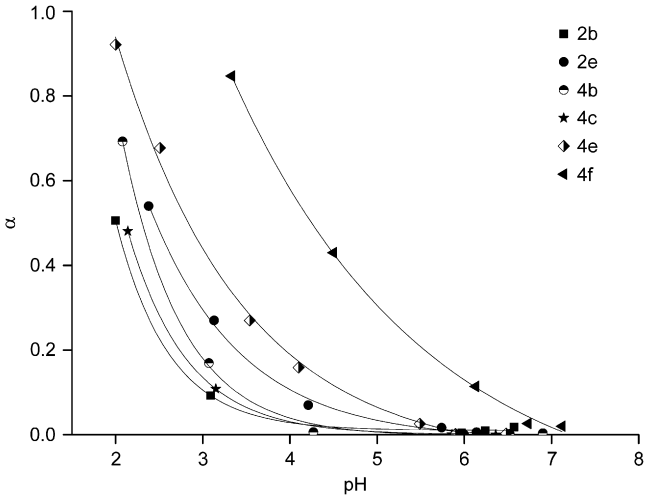
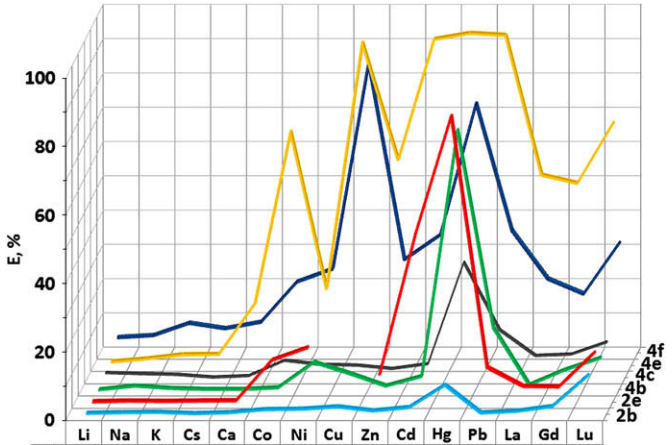


Figure 4. Effect of pH on a degree of transfer of HPic in the systems containing extractants **2b**,**e** and **4b**,**c**,**e**,**f**; [HPic]=2.5×10^{-4} M; [L_2]=2×10^{-3} M; [L_4]=0.5×10^{-3} M.

phase is negligible ($[L]_{aq}\sim0$). The presence of $[M^{z+}Pic^{-}{}_z]_{org}$ in the organic phase is also negligible. This was confirmed by blank control experiments.

The extraction percentages of metal picrates at equal effective concentrations of hydrazone groups are given in Figure 5. It was observed that the alkali metals ions are not extracted by hydrazones (E<3.5%). The more effective apparent extraction of these metals by compound **4f** is really caused by the above mentioned transfer of free picric acid from water to the organic phase at pH=6. Poor extraction was also observed for alkali-earth metal ion Ca^{2+} (from ~0.3% for **2b** to 18.1% for **4e**). Bishydrazone **2b** only insignificantly extracts Hg^{2+} (8.7%) and Lu^{3+} (11.6%) ions. The replacement of phenyl substituent in hydrazone fragment with a 2-pyridine substituent is resulted in an increase of the extraction yield for transition metal ions. The maxima of extraction for compound **2e** were observed for heavy metal ions—Cd^{2+} (49.2%) and Hg^{2+} (83.7%). It is probable that Cu^{2+} was also extracted by this compound with high yield, but because of precipitate formation the extraction yield could not be evaluated correctly.



	Li	Na	K	Cs	Ca	Co	Ni	Cu	Zn	Cd	Hg	Pb	La	Gd	Lu
2b	0,5	0,7	0,8	0,4	0,7	1,6	1,7	2,4	1,2	2,2	8,7	0,6	1,1	2,5	11,6
2e	0,3	0,5	0,4	0,5	0,6	12,4	16,1	_[a]	8,2	49,2	83,7	10,3	4,8	4,6	14,6
4b	0,2	1,3	0,6	0,3	0,3	0,8	8,2	4,9	1,3	4,1	76	18,3	1,6	6	9,5
4c	1,5	1,2	0,97	0,2	0,6	5,1	3,9	3,7	2,7	4,1	33,8	14	6,5	6,9	10,5
4e	1,2	2,1	3,3	3,4	18,1	68,4	22,5	94,3	60,1	95,3	97,1	96,5	55,7	53,3	70,9
4f	4,7	5,3	8,9	7,3	9,2	20,9	24,7	84,8	27,4	34,6	73	35,9	21,8	17,4	32,3

Figure 5. Extraction percentage (E%) of cations as a function of the nature of ligands **2b**,**e** and **4b**,**c**,**e**,**f**. [a] Percent was not determined due to formation of precipitate.

On going from bishydrazones **2** to calix[4]resorcinol derivatives **4**, the extraction yield was dramatically increased. The profiles of extraction selectivity of **4b** and **4c** are similar. However, the extraction efficiency of **4b** towards Hg^{2+} is much higher in comparison with other transition metals.

The introduction of pyridine as a substituent into the hydrazone fragments of compounds **4e** and **4f** leads to the substantial increase of extraction efficiency towards transition metal ions. All these data indicate that the sp^2-nitrogen pyridine atoms are involved into coordination with metal ions. However, the coordinating ability of 2-pyridine substituted compounds is higher than that for the 4-pyridine substituted analogues. The extraction of Cu^{2+} ion and heavy metal ions Cd^{2+}, Hg^{2+} and Pb^{2+} by **4e** is almost quantitative (94–97%). A high extraction yield was observed for Lu^{3+}, having the smallest radius among lanthanides. Obviously, it may be due to the geometrically favourable position of the nitrogen atom in the molecule **4e** leading to the *O*,*N*,*N*′-tri-dentate binding site formation. According to NMR data, the conformational equilibrium for amide fragments is shifted to the *trans*-conformer in nonpolar solvents and this also promotes the formation of a thermodynamically more effective binding site under the extraction conditions. The increase of extraction efficiency in the case of calix[4]resorcinol **4f** is essentially higher than the transfer contribution of free picric acid. This increase is probably connected with an additional coordination of sp^2-nitrogen pyridine atoms of neighbouring hydrazone fragments with metal ions.

The sequence ($Co^{2+}<Ni^{2+}<Cu^{2+}>Zn^{2+}$) of extraction efficiency values for compounds **2e** and **4f** is in accordance with Irving–Williams order for the relative stability of complexes formed by first transition series of metal ions.[28] However for **4e**, this regularity is disturbed. The Co^{2+} ion is extracted substantially better than Ni^{2+}. The *cis*-planar coordination of chelate groups of neighbouring aromatic fragments with metal ions becomes preferable when binding fragments are fixed at one of the rims of calixarene matrix. However, for mono-chelate ligands the symmetrical *trans*-planar coordination is more typical. Thus, the presence of tri-dentate donor fragments rigidly oriented relative to each other and the non-typical *cis*-coordination of chelate groups may be a reason for steric hindrance leading to the Irving–Williams order deviation.

The stoichiometry of the extracted complexes and the extraction constants ($\log K_{ex}$) have been determined for some of the metals, which were most effectively extracted by ligands **2e**, **4b**, **4c** and **4e** (Table 5). The extraction constant (K_{ex}) is evaluated from Eq. 2:

$$K_{ex} = [M^{z+}L_nPic^{-}{}_z]_{org}/[M^{z+}]_{aq}[Pic^{-}]^z{}_{aq}[L]^n{}_{org} \quad (2)$$

The extraction percent (E%) and extraction yield (α) can be calculated from Eq. 3:

$$E\% = \alpha\times100\% = [M^{z+}L_nPic^{-}{}_z]_{org}/([Pic^{-}]_{aq,init}/z)\times100\% \quad (3)$$

$[Pic^{-}]_{aq,init}$ is the initial concentration of the picrate anion in the aqueous phase.

When $M^{z+}L_n$ metal complexes are extracted as an ion-pair with the picrate anion into the organic phase, then the concentration of $M^{z+}L_nPic^{-}{}_z$ in the organic phase is determined by Eq. 4:

$$[M^{z+}L_nPic^{-}{}_z]_{org} = ([Pic^{-}]_{aq,init} - [Pic^{-}]_{aq})/z = \alpha[Pic^{-}]_{aq,init}/z \quad (4)$$

$[Pic^{-}]_{aq}$ is the final concentration of the picrate ion in the aqueous phase.

Substitution of Eq. 4 in Eq. 2 and taking logarithms gives Eq. 5:

$$\log K_{ex} = \log(\alpha/z(1-\alpha)^z) - (z-1)\log[Pic^{-}]_{aq,init} - \log[M^{z+}]_{aq} - n\log[L]_{org} \quad (5)$$

Table 5
The extraction constants and stoichiometry of complexes of hydrazones **2e**, **4b**, **4c** and **4e** with metal cations

Cation	Metal/ligand stoichiometry	log K_{ex}			
		2e	**4b**	**4c**	**4e**
Co^{2+}	1:1		6.5[a]		9.3±0.2
Ni^{2+}	1:1		7.6[a]		8.5±0.2
Cu^{2+}	1:1		7.3[a]		11.3±0.4
Zn^{2+}	1:1		6.8[a]		8.9±0.2
Cd^{2+}	1:1	8.8±0.2	7.2[a]		10.9±0.3
Hg^{2+}	1:1	8.7±0.4	9.2±0.2	8.2±0.1	10.2±0.3
Pb^{2+}	1:1		8.0[a]		11.7±0.4
La^{3+}	1:1		6.6[a]		13.1±0.3
Gd^{3+}	1:1		7.3[a]		12.9±0.4
Lu^{3+}	1:1		7.5[a]		13.7±0.4

[a] The extraction constant was evaluated from extraction yield for proposed complex stoichiometry 1:1.

The dependence of log Q is described as a function of the K_{ex} and the concentrations of the picrate anion and the ligand:

$$\log Q = \log K_{ex} + (z-1)\log[Pic^-]_{aq,init} + \log[M^{z+}]_{aq} + n\log[L]_{org} \quad (6)$$

where $Q=\alpha/z(1-\alpha)^z$.

If the extraction is very efficient and $[L]_{org,init}$ is less or comparable with $[M^{z+}]$ and $[Pic^-{}_z]_{aq,init}$ then the final concentration of $[L]_{org}$ becomes dramatically lower than $[L]_{org,init}$ The concentration of $[L]_{org}$ in such a case is determined by Eq. 7:

$$[L]_{org} = [L]_{org,init} - n\alpha[Pic^-]_{aq,init}/z \quad (7)$$

Under the assumption that $[M^{z+}]_{aq} \approx [M^{z+}]_{aq,init}$ (in our case $[M^{z+}]_{aq,init} > [L]_{org,init}$ and $[Pic^-]_{aq,init}$), a plot of log Q vs $\log[L]_{org}$ should be linear with a slope of n, where n indicates the number of ligands involved per cation in the extracted species. The experimental errors of the extraction yield determination leads to the very large dispersion of the plotted points in the range of rather high or low α. Therefore, for the correct construction of the graph log Q versus $\log[L]_{org}$ we have used only $\alpha=0.05\div0.95$ values. Extraction constants K_{ex} are calculated using the intercept values (b) of the plot with the log Q-axis and Eq. 8:

$$b = \log K_{ex} + (z-1)\log[Pic^-]_{aq,init} + \log[M^{z+}]_{aq} \quad (8)$$

All graphs of extraction dependences (log Q vs $\log[L]_{org}$) for metal ions have an equal slope ($n\approx1$) as well as in the case of excess and insufficiency of ligand (Fig. 6). This indicates the 1:1 (M^{z+}/L) stoichiometry of the extracted complexes across a wide concentration range. We had earlier shown[12] that under excess of extractant in the case of the tetrahydrazide of classical calix[4]arene, the bis-ligand complexes with all transition metal ions are formed. However, the more flexible conformational analogue tetrathiacalix[4]arene, having an increased size of the lower rim, only forms mono-ligand complexes with lanthanide ions. The high coordinating capacity and large size of calix[4]resorcinols is probably the reason for formation only mono-ligand complexes.

The K_{ex} (Hg^{2+}) values for acetylhydrazones with *N*,*O*-bidentate chelate center (**2e**, **4b** and **4c**) are similar to those for calix[4]arenes functionalized by hydrazide groups (K_{ex} (Hg^{2+})=$10^{8.1}$–$10^{9.1}$),[12] but in the case of calix[4]resorcinol **4e**, having an additional soft nitrogen atom in molecule, the K_{ex} (Hg^{2+}) value is more than one order of magnitude higher. Calix[4]resorcinol **4b** reveals high extraction selectivity towards Hg^{2+}, which amounts to more than one and a half or two orders of magnitude K_{ex} in the series of d- and f-elements, respectively.

The selectivity in the series of d-elements (Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}) with compound **4e** achieves two orders of magnitude

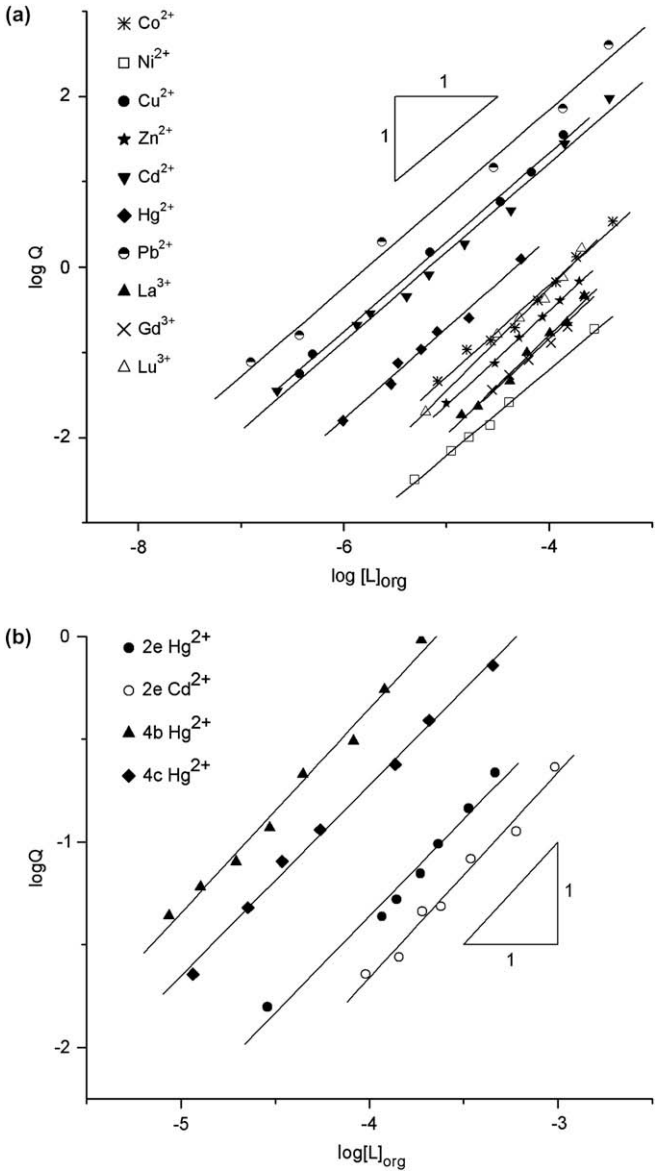


Figure 6. Log Q versus $\log[L]_{org}$ for some metal ions extracted by **4e**(a) and **2e**, **4b**,**c** (b) in $CHCl_3$; [HPic]=2.5×10^{-4} M, [M^{z+}]=1×10^{-2} M, pH=6.0.

($K_{ex}(Cu^{2+})/K_{ex}(Co^{2+})=10^2$). The extraction constants for heavy toxic metals varied from $10^{10.2}$ (Hg^{2+}) to $10^{11.7}$ (Pb^{2+}) (Table 5). It was interesting to notice that the maximum of extraction efficiency for this compound shifted from Hg^{2+} to Pb^{2+} compared with hydrazones **2b**, **2e**, **4b**, **4c** and **4f.** A similar shift in the maximum of extraction was also observed for tetrathiacalix[4]arene functionalized by hydrazide groups on going from 1,3-alternate to cone conformer, which, obviously, possesses more effective local concentration of donor centres.[12] The efficiency of extraction of lanthanide ions by the tetrahydrazone **2e** increased more than one and a half orders of magnitude ($K_{ex}=10^{12.9}$–$10^{13.7}$) as compared with tetrahydrazide derivatives of tetrathiacalix[4]arenes.

3. Conclusions

The synthesis and ion extraction abilities of the receptors based on calix[4]resorcinol derivatives **4b–f** and their monomer structural blocks **2a–f** have been studied. The spectroscopic data indicate that the investigated calix[4]resorcinols have the cone (*rccc*)

conformation. The diagnostically important IR spectral criteria required for the conformational analysis of polyacetylhydrazones have been considered. It was established that the population of *trans*-amide form of hydrazone fragments in solid state and solutions increased on going from mono-[23] to bis- **2a–f** and octahydrazones **4b–f.** The favourable formation of hydrogen bonds between NH···C(O) groups of neighbouring acetylhydrazone fragments having the less spatially hindered *trans*-configuration is the reason of this phenomenon. The irradiating or heating of polyhydrazones only in the case of picolinaldehyde bishydrazone **2e** resulted in the partly conversion of the $E_{C=N}$ into the $Z_{C=N}$ isomer. On going from resorcinols **2b**, **2e** to calix[4]resorcinols **4b**, **4e,** the value of the energy barrier increases, which is probably due to a formation of a large number of intra-molecular hydrogen bonds.

The solvent extraction data have demonstrated that at equal efficient concentrations of binding groups, the acetylhydrazones of calix[4]resorcinol are substantially more effective extractants of transition and heavy metal ions as compared to their monomer structural analogues. In spite of the high coordinating capacity of calix[4]resorcinols, only the metal/ligand 1:1 stoichiometry complexes are realized. The extraction efficiency in the series of metal ions ($Co^{2+}<Ni^{2+}<Cu^{2+}>Zn^{2+}$) for investigated compounds is in accordance with Irving–Williams order of the relative stability of complexes. An exception was observed for compound **4e**, which showed better extraction of Co^{2+} than Ni^{2+} cation. The Irving–Williams order deviation has been caused by the steric hindrances. The presence of rigidly oriented tri-dentate donor centres and non-typical *cis*-coordination of chelate groups at complexation may be a reason for this. The calix[4]resorcinol **4b** with benzene as a substituent in the hydrazone fragments reveals excellent selectivity towards Hg^{2+}. Thus, we can conclude that octahydrazones **4b** and **4e** have potential use in the extraction separation, phase transfer, recovery of metals and exclusion of toxic heavy metal ions.

4. Experimental

4.1. General

All chemicals were used as commercially received without further purification. $CHCl_3$ and DMFA were distilled over P_2O_5. $CDCl_3$ (99.8% isotopic purity) and DMSO-d_6 (99.5% isotopic purity) from Aldrich were used for NMR spectroscopy. The metal salts for extraction experiments were the following chlorides and nitrates: LiCl, NaCl, NaCl, CsCl, $CaCl_2$, $CoCl_2\cdot 6H_2O$, $NiCl_2$, $CuCl_2$, $ZnCl_2$, $CdCl_2\cdot 2.5H_2O$, $Hg(NO_3)_2\cdot H_2O$, $Pb(NO_3)_2$, $LaCl_3\cdot 7H_2O$, $Gd\cdot 6H_2O$, $LuCl_3\cdot 6H_2O$.

Microanalyses of C, H and N were carried out with a CHN-3 analyser. Melting points of compounds were measured with a Boetius hotstage apparatus. The purity of the compounds was monitored by TLC. NMR experiments were performed on a Bruker AVANCE-600 spectrometer at 303 K equipped of a 5 mm diameter broadband probe head working at 600.13 MHz in ^1H and 150.864 MHz in ^{13}C experiments. Chemical shifts were reported relative to TMS as an internal standard. Assignment was accomplished by means of 2D ^1H–^{13}C HSQC and 2D ^1H–^{13}C HMBC methods. The pulse programs of the HSQC and HMBC experiments were taken from Bruker software library. IR absorption spectra were recorded on a Vector-22 Bruker FT-IR spectrophotometer with a resolution of 4 cm^{-1} as Nujol emulsions and KBr pellets of compounds. The mass spectra (EI) were obtained on a Finnigan MAT-212 mass spectrometer (resolution was 1000; data were processed using the MSS MASPEC II data system 32; direct inlet of the sample into the ion source, programming of the temperature from 20 to 300 °C, the energy of ionizing electrons was 70 eV, the electron emission current was 1.0 mA). Mass spectra (MALDI) were detected on a Finnigan MALDI-TOF Dynamo mass spectrometer.

4.2. Synthesis

Figure 1 illustrates the successive synthetic steps of the compounds **2a–f** and **4b–f**. ^1H, ^{13}C NMR and IR data are presented in Tables 1–3.

4.3. 1,3-Bis[(*N′*-(propan-2-ylidene))-hydrazinocarbonylmethyloxy]benzene (2a)

To a suspension of **1** (1.02 g, 4 mmol) in water (10 ml) and acetone (20 ml) several drops of acetic acid were added. The reaction mixture was heated for 2 h at 70 °C. After cooling, the precipitate was filtered off. The precipitate was washed several times with acetone and recrystallized from mixture of EtOH and DMFA. Yield: 1.07 g (80%) as a white powder. Mp 223 °C. HRMS (EI), *m*/*z*: 334.1639 (calcd for $C_{16}H_{22}N_4O_4$ 334.1641). Anal. Calcd for $C_{16}H_{22}N_4O_4$ (334.38): C, 57.46; H, 6.64; N, 16.76. Found: C, 57.40; H, 6.80; N, 16.79.

4.4. General procedure for the preparation of hydrazone derivatives of resorcinol (2b–f)

To a suspension of **1** (1.02 g, 4 mmol) in 45 ml EtOH and 15 ml DMF under stirring 8.4 mmol of the corresponding aldehyde and several drops of acetic acid were added. The reaction mixture was heated for 5 h at 80 °C. After cooling, the formed precipitate was filtered off. During the synthesis of compounds **2e** and **2f** no precipitate was formed. In these cases, the solvent was removed from the reaction mixture by distillation. The residue was washed several times with a mixture of water/EtOH (1:1) and recrystallized from EtOH and DMFA.

*4.4.1. 1,3-Bis[(benzylidene)hydrazinocarbonylmethyloxy]-benzene (**2b**)*

Prepared similar to the general procedure using benzaldehyde (0.89 g). Yield: 1.13 g (66%) as a white powder. Mp 208 °C. HRMS (EI), *m*/*z*: 430.1640 (calcd for $C_{24}H_{22}N_4O_4$ 430.1641). Anal. Calcd for $C_{24}H_{22}N_4O_4$ (430.46): C, 66.97; H, 5.15; N, 13.02. Found: C, 66.98; H, 4.87; N, 13.18.

*4.4.2. 1,3-Bis[(4-bromobenzylidene)hydrazinocarbonyl-methyloxy]benzene (**2c**)*

Prepared similar to the general procedure using 4-bromobenzaldehyde (1.55 g). Yield: 2.2 g (94%) as a white powder. Mp 246 °C. HRMS (EI), *m*/*z*: 585.9847 (calcd for $C_{24}H_{20}Br_2N_4O_4$ 585.9851). Anal. Calcd for $C_{24}H_{20}Br_2N_4O_4$ (588.25): C, 49.00; H, 3.43; Br, 27.17; N, 9.52. Found: C, 49.10; H, 3.43; Br, 30.83; N, 9.52.

*4.4.3. 1,3-Bis[(4-nitrobenzylidene)hydrazinocarbonyl-methyloxy]benzene (**2d**)*

Prepared similar to the general procedure using 4-nitrobenzaldehyde (1.27 g, 8.4 mmol). Yield: 1.74 g (83%) as a light yellow powder. Mp 253–255 °C. HRMS (EI), *m*/*z*: 520.1348 (calcd for $C_{24}H_{20}N_6O_8$ 520.1343). Anal. Calcd for $C_{24}H_{20}N_6O_8$ (520.46): C, 55.39; H, 3.87; N, 16.15. Found: C, 55.47; H, 3.89; N, 16.26.

*4.4.4. 1,3-Bis[(2-pyridinylmethylidene)hydrazinocarbonyl-methyloxy]benzene (**2e**)*

Prepared similar to the general procedure using picolinaldehyde (0.89 g). Yield: 1.01 g (58%) as a white powder. Mp 205–207 °C. HRMS (EI), *m*/*z*: 432.1541 (calcd for $C_{22}H_{20}N_6O_4$ 432.1546). Anal. Calcd for $C_{22}H_{20}N_6O_4$ (432.43): C, 61.10; H, 4.66; N, 19.43. Found: C, 61.07; H, 4.93; N, 19.69.

*4.4.5. 1,3-Bis[(4-pyridinylmethylidene)hydrazinocarbonyl-methyloxy]benzene (**2f**)*

Prepared similar to the general procedure using isonicotinaldehyde (0.89 g). Yield: 1.31 g (75%) as a white powder. Mp

241 °C. HRMS (EI), *m/z*: 432.1544 (calcd for $C_{22}H_{20}N_6O_4$ 432.1546). Anal. Calcd for $C_{22}H_{20}N_6O_4$ (432.43): C, 61.10; H, 4.66; N, 19.43. Found: C, 61.31; H, 4.74; N, 19.47.

4.5. General procedure for the preparation of hydrazone derivatives of calix[4]resorcinol (4b–f)

To a suspension of **3** (0.63 g; 0.4 mmol) in EtOH (18 ml) and DMF (6 ml) under stirring 6.4 mmol of the corresponding aldehyde and several drops of acetic acid were added. The reaction mixture was heated for 24 h at 80 °C. The solvent was removed from the reaction mixture by distillation. Hexane was added to the residue and the mixture was heated again. After cooling, the precipitate was filtered off, washed several times with hexane and EtOH, recrystallized from EtOH and DMFA.

*4.5.1. 2,8,14,20-Tetranonyl-4,6,10,12,16,18,22,24-octa[(benzylidene)hydrazinocarbonylmethyloxy]pentacyclo[19,3,1,1^{3,7},1^{9,13},1^{15,19}]-octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23-dodecaene (**4b**)*

Prepared similar to the general procedure using benzaldehyde (0.68 g). Yield: 0.69 g (76%) as a white powder. Mp 145–147 °C. MS (MALDI-TOF), *m/z*: (2297) $[M+Na]^+$; (2315) $[M+K]^+$. Anal. Calcd for $C_{136}H_{160}N_{16}O_{16}$ (2274.8): C, 71.81; H, 7.09; N, 9.85. Found: C, 72.13; H, 7.40; N, 9.87.

*4.5.2. 2,8,14,20-Tetranonyl-4,6,10,12,16,18,22,24-octa[(4-bromobenzylidene)hydrazinocarbonylmethyloxy]pentacyclo-[19,3,1,1^{3,7},1^{9,13},1^{15,19}]octacosa-1(25),3,5,7(28),9,11,13(27),-15,17,19(26),21,23-dodecaene (**4c**)*

Prepared similar to the general procedure using 4-bromobenzaldehyde (1.19 g). Yield: 0.75 g (65%) as a white powder. Mp 152 °C. MS (MALDI-TOF), *m/z*: (2945) $[M+K]^+$. Anal. Calcd for $C_{136}H_{152}N_{16}O_{16}Br_8$ (2906.0): C, 56.21; H, 5.27; N, 7.71; Br, 22.00. Found: C, 56.23; H, 5.28; N, 7.65; Br, 21.72.

*4.5.3. 2,8,14,20-Tetranonyl-4,6,10,12,16,18,22,24-octa[(4-nitrobenzylidene)hydrazinocarbonylmethyloxy]pentacyclo-[19,3,1,1^{3,7},1^{9,13},1^{15,19}]octacosa-1(25),3,5,7(28),9,11,13(27),-15,17,19(26),21,23-dodecaene (**4d**)*

Prepared similar to the general procedure using 4-nitrobenzaldehyde (0.96 g). Yield: 0.93 g (87%) as a yellow powder. Mp 162–163 °C. MS (MALDI-TOF), *m/z*: (2636) $[M+H]^+$; (2658) $[M+Na]^+$. Anal. Calcd for $C_{136}H_{152}N_{24}O_{32}$ (2634.8): C, 62.00; H, 5.81; N, 12.76. Found: C, 61.71; H, 5.91; N, 12.38.

*4.5.4. 2,8,14,20-Tetranonyl-4,6,10,12,16,18,22,24-octa[(2-pyridinylmethylidene)hydrazinocarbonylmethyloxy]-pentacyclo[19,3,1,1^{3,7},1^{9,13},1^{15,19}]octacosa-1(25),3,5,7(28),-9,11,13(27),15,17,19(26),21,23-dodecaene (**4e**)*

Prepared similar to the general procedure using picolinaldehyde (0.68 g). Yield: 0.48 g (52%) as a white powder. Mp 145 °C. MS (MALDI-TOF), *m/z*: (2305) $[M+Na]^+$; (2327) $[M+2Na]^+$; (2368) $[M+2Na+K]^+$. Anal. Calcd for $C_{128}H_{152}N_{24}O_{16}$ (2282.73): C, 67.35; H, 6.71; N, 14.73. Found: C, 67.32; H, 6.96; N, 14.37.

*4.5.5. 2,8,14,20-Tetranonyl-4,6,10,12,16,18,22,24-octa[(4-pyridinylmethylidene)hydrazinocarbonylmethyloxy]-pentacyclo[19,3,1,1^{3,7},1^{9,13},1^{15,19}]octacosa-1(25),3,5,7(28),-9,11,13(27),15,17,19(26),21,23-dodecaene (**4f**)*

Prepared similar to the general procedure using isonicotinaldehyde (0.68 g). Yield: 0.84 g (92%) as a white powder. Mp 158–162 °C. MS (MALDI-TOF), *m/z*: (2285) $[M+H]^+$. Anal. Calcd for $C_{128}H_{152}N_{24}O_{16}$ (2282.73): C, 67.35; H, 6.71; N, 14.73. Found: C, 67.08; H, 7.18; N, 14.11.

4.6. Picrate extraction experiments

Aqueous metal picrate solution (5 ml), which was buffered at pH=6.0 and the solution of extractant (5 ml, 2.5×10^{-5} to 2×10^{-3} M for **2** and 2.5×10^{-5} to 0.5×10^{-3} M for **4**) in $CDCl_3$ were magnetically stirred in a flask. The extraction equilibrium was reached after vigorous stirring for 1.5 h at 20 °C. After that, two phases were allowed to settle for 1 h. The absorbances A_1 of the aqueous phase after extraction and A_0 of the aqueous phase before extraction were measured at 355 nm (the wavelength of maximum absorption of the picrate ion, λ_{max}=355 nm). All data were obtained from two independent experiments. Aqueous metal picrate solutions ([metal salt]=1×10^{-2} M; [picric acid]=2.5×10^{-4} M) were prepared by stepwise addition of a 2.5×10^{-4} M aqueous picric acid solution to the calculated amounts of metal salts. The obtained solutions were stirred at pH=6.0 with acetic-acetate buffer for 1 h. For alkaline ions, tris(hydroxymethyl)aminomethane–HCl (0.05 M) was used as a buffer. The percent of extraction was calculated as ratio $E\%=100\times(A_0-A_1)/A_0$. The $\log K_{ex}$ and n values were determined from the plot of $\log(\alpha/z(1-\alpha)^z)$ versus $\log[L]_{org}$.

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