

Synthesis, characterization, and metal extraction studies of a new macrobicyclic ligand

Halil Zeki GÖK*, Yaşar GÖK, Esra EKER

Department of Chemistry, Osmaniye Korkut Ata University, Osmaniye, Turkey

Received: 11.12.2014

Accepted/Published Online: 17.02.2015

Printed: 30.04.2015

Abstract: This article describes the synthesis, characterization, and metal ion binding properties of a new macrobicyclic ligand. Solvent extraction experiments were performed in order to determine the extraction behavior of new macrobicyclic ligand towards selected metal cations. Selective extraction of heavy metals and precious metals is highly demanded due to their toxicity and commercial importance. Based on our experimental results, macrobicyclic ligand **3** demonstrated remarkable affinity towards the Ag⁺ ion by 96.7% and 96.9% to the dichloromethane and chloroform phases, respectively. The extraction experiments with macrobicyclic ligand **3** for the Ag⁺ ion were repeated at different temperatures to calculate thermodynamic parameters. The negative values of thermodynamic parameters indicated that the formation of complex during solvent extraction was an exothermic process.

Key words: Macrocycle, macrobicyclic, transition metal, solvent extraction

1. Introduction

Macrocycles and related compounds have been one of the most actively studied research areas of chemistry since Pedersen reported the first synthesis of macrocyclic compounds.¹ Hundreds of macrocycles have been synthesized in order to understand and investigate their unique properties such as their metal-ion chemistry, and spectral, electrochemical, structural, kinetic, and thermodynamic stabilities.² In 1969, Lehn et al. revealed a new class of azapolyoxamacrocycles, which are known as cryptands.³ Cryptands have three-dimensional structures and a cage-like cavity capable of encapsulating the metal cation. The studies on these compounds showed that they have selective complexation towards specific alkali and alkaline earth cations and form more stable complexes than macrocyclic polyethers do.⁴ Because of their unique architecture, stabilities, and functions, macrobicyclic compounds are used in a wide variety of areas, for instance, in ion size recognition,⁵ separation of cations,⁶ transport process in biological systems, and in industrial, technological, and other applications.⁷

There is strong demand to extract and separate heavy metals and precious metals from aqueous solution due to their toxicity⁸ and commercial importance.⁹ A goal of research on macrocyclic chemistry is to achieve selective complexation of heavy metals and precious metals with macrocycles and macrobicyclics. For selective extraction of these metal cations, different parameters such as the ring size, the nature of substituents, and the type of donor atoms present in the cavity of macrocycles and macrobicyclics have been modified.^{10,11}

There are many reports on the synthesis of macrocyclic systems containing different types of donor atoms

*Correspondence: zekigok@osmaniye.edu.tr

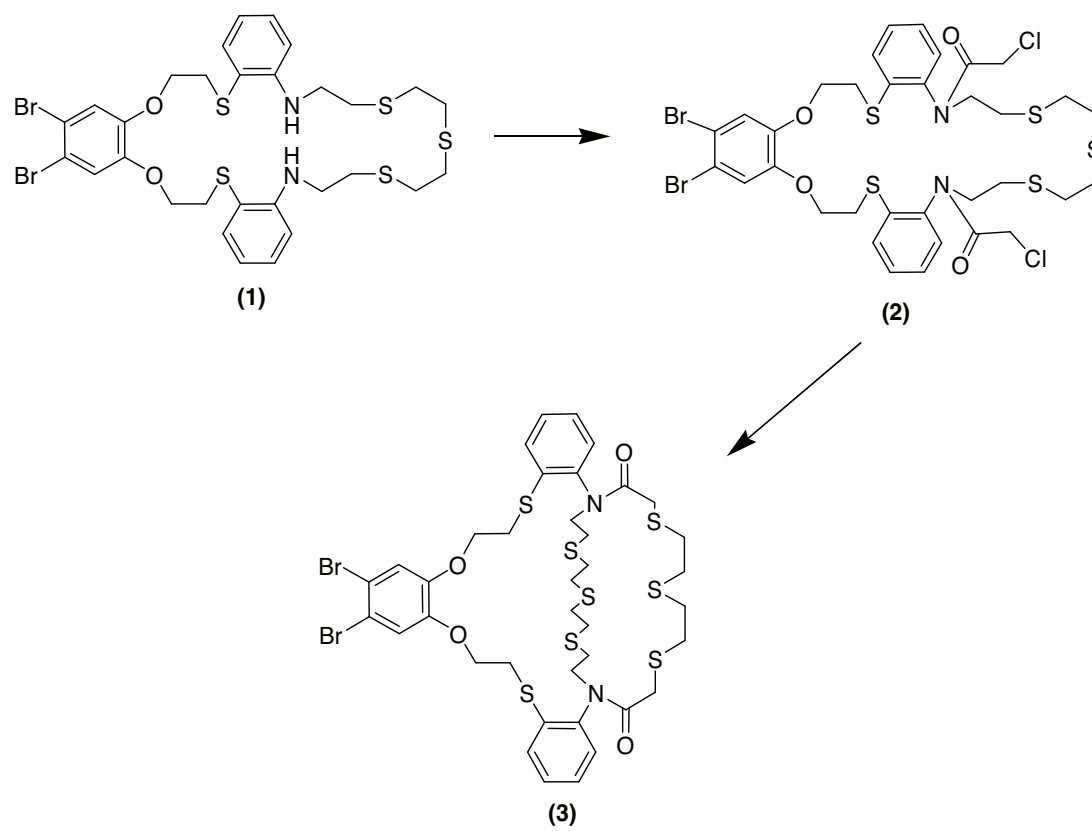
and their metal ion binding properties as extractants.^{12–14} Saito et al. synthesized thiacrown ether carboxylic acids and investigated their extraction properties towards metal ions.¹⁵ Bilgin et al. presented a new vic-dioxime containing bis(diazacrown)ether moieties and evaluated its extraction efficiency towards several alkali metal ions.¹⁴ Ashram et al. reported complexation and thermodynamic studies of oxathiadibenzocrown ethers with selected metal ions.¹² A series of closely related macrocyclic and macrobicyclic systems and their extractant properties were reported by Ocak et al. They demonstrated that the presence of soft donor atoms in the macrocyclic system enhanced the selective extraction for soft metal ions such as silver(I) and mercury(II).^{13,16,17} According to the HSAB concept, the attachment of nitrogen and sulfur donor atoms to a macrocyclic cavity increases their selectivity towards soft transition metal cations.¹⁰ Another interesting extractant used for metal cation and anion extraction is based on the calix[4]arene framework. Leng et al., Uysal Akkuş et al., and Memon et al. prepared selective chelating adsorbents with macrocycles and calix[4]arenes and investigated their extractant properties towards metal cations and anions.^{18–20} Qazi et al. synthesized a calix[4]arene derivative and demonstrated that it was an excellent copper selective chemsensor.²¹

The synthesis of macrobicyclic ligands and their metal ion binding properties is reported least in the literature due to the challenge in the synthesis of these compounds. Our study focused on selective and effective extraction of heavy metals and precious metals from solution and determining the extraction behavior of macrocycles in liquid–liquid medium. For these purposes, we have previously reported the synthesis of a series of macrocycles and their metal ion binding properties in solvent extraction.^{22,23} The present study, as our ongoing research on this area, describes the synthesis of a new lariat ether and macrobicyclic ligand, and investigates their extractant properties towards Ag^+ , Hg^{2+} , Cd^{2+} , Zn^{2+} , Cu^{2+} , Ni^{2+} , Pb^{2+} , and Co^{2+} ions in solvent extraction. The thermodynamic parameters for the extracted complex compositions in liquid–liquid extraction are also investigated.

2. Results and discussion

2.1. Synthesis and characterization

The N-pivot lariat ether **2** and macrobicyclic ligand **3** containing nitrogen, sulfur, and oxygen donors were prepared by the route shown in the Scheme. The structures of the new compounds were characterized by a combination of elemental analysis and ^1H NMR, ^{13}C NMR, IR, and MS spectral data. The reaction of 27,28-dibromo-6,7,9,10,12,13,16,17,23,24,31,32-dodecahydro-5H,15H-tribenzo[b,h,w] [1,4,7,13,16,19,25,10,22]dioxapentathiadiazacycloheptacosine **1** with 3 equivalents of chloroacetic anhydride in dichloromethane at 0–5 °C under argon atmosphere afforded 1,1'-(27,28-dibromo-6,7,9,10,12,13,15,16,23,24,31,32-dodecahydrotribenzo[b,h,w][1,4,7,13,16,19,25,10,22]dioxapentathiadiazacycloheptacosine-5,17-diyl)bis(2-chloroethanone) **2** in 90% yield. A free –NH stretching vibration at 3346 cm^{-1} in the IR spectrum of precursor compound **1**²⁴ disappeared after the introduction of chloroacetic anhydride as amide function. The appearance of a C=O vibration at 1663 cm^{-1} in the IR spectrum of **2** confirmed that the reaction had occurred. In the ^1H NMR spectrum of **2** (Figure 1), the singlet at $\delta = 3.79\text{ ppm}$ corresponded to methylene protons between C=O and Cl groups. The protons of the –NH group observed at $\delta = 9.66\text{ ppm}$ as a singlet in the ^1H NMR spectrum of **1** disappeared in the ^1H NMR spectrum of **2**. The C=O group of **2** gave a carbon resonance at $\delta = 166.37\text{ ppm}$ in the ^{13}C NMR spectrum of **2**. The appearance of a new peak at $\delta = 42.34\text{ ppm}$ concerning $\text{O}=\text{C}\underline{\text{C}}\text{H}_2\text{Cl}$ group in the ^{13}C NMR spectrum of **2** can be taken as clear evidence for the formation of N-pivot lariat ether. The formation of **2** was also supported by the presence of the characteristic molecular ion peak at $m/z = 930.8\text{ [M + H]}^+$ and 952.8 [M + Na]^+ in the mass spectrum.



Scheme. The synthetic route of the macrocyclic ligand **3**.

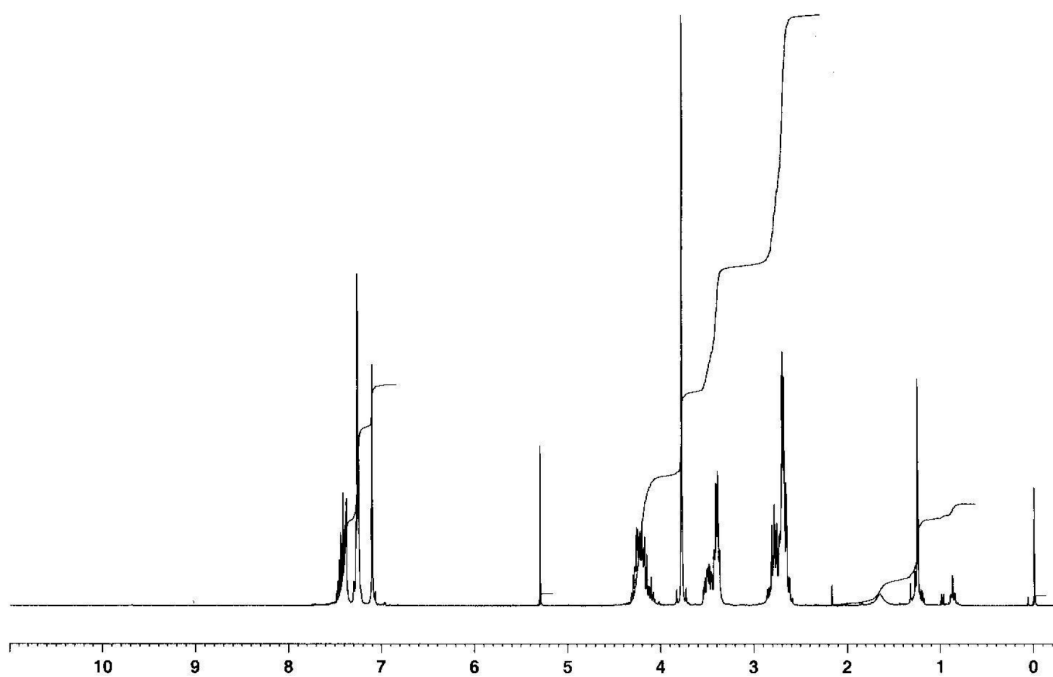


Figure 1. The ^1H NMR spectrum of macrocyclic ligand **2** in CDCl_3 .

The synthesis of macrobicyclic compound **3** was performed by adding a solution of 2,2'-dithioethanthiol and a solution of 1,1'-(27,28-dibromo-6,7,9,10,12,13,15,16,23,24,31,32-dodecahydrotribenzo[b,h,w][1,4,7,13,16,19,25,10,22]dioxapentathiadiazacycloheptacosine-5,17-diyl)bis(2-chloroethanone) **2** simultaneously into a CH₃CN solution containing Na₂CO₃ as a template agent at reflux temperature, affording the desired macrobicyclic compound **3** as the major product in 71% yield. Its IR spectrum showed an intense stretching vibration of C=O at 1660 cm⁻¹. The rest of the IR spectrum of **3** was almost identical to that of **2** with small changes in wavenumbers. The formation of macrobicyclic ligand was confirmed by the appearance of a new resonance for SCH₂ protons at around $\delta = 2.80$ ppm as a multiplet in the ¹H NMR spectrum of **3** in CDCl₃ (Figure 2). The ¹³C NMR spectrum of **3** also supports this structure, with signals at $\delta = 68.18$ ppm for the OCH₂ carbon, 48.56 ppm for the NCH₂ carbon, 35.60 ppm for O=CCH₂S carbon, and 33.03, 31.84, 31.41, and 30.90 ppm for the SCH₂ carbons. The resonance belonging to the C=O group was observed at $\delta = 169.81$ ppm in the ¹³C NMR spectrum of **3**. The molecular ion peak at $m/z = 1010.9$ [M + H]⁺ in the mass spectrum of **3** also confirms the proposed structure (Figure 3).

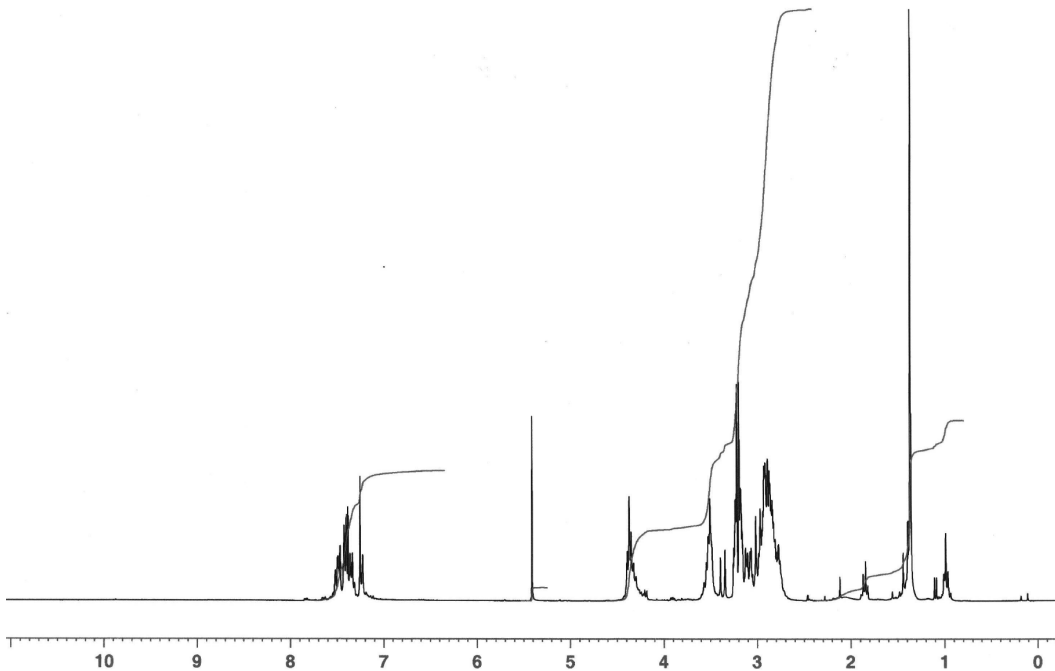


Figure 2. The ¹H NMR spectrum of macrobicyclic ligand **3** in CDCl₃.

2.2. Extraction of metal picrates

The metal ion binding properties of N-pivot lariat ether **2** and macrobicyclic ligand **3** were investigated using solvent extraction experiments in order to reveal the extractability of metal ions such as Ag⁺, Hg²⁺, Cd²⁺, Zn²⁺, Cu²⁺, Ni²⁺, Pb²⁺, and Co²⁺ from aqueous phase to organic phase. Two different organic solvents, dichloromethane and chloroform, were used in the liquid-liquid extraction experiments. The results related to the extractability of the above metal picrates from aqueous phase to organic phase are given in Table 1.

The metal ion binding properties of macrocyclic ligand **1** in dichloromethane and chloroform were reported before.²³ The cation-binding affinity of macrocyclic ligand **1** for Ag⁺ over other cations in both organic solvents was found to be the highest. Ligand **2**, which is a lariat ether compound having two side arms, showed behavior

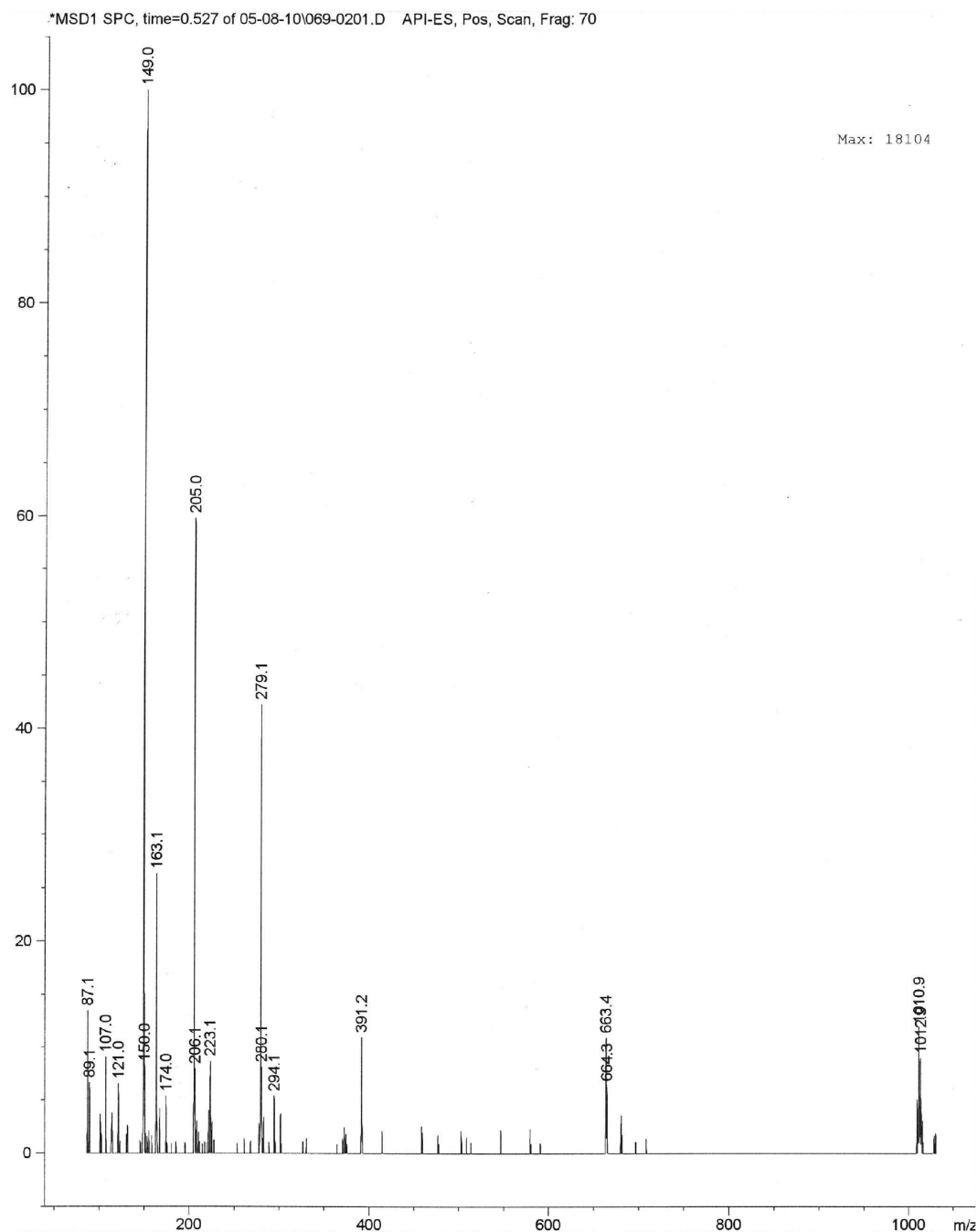


Figure 3. The ES-MS spectrum of macrobicyclic ligand **3**.

similar to ligand **1** in transferring metal cations from aqueous phase to organic phase. N-pivot lariat ether **2** extracted Ag^+ effectively with the values of 90.1% and 92.7% into the dichloromethane and chloroform phases, respectively. In this case, Hg^{2+} was extracted 61% and 53% into the dichloromethane and chloroform phases, respectively. The other metal cations were not extracted from aqueous solution with ligand **2**. This result showed that the macrocycle **2** has important selectivity for Ag^+ and Hg^{2+} . Macrocyclic ligand **1** and lariat ether **2** have the same macrocyclic cavity size with the same donor atoms. The only difference between ligand

Table 1. The extractability of aqueous metal picrates for **1–3** into the dichloromethane and chloroform phases.

Metal ion	Extractability ^{a,b} (%)			Extractability ^{a,c} (%)		
	1	2	3	1	2	3
Ni ²⁺	< 1	< 1	1.6 ± 0.5	< 1	0	< 1
Cu ²⁺	15.4 ± 1.1	1.3 ± 0.7	3.4 ± 0.9	4.5 ± 0.3	1.1 ± 0.8	6.4 ± 1.9
Hg ²⁺	81.6 ± 1.3	61 ± 2.4	22.5 ± 0.4	81.1 ± 1.2	53 ± 1.9	41.8 ± 2.5
Zn ²⁺	0	0	2.4 ± 0.9	0	0	15.7 ± 0.5
Ag ⁺	95.2 ± 1.3	90.1 ± 1.4	96.7 ± 0.6	92.7 ± 0.3	92.7 ± 0.7	96.9 ± 0.8
Cd ²⁺	< 1	< 1	2.8 ± 1.3	< 1	0	1.7 ± 0.5
Pb ²⁺	0	0	2.9 ± 0.5	0	< 1	1.7 ± 0.5
Co ²⁺	0	0	2.3 ± 0.1	2.2 ± 0.7	< 1	2.3 ± 0.5

^aTemperature: 20.0 ± 0.1 °C; aqueous phase (10 mL); [pic⁻] = 1.25 × 10⁻⁵ M, organic phase (10 mL); [L] = 1.25 × 10⁻⁴ M; The values calculated from three independent extraction experiments, ^b Dichloromethane, ^c Chloroform

1 and **2** is the two side arms attached to nitrogen atoms in macrocycle **2**. The studies on the interaction between macrocycles and cations showed that the selectivity is dependent on many factors such as cation size, macrocyclic cavity, and solvent.²⁵ The ionic diameters of Ag⁺ and Hg²⁺ cations are 2.20 Å and 2.52 Å, respectively. According to the extraction values, there should be good correlation between the sizes of Ag⁺ and Hg²⁺ cations and the cavity of both macrocycles. The other tested metal cations have ionic diameters smaller than 2.00 Å. In addition, it is well known that macrocycles with “soft” sulfur are selective against “soft” transition metal cations such as Ag⁺ and Hg²⁺ cations.^{10,26} These results indicated that the number and the kind of donors of the macrocyclic ligand are very important in selective extraction. There are similar results in the literature.^{27–29}

Macrocyclic ligand **3** with mixed oxygen–nitrogen–sulfur donors extracted all metal cations to the organic phase with different E% values. The results of extraction behavior of the hard, borderline, and soft metal ions with macrobicycle **3** indicated that the hard and borderline metal ions were hardly extracted. Macrocyclic ligand **3** shows good extractability but low selectivity towards Ag⁺ and Hg²⁺ cations for both organic solvents. Cadmium(II) was hardly extracted with macrobicycle **3**, whereas silver(I) was extracted the most by the macrobicycle **3** with the values of 96.7% for dichloromethane and 96.9% for chloroform. The extraction efficiency of Hg²⁺ with macrobicyclic ligand **3** to the dichloromethane and chloroform phases was 22.5% and 15.7%, respectively. This result can be explained according to Pearson’s acid-base classification. Pearson classified ions range from a very hard base, F⁻, less hard, O²⁻ and N³⁻, to soft base, S²⁻ and Ag⁺, and Hg²⁺ and Cd²⁺ as soft acid.³⁰ Soft acid and base mean that electrons in those molecules or atoms are distorted by interaction with other molecules or ions. The interactions are more favorable for soft–soft and hard–hard than for soft–hard and hard–soft in reactants.³⁰ During the solvent extraction at a divided interface, the sulfur in ligand **3** can be attracted by charges on other molecules such as Ag⁺, Hg²⁺, and Cd²⁺. Silver(I) is more polarizable than mercury(II) and cadmium(II). Thus, the high extraction efficiency of ligand **3** in both organic solvents towards Ag⁺ ions can be explained by the forming of a soft–soft interaction between the sulfur and Ag⁺ ions.

Figure 4 shows the evolution of log {D/[Pic⁻]ⁿ} versus log [L] at constant Ag-picrate concentration for macrocyclic ligands **1** and **2**, and macrobicyclic ligand **3** in chloroform. The calculated log *K_{ex}* values from the intercept by using Eq. (5) and complex composition for extracted Ag-complexes in chloroform are given

in Table 2. Macrocyclic ligand **2** and macrobicyclic ligand **3** gave 1:1 complex compositions with Ag^+ for chloroform. The $\log K_{ex}$ values for macrocyclic ligands **1** and **2**, and macrobicyclic ligand **3** were 10.75, 11.08, and 11.74, respectively, for chloroform. The extraction constant of extracted Ag -complex with macrocycle **2** is greater than that of extracted- Ag complex with macrocyclic ligand **1**. This may be attributed to the two side arms on nitrogen atoms in macrocycle **2**. Interactions of the side arms of lariat ethers with ring bound cations were reported in the literature.³¹

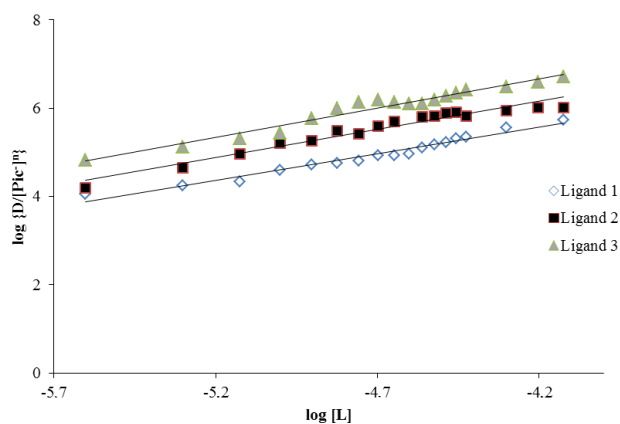


Figure 4. $\log \{D/[Pic^-]^n\}$ versus $\log [L]$ for the extraction of Ag -picrate with macrocyclic ligands **1** and **2**, and macrobicyclic ligand **3** for water–chloroform extraction.

Table 2. The relationship between composition and extraction constant for the macrocyclic ligands **1** and **2**, and macrobicyclic ligand **3**- Ag^+ complexes in the chloroform phase.

Ligand	Extraction constant ($\log K_{ex}$)	m	Complex Composition (L:M)
1	10.75 ± 0.17	1.24 ± 0.05	1:1
2	11.08 ± 0.60	1.19 ± 0.14	1:1
3	11.74 ± 0.20	1.24 ± 0.05	1:1

Macrobicyclic ligands, known as cryptands, have a cage-like cavity encapsulating the metal ions in it to form complexes. Cryptands form more stable complexes with metal cations than those of macrocycles due to the cryptate effect.⁴ The extracted Ag -complex in chloroform for macrobicyclic ligand **3** has the biggest extraction constants among the others in chloroform, indicating that macrobicyclic ligand **3** formed the most stable complex with Ag^+ cation due to the cryptate effect and the number of sulfur atoms with respect to macrocycles **1** and **2**.

Thermodynamic parameters for the complexation process are the free energy of the extraction process (ΔG°), change in the enthalpy extraction process (ΔH°), and change in entropy of the extraction process (ΔS°). The effect of temperature on the extraction constant was determined by repeating the extraction experiment at three different temperatures (20, 30, and 40 °C). Table 3 represents the calculated thermodynamic parameters of the extraction process of Ag^+ ion with macrobicyclic ligand **3**. Depending on the values of ΔG° from Table 3, the negative values of the free energy indicated spontaneous extraction processes for macrobicyclic ligand **3**.^{12,32} The changes in enthalpy for the extraction process of Ag^+ ion with macrobicyclic ligand **3** were a negative indication of the exothermic nature of the extraction process and formation of stable complex. The

negative value of the entropy change for macrobicyclic ligand **3** revealed that the randomness decreases after extraction of Ag^+ ion with ligand **3**. This situation is mostly attributed to the replacement of some water molecules with a positively charged species in the macrocyclic cavity. These results are in agreement with most published works.^{12,32,33} The negative values of thermodynamic parameters indicate that the formation of complex during solvent extraction is an exothermic process and occurs in a more ordered state.

Table 3. Thermodynamic parameters for extraction process of Ag^+ ion on macrobicyclic ligand **3**.

Ligand	Temperature (°C)	$-\Delta G^\circ$ (kJ/mol)	$-\Delta H^\circ$ (kJ/mol)	$-\Delta S^\circ$ (J/molK)	R^2
3	20	67	147	270	0.913
	30	66			
	40	61			

In summary, this work reports the synthesis of a new macrobicyclic ligand **3** in high yield (71%). The macrobicyclic ligand **3** and its precursor **2** were tested in the transfer of metal cations from aqueous phase to organic phase by liquid–liquid extraction experiments. Based on the experimental results, macrocyclic ligand **1** is very effective and selective for Ag^+ and Hg^{2+} cations, whereas compounds **2** and **3** show good extraction behavior without selectivity towards the Ag^+ cation. The highest Ag^+ extraction behavior among the tested ligands in both organic solvents was observed for macrobicyclic ligand **3**. Thermodynamic parameters revealed that the extraction process of the Ag^+ ion with macrobicyclic ligand **3** indicated exothermic behavior and a spontaneous extraction process. It can be concluded that all ligands have the potential to be used in extraction of the Ag^+ ion.

3. Experimental

3.1. Materials

Chloroform, dichloromethane, picric acid, $\text{Pb}(\text{NO}_3)_2$, $\text{Co}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$, $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$, $\text{Zn}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$, $\text{Ni}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$, $\text{Cd}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$, AgNO_3 , and $\text{Hg}(\text{NO}_3)_2 \cdot \text{H}_2\text{O}$ were reagent grade quality and were purchased from Merck. Demineralized water was used in the extraction experiments. The solvents were saturated with each other before use in order to prevent volume changes of the phases during extraction. 27,28-Dibromo-6,7,9,10,12,13,16,17,23,24,31,32-dodecahydro-5H,15H-tribenzo[b,h,w][1,4,7,13,16,19,25,10,22]dioxapentathiadiazacycloheptacosine **1** was prepared according to the literature.²⁴

3.2. Equipment

FTIR spectra were measured on a PerkinElmer Spectrum 65 spectrometer in KBr pellets. Analytical TLC was performed using Macherey-Nagel SIL G-25 UV254 plates. Flash chromatography (FC) was carried out with ROCC silica gel (0.040–0.063 mm). ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance 400 spectrometer as indicated, with chemical shifts reported in ppm relative to TMS, using the residual ratio solvent signal as standard. ^{13}C NMR spectra were recorded using the attached proton test. ESI-MS spectra were recorded with an Agilent LC/MSD mass spectrometer. A LECO Elemental Analyzer (CHNS 0932) was used for elemental analysis. The spectrophotometric measurements were recorded with a PG-T80+ spectrophotometer in 1-cm path length cuvettes at room temperature. In the solvent extraction experiment, a Selecta type shaker with a thermostat was used.

3.3. Synthesis

3.3.1. 1,1'-(27,28-Dibromo-6,7,9,10,12,13,15,16,23,24,31,32-dodecahydrotribenzo[b,h,w][1,4,7,13,16,19,25,10,22]dioxapentathiadiazacycloheptacosine-5,17-diyl)bis(2-chloroethanone) (2)

27,28-Dibromo-6,7,9,10,12,13,16,17,23,24,31,32-dodecahydro-5H,15H-tribenzo[b,h,w][1,4,7,13,16,19,25,10,22]dioxapentathiadiazacycloheptacosine **1** (10 g, 12.88 mmol) was placed in a two-necked round flask with CH_2Cl_2 (300 mL). Chloroacetic anhydride (4.36 g, 38.65 mmol) in CH_2Cl_2 (100 mL) was added dropwise through a dropping funnel over 3 h while the mixture was stirred under inert gas atmosphere at 0–5 °C. The progress of the reaction was monitored by thin layer chromatography using ethyl acetate/hexane (4:6) as the solvent system. The mixture was stirred for an additional 2 h under a nitrogen atmosphere at room temperature. At the end of this period, the reaction mixture was neutralized by adding saturated aqueous NaHCO_3 . The organic layer was separated and washed twice with a 100 mL portion of saturated aqueous NaHCO_3 and then twice with water, followed by drying over anhydrous Na_2SO_4 . The solvent was evaporated under reduced pressure to give the crude product, which was purified by silica gel chromatography. The elution was carried out with hexane/ethyl acetate (6:4). The product was obtained as oil. The yield was 11.75 g (90%). Anal. calcd for $\text{C}_{34}\text{H}_{38}\text{Br}_2\text{Cl}_2\text{N}_2\text{O}_4\text{S}_5$: C: 43.92; H: 4.12; N: 3.01; S: 17.24%. Found: C: 42.37; H: 4.01; N: 2.77; S: 16.30%. IR (KBr disc) $\nu_{\text{max}}/\text{cm}^{-1}$: 3062 (CH_{Ar}), 2924 (CH_{Al}), 1663 (C=O), 1583, 1477, 1446, 1376, 1313, 1277, 1260, 1185, 1147, 1089, 1047, 898, 752, 660, 546, 530. ^1H NMR (CDCl_3) (δ : ppm): 7.44 (m, 4H, ArH), 7.26 (m, 4H, ArH), 7.10 (s, 2H, ArH), 4.26 (m, 4H, OCH_2), 3.79 (s, 4H, $\text{O}=\text{CCH}_2$), 3.48–3.37 (m, 8H, $\text{NCH}_2 + \text{SCH}_2$), 2.81–2.66 (m, 12H, SCH_2). ^{13}C NMR (CDCl_3) (δ : ppm): 166.37 (C=O), 148.23, 138.17, 137.79, 136.62, 130.09, 126.48, 119.68, 119.42, 116.30 (ArC), 67.73 (OCH_2), 48.87 (NCH_2), 42.34 ($\text{O}=\text{CCH}_2\text{Cl}$), 32.15, 31.94, 31.69, 30.92, (SCH_2). MS (API-ES) m/z : 930.8 $[\text{M} + \text{H}]^+$, 952.8 $[\text{M} + \text{Na}]^+$.

3.3.2. Synthesis of dioxadiazaoctathia macrobicycle (3)

A solution of 2,2'-dithioethanthiol (0.90 g, 5.87 mmol) in dry acetonitrile (200 mL) in a dropping funnel and a solution of **2** (5.45 g, 5.87 mmol) in dry acetonitrile (200 mL) in a dropping funnel was added simultaneously under stirring and dry inert gas to dry acetonitrile (250 mL) containing anhydrous sodium carbonate (2.48 g, 23.48 mmol) over 2.5 h at reflux temperature. After addition was completed, the reaction mixture was stirred for another 16 h at reflux temperature. The reaction was monitored by thin layer chromatography [hexane/ethyl acetate (6:4)]. When the reaction was complete, the mixture was filtered and the filtrate was evaporated to dryness under reduced pressure. The yellowish oil was dissolved in CH_2Cl_2 . The organic layer was washed twice with 100 mL portions of a 5% Na_2CO_3 solution and then twice with water. The combined organic layer was dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure to give a crude product that was purified by silica gel chromatography. The elution was carried out with hexane/ethyl acetate (6:4). The product was obtained as oil. The yield was 4.25 g (71%). Anal. calcd for $\text{C}_{38}\text{H}_{46}\text{Br}_2\text{N}_2\text{O}_4\text{S}_8$: C: 45.14; H: 4.59; N: 2.77; S: 25.37%. Found: C: 44.82; H: 4.68; N: 2.96; S: 24.30%. IR (KBr disc) $\nu_{\text{max}}/\text{cm}^{-1}$: 3054 (CH_{Ar}), 2923, 2853 (CH_{Al}), 1660 (C=O), 1582, 1470, 1380, 1306, 1253, 1196, 1013, 850, 754, 562. ^1H NMR (CDCl_3) δ : 7.50–7.23 (m, 10H, ArH), 4.38 (m, 4H, OCH_2), 3.51 (m, 4H, NCH_2), 3.40–2.76 (m, 28H, $\text{O}=\text{CCH}_2 + \text{SCH}_2$). ^{13}C NMR (CDCl_3) δ : 169.81 (C=O), 148.55, 139.29, 136.37, 130.38, 129.45, 126.30, 119.68, 116.59 (ArC), 68.18 (OCH_2), 48.56 (NCH_2), 35.60 ($\text{O}=\text{CCH}_2\text{S}$), 33.03, 31.84, 31.41, 30.90, (SCH_2). MS (API-ES) m/z : 1010.9 $[\text{M} + \text{H}]^+$.

3.4. Extraction method

Picrate extraction experiments were performed according to published procedures.^{22,23,27-29} Solvent extraction experiments were carried out using aqueous metal picrate solutions, which were prepared from a mixture of the metal nitrates ($\text{Pb}(\text{NO}_3)_2$, $\text{Co}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$, $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$, $\text{Zn}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$, $\text{Ni}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$, $\text{Cd}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$, AgNO_3 , $\text{Hg}(\text{NO}_3)_2 \cdot \text{H}_2\text{O}$), and picric acid in deionized water. Dichloromethane and chloroform were tested as organic solvents in extraction experiments. An organic solution (10 mL) of ligand (1.25×10^{-4} M) and an aqueous solution (10 mL) containing 1.25×10^{-5} M picric acid and 1×10^{-2} M metal nitrate were placed in a stoppered flask and shaken for 2 h at 20 ± 0.1 °C. Then the resulting mixtures were allowed to stand for at least 2 h at the same temperature in order to complete the phase separation. The concentration of the picrate ion remaining in the aqueous phase was then determined by UV-Vis spectrophotometer at 355 nm. A blank experiment was performed in the absence of host and showed that no picrate extraction occurred.

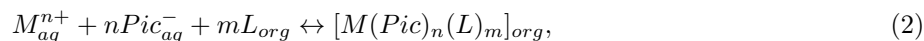
The extractability (E%) was determined as the absorbance of picrate in aqueous solutions. The extractability was calculated from the following equation:

$$E(\%) = \frac{[A_0 - A]}{A_0} \times 100, \quad (1)$$

where A_0 is the absorbance in the absence of ligand and A the absorbance in the aqueous phase after extraction.

The dependence of the distribution ratio D of the cation between the aqueous phase and the organic phase upon the ligand concentration was examined. The range of the ligand concentration was from 2.5×10^{-6} to 7.5×10^{-5} M.

The general extraction equilibrium was assumed from Eq. (2):



where the subscript “aq” denotes the aqueous solution and the subscript “org” denotes the organic solution. The extraction equilibrium constant is expressed as

$$K_{ex} = \frac{[M(\text{Pic})_n(\text{L})_m]}{[M^{n+}][\text{Pic}^-]^n[\text{L}]^m} \quad (3)$$

and the distribution ratio D is defined by

$$D = \frac{[M(\text{Pic})_n(\text{L})_m]}{[M^{n+}]} \quad (4)$$

By introducing Eq. (4) in Eq. (3) and taking the log of both sides gives the following logarithmic expression, which is valid for the above extraction system:^{22,23,27-29}

$$\log \left(\frac{D}{[\text{Pic}^-]^n} \right) = \log K_{ex} + m \log [L] \quad (5)$$

The plot of $\log \{D/[\text{Pic}^-]^n\}$ as a function of $\log [L]$ should give a straight line with a slope of m and $\log K_{ex}$ can be calculated from the intercept by using Eq. (5).

3.4.1. Thermodynamics of the extraction process

The extraction procedures were repeated at different temperatures (20, 30, and 40 °C) for obtaining thermodynamic parameters of macrobicycle **3**. The calculated $\log K_{ex}$ values from the intercept by using Eq. (5) were used for the following equation to calculate the change in standard free energy of the extraction process (ΔG°):

$$\Delta G^\circ = -RT \ln K_{ex} \quad (6)$$

The values of ΔH° and ΔS° were determined from the slope and the intercept on the Van't Hoff plot of $\log K$ versus $1/T$.^{12,32,34}

$$\log K_{ex} = \frac{\Delta S^\circ}{2.303R} - \frac{\Delta H^\circ}{2.303RT} \quad (7)$$

Acknowledgments

This study was supported the Research Fund of Osmaniye Korkut Ata University (project no. OKUBAP-2014-PT3-001). One of us, HZG, is grateful to the Scientific and Technological Research Council of Turkey (TÜBİTAK) for postdoctoral research scholarship (2219/1059B190900364). Technical assistance from the Department of Organic Chemistry (S4) at Ghent University is gratefully acknowledged.

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