

Synthesis, Extraction, and Anti-Bacterial Studies of Some New Bis-1,2,4-triazole Derivatives Part I

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ABSTRACT: A series of new bis triazole Schiff base derivatives (4) were prepared in good yields by treatment of 4-amino-3,5-diphenyl-4H-1,2,4-triazole (3) with bisaldehydes (1). Schiff bases (4) were reduced with NaBH₄ to afford the corresponding bisaminotriazoles (5). All the new compounds were characterized by IR, ¹H NMR and ¹³C NMR spectral data. Their overall extraction (log *K_{ex}*) constants for 1 : 1 (*M* : *L*) complexes and CHCl₃/H₂O systems were determined at 25 ± 0.1°C to investigate the relationship between structure and selectivity toward various metal cations. The extraction equilibrium constants were estimated using CHCl₃/H₂O membrane transfer with inductively coupled plasma-atomic

emission spectroscopy spectroscopy. The stability sequence of the triazole derivatives in CHCl₃ for the metal cations was exhibited a characteristic preference order of extractability to metal ions [Fe(III) > Cu(II) > Pb(II) > Co(II) > Ni(II) > Mn(II) > Zn(II) > Mg(II) > Ca(II)]. The compounds were tested for anti-microbial activity applying agar diffusion technique for 11 bacteria. © 2011 Wiley Periodicals, Inc. *J Appl Polym Sci* 123: 2011–2019, 2012

Key words: 4-Amino-4H-1,2,4-triazole; bis-1,2,4-triazoles; bisSchiff bases; extraction ability-selectivity; anti-bacterial activity

INTRODUCTION

There has been an increasing demand for the preparation of new anti-microbial agents due to the developing resistance toward conventional anti-biotics.^{1–3} 1,2,4-Triazole derivatives are among them which have been attracting widespread attention due to their diverse biological activities, including anti-microbial, anti-inflammatory, analgesic, and anti-tumoral.^{4–10} Their general structure includes a triazole ring fused to pyridine, pyridazine, pyrimidine, pyrazine, and triazine. Moreover, the structures incorporating triazoles fused to thiadiazine and thiazole display a broad spectrum of biological activities, even though few of them are available in the literature.^{11–16}

Solvent extraction is one of the most widely applied technique to separate metals from a mixture. The development of selective extraction techniques including selective extractants has expanded its use to metal recovery and purification, among which Schiff bases are one of the widely used extractants.^{17,18} Determination of ion-pair formation constants of organic ligands–metal ion complexes in

water can be examined by different methods through the extraction of metals to various organic solvents with organic ligands.^{19–24} The solvent extraction of metal cations containing ligands is generally preferred for its easy determination by spectrophotometric methods.^{25–27}

In this study, a novel series of bisSchiff base derivatives resulting from the reaction of 4-amino-3,5-diphenyl-4H-1,2,4-triazole **3** with bisaldehydes **1** and their corresponding reduced derivatives were synthesized and characterized by IR, ¹H NMR, and ¹³C NMR spectral data.

EXPERIMENTAL

General

Melting points were determined on a Barnstead Electrothermal melting point apparatus and are uncorrected. ¹H NMR and ¹³C NMR spectra (δ, ppm) were recorded on a Varian-Mercury 200 MHz spectrophotometer using tetramethylsilane as the internal reference. The IR spectra (ν, cm⁻¹) were obtained with a Perkin-Elmer 1600 FTIR spectrometer in KBr pellets, Extraction ability measured in inductively coupled plasma–atomic emission spectroscopy (ICP–AES): Perkin-Elmer Optima 2100 DV. Elemental analyses have been acquired with a Thermo Finnigan Flash EA 1112. The necessary chemicals were purchased from Merck and Fluka.

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Synthesis of bisaldehydes 1a–c

p-Hydroxy benzaldehyde (0.01 mol) was dissolved in hot ethanolic KOH (prepared by dissolving 0.01 mol of KOH in 100 mL of absolute ethanol) and the solvent was then removed *in vacuo*. The residue was dissolved in DMF (25 mL) and the appropriate dihalide (0.005 mol) was added. The reaction mixture was refluxed for 5 min, during which KCl separated out. The solvent was then removed in vacuum and the remaining material was washed with water and crystallized from an appropriate solvent to give compounds 1a–c.

4,4'-(ethane-1,2-diylbis(oxy)) dibenzaldehyde (1a) 4,4'-(2,2'-oxybis(ethane-2,1-diyl)bis(oxy)) dibenzaldehyde (1b) and 4,4'-(2,2'-(ethane-1,2-diylbis(oxy)) bis(ethane-2,1-diyl)) bis(oxy) dibenzaldehyde (1c) were prepared using the literature method.²⁸

Synthesis of hydrazone 2

A solution of an appropriate hydrazide (0.01 mol) in absolute ethanol (25 mL) was added to a solution of iminoester hydrochloride (0.01 mol) in absolute ethanol (25 mL). The mixture was stirred for 6 h at 0–5°C and subsequently for 2 h at room temperature. The reaction mixture was then poured into a beaker containing cold water (40 mL) and ice (10 g). The precipitate formed was washed with ice-water (50 mL), dried and the product was recrystallized from 1 : 2 benzene-petroleum ether to give compound 2.

Synthesis of amino compound 3

Compound 2 (0.005 mol) was added to a solution of hydrazine hydrate (0.01 mol) in 1-propanol (50 mL) and the mixture was refluxed for 24 h. After cooling a precipitate formed was filtered off, dried, and washed with benzene (20 mL). The product was then recrystallized from 1-propanol to give compound 3.

Synthesis of bisSchiff bases 4a–c

The corresponding bisaldehyde (0.01 mol) was added to a solution of compound 3 (0.005 mol) in glacial acetic acid (20 mL) and the mixture was refluxed for 16 h. After cooling, the mixture was poured into a beaker containing ice-water (100 mL). The precipitate formed was filtered. After drying in vacuum, the product was recrystallized from an appropriate solvent to give the desired compound.

N,N'-(4,4'-(ethane-1,2-diylbis(oxy))bis(4,1-phenylene)) bis(methane-1-yl-1-ylidene) bis(3,5-diphenyl-4H-1,2,4-triazole-4-amine) (4a)

Yield (0.99 g, 66%); m.p. 143–144°C (recrystallized from 1 : 2 benzene-petroleum ether); IR: 1597

(C=N), 1192 (C–O), 814, 744, 732 cm⁻¹ (aromatic ring); ¹H NMR (DMSO-*d*₆) δ (ppm): 4.42 (s, 4H, OCH₂), Ar–H: [7.11–7.20 (m, 3H), 7.22–7.44 (m, 3H), 7.45–7.76 (m, 11H), 7.77–7.84 (m, 11H)] [r, 8.52 (s, 2H, CH)]; ¹³C NMR (DMSO-*d*₆) δ (ppm): 163.17 (2C, N=CH), 150.86 (4C, triazole C₃, C₅), Ar–C: [131.85 (4C), 130.43 (8C), 129.59 (4C), 128.87 (8C), 127.21 (2C), 127.13 (4C), 123.73 (2C), 116.11 (4C)], 67.30 (2C, OCH₂). Anal. Calcd. for C, 74.77; H, 4.85; N, 15.85; O, 4.53; Found: C, 74.70; H, 4.80; N, 15.89; O, 4.61.

N,N'-(3,3'-(2,2'-oxybis(ethane-2,1-diyl)bis(oxy))bis(3,1-phenyl))bis(methane-1-yl-1-ylidene) bis(3,5-diphenyl-4H-1,2,4-triazole-4-amine) (4b)

Yield (1.24 g, 77%); m.p. 111–112°C (recrystallized from 1 : 2 benzene-petroleum ether); IR: 1576 (C=N), 1267 (C–O), 820, 768, 696 cm⁻¹ (aromatic ring); ¹H NMR (DMSO-*d*₆) δ(ppm): 3.80 (s, 4H, O–C–CH₂), 4.14 (s, 4H, O–CH₂), Ar–H: [7.19–7.31 (m, 4H), 7.34–7.39 (m, 4H), 7.46–7.60 (m, 12H), 7.75–7.90 (m, 8H)], 8.56 (s, 2H, CH); ¹³C NMR (DMSO-*d*₆) δ (ppm): 171.55 (2C, N=CH), 150.82 (4C, triazole C₃, C₅), Ar–C: [159.54 (2C), 133.31 (2C), 131.22 (2C), 130.50 (4C), 129.55 (8C), 129.13 (2C), 128.93 (8C), 127.06 (2C), 122.59 (2C), 120.46 (2C), 114.63 (2C)], 69.61 (2C, OCH₂), 68.16 (2C, O–C–CH₂). Anal. Calcd. for C, 73.58; H, 5.10; N, 14.92; O, 6.39; Found: C, 73.65; H, 5.05; N, 14.85; O, 6.43.

N,N'-(4,4'-(2,2'-(ethane-1,2-diylbis(oxy))bis(ethane-2,1-diyl))bis(oxy))bis(4,1-phenyl))bis(methane-1-yl-1-ylidene) bis(3,5-diphenyl-4H-1,2,4-triazole-4-amine) (4c)

Yield (0.84 g, 50%); m.p. 136–137°C (recrystallized from 1 : 2 benzene-petroleum ether); IR: 1598 (C=N), 1234 (C–O), 824, 744, 693 cm⁻¹ (aromatic ring); ¹H NMR (DMSO-*d*₆) δ (ppm): 3.79–3.82 (m, 6H, OCH₂), 4.18–4.20 (m, 6H, O–C–CH₂), Ar–H: [6.23–6.98 (m, 2H), 7.07–7.10 (m, 4H), 7.41–7.56 (m, 3H), 7.71–7.78 (m, 3H), 8.02–8.08 (m, 16H)], 8.20 (s, 2H, CH); ¹³C NMR(DMSO-*d*₆) δ (ppm): 162.63 (2C, N=CH), 151.91 (4C, triazole C₃, C₅), Ar–C: [134.82 (4C), 130.91 (2C), 130.22 (2C), 129.36 (2C), 129.13 (8C), 128.10 (8C), 126.85 (2C), 126.58 (2C), 119.78 (2C), 116.28 (4C)], 69.33 (2C, OCH₂), 68.37 (4C, O–C–CH₂). Anal. Calcd. for C, 72.53; H, 5.33; N, 14.10; O, 8.05; Found: C, 72.60; H, 5.36; N, 14.06; O, 8.00.

Synthesis of reduced compounds 5a–c

The corresponding compound 4a–c (0.005 mol) was dissolved in dried methanol (50 mL) and NaBH₄ (0.01 mol) was added in small portions to this solution. The mixture was refluxed for 20 min and then allowed to cool. After evaporation at 30–35°C under reduced pressure, the solid residue was washed

with cold water. After drying in vacuum, the solid product was recrystallized from an appropriate solvent to afford the desired compound.

N,N'-(4,4'-(ethane-1,2-diylbis(oxy))yl) bis (oxy) bis (4,1-phenylidene) bis (methylene) bis(3,5-diphenyl-4H-1,2,4-triazole-4-amine) (5a)

Yield (0.25 g, 51%); m.p. 201–202^o (recrystallized from 1 : 1 ethanol-water); IR: 3220 (NH), 1611 (C=N), 1246 (C–O), 824, 744, 693 cm⁻¹ (aromatic ring); ¹H NMR (DMSO-*d*₆) δ(ppm): 3.65 (d, 4H, NH–CH₂, *J* = 4.56 Hz), 4.16 (s, 4H, OCH₂), 6.69 (t, 2H, NH, *J* = 4.56 Hz), Ar–H: [6.68–6.74 (m, 6H), 7.44–7.53 (m, 2H), 7.54–7.60 (m, 10H), 7.64 (d, 2H, *J* = 7.80 Hz), 7.87–7.95 (m, 8H)]; ¹³C NMR (DMSO-*d*₆) δ(ppm): 149.01 (4C, triazole C₃, C₅), Ar–C: [130.88 (4C), 130.69 (4C), 130.48 (4C), 129.28 (4C), 129.25 (8C), 128.79 (2C), 128.69 (8C), 114.90 (2C)], 66.98 (2C, OCH₂), 54.15 (2C, NH–CH₂). Anal. Calcd. for C, 74.35; H, 5.39; N, 15.76; O, 4.50; Found: C, 74.48; H, 5.45; N, 15.70; O, 4.57

N,N'-(3,3'-(2,2'-oxybis(ethane-2,1-diyl) bis (oxy)-bis(3,1-phenyl)) bis (methylene) bis (3,5-diphenyl-4H-1,2,4-triazole-4-amine) (5b)

Yield (0.78 g, 55%); m.p. 172–173^oC (recrystallized from 1 : 1 ethanol-water); IR: 3306 (NH), 1599 (C=N), 1264 (C–O), 819, 769, 693 cm⁻¹ (aromatic ring); ¹H NMR (DMSO-*d*₆) δ(ppm): 3.70 (d, 4H, O–C–CH₂, *J* = 6.43 Hz), 3.80 (d, 4H, NH–CH₂, *J* = 4.56 Hz), 3.90–4.00 (m, 4H, OCH₂), 6.40 (bs, 2H, NH), Ar–H: [6.38–6.50 (m, 4H), 6.75 (d, 2H, *J* = 7.80 Hz), 7.00 (t, 2H, *J* = 8.00 Hz), 7.50–7.56 (m, 12H), 7.82–8.00 (m, 8H)]; ¹³C NMR (DMSO-*d*₆) δ(ppm): 154.59 (4C, triazole C₃, C₅), Ar–C: [137.59 (2C), 130.49 (4C), 129.83 (4C), 129.28 (8C), 128.69 (8C), 128.02 (4C), 121.55 (2C), 114.88 (4C)], 69.61 (2C, OCH₂), 67.52 (2C, O–C–CH₂), 54.62 (2C, NH–CH₂). Anal. Calcd. for C, 73.19; H, 5.61; N, 14.84; O, 6.36; Found: C, 73.23; H, 5.65; N, 14.79; O, 6.33.

N,N'-(4,4'-(2,2'-(ethane-1,2-diylbis(oxy)) bis (ethane-2,1-diyl)) bis(oxy) bis(4,1-phenyl)) bis (methylene) bis (3,5-diphenyl-4H-1,2,4-triazole-4-amine) (5c)

Yield (0.14 g, 62%); m.p. 169–170^oC (recrystallized from 1 : 1 ethanol-water); IR: 3220 (NH), 1611(C=N), 1246 (C–O), 819, 769, 693 cm⁻¹ (aromatic ring); ¹H NMR (DMSO-*d*₆) δ(ppm): 3.56–3.60 (m, 6H, OCH₂), 3.65 (d, 4H, NH–CH₂, *J* = 4.56 Hz), 3.95–4.00 (m, 6H, OCH₂), 6.65 (t, 2H, NH, *J* = 4.56 Hz), Ar–H: [6.68 (d, 8H, *J* = 7.60 Hz), 7.08 (s, 2H), 7.40–7.60 (m, 10H), 7.80–8.00 (m, 8H)]; ¹³C NMR (DMSO-*d*₆) δ(ppm): 154.55 (4C, triazole C₃, C₅), Ar–C: [130.64 (4C), 130.48 (4C), 129.25 (8C), 128.68 (8C), 128.58 (2C), 128.00 (4C), 127.95 (2C), 114.82 (4C)], 70.60 (2C, OCH₂), 69.57 (2C, O–C–CH₂), 67.78 (2C, O–C–CH₂), 54.15 (2C,

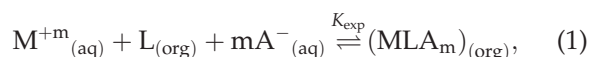
NH–CH₂). Anal. Calcd. for C, 72.16; H, 5.80; N, 14.03; O, 8.01; Found: C, 72.10; H, 5.70; N, 14.14; O, 8.06.

Anti-bacterial activity assay

Anti-bacterial activity was measured using the standard method of diffusion disc plates on agar.^{29,30} To test anti-bacterial activity, ligands were dissolved in DMSO and diluted by 5% aqueous solution of Tween 20 (5%). A preliminary assay with aqueous solutions of Tween 20 up to 5% was performed to assure that no micro-organism growth inhibition occurred. Twenty milliliters of Mueller Hinton Agar medium (Merck) was poured into each 12 cm Petridish. All bacterial strains were grown in Mueller Hinton Broth medium (Merck) for 24 h at 37^oC. Growth was adjusted to OD (600 nm) of 0.1 by dilution with Mueller Hinton Broth medium (Merck). One hundred microliters of suspension with approximately 10⁸ bacteria per milliliter was placed in Petri dishes and dispersed over agar. Then sterile paper discs (6 mm diameter) were placed on the agar to load 20 μL of each sample (10, 4, 2, 1, and 0.5 mg/mL). For bacteria, as a positive control, ampicillin (10 mg), streptomycin (10 mg), and kanamycin (30 mg) were used, and as negative control DMSO was used. Inhibition diameters were determined after incubation for 24 h at 37^oC. All tests were performed in triplicate.

Extraction studies

We studied in this work with a common formalism of equations,^{19,27,31} *K*_{ex} is extraction equilibrium constant; [M^{+m}] and [MLA_m] are the concentrations of metal cation in aqueous phase and organic phase, respectively. *K*_{D,L} denotes a distribution constant of ligand between organic solvent and water.



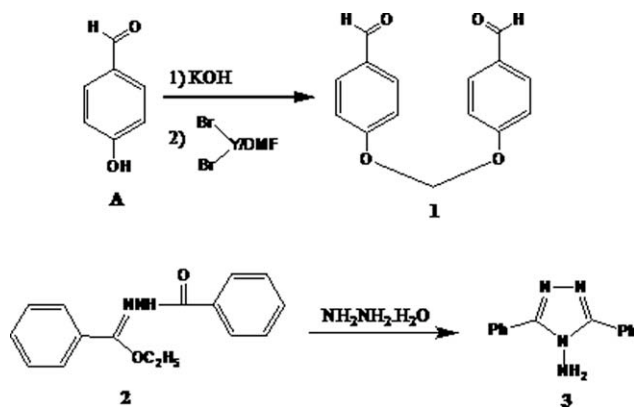
$$K_{ex} = \frac{[MLA_m]_{(org)}}{[M^{+m}]_{(aq)}[L]_{(org)}[A^{-}]_{(aq)}^m}, \quad (2)$$

$$K_{D,L} = [L]_{(org)} / [L]_{(w)}. \quad (3)$$

From selective extractions performed for 10 different transition metal cations under identical conditions (i.e., the same ligand and 10 metals the same concentrations), the selectivity factor, *S_f*, for *M*₁ over *M*₂ is determined as a ratio of *K*_{D,L} *M*₁ and *K*_{D,L} *M*₂, as described by eq. (4):

$$S_f = K_{dL M1} / K_{dL M2}. \quad (4)$$

Extraction and selectivity factor values, complexation and distribution constants of all synthesized ligands are collected in Tables II and III.



Scheme 1 Synthetic pathway for preparation of precursor compounds.

Extraction procedure

The overall extraction equilibrium constants for the 1 : 1 complexes of the synthesized compounds with metal ions, between the organic solvent and water, have been determined at $25 \pm 0.1^\circ\text{C}$. They were conducted in CHCl_3 -water systems maintaining an identical initial cation concentration in water, $[M_0^+]_{w}$, and a organic ligand concentration in the organic phase, $[L_0]_{org}$, so that in all extractions $[M_0^+]_{w} : [L_0]_{org}$ ratios were 1 : 1. An ion association complex formed between the metal-ligand complex ion and a metal anion was extracted into the CHCl_3 organic solvent, and then the metal concentration of the separated aqueous phase was measured with an ICP-AES spectrophotometer.

The extraction measurements were done in 100 mL glass thermostated cell compartment with a mechanical stirrer where a 25 mL solution of an aqueous salt ($1 \times 10^{-5} \text{ M}$) and ligand in CHCl_3 organic solvent in appropriate concentration were placed and stirred for 120 min at $25 \pm 0.1^\circ\text{C}$ and subsequently allowed to stand for 60 min to complete the phase separation. The optimum concentrations of the ligands were determined by extracting the metal ion with 10 mL of various concentrations of the ligands ($1 \times 10^{-5} \text{ M}$).

After extraction, complexation abilities of synthesized compounds with metal cation were determined with spectroscopic method. The extracted metal cation in the aqueous phases have been determined spectroscopically: ICP-AES Each value was the average of three subsequent measurements. Complexation and distribution constants are summarized in Table II.

RESULTS AND DISCUSSION

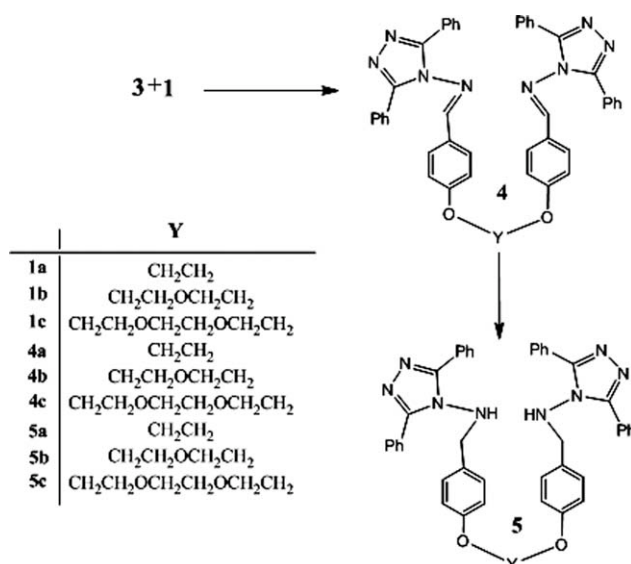
The Schiff bases and the ligands were prepared through a four-step syntheses, the starting materials of which bisaldehydes 1 and 3,5-diphenyl-4-amino-4*H*-1,2,4-triazole 3 were synthesized according to the

published procedures (Scheme 1).^{28,32} Treatment of the aldehyde A with potassium hydroxide and then addition of dibromoalkyl reagent into the medium gave the first starting material bisaldehydes 1. The second starting material triazole 3 was synthesized with the reaction of readily available imine 2 with hydrazine. Finally, the reactions of the compounds 1 and 3 afforded the desired products 4 (Scheme 2).

Although the reduction of imine type compounds have been well defined in the literature,³³ attempts of reducing the imines 4 we have in our hand could lead to the reduction of the heterocyclic ring. Then, the selective reduction of the imino group was achieved using NaBH_4 , the corresponding bisamino-triazoles 5 in good yields (Scheme 2).

In the IR spectra of compounds 4, the characteristic C=N stretching bands appeared between 1576 and 1598 cm^{-1} . While the ^1H NMR signals for the $-\text{N}=\text{CH}$ groups were observed at δ 8.20–8.56 ppm, their ^{13}C NMR signals were recorded at δ 162–171 ppm. The corresponding reduced compounds 5 showed IR bands around 3220 – 3300 cm^{-1} (νNH). The ^1H NMR signals of the $-\text{NH}-\text{CH}_2-$ groups were observed as a doublet or strong singlet at around δ 3.65–3.90 ppm and the proton signals of $-\text{NH}-\text{CH}_2-$ were recorded as a triplet or strong singlet between δ 6.40–6.69 ppm. The $\text{NH}-\text{CH}_2-$ carbon signals of the compounds 5 were recorded at δ 54 ppm. In addition, as C_3 and C_5 of the triazole moiety of the bisSchiff bases 4 gave signals between δ 150 and 151 ppm, similar carbons belonging to the same moiety of the reduced compounds 5 were observed between δ 149–154 ppm.

Anti-bacterial activity was measured using the standard method of diffusion disc plates on agar.



Scheme 2 Synthetic pathway for preparation of compounds 4 and 5 derivatives.

TABLE I
Antimicrobial Screening Data for the Selected Compounds

S. No.	Microorganisms	Zone of inhibition ^a						C ^b
		4a	4b	4c	5a	5b	5c	
1	<i>Enterobacter cloacae</i>	–	3	–	1	2	2	3
2	<i>Enterococcus faecalis</i>	1	2	1	2	4	3	–
3	<i>Salmonella typhimurium</i>	–	3	1	1	3	–	8
4	<i>Escherichia coli</i>	–	1	–	1	–	1	3
5	<i>Staphylococcus epidermidis</i>	1	10	3	3	3	7	8
6	<i>Proteus vulgaris</i>	1	3	2	3	2	1	29
7	<i>Yersinia pseudotuberculosis</i>	2	3	1	3	1	7	10
8	<i>Staphylococcus aureus</i>	3	2	2	1	2	1	23
9	<i>Pseudomonas aeruginosa</i>	2	4	2	4	3	2	–
10	<i>Klebsiella pneumonia</i>	3	2	1	1	2	2	8
11	<i>Bacillus subtilis</i>	1	3	7	2	1	3	–

DMSO has no values for negative control.

^a Millimeter values.

^b Positive control. sefpotec 200 mg was used.

However, only a few ligands showed biological activity against the studied microorganisms. Moderate activity was observed only in **4b** against *Staphylococcus epidermidis* bacteria. Anti-bacterial activity results of synthesized ligands are listed in Table I.

Extraction ability of the synthesized ligands

Heavy metal removal is an important task for the human health. Therefore, selective extraction power of organic ligands is extremely important. In this study, selective extraction abilities of the synthesized ligands were investigated. The affinities of the new bis-1,2,4-triazole derivatives of the some Schiff bases and amine analogs toward metal salts CuCl₂, PbCl₂, ZnCl₂, CdCl₂, NiCl₂, CaCl₂, MnCl₂, CoCl₂, FeCl₃, and Mg(NO₃)₂ were examined by solvent extraction experiment using chloroform–water biphasic system. The stability constants of the various metal complexes of the ligands with metal ions in chloroform are listed in Table II. It was assuming that the formation of 1 : 1 complexes of the metal cations were extracted at the natural pH of the aqueous metal salt solutions.

The log K_{ex} values of the ligands in chloroform generally decreased in the order of Fe(III) > Cu(II) > Pb(II) > Co(II) > Ni(II) > Mn(II) > Zn(II) > Mg(II) > Ca(II). The all hosts extracted metal ions with different extractability while, however, showing no affinity toward the alkaline earth metal ions. The selectivity constants of various metal complexes of the ligands as the interactions of the ligands with the metal ions in chloroform are listed in Table III. For selective extraction, a modified extraction technique was applied, considering S_f values of the metal cations. An aqueous solution of the metals (1×10^{-5} M) and a separate organic solution of the each ligand (1×10^{-5} M) were used. Competitive

metal salt extractions were conducted with a 10.00 cm³ of an aqueous solution containing the metal cations [Pb(II), Cd(II), Ni(II), Co(II), Cu(II), Zn(II), Ni(II), Mn(II), Fe(III) and Mg(II)] and 10.00 cm³ of an organic solution of the ligand.

One of the most important results is the increase in Fe(III) selectivity for all the ligands compare with the other the metal cations. The ligand **4b** exhibited remarkably high Fe(III) selectivity. For the Fe(III) cation in mixture, the S_f values, determined by competitive extraction, were approximately ~ 4.77 –1850.000,00 which is higher than those calculated from the results of selective extraction experiments of the other transition metal cations.

A graph of selectivity values was depicted in Figure 1. The results indicated that among the all studied metals, Fe (III) showed selective complexation toward the all the ligands. A graph of very high selectivity values of iron (III) was depicted in Figure 2. On the other hand, selectivity values of nonferrous was depicted in Figure 3. In copper (II) results in Figure 3, **4a** ligand was showed very high selectivity against Cd (II) and Ca(II), on the other hand **4b** ligand was only showed very high selectivity against Ni(II). Co(II) ion has the lowest complexation values in all transition metal ions. It was only showed selectivity against Ca(II) and Mg(II) ions. Podand compounds are open chain molecules, structures have the ability to move freely to hold metal ion during complexation.

In the supramolecular chemistry, some conformationally rigid cavitands are relatively slow in exchanging their metal–ligand solutions.^{34–38} The lipophilicity and functionality of specific terminal groups having various polyethylene frameworks could be useful in enhancing the cation transport and detection.^{38–40} The polyethylene glycol chains and their podands binding the cation by chelation

TABLE II
Equilibrium Constants for Extractions of the Metal Cations with Synthesized Ligands in CHCl₃ at 25 ± 0.1 °C^a

Metals	NL ^b		4a	4b	4c	5a	5b	5c
Cu ⁺²	0.22	<i>K</i> _{D,L}	1.76	1.12	1.37	1.32	1.29	1.43
		%ExL	63.81	52.79	57.83	56.88	56.25	58.93
		Log <i>K</i> _{ex}	11.13	10.70	10.89	10.85	10.83	10.93
Pb ⁺²	0.45	<i>K</i> _{D,L}	0.98	1.43	1.61	1.20	0.93	1.70
		%ExL	49.61	58.83	61.68	54.58	48.07	62.98
		Log <i>K</i> _{ex}	10.59	10.93	11.04	10.77	10.54	11.09
Zn ⁺²	0.01	<i>K</i> _{D,L}	0.12	0.06	0.15	0.16	0.10	0.86
		%ExL	10.86	5.50	13.30	13.76	9.33	46.18
		Log <i>K</i> _{ex}	9.19	8.81	9.31	9.33	9.10	10.47
Cd ⁺²	0.01	<i>K</i> _{D,L}	0.00	0.03	0.01	0.01	0.02	0.01
		%ExL	0.18	2.58	1.07	0.98	2.40	0.80
		Log <i>K</i> _{ex}	7.25	8.45	8.04	8.00	8.41	7.91
Ni ⁺²	–	<i>K</i> _{D,L}	0.28	0.00	0.25	0.11	0.46	0.29
		%ExL	21.64	0.17	20.10	9.88	31.35	22.49
		Log <i>K</i> _{ex}	9.65	7.23	9.60	9.13	9.99	9.68
Ca ⁺²	–	<i>K</i> _{D,L}	– ^c	– ^c	– ^c	– ^c	– ^c	– ^c
		%ExL	– ^c	– ^c	– ^c	– ^c	– ^c	– ^c
		Log <i>K</i> _{ex}	– ^c	– ^c	– ^c	– ^c	– ^c	– ^c
Mn ⁺²	0.08	<i>K</i> _{D,L}	0.15	0.09	0.19	0.10	0.12	0.19
		%ExL	13.11	8.20	15.66	9.11	10.38	15.85
		Log <i>K</i> _{ex}	9.30	9.03	9.42	9.08	9.16	9.42
Co ⁺²	0.09	<i>K</i> _{D,L}	0.94	0.88	1.11	1.08	1.00	1.02
		%ExL	48.56	46.69	52.63	51.95	49.92	50.42
		Log <i>K</i> _{ex}	10.55	10.49	10.69	10.67	10.60	10.62
Fe ⁺³	1.12	<i>K</i> _{D,L}	78.71	185.00	6.54	110.60	110.60	49.73
		%ExL	98.75	99.46	86.74	99.10	99.10	98.03
		Log <i>K</i> _{ex}	15.70	16.81	12.57	16.14	16.14	15.11
Mg ⁺²	–	<i>K</i> _{D,L}	0.03	0.06	– ^c	0.01	0.07	– ^c
		%ExL	3.29	8.56	– ^c	1.23	8.11	– ^c
		Log <i>K</i> _{ex}	5.35	8.80	– ^c	6.58	8.91	– ^c

Cu⁺²:CuCl₂, Pb⁺²:PbCl₂, Zn⁺²:ZnCl₂, Cd⁺²:CdCl₂, Ni⁺²:NiCl₂, Ca⁺²:CaCl₂, Mn⁺²:MnCl₂, Co⁺²:CoCl₂.

Fe⁺³:FeCl₃, Mg⁺²:Mg(NO₃)₂.

^a Correlation coefficient: 0.999.

^b *K*_{D,L} values for no ligand in solution.

^c The results were very small enough to be neglected.

have been well known because of the use of pure polyethylene glycols-glymes for the salt solvating. The end groups may play a specific role for the chelation depending on their polarity.⁴¹ Sometimes, surprisingly podands shows high complexation values compared with cyclic similar compounds.⁴²

The results concerning the study of the transition metal cations with these ligands very important in respect. Transition metals play important biological and environmental roles. Their selective detection is thus of high interest. First, in all cases of extraction studies, Fe(III) ion is found to be the best extracted metal cation for the all synthesized ligands as shown in Tables II and III. By using the selectivity results and graphics; selective metal recovery and removal studies are easily worked in these metal mixtures.

CONCLUSIONS

Development of a new selective complexation reagent and investigation of its ion extraction selectivity

are very important the mutual separation.⁴³ The ion binding role of polyglycols with specific end groups (so called podands) has been recognized. Such systems are of particular interest with respect to polymer studies. Flexible podands like polyethylene chains are relatively faster metal–ligand exchange of the complex.^{35–38} This remarkable range of specific selectivity for binding various metal ions depending on the size of the ligands and type of the donor atoms makes ligands a very useful extracting agent for separating metal ions. The metal ion-organic ligand binding strength is primarily controlled by the number of available electron donor sites within the ligand, donor atom basicity, the distance separating the metal ion and the oxygen, nitrogen and the alignment of the dipoles.^{44,45}

In this study, it has been showed that the synthesized ligands exhibit an extraordinary property of dissolving/extracting metal ions into nonpolar solvents. Moreover, they are very effective and highly selective for the separation of various metal ions. These properties are extremely important in separation science and

TABLE III
Selectivity Factor Values. S_f Determined for Pairs of Metal Cations in the Competitive Extraction of Metal Salts from Aqueous Solution into CHCl_3 with 4a–c and 5a–c Ligands

M		4a	4b	4c	5a	5b	5c
Cu^{+2}	M/Cu	1.00	1.00	1.00	1.00	1.00	1.00
	M/Pb	1.80	0.78	0.85	1.10	1.39	0.84
	M/Zn	14.67	18.67	9.13	8.25	12.90	1.66
	M/Cd	17,600.00	37.33	137.00	132.00	64.50	143.00
	M/Ni	6.29	11,200.00	5.48	12.00	2.80	4.93
	M/Ca	17,600.00	11,200.00	13,700.00	13,200.00	12,900.00	14,300.00
	M/Mn	11.73	12.44	7.21	13.20	10.75	7.53
	M/Co	1.87	1.27	1.23	1.22	1.29	1.40
	M/Fe	0.02	0.01	0.21	0.01	0.01	0.03
	M/Mg	58.67	18.67	13,700.00	132.00	18.43	14,300.00
Pb^{+2}	M/Cu	0.56	1.28	1.18	0.91	0.72	1.19
	M/Pb	1.00	1.00	1.00	1.00	1.00	1.00
	M/Zn	8.17	23.83	10.73	7.50	9.30	1.98
	M/Cd	9800.00	47.67	161.00	120.00	46.50	170.00
	M/Ni	3.50	14,300.00	6.44	10.91	2.02	5.86
	M/Ca	9800.00	14,300.00	16,100.00	12,000.00	9300.00	17,000.00
	M/Mn	6.53	15.89	8.47	12.00	7.75	8.95
	M/Co	1.04	1.63	1.45	1.11	0.93	1.67
	M/Fe	0.01	0.01	0.25	0.01	0.01	0.03
	M/Mg	32.67	23.83	16,100.00	120.00	13.29	17,000.00
Zn^{+2}	M/Cu	0.07	0.05	0.11	0.12	0.08	0.60
	M/Pb	0.12	0.04	0.09	0.13	0.11	0.51
	M/Zn	1.00	1.00	1.00	1.00	1.00	1.00
	M/Cd	1200.00	2.00	15.00	16.00	5.00	86.00
	M/Ni	0.43	600.00	0.60	1.45	0.22	2.97
	M/Ca	1200.00	600.00	1500.00	1600.00	1000.00	8600.00
	M/Mn	0.80	0.67	0.79	1.60	0.83	4.53
	M/Co	0.13	0.07	0.14	0.15	0.10	0.84
	M/Fe	0.00	0.00	0.02	0.00	0.00	0.02
	M/Mg	4.00	1.00	1500.00	16.00	1.43	8600.00
Cd^{+2}	M/Cu	0.00	0.03	0.01	0.01	0.02	0.01
	M/Pb	0.00	0.02	0.01	0.01	0.02	0.01
	M/Zn	0.00	0.50	0.07	0.06	0.20	0.01
	M/Cd	1.00	1.00	1.00	1.00	1.00	1.00
	M/Ni	0.00	300.00	0.04	0.09	0.04	0.03
	M/Ca	1.00	300.00	100.00	100.00	200.00	100.00
	M/Mn	0.00	0.33	0.05	0.10	0.17	0.05
	M/Co	0.00	0.03	0.01	0.01	0.02	0.01
	M/Fe	0.00	0.00	0.00	0.00	0.00	0.00
	M/Mg	0.00	0.50	100.00	1.00	0.29	100.00
Ni^{+2}	M/Cu	0.16	0.00	0.18	0.08	0.36	0.20
	M/Pb	0.29	0.00	0.16	0.09	0.49	0.17
	M/Zn	2.33	0.00	1.67	0.69	4.60	0.34
	M/Cd	2800.00	0.00	25.00	11.00	23.00	29.00
	M/Ni	1.00	1.00	1.00	1.00	1.00	1.00
	M/Ca	2800.00	1.00	2500.00	1100.00	4600.00	2900.00
	M/Mn	1.87	0.00	1.32	1.10	3.83	1.53
	M/Co	0.30	0.00	0.23	0.10	0.46	0.28
	M/Fe	0.00	0.00	0.04	0.00	0.00	0.01
	M/Mg	9.33	0.00	2500.00	11.00	6.57	2900.00
Ca^{+2}	M/Cu	0.00	0.00	0.00	0.00	0.00	0.00
	M/Pb	0.00	0.00	0.00	0.00	0.00	0.00
	M/Zn	0.00	0.00	0.00	0.00	0.00	0.00
	M/Cd	1.00	0.00	0.01	0.01	0.01	0.01
	M/Ni	0.00	1.00	0.00	0.00	0.00	0.00
	M/Ca	1.00	1.00	1.00	1.00	1.00	1.00
	M/Mn	0.00	0.00	0.00	0.00	0.00	0.00
	M/Co	0.00	0.00	0.00	0.00	0.00	0.00
	M/Fe	0.00	0.00	0.00	0.00	0.00	0.00
	M/Mg	0.00	0.00	1.00	0.01	0.00	1.00

TABLE III. Continued

M		4a	4b	4c	5a	5b	5c
Mn ⁺²	M/Cu	0.09	0.08	0.14	0.08	0.09	0.13
	M/Pb	0.15	0.06	0.12	0.08	0.13	0.11
	M/Zn	1.25	1.50	1.27	0.63	1.20	0.22
	M/Cd	1500.00	3.00	19.00	10.00	6.00	19.00
	M/Ni	0.54	900.00	0.76	0.91	0.26	0.66
	M/Ca	1500.00	900.00	1900.00	1000.00	1200.00	1900.00
	M/Mn	1.00	1.00	1.00	1.00	1.00	1.00
	M/Co	0.16	0.10	0.17	0.09	0.12	0.19
	M/Fe	0.00	0.00	0.03	0.00	0.00	0.00
Co ⁺²	M/Mg	5.00	1.50	1900.00	10.00	1.71	1900.00
	M/Cu	0.53	0.79	0.81	0.82	0.78	0.71
	M/Pb	0.96	0.62	0.69	0.90	1.08	0.60
	M/Zn	7.83	14.67	7.40	6.75	10.00	1.19
	M/Cd	9400.00	29.33	111.00	108.00	50.00	102.00
	M/Ni	3.36	8800.00	4.44	9.82	2.17	3.52
	M/Ca	9400.00	8800.00	11,100.00	10,800.00	10,000.00	10,200.00
	M/Mn	6.27	9.78	5.84	10.80	8.33	5.37
	M/Co	1.00	1.00	1.00	1.00	1.00	1.00
Fe ⁺³	M/Fe	0.01	0.00	0.17	0.01	0.01	0.02
	M/Mg	31.33	14.67	11,100.00	108.00	14.29	10,200.00
	M/Cu	44.72	165.18	4.77	83.79	85.74	34.78
	M/Pb	80.32	129.37	4.06	92.17	118.92	29.25
	M/Zn	655.92	3083.33	43.60	691.25	1106.00	57.83
	M/Cd	787,100.00	6166.67	654.00	11,060.00	5,530.00	4,973.00
	M/Ni	281.11	1850,000.00	26.16	1005.45	240.43	171.48
	M/Ca	787,100.00	1850,000.00	65,400.00	1106,000.00	1106,000.00	497,300.00
	M/Mn	524.73	2055.56	34.42	1106.00	921.67	261.74
Mg ⁺²	M/Co	83.73	210.23	5.89	102.41	110.60	48.75
	M/Fe	1.00	1.00	1.00	1.00	1.00	1.00
	M/Mg	2623.67	3083.33	65,400.00	11060.00	1580.00	497,300.00
	M/Cu	0.02	0.05	0.00	0.01	0.05	0.00
	M/Pb	0.03	0.04	0.00	0.01	0.08	0.00
	M/Zn	0.25	1.00	0.00	0.06	0.70	0.00
	M/Cd	300.00	2.00	0.01	1.00	3.50	0.01
	M/Ni	0.11	600.00	0.00	0.09	0.15	0.00
	M/Ca	300.00	600.00	1.00	100.00	700.00	1.00
M/Mn	0.20	0.67	0.00	0.10	0.58	0.00	
M/Co	0.03	0.07	0.00	0.01	0.07	0.00	
M/Fe	0.00	0.00	0.00	0.00	0.00	0.00	
M/Mg	1.00	1.00	1.00	1.00	1.00	1.00	

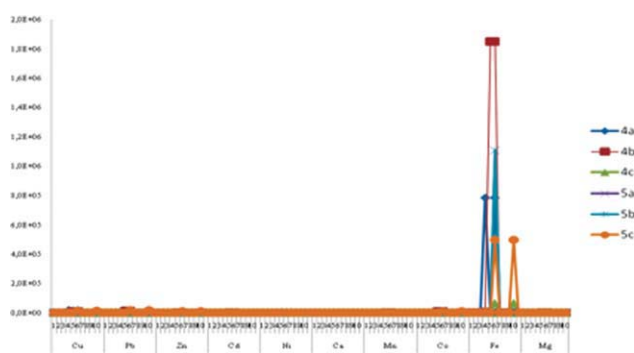


Figure 1 Selectivity factor graphic of all metals for 4a-c and 5a-c ligands. 1; M/Cu, 2; M/Pb, 3; M/Zn, 4; M/Cd, 5; M/Ni, 6; M/Ca, 7; M/Mn, 8; M/Co, 9; M/Fe, 10; M/Mg. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

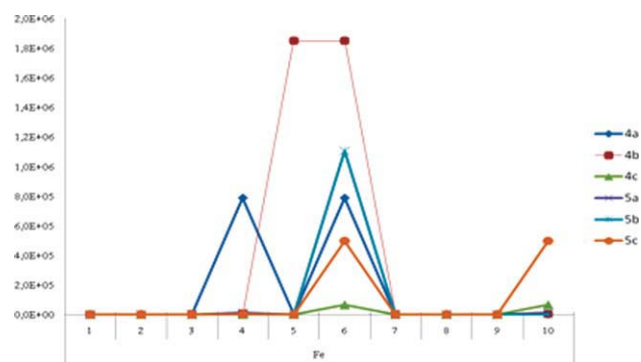


Figure 2 Selectivity factor graphic of iron for 4a-c and 5a-c ligands. 1; M/Cu, 2; M/Pb, 3; M/Zn, 4; M/Cd, 5; M/Ni, 6; M/Ca, 7; M/Mn, 8; M/Co, 9; M/Fe, 10; M/Mg. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

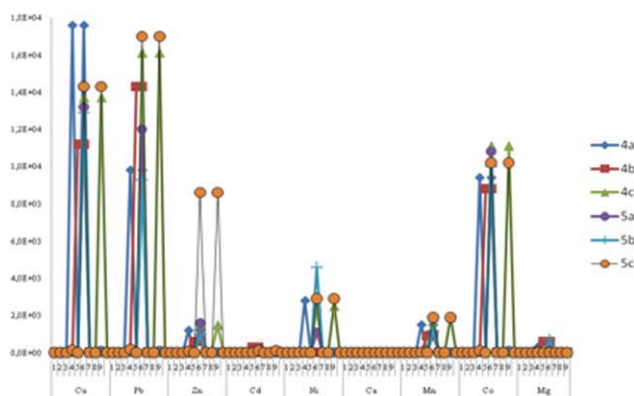


Figure 3 Selectivity factor graphic of all metals without iron for 4a–c and 5a–c ligands. 1; M/Cu, 2; M/Pb, 3; M/Zn, 4; M/Cd, 5; M/Ni, 6; M/Ca, 7; M/Mn, 8; M/Co, 9; M/Mg. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

technology. A convenient method was established for the syntheses of bis triazole Schiff bases **4a–c** and corresponding bis amino triazole compounds **5a–c** in good yields. Six new bis(4H-1,2,4-triazole) derivatives exhibited some biological activities.

The stability constants of metal complexes of the noncyclic and cyclic ligands as *N*-pivot side-armed podands and lariat ethers, i.e., **4a–c** and **5a–c**, are listed in Table II, as the interactions of these ligands with the alkali metal ions in CHCl_3 media. The $\log K_{\text{ex}}$ values of the ligands have been determined to be in the decreasing order of $\text{Fe} > \text{Cu} > \text{Pb} > \text{Co} > \text{Ni} > \text{Mn} > \text{Zn} > \text{Mg} > \text{Ca}$. Among the ligands, all the podands exhibited low extraction of alkali metals such as Ca^{+2} and Mg^{+2} . Relatively high extraction percentage was observed with all schiff bases and amine forms of the podands for transition metals. The $\log K_{\text{ex}}$ values indicated an extraction selectivity of the ligands toward Fe-organic salt compare with other metals. Fe-organic ligands proved to form more strong complexes with both imine and amine forms of the podands in the order of $4b > 5a = 5b > 4a > 5c > 4c$. The results strongly suggested that the selectivity results from the synergist coordination of oxygen atoms of appropriate polyglycol group length and nitrogen atom to Fe(III).

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