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ORIGINAL ARTICLE

Efficient synthesis and metal cations complexation of some novel dinaphthosulfide-substituted macrocyclic diamides

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Abstract Some dinaphthosulfide aza macrocycles (**3–9**) were synthesized based on the conventional route from the reaction of corresponding dinaphthosulfide diester and aliphathic diamines in refluxing methanol in good yields. Dinaphthosulfide diester were synthesized from the reaction of 1,1′-thiobis (2-hydroxy naphthalene) and methyl chloroacetate. The structures of these compounds were confirmed using IR, ^{1}H NMR, ^{13}C NMR, MASS spectroscopy and elemental analysis. Conductometric studies of the complexation of some metal ions with aza derivative **8** (**TDN**) in methanol as solvent implied the formation of 1:1 complexes. The stability of the 1:1 complexes of **TDN** decreases in the order $Hg^{2+} >> Pb^{2+} > Cu^{2+} > Zn^{2+} > Ca^{2+} > Mg^{2+} > Cd^{2+} > Sr^{2+} > Ag^{+} > Ba^{2+}$.

Keywords Azathia macrocycle · Dinaphthosulfide · Host-guest interactions · Conductometry · Complexation · Selective Hg^{2+}-carrier

Introduction

Macrocycles are possibly the most widely used family of host compounds in supramolecular chemistry. Pedersen's discovery of the macrocyclic polyethers has laid the foundation for a numerous studies of their ability to act as receptors for cationic, neutral and anionic species [1].

A rational design of macromolecular receptors is governed by a number of factors (the nature, the number, the relative structural and spatial placement of various ligating units, etc.), and the combination of these factors may induce an intrinsic balance of noncovalent binding forces optimum for specificity in host-uest recognition [2]. The amide group, so generously used by nature in a variety of antibiotic ionophores [3], has acquired a special status in the design of receptors because it displays dual (O or N and NH) ligating character, higher negative charge on oxygen than for ether and ester groups, and geometrical rigidity [4]. Amide-based macrocycles for selective recognition of metal cations [1b, 5] and organic molecules [1b, 6] typically adopt preorganization of their binding sites through hydrogen bonding or configurational rigidity around the amide carbon-itrogen bond.

Macrocyclic aza crown compounds have gained a great deal of attention due to their wide applications in chemistry, analysis, microanalysis, metal separation, sensoring, biology, biophysics and ecology [1b, 6]. Due to their high capability in selective and effective complexation with variety of transition and heavy metals, there is an increasing interest in the preparation of new crown ethers, including benzo-substituted macrocyclic diamides. It is well established that introduction of polar amide donors into a complexone plays an important role in the enhancement of the selectivity in cation binding.

Through N–C=O–metal interactions the amide group in many hosts directs the specificity of the host toward softer alkaline earth cations, whereas ether-ster macrocyclic ionophores show high selectivity in complex formation with alkali metal ions [7]. The amide group often plays a

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key role in the complexation of various guests in aza macrocycles. In our previous studies we have synthesized dibenzosulfide and dibenzosulfoxides aza macrocycles as metal cations receptors [8, 9]. In complexation studies, these macrocycles revealed high selectivities towards heavy metal ions such as Ag^{+}, Co^{2+}, Hg^{2+} and Cd^{2+} in the presence of other ions [10]. In biological studies these macrocycles showed inhibitor effects in some biological transformations [11]. These results have encouraged us to synthesize new dinaphthosulfide aza derivatives and undertake complexation studies for these macrocycles. In order to have a clue about the selectivity of the synthesized macrocycles, here we also report the conductance study of complexation of several different metal ions with 7,10, 13-triaza-1-thia-4,16-dioxa-2,3;17,18-dinaphto-cyclooctadecane-6,14-dione (**8**, **TDN**) in methanol solution at 25 °C.

Experimental

Chemicals and apparatus

All reactions were carried out in an efficient hood. The starting materials were purchased from Merck, Fluka and Aldrich chemical companies. Methanol was distilled and stored under Linde 4 Å molecular sieve. Column chromatography was performed on silica gel 60 (0.04–0.063 mm). Preparative thin layer chromatography was performed on silica gel 60 P F254.

Reagent-grade $Zn(NO_3)_2.4H_2O$, $Cd(NO_3)_2.6H_2O$, $Cu(NO_3)_2.3H_2O$ and methanol (all from Merck) were of the highest purity available and used as received. $AgClO_4.H_2O$, $Pb(ClO_4)_2.H_2O$, $Hg(ClO_4)_2.3H_2O$, $Mg(ClO_4)_2$ and $Ba(ClO_4)_2$ supplied from Fluka. $Sr(ClO_4)_2$ and $Ca(ClO_4)_2$ were prepared by treating $Sr(CO_3)_2$ and $Ca(CO_3)_2$, respectively, with small excess of 3 M perchloric acid, followed by evaporation to dryness, recrystallization three times from deionized water and drying at 120 °C.

Compound **1** was synthesized based on reported procedures [8–13]. The melting points (uncorrected) were measured with an Electrothermal Engineering LTD 9100 apparatus. Elemental analysis was performed by a CHNO-Rapid Heraeus elemental analyzer. IR spectra were measured on a Perkin-Elmer model 543. The ^{1}H NMR and ^{13}C NMR spectra were obtained using BRUKER AVANCE DRX 500 and BRUKER AVANCE DPX 300 MHz spectrometers and mass spectra were obtained with a Shimadzu GC-MS-QP 1100 EX model.

Conductance measurements were carried out with a CMD 500 WPA conductivity meter. A dip-type conductivity cell made of platinum black was used. The cell constant at the different temperatures used was determined by conductivity measurements of a 0.010 M solution of analytical-grade KCl (Merck) in triply distilled deionized water. The specific conductance of this solution at various temperatures has been reported in the literature [14]. In all measurements, the cell was thermostated at the desired temperature ± 0.03 °C using JULABO model F12-ED Refrigerated/Heating circulator.

Synthesis of 1,1′-thiobis-(2-naphthoxy (2-methyl acetate)) (**2**)

To a mixture of **1** (6.04 g, 19 mmol), potassium carbonate (5.24 g, 38 mmol) and potassium iodide (catalytic) in acetonitrile (100 mL) at room temperature, were added methylchloroacetate (3.35 mL, 38 mmol). Then the reaction mixture was refluxed for 24 h. After completion of the reaction (TLC), the mixture was cooled to room temperature, water was added and extracted with chloroform (3 × 50 mL), washed with sodium hydroxide solution (10%), dried and evaporated to afford a precipitate that was recrystallized from ethanol to give pure **2** in 91% yield. mp. 126.5–127 °C; IR (potassium bromide): 3040, 3000, 2970, 1750, 1595, 1500, 1450, 1300, 1250,1200, 1090, 1040, 810, 750 cm^{-1}; ^{1}H NMR (300 MHz, acetone-d_6) δ: 3.65 (6H, s), 4.65 (4H, s), 7.09 (2H, ddd, J = 8.46, J = 6.94, J = 1.32 Hz), 7.26 (2H, d, J = 9.05 Hz), 7.35 (2H, ddd, J = 7.98, J = 6.84, J = 1.11 Hz), 7.81 (2H, d, J = 7.91 Hz), 7.83 (2H, d, J = 9.02 Hz), 8.69 (2H, d, J = 8.59 Hz) ppm; Elemental analysis calculated for $C_{26}H_{22}O_6S$: C, 67.52; H, 4.79. Found: C, 67.45; H, 4.67.

General procedure for the synthesis of dinaphthosulfide aza macrocycles

To 2 mmol of diester (**2**) in methanol (100 mL) was added the appropriate diamine (2 mmol) at room temperature. After stirring for 20 min the resulting mixture was refluxed for 3 days. On completion of the reaction (TLC), the reaction mixture was allowed to cool to room temperature, water was added and the resulting mixture extracted with chloroform (3 × 50 mL), the combined chloroform layers was dried and evaporated to afford a precipitate that was purified by column chromatography on silica gel using appropriate solvent mixtures as eluent or purified by recrystallization from an appropriate solvent.

Synthesis of 7,10-diaza-1-thia-4,13-dioxa-6,11-dioxo-2,3;14,15-dinaphtho-cyclopentadecane (**3**)

This compound was synthesized based on the general procedure involving the reaction of **2** (2 mmol, 0.92 g),

and ethylenediamine (2 mmol, 0.14 mL) in refluxing methanol (100 mL).

The solid product was chromatographed on silica gel with dichloromethane /methanol (3:1) as eluent to afford **3** as a white solid in 66% yield, mp. 212–213 °C; IR (potassium bromide): 3390 (NH amide), 2941, 1691 (carbonyl), 1677 (carbonyl), 1618, 1584, 1513, 1439, 1345, 1315, 1263, 1206, 1143, 1080, 1018, 810, 773, 748 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ: 3.09 (4H, t), 4.30 (4H, s), 6.84 (2H, broad), 7.33 (2H, d, J = 9.1 Hz), 7.39–7.44 (4H, m), 7.90–7.94 (4H, m), 8.32 (2H, d, J = 8 Hz); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 168.64, 155.74, 134.73, 130.80, 130.34, 129.51, 128.05, 125.09, 125.07, 117.22, 114.86, 69.31, 38.26; MS (electron impact) m/z (relative intensity %): 458 (M^+, molecular ion) (79), 459 $(M+1)^+$ (38), 460 $(M+2)^+$ (11), 461 $(M+3)^+$ (5), 456 (6), 300 (24), 299 (18), 268 (17), 216 (10), 187 (62) 157 (22), 146 (20), 144 (33), 115 (37), 85 (86), 84 (100), 43 (17).

Anal. calcd. for $C_{26}H_{22}N_2O_4S$: C, 68.10; H, 4.84; N, 6.11. Found: C, 68.18; H, 4.76; N, 6.13.

Synthesis of 7,11-diaza-1-thia-4,14-dioxa-6,12-dioxo-2,3;15,16-dinaphtho-cyclohexadecane (**4**)

This compound was synthesized based on the general procedure involving the reaction of **2** (2 mmol, 0.92 g), and 1,3-diaminopropane (2 mmol, 0.17 mL) in refluxing methanol (100 mL). The product was recrystallized from ethanol to afford **4** as colorless crystals in 62% yield, mp. 256–257 °C; IR (potassium bromide): 3426, 3409, 2939, 1693, 1624, 1593, 1552, 1507, 1463, 1431, 1377, 1354, 1325, 1270, 1242,1150, 1075, 1031, 818, 752 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ**:** 1.68 (2H, m), 3.30–3.33 (4H, m), 4.47 (4H, s), 7.37 (2H, broad), 7.39 (2H, d, J = 4.61 Hz), 7.44 (2H, t, J = 7.46 Hz), 7.66 (2H, t, J = 5.62 Hz), 7.90 (4H, dd, J = 9.5 Hz), 8.44 (2H, d, J = 8.47 Hz) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 168.20, 157.01, 135.08, 131.15, 130.54, 129.53, 128.22, 125.09, 125.05, 118.28, 115.80, 69.33, 39.66, 28.43 ppm; MS (electron impact) m/z (relative intensity %): (M^+, molecular ion) 472 (64), 473 $(M+1)^+$ (17), 474 $(M+2)^+$ (12), 475 $(M+3)^+$ (4), 300 (33), 216 (24), 187 (62), 157 (31), 144 (39), 115 (46), 99 (60), 98 (100), 56 (39), 43 (21).

Anal. calcd. for $C_{27}H_{24}N_2O_4S$: C, 68.62; H, 5.12; N, 5.93. Found: C, 68.65; H, 5.10; N, 5.92.

Synthesis of 7, 12-diaza-1-thia-4, 15-dioxa-6, 13-dioxo-2, 3; 16,7-dinaphtho-cycloheptadecane (**5**)

This compound was synthesized based on the general procedure involving the reaction of **2** (2 mmol, 0.92 g), and 1,4-diaminobutane (2 mmol, 0.20 mL) in refluxing methanol (100 mL), the solid product was chromatographed on silica gel with chloroform/methanol (4:1) as eluent to afford **5** as a white solid in 58% yield, mp. 213–214 °C; IR (potassium bromide): 3388, 3062, 2974, 2941, 2882, 1680, 1624, 1591, 1530, 1505, 1463, 1449, 1354, 1299, 1274, 1216, 1156, 1085, 820 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 0.56 (4H, s, broad), 1.74 (1H, s, broad), 2.60 (4H, s, broad), 3.52–3.56 (1H, t, broad, J = 5.7 Hz), 4.38 (4H, s), 7.05 (2H, d, J = 9 Hz), 7.46 (2H, ddd, J = 7.5, 7.5, 0.9 Hz), 7.69 (2H, ddd, J = 7.8, 7.8, 1.2 Hz), 7.80 (4H, t, J = 9.3 Hz), 9.16(2H, d, J = 8.7 Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 168.07, 155.33, 135.92, 130.50, 129.05, 127.85, 127.65, 126.36, 124.95, 117.86, 112.09, 67.01, 36.44, 24.04 ppm; MS (electron impact) m/z (relative intensity %): (M^+, molecular ion) 488 (8), 489 $[M+1]^+$ (4), 300 (28), 271 (17), 239 (15), 216 (22), 187(34), 171 (11), 144 (33), 128 (27), 112 (58), 70 (36, 30 (57).

Anal. calcd. for $C_{28}H_{26}N_2O_4S$: C, 69.11; H, 5.39; N, 5.76. Found: C, 69.14; H, 5.38; N, 5.74.

Synthesis of 7, 16-diaza-1-thia-4, 10, 13, 19-tetraoxa-6, 17-dioxo-2, 3;20, 21-dinaphtho-cyclouneicosane (**6**)

This compound was synthesized based on the general procedure involving the reaction of **2** (2 mmol, 0.92 g), and 1,2-bis(2-aminoethoxy)ethane (2 mmol, 0.29 mL) in refluxing methanol (100 mL), the solid product was chromatographed on silica gel with chloroform/methanol (4:1) as eluent to afford **6** as a white solid in 64% yield, mp. 209–210 °C; IR (potassium bromide): 3384, 3358, 2931, 1683, 1617, 1589, 1535, 1500, 1460, 1429,1382, 1323, 1286, 1243, 1149, 1133, 1095, 810, 764 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 3.41–3.44 (8H, m), 3.48 (4H, t), 4.49 (4H, s), 7.15 (2H, broad), 7.18 (2H, d, J = 8.9 Hz), 7.40 (2H, t, J = 7.11 Hz), 7.48 (2H, t, J = 7.9 Hz), 7.80 (2H, d, J = 8.03 Hz), 7.83 (2H, d, J = 8.9 Hz), 8.52 (2H, d, J = 8.5 Hz) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.42, 155.89, 135.17, 130.97,130.78, 128.86, 127.91, 125.59, 125.17, 119.67, 115.34, 70.74, 69.96, 69.85, 39.42 ppm; MS (electron impact) m/z (relative intensity %): (M^+, molecular ion) 546 (17), $[M+1]^+$ 547 (5), 548 $[M+2]^+$ (4), 549 $[M+3]^+$ (4), 358 (8), 300 (43), 287 (21), 216 (54), 187 (100), 147 (34), 128 (43), 115 (64), 85 (60), 57 (29), 44 (57).

Anal. calcd. for $C_{30}H_{30}N_2O_6S$: C, 65.92; H, 5.53; N, 5.12. Found: C, 65.91; H, 5.56; N, 5.18.

Synthesis of 7,14-diaza-1,10,11-trithia-4,17-dioxa-6,15-dioxo-2,3;18,19-dinaphtho-cyclonona-decane (**7**)

This compound was synthesized based on the general procedure involving the reaction of **2** (2 mmol, 0.92 g),

and cystamine dihydrochloride (2 mmol, 0.45 g) in refluxing methanol (100 mL), and the solid product was chromatographed on silica gel with dichloromethane/methanol (4:1) as eluent to afford **7** as a white solid in 48% yield, mp. 206–207 °C; IR (potassium bromide): 3394, 3344, 1664, 1654, 1538, 1502, 1426, 1265, 1233, 1217, 1067, 1056 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 2.66 (4H, t, J = 5.4 Hz), 3.39 (4H, dd, J = 11.4, 5.7 Hz), 6.65 (2H, broad), 7.11 (2H, d, J = 9 Hz), 7.39 (2H, ddd, J = 7.5, 7.5, 1.2 Hz), 7.50 (2H, ddd, J = 7.5, 7.5, 1.2 Hz), 7.81 (4H, dd, J = 12.3, 8.1 Hz), 8.61 (2H, d, J = 8.7 Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 168.37, 155.63, 134.81, 130.80, 129.98, 128.35, 127.12, 125.37, 124.91, 118.51, 114.14, 68.78, 38.94, 38.54 ppm; MS (electron impact) m/z (relative intensity %): (M^+, molecular ion) 550 (55), 551 $[M+1]^+$ (7), 552 $[M+2]^+$ (5), 300 (15), 216 (26), 187 (50), 144 (100), 115 (74), 61 (20), 30 (35).

Anal. calcd. for $C_{28}H_{26}N_2O_4S_3$: C, 61.07; H, 4.76; N, 5.09. Found: C, 61.04; H, 4.73; N, 5.15.

Synthesis of 7,10,13-triaza-1-thia-4,16-dioxa-6,14-dioxo-2,3;17,18-dinaphtho-cyclooctadecane (**8**)

This compound was synthesized based on the general procedure involving the reaction of **2** (2 mmol, 0.92 g), and diethylene triamine (2 mmol, 0.22 mL) in refluxing methanol (100 mL), the solid product was chromatographed on silica gel with dichloromethane/methanol (3:1) as eluent to afford **8** as a white solid in 71% yield, mp. 260–261 °C; IR (potassium bromide): 3450, 3100, 3000, 2970, 2950, 1690, 1685, 1520, 1475, 1460, 1350, 1280, 1245, 1180, 1050, 800 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 2.56 (4H, t, J = 6 Hz), 3.13 (4H, q, J = 6 Hz), 4.47 (4H, s), 6.83 (2H, broad), 7.06 (2H, d, J = 6 Hz), 7.26–7.80 (4H, m), 7.79 (4H, t, J = 6 Hz), 8.64 (2H, d, J = 9 Hz) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.0, 155.6, 135.1, 130.4, 129.8, 128.4, 127.5, 125.4, 124.6, 118.2, 113.2, 68.1, 47.1, 38.2 ppm; MS (electron impact) m/z (relative intensity %): 501(M^+, molecular ion) (12), 483 (15), 300 (43), 287 (12), 216 (59), 187 (32), 147 (16), 144 (100), 128 (13), 115 (45), 85 (18), 56 (35), 44 (19), 30 (18).

Anal. calcd. for $C_{28}H_{27}N_3O_4S$: C, 67.05; H, 5.43; N, 8.38. Found: C, 67.08; H, 5.46; N, 8.32.

Synthesis of 7, 10-diaza-1-thia-4, 13-dioxa-6, 11-dioxo-8-methyl-2, 3; 14, 15-dinaphtho-cyclopentadecane (**9**)

This compound was synthesized based on the general procedure involving the reaction of **2** (2 mmol, 0.92 g), and 1,2-diaminopropane (2 mmol, 0.17 mL) in refluxing methanol (100 mL), and the solid product was chromatographed on silica gel with chloroform/methanol (4:1) as eluent to afford **9** as a white solid in 68% yield, mp. 256–257 °C; IR (potassium bromide): 3390, 3062, 2989, 2946, 1679, 1622, 1588, 1519, 1502, 1448, 1348, 1266, 1246, 1210, 1149, 1081, 1024, 990, 811, 779, 533 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 0.57 (3H, d, J = 7.2 Hz), 1.91 (1H, broad), 2.13 (1H, dt, J = 13.5, 3.9 Hz), 3.30 (1H, ddd, J = 12.9, 9.9, 1.5 Hz), 3.85–3.89 (1 H, m), 3.92 (1H, d, J = 15.3 Hz), 4.08 (1H, d, J = 15.3 Hz), 4.18 (1H, dd, broad, J = 9.3, 3.6 Hz), 4.24 (1H, d, J = 10.2 Hz), 4.49 (2H, dd, J = 26.7, 15 Hz), 7.08 (2H, dd, J = 9, 2.1 Hz), 7.47 (2H, td, J = 6.9, 1.2 Hz), 7.65 (2H, tdd, J = 6.3, 3, 1.2 Hz), 7.83 (4H, td, J = 7.5, 2.4 Hz), 9.03 (2H, dd, J = 9, 2.1 Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 168.16, 167.34, 154.55, 154.30, 135.71, 135.56, 130.68, 130.57, 129.47, 129.43, 128.27, 128.23, 127.66, 126.07, 125.88, 124.92, 124.86, 116.97, 116.84, 112.03, 111.70, 67.73, 66.98, 43.95, 42.01, 17.56, 17.54 ppm; MS (electron impact) m/z (relative intensity %): (M^+, molecular ion) 472 (78), 473 $[M+1]^+$ (28), 474 $[M+2]^+$ (12), 475 $[M+3]^+$ (3), 300 (31), 271 (18), 239 (21), 216 (54), 187 (62), 171 (11), 144 (34), 115 (68), 99 (100), 44 (63).

Anal. calcd. for $C_{27}H_{24}N_2O_4S$: C, 68.62; H, 5.12; N, 5.93. Found: C, 68.66; H, 5.14; N, 5.90.

Conductometric procedure

In a typical experiment, 10 mL of the desired metal ion (5.0×10^{-5} M) was placed in the titration cell, thermostated to the desired temperature and the conductance of solution was measured. Then, a known amount of a concentrated crown ether solution was added in a stepwise manner using a calibrated micropipette. The conductance of the solution was measured after each addition. The ligand solution was continually added until the desired ligand to cation mole ratio was achieved. The formation constants, K_f, and the limiting molar conductances, Λ_o, of the resulting complexes were calculated by fitting the observed molar conductance, Λ_{obs}, at varying [ligand]/[M^{n+}] mole ratios to a previously derived equation [15] and the formation constants were evaluated using a non-linear least-squares curve-fitting program KINFIT [16].

Results and discussion

Dinaphthosulfide aza macrocycles (**3–9**) were synthesized based on standard procedures (Scheme 1) [17]. Compound **1** was synthesized based on the reported procedure involving the reaction of sulfur dichloride and 2-naphthol [12], the corresponding diester (**2**) was prepared by the

reaction of dinaphthol (**1**) and chloromethyl acetate in refluxing acetonitrile in the presence of potassium carbonate and catalytic amounts of potassium iodide [18]. Dinaphthosulfide aza macrocycles were prepared from the reaction of diester (**2**) and appropriate diamine in refluxing dry methanol over three days [17].

It was found that the macrocyclization process in the present series of sulfide derivatives is more convenient and high yielding compared to the corresponding sulfoxide derivatives. This could be due to the *syn* structure of sulfide versus the *anti* structure of sulfoxide derivatives. X-ray crystallography of dibenzosulfide and dibenzosulfoxide derivatives proved the presence of *syn* structure for sulfide and *anti* structure for sulfoxide monomers [13]. This evidence was used to explain the behavior of their naphthalene derivatives. Based on these studies the proposed structure of dinaphthosulfide is *syn* and this is the preferred conformation for the synthesis of macrocycles in this work.

Solubility of these dinaphthosulfide macrocycles in organic solvents are higher compared to the corresponding dibenzosulfide counterparts reflecting the presence of naphthalene units in their structures. The latter property may be important for the application in host-guest studies of these macrocycles.

The molar conductance of the perchlorate salts of Tl^{+}, Mg^{2+}, Ca^{2+}, Sr^{2+}, Ba^{2+}, Ag^{+}, Pb^{2+}, Hg^{2+} and the nitrate salts of Ni^{2+}, Cu^{2+}, Zn^{2+} and Cd^{2+}, at a constant salt concentration (5.0×10^{-5} M) was monitored while increasing **TDN** crown ether concentration at 25 °C. The resulting molar conductance *vs* ligand/cation mole ratio plots are shown in Fig. 1.

As it is seen from Fig. 1, in all cases, there is a gradual decrease in the molar conductance with an increase in the crown ether concentration. This behavior indicates the lower mobility of the complexed cations compared to the solvated ones. Figure 1 show that, in the case of Pb^{2+}-TDN and especially Hg^{2+}-TDN systems, the addition of ligand to the metal ion solutions causes a continuous decrease in the molar conductance, which begins to level off at a mole ratio greater than one. Such a conductance behavior is indicative of the formation of fairly stable 1:1 complexes in solution. However, in other cases, the molar conductance does not show any tendency for leveling off even at a molar ratio of about 4 and the corresponding molar ratio data do not show considerable changes in their slopes at a molar ratio of about one, which emphasize the formation of some weaker 1:1 complexes.

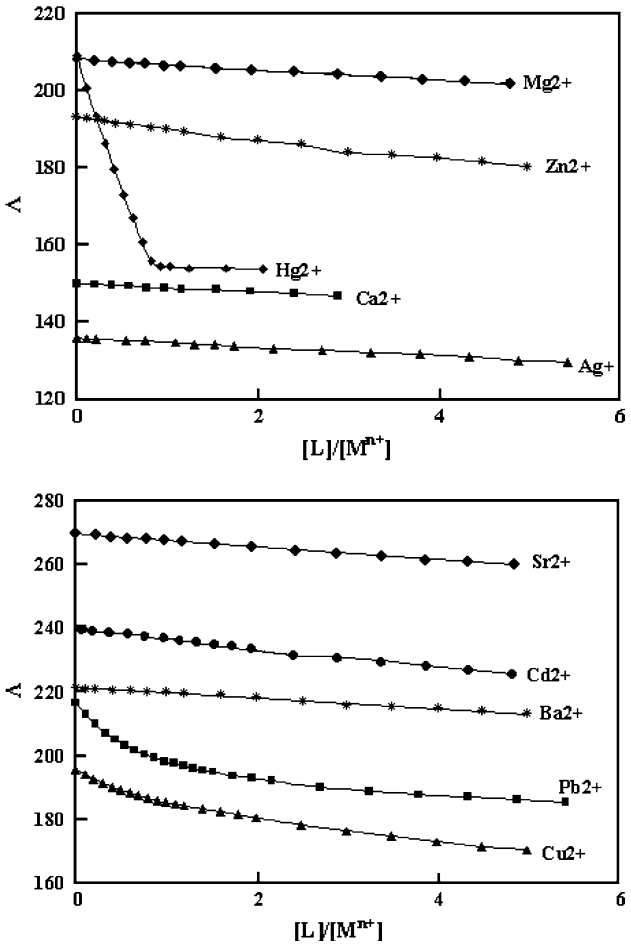
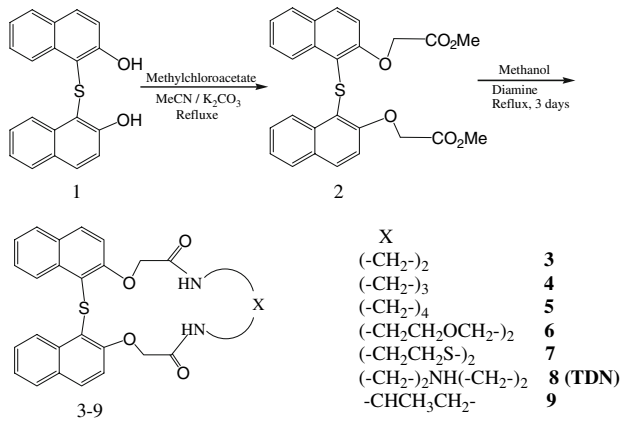


Fig. 1 Molar conductance (S cm^2 mol^{-1}) vs. [**TDN**]/[M^{n+}] for various cations in methanol at 25 °C



Scheme 1 Synthesis of macrocycles

The formation constants of all TDN–M^{n+} complexes in methanol at 25.00 ± 03 °C obtained by computer fitting of the molar conductance-mole ratio data [15, 16], are listed in Table 1. As is obvious, the stability of the resulting 1:1 complexes of **TDN** decreases in the order $Hg^{2+} \gg Pb^{2+} > Cu^{2+} > Zn^{2+} > Ca^{2+} > Mg^{2+} > Cd^{2+} > Sr^{2+} > Ag^{+} > Ba^{2+}$. The existence of nitrogen and especially

Table 1 Formation constants for TDN-metal ion complexes in methanol at 25 °C

Cation	Log K_f
Mg^{2+}	2.87 ± 0.04
Ca^{2+}	3.05 ± 0.05
Sr^{2+}	2.75 ± 0.04
Ba^{2+}	2.26 ± 0.07
Cu^{2+}	3.92 ± 0.07
Ag^{+}	2.34 ± 0.04
Zn^{2+}	3.19 ± 0.09
Cd^{2+}	2.81 ± 0.04
Hg^{2+}	6.49 ± 0.05
Pb^{2+}	4.64 ± 0.05

sulfur as soft donating atoms in **TDN** crown cavity results in a considerable increase in the stability of soft heavy metal cations such as Hg^{2+} ion in solution while diminishing the stability constants of their alkali and alkaline earth complexes. Complexing agents with soft coordination sites are known to generate a great affinity toward d^{10} transition metal ions such as Hg^{2+} [19]. It should be noted that Shamsipur et al. have already reported new benzo-substituted 18- and 15-membered aza-macrocyclic diamides which exhibited significantly high selectivity to Co^{2+} [20a] and Cu^{2+} [20b] ions, respectively, over alkali, alkaline earth and several transition metal ions.

On the basis of the selectivity orders obtained from the solution studies, the **TDN** can be used as a very suitable ionophore for the preparation of PVC-base ion-selective electrode for mercury(II). The work is undergoing in our laboratories in this respect and will be published subsequently.

To obtain more information about the conformational changes of **TDN** upon complexation with mercury ion, the molecular structures of the free ligand and its 1:1 complex with Hg^{2+} were built with the Hyperchem program version 7.0 [21], performed on a Pentium(IV) personal computer. The structure of free ligand was optimized using the 6-31G* basic set at the restricted Hartree-Fock (RHF) level of theory. The optimized structure of the ligand was then used to find out the initial structure of its mercury(II) complex. Finally, the structure of the resulting 1:1 complex was optimized using the Lan12mb basis set at the RHF level of theory. No molecular symmetry constraint was applied; rather, full optimization of all bond lengths, bond angles, and torsion angles was carried out using the Gaussian 98 program [22]. The optimized structures are shown in Fig. 2.

As is obvious from Fig. 2, in the case of free ligand, the molecule adopted a more or less planar rigid geometry so that all six donating atoms of the macrocyclic ring, including a sulfur atom two ethereal oxygens, two amide nitrogen atoms and an amine –NH-group are located within the same plane, while the two amide C=O groups are pointing out of the macrocyclic ring plane. However, upon complexation with Hg^{2+} ion, the planar geometry of the ligand cavity is quite distorted so that all six donatig atoms of the macrocyclic ring are bonded to the central metal ion to form a nice octahedral structure around the mecury(II) ion. Meanwhile the vibrational frequencies for the free ligand and its mercury complex were also calculated to check if the optimized geometry of the molecular system corresponds to a true energy minimum. All the calculated frequencies were found to be positive and also revealed good correlation with the experimentally recorded IR

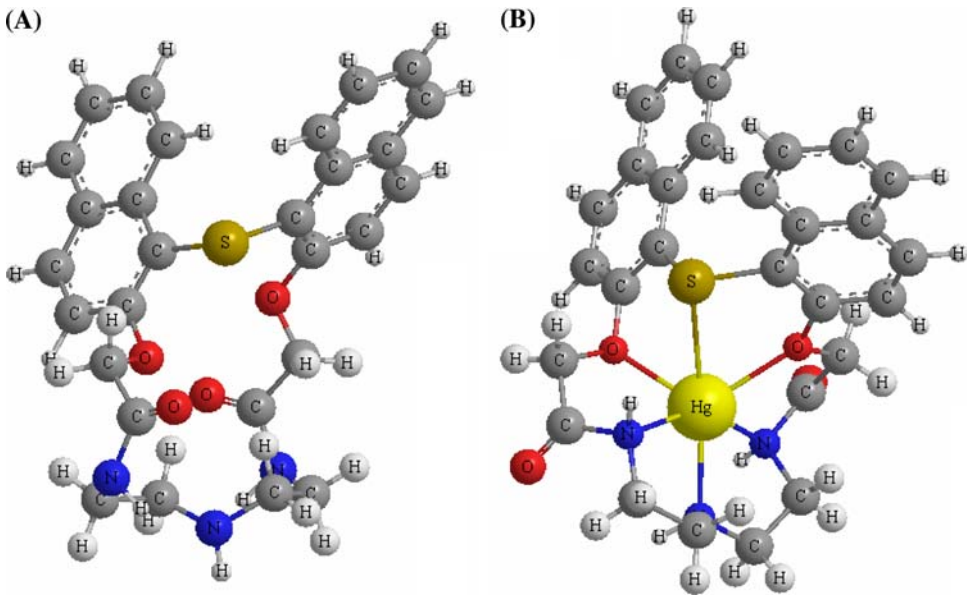


Fig. 2 Optimized structures of ligand **TDN** (**a**) and Hg^{2+}-**TDN** complex (**b**) obtained from HF/LANL2MB calculations

spectra for the free and mercury(II)-complexed ligand, nicely in support of the calculated geometric structures shown in Fig. 2 [23].

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