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Synthesis of a Novel Class of Macrocyclic Compounds Containing 1,3,4-Thiadiazole Rings as Subunits

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The synthesis and characterization of 12 new macrocycles containing two, four, or six 1,3,4-thiadiazole rings as subunits are described. The general methodology used is based on the nontemplated reaction of bis(4-methyl-5-(methylthio)-1,3,4-thiadiazolium) diperchlorates with α,ω-diamino compounds. Complexation properties of macrocycles **4a**–**4c** and **4e** toward Ag^+ are also reported.

Introduction

The wide interest in the construction of synthetic macrocyclic compounds containing five and six membered heterocyclic rings as subunits has led to the preparation of a range of such compounds which have been shown to possess very interesting properties in a variety of fields.[1] Pyridine and bipyridine have commonly been incorporated into macrocyclic frameworks, affording ligands which have been shown to form complexes with metal-transition ions and to be effective hosts for different kind of molecules.[2] There has also been much interest in designing certain polyazole-based macrocycles, with those containing pyrazole,[3] triazole,[4] and tetrazole[5] rings as well as 1,3,4-oxadiazole[6] being relevant. However, while much current attention has focused on those macrocycles, very little is known concerning the synthesis and chemical properties of macrocycles containing 1,3,4-thiadiazole rings.[7]

Thus, in view of the biological and analytical interest in 1,3,4-thiadiazole derivatives, we recently reported the synthesis of bipodands and macrocycles bearing two subunits of 2-imino-1,3,4-thiadiazoline[8] as well as tripodands bearing three subunits of that heterocyclic ring.[9]

In connection with our previous work in this field, the results described here provide an efficient and simple method for the one-pot preparation of a novel class of macrocycles bearing 1,3,4-thiadiazole rings as subunits, which permits, using the same general methodology, the tuning of the size and shape of the central hole as well as the grade of rigidity and solubility by controling the nature of the spacers linked to the 2- and 5-positions of the 1,3,4-thiadiazole units.

Results and Discussion

The macrocyclization step in this methodology involves the nontemplated reaction of bis(4-methyl-5-(methylthio)-1,3,4-thiadiazolium) diperchlorates **1** with the appropriate α,ω-diamino compound **2**, which was carried out in the presence of triethylamine, with dry DMF as the solvent most commonly used (Scheme 1).

The nature of the 2,2′-spacer could be aliphatic, aromatic, or heteroaromatic depending on the acid chloride used in the preparation of the open-chain precursors of the corresponding bis(1,3,4-thiadiazolium) salts **1**, while the structure of the 5,5′-spacer can be chosen by selecting the α,ω-diamino compound used as a reagent. The stoichiometry of the macrocycle thus obtained seems to be dependent on the structural properties, mainly length and rigidity, of both the 2,2′- and 5,5′-spacers. Moreover, on the basis of the previously reported X-ray crystal structure of 2,2′-bis[4,5-dihydro-5-((2-hydroxyethyl)imino)-4-methyl-1,3,4-thiadiazole],[8] we assume a *Z* geometry for the exocyclic C=N bond.

(A) Reactions of Bis(4-methyl-5-(methylthio)-1,3,4-thiadiazolium) Diperchlorates with Aliphatic and Xylylene Diamines. The macrocyclization of bis(1,3,4-thiadiazolium) diperchlorate (**1a**) and an equimolecular amount of 1,4-diaminobutane (**2b**), in the presence of triethylamine, was carried out by heating the corresponding dry DMF solution at 80 °C for 12 h. The (3 + 3) macrocycle **5a** was isolated in 45% yield and crystallized as orange prisms from DMSO.

Similarly, treatment of 2,2′-(2,6-pyridinediyl)bis(4-methyl-5-(methylthio)-1,3,4-thiadiazolium) diperchlorate (**1d**) and 1,3-diaminopropane (**2a**) under the same reaction conditions described above, but using dry chloroform as

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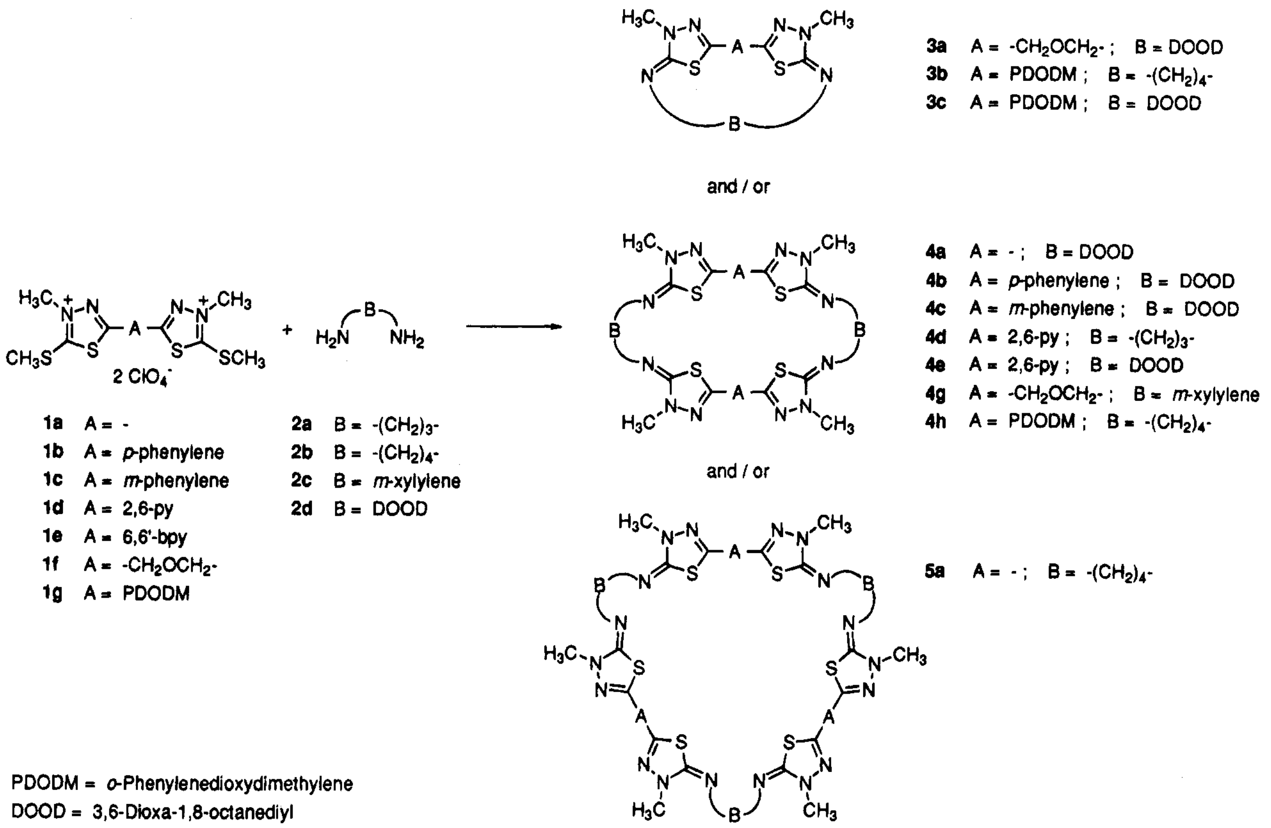
Scheme 1



1a A = -
1b A = *p*-phenylene
1c A = *m*-phenylene
1d A = 2,6-py
1e A = 6,6'-bpy
1f A = $-CH_2OCH_2-$
1g A = PDODM

2a B = $-(CH_2)_3-$
2b B = $-(CH_2)_4-$
2c B = *m*-xylylene
2d B = DOOD

3a A = $-CH_2OCH_2-$; B = DOOD
3b A = PDODM ; B = $-(CH_2)_4-$
3c A = PDODM ; B = DOOD

4a A = - ; B = DOOD
4b A = *p*-phenylene ; B = DOOD
4c A = *m*-phenylene ; B = DOOD
4d A = 2,6-py ; B = $-(CH_2)_3-$
4e A = 2,6-py ; B = DOOD
4g A = $-CH_2OCH_2-$; B = *m*-xylylene
4h A = PDODM ; B = $-(CH_2)_4-$

5a A = - ; B = $-(CH_2)_4-$

PDODM = *o*-Phenylenedioxydimethylene
DOOD = 3,6-Dioxa-1,8-octanediyl

a solvent, gave rise to the 28-membered macrocycle **4d**, isolated in 14% yield, thorugh a process which involves a (2 + 2) stoichiometry. Upon reaction of rigid bis(1,3,4-thiadiazolium) salts **1a–d** with 1,6-diaminohexane or 1,8-diaminooctane, only very insoluble materials, whose purification and characterization were not possible to be achieved, were obtained.

On the other hand, the reaction of 2,2'-((1,2-phenylenedioxy)dimethylene)bis(4-methyl-5-(methylthio)-1,3,4-thiadiazolium) diperchlorate (**1g**), which in turn was prepared from methyl 2-methyldithiocarbazate according to a previously described procedure,[8] with 1,4-diaminobutane (**2b**) in DMF, gave rise to the formation of a mixture of two products. Chromatography using silica gel and $MeOH/CH_2Cl_2$ (3:2) as eluent proved to be the most convenient method for the purification of the reaction mixture, allowing the isolation of both products in 60% ($R_f = 0.92$, mp 206–208 °C) and 8% yield ($R_f = 0.61$, mp 230 °C), which were identified as the 18- (**3b**) and 36-membered (**4h**) rings (1 + 1 and 2 + 2 products), respectively. It is worth noting the high solubility of these compounds in the common organic solvents in comparison with the macrocycles described in the above sections, which seems to be related to the presence of the two oxygen atoms in the 2,2'-spacer.

The incorporation of an aromatic ring into the tether connecting the two amino groups has also been studied. Thus, several bis(4-methyl-5-(methylthio)-1,3,4-thiadiazolium) diperchlorates **1** bearing rigid spacers linked to the 1,3,4-thiadiazole ring were reacted with *p*-phenylenediamine and *o*-, *m*-, and *p*-xylylenediamine under the same reaction conditions described above. However, the process yielded in all cases very insoluble polymeric precipitates from the hot reaction medium whose purification and identification was completely unsuccessful, even in the case of 2,2'-((*o*-phenylenedioxy)dimethylene)bis(4-methyl-5-(methylthio)-1,3,4-thiadiazolium) diperchlorate (**1g**) as starting material. Only when the reaction was carried out with 2,2'-(oxydimethylene)bis(4-methyl-5-(methylthio)-1,3,4-thiadiazolium) diperchlorate (**1f**) as substrate and *m*-xylylenediamine (**2c**) in dry DMF could a new oily specie be isolated from the reaction mixture which was purified by column chromatography using silica gel and EtOH/AcOEt (1:1) as eluent and identified as the 32-membered (2 + 2) macrocycle **4g**.

(B) Reactions of Bis(4-methyl-5-(methylthio)-1,3,4-thiadiazolium) Diperchlorates with 3,6-Dioxa-1,8-diaminooctane. When bis(1,3,4-thiadiazolium) diperchlorates **1a–e** were treated with an equimolecular amount of 3,6-dioxa-1,8-diaminooctane (**2d**) and triethylamine, under similar reaction conditions to that described above, (2 + 2) macrocycles **4a**, **4b**, **4c**, **4e**, and **4f** were the only products isolated in 11%, 24%, 27%, 16%, and 17% yields, respectively.

In the case of the very insoluble macrocycle **4f**, purification was difficult, but microanalytically pure samples could be obtained by crystallization using a high volumen of 1,4-dioxane. However, due to its high insolubility in the common organic deuterated solvents, we were not able to run the corresponding NMR spectra. Nevertheless, its molecular weight was ascertained by FAB mass spectra and, then, its structure assigned.

When the reaction was carried out using the same commercially available α,ω-diamino compound, but substrates bearing more flexible spacers between the two thiadiazole units such as 2,2'-(oxydimethylene)bis(4-methyl-5-(methylthio)-1,3,4-thiadiazolium) diperchlorate (**1f**) and 2,2'-((*o*-phenylenedioxy)dimethylene)bis(4-methyl-5-(methylthio)-1,3,4-thiadiazolium) diperchlorate (**1g**), the only isolated products were characterized as the (1 + 1) 19- and 22-membered macrocycles **3a** and **3c**, in 6% and 20% yields, respectively.

Table 1. Spectral Data of 4-Methyl-1,3,4-thiadiazolinophanes 3–5

	^1H NMR, δ (ppm)[a]			^{13}C NMR, δ (ppm)[a]					FAB-MS
entry	NCH_3	A	B	C5	C2	NCH_3	A	B	m/z (rel int)[b]
3a	3.36	4.56 (s, CH_2OCH_2)	3.55 (t, $NCH_2\mathit{CH}_2O$), 3.52 (s, OCH_2CH_2O), 3.17 (t, NCH_2)	157.00	143.99	34.85	69.84 (CH_2OCH_2)	69.84 (NCH_2CH_2O), 68.03 (OCH_2CH_2O), 57.89 (NCH_2)	387 (100)
3b	3.54	6.99 (s, ArH), 5.02 (s, CH_2OAr)	3.24 (t, NCH_2), 1.77 (t)	157.20	142.51	35.46	147.54 (s), 122.47 (d), 114.68 (d), 66.35 (CH_2OAr)	58.85 (NCH_2), 27.28	419 (61)
3c	3.52	6.99 (s, ArH), 5.02 (s, CH_2OAr)	3.73 (t, $NCH_2\mathit{CH}_2O$), 3.65 (s, OCH_2CH_2O), 3.33 (t, NCH_2)	158.30	142.90	35.35	147.53 (s), 122.52 (d), 114.61 (d), 66.56 (CH_2OAr)	71.05 (NCH_2CH_2O), 70.81 (OCH_2CH_2O), 58.06 (NCH_2)	479 (100)
4a	3.57		3.75 (t, $NCH_2\mathit{CH}_2O$), 3.68 (s, OCH_2CH_2O), 3.29 (t, NCH_2)	156.26	136.88	35.71		71.18 ($NCH_2\mathit{CH}_2O$), 70.50 (OCH_2CH_2O), 57.26 (NCH_2)	685 (11)
4b	3.62	7.59 (s, ArH)	3.76 (t, $NCH_2\mathit{CH}_2O$), 3.72 (s, OCH_2CH_2O), 3.34 (t, NCH_2)	157.51	143.32	35.66	131.64 (s), 125.65 (d)	71.30 ($NCH_2\mathit{CH}_2O$), 70.54 (OCH_2CH_2O), 57.53 (NCH_2)	837 (10)
4c	3.61	7.84 (br s), 7.55 (dd), 7.39 (t)	3.77 (t, $NCH_2\mathit{CH}_2O$), 3.72 (s, OCH_2CH_2O), 3.34 (t, NCH_2)	157.42	143.33	35.65	131.66 (s), 129.23 (d), 126.38 (d), 122.22 (d)	71.40 ($NCH_2\mathit{CH}_2O$), 70.63 (OCH_2CH_2O), 57.71 (NCH_2)	837 (14)
4d	4.10	8.29 (br s)	3.86 (t, NCH_2), 2.49 (quint.)	168.96	145.83	37.91	153.98 (s), 139.58 (d), 122.44 (d)	47.76 (NCH_2), 25.09	691 (100)
4e	3.62	7.77–7.67 (m, ArH)	3.79 (t, $NCH_2\mathit{CH}_2O$), 3.75 (s, OCH_2CH_2O), 3.37 (t, NCH_2)	158.48	145.36	35.69	148.52 (s), 136.75 (d), 118.36 (d)	71.34 ($NCH_2\mathit{CH}_2O$), 70.56 (OCH_2CH_2O), 57.26 (NCH_2)	839 (27)
4g	3.57	4.48 (s, CH_2OCH_2)	7.35–7.25 (m, ArH), 4.30 (s, NCH_2)	157.65	142.77	35.38	67.27 (CH_2OCH_2)	139.76 (s), 128.31 (d), 126.60 (d), 125.94 (d), 60.95 (NCH_2)	749 (20)
4h	3.50	6.70 (s, ArH), 5.01 (s, CH_2OAr)	3.10 (t, NCH_2), 1.68 (t)	156.95	142.84	35.48	147.93 (s), 122.82 (d), 115.37 (d), 67.04 (CH_2OAr)	58.14 (NCH_2), 29.03	837 (48)
5a	4.08		3.69 (t, NCH_2), 2.04 (t)	169.59	143.59	38.88		52.09 (NCH_2), 25.18	848 (10)

[a] NMR spectra were run in $CDCl_3$ solutions, except for compound **3a** which was run in DMSO-d_6, compound **4d** in DMSO-d_6/TFA, and compound **5a** in $CDCl_3$/TFA. [b] FAB mass spectra were recorded using *m*-nitrobenzyl alcohol as matrix, except for compounds **4a**, **4e**, and **4g** which were recorded in 2-hydroxyethyl disulfide and **3c** in *m*-nitrobenzyl alcohol/polyethylene glycol.

The structural characterization of compounds **3**, **4**, and **5** has been achieved by their analytical data and their ^1H- and ^{13}C-NMR spectra, with their FAB mass spectra of special significance. ^1H-NMR data show no evidence of temperature-dependent line broadening indicative of conformational flexibility occurring on the NMR timescale. Also, the simple well-defined ^1H- and ^{13}C-NMR spectra reveal that the monomers constituting these molecules are equivalent. Of special relevance are the signals corresponding to the NCH_3 group which appear in the range 3.36–3.62 ppm and 34.85–35.71 ppm in the ^1H- and ^{13}C NMR spectra, respectively, while the thiadiazole carbon atoms C2 and C5 resonate at 136.88–145.36 and 156.26–158.48 ppm, respectively, all of them lying within the normal characteristic ranges for neutral imino-1,3,4-thiadiazoline systems.[9] The only exceptions were compounds **4d** and **5a**, whose NMR spectra were recorded in TFA-containing deuterated solutions, and they displayed the expected signals in good agreement with the corresponding fully protonated amino-1,3,4-thiadiazolium derivatives[9] (Table 1).

Although none of these compounds gave the molecular ion peak in the electron-impact mass spectrum, FAB mass spectra have so far proved to be successful in confirming unambigously all the proposed structures (Table 1). We attempted to obtain X-ray quality crystals of these compounds from a variety of solvents, but in all cases we obtained either powders or small quantities of crystals unsuitable for that propose.

(C) Complexation Studies. We also wish to report herein the results obtained in the preliminary complexation studies of some of these macrocyclic ligands with metal ions. Thus, macrocycles **4a–c** were dissolved at room temperature in dry dichloromethane and then treated either with $AgClO_4$ or $AgCF_3SO_3$. After 1 h of stirring at room temperature, a yellow solid separated from the solution, showing in the IR spectrum the characteristic absorption bands of the noncoordinated counteranions at $\nu = 1081-1098$ cm^{-1} for ClO_4^-, and ca. 1280, 1251, and 1030 cm^{-1} for $CF_3SO_3^-$, and whose analytical data perfectly agree with a stoichiometric ratio 1:2 (ligand:metal). A different behavior is seen with macrocycle **4e**, which, under the same reaction conditions, gave rise to a complex with a 1:4 (ligand:metal) stoichiometry.

Unfortunately, it was impossible to determine whether or not NMR spectra of all the complexes differ from those of the corresponding free ligands because their very low solubility in the common deuterated organic solvents made impossible to obtain such data. Nevertheless, computer-based molecular modeling suggests that in the 1:2 complexes every metal ion should be attached in a linear fashion to the two sulfur atoms present in two of the 1,3,4-thiadiazoles belonging to different bis-thiadiazole moieties. The structural proposals for all complexes however can be considered highly speculative. The complexation study of the macrocycles described herein with other metal centers is in progress and will be reported elsewhere in a near future.

Conclusions

The present investigation has explored a new methodology which permits the synthesis of macrocycles containing two, four, or six 1,3,4-thiadiazole units and which is based on the reaction of bis(4-methyl-5-(methylthio)-1,3,4-thiadizolium) diperchlorates with several α,ω-diamino compounds. This route has no precedent and has the characteristic of tuning the size and shape of the central hole by connecting the 1,3,4-thiadiazole moieties by spacers which could have aliphatic, aromatic, or heteroaromatic nature. Elemental analysis and FAB mass spectra indicate the stoichiometry involved in every macrocyclization process studied.

Complexation reactions between some of these macrocycles and silver salts have also been carried out. Although we have no evidence, at the present time, for the real structure of the resulting complexes, their stoichiometry is obvious on the basis of their microanalytical data.

Experimental Section

Melting points were obtained in a Kofler hot-stage apparatus and are uncorrected. IR spectra were run using NaCl plates on a Nicolet FT-5DX spectrophotometer in Nujol emulsions. NMR spectra were recorded in $CDCl_3$ solutions unless otherwise stated, using a Varian Unity 300 apparatus (^{1}H at 299.95 MHz and ^{13}C at 75.43 MHz) and tetramethylsilane as internal reference. The signals were assigned by DEPT-135 and ^{13}C gate decoupled spectra, as well as by COSY-45 and ^{1}H–^{13}C 2D heteronuclear correlation experiments. The EI mass spectra were obtained with a Hewlett-Packard 5993 C spectrometer at 70 eV. The FAB mass spectra were recorded with a JEOL DX 300 (beam of Xe at 3 KeV), a Kratos MS-50 (beam of Xe at 8 Kv), or a VG-Autospec. L-SIMS spectrometer and using *m*-nitrobenzyl alcohol, 2-hydroxyethyl disulfide, or polyethylene glycol/*m*-nitrobenzyl alcohol as matrix. Elemental analyses were performed with an Eager 200 instrument.

2,2′-Bis(4-methyl-5-(methylthio)-1,3,4-thiadiazolium) Diperchlorates 1. The unreported compounds **1e** and **1g** were prepared according to the previously reported procedure.[9]

3,3′-(6,6′-Bipyridinediyldicarbonyl)bis(methyl 2-methyldithiocarbazate): 84% yield; white prisms (from 1,4-dioxane), mp >350 °C; IR 3313, 1699, 1586, 1365, 1263, 1246 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 2.46 (6H, s), 3.73 (6H, s), 8.20 (2H, t, $J = 7.5$ Hz), 8.29 (2H, d, $J = 7.5$ Hz), 9.25 (2H, d, $J = 7.5$ Hz), 11.94 (2H, s); ^{13}C NMR (DMSO-d_6) δ 18.95, 43.43, 123.30, 125.11, 139.05, 147.57 (s), 153.48 (s), 161.80 (s), 201.72 (s); EI-MS m/z (rel intensity) 480 (M^+, 1), 433 (13), 91 (100). Anal. Calcd for $C_{18}H_{20}N_6O_2S_4$: C, 45.00; H, 4.20; N, 17.49. Found: C, 45.21; H, 4.23; N, 17.63.

2,2′-(6,6′-Bipyridinediyl)bis(4-methyl-5-(methylthio)-1,3,4-thiadiazolium) Diperchlorate (1e): 85% yield; white prisms (from acetonitrile), mp 310–312 °C; IR 1580, 1563, 1088 cm^{-1}; ^{1}H NMR ($CDCl_3$/TFA) δ 3.26 (6H, s), 4.41 (6H, s), 8.62 (2H, t, $J = 7.5$ Hz), 8.69 (2H, d, $J = 7.5$ Hz), 8.86 (2H, d, $J = 7.5$ Hz); ^{13}C NMR ($CDCl_3$/TFA) δ 21.62, 43.37, 127.65, 129.70, 137.63, 144.29 (s), 145.98 (s), 149.88 (s), 183.16 (s); EI-MS m/z (rel intensity) 224 ($^1/_2 M^+ - ClO_4^-$, 10), 146 (100). Anal. Calcd for $C_{18}H_{18}Cl_2N_6O_8S_4$: C, 33.50; H, 2.81; N, 13.02. Found: C, 33.25; H, 2.63; N, 12.88.

3,3′-(((*o*-Phenylenedioxy)dimethylene)dicarbonyl)bis(methyl 2-methyldithiocarbazate): 95% yield; white prisms (from ethanol), mp 175–177 °C; IR 3200, 1704, 1506, 1359, 1257, 1234 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 2.42 (6H, s), 3.56 (6H, s), 4.76 (4H, s), 6.97–7.09 (4H, m), 11.21 (2H, s); ^{13}C NMR (DMSO-d_6) δ 19.20, 43.58, 67.72, 115.88, 122.65, 147.79 (s), 166.87 s), 201.64 (s); EI-MS m/z (rel intensity) 415 ($M^+ - SCH_3$, 7), 365 (27), 129 (100). Anal. Calcd for $C_{16}H_{22}N_4O_4S_4$: C, 41.56; H, 4.80; N, 12.12. Found: C, 41.42; H, 4.63; N, 11.98.

2,2′-((*o*-Phenylenedioxy)dimethylene)bis(4-methyl-5-(methylthio)-1,3,4-thiadiazolium) diperchlorate (1g): 74% yield; white needles (from methanol), mp 201–202 °C; IR 1512, 1093 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 3.10 (6H, s), 4.14 (6H, s), 5.66 (4H, s), 7.09 (2H, dd, $^3J = 6.0$ Hz, $^4J = 4.0$ Hz), 7.24 (2H, dd, $^3J = 6.0$ Hz, $^4J = 4.0$ Hz); ^{13}C NMR (DMSO-d_6) δ 20.81, 41.97, 65.08, 115.96, 123.34, 146.88 (s), 165.52 (s), 180.52 (s); EI-MS m/z (rel intensity) 398 ($M^+ - 2ClO_4^- - 2CH_3$, 1), 146 (100). Anal. Calcd for $C_{16}H_{20}Cl_2N_4O_{10}S_4$: C, 30.64; H, 3.21; N, 8.93. Found: C, 30.42; H, 2.98; N, 8.80.

Preparation of Macrocycles 3–5. General Procedure. To a solution of the corresponding 2,2′-bis(4-methyl-5-(methylthio)-1,3,4-thiadiazolium) diperchlorate (**1**) (2 mmol) in anhydrous DMF (40 mL) at 80 °C was added a mixture of dry triethylamine (4 mmol) and the adequate α,ω-diamino derivative **2** (2 mmol) dropwise for 30 min. The reaction mixture was stirred at this temperature for an additional 7 h and then poured into ice–water (250 mL). More insoluble compounds such as **4a**, **4b**, **4e**, **4f**, and **5a** precipited from the DMF–H_2O mixture and were collected by filtration, washed with water, and air-dried. Compounds **3b**, **3c**, **4g**, and **4h** were extracted with dichloromethane (3 × 150 mL), and the combined organic layers were washed with water (150 mL), dried over $MgSO_4$, filtered, and evaporated *in vacuo*.

In the case of compounds **3a**, **4c**, and **4d**, the reaction was carried out in refluxing methanol, acetonitrile, or chloroform, respectively. The first one was isolated by evaporation of the solvent followed by extraction in dichloromethane–water as mentioned, while the other two compounds were collected by filtration from the cooled solutions.

The purification method is stated below for every macrocycle prepared.

[5,5′-(3,6-Dioxa-1,8-octanediyldiamino)bis(4-methyl-1,3,4-thiadiazolo-5-ylidene-2-yl)(oxydimethylene)]phane (3a): 6% yield; white needles (chromatographed using methanol–butanol 1:1, $R_f = 0.56$, and crystallized from ethanol), mp 199–201 °C; IR 1641 cm^{-1}. Anal. Calcd for $C_{14}H_{22}N_6O_3S_2$: C, 43.52; H, 5.74; N, 21.75. Found: C, 43.21; H, 5.53; N, 21.49.

[5,5′-(1,4-Butanediyldiamino)bis(4-methyl-1,3,4-thiadiazolo-5-ylidene-2-yl)((*o*-phenylenedioxy)dimethylene)]phane (3b): 60% yield; white prisms (chromatographed using methanol–CH_2Cl_2 3:2, $R_f = 0.61$, and crystallized from ethanol), mp 206–208 °C; IR 1642 cm^{-1}. Anal. Calcd for $C_{18}H_{22}N_6O_2S_2$: C, 51.67; H, 5.30; N, 20.08. Found: C, 51.83; H, 5.46; N, 20.21.

[5,5′-(3,6-Dioxa-1,8-octanediyldiamino)bis(4-methyl-1,3,4-thiadiazolo-5-ylidene-2-yl)((*o*-phenylenedioxy)dimethylene)]phane (3c): 20% yield; yellow prisms (crystallized from ethanol), mp 143–145 °C; IR 1642 cm^{-1}. Anal. Calcd for $C_{20}H_{26}N_6O_4S_2$: C, 50.21; H, 5.48; N, 17.56. Found: C, 50.33; H, 5.76; N, 17.81.

Bis[5,5′-(3,6-dioxa-1,8-octanediyldiamino)bis(4-methyl-1,3,4-thiadiazolo-5-ylidene-2-yl)]phane (4a): 11% yield; yellow prisms (crystallized from ethanol), mp 147–149 °C; IR 1636 cm^{-1}. Anal. Calcd for $C_{24}H_{36}N_{12}O_4S_4$: C, 42.10; H, 5.30; N, 24.55. Found: C, 42.18; H, 5.44; N, 24.76.

Bis[5,5′-(3,6-dioxa-1,8-octanediyldiamino)bis(4-methyl-1,3,4-thiadiazolo-5-ylidene-2-yl)(*p*-phenylene)]phane (4b): 24% yield; yellow prisms (crystallized from ethanol), mp 153–155 °C; IR 1642 cm^{-1}. Anal. Calcd for $C_{36}H_{44}N_{12}O_4S_4$: C, 51.67; H, 5.30; N, 20.08. Found: C, 51.43; H, 5.16; N, 19.91.

Bis[5,5′-(3,6-dioxa-1,8-octanediyldiamino)bis(4-methyl-1,3,4-thiadiazolo-5-ylidene-2-yl)(*m*-phenylene)]phane (4c): 27% yield; white needles (crystallized from butanol), mp 155–158 °C; IR 1628 cm^{-1}. Anal. Calcd for $C_{36}H_{44}N_{12}O_4S_4$: C, 51.67; H, 5.30; N, 20.08. Found: C, 51.48; H, 5.17; N, 19.87.

Bis[5,5′-(1,3-propanediyldiamino)bis(4-methyl-1,3,4-thiadiazolo-5-ylidene-2-yl)(2,6-pyridinediyl)]phane (4d): 14% yield; orange prisms (crystallized from DMSO), mp 235–237 °C; IR 1646 cm^{-1}. Anal. Calcd for $C_{28}H_{30}N_{14}S_4$: C, 48.69; H, 4.38; N, 28.39. Found: C, 48.83; H, 4.55; N, 28.50.

Bis[5,5′-(3,6-dioxa-1,8-octanediyldiamino)bis(4-methyl-1,3,4-thiadiazolo-5-ylidene-2-yl)(2,6-pyridinediyl)]phane (4e): 16% yield; yellow prisms (crystallized from ethanol), mp 116–118 °C; IR 1619 cm^{-1}. Anal. Calcd for $C_{34}H_{42}N_{14}O_4S_4$: C, 48.68; H, 5.05; N, 23.38. Found: C, 48.53; H, 4.88; N, 23.17.

Bis[5,5′-(3,6-dioxa-1,8-octanediyldiamino)bis(4-methyl-1,3,4-thiadiazolo-5-ylidene-2-yl)(6,6′-bipyridinediyl)]phane (4f): 17% yield; white prisms (crystallized from 1,4-dioxane), mp 244–246 °C; IR 1636 cm^{-1}; FAB-MS (*m*-nitrobenzyl alcohol) m/z (rel intensity) 993 ($M^+ + 1$, 20). Anal. Calcd for $C_{44}H_{48}N_{16}O_4S_4$: C, 53.22; H, 4.87; N, 22.57. Found: C, 53.43; H, 4.98; N, 22.77.

Bis[5,5′-(*m*-xylylenediamino)bis(4-methyl-1,3,4-thiadiazolo-5-ylidene-2-yl)(oxydimethylene)]phane (4g): 27% yield; yellow oil (chromatographed using ethyl acetate–ethanol 1:1, $R_f = 0.66$); IR 1631 cm^{-1}. Anal. Calcd for $C_{32}H_{36}N_{12}O_2S_4$: C, 51.33; H, 4.85; N, 22.45. Found: C, 51.53; H, 4.95; N, 22.61.

Bis[5,5′-(1,4-butanediyldiamino)bis(4-methyl-1,3,4-thiadiazolo-5-ylidene-2-yl)((*o*-phenylenedioxy)dimethylene)]phane (4h): 8% yield; white prisms (chromatographed using methanol–CH_2Cl_2 3:2, $R_f = 0.92$, and crystallized from ethanol), mp 230–232 °C; IR 1632 cm^{-1}. Anal. Calcd for $C_{36}H_{44}N_{12}O_4S_4$: C, 51.67; H, 5.30; N, 20.08. Found: C, 51.83; H, 5.55; N, 20.30.

Tris[5,5′-(1,4-butanediyldiamino)tris(4-methyl-1,3,4-thiadiazolo-5-ylidene-2-yl)]phane (5a): 45% yield; orange prisms (crystallized from DMSO), mp 209–211 °C; IR 1636 cm^{-1}. Anal. Calcd for $C_{30}H_{42}N_{18}S_6$: C, 42.55; H, 5.00; N, 29.77. Found: C, 42.33; H, 4.74; N, 30.00.

Complexation of Macrocycles. General Procedure. To a solution of the corresponding macrocycle 4 (10^{-4} mol) in dichloromethane (10 mL) was added $AgClO_4$ or $AgCF_3SO_3$ (2×10^{-4} mol). Upon stirring for 1 h at rt, the solid formed was collected by filtration and crystallized from the adequate solvent.

[Ag$_2$(4a)](ClO$_4$)$_2$: 44% yield; yellow prisms (from dichloromethane–ether), mp 195 °C; IR 1620, 1098 cm^{-1}. Anal. Calcd for $C_{24}H_{36}Ag_2Cl_2N_{12}O_{12}S_4$: C, 26.22; H, 3.30; N, 15.29. Found: C, 26.56; H, 3.50; N, 15.58.

[Ag$_2$(4b)](ClO$_4$)$_2$: 57% yield; yellow prisms (from dichloromethane–ether), mp 123–124 °C; IR 1619, 1093 cm^{-1}; ^{1}H NMR (CD_2Cl_2) δ 3.82 (8H, t, J = 5.6 Hz), 3.90 (12H), 4.02 (8H, s), 4.13 (8H, t, J = 5.6 Hz), 7.88 (8H, s); ^{13}C NMR (CD_2Cl_2) δ 35.38, 58.56, 69.74, 70.18, 127.37, 129.67 (s), 145.40 (s), 163.19 (s). Anal. Calcd for $C_{36}H_{44}Ag_2Cl_2N_{12}O_{12}S_4$: C, 34.55; H, 3.54; N, 13.43. Found: C, 34.81; H, 3.27; N, 13.31.

[Ag$_2$(4c)](ClO$_4$)$_2$: 55% yield; yellow prisms (from dichloromethane–ether), mp 125–126 °C; IR 1620, 1081 cm^{-1}. Anal. Calcd for $C_{36}H_{44}Ag_2Cl_2N_{12}O_{12}S_4$: C, 34.55; H, 3.54; N, 13.43. Found: C, 34.29; H, 3.28; N, 13.22.

[Ag$_4$(4e)](ClO$_4$)$_2$: 49% yield; yellow prisms (from dichloromethane–ether), mp 200 °C (dec); IR 1620, 1093 cm^{-1}. Anal. Calcd for $C_{34}H_{42}Ag_4Cl_4N_{14}O_{20}S_4$: C, 24.48; H, 2.54; N, 11.76. Found: C, 24.30; H, 2.58; N, 11.53.

[Ag$_2$(4a)](CF$_3$SO$_3$)$_2$: 51% yield; yellow prisms (from dichloromethane–ether), mp 186–188 °C; IR 1620, 1280, 1251, 1030 cm^{-1}. Anal. Calcd for $C_{26}H_{36}Ag_2F_6N_{12}O_{10}S_6$: C, 26.06; H, 3.03; N, 14.03. Found: C, 26.10; H, 3.25; N, 14.31.

[Ag$_2$(4b)](CF$_3$SO$_3$)$_2$: 43% yield; yellow prisms (from dichloromethane–ether), mp 121–122 °C; IR 1620, 1280, 1251, 1030 cm^{-1}. Anal. Calcd for $C_{38}H_{44}Ag_2F_6N_{12}O_{10}S_6$: C, 33.79; H, 3.28; N, 12.44. Found: C, 33.82; H, 3.44; N, 12.41.

[Ag$_2$(4c)](CF$_3$SO$_3$)$_2$: 58% yield; yellow prisms (from dichloromethane–ether), mp 126–127 °C; IR 1620, 1285, 1251, 1030 cm^{-1}. Anal. Calcd for $C_{38}H_{44}Ag_2F_6N_{12}O_{10}S_6$: C, 33.79; H, 3.28; N, 12.44. Found: C, 33.51; H, 3.56; N, 12.70.

[Ag$_4$(4e)](CF$_3$SO$_3$)$_4$: 53% yield; yellow prisms (from dichloromethane–ether), mp 235–237 °C; IR 1620, 1282, 1258, 1030 cm^{-1}. Anal. Calcd for $C_{38}H_{42}Ag_4F_{12}N_{14}O_{16}S_8$: C, 24.46; H, 2.27; N, 10.51. Found: C, 24.45; H, 2.41; N, 10.23.

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