Pergamon

Tetrahedron 56 (2000) 885–895

TETRAHEDRON

Synthesis of New Benzo-substituted Macrocyclic Ligands Containing Pyridine or Triazole as Subcyclic Units

Ahmed H. M. Elwahy* and Ashraf A. Abbas

Department of Chemistry, Faculty of Science, Cairo University, Giza, A. R. Egypt

Received 16 September 1999; revised 17 November 1999; accepted 2 December 1999

Abstract—The macrocyclic diamides **11**–**21**, **42** and **43** were prepared by nucleophilic reaction of the bis phenols **22**–**29** with the appropriate dihalo compounds **2**, **3**, **40** and **41**, respectively. The macrocyclic dithiodiamides **30**–**33** were obtained in good yields upon treatment of **11**, **13**, **15** and **17** with Lawesson's reagent. The macrocycles **61**–**63** were prepared by condensation of the bis(aldehyde) **37** with the appropriate bis(aminotriazoles) **50**–**54** to give the corresponding Schiff bases **56**–**60** followed by $NaBH_4$ reduction.

Introduction

Heterocyclic groups incorporated in a macrocyclic ring provide rigidity and are able to participate in complexation through their soft donor atoms; for example macrocyclic ethers with pyridine and other nitrogen containing heterocyclic subunits were reported to form strong and selective interactions with various charged and neutral guest molecules.[1–5] If additional benzonuclei are condensed, ligand properties are altered. As a rule the complexation of cations decreases[6] due to the lower donor capacity of benzo compared to aliphatic bonded heteroatoms and as a consequence of conformational hindrance. On the other hand, the complexation of uncharged organic molecules is promoted.[7] In order to improve the binding ability of macrocyclic receptors for alkali metal cations, much attention has been paid to the development of functional groups in the ring.[8–11] For example incorporation of an amide linkage in a polyether macrocycle may modify the binding properties of crown ether compounds to favour the alkali earth cation over alkali metal cations.[12–16] Gokel and coworkers have found that diaza-18-crown-6 derivatives with amide groups in their side arms exhibit extraordinary Ca^{2+} binding strength and remarkable selectivity for Ca^{2+} over Na^+,[17] while a number of synthetic cyclopeptides are K^+ or Ca^{2+} ionophones.[18] Also macrocyclic diamides are precursors in the preparation of diazacrown compounds which are used as molecular receptors and for the synthesis of cryptands and related compounds.[19,20] Moreover some macrocyclic diamides have been recently used as new catalysts in the highly regioselective halogenation cleavage of epoxides with elemental halogens.[21]

In connection with these findings and in continuation of our interest in synthesizing macrocyclic crown compounds and their precursors from salicylic acid derivatives,[22–25] we report here the synthesis of a series of 17–19 and 25-26-membered benzo-fused macrocyclic diamides containing pyridine as a subcyclic unit. We also describe our attempts to synthesize benzo-fused macrocycles upon which are fused pyridine and triazole units and containing N, O and S inside the macrocyclic ring as donor atoms.

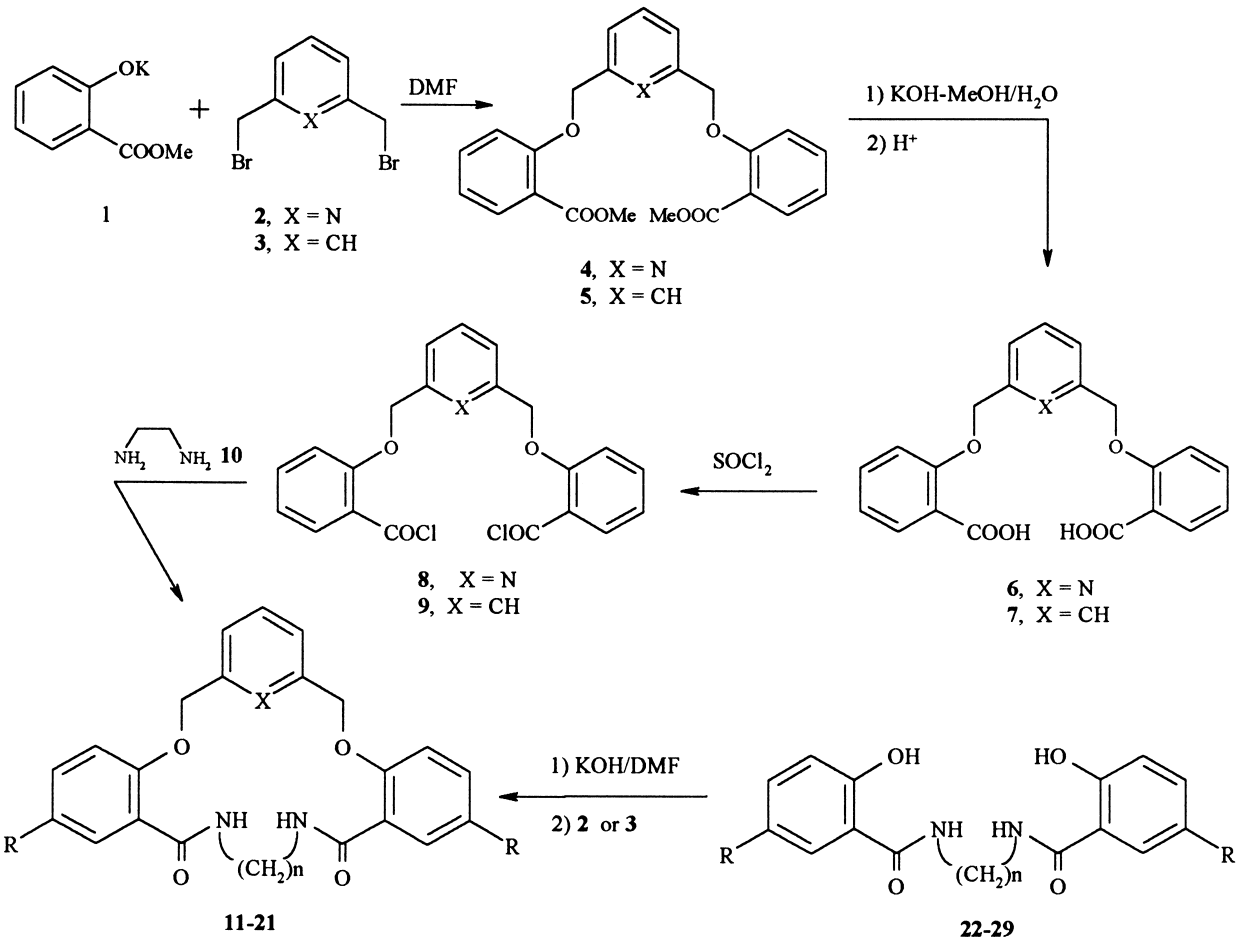
Results and Discussion

Several synthetic methods have been developed for the synthesis of macrocyclic diamides. Among these methods the high dilution technique is often used as the most versatile procedure.[19] This technique requires the simultaneous addition of a bis acid chloride and a diamino ether to a large volume of solvent over an extended period. Recently, Sharghi and coworkers[26] reported the synthesis of similar systems in good yields by reacting a diacid dichloride with a diamine in dichloromethane without the use of high dilution techniques. Using the above technique, Vogtle and others[27–33] have reported the synthesis of macrocyclic diamides containing pyridine as the subcyclic unit. In most cases 2,6-bis(chlorocarbonyl)pyridine was chosen as the starting material. The produced macrocycles in most cases have the amide linkage directly attached to the pyridine ring. We have now studied two synthetic routes towards modified derivatives of these macrocycles as outlined in Scheme 1. In the first route we applied a similar approach to that described by Sharghi et al.[26] for the synthesis of the macrocyclic diamides **11** and **17**. Thus, reaction of the potassium salt **1** (obtained upon treatment of methyl salicylate with methanolic potassium hydroxide solution) with 2,6-bis(bromomethyl)pyridine (**2**) in boiling DMF gave the

Keywords: triazole; pyridine; macrocyclic ligands.

* Corresponding author. E-mail: aelwahy@hrzpub.tu-darmstadt.de

0040–4020/00/$ - see front matter
PII: S0040-4020(99)01068-6

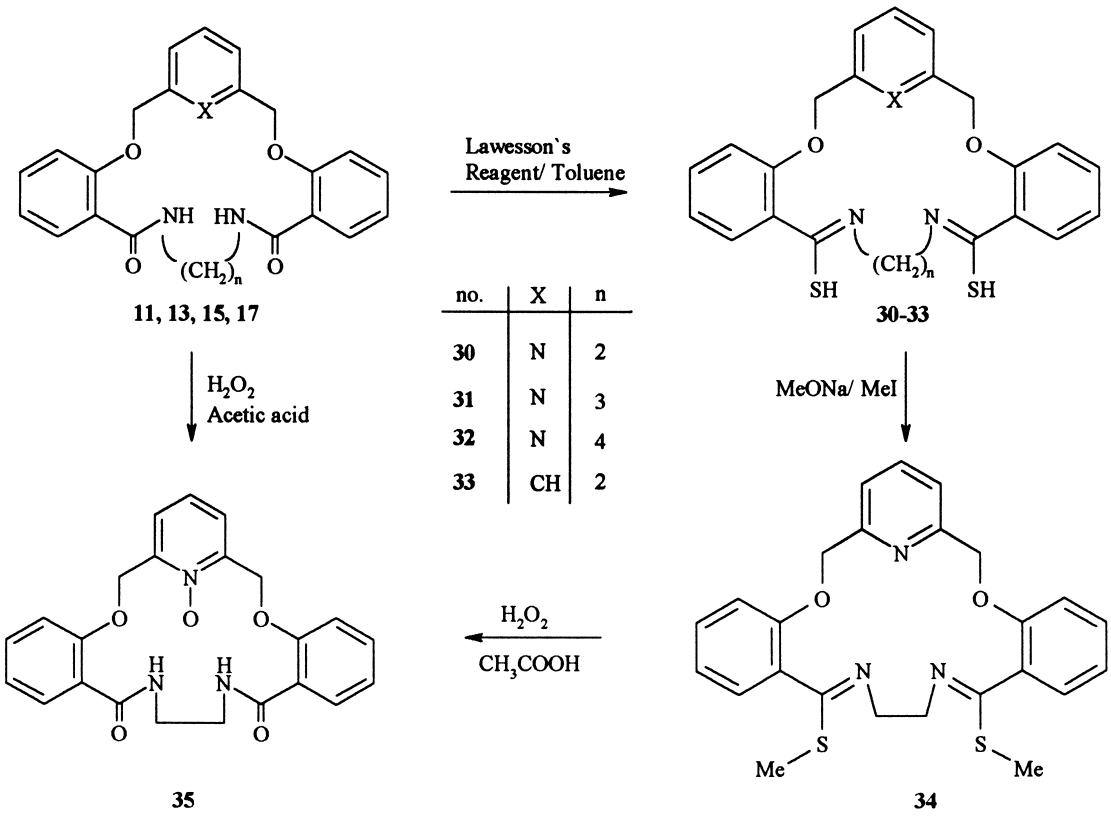


Compd. no	X	n	R
11	N	2	H
12	N	2	(p)$CH_3C_6H_4N_2$
13	N	3	H
14	N	3	(p)$CH_3C_6H_4N_2$
15	N	4	H
16	N	4	(p)$CH_3C_6H_4N_2$
17	CH	2	H
18	CH	2	$C_6H_5N_2$
19	CH	3	H
20	CH	3	(p)$CH_3OC_6H_4N_2$
21	CH	4	H

Compd. no	n	R
22	2	H
23	2	$C_6H_5N_2$
24	2	(p)$CH_3C_6H_4N_2$
25	3	H
26	3	(p)$CH_3C_6H_4N_2$
27	3	(p)$CH_3OC_6H_4N_2$
28	4	H
29	4	(p)$CH_3C_6H_4N_2$

Scheme 1.

corresponding diester **4** in 55% yield. Saponification of **4** followed by acid treatment afforded the dicarboxylic acid **6** in 62% yield. Treatment of **6** with $SOCl_2$ gave the corresponding dicarboxylic acid dichloride **8**. Cyclization was carried out with the fast addition of ethylenediamine (**10**) in CH_2Cl_2 into a solution of **8** in the same solvent. After vigorous stirring for 20 min at room temperature the macrocyclic diamide **11** was obtained in 6% yield. Similarly, the tribenzo analogue **17** was prepared in 8% yield by cyclization of the diacid dichloride **9** with ethylenediamine. Compound **9** was obtained by first reacting **1** with 1,3-di-(bromomethyl)benzene **3** in refluxing DMF to give **5** in 60% yield followed by saponification to give **7** in 70% yield. Reaction of the latter with $SOCl_2$ afforded the corresponding dicarboxylic acid dichloride **9**. Attempts to improve the yields of **11** and **17** by repeating the above reactions under the high dilution technique were unsuccessful. In anticipation of the low yield of the macrocyclic diamides **11**, **17** we



no.	X	n
30	N	2
31	N	3
32	N	4
33	CH	2

Scheme 2.

now apply our recently reported synthetic route for preparation of similar systems.[22] Thus, the bis phenol **22** was converted into its dipotassium salt upon treatment with methanolic KOH solution. Treatment of the salt with each of **2** and **3** in refluxing DMF for 5 min afforded **11** and **17** in 35 and 50% yield, respectively. Similarly, the macrocyclic diamides **12**–**16**, **18**–**21** could be obtained in 35–55% yields by reacting the potassium salt of the appropriate bis phenols **22**,[22] **23**,[34] **24**,[35] (**25**, **28**),[36] **26**, **27**, **29** with each of **2** and **3** in refluxing DMF. It is noteworthy that this reaction proceeds in a short time affording moderate to good yields of the macrocycles. The present findings are comparable to our recently reported synthesis of similar systems where reasonable explanations were given.[22] The new bis azo compounds **26**, **27**, **29** were prepared by coupling the corresponding bis phenols **25** and **28** with two equivalents of the appropriate arenediazonium chloride in aqueous NaOH solution. The arylazo groups in the latter compounds were proved by ^{1}H NMR study to occupy the 5-postion of the aryl group and excluded the possible formation of the other isomeric azo derivatives.[34] The introduction of the bis azo groups in the macrocycles as potential chromophores should be useful for spectrophotometric applications.

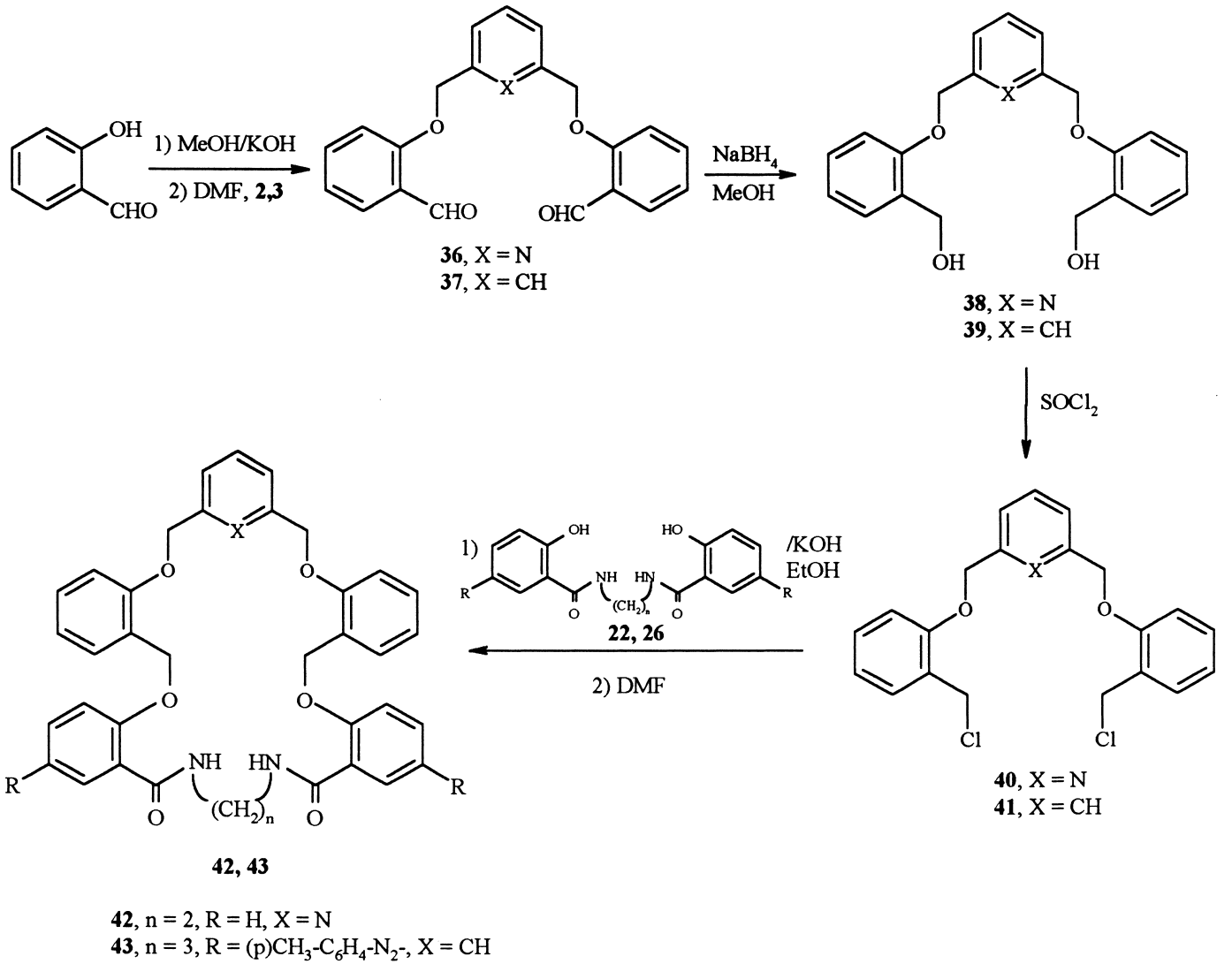
The novel macrocyclic diamides, now available, prompted us to study their possible transformation to other functionalised derivatives (Scheme 2).

The dithiodiamides **30**–**33** were obtained in 50–72% yields upon treatment of **11**, **13**, **15** and **17** with Lawesson's reagent in refluxing toluene. Treatment of **30** with MeI in methanolic sodium methoxide solution afforded the corresponding di(methylthio) derivative **34** in 50% yield. The structure of the latter was chemically established by its ready oxidation with H_2O_2 in refluxing acetic acid to give the corresponding **35** in 60% yield. Compound **35** was alternatively obtained in 65% yield by oxidation of **11** with H_2O_2 in refluxing acetic acid.

In an attempt to extend the spacing between the terminal bis functional group in compounds **2** and **3** and to increase the number of intervening ether functions we also report the synthesis of the novel 25-26-membered macrocyclic diamides **42** and **43** as outlined in Scheme 3.

Thus, salicylaldehyde was converted to its potassium salt upon treatment with methanolic KOH. Reaction of the latter with each of **2** and **3** in boiling DMF afforded the corresponding bis aldehyde derivatives **36**, **37** in 50 and 60% yields, respectively. Reduction of **36** and **37** with $NaBH_4$ gave the corresponding bis(hydroxymethyl) ethers **38**, **39** in 60–80% yields, which on treatment with $SOCl_2$ in $CHCl_3$ gave the corresponding bis(chloromethyl) ethers **40**, **41** in 70 and 75% yields, respectively. Macrocycles **42** and **43** were obtained in 8–10% yields by heating the dipotassium salts of each of **22**, **26** with **40** and **41**, respectively.

Our study was extended to investigate the reactivity of the bis aldehyde **36** towards the bis(aminotriazole) derivatives **50**–**52**,[37] **53**, **54** (prepared by heating the dibromo alkanes **47**–**49** with 4-amino-1,2,4-triazole derivatives **44**–**46** in aqueous ethanol (50%) containing NaOH) in an attempt to obtain the corresponding novel macrocycles **56**–**60** (X=N) (Scheme 4).



36, X = N
37, X = CH

38, X = N
39, X = CH

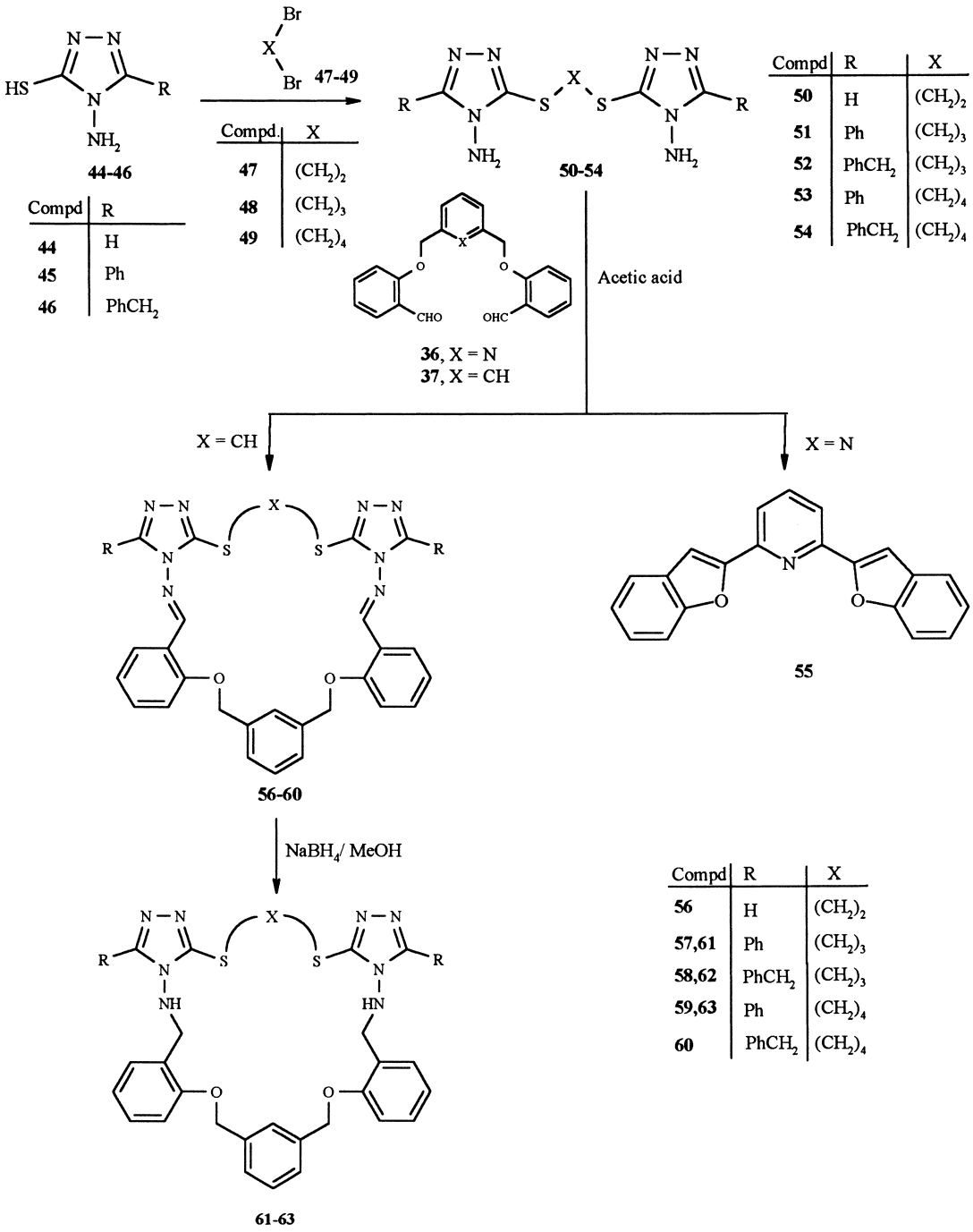
40, X = N
41, X = CH

22, 26

42, 43

42, n = 2, R = H, X = N
43, n = 3, R = (p)CH_3-C_6H_4-N_2-, X = CH

Scheme 3.



Compd	R
44	H
45	Ph
46	$PhCH_2$

Compd	X
47	$(CH_2)_2$
48	$(CH_2)_3$
49	$(CH_2)_4$

Compd	R	X
50	H	$(CH_2)_2$
51	Ph	$(CH_2)_3$
52	$PhCH_2$	$(CH_2)_3$
53	Ph	$(CH_2)_4$
54	$PhCH_2$	$(CH_2)_4$

Compd	R	X
56	H	$(CH_2)_2$
57,61	Ph	$(CH_2)_3$
58,62	$PhCH_2$	$(CH_2)_3$
59,63	Ph	$(CH_2)_4$
60	$PhCH_2$	$(CH_2)_4$

Scheme 4.

However, the reaction of bis(aminotriazoles) **50**–**54** with **36** in refluxing acetic acid under the high dilution conditions did not afford the corresponding pyridinomacrocycles but gave instead the 2,6-bis[benzo(*b*)furan-2-yl]pyridine **55** in 50% yield. The latter could be obtained by heating only **36** in refluxing acetic acid. On the other hand, reaction of **37** with the bis amino derivatives **50**–**54** in refluxing acetic acid under the high dilution conditions afforded the corresponding Schiff bases **56**–**60** in 55–62% yields. Reduction of these with $NaBH_4$ gave the corresponding macrocycles **61**–**63** in 65–75% yields. We attribute the reactivity of the methylene group in compound **36** compared to **37** to the greater electron withdrawing effect of C-2 and C-6 in the pyridine ring especially when protonated.

In conclusion, we prepared a series of new benzo-substituted macrocyclic-diamides containing pyridine as the subcyclic unit and their corresponding dithiodiamide derivatives. Contrary to the other known pyridinomacrocyclic diamides, the amide group in the macrocyclic ring is not directly attached to the pyridine unit. This should modify the cation binding ability of the new macrocycles. Some derivatives showed promising cation binding properties in a preliminary spectrophotometric study, which is still under way. We also prepared a series of new macrocycles

upon which are fused three benzo and two triazole rings and containing N, O and S as donor atoms. Further studies to develop new synthetic routes to introduce the pyridine ring into these macrocycles are in progress.

Experimental

All melting points are uncorrected. IR spectra (KBr) were recorded on a Perkin–Elmer 1430 spectrophotometer. NMR spectra were measured with a Varian GEMINI 200 spectrometer (200 MHz ^{1}H NMR) or Brucker WM-300 instrument and chemical shifts are given in ppm from TMS. Mass spectra were recorded on a Varian 311 A or DCMS-QP 1000 EX (EI, 70 eV) or Field Desorption (FD). Elemental analyses were carried out at the Microanalytical Centre, Cairo University. 1,2-Diaminoethane, 1,3-diaminopropane, 1,4-diaminobutane and 1,4-dibromobutane were used as purchased from Aldrich.

Synthesis of compounds 4, 5, 36 and 37

General procedure. Each of methyl salicylate (**1**) and salicylaldehyde (20 mmol) was dissolved in hot ethanolic KOH (prepared by dissolving 1.12 g (20 mmol) of KOH in 20 ml of absolute ethanol), and the solvent was then removed in vacuo. The remaining material was dissolved in DMF (15 ml) and the appropriate dibromide **2**, **3** (10 mmol) was added. The reaction mixture was refluxed for 5 min during which KCl was separated. The solvent was then removed in vacuo and the remaining materials was washed with water and purified by crystallization to give compounds **4**, **36**, **37** or by chromatography to give compound **5**.

2,6-Bis[2-(methoxycarbonylphenoxy)methyl]pyridine (4). With the use of the general procedure, the potassium salts of **1** and **2** gave crude **4** which crystallized from methanol as colorless crystals (55%), mp 158–60°C; ^{1}H NMR ($CDCl_3$) δ 3.99 (s, 6H, CH_3), 5.63 (s, 4H, OCH_2), 7.04–8.27 (m, 11H, ArHs) ppm. (Calcd for $C_{23}H_{21}NO_6$ (407.42): C, 67.81; H, 5.20; N, 3.44. Found: C, 67.50; H, 5.30; N, 3.70.

1,3-Bis[2-(methoxycarbonylphenoxy)methyl]benzene (5). With the use of the general procedure, the potassium salt of **1** and **3** gave crude **5** as an oil which purified by chromatography over a silica gel column using $CHCl_3$ as an eluent (60%), ^{1}H NMR ($CDCl_3$) δ 3.84 (s, 6H, CH_3), 5.12 (s, 4H, OCH_2), 6.94–7.83 (m, 12H, ArHs) ppm. (Calcd for $C_{24}H_{22}O_6$ (406.43): C, 70.93; H, 5.46. Found: C, 70.70; H, 5.30).

2,6-Bis[2-(formylphenoxy)methyl]pyridine (36). With the use of the general procedure, the potassium salt of salicylaldehyde **35** and **2** gave crude **36** which crystallized from ethanol as colorless crystals, (50%), mp 145–146°C (lit.[38] mp 141–145°C); ^{1}H NMR ($CDCl_3$) δ 5.31 (s, 4H, OCH_2), 7.09–7.88 (m, 11H, ArHs), 10.55 (s, 2H, CHO) ppm.

1,3-Bis[2-(formylphenoxy)methyl]benzene (37). With the use of the general procedure, the potassium salt of salicylaldehyde **35** and **3** gave crude **37** which crystallized from ethanol as colorless crystals, (60%) mp 114–116°C (lit.[39] mp 115–117°C); ^{1}H NMR ($CDCl_3$) δ 5.19 (s, 4H, OCH_2), 6.90–7.33 (m, 12H, ArHs), 10.36 (s, 2H, CHO) ppm.

Synthesis of compounds 6 and 7

General procedure. A solution of each of **4** and **5** (0.1 mol) in 10% aqueous KOH (500 ml) was refluxed for 3 h. The mixture was cooled, washed and acidified with 6 N HCl and the solid obtained was collected and crystallized from ethanol as colorless crystals of **6** and **7**, respectively.

2,6-Bis[2-(carboxyphenoxy)methyl]pyridine (6). (62%), mp 185–187°C; IR (cm^{-1}) 2557–2400 (OH), 1720 (C=O); ^{1}H NMR (DMSO) δ 12.71 (brs, 2H, COOH), 5.31 (s, 4H, OCH_2), 7.01–8.11 (m, 11H, ArHs) ppm. (Calcd for $C_{21}H_{17}NO_6$ (379.37): C, 66.49; H, 4.52; N, 3.69. Found: C, 66.70; H, 4.60; N, 3.30).

1,3-Bis[2-(carboxyphenoxy)methyl]benzene (7). (70%), mp 153–155°C; IR (cm^{-1}) 2555–2360 (OH), 1747 (C=O); ^{1}H NMR ($CDCl_3$) δ 12.81 (brs, 2H, COOH), 5.32 (s, 4H, OCH_2), 7.09–8.19 (m, 12H, ArHs) ppm. (Calcd for $C_{22}H_{18}O_6$ (378.38): C, 69.83; H, 4.79. Found: C, 69.80; H, 5.00).

2,6-Bis(2-chloroformylphenoxymethyl)pyridine (8), 1,3-bis(2-chloroformylphenoxymethyl)benzene (9). A solution of each of **6** and **7** (10 mmol) in $SOCl_2$ (10 ml) was heated under reflux for 2 h. The solvent was then removed in vacuo and the remaining material was used in the next step without further purification.

Preparation of the potassium salts of 22–29

A solution of each of compounds **22**–**29** (10 mmol) and KOH (1.14 g, 20 mmol) in ethanol (10 ml) was stirred at room temperature for 10 min. The solvent was then removed in vacuo and the remaining solid was triturated with dry ether, collected, dried, and used in the next step without further purification.

Synthesis of the cyclic diamides 11–21, 42, 43

General procedure A. A solution of each of the appropriate potassium salt of **23**–**29** (10 mmol) and the appropriate dichloro compound **2**, **3** and **40**, **41** (10 mmol) in DMF (20 ml) was heated under reflux for 15 min during which KCl was precipitated. The solvent was then removed in vacuo and the remaining material was washed with water (50 ml) and crystallized from the proper solvent to give compounds **11**–**21** and **42**, **43**, respectively.

General procedure B: (for compounds 11 and 17). A solution of ethylenediamine (10 mmol) and triethylamine (40 mmol) in CH_2Cl_2 (250 ml) was added quickly (5 s) to a vigorously stirring solution of diacid chloride **8**, **9** (10 mmol) in CH_2Cl_2 (250 ml) at 0°C. The reaction mixture was stirred at room temperature for 10–30 min. The precipitate was filtered off and the filtrate washed with water (2×100 ml) and 10% aqueous NaOH solution (100 ml) and then water (100 ml). The organic layer was dried over

$MgSO_4$ and the solvent was evaporated to give compounds **11** and **17**, respectively.

7,11-Nitrilo-2,12,20,21-tetrahydrodibenzo[*b,j*][1,12,5,8]-dioxadiazacyclononadecin-18,23(19*H*,22*H*)-dione (11). With the use of the general procedure A, the potassium salt of **22** and **2** gave crude **11** which crystallized from ethanol as colorless crystals (35%), mp 255–256°C; IR (cm^{-1}) 3396 (NH), 1647 (C=O); MS: *m/z* 404 (M^++1, 30%); ^{1}H NMR ($CDCl_3$) δ 3.62 (m, 4H, CH_2NH), 5.24 (s, 4H, OCH_2), 7.01–8.18 (m, 13H, ArHs, NH) ppm; ^{13}C NMR ($CDCl_3$) δ 40.27 (CH_2N), 70.12 (OCH_2), 113.6, 121.06, 122.95, 130.67, 132.24, 137.81 (ArCHs), 123.09, 155.31, 155.72 (ArCs), 164.97 (C=O) ppm. (Calcd for $C_{23}H_{21}NO_4$ (403.44): C, 68.47; H, 5.25; N, 10.42. Found: C, 68.70; H, 5.40; N, 10.60).

With the use of the general procedure B, **8** and **10** gave **11** (6%).

7,11-Nitrilo-2,16-di(*p*-methylphenylazo)-2,12,20,21-tetrahydrodibenzo[*b,j*][1,12,5,8]dioxadiazacyclononadecin-18,23(19*H*,22*H*)-dione (12). With the use of the general procedure A, the potassium salt of **24** and **2** gave crude **12** which crystallized from acetic acid as yellow crystals (50%), mp 290–292°C; IR (cm^{-1}) 3379 (NH), 1645 (C=O); MS: *m/z* 640 (M^+, 16.1%); ^{1}H NMR (DMSO) δ 2.41 (s, 6H, CH_3), 3.50 (brs, 4H, CH_2NH), 5.47 (s, 4H, OCH_2), 7.38–8.51 (m, 19H, ArHs, NH) ppm. (Calcd for $C_{37}H_{33}N_7O_4$ (639.71): C, 69.47; H, 5.20; N, 15.33. Found: C, 69.30; H, 5.40; N, 15.00).

7,11-Nitrilo-22*H*-6,12,20,21-tetrahydrodibenzo[*b,k*]-[1,13,5,9]dioxadiazacycloeicosin-18,24(19*H*,23*H*)-dione (13). With the use of the general procedure A, the potassium salt of **25** and **2** gave crude **13** which crystallized from methanol as colorless crystals (40%), mp 215–217°C; IR (cm^{-1}) 3396 (NH), 1643 (C=O); MS: *m/z* 417 (M^+, 23.7%); ^{1}H NMR ($CDCl_3$) δ 1.84 (quintet, *J*=6.2 Hz, 2H, CH_2CH_2NH), 3.51 (m, 4H, CH_2NH), 5.29 (s, 4H, OCH_2), 7.08–8.41 (m, 13H, ArHs, NH) ppm. (Calcd for $C_{24}H_{33}N_3O_4$ (417.46): C, 69.05; H, 5.55; N, 10.70. Found: C, 68.90; H, 5.60; N, 10.30).

7,11-Nitrilo-22*H*-2,16-di(*p*-methylphenylazo)-6,12,20,21-tetrahydrodibenzo[*b,k*][1,13,5,9]dioxadiazacycloeicosin-18,24(19*H*,23*H*)-dione (14). With the use of the general procedure A, the potassium salt of **26** and **2** gave crude **14** which crystallized from acetic acid as orange crystals (55%), mp 260–262°C; IR (cm^{-1}) 3394 (NH), 1649 (C=O); ^{1}H NMR ($CDCl_3$) δ 1.93 (quintet, *J*=6.1 Hz, 2H, CH_2CH_2NH), 2.42 (s, 6H, CH_3), 3.57 (m, 4H, CH_2NH), 5.35 (s, 4H, OCH_2), 7.19–8.70 (m, 19H, ArHs, NH) ppm. (Calcd for $C_{38}H_{35}N_7O_4$ (653.74): C, 69.82; H, 5.40; N, 15.00. Found: C, 69.70; H, 5.20; N, 14.70).

7,11-Nitrilo-6,12,20,21,22,23-hexahydrodibenzo[*b,l*]-[1,14,5,10]dioxadiazacyclohenicosin-18,25(19*H*,24*H*)-dione (15). With the use of the general procedure A, the potassium salt of **28** and **2** gave crude **15** which crystallized from dil. acetic acid as colorless crystals (45%), mp 239–240°C; IR (cm^{-1}) 3398 (NH), 1649 (C=O); MS: *m/z* 431 (M^+, 15.1%); ^{1}H NMR (DMSO) δ 1.21 (brs, 4H, CH_2CH_2NH), 3.16 (m, 4H, CH_2NH), 5.27 (s, 4H, OCH_2), 7.08–8.03 (m, 13H, ArHs, NH) ppm. (Calcd for $C_{25}H_{35}N_3O_4$ (431.49): C, 69.59; H, 5.84; N, 9.74. Found: C, 69.30; H, 5.50; N, 9.60).

7,11-Nitrilo-2,16-di(*p*-methylphenylazo)-6,12,20,21,22,23-hexahydrodibenzo[*b,l*][1,14,5,10]dioxadiazacyclohenicosin-18,25(19*H*,24*H*)-dione (16). With the use of the general procedure A, the potassium salt of **29** and **2** gave crude **16** which crystallized from acetic acid as yellow crystals (50%), mp 230–232°C; ^{1}H NMR (DMSO) δ 1.22 (brs, 4H, CH_2CH_2NH), 2.41 (s, 6H, CH_3), 3.16 (brs, 4H, CH_2NH), 5.28 (s, 4H, OCH_2), 6.95–8.03 (m, 19H, ArHs, NH) ppm. (Calcd for $C_{39}H_{37}N_7O_9$ (667.78): C, 70.15; H, 5.58; N, 14.68. Found: C, 70.30; H, 5.70; N, 14.90).

7,11-Metheno-2,12,20,21-tetrahydrodibenzo[*b,j*][1,12,5,8]-dioxadiazacyclononadecin-18,23(19*H*,22*H*)-dione (17). With the use of the general procedure A, the potassium salt of **22** and **3** gave crude **17** which crystallized from acetic acid as colorless crystals (50%), mp 290–292°C; IR (cm^{-1}) 3394 (NH), 1639 (C=O); MS: *m/z* 402 (M^+, 4.8%); ^{1}H NMR (DMSO) δ 4.0 (m, 4H, CH_2NH), 5.84 (s, 4H, OCH_2), 7.49–8.89 (m, 14H, ArHs, NH) ppm; ^{13}C NMR (DMSO) δ 40.2 (CH_2N), 68.9 (OCH_2), 113.05, 120.74, 125.46, 127.34, 128.27, 130.62, 132.17 (ArCHs), 122.95, 137.05, 155.56 (ArCs), 165.23 (C=O) ppm. (Calcd for $C_{24}H_{22}N_2O_4$ (402.45): C, 71.63; H, 5.51; N, 6.96. Found: C, 71.90; H, 5.20; N, 6.80).

With the use of the general procedure B, **9** and **10** gave **17** (8%).

7,11-Metheno-2,16-diphenylazo-2,12,20,21-tetrahydrodibenzo[*b,j*][1,12,5,8]dioxadiazacyclononadecin-18,23(19*H*,22*H*)-dione (18). With the use of the general procedure A, the potassium salt of **23** and **3** gave crude **18** which crystallized from acetic acid as yellow crystals (55%), mp 228–230°C; IR (cm^{-1}) 3406 (NH), 1643 (C=O); MS (FD): *m/z* 611 (M^++1, 100%); ^{1}H NMR (DMSO) δ 3.52 (brs, 4H, CH_2NH), 5.46 (s, 4H, OCH_2), 7.01–8.50 (m, 22H, ArHs, NH) ppm. (Calcd for $C_{36}H_{30}N_6O_4$ (610.67): C, 70.81; H, 4.95; N, 13.76. Found: C, 70.90; H, 4.60; N, 14.00).

7,11-Metheno-22*H*-6,12,20,21-tetrahydrodibenzo[*b,k*]-[1,13,5,9]dioxadiazacycloeicosin-18,24(19*H*,23*H*)-dione (19). With the use of the general procedure A, the potassium salt of **25** and **3** gave crude **19** which crystallized from acetic acid as colorless crystals (40%), mp 268–270°C; IR (cm^{-1}) 3379 (NH), 1637 (C=O); ^{1}H NMR ($CDCl_3$) δ 1.39 (quintet, *J*=6.6 Hz, 2H, CH_2CH_2NH), 3.33 (m, 4H, $NHCH_2$), 5.15 (s, 4H, OCH_2), 7.09–8.21 (m, 14H, ArHs, NH) ppm. (Calcd for $C_{25}H_{24}N_2O_4$ (416.47): C, 72.10; H, 5.81; N, 6.73. Found: C, 72.21; H, 5.70; N, 6.80).

7,11-Metheno-22*H*-6,16-di(*p*-methoxyphenylazo)-6,12,20,21-tetrahydrodibenzo[*b,k*][1,13,5,9]dioxadiazacycloeicosin-18,24(19*H*,23*H*)-dione (20). With the use of the general procedure A, the potassium salt of **27** and **3** gave crude **20** which crystallized from DMF as orange crystals (45%), mp 320–322°C; IR (cm^{-1}) 3382 (NH), 1652 (C=O); MS: *m/z* 684 (M^+, 4.33%); ^{1}H NMR (DMSO) δ 1.55

(quintet, J=6.3 Hz, 2H, CH_2CH_2NH), 3.36 (brs, 4H, $NHCH_2$), 3.88 (s, 6H, OCH_3), 5.35 (s, 4H, OCH_2), 7.12–8.18 (m, 20H, ArHs, NH) ppm. (Calcd for $C_{39}H_{36}N_6O_6$ (684.75): C, 68.41; H, 5.30; N, 12.27. Found: C, 68.20; H, 5.60; N, 11.90).

7,11-Metheno-6,12,20,21,22,23-hexahydrodibenzo[*b,l*]-[1,14,5,10]dioxadiazacyclohenicosin-18,25(19*H*,24*H*)-dione (21). With the use of the general procedure A, the potassium salt of **28** and **3** gave crude **21** which crystallized from acetic acid as colorless crystals (35%), mp 258–260°C; IR (cm^{-1}) 3375 (NH),1643 (C=O); ^1H NMR ($CDCl_3$) δ 1.13 (brs, 4H, CH_2CH_2NH), 3.24 (brs, 4H, $NHCH_2$), 5.11 (s, 4H, OCH_2), 7.08–8.26 (m, 14H, ArHs, NH) ppm. (Calcd for $C_{26}H_{26}N_2O_4$ (398.50): C, 78.36; H, 6.58; N, 7.03. Found: C, 78.40; H, 6.70; N, 7.20).

13,17-Nitrilo-6,12,18,24,32,33-hexahydrotetrabenzo-[*b, f,n,r*][1,5,16,20,9,12]tetraoxadiazacycloheptacosin-30,35(31*H*,34*H*)-dione (42). With the use of the general procedure A, the potassium salt of **23** and **40** gave crude **42** which crystallized from ethanol as colorless crystals (8%), mp 178–179°C; IR (cm^{-1}) 3385 (NH), 1649 (C=O); MS: m/z 616 (M^++1, 23.2%); ^1H NMR ($CDCl_3$) δ 2.86 (m, 4H, CH_2NH), 5.10 (s, 4H, OCH_2 pyridine), 5.22 (s, 4H, OCH_2 Ar), 6.95–8.08 (m, 21H, ArHs, NH) ppm. (Calcd for $C_{37}H_{33}N_3O_6$ (615.68): C, 72.18; H, 5.40; N, 6.82. Found: C, 72.15; H, 5.32; N, 6.79).

13,17-Metheno-34*H*-2,28-di(*p*-methylphenylazo)-6,12, 18,24,32,33-hexahydrotetrabenzo[*b, f,n,r*][1,5,17,21, 9,13]tetraoxadiazacyclooctacosin-30,36(31*H*,35*H*)-dione (43). With the use of the general procedure A, the potassium salt of **26** and **41** gave crude **43** which crystallized from ethanol as pale yellow crystals (10%), mp 212–214°C; IR (cm^{-1}) 3388 (NH), 1651 (C=O); MS (FD): m/z 864 (M^+, 100%); ^1H NMR ($CDCl_3$) δ 1.25 (brs, 2H, CH_2CH_2NH), 2.44 (s, 6H, CH_3), 3.06 (m, 4H, CH_2NH), 5.03 (s, 4H, OCH_2 Ar), 5.28 (s, 4H, OCH_2 Ar-azo), 6.97–8.04 (m, 26H, ArHs, NH), 8.73 (m, 2H, NH) ppm. (Calcd for $C_{53}H_{48}N_6O_6$ (864.99): C, 73.59; H, 5.59; N, 9.72. Found: C, 73.62; H, 5.50; N, 9.81).

Synthesis of 1,ω-bis(2-hydroxy-5-arylazobenzoylamino)-alkane 26, 27, 29

General procedure. A solution of the appropriate aromatic amine (10 mmol) in water (5 ml) and conc. HCl (3 ml) was diazotized at −5°C with a solution of $NaNO_2$ (0.7 g in 5 ml of water) during 10 min. These diazonium salts were added dropwise with stirring over a period of 30 min to a cold (−5°C) solution of the appropriate bis(phenols) **25**, **28** (5 mmol) in aqueous NaOH (20 ml, 30%). After the mixture had been kept overnight in the freezer, acidification with HCl (3 N) afforded the crude products **26**, **27**, **29** which were collected and crystallized from the proper solvent as orange crystals.

1,3-Bis(2-hydroxy-5-*p*-methylphenylazobenzoylamino)-propane (26). With the use of the general procedure, *p*-toluidene was diazotized and coupled with **25** to give crude **26** which crystallized from DMF/ethanol as orange crystals (60%), mp 264–266°C, ^1H NMR (DMSO) δ 1.91 (brs, 2H, CH_2CH_2NH), 2.42 (s, 6H, CH_3), 3.23 (m, 4H, CH_2NH), 7.07–8.52 (m, 14H, ArHs), 9.21 (brs, 2H, NH), 12.95 (s, 2H, OH) ppm. (Calcd for $C_{31}H_{30}N_6O_4$ (550.62): C, 67.62; H, 5.49; N, 15.26. Found: C, 67.70; H, 5.70; N, 14.90).

1,3-Bis(2-hydroxy-5-*p*-methoxylphenylazobenzoyl-amino)propane (27). With the use of the general procedure, *p*-anisidine was diazotized and coupled with **25** to give crude **27** which crystallized from DMF/water as brown crystals (60%), mp 224–225°C, ^1H NMR (DMSO) δ 1.93 (brs, 2H, CH_2CH_2NH), 3.44 (m, 4H, CH_2NH), 3.87 (s, 6H, OCH_3), 7.06–8.49 (m, 14H, ArHs), 9.19 (brs, 2H, NH), 13.22 (s, 2H, OH) ppm. (Calcd for $C_{31}H_{30}N_6O_6$ (582.61): C, 63.91; H, 5.19; N, 14.42. Found: C, 64.10; H, 5.30; N, 14.70).

1,3-Bis(2-hydroxy-5-*p*-methylphenylazobenzoylamino)-butane (29). With the use of the general procedure, *p*-toluidine was diazotized and coupled with **28** to give crude **29** which crystallized from ethanol as yellow crystals (65%), mp 210–212°C, ^1H NMR (DMSO) δ 1.64 (brs, 4H, CH_2CH_2NH), 2.4 (s, 6H, CH_3), 3.23 (brs, 4H, CH_2NH), 6.85–8.54 (m, 14H, ArHs), 8.86 (brs, 2H, NH), 12.74 (s, 2H, OH) ppm. (Calcd for $C_{32}H_{32}N_6O_4$ (564.64): C, 68.07; H, 5.71; N, 14.88. Found: C, 67.95; H, 5.65; N, 14.95).

Synthesis of the macrocyclic dithiodiamides 30–33

General procedure. To a boiling solution of **10**–**12** and **17** (10 mmol) in toluene (30 ml) was added Lawesson's reagent (8.1 g, 20 mmol). The reaction mixture was heated under reflux for 3 h. After cooling the yellow precipitate was collected and crystallized from the proper solvent to give yellow crystals of **30**–**33**, respectively.

7,11-Nitrilo-2,12,20,21-tetrahydrodibenzo[*b, j*][1,12,5,8]-dioxadiazacyclodecin-18,23(19*H*,22*H*)-dithione (30). With the use of the general procedure, **11** gave crude **30** which crystallized from DMF/ethanol as yellow crystals (72%), mp 241–242°C; IR (cm^{-1}) 2216 (SH); ^1H NMR (DMSO) δ 4.07 (brs, 4H, NCH_2), 5.28 (s, 4H, OCH_2), 6.90–7.95 (m, 11H, ArHs, pyridine Hs) 10.38 (brs, 2H, SH) ppm. (Calcd for $C_{23}H_{21}N_3O_2S_2$ (435.57): C, 63.42; H, 4.86; N, 9.65; S, 14.72. Found: C, 63.30; H, 5.00; N, 9.90; S, 14.90).

7,11-Nitrilo-22*H*-6,12,20,21-tetrahydrodibenzo[*b,k*]-[1,13,5,9]dioxadiazacycloeicosin-18,24(19*H*,23*H*)-dithione (31). With the use of the general procedure, **13** gave crude **31** which crystallized from toluene as yellow crystals (70%), mp 236–238°C; MS: m/z 449 (M^+, 3.5%); ^1H NMR (DMSO) δ 1.99 (brs, 2H, NCH_2CH_2), 3.83 (m, 4H, NCH_2), 5.32 (s, 4H, OCH_2), 6.99–7.95 (m, 11H, ArHs, pyridine Hs) 10.42 (brs, 2H, SH) ppm. (Calcd for $C_{24}H_{23}N_3O_2S_2$ (449.59): C, 64.12; H, 5.16; N, 9.35; S, 14.26. Found: C, 63.99; H, 5.25; N, 9.28; S, 14.33).

7,11-Nitrilo-6,12,20,21,22,23-hexahydrodibenzo[*b,l*]-[1,14,5,10]dioxadiazacyclohenicosin-18,25(19*H*,24*H*)-dithione (32). With the use of the general procedure, **15** gave crude **32** which crystallized from toluene as yellow crystals (60%), mp 245–246°C; ^1H NMR (DMSO) δ 1.37

(brs, 4H, NCH_2CH_2), 3.59 (brs, 4H, NCH_2), 5.28 (s, 4H, OCH_2), 6.98–8.06 (m, 11H, ArHs, pyridine Hs) 10.11 (brs, 2H, SH) ppm. (Calcd for $C_{25}H_{25}N_3O_2S_2$ (463.62): C, 64.77; H, 5.43; N, 9.06; S, 13.83. Found: C, 64.70; H, 5.20; N, 8.90; S, 13.50).

7,11-Metheno-2,12,20,21-tetrahydrodibenzo[*b*,*j*]-[1,12,5,8]dioxadiazacyclononadecin-18,23(19*H*,22*H*)-dithione (33). With the use of the general procedure, **17** gave crude **33** which crystallized from DMF/ethanol as yellow crystals (50%), mp 243–245°C; IR (cm^{-1}) 2327 (SH); ^{1}H NMR (DMSO) δ 4.03 (brs, 4H, NCH_2), 5.24 (s, 4H, OCH_2), 6.95–7.68 (m, 12H, ArHs) 10.34 (brs, 2H, SH) ppm. (Calcd for $C_{24}H_{22}N_2O_2S_2$ (434.58): C, 66.33; H, 5.10; N, 6.45; S, 14.76. Found: C, 66.40; H, 5.30; N, 6.10; S, 14.40).

7,11-Nitrilo-18,23-dimethylthio-2,12,20,21-tetrahydrodibenzo[*b*,*j*][1,12,5,8]dioxadiazacyclononadecin (34). To a solution of **30** (5 mmol) in sodium methoxide solution (prepared from 0.23 g sodium and 20 ml dry methanol) was added MeI (10 mmol). The reaction mixture was heated under reflux for 1 h. After cooling and dilution with water the precipitate was collected and crystallized from DMF to give colorless crystals of **34** (50%), mp 275–277°C; ^{1}H NMR (DMSO) δ 2.19 (s, 6H, SCH_3), 3.58 (s, 4H, NCH_2), 5.22 (s, 4H, OCH_2), 6.99–7.9 (m, 11H, ArHs) ppm. (Calcd for $C_{25}H_{25}N_3O_2S_2$ (463.62): C, 64.77; H, 5.43; N, 9.06; S, 13.83. Found: C, 65.00; H, 5.60; N, 9.20; S, 14.01).

7,11-Nitrilo-2,12,20,21-tetrahydrodibenzo[*b*,*j*][1,12,5,8]-dioxadiazacyclononadecin-18,23(19*H*,22*H*)-dione-24-oxide (35). To a solution of each of **11** and **34** (0.5 g) in acetic acid (5 ml) was added 30% H_2O_2 (1 ml). The reaction mixture was heated under reflux for 10 min and allowed to stand at room temperature overnight. After dilution with water the precipitate was collected and crystallized from acetic acid to give colorless crystals of 35 (65 and 60% yields, respectively) mp 284–286°C; MS: *m*/*z* 419 (M^+, 5%); ^{1}H NMR (DMSO) δ 3.54 (brs, 4H, NCH_2), 5.54 (s, 4H, OCH_2), 7.07–8.07 (m, 11H, ArHs pyridine Hs), 9.02 (brs, 2H, NH) ppm. (Calcd for $C_{23}H_{21}N_3O_5$ (419.43): C, 65.86; H, 5.08; N, 10.02. Found: C, 65.72; H, 5.12; N, 9.99).

Synthesis of bis(hydroxymethyl) ethers 38 and 39

To a stirred solution of the appropriate bis(carbonyl) ethers **36**, **37** (10 mmol) in MeOH (10 ml) was added solid $NaBH_4$ (0.89 g, 20 mmol) over a period of 5 min. The reaction mixture was heated under reflux for 30 min. The solvent was then removed in vacuo and water 10 ml was added. The solid obtained was collected and crystallized from the proper solvent to give **38** and **39**.

2,6-Bis[2-(hydroxymethylphenoxy)methyl]pyridine (38). With the use of the general procedure, **36** gave crude **38** which crystallized from methanol as colorless crystals (60%), mp 136–137°C; ^{1}H NMR ($CDCl_3$) δ 3.89 (brs, 2H, OH), 4.75 (d, J=5.4 Hz, 4H, CH_2OH), 5.27 (s, 4H, OCH_2Ar), 6.90–7.81 (m, 11H, ArHs) ppm. (Calcd for $C_{21}H_{21}NO_4$ (351.40): C, 71.78; H, 6.02; N, 3.99. Found: C, 72.00; H, 6.30; N, 4.10).

1,3-Bis[2-(hydroxymethylphenoxy)methyl]benzene (39). With the use of the general procedure, **37** gave crude **39** which crystallized from toluene as colorless crystals (80%), mp 95–97°C; ^{1}H NMR ($CDCl_3$) δ 2.75 (brs, 2H, OH), 4.75 (d, J=5.4 Hz, 4H, CH_2OH), 5.16 (s, 4H, OCH_2Ar), 6.94–7.42 (m, 12H, ArHs) ppm. (Calcd for $C_{22}H_{22}O_4$ (350.41): C, 75.41; H, 6.33. Found: C, 75.60; H, 6.60).

Synthesis of bis(chloromethyl) ethers 40 and 41

General procedure. To a cold stirred solution (−10°C) of each of the diols **38**, **39** (10 mmol) in chloroform (100 ml) was added dropwise thionyl chloride (5 ml). Stirring was continued for 2 h. The solvent was then removed in vacuo and the remaining solid was used in next step without further purification.

2,6-Bis[2-(chloromethylphenoxy)methyl]pyridine (40). With the use of the general procedure, **38** gave **40** as colorless crystals (70%), mp 175–176°C; ^{1}H NMR ($CDCl_3$) δ 4.77 (s, 4H CH_2Cl), 5.34 (s, 4H, OCH_2), 6.94–7.91 (m, 11H, ArHs) ppm. (Calcd for $C_{21}H_{19}Cl_2NO_2$ (388.29): C, 64.96; H, 4.93; N, 3.61; Cl, 18.26. Found: C, 65.20; H, 4.90; N, 3.50; Cl, 18.31).

1,3-Bis[2-(chloromethylphenoxy)methyl]benzene (41). With the use of the general procedure, **39** gave **41** as colorless crystals (75%), mp 110–112°C; ^{1}H NMR ($CDCl_3$) δ 4.72 (s, 4H CH_2Cl), 5.18 (s, 4H, OCH_2), 6.93–7.59 (m, 12H, ArHs) ppm. (Calcd for $C_{22}H_{20}Cl_2O_2$ (387.30): C, 68.23; H, 5.20; Cl, 18.31. Found: C, 68.10; H, 5.40; Cl, 18.60).

Synthesis of bis(4-amino-1,2,4-triazol-3-ylsulfanyl)alkanes 53, 54

General procedure. To a solution of each of **45**, **46** (50 mmol) in aqueous ethanol (50 ml, 50%) containing NaOH (2 g, 50 mmol) was added 1,4-dibromobutane (25 mmol). The reaction mixture was heated under reflux for 1 h. The solvent was then removed in vacuo and the remaining solid was collected and crystallized from DMF to give colorless crystals of compounds **53**, **54**.

1,4-Bis(4-amino-5-phenyl-1,2,4-triazol-3-ylsulfanyl)-butane (53). With the use of the general procedure, **45** gave **53** (65%), mp 241–243°C; ^{1}H NMR (DMSO) δ 1.9 (brs, 4H, SCH_2CH_2), 3.24 (brs, 4H, SCH_2), 6.12 (s, 4H, NH_2), 7.51–8.03 (m, 10H, ArHs) ppm. (Calcd for $C_{20}H_{22}N_8S_2$ (438.58): C, 54.77; H, 5.06; N, 25.55; S, 14.62. Found: C, 54.70; H, 4.90; N, 25.30; S, 14.30).

1,4-Bis(4-amino-5-benzyl-1,2,4-triazol-3-ylsulfanyl)-butane (54). With the use of the general procedure, **46** gave **54** (60%), mp 231–233°C; ^{1}H NMR (DMSO) δ 1.79 (brs, 4H, SCH_2CH_2), 3.12 (brs, 4H, SCH_2), 4.01 (s, 4H, CH_2Ph), 5.87 (s, 4H, NH_2), 7.29 (brs, 10H, ArHs) ppm. (Calcd for $C_{22}H_{26}N_8S_2$ (466.63): C, 65.63; H, 5.62; N, 24.01; S, 13.74. Found: C, 65.70; H, 5.80; N, 24.20; S, 13.40).

2,6-Bis[benzo(*b*)furan-2-yl]pyridine (55). A solution of **36** (10 mmol) in acetic acid (20 ml) was heated under reflux for 1 h. The solid obtained upon cooling was collected and crystallized from acetic acid as colorless crystals (50%),

mp 233–235°C; MS: *m/z* 311 (M^+, 100%); ^{1}H NMR (DMSO) δ 7.31–8.15 (m, 13H, ArHs pyridin Hs, furan Hs) ppm. (Calcd for $C_{21}H_{13}NO_2$ (311.34): C, 81.01; H, 4.21; N, 4.50. Found: C, 81.10; H, 4.40; N, 4.20).

Synthesis of macrocycles 56–60

General procedure. To a solution of **37** (10 mmol) in glacial acetic acid (30 ml) was added a solution of the appropriate bis(4-amino-1,2,4-triazol-3-ylsulfanyl)alkanes **50**–**54** (10 mmol) in glacial acetic acid (30 mmol). The reaction mixture was then heated under reflux for 2 h. The solvent was then removed in vacuo and the remaining solid was crystallized from acetic acid to give colorless crystals of **56**–**60**.

13,17-Metheno-12,18,31,32-tetrahydrobis[1,2,4]triazolo-[4,3-*f*:3,4-*l*]dibenzo[*b*,*l*][1,18,5,6,13,14,8,11]dioxatetraazadithiacyclopentacosine (56). With the use of the general procedure, **50** and **37** gave **56** (50%), mp 238–240°C; ^{1}H NMR (DMSO) δ 3.62 (s, 4H, SCH_2), 5.32 (s, 4H, OCH_2), 7.06–7.82 (m, 12H, ArHs), 8.92 (s, 2H, CH triazol), 9.08(s, 2H, CH=N) ppm. (Calcd for $C_{28}H_{24}N_8O_2S_2$ (568.68): C, 59.14; H, 4.25; N, 19.70; S, 11.28. Found: C, 59.30; H, 4.10; N, 19.50; S, 11.40).

13,17-Metheno-3,27-diphenyl-33*H*-12,18,32,33-tetrahydrobis[1,2,4]triazolo[4,3-*f*:3,4-*m*]dibenzo[*b*,*q*]-[1,19,5,6,14,15,8,12]dioxatetraazadithiacyclohexacosine (57). With the use of the general procedure, **51** and **37** gave **57** (55%), mp 262–264°C; MS (FD): *m/z* 735 (M^+, 100%); ^{1}H NMR ($CDCl_3$) δ 2.25 (quintet, J=6.2 Hz, 2H, SCH_2CH_2), 3.36 (t, J=6.4 Hz, 4H, SCH_2), 5.18 (s, 4H, OCH_2), 7.06–8.08 (m, 22H, ArHs), 9.25 (s, 2H, CH=N) ppm. (Calcd for $C_{41}H_{34}N_8O_2S_2$ (734.90): C, 67.01; H, 4.66; N, 15.25; S, 8.73. Found: C, 67.30; H, 4.30; N, 15.10; S, 8.90).

13,17-Metheno-3,27-dibenzyl-33*H*-12,18,32,33-tetrahydrobis[1,2,4]triazolo[4,3-*f*:3,4-*m*]dibenzo[*b*,*q*]-[1,19,5,6,14,15,8,12]dioxatetraazadithiacyclohexacosine (58). With the use of the general procedure, **52** and **37** gave **58** (62%), mp 240–242°C; MS (FD): *m/z* 764 (M^++1, 100%); ^{1}H NMR (DMSO) δ 1.94 (quintet J=6 Hz, 2H, SCH_2CH_2), 3.03 (t, J=6.8 Hz, 4H, SCH_2), 4.21 (s, 4H, CH_2Ph), 5.19 (s, 4H, OCH_2), 7.19–7.94 (m, 22H, ArHs), 9.15 (s, 2H, CH=N) ppm. (Calcd for $C_{43}H_{38}N_8O_2S_2$ (762.96): C, 67.69; H, 5.02; N, 14.69; S, 8.41. Found: C, 67.70; H, 4.80; N, 14.30; S, 8.60).

13,17-Metheno-3,27-diphenyl-12,18,31,32,33,34-hexahydrobis[1,2,4]triazolo[4,3-*f*:3,4-*n*]dibenzo[*b*,*q*][1,20,5,6,15,16,8,13]dioxatetraazadithiacycloheptacosine (59). With the use of the general procedure, **53** and **37** gave **59** (55%), mp 265–267°C; ^{1}H NMR (DMSO) δ 1.73 (brs, 4H, SCH_2CH_2), 3.14 (brs, 4H, SCH_2), 5.27 (s, 4H, OCH_2), 7.11–7.97 (m, 22H, ArHs), 9.22 (s, 2H, CH=N) ppm. (Calcd for $C_{42}H_{36}N_8O_2S_2$ (748.93): C, 67.36; H, 4.84; N, 14.96; S, 8.56. Found: C, 62.50; H, 4.50; N, 15.10; S, 8.40).

3,17-Metheno-3,27-dibenzyl-12,18,31,32,33,34-hexahydrobis[1,2,4]triazolo[4,3-*f*:3,4-*n*]dibenzo[*b*,*q*][1,20,5,6,15,16,8,13]dioxatetraazadithiacycloheptacosine (60). With the use of the general procedure, **54** and **37** gave **60** (60%), mp 250–252°C; MS (FD): *m/z* 777 (M^+, 100%); ^{1}H NMR (DMSO) δ 1.66 (brs, 4H, SCH_2CH_2), 3.11 (brs, 4H, SCH_2), 4.22 (s, 4H, CH_2Ph), 5.23 (s, 4H, OCH_2), 7.05–7.96 (m, 22H, ArHs), 9.12 (s, 2H, CH=N) ppm. (Calcd for $C_{44}H_{40}N_8O_2S_2$ (776.98): C, 68.02; H, 4.19; N, 14.42; S, 8.25. Found: C, 68.10; H, 5.30; N, 14.70; S, 8.40).

Action of sodium borohydride on 57–59

General procedure. To a stirred hot (40–50°C) solution of each of **57**–**59** (0.7 mmol) in methanol (10 ml) was added sodium borohydride (0.4 g) over a period of 15 min. The reaction mixture was heated under reflux for 1 h. The solvent was then removed in vacuo and the remaining solid was collected, washed with water and crystallized from methanol to give colorless crystals of **61**–**63**.

13,17-Metheno-3,27-diphenyl-33*H*-5,6,12,18,24,25,31,32-octahydrobis[1,2,4]triazolo[4,3-*f*:3,4-*m*]dibenzo-[*b*,*q*][1,19,5,6,14,15,8,12]dioxatetraazadithiacyclohexacosine (61). With the use of the general procedure, **57** gave **61** (70%), mp 182–184°C; ^{1}H NMR ($CDCl_3$) δ 2.08 (quintet, J=6.6 Hz, 2H, SCH_2CH_2), 3.09 (t, J=6.4 Hz, 4H, SCH_2), 4.15 (d, J=6.4 Hz, 4H, $NHCH_2Ar$), 5.13 (s, 4H, OCH_2), 5.55 (t, J=6.6 Hz, 2H, NH), 6.85–8.09 (m, 22H, ArHs) ppm. (Calcd for $C_{41}H_{38}N_8O_2S_2$ (738.93): C, 66.64; H, 5.18; N, 15.16; S, 8.68. Found: C, 66.90; H, 5.20; N, 15.30; S, 8.59).

13,17-Metheno-3,27-dibenzyl-33*H*-5,6,12,18,24,25,31,32-octahydrobis[1,2,4]triazolo[4,3-*f*:3,4-*m*]dibenzo-[*b*,*q*][1,19,5,6,14,15,8,12]dioxatetraazadithiacyclohexacosine (62). With the use of the general procedure, **58** gave **62** (75%), mp 220–222°C; IR (cm^{-1}) 3182 (NH); ^{1}H NMR ($CDCl_3$) δ 2.0 (quintet, J=6.4 Hz, 2H, SCH_2CH_2), 3.04 (t, J=6.8 Hz, 4H, SCH_2), 3.84 (d, J=6.2 Hz, 4H, $NHCH_2Ar$), 3.97 (s, 4H, $PhCH_2$), 5.09 (m, 6H, OCH_2, NH), 6.93–7.43 (m, 22H, ArHs) ppm; ^{13}C NMR ($CDCl_3$) δ 28.45 (SCH_2CH_2), 30.9 (CH_2Ph), 31.36 (SCH_2), 51.72 (CHNH), 70.21 (CH_2O) 111.89, 121.48, 127.15, 127.24, 127.94, 128.88, 129.08, 130.19, 131.90 (ArCHs), 123.92, 136.14, 136.82, 150.54, 154.74, 157.49 (ArCs) ppm. (Calcd for $C_{43}H_{42}N_8O_2S_2$ (766.98): C, 67.34; H, 5.52; N, 14.61; S, 8.36. Found: C, 67.70; H, 5.60; N, 14.34; S, 8.18).

13,17-Metheno-3,27-diphenyl-5,6,12,18,24,25,31,32,33,34-decahydrobis[1,2,4]triazolo[4,3-*f*:3,4-*n*]dibenzo-[*b*,*q*][1,20,5,6,15,16,8,13]dioxatetraazadithiacycloheptacosine (63). With the use of the general procedure, **59** gave **63** (65%), mp 185–187°C; MS: *m/z* 752 (M^+, 7%); ^{1}H NMR $CDCl_3$) δ 1.76 (brs, 4H, SCH_2CH_2), 3.11 (brs, 4H, SCH_2), 4.14 (d, J=6.4 Hz, 4H, $NHCH_2$), 5.13 (s, 4H, OCH2), 5.50 (t, J=6.6 Hz, 2H, NH), 6.83–8.05 (m, 22H, ArHs) ppm. (Calcd for $C_{42}H_{40}N_8O_2S_2$ (752.96): C, 67.00; H, 5.35; N, 14.88; S, 8.52. Found: C, 67.21; H, 5.17; N, 15.00; S, 8.29).

References

1. Izatt, R. M.; Bordunov, A. V.; Zhu, C. Y.; Hathaway, J. K. In *Comprehensive Supramolecular Chemistry*, Gokel, G. W., Ed.; Pergamon: New York, 1996; Vol. 1, p 3595.

2. Izatt, R. M.; Pawlak, K.; Bradshaw, J. S.; Bruening, R. L. *Chem. Rev.* **1991**, *91*, 1721.
3. Gokel, G. W. *Crown Ethers and Cryptands* (Monographs in Supramolecular Chemistry); The Royal Society of Chemistry: Cambridge, 1991; Vol. 3; Cram, D. J.; Cram, J. M. *Container Molecules and their Guests* (Monographs in Supramolecular Chemistry); The Royal Society of Chemistry: Cambridge, 1994; Vol. 4; Bell, T. W.; Salmi, S. K. In *Inclusion Compounds*; Atwood, J. L., Davies, J. E. D., Macnicol, D. D., Eds.; Oxford University Press: Oxford, 1991; Vol. 4, p 325.
4. Weber, E.; Kohler, H. J.; Reuter, H. *J. Org. Chem.* **1991**, *56*, 1236.
5. Weber, E.; Kohler, H. J. *J. Prakt. Chem.* **1995**, *337*, 451.
6. Heitzsch, O.; Gloe, K.; Sabela, A.; Koryta, J.; Weber, E. *J. Incl. Phenom.* **1992**, *13*, 311.
7. Weber, E. *Synthesis of Macrocycles—the Design of Selective Complexing Agents*; In *Progress in Macrocyclic Chemistry*, Izatt, R. M., Christensen, J. J., Eds.; Wiley: New York, 1987; Vol. 3, p 337.
8. Irie, S.; Yamamoto, M.; Kishikawa, K.; Kohmoto, S.; Yamada, K. *Synthesis* **1995**, 1179.
9. Cram, D. J. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1035.
10. Fujita, T.; Lehn, J. M. *Tetrahedron Lett.* **1988**, *29*, 1709.
11. Grammenudi, S.; Vogtle, F. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1122.
12. Nakatsuji, Y.; Kobayashi, H.; Okahara, M.; Matsuchima, K. *Chem. Lett.* **1982**, 1571.
13. Petranek, J.; Ryba, O. *Anal. Chim. Acta* **1981**, *128*, 129.
14. Duriez, M. C.; Pigot, T.; Picard, C.; Cazaux, L.; Tinses, P. *Tetrahedron* **1992**, *48*, 4347.
15. Pigot, T.; Duriez, M. C.; Picard, C.; Cazaux, L.; Tisnes, P. *Tetrahedron* **1992**, *48*, 4359.
16. Elshani, S.; Wai, C. M.; Natale, N. R.; Bartsch, R. A. *Tetrahedron* **1999**, *55*, 9425.
17. Trafton, Y. E.; Mallen, C. L. J.; Miller, S. R.; Nakano, A.; Schall, O. F.; Gokel, G. W. *J. Chem. Soc., Chem. Commun.* **1990**, 1266.
18. Ozeki, E.; Kimura, S.; Truanislu, Y. *J. Chem. Soc., Perkin Trans 2* **1988**, 1743.
19. Krakowiak, K. E.; Bradshaw, J. S.; Zamecka-Krakowiak, D. *Chem. Rev.* **1989**, *89*, 929.
20. Dietrich, B. *Comprehensive Supramolecular Chemistry*; Gokel, G. W. Ed.; Pergamon: New York, 1996, pp 153–212.
21. Sharghi, H.; Massah, A. R.; Eshgi, H.; Niknam, K. *J. Org. Chem.* **1998**, *63*, 1455.
22. Ibrahim, Y. A.; Elwahy, A. H. M. *Synthesis* **1993**, 503.
23. Ibrahim, Y. A.; Elwahy, A. H. M. *J. Chem. Res. (S)* **1993**, 852; *J. Chem. Res. (M)* **1993**, 1684.
24. Ibrahim, Y. A.; Elwahy, A. H. M.; Elkareish, G. M. M. *J. Chem. Res. (S)* **1994**, 414; *J. Chem. Res. (M)* **1994**, 2321.
25. Ibrahim, Y. A.; Elwahy, A. H. M.; Abbas, A. A. *J. Chem. Res. (S)* **1998**, 548; *J. Chem. Res. (M)* **1998**, 2501.
26. Sharghi, H.; Eshgi, H. *Tetrahedron* **1995**, *51*, 913.
27. Weber, E.; Vogtle, F. *Chem. Ber.* **1976**, *109*, 1803.
28. Si, J.; Wu, Y.; Cai, L.; Liu, Y.; Du, B.; Xu, T.; An, H. *J. Incl. Phenom.* **1994**, *17*, 249.
29. Weber, E.; Ahrendt, J.; Bruck, F. J.; Reddy, R. Y.; Chacko, K. K. *J. Prakt. Chem.* **1993**, *335*, 235.
30. Kumar, S.; Humdal, M. S.; Hundal, G.; Singh, P.; Bhalla, V.; Singh, H. *J. Chem. Soc., Perkin Trans 2* **1998**, 925.
31. Kumar, S.; Kaur, N.; Singh, H. *Tetrahedron* **1996**, *52*, 13483.
32. Mikhura, I. V.; Formanovski, A. A. *Khim. Geterosikl Soedin* **1989**, *11*, 1559; *Chem. Abstr.* **1990**, *113*, 59133.
33. Kumar, S.; Bhalla, V.; Singh, H. *Tetrahedron* **1998**, *54*, 5575.
34. Ibrahim, Y. A.; Elwahy, A. H. M.; Elkareish, G. M. M. *Heteroatom Chem.* **1995**, *6*, 183.
35. Kassab, R. M. M.Sc. Thesis, 1999, Cairo University, Faculty of Science, Chemistry Department.
36. Djurendic, E. A.; Sauranyj, T. M.; Miljkovic, D. A. *Collect. Czech. Chem. Commun.* **1990**, *55*, 1763.
37. Elwahy, A. H. M.; Abbas, A. A.; Ibrahim, Y. A. *J. Chem. Res. (S)* **1996**, 183; *J. Chem. Res. (M)* **1996**, 1066.
38. Baily, N. A.; Fenton, D. E.; Kitchen, S. J.; Lilley, T. H.; Williams, M. G.; Tasker, P. A.; Leong, A. J.; Lindoy, L. F. *J. Chem. Soc., Dalton Trans.* **1991**, 627.
39. Reddy, D.; Chandrashekar, T. K. *J. Chem. Soc., Dalton Trans.* **1992**, 619.