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Regioselective N-alkylation for the Synthesis of Novel Aminotriazolophanes

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ABSTRACT: *Regioselective synthesis of macrocycles, incorporating 3-oxo-4-amino-1,2,4-triazole derivatives, has been achieved by reactions involving N-alkylation, utilizing appropriate 1,ω-dihaloalkanes in the presence of metal hydroxide.* © 2006 Wiley Periodicals, Inc. Heteroatom Chem 17:329–336, 2006; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20211

INTRODUCTION

Crown compounds have generated considerable interest in the past three decades because of their ability to form stable complexes with a variety of metal and organic cations and anions [1–5]. They also have wide applications in phase transfer catalysis [6,7]. In recent years, various structural changes have been made to the basic "crown ether" structure in order to enhance the selective activity of the ligands [8].

Incorporation of heterocyclic subunits provides rigidity to the macrocycle and assists in increasing the stability of complexes formed with both metals and organic cations [8]. The observation that certain triazoles were capable of inhibiting fog formation [9] in photographic emulsions and that others were useful as anticonvulsants [9] and herbicides [9] has led to a renewed attention particularly by the chemical industry, to simple and fused triazole systems. 1,2,4-Triazoles also have potent antimicrobial activity [9]. We have recently reported various triazolophane lariats containing amino side arm [10].

In continuation of our work, we now report a facile regioselective synthesis of aminotriazolophanes involving N-alkylation.

RESULTS AND DISCUSSION

In Scheme 1, the starting synthon, 3-oxo-4-amino-5-mercapto-1,2,4-triazole, **1** was prepared in good yields from thiocarbohydrazide by its reaction with carbonoxysuphide [11].

The synthon **1** was treated with 1,2-bis(bromomethyl)benzene and bis(iodoethyl)ether in aqueous methanol in the presence of metal hydroxide to afford 1,2-bis[(3-oxo-4-amino-1,2,4-triazol-5-yl) mercaptomethyl]benzene, **5** and 1,5-bis[(3-oxo-4-amino-1,2,4-triazol-5-yl) mercaptoethyl]ether **6**. **1** was also treated with various 1,ω-dihaloalkanes to yield 1,ω-bis(3-oxo-4-amino-1,2,4-triazol-5-yl)-mercaptoalkanes **7a–d**.

For compound **5**, IR spectrum gave a strong absorption at 1710 cm^{-1} for >C=O. ^1H NMR showed a singlet at δ 4.38 (S—C$\underline{H}_2$), a singlet at δ 5.30 (—N$\underline{H}_2$), a multiplet at δ 7.25–7.39 (aromatic protons), and a singlet at δ 11.71 (—N$\underline{H}$, amido, D_2O-exchangeable). ^{13}C NMR showed signals at 30.76 ppm (S—CH_2), at 127.97–135.32 ppm (aromatic carbons), at 145.01 ppm (>C=N), and at 154.64 ppm (>C=O).

From the above data, the compound **5** was identified as 1,2-bis(3-oxo-4-amino-1,2,4-triazol-5-yl) mercaptomethylbenzene.

The absence of a peak for —S$\underline{H}$ in ^1H NMR, and the absence of signal for >$\underline{C}$=S in ^{13}C NMR of

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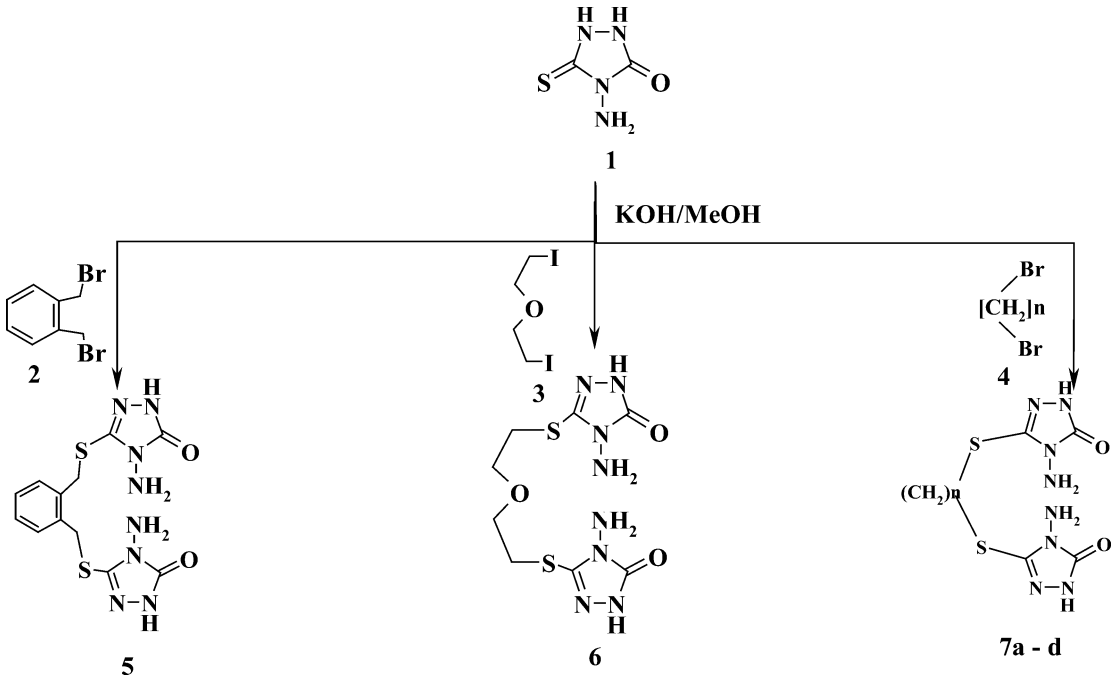


SCHEME 1

compound **5**, indicated that S-alkylation had taken place. The singlet for the amido —N<u>H</u> proton in the ^{1}H NMR of compound **5**, and the signal for carbonyl carbon of the amido group in the ^{13}C NMR, indicated that the compound exists in the amido form and not in the iminol form. The spectra of compounds **6** and **7a–d** also led to similar conclusions.

In Scheme 2, the crown precursors **5, 6**, and **7a–d** were reacted with 1,2-bis(bromomethyl)benzene, 2,2′-diiodoethylether **3** and with various 1,ω-dihaloalkanes **4** to afford the novel aminotriazolophanes **8–13**.

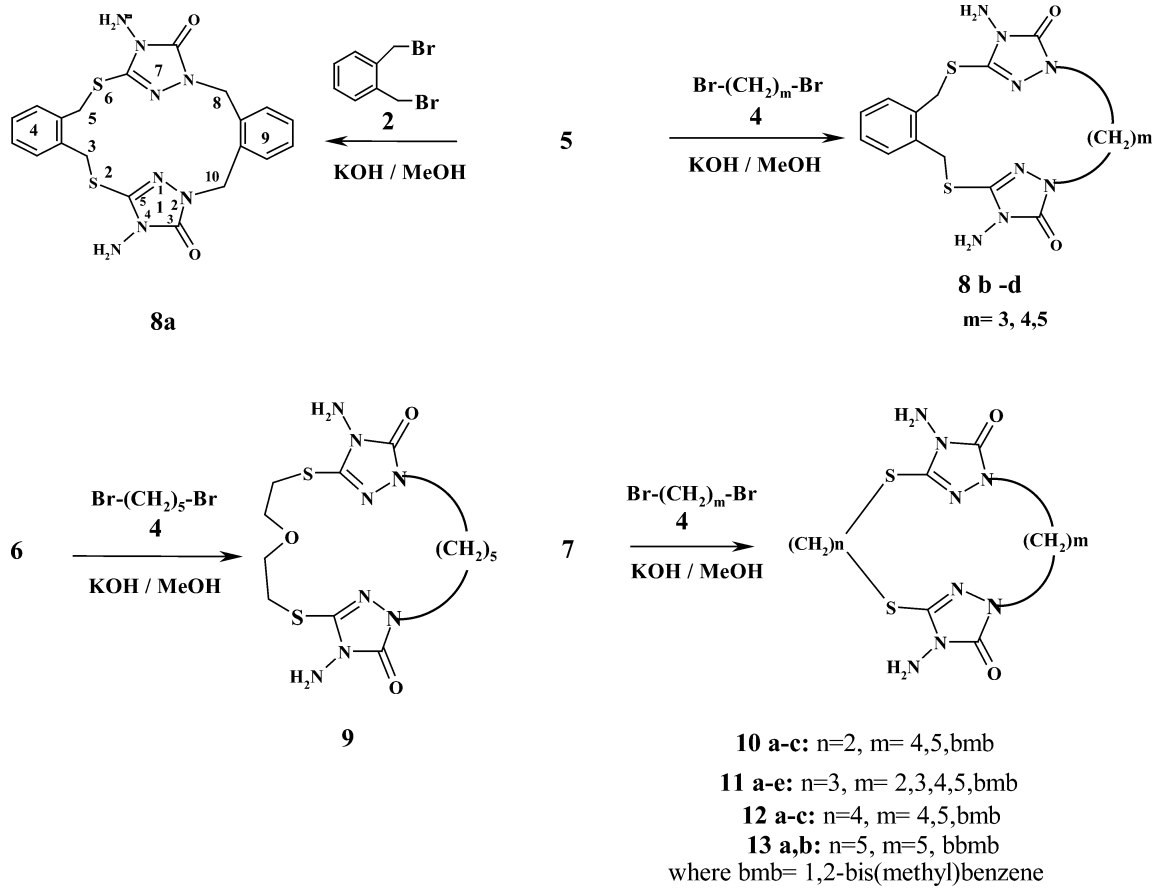
IR spectrum of compound **8a** gave a strong absorption at 1698 cm^{-1} (>C=O). ^{1}H NMR showed a singlet at δ 4.51(S—C<u>H</u>$_2$–), a singlet at 5.19 (N–C<u>H</u>$_2$–), a singlet at 5.42 (—N<u>H</u>$_2$), and a multiplet at 7.22–7.40 (aromatic protons). ^{13}C NMR gave a signal at 29.71 ppm (S—<u>C</u>H$_2$), 45.75 ppm (—N—<u>C</u>H$_2$), multiple signals at 128.14, 129.51, 130.88, 135.05, and 135.6 ppm (aromatic carbons), a signal at 144.94 ppm (><u>C</u>=N), and a signal at 153.59 ppm (><u>C</u>=O).

From the above data, the compound **8a** was identified as 2,6-dithia-1^4,7^4-diamino-4(1,2)-9(1,2)-dibenzena-1(2,5),7(5,2)-di(3-oxo-1,2,4-triazola)-cyclodecaphane [12].

The strong absorptions for >C=O in IR spectrum and the signal for ><u>C</u>=O in the ^{13}C NMR spectrum of the compound **8a** indicated that *N-alkylation* had taken place. This was further confirmed by the clear absence of the amido proton (—N<u>H</u>—) peaks, which were very prominent in the ^{1}H NMR spectra of compounds **5, 6**, and **7a–d**.

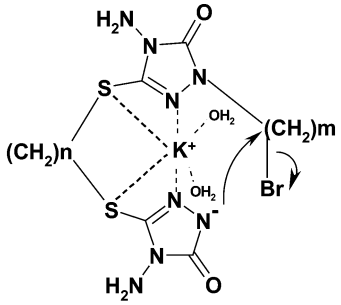
Also, the presence of a distinct peak for —NH$_2$ protons in the proton NMR showed that cyclization did not involve the N—NH$_2$ group. The spectral data of the other aminotriazolophanes synthesized were in agreement with the above observations.

The intramolecular alkylation, which regioselectively occurs at amido nitrogen, is mainly because of the template formation due to the presence of the hexadentate potassium ions where two ligands are water molecules [13a,b]. The reactions were carried out in large excess of solvent for ensuring intramolecular cyclization (high-dilution condition). In Scheme 3, the starting synthons 1,ω-bis-(4-amino-3-oxo-1,2,4-triazol-5-yl) alkanes **16a–b** were synthesized by fusing 1,ω-dicarboxylic acids with carbohydrazide in an oil bath at 140°C for 4 h. IR spectrum of compound **16b** gave a strong absorption at 1709 cm^{-1}(>C=O). ^{1}H NMR showed a pentet at δ 1.64(CH$_2$—C<u>H</u>$_2$—C<u>H</u>$_2$—CH$_2$), a triplet at δ 2.47(N=C—C<u>H</u>$_2$), a singlet at δ 5.1 (—N<u>H</u>$_2$), and a singlet at δ 11.26 (—N<u>H</u>). ^{13}C NMR showed signals at 24.18 and 24.91 (aliphatic carbons), a signal at 148.36 ppm (><u>C</u>=N), and at 154.59 ppm (><u>C</u>=O). M$^+$, *m/z* (%) 254(45), 223(35), 141(55), 127(100), 82(20), 55(30). From the above data, the compound **16b** was identified as 1,4-bis(4-amino-3-oxo-1,2,4-triazol-5-yl)butane.



SCHEME 2

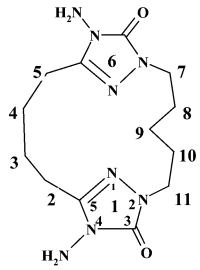
The spectra of compound **16a** also led to similar conclusions.



Template Effect

The crown precursors **16a,b** were reacted with 1,2-bis(bromomethyl)benzene and with various 1,ω-dihaloalkanes to afford the novel aminotriazolophanes **17a–c** and **18a–d**.

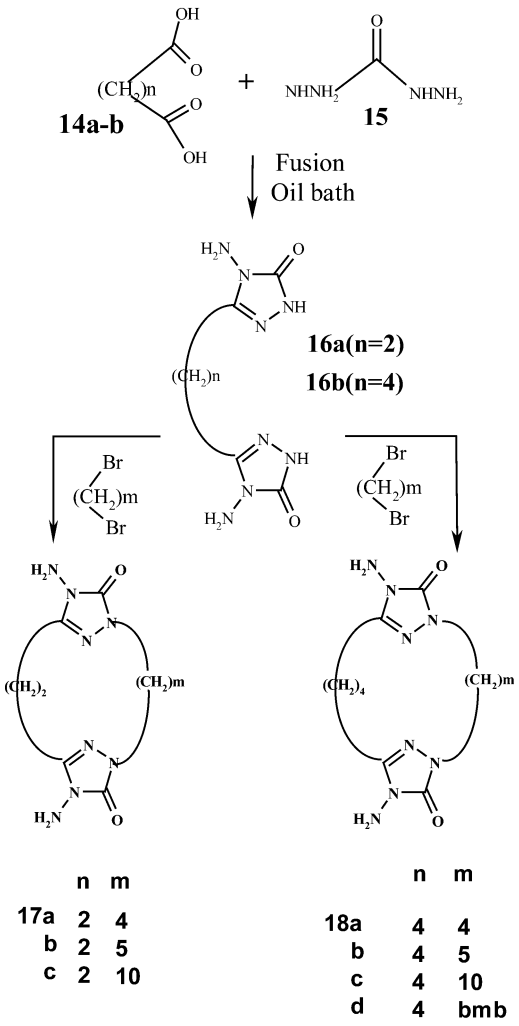
IR spectrum of compound **18b** gave a strong absorption at 1695 cm^{-1} (>C=O). ^1H NMR showed a pentet at δ 1.08 (N–CH_2–CH_2–$C\underline{H}_2$), a pentet at δ 1.57 ($2 \times$ N–CH_2–$C\underline{H}_2$ and $2 \times$ N=C–CH_2–$C\underline{H}_2$), a triplet at δ 2.48 ($2 \times$ C=N–$C\underline{H}_2$), a triplet at 3.68 (–N–$C\underline{H}_2$), and a singlet at 5.22 (–$N\underline{H}_2$). ^{13}C NMR gave signals at 20.02, 24.37, 25.84, 28.53, and 42.83 (aliphatic carbons), a signal at 147.06 (>$\underline{C}$=N), and a signal at 153.16 ppm (>$\underline{C}$=O). M^+, *m/z* (%) 322(40), 306(20), 291(45), 224(10), 154(8), 108(58), and 82(100). From the above data, the compound **18b** was identified as 1^4,6^4-diamino-1(2,5),6(2,5)-di-(3-oxo-1,2,4-triazola)-cycloundecaphane.



18 b

EXPERIMENTAL

Melting points were determined on Tempo melting point apparatus in open capillaries and are uncorrected. The IR spectra (potassium bromide, ν in cm^{-1}) were recorded on a Perkin-Elmer 257-FTIR



bmb= 1,2-bis (methylene)benzene

SCHEME 3

1600 spectrophotometer. ^{1}H NMR spectra (deuterochloroform and deuterodimethylsulfoxide, δ in ppm) were run on a Bruker AMX 500 spectrometer, using trimethylsilane as the internal standard. Mass spectra (70 eV) were recorded on Shimadzu QP 2010 GC-MS spectrometer, and the elemental analyses were carried out at Mumbai University Institute of Chemical Technology, Matunga, Mumbai, India.

Synthesis of 1,2-Bis(3-oxo 4-amino-5-mercapto-1,2,4-triazol-5-ylmethyl)benzene **5**

A solution of **1** (2.64 g, 20 mmol), potassium hydroxide (1.3 g, 20 mmol in minimum water), 1,2 bis(bromomethyl)benzene, **2** (2.64 g, 10 mmol) in 100 mL methanol was warmed to reflux for 4 h. A white solid was formed in the reaction mixture in 3 h. This was collected by filtration, washed with water and crystallized from dimethylsulfoxide to give **5**. This compound was isolated (2.4 g, 65%) mp 235°C. IR : ν 1710. ^{1}H NMR (DMSO-d_6) δ 4.38 (s, 2H, S—C$\underline{H}_2$), 5.30 (s, 2H, —N$\underline{H}_2$), 7.25–7.39 (m, 4H, Ar-H), 11.71 (s, 2H, 2 × N$\underline{H}$, amido). ^{13}C NMR (DMSO-d_6): δ 30.76 (S—$\underline{C}$H$_2$), 127.97–135.32 (Ar-C), 145.01 (>C=N), and 154.64 ppm (>C=O). MS, *m/z* (%): M$^+$, 366(25), 234(22), 219(29), 132(98), 104(74). Elemental analysis for $C_{12}H_{14}O_2N_8S_2$. MW: 366. Calc: C 39.34, H 3.82, O 8.74, N 30.60, S 17.48; Found: C 39.36, H 3.83, O 8.75, N 30.61, S 17.47.

Synthesis of 1,2-Bis(3-oxo 4-amino-5-mercapto-1,2,4-triazol-5-yl) Diethyl Ether, **6**

A solution of **1** (2.64 g, 20 mmol), potassium hydroxide (1.3 g, 20 mmol in minimum water), 2,2′-diiodoethylether **3** (3.26 g, 10 mmol) in 100 mL methanol was warmed to reflux for 4 h. A white solid was formed in the reaction mixture in 3 h. This was collected by filtration, washed with water, and crystallized from dimethylsulfoxide to give **6**. This compound was isolated (1.70 g, 51%), mp 205°C. IR : ν 1710. ^{1}H NMR (DMSO-d_6) δ 3.16 (t, 4H, 2 × O—C$\underline{H}_2$), 3.60 (t, 4H, 2 × S—C$\underline{H}_2$), 5.26 (s, 4H, 2 × —N$\underline{H}_2$), 11.63 (s, 2H, 2 × —N$\underline{H}$, D_2O-exchangeable); ^{13}C NMR: (DMSO-d_6): 28.63 (—S—$\underline{C}$H$_2$), 68.46 (—O—$\underline{C}$H$_2$), 145.66 (>$\underline{C}$=N), 154.74 ppm (>$\underline{C}$=O). MS, *m/z* (%) M$^+$334(10), 159(23), 117(100), 105(25). Element. anal. for $C_8H_{14}O_3N_8S_2$ mw: 366. Calc: C 28.74, H 4.19, N 33.53, S 19.15; Found C 28.72, H 4.20, N 33.54, S 19.14

General Procedure for Synthesis of 1,ω-Bis(3-oxo-4-amino-5-mercapto-1,2,4-triazol-5-yl)-alkanes **7a–d**

A solution of **1** (2.64 g, 20 mmol), potassium hydroxide (1.3 g, 20 mmol in minimum water), 1,ω-dibromo alkane **4** (10 mmol) in 100 mL of methanol was warmed to reflux for 4 h. A white solid was formed in the reaction mixture in 3 h. This was collected by filtration, washed with water, dried and crystallized from dimethylsulfoxide to give **7a–d**. The physical constants and the spectral data of the compounds **7a–d** are included in Tables 1 to 3.

Synthesis of 2 6-Dithia-1^4, 7^4-diamino-4 (1,2)-9(1,2)-dibenzena-1(2,5),7(5,2)-di(3-oxa-1,2,4 triazola)-cyclodecaphane, **8a**

A solution of **5** (3.66 g, 10 mmol), potassium hydroxide (1.3 g, 20 mmol), and 1,2-bis (bromomethyl) benzenes **2** (2.64 g, 10 mmol) in 200 mL of 80:20 aqueous methanol was warmed to reflux for 4 h. By

TABLE 1 Physical and Chemical Characteristics and Data Analysis

No.	Molecular Formula	Found/Calculated (%)				mp (°C)	Yield (%)
		C	H	N	S		
7a	$C_6H_{10}O_2N_8S_2$	24.81/24.82	3.44/3.47	38.63/38.62	22.08/22.09	263	56
7b	$C_7H_{12}O_2N_8S_2$	27.62/27.63	3.97/3.97	36.84/36.82	21.06/21.07	222	52
7c	$C_8H_{14}O_2N_8S_2$	30.16/30.18	4.41/4.43	10.07/10.19	20.18/20.12	239	57
7d	$C_9H_{16}O_2N_8S_2$	32.54/32.53	4.83/4.85	33.69/33.71	19.21/19.29	222	62
8b	$C_{15}H_{18}O_2N_8S_2$	44.31/44.32	4.47/4.46	25.56/25.57	15.77/15.78	256	23
8c	$C_{16}H_{20}O_2N_8S_2$	45.72/45.70	4.79/4.79	26.67/26.65	15.23/15.25	267	28
8d	$C_{17}H_{22}O_2N_8S_2$	46.96/46.99	5.09/5.10	25.78/25.79	14.76/14.76	285	30
10a	$C_{10}H_{16}O_2N_8S_2$	34.88/34.87	4.67/4.68	32.54/32.53	18.59/18.62	285	31
10b	$C_{11}H_{18}O_2N_8S_2$	36.85/36.86	5.03/5.06	31.29/31.26	17.86/17.89	255	22
10c	$C_{14}H_{16}O_2N_8S_2$	42.84/42.85	4.12/4.11	28.54/28.55	16.33/16.34	241	30
11a	$C_9H_{14}O_2N_8S_2$	32.72/32.72	4.27/4.27	33.92/33.92	19.41/19.41	245	32
11b	$C_{10}H_{16}O_2N_8S_2$	34.86/34.87	4.67/4.68	32.54/32.53	18.62/18.62	248	35
11c	$C_{11}H_{18}O_2N_8S_2$	36.88/36.86	5.07/5.06	31.55/31.56	17.89/17.89	279	31
11d	$C_{12}H_{20}O_2N_8S_2$	38.72/38.70	5.39/5.41	30.11/30.08	17.21/17.22	271	33
11e	$C_{15}H_{18}O_2N_8S_2$	44.33/44.32	4.47/4.46	27.55/27.57	15.78/15.78	247	30
12a	$C_{12}H_{20}O_2N_8S_2$	38.72/38.70	5.42/5.41	30.09/30.08	17.21/17.22	272	25
12b	$C_{13}H_{22}O_2N_8S_2$	40.42/40.40	5.73/5.74	28.98/28.99	16.62/16.59	255	29
12c	$C_{16}H_{20}O_2N_8S_2$	45.73/45.70	4.78/4.79	26.64/26.65	15.26/15.25	285	26
13a	$C_{14}H_{24}O_2N_8S_2$	41.97/41.98	6.06/6.04	27.96/27.98	16.01/16.01	259	27
13b	$C_{17}H_{22}O_2N_8S_2$	46.98/46.99	5.11/5.10	25.80/25.79	14.76/14.76	265	21
16a	$C_6H_{10}O_2N_8$	31.88/31.86	4.44/4.46	49.53/49.55	–	¿300	50
16b	$C_8H_{14}O_2N_8$	37.85/37.79	5.51/5.50	44.10/44.07	–	¿300	40
17a	$C_{10}H_{16}O_2N_8$	42.88/42.85	5.68/5.75	40.10/39.98		¿300	22
17b	$C_{11}H_{18}O_2N_8$	44.86/44.89	6.13/6.16	38.05/38.07	–	¿300	25
17c	$C_{16}H_{28}O_2N_8$	52.80/52.73	7.68/7.74	30.70/30.75	–	275	28
18a	$C_{12}H_{20}O_2N_8$	46.70/46.74	6.48/6.50	36.4036.34/	–	¿300	20
18b	$C_{13}H_{22}O_2N_8$	48.45/48.44	6.82/6.83	–	–	270	21
18c	$C_{18}H_{32}O_2N_8$	55.12/55.08	8.18/8.22	28.55/28.55	–		28
18d	$C_{16}H_{20}O_2N_8$	53.91/53.92	5.65/5.66	31.48/31.44	–		24

concentrating the reaction mixture to 50%, a crystalline white solid was formed. This was collected by filtration and washed carefully with a dilute solution of potassium hydroxide to dissolve any polymeric material that may have precipitated out. The solid was then washed well with water, and crystallized from dimethylsulfoxide to give **8a**. This compound was isolated (1.35 g, 29%). mp 269°C. IR : ν 1698 (>C=O), ^{1}H NMR (DMSO-d_6) δ 4.51 (s, 2H, S—C$\underline{H}_2$—), 5.19 (s, 2H, —N—C$\underline{H}_2$—), 5.42 (s, 2H, —N$\underline{H}_2$), 7.22–7.40 (m, 8H, Ar-H). ^{13}C NMR: (DMSO-d_6): 29.71 (—S—$\underline{C}H_2$), 45.75 (—N—$\underline{C}H_2$), 128.14, 129.51, 130.88, 135.05, and 135.6 ppm (Ar-C), 144.94 (>$\underline{C}$=N) 153.59 ppm (>$\underline{C}$=O). MS, *m/z* (%). M$^+$ 468(11), 168(18), 135(42), 1004(35), 41(100). Elemental analysis for $C_{20}H_{20}O_2N_8S_2$ mw: 468; Calc C 51.28, H 4.27, N 23.93, S 13.67; Found C 51.27, H 4.28, N 23.95, S 13.65.

Synthesis of 2,6-Dithia-1^4, 7^4-diamino-4(1,2)-benzena-1(2,5),7(5,2)-di(3-oxa-1,2,4-triazola)-cyclodecaphanes **8b–d**

A solution of **5** (3.66 g, 10 mmol), potassium hydroxide (1.3 g, 20 mmol), 1,ω-dibromo alkane **4** (10 mmol) in 200 mL of 80:20 aqueous methanol was warmed to reflux for 4 h. By concentrating the reaction mixture to 50%, a crystalline white solid was formed. This was collected by filtration and washed carefully with a diluted solution of potassium hydroxide to dissolve any polymeric material that may have precipitated out. The solid was then washed well with water, and crystallized from dimethylsulfoxide to give **8b–d**. The physical constants and the spectral data of the compounds **8b–d** are included in Table 1.

Synthesis of 2,8-Dithia-1^4, 9^4-diamino-5-oxa-1-(2,5),9(5,2)-di(3-oxa-1,2,4-triazola)-cyclotetradecaphane **9**

A solution of **6** (3.34 g, 10 mmol), potassium hydroxide (1.3 g, 20 mmol), 1, 5, ω-dibromo pentane **4** (10 mmol) in 200 mL of 80:20 aqueous methanol were warmed to reflux for 4 h. By concentrating the reaction mixture to 50%, a crystalline white solid was formed. This was collected by filtration and washed carefully with a diluted solution of potassium hydroxide to dissolve any polymeric material that may have precipitated out. The solid was

TABLE 2 **2** ^{1}H NMR Data

7a	δ: 3.26, (s, 4H,—S—C$\underline{H_2}$), 5.24 (s, 4H, 2× —N$\underline{H_2}$), 11.62 (s, 2H, 2× —N$\underline{H}$, D_2O-exchangeable
7b	2.015, (p, 2H, —S—CH_2—C$\underline{H_2}$—), 3.08 (t, 4H, 2× —S—C$\underline{H_2}$), 5.26 (s, 4H, 2× —N$\underline{H_2}$), 11.63 (s, 2H, 2×—N$\underline{H}$, D_2O-exchangeable
7c	1.69 (p, 4H, —S—CH_2—C$\underline{H_2}$—), 2.95 (t, 4H, —S—C$\underline{H_2}$) 5.21 (s, 4H, 2× —N$\underline{H_2}$), 11.63 (s, 2H, 2× —N$\underline{H}$, D_2O-exchangeable
7d	1.46 (p, 2H, —S—CH_2—CH_2—C$\underline{H_2}$), 1.65 (p, 4H, 2× —S—CH_2—C$\underline{H_2}$), 2.97 (t, 4H, 2× —S—C$\underline{H_2}$), 5.23 (s, 4H, 2× —N$\underline{H_2}$), 11.61 (s, 2H, 2× NH, D_2O-exchangeable
8b	2.18 (p, 2H, —N—CH_2—C$\underline{H_2}$, $J = 5.5$ Hz), 3.68 (t, 4H, 2× N—C$\underline{H_2}$, $J = 5.5$ Hz), 4.39 (s, 4H, 2 S—C$\underline{H_2}$) 5.31 (s, 4H, 2× —N$\underline{H_2}$)7.28—7.38 (m, 4H, Ar-H)
8c	1.41 (p, 4H, —N—CH_2—C$\underline{H_2}$, $J = 5.5$ Hz), 2.15 (t, 4H, 2× —N—C$\underline{H_2}$, $J = 5.5$ Hz), 4.19 (s, 4H, 2× S—C$\underline{H_2}$), 5.25 (s, 4H, 2× —N$\underline{H_2}$), 7.22—7.45 (m, 4H, Ar-H)
8d	δ 1.24 (p, 2H, —N—CH_2—CH_2—C$\underline{H_2}$, $J = 6.5$ Hz), 1.63 (p, 4H, 2× —N—CH_2—C$\underline{H_2}$, $J = 6.5$ Hz), 3.70 (t, 4H, 2× —N—CH_2, $J = 6.5$ Hz), 4.38 (s, 4H, 2× —S—C$\underline{H_2}$), 5.41 (s, 4H, 2× —N$\underline{H_2}$), 7.34—7.45 (m, 4H, Ar-H)
10a	1.52 (p, 4H, 2× —N—CH_2—C$\underline{H_2}$, $J = 6.5$ Hz), 3.28 (s, 4H, 2× —S—C$\underline{H_2}$), 3.58 (t, 4H, 2× —N—C$\underline{H_2}$, $J = 6.5$ Hz), 5.38 (s, 4H, 2× —N$\underline{H_2}$)
10b	1.40 (p, 2H, —N—CH_2—CH_2—C$\underline{H_2}$, $J = 6.5$ Hz), 1.63 (p, 4H, 2× —N—CH_2—C$\underline{H_2}$, $J = 6.5$ Hz), 3.31 (s, 4H, 2× —S—C$\underline{H_2}$), 3.67 (t, 4H, 2× —N—C$\underline{H_2}$, $J = 6.5$ Hz), 5.35 (s, 4H, 2× —N$\underline{H_2}$)
10c	2.99 (s, 4H, 2× —S—C$\underline{H_2}$), 4.89 (s, 4H, 2× N—C$\underline{H_2}$), 5.40 (s, 4H, 2× —N$\underline{H_2}$), 7.28—7.31 (m, 4H, Ar-H)
11a	2.03 (p, 2H, —S—CH_2—, $J = 7$ Hz), 3.09 (t, 4H, 2× —S—C$\underline{H_2}$, $J = 7$ Hz), 3.33 (s, 4H, 2× —N—C$\underline{H_2}$), 5.28 (s, 4H, 2× —NH_2)
11b	2.24 (p, 2H, —S—CH_2—, $J = 7$ Hz), 2.35 (p, 2H, —N—C$\underline{H_2}$—C$\underline{H_2}$, $J = 6.5$ Hz), 3.18 (t, 4H, 2× S—C$\underline{H_2}$, $J = 7$ Hz), 3.89 (t, 4H, 2× N—C$\underline{H_2}$, $J = 6.5$ Hz), 4.36 (s, 4H, 2× N—N$\underline{H_2}$)
11c	δ 1.58 (p, 4H, —N—CH_2—C$\underline{H_2}$, $J = 6.5$ Hz), 2.19 (p, 2H, —S—CH_2—C$\underline{H_2}$, $J = 7$ Hz), 2.95 (t, 4H, 2× —S—C$\underline{H_2}$, $J = 7$ Hz), 3.66 (t, 4H, 2× —N—C$\underline{H_2}$, $J = 6.5$ Hz), 5.22 (s, 4H, 2× —N$\underline{H_2}$)
11d	1.20 (p, 2H, —N—CH_2—C$\underline{H_2}$—, $J = 5.5$ Hz), 1.54 (p, 4H, —N—CH_2—C$\underline{H_2}$, J =5.5 Hz), 1.96 (p, 2H, —S—CH_2—C$\underline{H_2}$, $J = 6.5$ Hz), 2.94 (p, 4H, —S—C$\underline{H_2}$, $J = 6.5$ Hz), 3.61 (t, 4H, —N—C$\underline{H_2}$, $J = 5.5$ Hz), 5.31 (s, 4H, 2× —N$\underline{H_2}$)
11e	δ 1.94 (p, 2H, S—CH_2—, $J = 7$ Hz), 2.94 (t, 4H, 2× —S—C$\underline{H_2}$, $J = 7$ Hz), 4.89 (s, 4H, 2× —N—C$\underline{H_2}$), 5.48 (s, 4H, 2× —N—N$\underline{H_2}$), 7.24—7.35 (m, 4H, Ar-H)
12a	1.53 (p, 4H, 2× —N—CH_2—C$\underline{H_2}$, $J = 5.5$ Hz), 1.64 (p, 4H, 2× —S—CH_2—C$\underline{H_2}$, $J = 6.5$ Hz), 2.98 (t, 4H, 2× —S—C$\underline{H_2}$, $J = 6.5$ Hz), 3.61 (t, 4H, 2× —N—C$\underline{H_2}$, $J = 5.5$ Hz), 5.36 (s, 4H, 2× —N$\underline{H_2}$)
12b	1.20 (p, 2H, —N—CH_2—CH_2—C$\underline{H_2}$, $J = 5.5$ Hz), 1.57 (p, 4H, 2× —N—CH_2—C$\underline{H_2}$, $J = 5.5$ Hz), 1.70 (p, 4H, 2× —S—CH_2—C$\underline{H}$, $J = 6.5$ Hz), 2.96 (t, 4H, 2× —S—C$\underline{H_2}$, $J = 6.5$ Hz), 3.65 (t, 4H, 2× —N—C$\underline{H_2}$, $J = 5.5$ Hz), 5.30 (s, 4H, 2× —N$\underline{H_2}$)
12c	1.59 (p, 4H, 2× —S—CH_2—C$\underline{H_2}$, $J = 6.5$ Hz), 2.89 (t, 4H, 2× —S—C$\underline{H_2}$, $J = 6.5$ Hz), 5.08 (s, 4H, 2× —N—C$\underline{H_2}$), 5.38 (s, 4H, 2× —N$\underline{H_2}$), 7.11—7.23 (m, 4H, Ar-H)
13a	1.16 (p, 2H, —N—CH_2—CH_2—C$\underline{H_2}$, $J = 7$ Hz), 1.42 (p, 2H, —S—CH_2—C$\underline{H_2}$, $J = 7$ Hz), 1.60 (p, 4H, 2×—N—CH_2—C$\underline{H_2}$, $J = 7$ Hz), 1.66 (p, 4H, —S—CH_2—C$\underline{H_2}$, $J = 7$ Hz), 2.92 (t, 4H, 2× —S—C$\underline{H_2}$, $J = 7$ Hz), 3.59 (t, 4H, 2× —N—C$\underline{H_2}$, $J = 7$ Hz), 5.30 (s, 4H, 2× —N$\underline{H_2}$)
13b	1.48 (p, 2H, S—CH_2—CH_2—C$\underline{H_2}$, $J = 6.5$ Hz), 1.68 (p, 2H, —S—CH_2—C$\underline{H_2}$, J = 6.5 Hz), 2.93 (t, 4H, 2 × S—, $J = 6.5$ Hz), 5.17 (s, 4H, 2 × —N—C$\underline{H_2}$—), 5.43 (s, 4H, 2 × N—N$\underline{H_2}$), 7.07 — 7.26 (m, 4H, Ar-H)
16a	^{1}H NMR (DMSO-d_6): δ 2.82 (t, 4H, 2× CH_2—C$\underline{H_2}$), 5.15 (s, 4H, 2× N—N$\underline{H_2}$), 11.36 (s, 2H, 2× N$\underline{H}$ D_2O exchangeable
16b	^{1}H NMR (500 MHz/DMSO-d_6): δ 1.64 (p, 4H, —CH_2—C$\underline{H_2}$—), 2.47 (t, 2H, C═N—C$\underline{H_2}$), 5.10 (s, 4H, 2× N—N$\underline{H_2}$), 11.26 (s, 2H, 2× N$\underline{H}$)
17a	^{1}H NMR (DMSO-d_6): δ 1.21 (p, 4H, 2× C$\underline{H_2}$—C$\underline{H_2}$), 2.82 (t, 4H, 2× N═C—C$\underline{H_2}$), 3.41 (t, 4H, 2× N—C$\underline{H_2}$), 5.33 (s, 4H, 2× N—N$\underline{H_2}$)
17b	^{1}H NMR (DMSO-d_6): δ 0.99 (p, 2H, N—CH_2—CH_2—CH_2), 1.49 (p, 4H, 2× N—CH_2—CH_2), 2.83 (t, 4H, 2× N═C—CH_2), 3.43 (t, 4H, 2× N—CH_2), 5.32 (s, 4H, 2× N—NH_2)
17c	^{1}H NMR (DMSO-d_6): pentets at δ 1.40, 1.53, 1.63, and 1.73 (aliphatic-H), 3.01 (t, 4H, 2× N═C—C$\underline{H_2}$), 3.75 (t, 4H, 2× N—C$\underline{H_2}$), 5.42 (s, 4H, 2× N—N$\underline{H_2}$)
18a	^{1}H NMR (DMSO-d_6): δ 1.53 (p, 4H, 2× N—CH_2—C$\underline{H_2}$), 1.60 (p, 4H, 2× C═N—CH_2—C$\underline{H_2}$), 2.46 (t, 4H, 2× N═C—CH_2—C$\underline{H_2}$), 3.53 (t, 4H, 2× N—C$\underline{H_2}$), 5.21 (s, 4H, 2× N—N$\underline{H_2}$)
18b	^{1}H NMR (500 MHz/ DMSO-d_6): δ 1.08 (p, 2H, N—CH_2—CH_2—C$\underline{H_2}$), 1.57 (p, 8H, 2× N—CH_2—C$\underline{H_2}$ and 2× C═N—CH_2—C$\underline{H_2}$), 2.48 (t, 4H, 2× C═N—C$\underline{H_2}$), 3.61 (t, 4H, 2× N—C$\underline{H_2}$), 5.22 (s, 4H, 2× N—N$\underline{H_2}$)
18c	^{1}H NMR (500 MHz/DMSO-d_6): δ 1.08 (p, 2H, N—CH_2—CH_2—C$\underline{H_2}$), 1.57 (p, 8H, 2× N—CH_2—C$\underline{H_2}$ and 2× C═N—CH_2—C$\underline{H_2}$), 2.48 (t, 4H, 2× C═N—C$\underline{H_2}$), 3.61 (t, 4H, 2× N—C$\underline{H_2}$), 5.22 (s, 4H, 2× N—N$\underline{H_2}$)
18d	^{1}H NMR (DMSO-d_6) δ: 1.79 (p, 4H, 2× N═C—CH_2—C$\underline{H_2}$), 2.67 (t, 4H, 2× N═C—C$\underline{H_2}$), 3.50 (t, 4H, 2× N—C$\underline{H_2}$), 5.43 (s, 4H, 2× N—N$\underline{H_2}$), 7.20—7.58 (m, 4H, Ar-H)

TABLE 3 ^{13}C NMR (DMSO-d_6) Data

1	152.53 (C-3, ¿C=O); 167.33 (C-5, ¿C=S)
7b	28.43 and 29.17 (aliphatic C), 145.91 (¿C=N), 155.15 ppm (¿C=O)
7d	27.13, 28.35, 28.87 (aliphatic C), 145.75 (¿C=N), 154.72 ppm (¿C=O)
8d	23.56, 27.58, 30.65, and 45.53 (aliphatic C), 128.59, 130.89, 134.60 (aromatic C), 144.18 (¿C=N), 153.01 ppm (¿C=O)
10b	23.93, 28.31,31.00, and 44.78 (aliphatic C), 143.72 (¿C=N), 153.41 ppm (¿C=O)
10c	31.53 (S—CH_2), 45.51 (N—CH_2), 128.25, 130.51, and 135.99 (aromatic carbons), 143.92 (¿C=N), 153.57 ppm (¿C=O)
11a	14.59, 27.86, 28.64 (aliphatic carbons), 145.46 (¿C=N), 154.66 ppm (¿C=O)
11b	26.58, 27.37, 28.22, and 43.16 (aliphatic carbons), 142.79 (¿C=N), 153.11 ppm (¿C=O)
12c	28.55, 29.03, 46.12 (aliphatic carbons), 128.36, 129.43, and 135.67 (aromatic C), 145.69 (¿C=N), 154.14 ppm (¿C=O)
13a	22.85, 26.42, 27.62, 28.03, 45.15 (aliphatic carbons), 144.28 (¿C=N), 153.09 ppm (¿C=O)
13b	26.63, 27.14, 27.60, 46.38 (aliphatic carbons), 128.14, 128.61, and 135.16 (aromatic C), 145.98 (¿C=N), 153.83 ppm (¿C=O)
16a	21.20 (N=C—CH_2—), 147.47 (¿C=N), and 154.62 ppm (¿C=O)
16b	^{13}C NMR (DMSO-d_6): 24.18 (2× CH_2—CH_2), 24.91 (2× ¿C=N—CH_2) 148.36 (C=N) and 154.59 ppm (¿C=O)
17c	^{13}C NMR (DMSO-d_6): 21.21, 25.85, 28.47, 28.79, 32.23, 44.62, (aliph-C), 146.03 (¿C=N), 152.90 ppm (¿C=O)
18b	^{13}C NMR (solid state NMR): 20.02 (N—CH_2—CH_2—CH_2), 24.37 (2× C=N—CH_2—CH_2), 25.84 (2× C=N—CH_2), 28.53 (2× N—CH_2—CH_2), 42.83 (2× N—CH_2), 147.06 (2× ¿C=N), 153.16 ppm (2× ¿C=O)
18c	^{13}C NMR (DMSO-d_6): 24.58, 25.66, 26.49, 28.68, 29.61 (aliphatic carbons), 32.78 (N=C—C—CH_2), 34.02 (N—C—CH_2), 147.40 (¿C=N), and 153.78 ppm (¿C=O)
18d	^{13}C NMR (DMSO-d_6): 25.14 (N=C—CH_2—CH_2), 29.66 (N=C—C—CH_2), 46.04(N—C—Ar), 128.22, 129.30, 135.14 (aromatic carbons), 145.28 (¿C=N), and 153.55 ppm (¿C=O)

then washed well with water, and crystallized from dimethylsulfoxide to give **9**.

This compound was isolated (0.64 g, 16%) mp 276°C. IR : ν 1698 (>C=O). ^1H NMR (DMSO-d_6) δ 1.18 (p, 2H, —N—CH_2—CH_2—CH_2, $J = 6.5$ Hz), 1.57 (p, 4H, 2 × —N—CH_2—CH_2, $J = 6.5$ Hz), 3.08 (t, 4H, 2 × —S—CH_2, $J = 7$ Hz), 3.61 (t, 4H, 2× —N—, $J = 6.5$ Hz), 4.32 (t, 4H, 2 × —O—CH_2, $J = 6$ Hz), 5.34 (s, 4H, 2 × NH_2); MS, *m/z* (%) M^+ 402(100), 240(41), 159(60), 91(115), 69(29). Elemental analysis for $C_{13}H_{22}O_3N_8S_2$, mw: 402; Calcd C 38.81, H 5.47, N 27.86, S 15.92; Found C 38.79, H 5.51, N 27.84, S 15.93.

General Procedure for the Synthesis of 2,ω-Dithia-1⁴,7⁴-diamino-4(1,2)-9(1,2)-dibenzena-1(2,5),7(5,2)-di(3-oxa-1,2,4-triazola)-cyclodecaphanes, **10a–c, 11a–e, 12a–c, and 13a,b**

A solution of **7a–d** (10 mmol), potassium hydroxide (1.3 g, 20 mmol), and 1,2-bis(bromomethyl) benzene **2** (2.64 g, 10 mmol) or 1,ω-dibromo alkane **4** (10 mmol) in 200 mL of 80:20 aqueous methanol was warmed to reflux for 4 h. By concentrating the reaction mixture to 50%, a crystalline white solid was formed. This was collected by filtration and washed carefully with a dilute solution of potassium hydroxide to dissolve any polymeric material that may have precipitated out. The solid was then washed well with water, and crystallized from dimethylsulfoxide to give compounds **10a–c, 11a–e, 12a–c**, and **13a,b**. The physical constants and the spectral data of the compounds **10a–c, 11a–e, 12a–c**, and **13a,b** are included in Table 1.

General Procedure for the Synthesis of 1,ω-Bis(4-amino-5-oxo-1, 2,4-triazol-3-yl) Alkanes **16a–b**

Aliphatic dicarboxylic acids (10 mmol) and carbohydrazide (2 ommol) were mixed properly. The mixture was heated at 140°C in oil bath for 4 h. Water (50 mL) was added to the sticky mass and was kept overnight. A white solid was formed and was filtered, washed with water, and dried.

General Procedure for the Synthesis of 1⁴, ω⁴-Diamino-1(1,3),ω-(1,3)-di-(5-oxa-1,2,4-triazola)-cyclophanes **17a–c, 18a–d**

A solution of **16a** (10 mmol), potassium hydroxide (1.3 g, 20 mmol), 1,ω-dibromo alkane (10 mmol), and aqueous methanol (80:20, 200 mL) was refluxed together in a round-bottomed flask for 14 h. By concentrating the reaction mixture, a white solid was

formed. This was filtered and washed carefully with a diluted solution of potassium hydroxide to dissolve any polymeric material that may have precipitated out. The solid was then washed well with water and crystallized from DMF.

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