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## Synthesis of new estermacrocycles bearing xylyl structure

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### ABSTRACT

In this study 2,2'-thiobis (1-naphthoxy acetic acid) (diacid, NA) was prepared from the hydrolysis of corresponding diester. Diester crown was synthesized from the reaction of diacid and 1,2-bis(bromomethyl)benzene in nucleophilic conditions. Similar to this diester crown 2-naphthol derivative was prepared based on this procedure. A new diacid (benzo diacid, BA) was prepared from the reaction of 1,2-bis (bromomethyl)benzene and thiosalysilic acid. A new diester crown was prepared from the reaction of benzo diacid and 1,2-bis(bromomethyl)benzene. Also, a new pyridine containing diester was prepared from the reaction of 2,6-dichloropyridine and methylthioglycolate. Corresponding diacid was prepared from pyridine diester. Two new ester crowns, diester (1:1) and tetra ester (2:2) crowns were prepared from the reaction of pyridine diacid and 1,2-bis(bromomethyl)benzene. © 2012 Trade Science Inc. - INDIA

### KEYWORDS

Dinaphthosulfide;  
Diester crown;  
2,6-Dichloropyridine;  
Methylthioglycolate;  
Synthesis;  
1,2-  
bis(bromomethyl)benzene.

### INTRODUCTION

Since the first preparation by Pedersen in 1967<sup>[1]</sup>, crown ethers have played a significant role in many areas of chemistry. A distinctive feature of these compounds is the non-covalent nature of interactions with a series of guests such as their metal-ion complexations. Non-covalent chemical bonding is covered by the special broad field of chemistry called supramolecular chemistry and host-guest chemistry<sup>[2]</sup>. Supramolecular chemistry has received widespread acceptance and interest in many areas such as nanotechnology and biotechnology<sup>[3]</sup>. Nowadays, supramolecular compounds include not only cyclic polyethers, aza crown ethers, estercrowns, cyclic peptides and similar compounds, but also various more complex three-dimensional molecular structures and machines. These compounds

find wide applications in such new fields as nanotechnology<sup>[4]</sup>, nuclear waste separations<sup>[5]</sup>, enzymes<sup>[6]</sup> and new optical devices<sup>[7]</sup>.

There are several factors that influence the complexation abilities of crown ethers, aza crowns and estercrowns. The most important factor is the relationship between the macrocycle cavity size and the cation diameter<sup>[8]</sup>. If the metal ion is too large for the macrocycle cavity, sandwich complexes may be formed<sup>[9]</sup>. It has also been revealed that a closed macrocycle ring has much higher complexing ability than its corresponding open-chained structure named podand. An important property on macrocycles in host-guest chemistry in interaction between hosts and guests is preorganization. In this process before complete complex formation the structure of macrocycle rearrange to fit with guest and led to a more stable complex in comparison with open

chain receptors; this phenomena is called “the macrocyclic effect”. The potassium ion complexation strength with 18-crown-6 was found to be 6000-fold higher than that of its open-chained analog<sup>[10]</sup>.

A series of factors that influence the complexation strength of guests with receptors include the identities and placement of the heteroatoms, the number of heteroatoms in the cavity, the flexibility of the macrocycle ring and the addition of the side arms that provide additional ligating functionalities to the complexing species. The identities and placement of the heteroatoms influence complexation according to the Hard-Soft Acid Base theory of Pearson<sup>[11]</sup>. According to this theory, oxygen atoms that are hard Lewis base as donor atoms in the macrocyle ring favor significant interaction with hard cations, such as alkali and alkaline earth metal cations. Soft Lewis base donors, such as sulfur or nitrogen, into the macrocycle ring binds stronger towards softer cations, such as transition metals.

Addition of side arms with desirable functional groups that cannot be introduced directly into the ring is also an important route in supramolecular and host-guest chemistry<sup>[12]</sup>. In this case, three-dimensional ligation involves not only the cation being involve by the macrocycle ring,

but also the side arm of the macrocycle which wraps around the cation making the complex more stable.

In continuation of research on the synthesis of macrocycles<sup>[13]</sup>, in this research work new ester crowns were prepared.

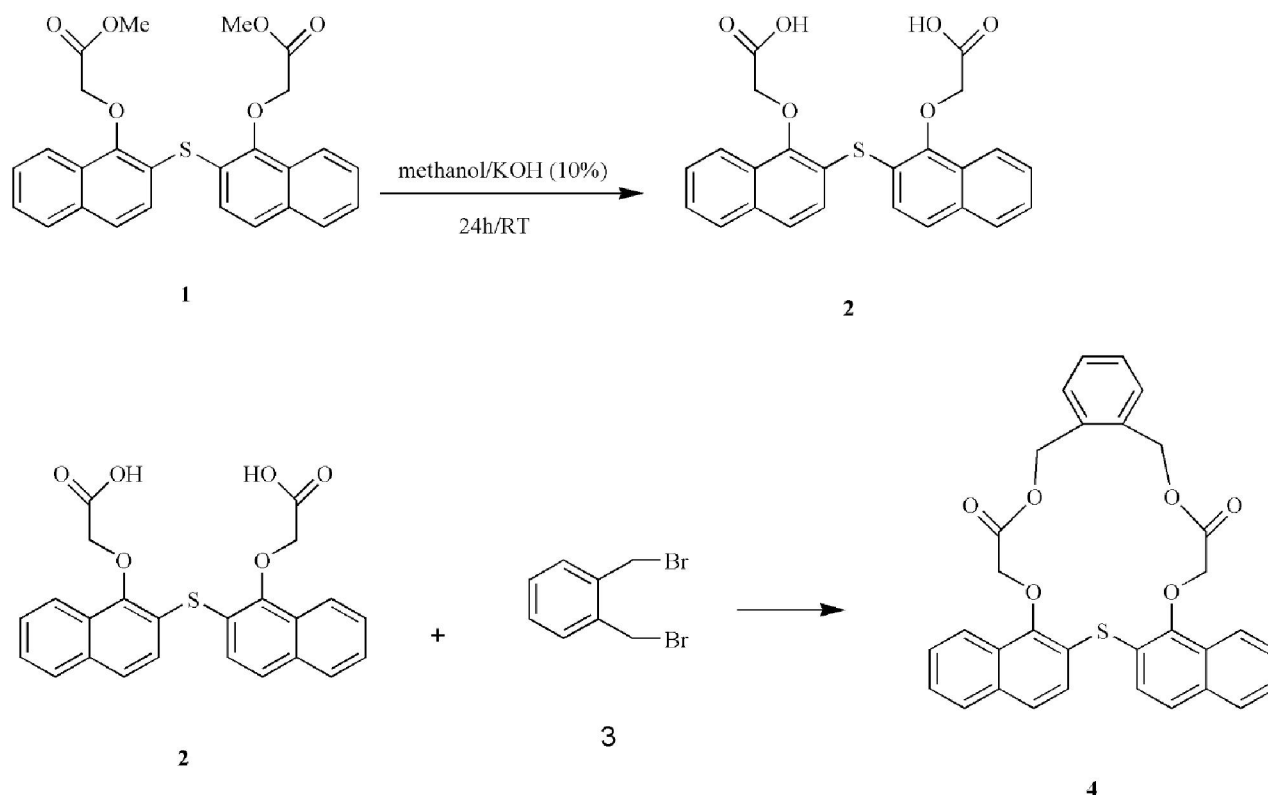
## RESULTS AND DISCUSSION

Dinaphthosulfide diester (1) and dinaphthosulfide diacid (2) were prepared according to the published procedure<sup>[14,15]</sup>. Nucleophilic reaction of diacid (2) and 1,2-bis(bromomethyl)benzene at room temperature afforded the diester macrocycle (4) in good yield.

Dinaphthosulfide diacid of 2-nphthol derivative (5) was prepared previously<sup>[16]</sup>. Diester macrocycle (6) was prepared from the reaction of diacid (5) and 1,2-bis(bromomethyl)benzene in acetonitrile and dimethylformamide (DMF) at room temperature in good yield.

Pyridine sulfide diacid (7) was reported previously<sup>[17]</sup>. Reactions of diacid (7) and dibromide (3) afforded two ester crowns, 8 and 9.

Benzene diacid (10) was prepared according to the published procedure<sup>[18]</sup> from the reaction of ben-



Scheme 1 : Synthesis of 1-naphthol ester crown.

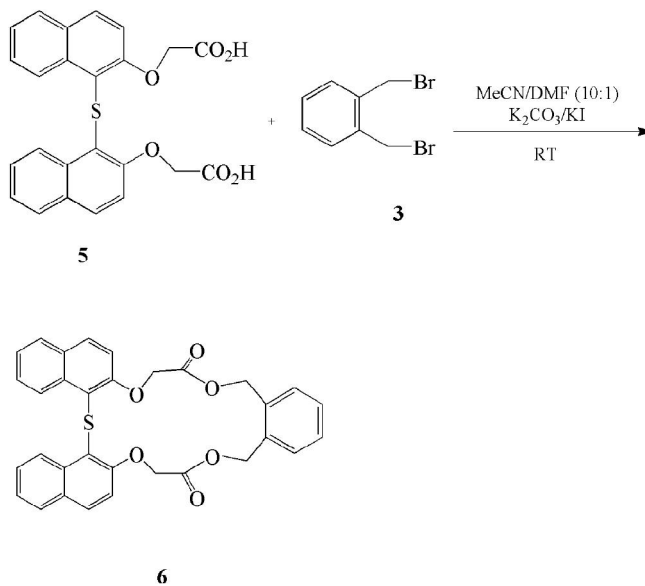
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zene diacid (10) and dibromide (3), diester crown (11) was prepared in good yield.

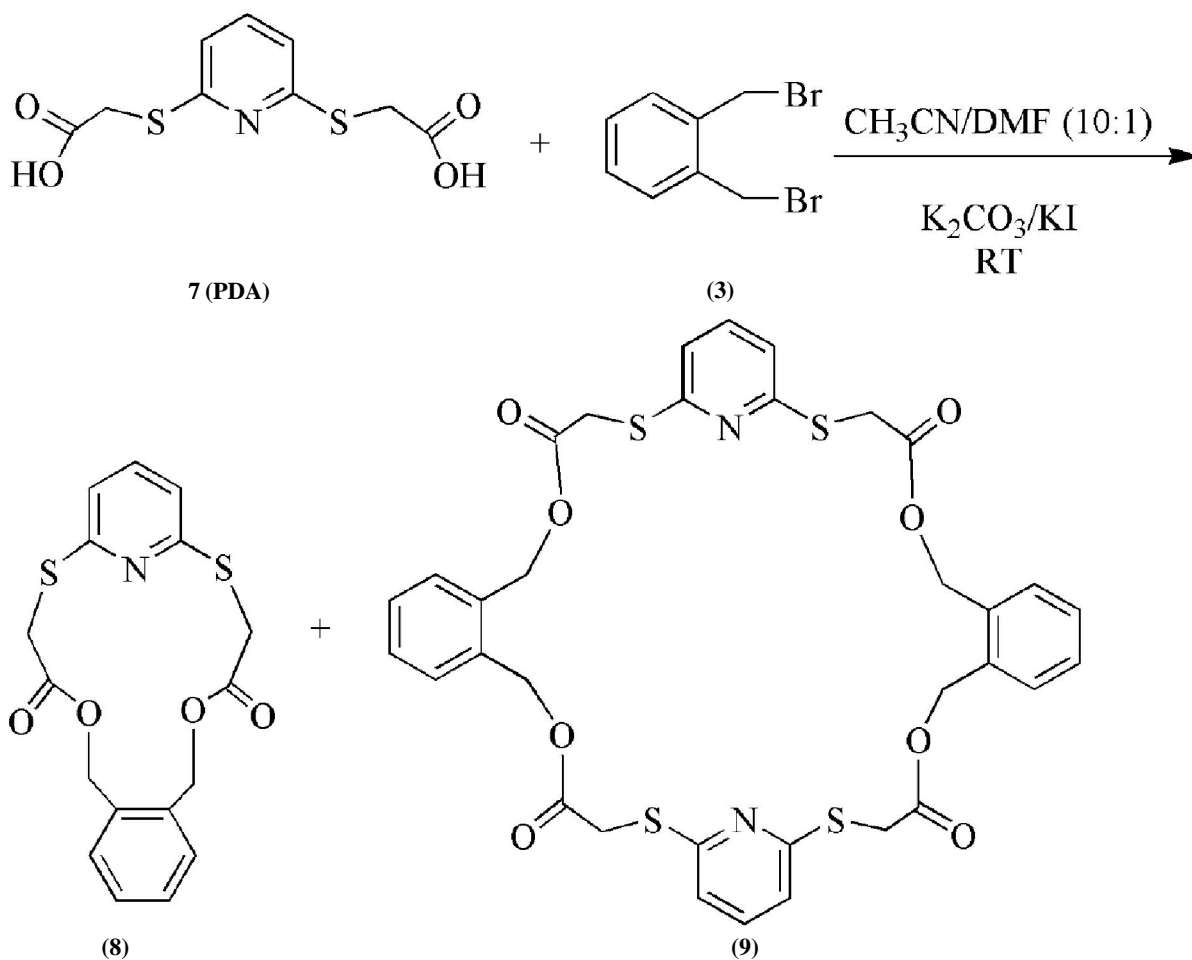
The key step for the synthesis of macrocycles is macrocyclization. Oligomerization and polymerization compete with macrocyclization, in high dilution conditions the macrocyclization overcomes to the oligomerization and polymerization. In high dilution experiments a large volume of solvent is required and is an expensive process. The structure of reacting species make difference between macrocyclization and oligomerization (and polymerization), the active groups near to each other raise the macrocyclization yields versus the preparation of linear products (oligomers and polymers). In some cases, far reacting groups afforded 1:1 (diacid:dibromide) and 2:2 products similar to **8** and **9**.

The reaction of diacids and dibromide under nucleophilic conditions afford the ester crowns. DMF is an aprotic nucleophilic solvent and the nucleophilic reactions perform at room temperature in this solvent. In the binary systems of DMF and acetonitrile the reac-

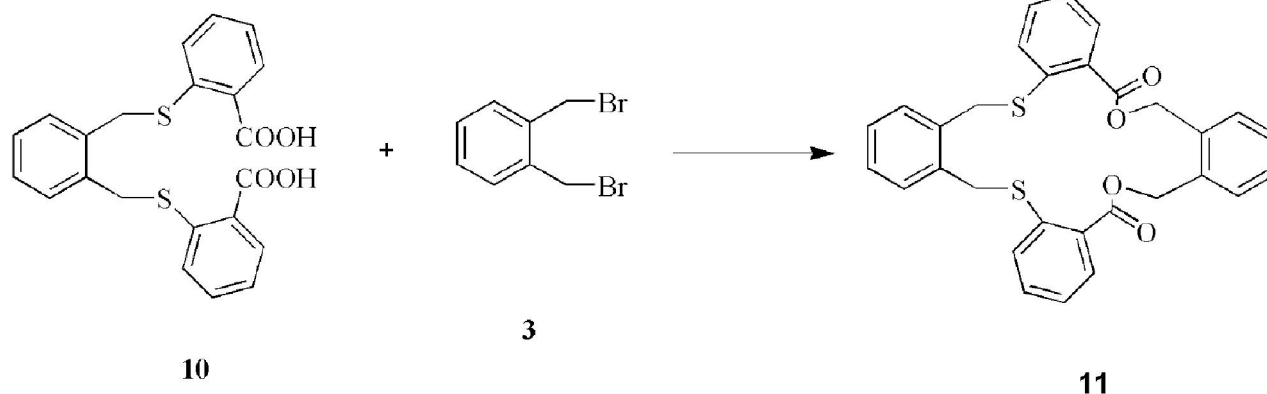
tions were carried out at room temperature. In the absence of DMF, the reactions perform under reflux conditions.



Scheme 2 : Synthesis of 2-naphthol ester crown.



Scheme 3 : Synthesis of pyridine ester crowns.



Scheme 4 : Synthesis of benzo ester crown.

## EXPERIMENTAL

The reactions were carried out in an efficient hood cupboard. All the materials were purchased from Merck, Fluka, Across Organics and Aldrich chemical companies. Acetonitrile and methanol were distilled and stored over molecular sieves. DMF was distilled over molecular sieves under reduced pressure and stored over them. Merck silica gel 40 was used for column chromatography. Merck silica gel 60 F254 TLC plates were used for thin layer chromatography (TLC). Compounds 1<sup>[14]</sup>, 2<sup>[14,15]</sup>, 5<sup>[16]</sup>, 7<sup>[17]</sup>, 10<sup>[18]</sup> were reported previously. The melting points (uncorrected) were measured with an Electrothermal engineering LTD 9100 apparatus. Elemental analysis was performed by a CHN-O- Rapid Heraeus elemental analyzer. IR spectra were measured on a Perkin-Elmer model 543 and FT-IR BRUKER spectrometers. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were obtained using BRUKER AVANCE DRX 500 MHz <sup>1</sup>H NMR and 125 MHz <sup>13</sup>C NMR instrument and mass spectra were obtained with Shimadzu GC-MS-QP 1100 EX model.

### General procedure for the synthesis of ester crowns

To diacid (**2** or **5** or **7** or **10**, 1mmol) in acetonitrile (50mL) were added dimethylformamide (DMF, 10mL), 1,2-bis(bromomethyl)benzene (1mmol), K<sub>2</sub>CO<sub>3</sub> (2mmol, 0.26g) and KI (catalytic). The reaction mixture was stirred at room temperature for 48h. After completion of the reaction (monitored by TLC), water was added (100mL) and extracted with chloroform (3×50mL), the chloroform layers were washed with

water (50mL) and HCl (10%, 50mL), respectively. The combined chloroform layers were dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated to afford the crude product which was purified by column chromatography on silica gel using appropriate solvents as eluent.

### Synthesis of 9,10-benzo-2,3;16,17-dinaphtho-4,7,12,15-tetraoxa-6,13-dioxo-1-thia-cycloheptadecane (**4**)

According to the general procedure this ester crown was prepared from the reaction of **2** and 1,2-bis(bromomethyl)benzene (**3**) and then purified by column chromatography using n-hexane/ethylacetate (4:1) as eluent to afford **4** in 76% yield and melting point of 153-154°C; IR (KBr): 3056, 2918, 1751, 1460, 1197, 1089, 855, 746cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) δ: 4.71 (s, 4H), 5.22 (s, 4H), 7.34-7.73 (m, 3H), 7.38-7.42 (m, 6H), 7.46-7.49 (m, 2H), 7.87 (d, J = 9.4Hz, 2H), 7.89 (d, J = 6Hz, 2H), 8.31 (d, J = 8Hz, 2H)ppm; <sup>13</sup>C NMR (125MHz, DMSO-d<sub>6</sub>) δ: 169.02, 157.27, 135.82, 134.64, 132.92, 130.76, 130.62, 130.14, 129.52, 128.10, 125.24, 125.02, 119.14, 117.87, 67.89, 65.15cm<sup>-1</sup>; MS (electron impact) m/z (relative intensity %): 536 [M]<sup>+</sup> (65), 478 (7), 316 (17), 300 (28), 187 (36), 144 (31), 119 (54), 105 (34), 91 (100), 44 (46); Anal. Cal. C<sub>32</sub>H<sub>24</sub>O<sub>6</sub>S: C, 71.63; H, 4.51. Found: C, 71.61; H, 4.52.

### Synthesis of synthesis of 9,10-benzo-2,3;16,17-dinaphtho-4,7,12,15-tetraoxa-6,13-dioxo-1-thia-cycloheptadecane (**6**)

Similar to general procedure this ester crown was prepared from the reaction of **5** and 1,2-bis(bromomethyl)benzene (**3**) and purified by column

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chromatography using n-hexane/ethylacetate (4:1) as eluent to afford **6** in 72% yield and melting point of 142-143°C; IR (KBr): 2976, 1926, 1783, 1625, 1573, 1452, 1267, 1041, 771 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) δ: 4.35 (s, 4H), 4.46 (s, 4H), 7.24 (t, J = 6Hz, 2H), 7.29-7.31 (m, 4H), 7.41 (dd, J = 6, 10Hz, 2H), 7.46 (dd, J = 7.4, 9.5Hz, 2H), 7.52 (s, 6H), 7.78 (dd, J = 6, 10Hz, 2H), 7.89 (d, J = 6Hz, 2H), 8.67 (d, J = 14Hz, 2H) ppm; <sup>13</sup>C NMR (125MHz, DMSO-d<sub>6</sub>) δ: 172.26, 169.89, 168.14, 168.07, 154.62, 141.85, 136.45, 135.12, 131.53, 131.47, 130.46, 130.17, 129.91, 129.33, 128.94, 128.61, 128.45, 128.28, 126.57, 125.42, 124.65, 118.21, 113.26, 68.11, 67.43 ppm; MS (electron impact) m/z (relative intensity %): 536 [M]<sup>+</sup> (76), 478 (4), 300 (24), 187 (26), 119 (51), 104 (53), 91 (100), 44 (52); Anal. Cal. C<sub>32</sub>H<sub>24</sub>O<sub>6</sub>S: C, 71.63; H, 4.51. Found: C, 71.66; H, 4.50.

### Synthesis of 1-aza-8,9-benzo-6,11-dioxa-5,12-dioxo-2,15-dipyridile-3,14-dithia-cyclopentadecane (**8**) and 1,16-diazo-8,9;23,24-dibenzo-6,11,21,26-tetraoxa-5,12,20,27-tetraoxo-2,30;15,17-dipyridile-3,14;18,29-tetrathia-cyclotriacontane (**9**)

Based on the general procedure these ester crowns were prepared from the reaction of **7** and 1,2-bis(bromomethyl)benzene (**3**) and purified by column chromatography using n-hexane/ethylacetate (3:1) as eluent to afford **8** and **9** in 65% and 23% yields and melting point of 154-155°C and 171-172°C, respectively.

#### Spectral data of **8**

IR (KBr): 3041, 2912, 2873, 1713, 1618, 1537, 1472, 1209, 1151, 1062, 732 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) δ: 4.15 (s, 4H), 5.24 (s, 4H), 7.06 (d, J = 10Hz, 1H), 7.19-7.23 (m, 1H), 7.25-7.27 (m, 1H), 7.46 (d, J = 8Hz, 1H), 7.51 (d, J = 7Hz, 1H), 7.82 (d, J = 9.5Hz, 2H) ppm; <sup>13</sup>C NMR (125MHz, DMSO-d<sub>6</sub>) δ: 174.21, 171.18, 168.94, 168.11, 159.26, 152.33, 144.86, 138.43, 137.77, 136.49, 133.54, 132.43, 131.45, 130.36, 128.91, 127.53, 127.26, 126.63, 125.57, 121.72, 120.43, 68.45, 55.73, 57.38 ppm; MS (electron impact) m/z (relative intensity %): 362 [M]<sup>+</sup> (11), 346 (28), 263 (17), 158 (100), 144 (95), 114 (87), 105 (63), 91 (52); Anal. Cal. C<sub>34</sub>H<sub>30</sub>N<sub>2</sub>O<sub>8</sub>S<sub>4</sub>: C, 56.49; H, 4.18; N, 3.88.

Found: C, 56.48; H, 4.17; N, 3.92.

#### Spectral data of **9**

IR (KBr): 3027, 2956, 2875, 1722, 1578, 1468, 1281, 1143, 791 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) δ: 4.18 (s, 8H), 5.27 (s, 8H), 7.07 (d, J = 10Hz, 2H), 7.21-7.26 (m, 2H), 7.31-7.33 (m, 2H), 7.49 (d, J = 7.5Hz, 2H), 7.53 (d, J = 7Hz, 2H), 7.85 (d, J = 9.5Hz, 4H) ppm; <sup>13</sup>C NMR (125MHz, DMSO-d<sub>6</sub>) δ: 174.26, 174.08, 171.58, 171.17, 169.97, 169.16, 164.13, 155.34, 153.39, 144.86, 144.54, 138.42, 137.77, 137.75, 136.47, 133.53, 133.49, 131.52, 130.37, 128.95, 127.51, 126.95, 126.61, 125.52, 121.70, 120.47, 68.47, 68.26, 57.72, 57.30 ppm; MS (electron impact) m/z (relative intensity %): 724 [M]<sup>+</sup> (4), 611 (100), 563 (74), 466 (100), 419 (27), 346 (24), 158 (100), 114 (93), 105 (76), 91 (57); Anal. Cal. C<sub>34</sub>H<sub>30</sub>N<sub>2</sub>O<sub>8</sub>S<sub>4</sub>: C, 56.49; H, 4.18; N, 3.88. Found: C, 56.51; H, 4.17; N, 3.90.

### Synthesis of 2,3;7,8;12,13;16,17-tetrabenzo-5,10-dioxa-4,11-dioxo-1,14-dithia-cyclooctadecane (**11**)

According to the general procedure this ester crown was prepared from the reaction of **10** and 1,2-bis(bromomethyl)benzene (**3**) and purified by column chromatography using n-hexane/ethylacetate (3:1) as eluent to afford **11** in 79% yield and melting point of 147-148 °C ; IR (KBr): 2915, 2643, 1691, 1461, 1318, 1256, 1054, 746 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) δ: 4.19 (s, 4H), 5.33 (s, 4H), 6.96 (d, J = 7.5Hz, 1H), 6.97 (d, J = 7.4Hz, 1H), 7.26 (d, J = 3.5Hz, 1H), 7.27 (d, J = 3Hz, 1H), 7.32-7.40 (m, 4H), 7.43-7.47 (m, 4H), 7.52 (d, J = 7.5Hz, 2H), 7.56 (t, J = 3.5Hz, 1H), 7.57 (d, J = 5.5Hz, 1H) ppm; <sup>13</sup>C NMR (125MHz, DMSO-d<sub>6</sub>) δ: 173.27, 168.88, 168.27, 143.81, 142.27, 136.79, 136.42, 133.52, 132.48, 130.94, 130.12, 129.87, 129.38, 128.65, 126.28, 59.13, 58.33 ppm; MS (electron impact) m/z (relative intensity %): 512 [M]<sup>+</sup> (78), 393 (14), 256 (11), 238 (21), 178 (18), 137 (100), 104 (81), 91 (53); Anal. Cal. C<sub>30</sub>H<sub>24</sub>O<sub>4</sub>S<sub>2</sub>: C, 70.29; H, 4.72. Found: C, 70.27; H, 4.73.

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