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# Synthesis of Redox-Active Macrocyclic Diimine Ligands as Flexible Building Blocks

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Large macrocyclic compounds have proven themselves as important building blocks in molecular design due to their interesting structures and properties. Application of these compounds to molecular machines and devices has also attracted much attention. A muti-step synthesis was successfully accomplished to obtain the bipyridyl containing macrocyclic ligand with potential redox-activities. The possible controllable binding properties of these compounds will examined later on. Subsequent coordination of the ligands to suitable transition metal centers and examination for the potential communications between these meal centers is also undergoing.

**Key Words: Macrocycle, Redox-active, Disulphide.**

## INTRODUCTION

Macrocycles form a major class of molecules that encompasses a wide range of structures and functional groups. Important recognition to the field of 'macrocycle chemistry' or the so-called 'host-guest chemistry' in the late 1980s inspired continually research interests in this area. Great efforts and much progress have been made since then to create macrocycles that possess numerous remarkable attributes such as binding[1], ion transport[2,3], gelation[4,5] and catalysis[6]. With the great current interest in nanoscience, materials science and supramolecular chemistry, numerous novel structures based on crowns have been prepared which ranged from nanotubes[7], light-emitting devices[8], to polymeric systems[9], *etc*. In recent years, much attention have also been focused on the exploration of supramolecular interactions between crowns and guest compounds as well[10,11]. Crowns have been integrated with other structural units and technologies, resulting in an array of novel compounds and materials.

Redox reactions between thiol and disulphide are very useful to control molecular structures and functions simultaneously[12]. However, using disulphide as a controller for macrocyclic structure is relative scare. It was reported that the binding properties of a macrocycle were controllable by chemical redox reactions of the disulphide linkage within the macrocycle[13]. Delius *et al.*[14] and others reported a macrocycle containing both a hydrazone and a disulphide linkage in which selective ring-opening of the macrocycle under thermodynamic control could be achieved at either the disulphide or the hydrazone linkage.

Here, we reported the synthesis of a new series of macrocyclic ligands both in close form and open form. In the molecule, two bipyridyls each covalently bonded to a phenol ring were bridged by a macrocyclic moiety that contained a sulphur unit, which are expected to be potential flexible building blocks for controllable binding or redox-active molecular switches.

## EXPERIMENTAL

Diethylene glycol, 2-bromopyridine, N,N-dimethylformamide, *m*-xylene, triethylamine and trifluoroacetic anhydride (TFAA) were distilled using standerd procedures[15] and were used freshly after distillation or kept under suitable environments. Anhydrous tetrahydrofuran, diethyl ether and toluene for synthesis were obtained from the Pure Solv-MD solvent purification system by Innovative Technology, Inc. and stored under nitrogen before use. Ammonium chloride and potassium nitrate were recrystallized from absolute ethanol prior to use. *Tetrakis*(triphenylphosphine) palladium[16], 2-trimethylstannylpyridine[17], were prepared according to literature procedures. All other reagents and solvents were purchased of analytical grade from Acros or Fluka and used as received.

### General procedure

**2: O-(4-Bromo-2,6-dimethylphenyl)dimethylthiocarbamate:** N,N-dimethylformamide (160 mL) was freshly distilled

over calcium hydride and placed in a 500 mL three-necked round bottom flask; to which 4-bromo-2,6-dimethyl phenol (**1**) (30 g, 150 mmol) was added to give a deep yellow to brown solution. The solution was then cooled to 0 ºC with an ice-water bath and degassed, followed by the slow addition of sodium hydride (60 % dispersion in mineral oil, 8.3 g, 200 mmol). The reaction mixture was stirred at 0 ºC for 1 h and allowed to warm up to room temperature before dimethylthiocarbamoyl chloride (22 g, 180 mmol) was added in slowly. The so-formed reaction mixture was stirred at room temperature for 1.5 h and then at 100 ºC for overnight under nitrogen. The thick reaction mixture was then cooled to room temperature and slowly poured into 250 mL of ice-water mixture. On standing, dark brown solids formed which were filtered off and recrystallized from absolute ethanol to remove most of the coloured impurities. Column chromatography on silica gel with pet. ether-$Et_2O$ (4:1, v/v) as eluent afforded the product as a white solid. Yield: 32.2 g, 75 %. $^1$H NMR ($CDCl_3$): δ 2.14 (s, -$CH_3$), 3.37 (s, 3H, -$NCH_3$), 3.47 (s, 3H, -$NCH_3$), 7.21 (s, 2H, -Ph).

**3: S-(4-Bromo-2,6-dimethylphenyl)dimethylthiocarbamate:** This was synthesized by modification of a literature procedure[19]. Compound **2** (20 g, 70 mmol) was placed into a 250 mL one-necked round bottom flask. To which 50 mL freshly distilled phenyl ether was added. The mixture was heated to reflux for 4 h with a heating mantle. During heating, the reaction mixture would change from yellow to dark brown and the reaction progress was monitored by TLC. After completion of the reaction, phenyl ether was distilled out under reduced pressure and the black residue was recrystallized from absolute ethanol, followed by column chromatography on silica gel with petroleum ether-$Et_2O$ (4:1, v/v) as eluent to afford the product as a white solid. Yield: 11 g, 55 %. $^1$H NMR ($CDCl_3$): δ 2.39 (s, 6H, -$CH_3$), 3.00 (s, 3H, -$NCH_3$), 3.25 (s, 3H, -$NCH_3$), 7.30 (s, 2H, -Ph).

**4: 4-Bromo-2,6-dimethylthioanisole:** Compound **3** (10 g, 35 mmol) was added to MeOH (60 mL) to give a suspension. With stirring, an aqueous NaOH solution (15 M, 4.7 mL) was added, followed by the addition of tetrahydrofuran (THF, 20 mL). The resulting yellow mixture was heated to reflux for overnight under nitrogen. A second portion of NaOH (15 M, 1.2 mL) was added and the reaction mixture was further refluxed for another 6 h and then cooled to room temperature. MeI (5.3 mL, 87 mmol) was added and the reaction mixture was stirred for overnight at room temperature. After completion of the reaction, the solvent was removed and dissolved in deionized water (150 mL) and extracted with $CHCl_3$. Subsequent drying over anhydrous $MgSO_4$, followed by filtration and distillation under reduced pressure gave the crude product as a yellow oil. Further distillation with a micro-distillation setup under reduced pressure gave the pure product as a colourless oil. Yield: 7.07 g, 94 %. $^1$H NMR ($CDCl_3$): δ 2.20 (s, 3H, -$SCH_3$), 2.52 (s, 6H, -$CH_3$), 7.23 (s, 2H, -Ph).

**5: 4-Bromo-2,6-*bis*(bromomethyl)thioanisole:** Compound **4** (10 g, 43.5 mmol) was dissolved in benzene (150 mL) in a 250 mL two-necked round bottom flask; to the solution was added N-bromosuccinimide (NBS, 21 g, 109 mmol) followed by addition of a catalytic amount of dibenzoyl peroxide (300 mg). A lamp was used to generate radicals for this photo-induced reaction and the reaction was heated to reflux in the presence of light under nitrogen for 5 h. The reaction progress was monitored by TLC using hexane as developing solvent. The resulting red reaction mixture was then allowed to cool to room temperature, filtered and washed with benzene. The combined filtrate was washed with aqueous $Na_2S_2O_3$ for three times followed by saturated brine. It was subsequently dried over anhydrous $MgSO_4$, followed by filtration and solvent evaporation under reduced pressure to give the crude product as a light-yellow solid. Finally, recrystallization from acetone-hexane (1:1, v/v) afforded the product as a white solid. Yield: 4.87 g, 28 %. $^1$H NMR ($CDCl_3$): δ 2.46 (s, 3H, -$SCH_3$), 4.82 (s, 4H, -$CH_2$Br), 7.62 (s, 2H, -Ph).

**6: 4-Bromo-2,6-*bis*(7-hydroxy-2,5-dioxahepty)thio anisole:** Sodium metal (1.5 g, 65 mmol) was cut and added slowly into freshly distilled diethylene glycol (100 mL) at room temperature. The reaction mixture was heated to around 40 ºC until all the sodium metal reacted. Compound **5** (5 g, 13 mmol) was then added and the reaction was heated to 100 ºC and stirred at this temperature overnight to give a light-yellow solution. The reaction mixture was cooled to room temperature, dilute with water (200 mL) and then extracted with $CHCl_3$ (3 mL × 200 mL). The combined organic layer was washed with deionized water for no less than six times and subsequently dried over anhydrous $MgSO_4$, followed by filtration and solvent evaporation under reduced pressure. Column chromatography on silica gel using EtOAc as the eluent followed by solvent removal to afford the product as a pale yellow oil. Yield: 5.12 g, 96 %. $^1$H NMR ($CDCl_3$): δ 2.23 (s, 3H, -$SCH_3$), 3.76-3.62 (m, 16H, O-$CH_2$-$CH_2$-O), 4.83 (s, 4H, Ph-$CH_2$-O), 7.64 (s, 2H, -Ph).

**7: Br-CROWN$_{SMe}$-Br:** NaH (60 % dispersion in mineral oil, 0.16 g, 6.8 mmol) was placed in a 250 mL three-necked round bottom flask connected with two dropping funnels and a reflux condenser. The system was degassed for no less than three pump-fill cycles and then anhydrous THF (100 mL) was added to the flask *via* cannula under nitrogen. Degassed solutions of **5** (0.9 g, 2.28 mmol) in anhydrous THF (10 mL) and **6** (1.0 g, 2.28 mmol) in anhydrous THF (10 mL) were transferred *via* cannula into each of the dropping funnels of the reaction setup. Additional anhydrous THF (*ca*. 30 mL) was transferred into each of the dropping funnels. After the reaction was heated to reflux, the solutions in the dropping funnels were added dropwise. The dropping rate was monitored from time to time to ensure both reagents added at the same rate and finished in *ca*. 4 h. After that the reaction mixture was heated to reflux for overnight before cooling to room temperature. The reaction mixture was then filtered and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel with $CHCl_3$-acetone (50:1, v/v) as eluent to afford the product as a white solid. Yield: 0.38 g, 25 %. $^1$H NMR ($CDCl_3$): δ 2.02 (s, 6H, -$SCH_3$), 3.69 (s, 16H, O-$CH_2$-$CH_2$-O), 4.76 (s, 8H, Ph-$CH_2$-O), 7.53 (s, 4H, -Ph).

**8: (HO)$_2$B-CROWN$_{SMe}$-B(OH)$_2$:** Compound **7** (0.5 g, 0.75 mmol) was dissolved in anhydrous THF (60 mL) in a 100 mL two-necked round bottom flask. *n*-BuLi (0.9 M in hexane, 1.8 mL, 1.65 mmol) was added dropwise to the solution at -78 ºC. The reaction mixture was stirred at -78 ºC for 0.5 h and tri-*n*-butyl borate (0.41 mL, 1.51 mmol) was added after which the

reaction mixture was kept at -78 ºC for 5 h. Then dilute hydrochloric acid (2 M, 2.6 mL, 5.25 mmol) was added and the reaction was allowed to warm to room temperature and stirred overnight. Deionized water (10 mL) was added to the resulting pale yellow solution and the product was extracted with $Et_2O$ (4 mL × 60 mL) and the organic extract was washed with deionized water (3 mL × 30 mL). The product was extracted with aqueous NaOH solution (2 M, 4 mL × 1 mL) and the product was precipitated from the combined aqueous layer upon slow addition of dilute hydrochloric acid (2 M) with stirring. The white solids precipitated were collected by filtration and washed adequately with water before drying in vacuum. Yield: 0.28 g, 59 %. $^1$H NMR (DMSO): δ 1.97 (s, 6H, -$SCH_3$), 3.56 (s, 16H, O-$CH_2$-$CH_2$-O), 4.69 (s, 8H, Ph-$CH_2$-O), 7.76 (s, 4H, -Ph), 8.10 (s, 4H, -$B(OH)_2$).

**9: 5-Bromo-2,2'-bipyridine:** 5-Bromo-2,2'-bipyridine was synthesized by modification of a literature procedure[17]. Freshly distilled 2-bromopyridine (1 g, 6.33 mmol) was reacted with *n*-BuLi (1.6 M in hexane, 4.3 mL, 6.96 mmol) at -78 ºC for 2 h followed by addition of a solution of $Me_3SnCl$ (1.3 g, 6.40 mmol) dissolved in dried $Et_2O$ (20 mL)-THF (5 mL). The reaction mixture was stirred at the same temperature for an additional hour before it was allowed to stir at room temperature overnight under nitrogen. After completion of the reaction, the reaction mixture turned into a yellow suspension. The solids were filtered off under nitrogen and the solvents were removed under reduced pressure to afford 2-trimethylstannylpyridine as a light yellow oil and used directly in the next step without further purification.

2,5-Dibromopyridine (1.5 g, 6.35 mmol) was added into a 50 mL two-necked round bottom flask and degassed. 2-Trimethylstannylpyridine dissolved in freshly distilled *m*-xylene (20 mL) was added *via* a cannula. The pale yellow solution was degassed by passing through nitrogen gas bubbles for 10 min before $Pd(PPh_3)_4$ (20 mg) was added. The reaction was stirred at 120 ºC overnight and the colour of the reaction mixture turned to dark brown. After cooling to room temperature, the reaction mixture was poured into aqueous NaOH solution (2 M, 50 mL) and the product was extracted with toluene (3 mL × 20 mL). The combined organic layers were subsequently dried over anhydrous $MgSO_4$, followed by filtration and evaporation under reduced pressure to afford the crude product as a yellow brown solid. Susequent purification by column chromatography on alumina with hexane-EtOAc (5:1, v/v) as eluent or on silica gel with $CHCl_3$-MeOH (200:1, v/v) as eluent afforded the product as a white solid. Yield: 0.32 g, 21 % for the two steps. $^1$H NMR ($CDCl_3$): δ 7.31 (m, 1H, py), 7.80 (td, $J_1$ = 8.0 Hz, $J_2$ = 1.8 Hz, 1H, py), 7.93 (dd, $J_1$ = 8.5 Hz, $J_2$ = 2.4 Hz, 1H, py), 8.32 (d, $J$ = 9.0 Hz, 1H, py), 8.37 (d, $J$ = 8.8 Hz, 1H, py), 8.67 (dt, $J$ = 4.8 Hz, 1H, py), 8.72 (d, $J$ = 2.3 Hz, 1H, py).

**10: 5-Bromo-5'-methyl-2,2'-bipyridine:** The procedure was similar to that of synthesis of compound **9** except that 2-bromo-5-methylpyridine (1.1 g, 6.34 mmol) was used instead of 2-bromopyridine as the starting material. Yield: 0.35 g, 22 % for two steps. $^1$H NMR ($CDCl_3$): δ 2.43 (s, 3H, -$CH_3$), 7.20 (m, 1H, bpy), 7.76 (t, $J$ = 6.0 Hz, 1H, bpy), 7.83 (d, $J$ = 7.2 Hz, 1H, bpy), 8.32 (d, $J$ = 6.5 Hz, 1H, bpy), 8.35 (d, $J$ = 6.2 Hz, 1H, bpy), 8.63 (d, $J$ = 5.6 Hz, 1H, bpy), 8.75 (d, $J$ = 8.0 Hz, 1H, bpy).

**11: 4-Bromo-2,2'-bipyridine:** 4-Bromo-2,2'-bipyridine was synthesized by modification of literature procedures[18] in three steps. 3-Chloroperoxybenzoic acid (MCPBA, 50-55 %, 2.4 g, 6.2 mmol) was dissolved in $CHCl_3$ (20 mL) and added dropwise into a solution of 2,2-bipyridine (1 g, 6.4 mmol) in $CHCl_3$ (20 mL). The reaction solution was stirred at room temperature for 30 h. The brown reaction mixture was washed with three portions of aqueous $Na_2CO_3$ solution (5 %, 20 mL) and the combined aqueous layers was extracted by $CHCl_3$ (3 mL × 10 mL). The combined organic layers were subsequently dried over anhydrous $MgSO_4$, followed by filtration and solvent evaporation under reduced pressure to afford the crude 2,2'-bipyridine N-oxide as a pale yellow solid. Subsquent purification by column chromatography on silica gel with EtOAc followed by EtOAc-MeOH (20:1, v/v) as eluent to afford the pure product as a white solid. Yield: 0.84 g, 65 %. $^1$H NMR ($CDCl_3$): δ 7.18-7.40 (m, 3H, bpy), 7.82 (t, $J$ = 6.8 Hz, 1H, bpy), 8.17 (d, $J$ = 6.7 Hz, 1H, bpy), 8.33 (d, $J$ = 7.2 Hz, 1H, bpy), 8.73 (d, $J$ = 5.0 Hz, 1H, bpy), 8.88 (d, $J$ = 8.0 Hz, 1H, bpy).

Concentrated sulphuric acid (98 %, 5 mL) was added carefully to a mixture of 2,2'-bipyridine N-oxide (0.5 g, 2.5 mmol) and $KNO_3$ (2 g) at 0 ºC in a 10 mL conical flask. The yellow solution was heated to reflux for 22 h. Then the reaction mixture was allowed to cool to room temperature and carefully poured onto crashed ice (50 g). The pH of the solution was adjusted to *ca.* 8.5 by adding aqueous NaOH solution (40 %) during which lots of yellow solids precipitated. The solids were filtered off and air-dried followed by recrystallization from $CH_2Cl_2$-hexane (1:2, v/v) to afford 4-nitro-2,2'-bipyridine N-oxide as light yellow crystals. Yield: 0.34 g, 53 %. $^1$H NMR ($CDCl_3$): δ 7.44 (m, 1H, bpy), 7.88 (td, $J_1$ = 8.0 Hz, $J_2$ = 1.8 Hz, 1H, bpy), 8.06 (dd, $J_1$ = 7.9 Hz, $J_2$ = 3.3 Hz, 1H, bpy), 8.36 (d, $J$ = 7.6 Hz, 1H, bpy), 8.80 (dd, $J_1$ = 5.6 Hz, $J_2$ = 1.6 Hz, 1H, bpy), 8.88 (d, $J$ = 8.0 Hz, 1H, bpy), 9.17(d, $J$ = 3.2 Hz, 1H, bpy).

Acetyl bromide (4 mL) and phosphorus tribromide (4 mL) was added sequentially to a solution of 4-nitro-2,2'-bipyridine N-oxide (1 g, 4.6 mmol) dissolved in glacial acetic acid (15 mL) at 0 ºC. The reaction mixture was heated to reflux for 3 h and cooled to room temperature before transferred onto ice (150 mL). The solution was neutralized with aqueous NaOH (40 %) till maximum of solids precipitaded. The white solids were filtered off and subjected to column chromatography on silica gel with $CH_2Cl_2$ as the eluent. 4-Bromo-2,2'-bipyridine was obtained as a colourless oil after solvent evaporation and crystallized on standing. Yield: 0.52 g, 45 %. $^1$H NMR ($CDCl_3$): δ 7.32 (t, $J$ = 5.5 Hz, 1H, bpy), 7.46 (dd, $J$ = 5.2 Hz, 1H, bpy), 7.80 (td, $J$ = 7.8 Hz, 1H, bpy), 8.37 (d, $J$ = 8.0 Hz, 1H, bpy), 8.46 (dd, $J$ = 6.5 Hz, 1H, bpy), 8.61 (d, $J$ = 2.0 Hz, 1H, bpy), 8.67(dd, $J_1$ = 4.4 Hz, $J_2$ = 1.0 Hz, 1H, bpy).

**12: (5-bpy)-CROWN$_{SMe}$-(5'-bpy) (LSMebpy):** Macrocyclic boronic acid $(HO)_2$B-CROWN$_{SMe}$-$B(OH)_2$ (66 mg, 0.11 mmol) and 5-bromo-2,2'-bipyridine (58 mg, 0.28 mmol) were placed in a 25 mL two-necked round bottom flask and to which an aqueous solution of $K_2CO_3$ (150 mg in 1 mL $H_2O$) was added followed by EtOH (0.5 mL). The reaction mixture was degassed and anhydrous toluene (15 mL) was added. It was degassed again before addition of $Pd(PPh_3)_4$ (20 mg). The

reaction mixture was heated to reflux overnight and subsequently cooled to room temperature. The reaction mixture was washed with deionized water (10 mL) and the aqueous layer was extracted by toluene (2 mL × 10 mL). The combined organic layer was washed by water for three times and dried over anhydrous $MgSO_4$ followed by filtration and solvent evaporation to afford the crude product as pale-yellow powders. The solid was washed with $Et_2O$ and EtOH followed by recrystallization from $CH_2Cl_2$-$Et_2O$ to give the pure product as white solid. Yield: 56 mg, 63 %. $^1$H NMR ($CDCl_3$): δ 2.04 (s, 6H, -$SCH_3$), 3.76 (s, 16H, O-$CH_2$-$CH_2$-O), 4.82 (s, 8H, Ph-$CH_2$-O), 7.30 (t, *J* = 5.8 Hz, 2H, bpy), 7.69 (s, 4H, Ph), 7.83 (t, *J* = 6.8 Hz, 2H, bpy), 7.97 (d, *J* = 6.4 Hz, 2H, bpy), 8.38 (d, *J* = 8.0 Hz, 2H, bpy), 8.47 (d, *J* = 8.0 Hz, 2H, bpy), 8.67 (d, *J* = 4.0 Hz, 2H, bpy), 8.80 (d, *J* = 1.6 Hz, 2H, bpy).

**13: (5-Mebpy)-CROWN$_{SMe}$-(5'-Mebpy) (MeL$_{SMe}$bpy):** The procedure was similar to that of synthesis of compound **12** except that 5-bromo-5'-methyl-2,2'-bipyridine (61 mg, 0.28 mmol) was used instead of 5-bromo-2,2'-bipyridine. Yield: 55 mg, 60 %. $^1$H NMR ($CDCl_3$): δ 2.03 (s, 6H, -$SCH_3$), 2.35 (s, 6H, -$CH_3$-bpy), 3.75 (s, 16H, O-$CH_2$-$CH_2$-O), 4.82 (s, 8H, Ph-$CH_2$-O), 7.56 (dd, $J_1$ = 8.0 Hz, $J_1$ = 1.6 Hz, 2H, bpy), 7.67 (s, 4H, Ph), 7.88 (dd, $J_1$ = 8.3 Hz, $J_1$ = 2.3 Hz, 2H, bpy), 8.25 (d, *J* = 8.1 Hz, 2H, bpy), 8.46 (s, 2H, bpy), 8.77 (d, *J* = 2.0 Hz, 2H, bpy).

**14: (4-bpy)-CROWN$_{SMe}$-(4'-bpy) (L'$_{SMe}$bpy):** The procedure was similar to that of synthesis of compound **12** except that 4-bromo-2,2'-bipyridine (58 mg, 0.28 mmol) was used instead of 5-bromo-2,2'-bipyridine. Yield: 49 mg, 55 %. $^1$H NMR ($CDCl_3$): δ 2.10 (s, 6H, -$SCH_3$), 3.75 (s, 16H, O-$CH_2$-$CH_2$-O), 4.80 (s, 8H, Ph-$CH_2$-O), 7.32 (t, *J* = 4.0 Hz, 2H, bpy), 7.46 (s, 2H, bpy), 7.80 (m, 6H, 4H on Ph and 2H on bpy), 8.40 (d, *J* = 7.6 Hz, 2H, bpy), 8.59-8.69 (m, 6H, bpy).

**15: (5-bpy)-CROWN$_{SS}$-(5'-bpy) (L$_{SS}$bpy):** This was synthesized by modification of a literature procedure[20]. Compound **12** (40 mg, 0.049 mmol) was dissolved in $CHCl_3$ and cooled to 0 ºC, to which a $CHCl_3$ solution of 3-chloroperoxybenzoic acid (50-55 %, 34 mg, 0.1 mmol) was added dropwise over 1 h. The reaction was stirred at 0 ºC for additional 2 h before warming up to room temperature and the addition of $Ca(OH)_2$ (7.3 mg, 0.1 mmol). The reaction mixture was filtered and the filtrate was dried in vacuum. Freshly distilled trifloroacetic anhydride (4 mL) was added and the mixture was heated to reflux for 1 h. The remaining acid was evaporated under reduced pressure and the residue was cooled down with an ice-water bath followed by carefully addition of ice-cooled $Et_3$N-MeOH (5 mL, 1:1, v/v). The reaction mixture was stirred at room temperature for 0.5 h and solvents were evaporated. Saturated aqueous $NH_4Cl$ solution was added and the product was extracted by $CHCl_3$. The combined organic layers were subsequently dried over anhydrous $MgSO_4$, followed by filtration and solvent removal under reduced pressure. The residue was redissolved in $CH_2Cl_2$ (15 mL) to which $I_2$ (12.5 mg, 0.05 mmol) was added and the reaction mixture was stirred at room temperature for 4 h. It was washed with aqueous $Na_2S_2O_3$ for three times followed by saturated aqueous NaCl for once. The aqueous layer was extracted by $CHCl_3$ (3 mL × 10 mL) and the combined organic layers were subsequently dried over anhydrous $MgSO_4$, filtrated and solvent evaporated. The residue was washed with EtOH to afford the product as yellow solid. Yield: 7.7 mg, 20 %. $^1$H NMR ($CDCl_3$): δ 3.73-3.83 (d, 16H, O-$CH_2$-$CH_2$-O), 4.89 (s, 8H, Ph-$CH_2$-O), 7.30 (m, 2H, bpy), 7.74 (s, 4H, Ph), 7.81 (td, $J_1$ = 8.5 Hz, $J_1$ = 2.1 Hz, 2H, bpy), 8.07 (dd, $J_1$ = 8.3 Hz, $J_1$ = 2.4 Hz, 2H, bpy), 8.46 (t, *J* = 9.4 Hz, 4H, bpy), 8.70 (d, *J* = 6.2 Hz, 2H, bpy), 8.96 (d, *J* = 2.4 Hz, 2H, bpy).

**16: (4-bpy)-CROWN$_{SS}$-(4'-bpy) (L'$_{SS}$bpy):** The procedure was similar to that of compound **15** except that compound **14** (45 mg, 0.055 mmol) was used instead of **12**. Yield: 7.4 mg, 17 %. $^1$H NMR ($CDCl_3$): δ 3.74-3.82 (d, 16H, O-$CH_2$-$CH_2$-O), 4.86 (s, 8H, Ph-$CH_2$-O), 7.35 (dd, $J_1$ = 8.2 Hz, $J_1$ = 2.3 Hz, 2H, bpy), 7.60 (dd, $J_1$ = 8.0 Hz, $J_1$ = 1.8 Hz, 2H, bpy), 7.84 (m, 6H, 4H on Ph and 2H on bpy), 8.46 (d, *J* = 7.4 Hz, 2H, bpy), 8.68-8.74 (d, d, s, 6H, bpy).

**Detection method:** $^1$H NMR spectra were recorded on a Bruker DPX 300 (300 MHz) or Bruker DPX 400 (400 MHz) Fourier-transform NMR spectrometers with chemical shifts reported relative to tetramethylsilane, $Me_4Si$.

## RESULTS AND DISCUSSION

**2** was synthesized by reaction of the starting material 4-bromo-2,6-dimethyl phenol (**1**) with dimethylthiocarbamoyl chloride in DMF under nitrogen using NaH as the base. A S-O rearrangement occurred in the high-boiling-point solvent phenyl ether according to a literature procedure[19]. The unstable carbamoyl group was cleaved by NaOH and the molecule was treated with MeI so as to form a methylthio group to protect the thiol. Dibromination with NBS in benzene in presence of light gave **5** and this could further be reacted with diethylene glycol under nitrogen in the presence of Na. The so-obtained **6** was used to react with **5** in a 1:1 ratio in dried THF using NaH as the base and the macrocyclic compound, Br-crown-Br(7), was synthesized. *n*-BuLi and *n*-butyl borate were used at -78 ºC to covert the di-bromo-crown compound to the corresponding di-boronic acid-containing crown. Various monobromo-2,2'-bipyridine compounds were synthesized by modification of literature procedures[14] and were reacted with the di-boronic acid-containing crown *via* Suzuki coupling reactions to afford the macrocyclic diimine ligands in open form (*i.e.*, SMe derivatives, **12-14**). Actually, we also tried the still coupling reaction as an alternative route in this stage, because this can shorten the total synthetic route for one step. After the reaction column chromatography on base alumina was found to be necessary for separating the pure product in this case. And result in an around 5-10 % improvement in yield but with slightly less purity due to NMR spectrum.

Disulphide formation reaction is the last and key step of this synthesis to realize our proposal. Unfortunately, almost all possible procedures to make disulphide compounds were tried and all failed but one. Although with a relatively low yield, the synthetic procedure described as following is the only one works in this system as we have found. The -SMe groups were first oxidized to -SOMe by 3-chloroperoxybenzoic acid, as revealed by NMR and mass spectrometry and the compound was then treated with trifluoroacetic anhydride, which was followed by oxidation with $I_2$, which after further purification gave the closed form ligands (*i.e.*, S-S derivatives, **15** and **16**). Formation of the disulphide-bridged ligands was

confirmed by NMR spectroscopy, which showed the disappearance of the $^1$H NMR signals of the methyl groups due to the -SMe group upon completion of the reaction.

## Conclusion

We have successfully synthesized a series of macrocyclic diimine ligands with the synthetic route as shown in Fig. 1. This kind of building blocks is potentially controllable due to the redox property of the disulphide linkage in the macrocycle. The complexation of macrocyclic diimine ligands with transition metal centers is undergoing and it is expected that the energy or electron transfer properties could be somehow affected by the switching of the disulphide linkage. Furthermore, the crown ether can perform as a potential host for molecule recognition.

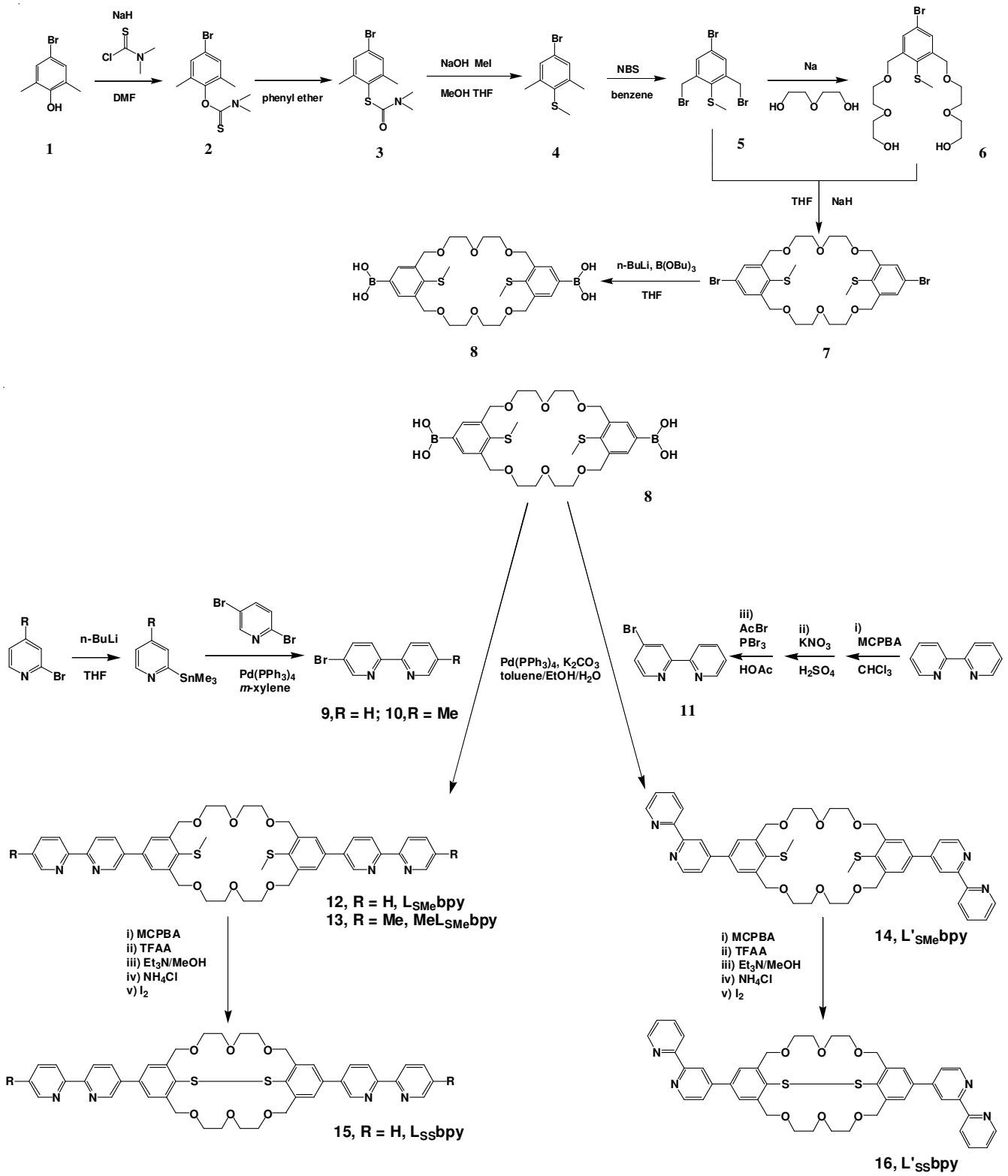


Fig. 1. Synthetic routes for the target ligands, **12-16** where R = H or Me

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