Synthesis of Hexaazacryptands Containing Furan and Benzene Groups in the Bridging Arms

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Two new hexaazacryptands were prepared. One contains two propylene groups and a 2,5-furandimethylene unit between the nitrogen atoms of each bridge. The other has two propylene groups and a *p*-phenylene unit between the nitrogen atoms of each bridge.

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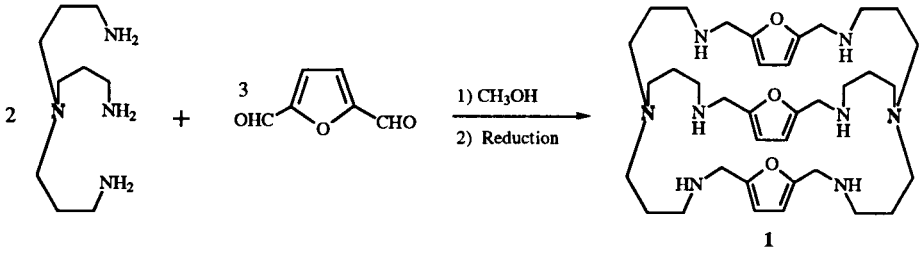
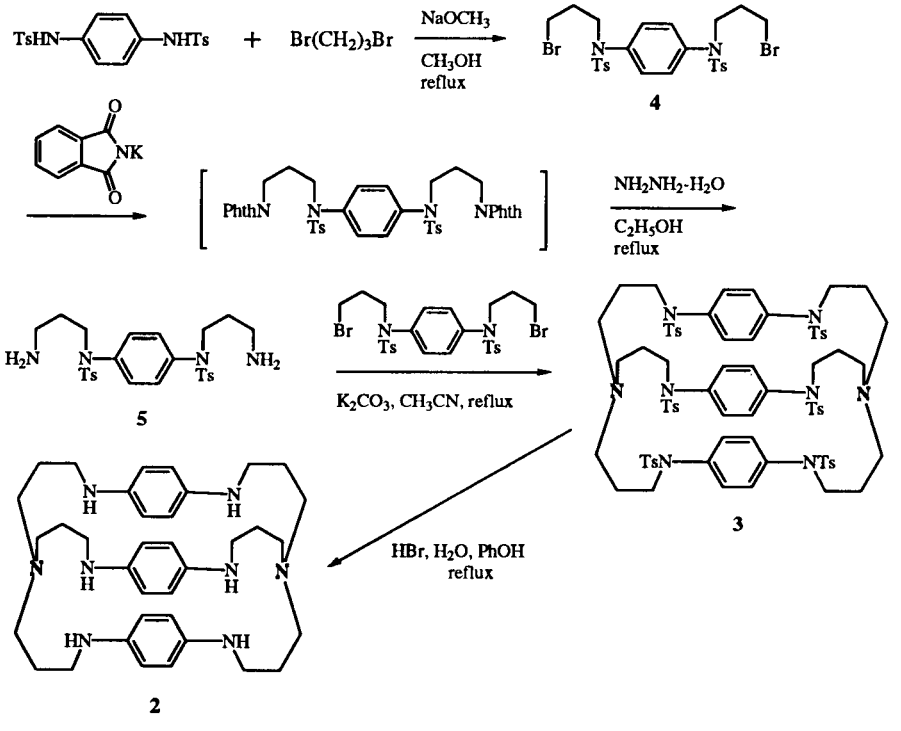
The cryptands have been prepared by a number of methods. The first synthetic method was a step-by-step procedure wherein an oligoethylene glycol diamine was treated with the corresponding diacid chloride followed by reduction of the cyclic diamide to form the cyclic diamine. The cyclic diamine was treated again with the diacid chloride and the cryptand diamide was reduced [1-5]. Some new one- and two-step procedures have been developed for the preparation of the traditional aliphatic polyether cryptands [6-12]. The cryptands form very strong complexes and are selective for certain metal ions [13,14].

Scheme 1



Scheme 2



The polyazacryptands have been studied in recent years. These aza cage compounds have interesting complexation properties [14-16]. In the first place, they are reasonably strong bases, at least in the first protonation step [15]. The small perazacryptands form especially strong complexes with lithium ions [16]. We herein report the synthesis of two new hexaazacryptands containing furan (**1**) and benzene (**2**) subcyclic groups.

Trifuran-containing hexaazacryptand **1** was prepared by treating two equivalents of tris(3-aminopropyl)amine with three equivalents of 2,5-furandicarbaldehyde to form the hexa-Schiff base followed by reduction as shown in Scheme 1. This cyclic condensation method has been used previously to prepare the perazacryptands containing only ethylene units between nitrogen atoms [17-22]. Hexaazacryptand **1** has both propylene and 2,5-furandimethylene units between the nitrogen atoms in the three connecting arms. The condensation reaction was carried out in methanol. The reaction was not successful in acetonitrile. The hexa Schiff base intermediate was not isolated.

Tribenzene-containing hexaazacryptand **2** was prepared by a one-step cyclization reaction between one equivalent of *N,N'*-ditosyl-*N,N'*-bis(1-aminopropyl)-*p*-phenylenediamine (**5**) with two equivalents of *N,N'*-ditosyl-*N,N'*-bis(3-bromopropyl)-*p*-phenylenediamine (**4**) to form hexatosyl intermediate **3** in a 31% yield (Scheme 2). Cryptand **3** was detosylated using the hydrobromic acid/phenol method to give the desired hexaazacryptand **2** in a 96% yield. Scheme 2 also shows the preparation of dibromide **4** by treating *N,N'*-ditosyl-*p*-phenylenediamine with an excess of 1,3-dibromopropane. An excess of 1,3-dibromopropane was used to suppress the 2:2 cyclization reaction which would form a dibenzotetraazacrown. Dibromide **4** was converted into diamine **5** by the Ing-Manske modification to the Gabriel synthesis which uses hydrazine to convert the bisphthalimide to the diamine [23].

EXPERIMENTAL

Proton nmr spectra were obtained at 200 MHz in deuteriochloroform. Molecular weights were determined by electron impact hrms. 2,5-Furandicarbaldehyde was prepared from 2,5-furandimethanol [24]. Starting materials were purchased from TCI (tris(3-aminopropyl)amine) or the Aldrich Chemical Company. Silica gel (230-400 mesh) (Merck) was used for column chromatography. Combustion analyses were obtained from MHW Labs, Phoenix, Arizona.

Preparation of Trifuran-containing Hexaazacryptand 1 (Scheme 1).

To 300 ml of methanol containing 0.75 g (0.04 mole) of tris(3-aminopropyl)amine was dropped 0.75 g (0.06 mole) of 2,5-furandicarbaldehyde in 100 ml of methanol. The mixture was stirred at room temperature for 20 hours. Sodium borohydride (3 g, 78 mmoles) was added and the mixture was stirred at 60° for five hours. The solvent was evaporated and 10 ml of 5% aqueous sodium hydroxide was added to the residue. This mixture was extracted three times with 10-ml portions of methylene chloride. The organic layers were dried over anhydrous sodium sulfate, filtered and the solvent was evaporated. The residue was purified on silica gel using methanol/ammonium hydroxide: 40/1 as eluant to give 0.10 g (75%) of **1** as an oil; ^{1}H nmr: δ 1.6 (t, 12 H), 1.75 (s, 6 H), 2.35 (m, 12 H), 2.6 (t, 12 H), 3.65 (s, 12 H), 6.1 (s, 6 H); ms: m/z 652.

Anal. Calcd. for $C_{36}H_{60}N_8O_3$: C, 66.22; H, 9.26. Found: C, 66.31; H, 9.38.

Preparation of *N,N'*-Ditosyl-*N,N'*-bis(3-bromopropyl)-*p*-phenylenediamine (**4**, Scheme 2).

Sodium (2 g) was dissolved in 250 ml of dry methanol and 8 g (19 mmoles) of *N,N'*-ditosyl-*p*-phenylenediamine was added. The mixture was stirred and refluxed for 30 minutes, then 37 g (0.27 mole) of 1,3-dibromopropane was added. The reaction mixture was refluxed for 12 hours. The methanol was evaporated and the excess of 1,3-dibromopropane was removed under high vacuum. The residue was crystallized twice from ethyl acetate to give 52% of **4**, mp 150-152°; ^{1}H nmr δ: 2.05 (m, 4 H), 2.44 (s, 6H), 3.46 (t, 4 H), 3.69 (t, 4 H), 7.01 (s, 4 H), 7.26 (d, 4 H), 7.43 (d, 4 H).

Anal. Calcd. For $C_{26}H_{30}Br_2N_2S_2O_4$: C, 47.42; H, 4.56. Found: C, 47.53; H, 4.55.

Preparation of *N,N'*-Ditosyl-*N,N'*-bis(3-aminopropyl)-*p*-phenylenediamine (**5**, Scheme 2).

Compound **4** (10 g, 15.2 mmoles) was stirred with 7 g (38 mmoles) of potassium phthalimide in 120 ml of dimethylformamide at 90° for 2 days. The solvent was evaporated and the residue was mixed with 30 ml of water. The mixture was filtered, washed with water and methanol and the residue was dried under vacuum. The residue (10 g, 12.7 mmoles) was added to 15 ml of hydrazine hydrate and 80 ml of ethanol. This mixture was refluxed for 1 day, 40 ml of 25% aqueous hydrochloric acid was added, and the resulting mixture was refluxed for 4 hours. The reaction mixture was cooled and mixed with 50 ml of ethanol and 50 ml of 25% aqueous hydrochloric acid. The solution was washed with chloroform, neutralized, and extracted with chloroform again. The chloroform layer was dried under anhydrous sodium sulfate and evaporated to give **5** in an 84% yield, mp, 147-149°; ^{1}H nmr: δ 1.58 (m, 4 H), 2.05 (b, 4 H), 2.42 (s, 6 H), 2.80 (t, 4 H), 3.63 (t, 4 H), 7.00 (s, 4 H), 7.24 (d, 4 H), 7.45 (d, 4 H).

Anal. Calcd for $C_{26}H_{34}N_4S_2O_4$: C, 58.87; H, 6.42. Found: C, 58.94; H, 6.58.

Preparation of Per-*N*-tosylated Tribenzene-containing Hexaazacryptand **3** (Scheme 2).

Intermediates **5** (2 g, 3.8 mmoles), **4** (5.1 g, 7.8 mmoles) and 6 g of potassium carbonate were refluxed in 150 ml of acetonitrile for 4 days. The solvent was evaporated under the vacuum and the residue was extracted with 150 ml of a 1/3 water/methylene chloride mixture. The organic layer was washed with 50 ml of water, dried, and evaporated. Compound **3** was purified on silica gel using chloroform/tetrahydrafuran, 10/1 as eluent to give a 31% yield of an oil; ^{1}H nmr: δ 1.38 (m, 12 H), 2.15 (m, 12 H), 2.46 (s, 18 H), 3.39 (m, 12 H), 6.82 (s, 12 H), 7.28 (d, 12 H), 7.43 (d, 12 H).

Anal. Calcd. for $C_{78}H_{90}N_8S_6O_{12}$: C, 61.50; H, 5.91. Found: C, 61.68; H, 6.09.

Preparation of Tribenzene-containing Hexaazacryptand **2** (Scheme 2).

Compound **3** (2.2 g, 1.4 mmoles) was refluxed with 100 ml of 48% aqueous hydrobromic acid and 6 g of phenol for 1 day. The reaction mixture was cooled and extracted twice with 60 ml portions of ether. The ether was evaporated and the solid was filtered and washed with ether. The solid was dissolved in 10 ml of water and neutralized with sodium carbonate and extracted with dichloromethane. The organic layer was washed with water, dried over sodium sulfate, and evaporated to give a 96% yield of **2** as an oil; ^1H nmr: δ 1.81 (m, 12 H), 2.51 (t, 12 H), 3.22 (m, 18 H), 6.42 (s, 12 H); M^+ (CI) m/z 598.

Anal. Calcd. for $C_{36}H_{54}N_8$: C, 72.24; H, 9.03. Found: C, 72.37; H, 9.12.

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