Synthesis and Characterization of Some Bifunctional 2B:2:1 Cryptands

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Methods for the synthesis of aromatic substituted diaza-polyoxamacrobicyclic compounds (benzocryptands) are described. New synthetic routes to cryptand precursors are developed and improvements in cryptand synthesis discussed and employed to prepare some bifunctional cryptands.

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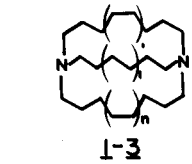
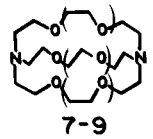
Introduction.

The chemistry of macrocyclic multidentate compounds with cation complexing ability has been explored extensively only during the past decade. Simmons and Park reported (1) the high dilution synthesis of a class of macrocyclic diamines such as **1-3** in 1968, while in the preceding year Pederson (2) had published his discovery of a broad range of polyether crown compounds of the type **4-6**. Lehn and co-workers (3) in 1969 succeeded in combining chemical features of these two closely related classes of molecules in forming the diaza-polyoxa-macrocycles, known as cryptands **7-9**, which have as their principal structural feature a central cavity which may serve to encapsulate a cation. It is the current objective of our research to synthesize a series of bifunctional cryptands, *i.e.*, cryptands which possess, in addition to the metal ion binding functionality, a reactive functional group which allows entire cryptands (or metal cryptates) to be covalenty attached to host molecules and thereby act as spin labels or tracers. Other efforts of this genre have been limited to preparations of derivatized EDTA-type ligands (4).



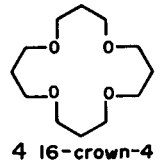
1-3

1 l-m-o; n=1
2 l-m=n=l
3 l=m=l; n=2

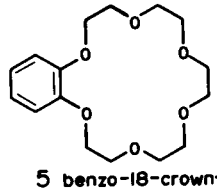


7-9

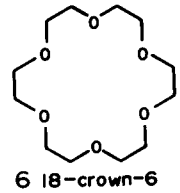
7 l=l, m=n=O 2:l:l
8 l=m=l, n=O 2:2:l
9 l=m=n=l 2:2:2



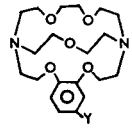
4 16-crown-4



5 benzo-18-crown-6



6 18-crown-6



10 Y = H
11 Y = NO_2
12 Y = NH_2
13 Y = N_2^+

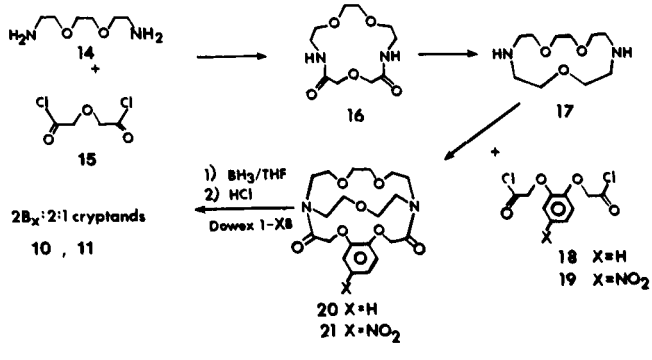
Herein is discussed the preparation of benzocryptand **10** and several derivatives **11-13** thereof in which reactive nitrogen containing groups have been introduced into the aromatic ring to produce bifunctional cryptands. The cation complexation properties of these materials will be reported elsewhere.

In detailed descriptions of preparative methods for cryptand syntheses (3c), high dilution condensations of diacid chlorides with diamines are seen to be the most important reaction steps. Since neither of the required starting materials are commercially available, and since the reported synthetic methods were found to be lengthy, we herein suggest simpler, more efficient syntheses. Modifications of literature procedures for cryptand cyclizations were employed to prepare the benzocryptands. Although Lehn, in a review article (3b), listed a few complexation constants for benzocryptands, their synthesis and characterization have never been detailed in the literature.

Syntheses.

The essential features of the benzocryptand syntheses are shown in Scheme I. Diamine **14** was initially prepared according to the Gabriel phthalimide method (3c), but we learned that this laborious procedure could conveniently be replaced by reduction of the diazide N_3-$(CH_2)_2$-O-$(CH_2)_2$-O-$(CH_2)_2$-N_3 **22** obtained either by direct reaction of sodium azide with Cl-$(CH_2)_2$-O-$(CH_2)_2$-O-$(CH_2)_2$-Cl or with the ditosylate of triethylene glycol **23**. **Caution: the diazide 22 is explosive.** Reaction of phosphorus pentachloride with diglycolic acid results in an improved synthesis of the other starting material, the diacid chloride **15**.

SCHEME I



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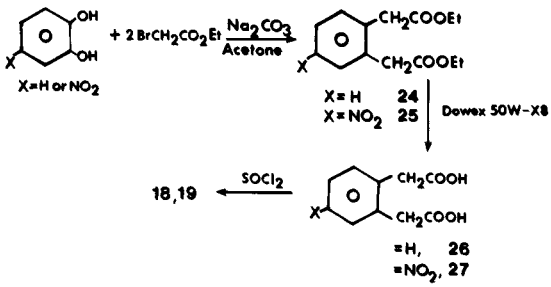
All cyclization steps were performed under high dilution conditions in toluene solution. Yields were higher than those obtained using benzene as solvent, possibly because lower reaction temperatures could be employed. Procedures used to make the monocyclic diamine **17** were otherwise the same as has been reported (3c).

The benzodiacidchlorides **18** and **19** required for the second cyclization step of Figure 1 were obtained as outlined Scheme II. Treatment of catechol or 4-nitrocatechol with ethyl bromoacetate gives diesters which are easily converted to the corresponding diacids by reaction with an aqueous slurry of a strong acid ion exchange resin. The desired diacid chlorides are obtained from thionyl chloride reaction with the diacids.

The second condensation step to form **20** and **21** proceeds in very high yield when toluene solvent is used and triethylamine base added to consume the hydrogen chloride formed during reaction. Subsequent borane reduction was performed strictly according to literature methods.

SCHEME II



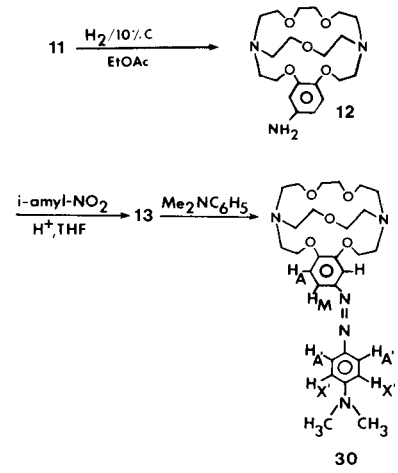
The nitro-cryptand **11** can also be obtained by direct nitration of **10** with nitric acid/acetic acid in chloroform. That reaction goes smoothly to give the hydronitrate salt which is passed through basic ion exchange column to produce pure product after one recrystallization from methanol.

The major objective of this synthesis project, the preparation of a bifunctional cryptand was accomplished by reduction of **11** to the aminobenzo cryptand **12** and its subsequent oxidation to the diazonium cryptand **13** as sketched in Scheme III. Verification of the ability of **13** to form covalent bonds with suitable substrates was obtained by reaction with dimethylaniline to produce the coupled azoaniline cryptand **30**. Encryptation of a paramagnetic lanthanide ion subsequent or prior to coupling will produce the desired covalently bonded spin label or T_1 relaxation agent (5,6).

Characterization of Compounds.

Cryptate precursors already reported were routinely checked for spectral purity. Characterization of new compounds was accomplished by examination of their proton nmr, mass, i.r. and uv spectra and by combustion analysis.

SCHEME III

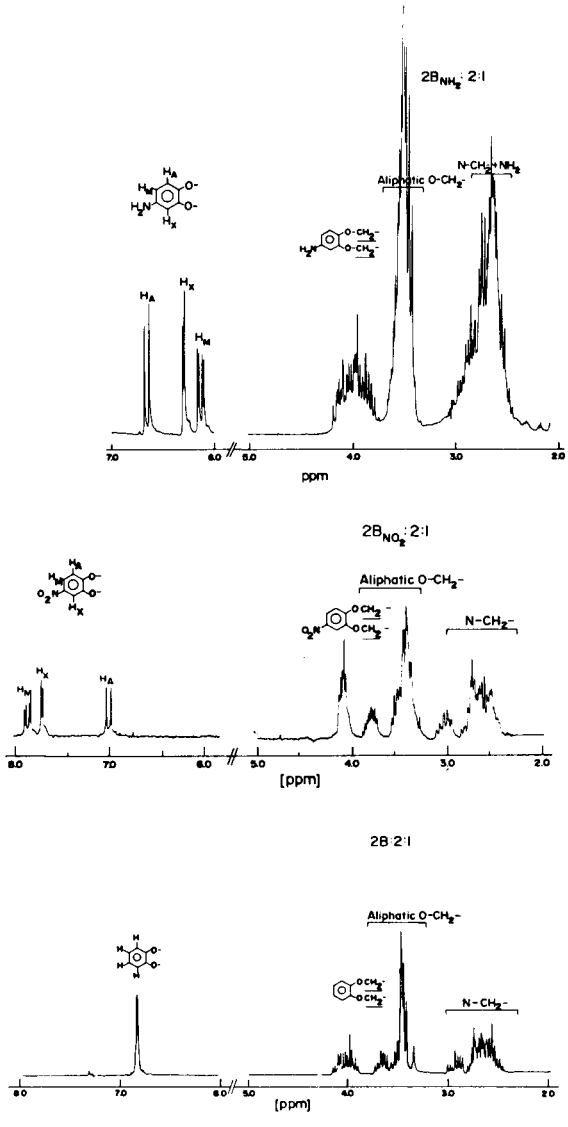


Detailed discussion of some spectral properties of only the principal target compounds, **10, 11,** and **12,** will be presented with data for other precursors being summarized in the Experimental, as are all mass spectral data.

The 2B:2:1 cryptand **10** is a white solid, whose ir spectrum in nujol confirmed (2) the presence of an ether linkage by a strong, broad band centered at 1132 cm^{-1}. Evidence for *ortho* substitution was gained from the aromatic ring C-H bending mode centered at 740 cm^{-1}. These features were maintained in all substituted cryptands prepared. Ultraviolet spectra were measured in both acetonitrile and water, and were compared with the model compound 1,2-dimethoxybenzene, which shows a bond absorption at λ max 275 nm characteristic of catechol derivatives. Compound **10** gave λ max 274 nm in acetonitrile and 275 nm in water.

The 180 MHz proton nmr spectrum of **10** in acetonitrile solution presented in Figure 1 contains separate, complex multiplets of intensity ratio 12:16 for the $N\text{-}CH_2$ and $O\text{-}CH_2$ protons. The twelve methylene hydrogens adjacent to the bridgehead appeared between 2.46-3.06 ppm, while protons next to oxygen were found between 3.44-4.18 ppm, in agreement with nmr data reported for the aliphatic cryptands (3c). The four protons of the aromatic oxyethylenes are found downfield from those of the similar aliphatic groups and are split into an AA'BB' multiplet. A broad aromatic resonance with intensity corresponding to four protons, centered at 6.90 ppm, completed the spectrum.

The uv spectra for the nitro-**11** and amino-**12** benzocryptands were recorded in acetonitrile-d_3 and compared to those for the model compounds 1,2-diethoxy-4-nitrobenzene **28** or 1,2-diethoxy-4-aminobenzene **29**. Absorptions for **11** had λ max 238, 340 nm, while those of **28** in ethanol were seen at 241, 338 nm. The aminobenzene **29** showed λ max 243, 299 nm, and can be compared to λ max 249, 304 nm for cryptand **12.**



1. Proton nmr spectra of benzocryptands **10, 11, 12.**

Proton nmr spectra for **11, 12** differ from that of the unsubstituted cryptand **10** in that multiplet patterns are detected for the benzenoid ring protonsin the substituted species. The aromatic AMX patterns assigned for **11, 12** are quite similar to those reported (7) for the model compounds **28,** and **29,** respectively. Spectral assignments for the aliphatic proton of the substituted cryptands are recorded in Figure 1. Taken together with elemental analysis data, spectral results therefore confirm the structures of this new series of benzo-cryptands.

The utility of **12** as a bifunctional cryptate was subsequently demonstrated as shown in Chart III. Non-aqueous diazotization with iso-amylnitrite (8) and coupling to *N,N'*-dimethylaniline (9) resulted in the azo-coupled cryptand **30** which showed the expected strong uv absorptions at λ max 290, 375 nm and the correct nmr spectrum as assigned in Figure 2. Studies employing these and other bifunctional cryptands and cryptates as covalently attachable nmr spin labels and relaxation agents are now in progress.

EXPERIMENTAL

Most reactions were performed under dry nitrogen atmosphere unless water was used as solvent. Toluene for high dilution condensations was purified by distillation over sodium metal. All other solvents were reagent grade and used without purification.

Diglycolic acid and 4-nitrocatechol were purchased from Aldrich Chemical Company. The resins, Dowex 1-8 (Cl form) 50-100 mesh and Dowex 50W-8 (H^+ form) 100-200 mesh, were obtained from J. T. Baker Chemical Company.

Melting points were determined in air employing a Thomas-Hoover apparatus using a capillary tube and are uncorrected. Ultraviolet spectra were taken by using a Cary-17 spectrophotometer. Infrared spectra were recorded with a Perkin-Elmer Model 457 spectrophotometer. Proton nmr spectra were obtained by using a Bruker WH-180 or a Varian T-60 spectrometer. Mass spectra were obtained locally employing a Hitachi RMU-6 spectrometer operating at 70 eV. Elemental analyses were performed by Spang Laboratories of Eagle Harbor, Michigan or Galbraith Laboratories of Knoxville, Tennessee.

Triethyleneglycol Disosylate (**23**).

To an erlenmeyer flask equipped with a stir bar was added 400 ml. of pyridine and 75 g. (0.5 mole) of triethyleneglycol. After cooling to 5-10° in an ice bath, 95.33 g. (0.5 mole) of *p*-toluenesulfonyl chloride was next added to the reaction flask in two protions over a period of 20 minutes. Then another 95.33 g. (0.5 mole) of *p*-toluenesulfonyl chloride was added in the same way. Near the completion of this addition, a slurry formed. Stirring was continued for another one and one-half hours after the addition had been completed. Next the slurry was poured into a solid ice and water mixture whereupon the ditosylate solidified and pyridine hydrochloride salt dissolved. After filtration, triethyleneglycol ditosylate was recrystallized from ethanol (yield 178 g., 78%, m.p. 78° [lit. (10) m.p. 78°]; ^{1}H nmr (deuteriochloroform): δ 2.4 (6H, singlet), 3.43-3.62 (8H, singlet and triplet), 4.1 (4H, triplet) and 7.2-7.65 (4H, two doublets, J = 8.0 Hz); ms: m/e 458.

1,8-Diazido-3,6-dioxaoctane (**22**).

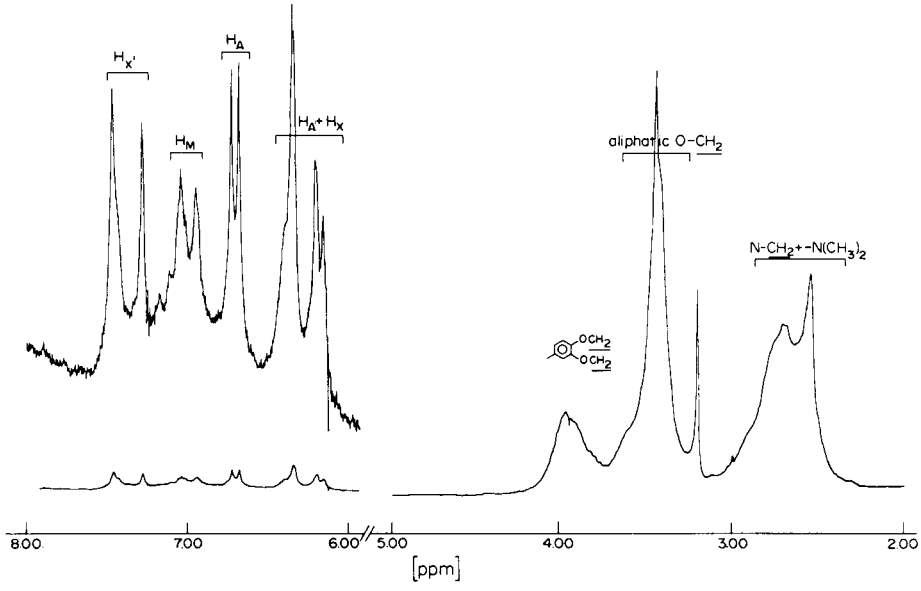
NOTE: All organic azides are known to be explosive. Although this particular diazide can be distilled, it is advisable to use it immediately after preparation and without further purification.

The ditosylate **23**, 45.8 g. (0.1 m), was placed in a round bottom flask and 100 ml. of ethanol and 50 ml. of water were added. To this slurry, 15 g. of sodium azide was next added. The mixture dissolved upon heating to 60° after one-half hour and was refluxed for 8-10 hours. The solvent was rotary evaporated to a wet paste, which was extracted with ether. The ether was then evaporated, yielding the crude 2-diazide as a yellow oil [16 g., 80% b.p. 83° at 0.3 mm, lit (11) b.p.]: ir (neat): 1890 cm^{-1} due to asymmetrical azide stretches; ^{1}H nmr (deuteriochloroform): δ 3.3 (4H, triplet) and 3.55 (8H, singlet and triplet); ms: m/e, 178.

CAUTION: Upon one occasion, the original azide reaction slurry was let go to dryness resulting in a violent explosion.

1,8-Diamino-3,6-dioxaoctane (**14**).

A three neck flash equipped with a mechanical stirrer, a reflux condenser, and a dropping funnel was charged with 5 g. of lithium aluminum hydride. The flask was evacuated, filled with dry nitrogen and attached to a bubbler to monitor the flow of nitrogen. To this was slowly added 300 ml. of dry THF (predistilled over lithium aluminum hydride) through dropping funnel while the flask was kept cold (5-10°) in an ice bath. Next, 10 g. of **22** in 30 ml. dry THF was added to the slurry of lithium aluminum hydride in THF over a period of one hour. After the addition was complete, the slurry was refluxed for 10 hours. Excess hydride was



2. Proton nmr spectrum of the dimethylaniline coupled cryptate **30**.

destroyed by dropwise addition of an aqueous 5% sodium hydroxide solution until evolution of hydrogen ceased. The slurry was filtered to remove hydroxide salts. Solvent from the filtrate was rotary evaporated and a yellow oil obtained. The crude reaction product was distilled to give the colorless product [6.1 g., 82%, b.p. 78°/0.2 mm, lit. b.p. (3c) 78-79°/0.2 mm]; ^{1}H nmr (deuteriochloroform): δ 1.38 (4H, broad singlet), 2.85 (4H, triplet), 3.48-3.60 (8H, singlet and triplet); ms: m/e, 148.

Diacid Chloride of Diglycolic Acid (**15**).

To a stirred mixture of 125 g. of phosphorus pentachloride in 400 ml. of chloroform at room temperature under a nitrogen atmosphere, was added 40.2 g. of diglycolic acid in small portions (2-3 g.). After a short while, a slurry formed. Stirring and addition were continued at room temperature for 5-6 hours. During this time the slurry dissolved. The solvent was removed by using a rotary evaporator and an oil was obtained. Upon distillation under vacuum (1.05 mm), phosphorus oxychloride first distilled at 25° and then the diacid chloride was collected as a colorless oil [b.p. 37-38°, lit. (3c) b.p. 56-57°/5 mm]; ^{1}H nmr (deuteriochloroform): δ 4.52 (4H, singlet); ms: m/e, 170.

1,7,13-Trioxa-4,10-diazacyclopentadecane (**17**).

i) Cyclization to Form 5,9-Dioxo-1,7,13-trioxa-4,10-diazacyclopentadecane (**16**).

The reaction of **14** with **15** was performed under high dilution conditions and at low temperature (0°) to minimize formation of polymers in the same general way described by Lehn (3c) except that use of toluene as solvent gave better yields.

To a 5-liter three neck flask equipped with mechanical stirrer and two pressure equalizing dropping funnels, all kept under a nitrogen atmosphere, 1.5 l. of dry toluene was first added. After cooling the vessel with an ice bath, the diamine **14**, 14.5 g. in 500 ml. of toluene, and the diacid chloride **15**, 17.1 g. in 500 ml. of toluene, were added separately to the two dropping funnels. The temperature of the toluene in the flask was lowered to 0° and kept cold throughout the reaction. Dropwise, simultaneous, addition was begun along with stirring. Addition was completed in 7 hours. The resulting mixture was stirred overnight and then filtered. The recipitated amine hydrochloride salt was removed by filtration and the solute stripped to dryness on a rotary evaporator. The white solid obtained was taken up and eluted with 50/50 v/v chloroform-benzene from a column (18 inches long, 1 inch diameter) packed with 50 g. of neutral alumina. After evaporation of solvent, the unreduced diamido monocycle **16** was obtained as a white solid [m.p. 149-150°, lit. (3c) m.p. 149-150°, yield 60%]; ^{1}H nmr (deuteriochloroform): δ 3.50-3.67 (singlet and multiplet), 4.08 (singlet) and 7.15 (singlet); ms: m/e, 246.

ii) Reduction to Form Monocyclic 2:1 (**17**).

A one liter three neck flask was equipped with a mechanical stirrer, a dropping funnel, and a reflux condenser. The flask was evacuated and kept under a nitrogen atmosphere. Then, 5 g. of lithium aluminum hydride and 200 ml. of dry THF was added to the flask which was cooled in an ice bath (5-10°). To this cold slurry, 5 g. of the diamide **16** monocycle was added as a solid in portions not exceeding more than 3/4 g. After 8 hours of reflux, excess lithium aluminum hydride was destroyed by dropwise addition of 5% sodium hydroxide solution. The hydroxide salt was filtered and the filtrate concentrated on a rotary evaporator. This yielded the white solid **17** which was recrystallized from petroleum ether [m.p. 89-90°, lit. (3c) m.p. 89-90°, yield 85%]; ^{1}H nmr (deuteriochloroform): δ 1.9 (2H, singlet), 2.75 (8H, triplet) and 3.60 (12H, singlet and triplet); ms: m/e, 218.

Bis(1,2-ethylacetoxy)benzene (**24**).

Ethylbromoacetate (30.3 g.) was slowly added to a stirred mixture of 27 g. of anhydrous potassium carbonate in 500 ml. acetone at room temperature. Next, 7 g. of cathecol in 100 ml. of acetone was added dropwise over a period of one-half hour. After addition, the mixture was refluxed overnight. The salts formed were removed by filtration and the sovlent was rotary evaporated leaving the oil **24** which was distilled (b.p. 145°/0.1 mm, yield 85%); ^{1}H nmr (deuteriochloroform): δ 1.4 (6H, triplet), 4.32 (4H, quartet), 4.85 (4H, singlet) and 6.98 (4H, singlet); ms: m/e, 282.

Anal. Calcd. $C_{14}H_{18}O_6$: C, 59.59; H, 6.38. Found: C, 59.36; H, 6.46.

Bis(1,2-ethylacetoxy)-4-nitrobenzene (**25**).

The procedure described for preparation of **24** was employed. After the rotary evaporation step, a solid was obtained which was recrystallized from ethanol to yield light yellow crystals of **25** (m.p. 74-76°, yield 88%); ^{1}H nmr (deuteriochloroform): δ 1.45 (6H, triplet), 4.30 (4H, quartet), 4.8 (4H, singlet), 6.92 (1H, doublet), 7.7 (1H, doublet) and 7.82 (1H, quartet); ms: m/e, 327.

Anal. Calcd. for $C_{14}H_{17}NO_8$: C, 51.37; H, 5.19. Found: C, 51.12; H, 5.11.

Hydrolysis of **24** to Form 1,2-Bis(oxyacetic acid)benzene (**26**).

Compound **24** (5 g.) was refluxed in water with 0.5 g. of Dowex 50W-x8 (H^+ form). The ethanol formed upon hydrolysis was distilled as the azeotrope in order to drive the reaction to completion, thus forming the diacid **26**. After 8 hours of reflux, the mixture was filtered to remove the resin. Upon cooling the diacid solidified and recrystallized from hot water [m.p. 181-182°, lit. (12) m.p. 181° yield 78%]; ^1H nmr (DMSO-d_6): δ 4.80 (4H, singlet), 6.98 (4H, singlet); ms: m/e, 226.

Hydrolysis of **25** to Form 1,2-Bis(oxayacetic acid)-4-nitrobenzene (**27**).

The same procedure was used as described for the preparation of **26**. Upon recrystallization from hot water, a light yellow solid was obtained (m.p. 173-176°, yield 85%); ^1H nmr (DMSO-d_6): δ 4.88 (4H, singlet), 6.95 (1H, doublet), 7.55 (1H, doublet) and 7.74 (1H, quartet); ms: m/e, 271.

Anal. Calcd. for $C_{10}H_9NO_8$: C, 44.28; H, 3.32. Found: C, 41.43; H, 3.82.

Note: Calcd. with 1 mole of water of crystallization: C, 41.52; H, 3.80, presence of water confirmed by ir.

1,2-Bis(oxacetylchloride)benzene (**18**).

To a one liter three neck flask equipped with a dropping funnel, a reflux condenser, and a mechanical stirrer, 10 g. of diacid **26** was added. The flask was evacuated and kept under nitrogen atmosphere. Then 40 ml. of freshly distilled thionyl chloride was added dropwise. The suspension was heated slowly and then to reflux. The solid goes into solution after one hour. After 5 hours of reflux, the excess thionyl chloride was evaporated using a water aspirator. A solid was obtained in this way, which was recrystallized from petroleum ether/acetone to yield white crystals of diacid chloride **18** (m.p. 50.5-51.5°, yield 90%); ^1H nmr (deuteriochloroform): δ 4.99 (4H, singlet), 6.95 (4H, singlet); ms: m/e, 263.

Anal. Calcd. for $C_{10}H_6Cl_2O_4$: C, 45.63; H, 3.04. Found: C, 45.81; H, 3.20.

1,2-Bis(oxyacetylchloride)-4-nitrobenzene (**19**).

The procedure applied was the same as that used for the preparation of **18**. Recrystallization from petroleum ether/acetone yielded a light yellow solid (m.p. 76-78°, yield 95%); ^1H nmr (deuteriochloroform): δ 5.15 (4H, singlet), 6.98 (1H, doublet), 7.70 (1H, doublet) and 7.88 (1H, quartet); ms: m/e, 308.

Anal. Calcd. for $C_{10}H_7Cl_2NO_6$: C, 38.96; H, 2.27. Found: C, 38.90; H, 2.32.

Preparation of 4,7,13,18,21-Pentaoxa-5,6-benzo-1,10-diazabicyclo[8.5.8]-tricosane, the 2B:2:1 Cryptand (**10**).

i) Cyclization to Form 2,9-Dioxo-4,7,13,18,21-pentaoxa-5,6-benzo-1,10-diazabicyclo[8.5.8]tricosane (**20**).

A three liter three neck flask equipped with a mechanical stirrer and two dropping funnels was evacuated and refilled with nitrogen. Then, 800 ml. of dry toluene was added and the solution was cooled to 0° in an ice bath. Next, 5 g. of monocycle 2:1 **17** and 6 g. of triethyl amine were mixed together in a separate flask and adjusted to a 250 ml. volume by adding toluene. Separately, 6.02 g. of the diacid chloride **18** was dissolved in a volume of 250 ml. with toluene. These two solutions were added to the two dropping funnels. Then, stirring was begun. Next, the solutions from the dropping funnels were added dropwise simultaneously to the cold toluene in the flask. Addition was completed in 5 hours, and stirring was continued for another 12 hours. The triethylamine hydrochloride salt which formed was then filtered and the supernatnat liquid was rotary evaporated. A paste was obtained which was dissolved in 50 ml. of 50/50 chloroform/benzene and was passed through a column (18" long, 1" diameter) packed with 30 g. of neutral alumina. Following rotary evaporation of the solvent, a fluffy solid of the diamide **20** was obtained which was used in the following reduction procedure (m.p. 154-157°, yield 86%). This compound was somewhat unstable. Attempts to purify it for analysis led to decomposition.

ii) Diborane Reduction of **20**.

Compound **20** (6.0 g.) was dissolved in 25 ml. of THF in a one liter three neck flask. Then, 30 ml. of 1*M* diborane in THF solution was added dropwise to the flask. The resulting solution was refluxed for 8 hours. Excess diborane was destroyed by the dropwise addition of water. Upon removal of the solvent by rotary evaporation, the diborane salt of 2B:2:1 was obtained as a white solid.

iii) Hydrochloride Salt Formation.

The diborane salt of 2B:2:1 obtained in the previous step was dissolved in 50 ml. of 6*N* hydrochloric acid and was refluxed for 8 hours. Water was rotary evaporated to yield the dihydrochloride salt of the 2B:2:1 cryptand.

iv) Cryptand 2B:2:1 (**10**).

A column 18" long and 1" in diameter was packed with Dowex 1-8 ion exchange resin (OH form). The resin commercially obtained was in the chloride ion form and was treated with potassium hydroxide to obtain the hydroxide form. The dihydrochloride salt of the 2B:2:1 cryptand was dissolved in 50 ml. of water and passed through the column and washed with water until the effluent tested neutral to litmus paper. The effluent was next rotary evaporated to yield the white solid of 2B:2:1 **10**. Upon recrystallization from methanol, pure white crystals of product were obtained (m.p. 74-75°, yield 78%); ^1H nmr (acetonitrile-d_6): δ 2.46-3.06 (12H, multiplets), 3.44-4.18 (16H, multiplets) and 6.90 (4H, singlet); ms: m/e 380; uv: λ max at 274 nm.

Anal. Calcd. $C_{20}H_{32}N_2O_5$: C, 63.16; H, 8.42. Found: C, 62.99; H, 8.60.

Preparation of 4,7,13,18,21-Pentaoxa-5,6,4-(nitro)benzo-1,10-diazabicyclo[8.5.8]tricosane, Cryptand 2BNO2:2:1 (**11**).

i) Cyclization to Form 2,9-Dioxo-4,7,13-18,21-pentaoxa-5,6,4-nitrobenzo-1,10-diaza bicyclo[8.5.8]tricosane (**21**).

The same procedure was used for the preparation of **20**. A light yellow fluffy solid was reduced to form the nitrobenzo cryptand, which decomposed when attempts were made to purify it.

ii) Diborane Reduction and Formation of 2BNO2:2:1 (**11**).

The same procedures were used as described in the synthetic scheme for 2B:2:1. Upon recrystallization from methanol, yellow crystals of 2BNO2:2:1 were obtained (m.p. 125°, yield 83%); ^1H nmr (acetonitrile-d_6):δ 2.44-3.14 (12H, multiplets), 3.24-4.24 (16H, multiplets), 6.98 (1H, doublet), 7.70 (1H, doublet) and 7.83 (1H, quartet); ms: m/e 425; uv (acetonitrile): λ max at 238, 300 and 338 nm.

Anal. Calcd. for $C_{20}H_{31}N_3O_7$: C, 56.47; H, 7.29. Found: C, 56.53; H, 7.40.

Preparation of 4,7,13,18,21-Pentaoa-5,6,4-(amino)benzo-1,10-diazabicyclo[8.5.8]tricosane, Cryptand 2BNH2:2:1 (**12**).

One hundred mg. of 2BNO2:2:1 **11** was dissolved in 10 ml. of dry ethylacetate, and 30 mg. of 10% palladium on charcoal, obtained from ROC/RIC Chemical Co., was added to the solution. This mixture was hydrogenated at room temperature and atmospheric pressure for 24 hours. The catalyst was removed by filtration and the solvent was rotary evaporated to yield 85 mg. of a light brown paste; ^1H nmr (acetonitrile-d_6): δ 2.35-3.30 (14H, multiplets), 3.35-4.26 (16H, multiplets), 6.10 (1H, quartet), 6.26 (1H, doublet) and 6.62 (1H, doublet); ms: m/e 395.

Anal. Calcd. for $C_{20}H_{33}N_3O_5$: C, 58.11; H, 8.47. Found: C, 58.27; H, 8.20.

Literature procedures (8) were employed to effect the non-aqueous diazotization of **12** and to coupel (9) it to dimethyl aniline in order to form the unstable azo derivative **30**.

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