Synthesis and Properties of a New Series of Trögerophanes

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A new series of macrocyclic compounds with one or two Tröger base skeletons has been synthesized by condensing mono-, di-, tri-, and teraethyleneglycol bis(*p*-aminophenoxy) ethers with formalin in the presence of concentrated hydrochloric acid in ethanol at room temperature for 13 days. This simple one-step cyclization provided **19** in remarkably high yield (46%) and **17**, **18**, and **20** in yields reflecting the strain of the rings and statistical factors. Complexation with lithium thiocyanate was observed for **20**, the structure of which was elucidated by X-ray crystallography.

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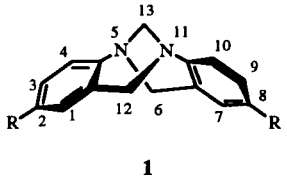
The Tröger base, 2,8-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine, **1** (R = Me) is a well-known chiral compound which was first synthesized by Tröger in 1887 by treating *p*-toluidine with formalin in the presence of hydrochloric acid in ethanol [1]. After its correct structure by Spielman was proposed in 1935 [2], chromatographic optical resolution of the Tröger base by means of a *d*-lactose column was achieved by Prelog and Wieland in 1944 [3]. This is well-known as the first classical demonstration that optical activity can originate from the asymmetric nature of trivalent nitrogen atoms. The chiral, rigid, and folded geometry of the Tröger base has recently attracted many chemists as a well-defined building block in designing ligands and host molecules. The most notable examples are molecular receptors by Wilcox and his co-workers [4]. It has been shown by Weber *et al.* [5] and Bond and Scott [6] that the quarternized Tröger bases can form inclusion complexes with aliphatic and aromatic solvents.



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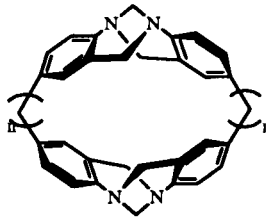


2-4 (n=1-3)

With the hope of obtaining chiral macrocycles having cavities suitable for selective inclusion of some chiral guests, several macrocycles containing Tröger base skeletons, **2-4**, have been synthesized in our laboratory [7]. Unfortunately, those compounds had only very low solubilities in common organic solvents for the inclusion and complexation studies to be made.

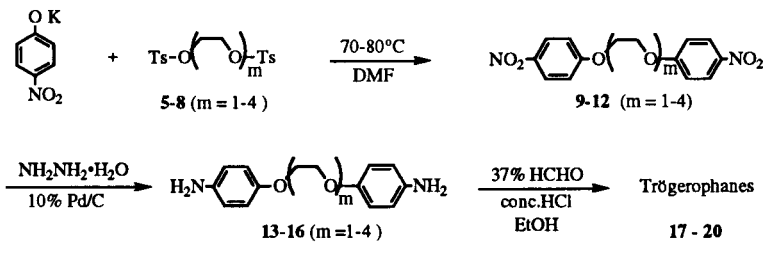
In this paper we report the synthesis of a new series of macrocycles including oxygen atoms in the ring that can, by taking advantage of the flexibility of the ether linkages, increase the solubility in organic solvents. In addition, the inclusion of ether oxygens of the crown ether type was thought to endow the macrocycles with complexing capabilities.

Results and Discussion.

The requisite precursors for the cyclization were synthesized *via* simple processes (Scheme 1).

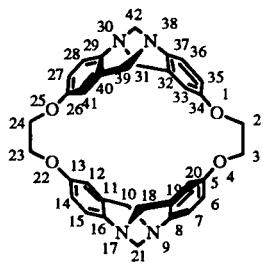
The bis(*p*-nitrophenyl) compounds **9-12** were prepared by treating the corresponding bis(*p*-toluenesulfonyl) compounds **5-8** with potassium *p*-nitrophenolate in *N*,*N*-dimethylformamide for one day. Reduction of **9-12** with hydrazine hydrate in the presence of 10% palladium on carbon in refluxing ethanol for 13 hours afforded the corresponding bis(*p*-aminophenyl) compounds **13-16** in excellent yields. These amines were very sensitive toward oxidation and had to be used immediately in the next condensation.

Scheme 1



Cyclizations of **13-16** were effected by reaction with 37% formalin in the presence of concentrated hydrochloric acid under moderately dilute conditions in ethanol at room temperature for 13 days. In the cases of ethylenedioxy and diethylenetrioxy units as the connecting chain, only dimeric Tröger base macrocycles were obtained in very low yields; 1,4,22,25-tetraoxa[4.4](2,8)trögerophane **17** in 2.5% yield, and 1,4,7,25,28,31-hexaoxa[7.7](2,8)trögerophane **18** in 3.0% yield, respectively [8].

changed when it is incorporated in the monomeric or dimeric cyclophane structures as can be seen from the ^{1}H nmr data. For example, the dimer **17** shows two doublets at δ 3.91 ppm (J = 17 Hz) and 4.60 ppm (J = 17 Hz) as well as a singlet for the endomethylene protons at 4.31 ppm. The ^{1}H nmr spectrum of the monomeric **20** reveals a characteristic AB quartet for the benzylic protons, doublets at 4.00 ppm (J = 17 Hz) and 4.60 ppm (J = 17 Hz), and a singlet at 4.36 ppm for the endomethylene protons.



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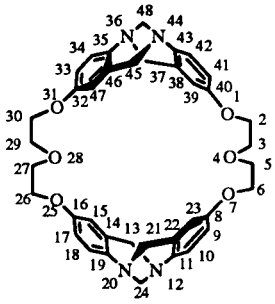

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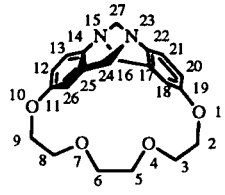
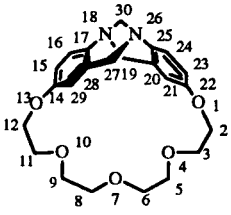


19



20

On the other hand, in the case of triethylenetetraoxy and tetraethylenepentaoxy chain, the monomeric cyclic Tröger bases; 1,4,7,10-tetraoxa[10](2,8)trögerophane **19** and 1,4,7,10,13-pentaoxa[13](2,8)trögerophane **20** were obtained in 46% and 34% yield, respectively. Evidently, since the Tröger base-forming condensation is slow, only the less strained trögerophanes could be produced effectively. While the dimeric compounds **17** and **18** have no strain problems, the necessity for the formation of the two Tröger base skeletons suffers from many competing side reactions. Actually, the formation of the dimers were, for unknown reasons, very difficult to reproduce. In contrast, the monomeric compounds **19** and **20** were prepared reproducibly in good yields.

Although, due to the paucity of the dimers **17** and **18**, we could not purify the samples sufficiently for obtaining correct elemental analyses, the following ^{1}H nmr spectral data, which are characteristic of the Tröger base unit as discussed below, and the molecular ions in their low resolution EI mass spectra established the structures. For the monomeric **19** and **20** the structures were determined by elemental analyses, ^{1}H and ^{13}C nmr and mass spectroscopic methods.

The most characteristic feature of the rigid Tröger base moiety is the appearance of an AB quartet for the nonequivalent benzylic protons as well as a singlet for the endomethylene protons in the ^{1}H nmr spectrum. For the open chain dimethoxy Tröger base **1** (R = OMe) [9] the benzylic protons appear as doublets at δ 4.08 ppm (J = 17 Hz) and 4.65 (J = 17 Hz) together with a singlet at 4.29 ppm. The structure around the Tröger base moiety is little

According to the initial CPK model examinations of the trögerophanes **19** and **20**, the cavity sizes were thought to be promising for inclusion of some small organic molecules. Although, as we had hoped, the trögerophanes synthesized this time had rather good solubilities in common organic solvents, no sign of inclusion of solvent molecules was detected on crystallization. In order to find the clue to the failure of inclusion, we searched for the most stable structures of **19** and **20** by molecular calculations. The lowest energy structures obtained by means of repeated MM3 stochastic searches [10] and semiempirical MOPAC-AM1-EF optimizations [11] are shown in Figures 1 and 2.

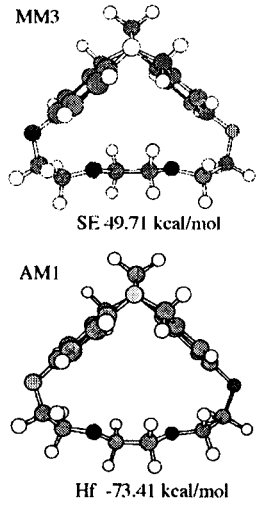


Figure 1. Lowest Energy Structures of **19** from Calculations.

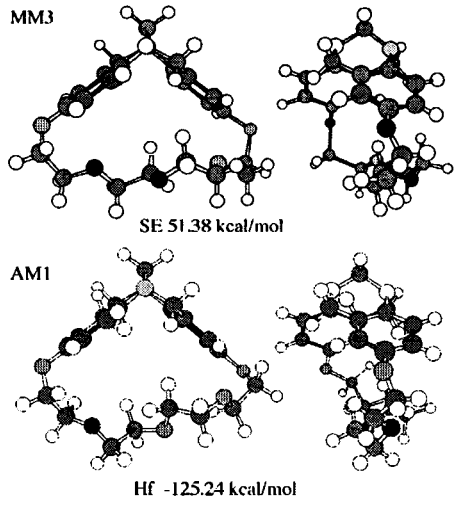


Figure 2. Lowest Energy Structures of **20** from Calculations.

In accord with the highest yield obtained in the present series, the aromatic rings of the Tröger base unit in **19** is spanned by the polyether chain with the right length. The longer polyether chain in **20**, therefore, has to be folded out of the mean molecular plane. If this were correct, the cavity surrounded by the resultant higher wall and the rigid Tröger base skeleton would have been more favorable for inclusion, even though it is considerably small.

Table 1
Crystal Data for **20**

Formula	$C_{23}H_{28}O_5N_2$
Crystal size(mm)	0.3 x 0.3 x 0.3
Molecular weight	412.48
Color	Colorless
Crystal system	Monoclinic
Space goup	$P2_1/a$ (No. 14)
a (Å)	11.590 (2)
b (Å)	11.143 (2)
c (Å)	16.348 (2)
β (degree)	103.411 (10)
V (Å^3)	2053.8 (4)
Z value	4
ρ_{calc} (g/cm^3)	1.334
μ (MoKα)	0.94 cm^{-1}
F(000)	880
Radiation	MoKα (λ = 0.71069)
Diffractometer	Rigaku AFC7R
Scan type	ω-2θ
Data collection range	6.0°<2θ<55.0°
Unique reflections	4972
Observed reflections	3174 [I > 3σ(I)]
Refined parameters	271
R [a]	0.042
R_w [b]	0.040
GOF	2.58
Residual positive peak	<0.18 e/Å^3
Residual ngative peak	<-0.20 e/Å^3

[a] $R = \Sigma||F_o|-|F_o||/\Sigma|F_o|$. [b] $R_w = [\Sigma w(|F_o|-|F_c|)^2/\Sigma w(F_o)^2]^{1/2}$ where $w = 4F_o^2/\sigma^2(F_o^2)$

Since the molecular calculations are basically for an isolated molecule, we performed an X-ray crystallographic analysis on **20** in order to get the information on the structural features of the cavity. The pertinent crystallographic data are summarized in Tables 1 and 2.

Table 2
Positional and Equivalent Isotropic Temperature Parameters of Nonhydrogen Atoms for **20**

Atom	X	Y	Z	B(eq)
O1	0.8599(1)	0.7272(1)	0.93882(8)	4.06(4)
O4	0.8400(1)	0.4527(1)	0.90978(9)	4.16(4)
O7	0.8460(1)	0.1995(1)	0.8799(1)	5.82(5)
O10	0.9701(1)	0.0618(1)	0.76534(9)	4.03(4)
O13	0.9014(1)	0.0962(1)	0.5855(1)	5.24(4)
N18	0.8992(1)	0.5970(1)	0.58382(9)	3.19(4)
N26	1.0900(1)	0.6070(1)	0.6842(1)	3.20(4)
C2	0.8424(2)	0.6297(2)	0.9924(1)	4.42(6)
C3	0.7684(2)	0.5303(2)	0.9452(1)	4.89(6)
C5	0.7799(2)	0.3927(2)	0.8354(1)	4.43(6)
C6	0.8539(2)	0.2891(2)	0.8201(1)	4.46(6)
C8	0.9415(2)	0.1183(2)	0.8994(1)	5.34(7)
C9	0.9363(2)	0.0189(2)	0.8383(1)	4.37(6)
C11	0.9689(2)	-0.0309(2)	0.7062(1)	4.45(6)
C12	0.9960(2)	0.0216(2)	0.6287(1)	4.78(6)
C14	0.9075(2)	0.2192(2)	0.5949(1)	3.20(4)
C15	0.8028(2)	0.2786(2)	0.5596(1)	3.15(4)
C16	0.8004(2)	0.4025(2)	0.5577(1)	2.98(4)
C17	0.9021(2)	0.4686(2)	0.5929(1)	2.61(4)
C19	0.8346(2)	0.6567(2)	0.6401(1)	3.37(4)
C20	0.9079(2)	0.6622(1)	0.7297(1)	2.60(4)
C21	0.8537(2)	0.6944(2)	0.7939(1)	2.90(4)
C22	0.9178(2)	0.6951(2)	0.8764(1)	2.94(4)
C23	1.0376(2)	0.6675(2)	0.8963(1)	3.13(4)
C24	1.0920(2)	0.6372(2)	0.8326(1)	2.95(4)
C25	1.0281(2)	0.6340(1)	0.7488(1)	2.62(4)
C27	1.1143(2)	0.4777(2)	0.6778(1)	3.58(5)
C28	1.0046(2)	0.4087(2)	0.6335(1)	2.74(4)
C29	1.0075(2)	0.2835(2)	0.6332(1)	3.32(5)
C30	1.0197(2)	0.6452(2)	0.6018(1)	3.84(5)

As shown in Figure 3, the structure around the Tröger base moiety is almost the same as has been found for the Tröger base [12] and its derivatives [13].

For example, the dihedral angle between the least-squares planes containing the two aryl rings was 102.5° and in the range of 89-104° for the open chain compounds [13]. The most notable is the fact that a part of the polyether chain of **20** is folded inward filling the cavity of the macro ring, unlike the prediction by the molecular calculations that the methylene protons are directed away from the molecular cavity. This self-filling apparently precluded inclusion of a guest molecule, although the crystal packing force should be taken into account in the solid state.

Actually, in solution the polyether chain appears symmetrical in structure judging from the ^{1}H nmr spectrum at room temperature [Figure 4 (a)]. Even when the temperature was lowered to -115° in deuteriomethylene chloride-carbon disulfide, no appreciable change in the spectrum was observed.

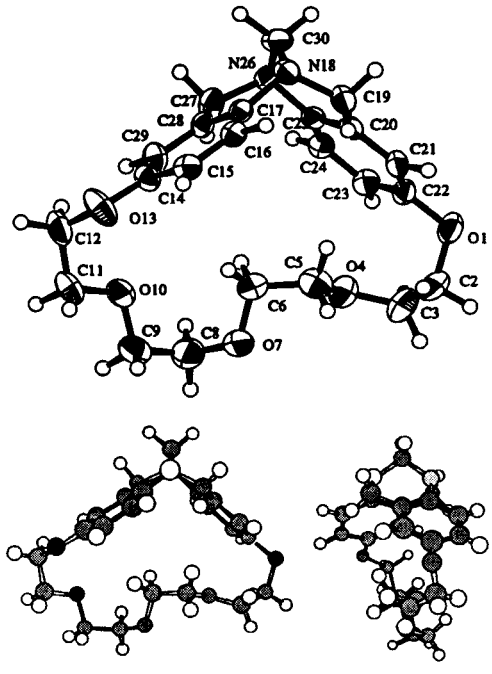


Figure 3. X-Ray Structure of **20**.

Therefore, the polyether chain is rapidly moving in solution and, on crystallization, the cavity of the molecule is filled not by the other molecule as we hoped, but by part of the chain.

Interestingly, however, this very fact of folding of the flexible polyether chain allows it to behave as a crown ether in complexation. Namely, when a solution of **20** in deuteriochloroform was mixed with anhydrous powdered metal thiocyanates (lithium, sodium, potassium), only the lithium salt was solubilized and the polyether protons showed significant downfield shifts of 0.4-0.6 ppm in the ^{1}H nmr spectrum [Figure 4 (b)].

In contrast, no sign of complexation was observed for **19** with the shorter straight polyether chain. Unfortunately, the complexation of **20** with the lithium salt is very weak and evaporation of the solution recovered only uncomplexed **20**. Likewise, in donating solvents as d_4-methanol, d_6-dimethyl sulfoxide, no complexation was observed.

Although inclusion phenomenon was not observed, we tried separation of the trögerophanes **19** and **20** to their optical anipodes. However, the optically active column, CHIRALPAK OP(+) (Daicel Chemical Industries Inc.), which was the most effective column for resolution of the Tröger base, did not show any resolution, maybe because the aromatic part of the Tröger base is responsible for the resolution and that part is blocked in the case of the trögerophanes. Attempts at resolution by salt formation with chiral acids were so far also unsuccessful.

Conclusions.

Both monomeric and dimeric trögerophanes could be synthesized *via* one-step condensation of bis(*p*-anilines) joined by a polyether chain with formalin under acidic

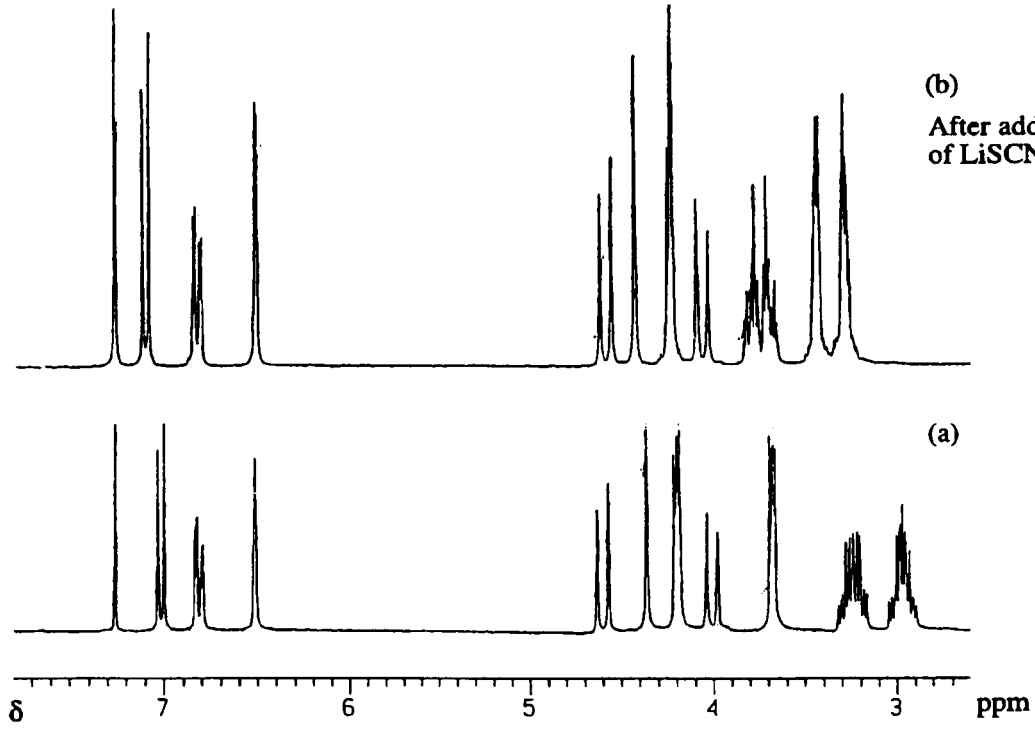


Figure 4. The 270 MHz ^{1}H nmr Spectra of **20** in Deuteriochloroform (a) Before and (b) After Addition of Lithium Thiocyanate.

conditions. However, the condensation is slow and only sterically favorable trögerophanes **19** and **20** could be synthesized in good yields. Although sufficient solubilities of these macrocycles in common organic solvents were attained, all of the complexation and inclusion experiments did not provide the expected products, except for the **20**•lithium thiocyanide complex, which was observed only in deuteriochloroform by ^{1}H nmr spectroscopy.

EXPERIMENTAL

General.

All the melting points were measured in open capillaries on a Yamato MP-21 melting point apparatus and are uncorrected. Infrared spectra were measured using potassium bromide disks on a JASCO IR-700 infrared spectrophotometer. Both ^{1}H and ^{13}C nmr spectra were measured in deuteriochloroform, unless otherwise stated, on a JEOL JNM-EX270H spectrometer. Mass spectra were recorded on a JEOL JMS-SX102 mass spectrometer using the FAB mode. Elemental analyses were performed at the Center of the Elementary Analysis of Organic Compounds affiliated to Faculty of Science in Kyushu University.

Mono-, Di-, Tri-, and Tetraethylene Glycol Bis(*p*-toluenesulfonates) **5-8**.

A solution of *p*-toluenesulfonyl chloride (80.0 g, 0.42 mole) in dioxane (100 ml) was added portionwise to a mechanically stirred solution of the glycol (0.188 mole) and sodium hydroxide (20 g, 0.5 mole) in water (100 ml). The mixture was stirred for 2 hours and left overnight at room temperature. The reaction mixture was extracted with benzene (70 ml x 3). The combined benzene layer was washed with water, aqueous sodium carbonate, and water, then dried (magnesium sulfate) and evaporated *in vacuo* to give the corresponding bis(*p*-toluenesulfonate) in good yields.

Ethylene glycol bis(*p*-toluenesulfonate) (**5**) was obtained in 85% yield as colorless needles (ethanol), mp 123-124° (lit [14] mp 128°).

Diethylene glycol bis(*p*-toluenesulfonate) (**6**) was obtained in 89% yield as colorless needles (ethanol), mp 86.5-87° (lit [15] mp 88-89°).

Triethylene glycol bis(*p*-toluenesulfonate) (**7**) was obtained in 60% yield as white crystals (methanol), mp 79-80° (lit [16] mp 81-82°).

Tetraethylene glycol bis(*p*-toluenesulfonate) (**8**) was obtained in 79% yield as a colorless viscous liquid [16].

Mono-, Di-, Tri-, and Tetraethylene Glycol Bis(*p*-nitrophenyl) ethers **9-12**.

A mixture of potassium *p*-nitrophenolate (40.0 g, 0.224 mole) and bis(*p*-toluenesulfonate) of each glycol **5-8** (0.112 mole) in dimethylformamide (150 ml) was stirred at 70-80° for 22-26 hours. The reaction mixture was allowed to stand overnight at room temperature. The workup procedure depends upon the solubility of the product as follows.

(1) Ethylene Glycol Bis(*p*-nitrophenyl) Ether (**9**).

The precipitate formed was collected by filtration, washed with water, dried (magnesium sulfate), and recrystallized from ethanol to give **9** in 94% yield as pale yellow needles: mp 163-165° (lit [17] mp 164-166°); ^{1}H nmr: δ (ppm) 4.38 (s, 4H), 7.03 (d, 4H, J = 9.2 Hz), 8.23 (d, 4H, J = 9.2 Hz); ^{13}C nmr: δ 163.3, 141.9, 125.9, 114.6, 66.8 ppm.

Anal. Calcd. for $C_{14}H_{12}N_2O_6$: C, 55.26; H, 3.95; N, 9.21. Found: C, 55.29; H, 4.00; N, 9.12.

(2) Diethylene Glycol Bis(*p*-nitrophenyl) Ether (**10**).

The separation procedure was the same as for **9**. The product was isolated in 77% yield as pale yellow fine needles, mp 153-154° (ethanol) (lit [18] mp 153°); ^{1}H nmr: δ 3.98 (t, 4H, J = 4.6 Hz), 4.26 (t, 4H, J = 4.6 Hz), 6.98 (d, 4H, J = 9.2 Hz), 8.19 (d, 4H, J = 9.2 Hz) ppm; ^{13}C nmr: δ 163.6, 141.9, 125.9, 114.5, 69.7, 68.1 ppm.

Anal. Calcd. for $C_{16}H_{16}N_2O_7$: C, 55.20; H, 4.60; N, 8.00. Found: C, 55.10; H, 4.55; N, 8.01.

(3) Triethylene Glycol Bis(*p*-nitrophenyl) Ether (**11**).

The same procedure as for **9** was used. The product was isolated in 70% yield as yellowish fine granules, mp 97-98° (ethanol); ^{1}H nmr: δ 3.76 (s, 4H), 3.89 (t, 4H, J = 4.6 Hz), 4.22 (t, 4H, J = 4.6), 6.97 (d, 4H, J = 9.2 Hz), 8.19 (d, 4H, J = 9.2 Hz) ppm; ^{13}C nmr: δ 163.8, 141.6, 125.9, 114.5, 70.9, 69.5, 68.1 ppm.

Anal. Calcd. for $C_{18}H_{20}N_2O_8$: C, 55.01; H, 5.14; N, 7.14. Found: C, 54.97; H, 5.19; N, 7.03.

(4) Tetraethylene Glycol Bis(*p*-nitrophenyl) Ether (**12**).

The reaction mixture obtained as above was poured into water and extracted with chloroform (70 ml x 3). After washing with water, the extract was dried (magnesium sulfate) and evaporated *in vacuo* to give a crude product which was purified by column chromatography (silica gel 60, 4 cm x 15 cm, chloroform). After evaporation, compound **12** was obtained in 56% yield as fine colorless needles after recrystallization from ethanol, mp 77-78°; ^{1}H nmr: δ 3.68-3.76 (m, 8H), 3.89 (t, 4H, J = 4.6 Hz), 4.22 (t, 4H, J = 4.6 Hz), 6.97 (d, 4H, J = 9.2 Hz), 8.18 (d, 4H, J = 9.2 Hz) ppm; ^{13}C nmr: δ 163.8, 141.5, 125.8, 114.5, 70.8, 70.4, 69.3, 68.1 ppm.

Anal. Calcd. for $C_{20}H_{24}N_2O_9$: C, 55.04; H, 5.50; N, 6.42. Found: C, 54.51; H, 5.57; N, 6.23.

Mono-, Di-, Tri-, and Tetraethylene Glycol Bis(*p*-aminophenyl) Ethers **13-16**.

A stirred mixture of the bis(*p*-nitrophenyl)ether (25 mmoles) in ethylene glycol (500 ml) and ethanol (100 ml) in a three-necked flask, equipped with a refluxing condenser and a dropping funnel, was heated at 80-90° until a clear solution was obtained. To the refluxing solution was added 10% palladium on carbon catalyst (400 mg), followed by dropwise addition of hydrazine monohydrate (8.9 ml) during 1 hour. After the addition, an additional 80 mg of the palladium catalyst was added and the reaction mixture was refluxed for further 8-12 hours. The following workup procedures were used to isolate the products. Since the liquid diamines were particularly sensitive toward air-oxidation, they did not give correct elemental analyses and were used immediately in the next step.

(1) Ethylene Glycol Bis(*p*-aminophenyl) Ether (**13**).

After filtering the palladium catalyst and rinsing with hot ethanol, the reaction mixture was cooled to room temperature, poured into water, and extracted with methylene chloride (70 ml x 3). The combined organic layer was dried (magnesium sulfate) and evaporated to give **13** in 80% yield as colorless needles after recrystallization from ethanol, mp 174.5-176°; ir: 3394, 3320 (NH_2) cm^{-1}; ^{1}H nmr: δ 3.44 (bs, 4H), 4.21 (s, 4H), 6.64 (d, 4H, J = 8.9 Hz), 6.79 (d, 4H, J = 8.9 Hz) ppm; ^{13}C nmr: δ 151.9, 140.3, 116.4, 116.0, 67.5 ppm.

Anal. Calcd. for $C_{14}H_{16}N_2O_2$: C, 68.85; H, 6.56; N, 11.48. Found: C, 68.82; H, 6.58; N, 11.51.

(2) Diethylene Glycol Bis(*p*-aminophenyl) Ether (**14**).

It was obtained as a reddish oil in 89% yield using the same procedure as for **13**; ^{1}H nmr: δ 3.89 (bs, 4H), 3.84 (t, 4H, J = 4.6 Hz), 4.11 (t, 4H, J = 4.6 Hz), 6.59 (d, 4H, J = 8.8 Hz), 6.83 (d, 4H, J = 8.8 Hz) ppm; ^{13}C nmr: δ 151.9, 140.2, 116.3, 115.9, 70.0, 68.2 ppm.

(3) Triethylene Glycol Bis(*p*-aminophenyl) Ether (**15**).

The reaction mixture obtained was filtered hot, washed with a small amount of hot ethanol, concentrated under vacuum, and diluted with a large amount of hot water. When the solution was allowed to cool, the precipitated white fine needles were collected by filtration and dried to give **15** in 78% yield, mp 89-90°; ir 3404, 3314 (NH_2) cm^{-1}; ^{1}H nmr: δ 2.93 (bs, 4H), 3.74 (s, 4H), 3.82 (t, 4H, J = 4.6 Hz), 4.05 (t, 4H, J = 4.6 Hz), 6.62 (d, 4H, J = 8.8 Hz), 6.76 (d, 4H, J = 8.8 Hz) ppm; ^{13}C nmr: δ 151.9, 140.1, 116.3, 116.0, 70.8, 69.9, 68.1 ppm.

Anal. Calcd. for $C_{18}H_{24}N_2O_4$: C, 65.01; H, 7.28; N, 8.43. Found: C, 64.81; H, 7.25; N, 8.34.

(4) Tetraethylene Glycol Bis(*p*-aminophenyl) Ether (**16**).

It was obtained as a reddish viscous liquid in 96% yield by the same method as for **13**; ir (neat): 3398, 3308 (NH_2) cm^{-1}; ^{1}H nmr: δ 3.35 (bs, 4H), 3.67-3.73 (m, 8H), 3.8 (t, 4H, J = 4.6 Hz), 4.03 (t, 4H, J = 4.6 Hz), 6.60 (d, 4H, J = 8.9 Hz), 6.74 (d, 4H, J = 8.9 Hz) ppm; ^{13}C nmr: δ 151.9, 140.14, 116.4, 116.1, 70.8, 70.0, 68.1, 68.0 ppm.

Synthesis of Trögerophanes.

(1) 1,4,22,25-Tetraoxa[4.4](2,8)trögerophane (**17**).

To a stirred solution of ethylene glycol bis(*p*-aminophenyl) ether **13** (1.6 mmoles) in acetic acid (200 ml) and 35% hydrochloric acid (20 ml) was added paraformaldehyde (10.0 g) at room temperature. Stirring was continued until a clear solution was obtained. After standing for 10 days at room temperature with occasional shaking, the reaction mixture was concentrated *in vacuo* and the residue was basified with 28% aqueous ammonia, extracted with chloroform, and evaporated under reduced pressure to give a crude product which was separated by column chromatography (silica gel 60, 4 cm x 20 cm, ethyl acetate). The powder obtained was recrystallized to give **17** as colorless prisms in 3.5% yield; mp >280° (chloroform/ethanol); ir: 3020, 2940, 2895, 1608 cm^{-1}; ^{1}H nmr (90 MHz): δ 3.91 (d, 4H, J = 17 Hz), 4.21 (s, 8H), 4.31 (s, 4H), 4.60 (d, 4H, J = 17 Hz), 6.31 (d, 4H, Jm = 2.7 Hz), 6.69 (dd, 4H, J_o = 8.6 Hz, J_m = 2.7 Hz), 7.02 (d, 4H, Jo = 8.6 Hz) ppm; ms: m/z 560 (M^+).

(2) 1,4,7,25,28,31-Hexaoxa[7.7](2,6)trögerophane (**18**).

Compound **18** was obtained as colorless powder in 3.0% yield, mp 216-217.5° (benzene) by the same procedure as for **17** from diethylene glycol bis(*p*-aminophenyl) ether **14**; ir: 3005, 2930, 2880, 1600 cm^{-1}; ^{1}H nmr (90 MHz): δ 3.72-3.86 (m, 8H), 3.86-4.01 (m, 8H), 3.97 (d, 4H, J = 16.2 Hz), 4.28 (s, 4H), 4.60 (d, 4H, J = 16.2 Hz), 6.36 (d, 4H, Jm = 2.6 Hz), 6.69 (dd, 4H, J_o = 8.6 Hz, J_m = 2.6 Hz), 6.99 (d, 4H, Jo = 8.6 Hz) ppm; ms: m/z 648 (M^+).

(3) 1,4,7,10-Tetraoxa[10](2,8)trögerophane (**19**).

A mixture of triethylene glycol bis(*p*-aminophenyl) ether **15** (1.87 mmole), ethanol (240 ml), and concentrated hydrochloric acid (114 ml) was stirred with cooling in an ice bath to 5-10°. To this mixture, 114 ml of 38% formalin was added dropwise with stirring. After standing for 13 days at room temperature, the reaction mixture was concentrated, basified with 28% ammonia solution, and extracted with methylene chloride (100 ml x 3). The methylene chloride phases were combined, dried (magnesium sulfate), and evaporated under vacuum to give a crude product which was purified by column chromatography (20 cm x 4 cm, silica gel 60, chloroform) to give **19** as colorless cubic crystals in 46% yield after recrystallization from ethanol/methylene chloride; mp 234-235°; ir: 3030, 3000, 2930, 2900, 1605 cm^{-1}; ^{1}H nmr: δ 2.53-2.70 (m, 4H), 3.50-3.63 (m, 4H), 3.98 (d, 2H, J = 16.2 Hz), 4.09-4.22 (m, 4H), 4.46 (s, 2H), 4.57 (d, 2H, J = 16.2 Hz), 6.49 (d, 2H, Jm = 2.6 Hz), 6.83 (dd, 2H, J_o = 8.6 Hz, J_m = 2.6 Hz), 7.01 (d, 2H, Jo = 8.6 Hz) ppm; ^{13}C nmr: δ 155.4, 141.5, 128.7, 125.1, 118.2, 116.9, 72.8, 69.9, 69.5, 68.4, 60.6 ppm; ms: m/z 368 (M^+).

Anal. Calcd. for $C_{21}H_{24}N_2O_4$: C, 68.46; H, 6.57; N, 7.60. Found: C, 68.29; H, 6.57; N, 7.45.

(4) 1,4,7,10,13-Pentaoxa[13](2,8)trögerophane (**20**).

Treating tetraethylene glycol bis(*p*-aminophenyl) ether **16** under the same conditions as with **15**, afforded a crude product which was separated by column chromatography (silica gel 60, 20 cm x 4 cm, acetonitrile) to give **20** as colorless long rectangular prisms in 34% yield after recrystallization from ethanol; mp 128-129°; ir: 3032, 3001, 2935, 2902, 1607 cm^{-1}; ^{1}H nmr: δ 2.86-3.01 (m, 4H), 3.13-3.29 (m, 4H), 3.65-3.68 (m, 4H), 4.00 (d, 2H, J = 16.5 Hz), 4.18-4.21 (m, 4H), 4.36 (s, 2H), 4.60 (d, 2H, J = 16.5 Hz), 6.51 (d, 2H, Jm = 2.6 Hz), 6.81 (dd, 2H, J_o = 8.6 Hz, J_m = 2.6 Hz), 7.01 (d, 2H, Jo = 8.6 Hz) ppm; ^{13}C nmr: δ 155.2, 141.0, 128.4, 125.3, 116.3, 113.9, 71.0, 70.3, 70.1, 68.0, 67.70, 59.7 ppm; ms: m/z 412 (M^+).

Anal. Calcd. for $C_{23}H_{28}N_2O_5$: C, 66.97; H, 6.84; N, 6.79. Found: C, 67.04; H, 6.87; N, 6.72.

Crystal Structure Determination.

The X-ray reflection data were collected on a Rigaku AFC7R X-ray diffractometer and solved by direct methods (MULTAN 88 [19]) and refined by full-matrix least-squares techniques as implemented in the teXsan system [20] on a Silicon Graphics Indy computer. The non-hydrogen atoms were refined anisotropically. All the hydrogen atoms were located in the difference Fourier map and included, but not refined in the final least squares calculations.

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