Doubly and Triply Bridged Polyoxapolyazaheterophanes Derived from 2,4,6-Trichloro-*s*-triazine

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Doubly and triply bridged polyoxapolyazaheterophanes (**1**, **2**) have been synthesized from 2,4,6-trichloro-*s*-triazine by using the different reactivity of the three chlorine atoms toward neutral nucleophiles. Introduction of alkyl groups and/or of heteroatoms in the bridging chains makes these systems soluble in organic solvents. Triazinophanes **1h** and **2b**, with NH groups in the bridging chains, may be used as phase-transfer catalysts in nucleophilic aliphatic substitutions. ^{13}C NMR spectra indicate that molecules **1** and **2** either exist in a single nonsymmetric conformation up to about room temperature or, more likely, that there are two or more differently populated conformations separated by a high interconversion barrier.

An exciting and rapidly growing development in the chemistry of host molecules capable of molecular recognition has occurred in the last few years: coronands, cryptands, podands,[1] cylindranes,[2-5] and spherands[2] have been designed and synthesized. Numerous factors influence the selectivity of these compounds in binding cations or host molecules, among them are the cavity size, the conformational freedom, the lipophilicity, and the nature and the number of coordination sites. The synthetic approaches to these structurally sophisticated systems are complex, although a few attempts to simplify the classical routes have been reported.[6]

In the present paper we describe the synthesis of triazinophanes (**1**, **2**), doubly and triply bridged with polyheteroatomic alkyl chains by using 2,4,6-trichloro-*s*-triazine (**3**) as the building block.[7] 2,4,6-Trichloro-*s*-triazine shows the unusual feature of a stepwise replacement of the three halogens by nucleophiles, particularly in the case of neutral nucleophiles.[8] Hence, macropolycyclic ligands may be synthesized by the stepwise connection of two triazine rings with one, two, or three bridging chains.

Doubly bridged polyazatriazinophanes have been prepared by Borodkin, and a few systems containing isoindoline and pyridine subunits have been characterized as transition metals complexes.[9] Polyoxapolyazaheterophanes containing pyridine subunits have been described by Newkome:[10] a few doubly bridged systems are structurally related to those described in this paper. Triply bridged cyclophanes with polyoxyethylene chains have been prepared from phloroglucinol[11] and from 1,3,5-trihydroxymethylbenzene.[12] However, the identity of the three points of attack of the subunits gives rise to very low yields of these cyclophanes.

Results and Discussion

Synthesis. The diamines used to bridge **3** leading to compounds **6**, **1**, and **2** are listed in Table II. To prevent formation of structural isomers, symmetrically substituted chains were used. Alkyl groups were introduced via bis(acylation) of α,ω-diamines or bis(amination) of α,ω-dicarboxylic acids to give diamides **4** (Table I) and successive reduction of **4** to **5** with $LiAlH_4$. Triamine **5f** was obtained from commercial diethylenetriamine by protection of the primary amino groups with phthalic anhydride, benzylation of the NH group, and deprotection and final alkylation of the primary amino groups by the above procedure. Diamine **5g** was prepared by an improvement of a described[13] procedure. Physical data and yields of diamides **4** and diamines **5** are reported in Tables I and II.

Attack of the first chain on the triazine rings was conducted at 0–5 °C in aqueous acetone in the presence of a slight molar excess of KOH or NaOH. Alternatively, anhydrous acetone was used, in the presence of triethylamine or solid K_2CO_3, as base, with comparable results. The second chain was inserted working under high dilution conditions in tetrahydrofuran (THF) or acetone at 55–65 °C, again with a slight excess of aqueous KOH or NaOH. The third chain was inserted under high dilution conditions in dimethyl sulfoxide (Me_2SO) at 160–180 °C with anhydrous K_2CO_3 (Scheme I). Yields are fair to good in the two first steps, low to fair in the third, and are reported

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Table I. Diamides

RNHCOZCONHR (4a–c) R'CONHZNHCOR' (4d,e)

compd	Z	R	R'	mp, °C (solvent)	yield, %	^{1}H NMR ($CDCl_3$), δ
4a	CH_2OCH_2	n-C_4H_9		97–99 (cyclohexane–benzene)	65	1.0 (t, 6 H), 1.2–1.8 (m, 8 H), 3.4 (q, 4 H) 4.1 (s, 4 H), 6.6 (br s, 2 H)
4b	$(CH_2OCH_2)_2$	n-C_4H_9		68–70 (cyclohexane–benzene)	82	0.95 (t, 6 H), 1.1–1.7 (m, 8 H), 3.3 (q, 4 H) 3.7 (s, 4 H), 4.0 (s, 4 H), 6.6 (br s, 2 H)
4c	$(CH_2OCH_2)_2$	n-C_8H_{17}		79–80 (n-hexane)	83	0.9 (t, 6 H), 1.2–1.7 (m, 24 H), 3.25 (q, 4 H) 3.7 (s, 4 H), 4.0 (s, 4 H), 6.6 (br s, 2 H)
4d	$CH_2CH_2(CH_2OCH_2)_3CH_2CH_2$		n-C_3H_7	64–66 (cyclohexane–benzene)	83	0.95 (t, 6 H), 1.4–1.95 (m, 8 H), 2.15 (t, 4 H) 3.35 (t, 4 H), 3.45–3.75 (m, 12 H), 6.25 (br s, 2 H)
4e	$CH_2CH_2N(CH_2Ph)CH_2CH_2$		n-C_3H_7	69–71 (n-heptane)	93	0.95 (t, 6 H), 1.6 (m, 4 H), 2.2 (t, 4 H), 2.5 (t, 4 H) 3.3 (q, 4 H), 3.5 (s, 2 H), 6.2 (br s, 2 H), 7.2 (s, 5 H)

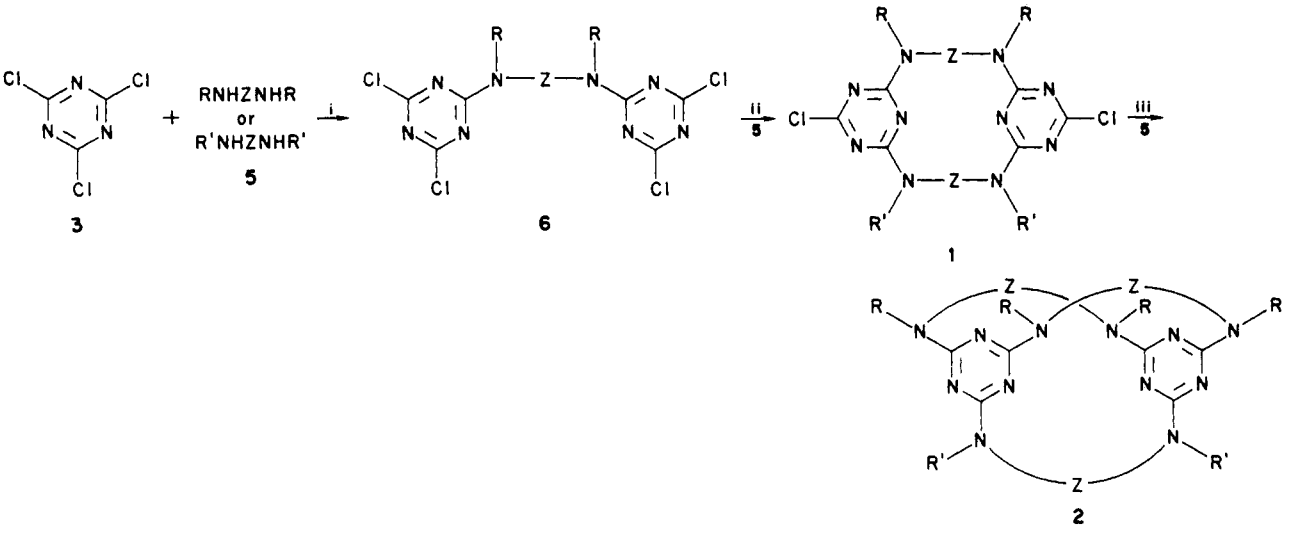
Table II. Diamines

RNHCH$_2$ZCH$_2$NHR (5)

compd	Z	R	yield, %	^{1}H NMR ($CDCl_3$), δ
5a	CH_2OCH_2	n-C_4H_9	76	0.9 (t, 6 H), 1.1–1.7 (m, 10 H), 2.65 (t, 4 H), 2.8 (t, 4 H) 3.6 (t, 4 H)
5b	$(CH_2OCH_2)_2$	n-C_4H_9	86	0.9 (t, 6 H), 1.1–1.7 (m, 10 H), 2.65 (t, 4 H), 2.8 (t, 4 H) 3.5–3.7 (m, 8 H)
5c	$(CH_2OCH_2)_2$	n-C_8H_{17}	85	0.9 (t, 6 H), 1.1–1.8 (m, 26 H), 2.6 (t, 4 H), 2.8 (t, 4 H) 3.5–3.9 (m, 8 H)
5d	$CH_2(CH_2OCH_2)_3CH_2$	n-C_4H_9	77	0.9 (t, 6 H), 1.1–1.6 (m, 10 H), 1.7 (q, 4 H), 2.5–2.9 (m, 8 H) 3.4–3.7 (m, 12 H)
5e	$CH_2N(CH_2Ph)CH_2$	n-C_4H_9	87	0.9 (t, 6 H), 1.1–1.7 (m, 10 H), 2.4–2.85 (m, 12 H), 3.6 (s, 2 H) 7.25 (s, 5 H)
5f	$CH_2N(CH_2Ph)CH_2$	H	98	1.3 (s, 4 H), 2.4–2.9 (m, 8 H), 3.6 (s, 2 H), 7.3 (s, 5 H)
5g	$(CH_2OCH_2)_2$	H	78	[a]

[a] Reference 13.

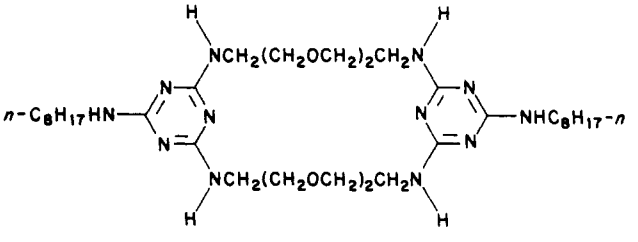
Scheme I[a]



[a] i, 0–5 °C, 3 h, acetone–H_2O, KOH; ii, 50–70 °C, 20 h, tetrahydrofuran–H_2O, KOH; iii, 160–180 °C, 20 h, Me_2SO–H_2O, K_2CO_3.

in Tables III–V together with the physical properties of **1**, **2**, and **6**.

Heteroatoms in the bridges and alkyl chains exert a marked influence on the physical properties. For example, bis(triazinyl) derivative **6g** (Z = CH_2CH_2; R = H) and **1g** [Z = $CH_2(CH_2OCH_2)_2CH_2$; R, R' = H] have mp >300 °C and are insoluble in most organic solvents. Introduction of one and two oxyethylene groups in the bridging chain of **6g** decreases the melting point (Table III) with a concomitant solubility increase in the organic solvents. Lipophilicity of **1** and **2** was obtained by bonding alkyl groups to the bridging nitrogen atoms. A lipophilic ligand **1h** was obtained by replacing the third chlorine atom of both triazine rings in **1** with octylamine.



1h

^{13}C NMR Spectra. Due to the complexity of the molecules investigated, ^{13}C NMR spectroscopy is best

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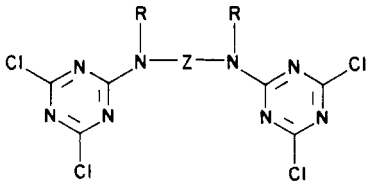
Table III. Bis(dichlorotriazinyl) Derivatives

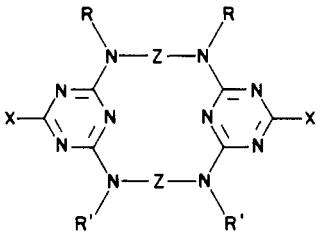


6

compd	Z	R	mp, °C (solvent)	yield, %	^{1}H NMR ($CDCl_3$), δ
6a	$CH_2CH_2OCH_2CH_2$	*n*-C_4H_9	90–91 (*n*-hexane)	46	0.95 (t, 6 H), 1.1–1.8 (m, 8 H), 3.5–3.9 (m, 12 H)
6b	$CH_2(CH_2OCH_2)_2CH_2$	H	127–129 (acetonitrile)	74	3.75 (s, 6 H), 3.80 (s, 8 H), 7.0 (br s, 2 H)
6c	$CH_2(CH_2OCH_2)_2CH_2$	*n*-C_4H_9	70–72 (light petroleum)	45	0.95 (t, 6 H), 1.0–1.8 (m, 8 H), 3.4–3.9 (m, 16 H)
6d	$CH_2CH_2(CH_2OCH_2)_3CH_2CH_2$	*n*-C_4H_9	oil	47	0.95 (t, 6 H), 1.1–2.1 (m, 12 H), 3.4–3.8 (m, 20 H)
6e	$CH_2CH_2N(CH_2Ph)CH_2CH_2$	*n*-C_4H_9	oil	69	0.95 (t, 6 H), 1.1–1.8 (m, 8 H), 2.75 (t, 4 H) 3.3–3.8 (m, 10 H), 7.2 (s, 5 H)
6f	$CH_2(CH_2OCH_2)_2CH_2$	*n*-C_8H_{17}	49–51 (light petroleum)	47	0.90 (t, 6 H), 1.1–1.8 (m, 24 H), 3.4–3.9 (m, 16 H)
6g[a]	CH_2CH_2	H			
6h	$CH_2CH_2OCH_2CH_2$	H	162–164 (benzene)	76	3.6 (m, 8 H), 9.2 (br s, 2 H)

[a] Reference 14.

Table IV. Doubly Bridged Triazinophanes



1

compd	Z	R	R′	X	mp, °C (solvent)	yield, %	^{1}H NMR ($CDCl_3$), δ
1a	$CH_2CH_2OCH_2CH_2$	*n*-C_4H_9	*n*-C_4H_9	Cl	90–92 (methanol)	63	0.9 (t, 12 H), 1.05–1.75 (m, 16 H), 2.7–4.6 (m, 24 H)
1b	$CH_2(CH_2OCH_2)_2CH_2$	H	*n*-C_8H_{17}	Cl	127–128 (acetonitrile)	43	0.9 (t, 6 H), 1.0–1.3 (m, 20 H), 1.3–1.6 (m, 4 H) 3.2–3.7 (m, 28 H), 6.8–7.2 (br s, 2 H)
1c	$CH_2(CH_2OCH_2)_2CH_2$	*n*-C_4H_9	*n*-C_4H_9	Cl	89–90 (methanol)	53	0.9 (t, 12 H), 1.3 (m, 8 H), 1.45 (m, 8 H) 3.4–3.7 (m, 32 H)
1d	$CH_2CH_2(CH_2OCH_2)_3CH_2CH_2$	*n*-C_4H_9	*n*-C_4H_9	Cl	oil	57	0.9 (t, 12 H), 1.1–2.1 (m, 24 H), 3.3–3.8 (m, 40 H)
1e	$CH_2CH_2N(CH_2Ph)CH_2CH_2$	*n*-C_4H_9	*n*-C_4H_9	Cl	oil	59	0.9 (t, 12 H), 1.0–1.7 (m, 26 H), 2.4–4.5 (m, 28 H)
1f	$CH_2CH_2NHCH_2CH_2$	*n*-C_4H_9	*n*-C_4H_9	Cl	>220 (benzene–*n*-hexane)	55	0.9 (t, 12 H), 1.35 (m, 8 H), 1.55 (m, 8 H) 2.75 (t, 6 H), 3.45–3.65 (m, 14 H)
1g	$CH_2(CH_2OCH_2)_2CH_2$	H	H	Cl	~300 (*o*-dichlorobenzene)	89	3.2–3.8 (m, 24 H), 7.5–7.9 (br s, 4 H)
1h	$CH_2(CH_2OCH_2)_2CH_2$	H	H	NHC_8H_{17}-*n*	178–180 (benzene–hexane)	70	0.9 (t, 6 H), 1.1–1.7 (m, 24 H), 3.2–3.8 (m, 28 H), 4.9–5.2 (br s, 2 H), 7.4–8.2 (br s, 4 H)

suited to ascertain their structural and conformational properties. Compounds analogous to those reported here have been shown to exist at least in two conformations, with barriers high enough to be detectable by variable temperature NMR.[15-19] This temperature dependent behavior explains why the room temperature ^{13}C NMR spectra showed either more lines than expected on the basis of the number of "chemically equivalent" carbons (as observed in the case of doubly bridged derivatives) or quite broad spectral lines (as observed in the case of triply bridged derivatives). Two such examples (namely **1c** and **2b**) have been examined over a wide temperature range to prove that the observed spectral features were consistent with the molecular structure proposed.

The room temperature spectrum (^{13}C at 75.5 MHz) of **1c** display, for each "chemically equivalent" carbon, a large number of lines of different relative intensity. In particular the carbons of the chains linking the two aromatic rings display so many lines that, despite the good resolution, they could not be counted with certainty.

On the other hand the number of lines is much smaller for the carbons belonging to the C_4H_9 moiety: the number decreases going from the β carbon (4 lines) to the δ carbon

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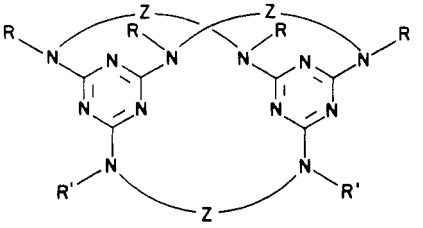
Table V. Triply Bridged Triazinophanes



2

compd	Z	R	R′	mp, °C (solvent)	yield, %	^{1}H NMR ($CDCl_3$), δ
2a	$CH_2CH_2OCH_2CH_2$	n-C_4H_9	n-C_4H_9	88–90 (methanol)	14	0.85 (t, 18 H), 1.2 (m, 12 H), 1.45 (m, 12 H) 2.5–4.5 (m, 36 H)
2b	$CH_2(CH_2OCH_2)_2CH_2$	H	n-C_8H_{17}	oil	28	0.85 (t, 6 H), 1.05–1.20 (m, 20 H), 1.35–1.55 (m, 4 H) 3.1–4.0 (m, 44 H)
2c	$CH_2(CH_2OCH_2)_2CH_2$	n-C_4H_9	n-C_4H_9	oil	22	0.85 (t, 18 H), 1.25 (m, 12 H), 1.5 (m, 12 H) 2.8–4.1 (m, 48 H)
2d	$CH_2CH_2(CH_2OCH_2)_3CH_2CH_2$	n-C_4H_9	n-C_4H_9	oil	24	0.9 (t, 18 H), 1.1–2.1 (m, 36 H), 3.3–4.3 (m, 60 H)

Table VI. ^{13}C NMR Chemical Shifts (ppm from Me_4Si) of 1c and 2b Obtained at 75.49 MHz at Temperatures Where Average Signals Are Observable

compd **1c** in hexachloroacetone at +120 °C[a]	compd **2b** in $CDCl_3$ at +50 °C
165.7 (4 C), aromatic carbons bonded to N	166.0 (4 C), aromatic carbons
70.9 (4 C), CH_2O	165.3 (2 C), aromatic carbons
69.3 (4 C), CH_2O	70.7 (2 C), CH_2O
48.3 (4 C), CH_2N	70.6 (4 C), CH_2O
47.65 (4 C), CH_2N	70.4 (4 C), CH_2O
30.4 (4 C), CH_2 in position β of C_4H_9	69.2 (2 C), CH_2O
20.4 (4 C), CH_2 in position γ of C_4H_9	47.7 (2 C), CH_2N
14.1 (4 C), CH_3	46.7 (2 C), CH_2N
	40.7 (4 C), CH_2NH
	31.9 (2 C) }
	29.5 (2 C) } CH_2 carbons of
	29.4 (2 C) } the chain
	28.1 (2 C) } C_8H_{17}
	27.2 (2 C) }
	22.6 (2 C) }
	14.0 (2 C), CH_3

[a] The aromatic carbons bonded to chlorine have too long relaxation times to be detectable at this temperature.

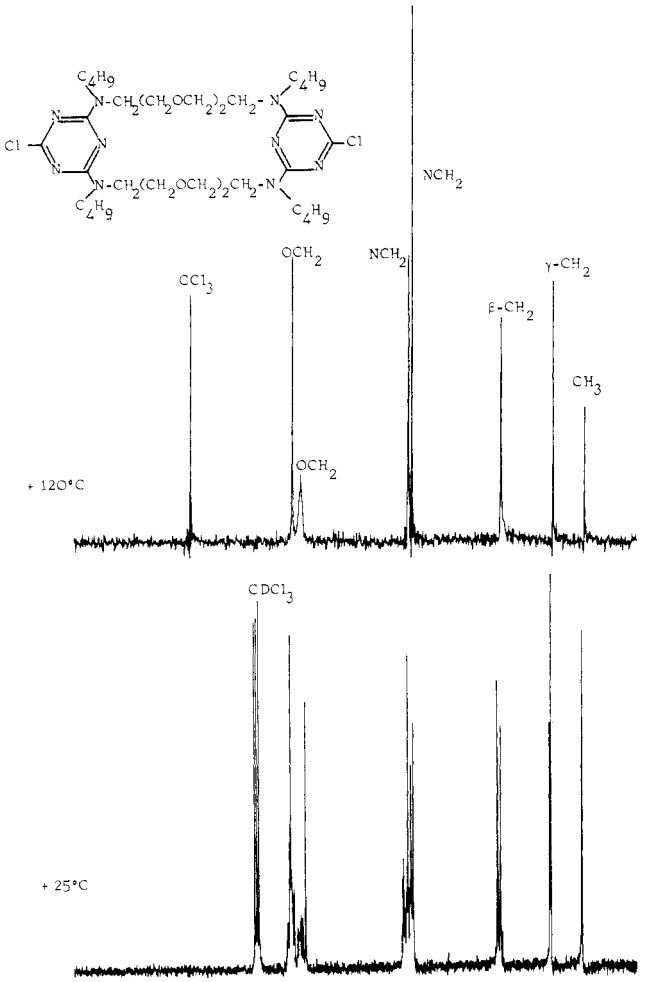


Figure 1. Aliphatic region of the ^{13}C NMR spectrum (at 75.5 MHz) of **1c** at 25 °C in $CDCl_3$ and at 120 °C in $(CCl_3)_2CO$. The lines of the solvents are marked in the picture. The large number of lines for each type of carbon of the compound coalesce at high temperature into a single line. One of them (i.e., one line for the pair of OCH_2) is still broad, and only at temperatures higher than 120 °C is its sharpening completed.

(2 lines). Very few lines were also observed for each aromatic carbon. These observations seem to suggest that the molecule is locked in at least two syn,anti conformers of different stability, as described in ref 15 and 16. In these conformers the chains connecting the two rings are "frozen" (on the NMR time scale) in a definite spatial arrangement: as a consequence they can, in principle, give rise to a line for each of their carbons, thus accounting for the large number of observed signals. The great number of lines observed seems actually to indicate that these conformers have very low symmetry. However the C_4H_9 chains are free to move rapidly on the NMR time scale and the different lines for each "chemically equivalent" carbon depend only on the type of conformer they belong to and on the asymmetry of the conformer itself. Unfortunately the complexity of the molecule and of the observed spectra do not currently allow a more precise hypothesis for the geometry of these conformers.

On warming **1c** to +120 °C in hexachloroacetone all the lines broaden and coalesce into single lines for each "chemically equivalent" carbon, as shown in Figure 1 and in Table VI. At 120 °C the conformational interconversions are fast on the NMR time scale and a single averaged signal is seen for each carbon. A very rough estimate of the barrier required for this interconversion indicates a $\Delta G^{\ddagger}$ value of about 20 kcal mol^{-1}.

Similar spectral features are also observed in the case of **2b**, but the temperature range where the dynamic phenomenon occurs is lower. At room temperature in fact there are already single (broad) lines for each carbon, and warming up +50 °C is sufficient to sharpen all the lines and assign their averaged shifts (see Table VI), whereas on lowering the temperature below −50 °C (in CHF_2Cl) the

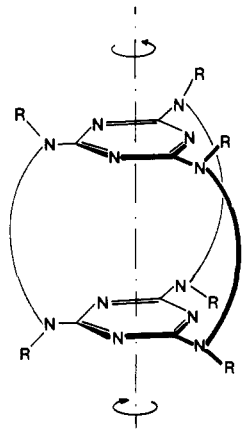


Figure 2. Disrotation around the vertical axis of cyclophanes **2** leading to folded conformations.

lines first broaden and finally split into many lines of different relative intensities. The behavior of triply bridged **2b** is similar to that of the doubly bridged **1c**: the number of different carbons is much higher for the chains linking the aromatic rings than for the carbons of the C_8H_{17} moiety. The corresponding free energy of activation for this motion can be estimated in the proximity of 15 kcal mol^{-1}.

Such a feature might suggest the existence of two, or more than two, "folded" conformers of the type illustrated in the following section. Again the atoms of the chains linking the aromatic rings would stay, at low temperature, in a definite spatial arrangement (on the NMR time scale), thus showing, in principle, a line for each carbon. The atoms of the C_8H_{17} chains would be free to move and the difference, observed at low temperature, in the shifts of their "chemically equivalent" carbons would only depend on the asymmetry and the number of the "folded" conformers, hence the fewer lines detectable for each of these carbons.

The difference in the dynamic properties of the doubly and triply bridged derivatives has been confirmed by the temperature dependence of the spectra of **2c** (similar to that of **2b**) and of **1b** (similar to that of **1c**).

The difference in the temperature range seems to reflect the difference in the kind of dynamic process occurring in the doubly bridge derivatives with respect to the triply bridged derivatives. The first is probably a syn–anti isomerization, the second an interconversion between folded conformers which would be expected to have a smaller free energy of activation.

Catalytic Activity and Complexation. Terminal nitrogens of the bridging chains in **1** and **2** lie in the same plane as the triazine rings. As a consequence, the bridging chains are forced outside of the molecule core, making the internal cavity too large for hosting simple inorganic cations. Furthermore, both heterocyclic and bridging nitrogens are poor electron donors, so that only the central heteroatoms of the chains act as efficient binding sites.

However, as shown by CPK models, complexation of small cations by **1** and **2** may become possible if both assume folded conformations. For example, in triply bridged triazinophanes **2** the triazine rings get closer by simultaneous disrotation around the vertical axis passing through them (Figure 2). Accordingly, interatomic distances inside bridging chains are markedly diminished. Among **1** and **2**, only **1h** and **2b** can complex alkali cations, acting therefore as catalysts in nucleophilic aliphatic substitutions under PTC conditions. Differently from the other cyclophanes **1** and **2**, **1h** and **2b** bear only two alkylated nitrogens in the bridging chains. The absence of

Table VII. Observed Pseudo-First-Order Kinetic Constants as a Function of Cation[a]

	$10^6 k_{obsd}$, s^{-1}			
catalyst[b]	Na^+	K^+	Cs^+	NH_4^+
1h[c]	11.3	10.6	12.2	10.2
2b	19.8	3.3	4.0	
7	12.0	93.0[d]	6.8	

[a] For reaction 1 in toluene–H_2O at 60 °C. [b] 0.05 Molar equiv. [c] Kinetics performed in 1,2-dichloroethane–H_2O. [d] Reference 20.

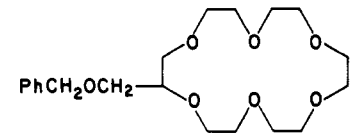
steric hindrance and/or the possibility of forming intramolecular hydrogen bonds by the NH groups favor the presence of folded conformations (see ^{13}C NMR spectra), likely capable of complexing cations.

In nucleophilic substitution of the methanesulfonic group in *n*-octyl methanesulfonate by I^- conducted under two-phase conditions in the presence of catalytic amounts of **2b** (eq 1), the reactivity scale as a function of cation is

$$n\text{-}C_8H_{17}OMes + I^- \xrightarrow[\text{toluene–}H_2O,\ 60\ °C]{\text{cat (0.05 mol equiv)}} n\text{-}C_8H_{17}I + MesO^- \quad (1)$$

cat = **1h**, **2b**, **7**

in the order: $Na^+ > K^+ \sim Cs^+$ (Table VII). The catalytic activity found in the presence of NaI is slightly higher than that of [(benzyloxy)methyl]-18-crown-6 (**7**), but it is noticeably lower than that shown by the same crown ether when KI is used instead of NaI. Complexation mea-



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surements performed under the same conditions of PTC reactions indicated that only 11.5% of **2b** in the organic phase is complexed with NaI.[21]

Macrocycle **1h** has a catalytic activity slightly lower or equal to that of **2b**. Unlike the latter, no significant dependence on the nature of cation was observed (Table VII).

No appreciable catalytic activity was found with lithium iodide. Doubly and triply bridged hexabutyl-substituted heterophanes showed no detectable phase-transfer catalytic activity with any cation.

Experimental Section

^{13}C NMR spectra were recorded at 75.5 MHz on a Bruker CXP-300 instrument. The samples in CHF_2Cl were obtained by condensing the gaseous solvent in the NMR tube connected to a vacuum line: samples were subsequently sealed in vacuo and introduced in the precooled probe of the spectrometer. ^1H NMR spectra were recorded at 90 MHz on a Varian EM-390 spectrometer with Me_4Si as an internal standard. Infrared spectra were obtained with a Perkin Elmer 377 spectrometer. GLC analyses were performed on a Hewlett-Packard Model 5840 flame ionization instrument (2 ft × 0.125 in. UCW 982-10% on Chromosorb W column). Potentiometric titrations were performed with a Metrohm Titroprocessor E636 and Metrohm Dosimat E635. Melting points were measured on a Büchi 510 apparatus and are uncorrected. Satisfactory combustion analyses were obtained (C = ±0.40, H = ±0.20, N = ±0.40) for all new compounds.

Organic and inorganic reagents, ACS grade, were used without further purification. 3,6-Dioxa-1,8-octanedioyl dichloride[22] and

(20) Anelli, P. L.; Czech, B.; Montanari, F.; Quici, S. *J. Am. Chem. Soc.* **1984**, *106*, 861–869.

(21) Doubly bridged polyazaheterophane **1e** partially complexes Ag^+, and the complexation constant noticeably increases in the corresponding debenzylated system **1f**: unpublished results from this laboratory.

(22) Dietrich, B.; Lehn, J.-M.; Sauvage, J. P.; Blanzat, J. *Tetrahedron* **1973**, *29*, 1629–1645.

n-octyl methanesulfonate[23] were prepared following standard procedures.

***N,N'*-Dioctyl-3,6-dioxa-1,8-octanediamide (4c).** A solution of 5.37 g (25 mmol) of 3,6-dioxa-1,8-octanedioyl dichloride in 30 mL of anhydrous benzene was added dropwise to a solution of 6.46 g (50 mmol) of *n*-octylamine and 5.05 g (50 mmol) of dry Et_3N in 50 mL of benzene. The mixture was stirred for 2 h at 25 °C and then filtered, and the precipitate washed with 50 mL of benzene. The combined benzene was washed with water (2 × 80 mL), 3 N HCl (2 × 80 mL), and water (80 mL) and dried over Na_2SO_4. Evaporation of the solvent afforded 8.30 g (83%) of a pale yellow solid: mp 79–80 °C (*n*-hexane); IR (nujol) cm^{-1} 3260, 1640, 1530; ^1H NMR ($CDCl_3$) δ 0.9 (t, 6 H), 1.2–1.7 (m, 24 H), 3.25 (q, 4 H), 3.7 (s, 4 H), 4.0 (s, 4 H), 6.6 (br s, 2 H). The same procedure was applied in the synthesis of dicarboxamides **4a** and **4b** (Table I).

***N,N'*-Dioctyl-3,6-dioxa-1,8-octanediamine (5c).** A solution of 6.8 g (17 mmol) of **4c** in 50 mL of anhydrous tetrahydrofuran (THF) was slowly added to a suspension of 3.2 g (85 mmol) of $LiAlH_4$ in 50 mL of THF. The mixture was refluxed, magnetically stirred for 40 h, and then cooled at 0 °C with an ice bath. The excess of hydride was destroyed by adding 12 mL of 2:1 THF–H_2O dropwise under a vigorous stirring. The mixture was filtered and the precipitate washed with boiling toluene (3 × 80 mL). The organic solution was evaporated in vacuo, and the residue was dissolved in 100 mL of toluene and dried with Na_2SO_4. Evaporation of the solvent gave 5.37 g (85%) of pale yellow oil: ^1H NMR ($CDCl_3$) δ 0.85 (t, 6 H), 1.1–1.8 (m, 26 H), 2.6 (t, 4 H), 2.8 (t, 4 H), 3.5–3.9 (m, 8 H). The same procedure was applied in the synthesis of diamines **5a,b,d,e** (Table II).

***N,N'*-Dibutanoyl-4,7,10-trioxa-1,13-tridecanediamine (4d).** A solution of 47.4 g (0.30 mol) of butyric anhydride in 100 mL of toluene was added dropwise to a stirred solution of 33.05 g (0.15 mol) of 4,7,10-trioxa-1,13-tridecanediamine in 200 mL of toluene. The mixture was heated at 50 °C for 1 h, cooled to 25 °C, and extracted with 3 N HCl (3 × 100 mL). The aqueous solution was neutralized with solid $NaHCO_3$ and evaporated in vacuo, and the solid residue extracted in sohxlet for 2 h with EtOH (200 mL). Evaporation of the solvent gave 44.9 g (83%) of a white solid: mp 64–65 °C (cyclohexane/benzene 1/1); IR (nujol) cm^{-1} 3250, 1620, 1550; ^1H NMR ($CDCl_3$) δ 0.95 (t, 6 H), 1.40–1.95 (m, 8 H), 2.15 (t, 4 H), 3.35–3.75 (m, 16 H), 6.25 (br s, 2 H).

3-Benzyl-3-aza-1,5-pentanediamine (5f). Diethylenetriamine (51.6 g, 0.5 mol) was added dropwise with vigorous stirring to 148.1 g (1.0 mol) of phthalic anhydride at 180 °C. Steam which developed from the reaction was removed. The temperature was kept at 180 °C until solidification of the reaction mixture. Crystallization from xylene afforded 128.8 g (71%) of 1,5-diphthalimido-3-azapentane: mp 176–178 °C; ^1H NMR ($CDCl_3$) δ 1.75 (br s, 1 H), 2.95 (t, 4 H), 3.75 (t, 4 H), 7.65 (s, 8 H).

A solution of 34.20 g (94 mmol) of 1,5-diphthalimido-3-azapentane and 17.72 g (104 mmol) of benzyl bromide in 300 mL of dry MeCN was refluxed with stirring for 15 h in the presence of 39.06 g (282 mmol) of anhydrous K_2CO_3. The mixture was filtered and the precipitate washed with CH_2Cl_2. The combined organic phases were evaporated and the residue was dissolved in water and CH_2Cl_2. The organic solution was dried over anhydrous Na_2SO_4 and evaporated to give 32.8 g (77%) of 3-benzyl-1,5-diphthalimido-3-azapentane: mp 130–132 °C (MeCN); ^1H NMR ($CDCl_3$) δ 2.8 (t, 4 H), 3.7–3.8 (m, 6 H), 6.8–7.1 (m, 5 H), 7.7 (s, 8 H).

A solution of 31.7 g (0.069 mol) of 3-benzyl-1,5-diphthalimido-3-azapentane and 34.5 g (0.69 mol) of hydrazine hydrate in 700 mL of EtOH was refluxed with vigorous stirring for 3 h. The mixture was filtered and washed with EtOH. The solvent was evaporated, 200 mL of $CHCl_3$ were added, and after cooling with an ice bath, the insoluble phthalhydrazide was filtered. Evaporation of $CHCl_3$ gave 13.05 g (98%) of **5f** as a yellow oil: ^1H NMR ($CDCl_3$) δ 1.3 (s, 4 H), 2.4–2.9 (m, 8 H), 3.6 (s, 2 H), 7.3 (s, 5 H).

3-Benzyl-*N,N'*-dibutanoyl-3-aza-1,5-pentanediamine (4e). Butyric anhydride (21.17 g, 0.134 mol) in 100 mL of toluene was added dropwise to a stirred solution of 13.05 g (0.067 mol) of **5f** in 150 mL of toluene. The solution was heated at 50 °C for 1 h, cooled to 25 °C, and extracted with 3 N HCl (3 × 70 mL). The aqueous phase, neutralized with solid $NaHCO_3$, gave a yellow precipitate that after filtration was dissolved in ethyl ether/H_2O; evaporation of the organic phase afforded 21.4 g (93%) of **4e** as a yellow solid: mp 69–71 °C (*n*-heptane); IR (nujol) cm^{-1} 3290, 1640, 1540; ^1H NMR ($CDCl_3$) δ 0.95 (t, 6 H), 1.6 (m, 4 H), 2.2 (t, 4 H), 2.5 (t, 4 H), 3.3 (q, 4 H), 3.5 (s, 2 H), 6.2 (br s, 2 H), 7.2 (s, 5 H).

3,6-Dioxa-1,8-octanediamine (5g). A mixture of 23.5 g (0.36 mol) of NaN_3 and 0.6 g (3.6 mmol) of KI in 55 mL of H_2O and 3.75 g (0.074 mol) of hexadecyltributylphosphonium bromide in 28.0 g (0.15 mol) of 1,8-dichloro-3,6-dioxaoctane was refluxed with stirring for 17 h. The reaction mixture was separated and the aqueous phase washed with ethyl ether (3 × 50 mL). The combined organic solution was dried (Na_2SO_4), and evaporation of the solvent at 25 °C gave 28.8 g (96%) of crude diazide. The crude product was dissolved in 250 mL of 95% ethanol and hydrogenated at 25 °C and 30 atm in the presence of 10% Pd/C (2.88 g) to afford 16.7 g (78%) of **5g**: bp 84–85 °C (0.5 torr); n_D 1.4262 (lit.[13] bp 78–79 °C (0.2 torr)).

***N,N'*-Bis(dichloro-*s*-triazinyl)-*N,N'*-dibutyl-3-oxa-1,5-pentanediamine (6a).** A solution of 4.53 g (0.021 mol) of **5a** and 5.05 g (0.050 mol) of dry Et_3N in 80 mL of acetone was slowly dripped into a stirred solution of 7.75 g (0.42 mol) of cyanuric chloride (**3**) in 70 mL of acetone, kept at 0–5 °C. The mixture was stirred for another 2 h at 0 °C and then filtered and the precipitate washed with acetone. The solvent was evaporated and the residue dissolved in CH_2Cl_2 and washed with water. Evaporation of the solvent gave 10.0 g of an orange oil. Column chromatography (silica gel, ethyl ether–light petroleum) afforded 4.92 g (46%) of **6a**: mp 90–91 °C (*n*-hexane); ^1H NMR ($CDCl_3$) δ 0.95 (t, 6 H), 1.1–1.8 (m, 8 H), 3.5–3.9 (m, 12 H).

***N,N'*-Bis(dichloro-*s*-triazinyl)-3,6-dioxa-1,8-octanediamine (6b).** Solutions A and B [A, 2.96 g (20 mmol) of 1,8-diamino-3,6-dioxaoctane (**5g**) in 20 mL of acetone; B, 1.76 g (44 mmol) of sodium NaOH in 20 mL of water] were simultaneously dripped (2 h) into a vigorously stirred solution of 7.38 g (40 mmol) of cyanuric chloride (**3**) in 200 mL of 3:1 water–acetone, at 0–5 °C. The mixture was stirred for another 2 h at this temperature and then filtered, and the precipitate washed with water, cold ethanol, and light petroleum. Crystallization from MeCN gave 6.57 g (74%) of a white solid: mp 127–129 °C; ^1H NMR ($CDCl_3$) δ 3.7–3.8 (double s, 12 H), 7.0 (br s, 2 H). The same procedure was applied in the synthesis of bis(triazinyl) derivatives **6c** and **6f** (Table III).

***N,N'*-Bis(dichloro-*s*-triazinyl)-*N,N'*-dibutyl-4,7,10-trioxa-1,13-tridecanediamine (6d).** A solution of 2.65 g (8 mmol) of **5d** in 70 mL of acetone was dripped in 1 h into a vigorously stirred suspension of 2.94 g (16 mmol) of **3** and 2.21 g (16 mmol) of anhydrous K_2CO_3 in 70 mL of acetone at 0–5 °C. The mixture was stirred for 2 h at 0–5 °C and then filtered, and the solvent evaporated. The residue was dissolved in CH_2Cl_2, washed with water, and dried over Na_2SO_4. Evaporation of the solvent gave a yellow oil, which by column chromatography (silica gel, ethyl ether–light petroleum) afforded 2.38 g (47%) of **6d** as a colorless oil: ^1H NMR ($CDCl_3$) δ 0.95 (t, 6 H), 1.1–2.1 (m, 12 H), 3.4–3.8 (m, 20 H). The same procedure was applied in the synthesis of bis(triazinyl) derivative **6e** (Table III).

10,23-Dichloro-1,7,14,20-tetrabutyl-4,17-dioxa-1,7,9,11,13,14,20,22,24,26-decaaza[7.7](2,6)triazinophane (1a). Solutions A, B, and C [A, 4.10 g (8 mmol) of **6a** in 100 mL of THF; B, 1.73 g (8 mmol) of **5a** in 100 mL of THF; C, 1.19 g (18 mmol) of 85% KOH in 100 mL of water] were simultaneously dripped (4.5 h) into 150 mL of boiling THF. Reflux was maintained for 15 h, then the solvent was evaporated, and the residue dissolved in CH_2Cl_2 and washed with water. Evaporation of CH_2Cl_2 gave a viscous oil, which was purified by column chromatography (silica gel, ethyl ether–light petroleum) to afford 3.30 g (63%) of a white solid: mp 90–92 °C (MeOH); ^1H NMR ($CDCl_3$) δ 0.9 (t, 12 H), 1.05–1.75 (m, 16 H), 2.7–4.6 (m, 24 H). The same procedure was applied in the synthesis of triazinophanes **1c–e** (Table IV).

13,29-Dichloro-1,10-dioctyl-4,7,20,23-tetraoxa-1,10,12,14,16,17,26,28,30,32-decaaza[10.10](2,6)triazinophane (1b). Solutions A and B [A, 5.32 g (12 mmol) of **6b** in 250 mL of acetone; B, 4.46 g (12 mmol) of **5c** and 1.10 g (27 mmol) of NaOH in 250 mL of 3:2 acetone–water] were simultaneously

(23) Williams, M. R.; Mosher, H. S. *J. Am. Chem. Soc.* **1954**, *76*, 2984–2987.

dripped (6 h) into 300 mL of boiling acetone. Reflux was maintained for 16 h, acetone was evaporated, and the suspension filtered. The solid material was purified by column chromatography (silica gel, ethyl ether) to afford 3.80 g (43%) of **1b**: mp 127–128 °C (MeCN); ^{1}H NMR ($CDCl_3$) δ 0.85 (t, 6 H), 1.0–1.6 (m, 24 H), 3.2–3.7 (m, 30 H); mass spectrum, m/z 742 (M^+); $m/2z$ 371 ($M^+/2$). The same procedure was applied in the synthesis of triazinophane **1g** (Table IV).

10,23-Dichloro-1,7,14,20-tetrabutyl-1,4,7,9,11,13,14,17,20,22,24,26-dodecaaza[7.7](2,6)triazinophane (1f). A sample of 834 mg (1 mmol) of **1e** dissolved in 40 mL of 95% ethanol containing 2 drops of concentrated HCl was hydrogenated for 20 h at 25 °C in the presence of $PdCl_2$ (71 mg, 0.4 mmol). After filtration of the catalyst, the solvent was evaporated and the residue dissolved in $CHCl_3$ and extracted with 3 N HCl. The aqueous phase was made alkaline with NaOH and extracted with $CHCl_3$ to afford 360 mg (55%) of **1f**: mp 220 °C (benzene–*n*-hexane); ^{1}H NMR ($CDCl_3$) δ 0.9 (t, 12 H), 1.35 (m, 8 H), 1.55 (m, 8 H), 2.75 (t, 6 H), 3.45–3.65 (m, 14 H).

13,29-Bis(octylamino)-4,7,20,23-tetraoxa-1,10,12,14,16,17,26,28,30,32-decaaza[10.10](2,6)triazinophane (1h). A solution of 2.08 g (4 mmol) of **1g** and 1.14 g (8.8 mmol) of *n*-octylamine in 50 mL of Me_2SO was stirred at 160 °C for 5 h in the presence of 2.76 g (20 mmol) of K_2CO_3. The solvent was distilled in vacuo, and the residue dissolved in $CHCl_3$ and washed with H_2O, 3 N HCl, and H_2O. Evaporation of the solvent and column chromatography (silica gel, EtOAc–MeOH) afforded 1.97 g (70%) of **1h**: mp 178–180 °C (benzene–hexane); ^{1}H NMR ($CDCl_3$) δ 0.9 (t, 6 H), 1.1–1.7 (m, 24 H), 3.2–3.8 (m, 28 H), 4.9–5.2 (br s, 2 H), 7.4–8.2 (br s, 4 H).

1,7,14,20,27,33-Hexabutyl-4,17,30-trioxa-1,7,9,11,13,14,20,22,24,26,27,33-dodecaaza[7.7.7](2,4,6)triazinophane (2a). Solutions A and B [A, 2.16 g (3.3 mmol) of **1a** in 80 mL of Me_2SO; B, 0.713 g (3.3 mmol) of **5a** in 80 mL of Me_2SO] were simultaneously dripped (6 h) into a stirred suspension of 1.83 g (13.2 mmol) of K_2CO_3 in 50 mL of Me_2SO at 170 °C, and the mixture was refluxed for another 15 h. The solvent was distilled in vacuo, the residue dissolved in $CHCl_3$, and washed with brine. Evaporation of the solvent and column chromatography (silica gel, ethyl ether–light petroleum) afforded 368 mg (14%) of **2a**: mp 88–90 °C (MeOH); ^{1}H NMR ($CDCl_3$) δ 0.85 (t, 18 H), 1.20 (m, 12 H), 1.45 (m, 12 H), 2.5–4.5 (m, 36 H); mass spectrum, m/z 798 (M^+), $m/2z$ 399 ($M^+/2$). The same procedure was applied in the synthesis of triazinophanes **2b–d** (Table V).

Kinetic Measurements. Kinetics were run in a 10-mL flask, equipped with a teflon-lined screw cap, thermostated at 60 °C with circulating butyl phthalate and magnetic stirrer. The temperature was controlled to within ±0.01 °C by a Exacal 200 Bath Circulator. Stirring speed (1300 ± 50 rpm) was controlled by using a strobe light. The flask was charged with 2.5 mL of a 4 M aqueous solution of the appropriate iodide, 0.5 mL of a 0.1 M solution of catalyst in toluene, and tetradecane as internal standard (0.5 mL of a 0.1 M solution in toluene). *n*-Octyl methanesulfonate (1 mL of a 1M solution in toluene) was added at zero time. Kinetics were followed by GLC analysis, and the pseudo-first-order rate constants (k_{obsd}) were obtained by plotting ln [substrate] vs. time and determining the slope of the straight lines.

Extent of Complexation of Triazinophane 2b. A mixture of a 2.5×10^{-2} M toluene solution (6 mL) of **2b** and a 4 M aqueous solution (5 mL) of NaI was stirred for 2 h in a flask thermostated at 60 °C. The mixture was left without stirring for an additional 2 h to allow good separation of the two phases. Potentiometric titration of a 2-mL sample of the organic phase with 0.01 N aqueous silver nitrate showed that 11.5% of the ligand was complexed (average of three measurements).

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Registry No. **1a**, 86577-71-1; **1b**, 86577-69-7; **1c**, 86577-70-0; **1d**, 91817-02-6; **1e**, 91817-03-7; **1f**, 91817-04-8; **1g**, 91817-05-9; **1h**, 91817-06-0; **2a**, 86577-74-4; **2b**, 86577-72-2; **2c**, 86577-73-3; **2d**, 91817-07-1; **3**, 108-77-0; **4a**, 31353-28-3; **4b**, 32775-05-6; **4c**, 23243-82-5; **4d**, 91817-08-2; **4e**, 91817-09-3; **5a**, 2620-28-2; **5b**, 86577-64-2; **5c**, 86577-65-3; **5d**, 91817-10-6; **5e**, 91817-11-7; **5f**, 23539-10-8; **5g**, 929-59-9; **6a**, 86577-68-6; **6b**, 86577-66-4; **6c**, 86577-67-5; **6d**, 91817-12-8; **6e**, 91817-13-9; **6f**, 91841-55-3; **6g**, 4700-88-3; **6h**, 18426-53-4; Na^+, 17341-25-2; K^+, 24203-36-9; Cs^+, 18459-37-5; 3,6-dioxa-1,8-octanedioyl dichloride, 31255-09-1; butyric anhydride, 106-31-0; 4,7,10-trioxa-1,13-tridecanediamine, 4246-51-9; phthalic anhydride, 85-44-9; 1,5-diphthalimido-3-azapentane, 63563-83-7; 3-benzyl-1,5-diphthalimido-3-azapentane, 23538-88-7; octylamine, 111-86-4; diethylenetriamine, 111-40-0; benzyl bromide, 100-39-0; 1,8-dichloro-3,6-dioxaoctane, 112-26-5; ammonium, 14798-03-9.

Catalytic Hydrogenation of Pyrroles at Atmospheric Pressure[1]

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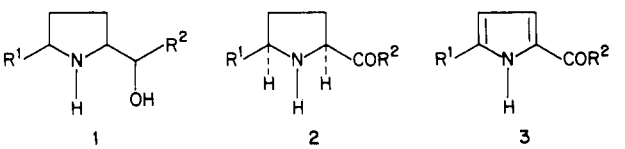
N-(*tert*-Butoxycarbonyl)pyrroles are catalytically hydrogenated to the corresponding pyrrolidines, over 5% platinum on carbon catalyst, at room temperature and atmospheric pressure. Under these conditions *O*-benzyl groups are retained and 2,5-disubstituted pyrroles are reduced predominantly or exclusively to the *cis*-2,5-disubstituted pyrrolidines. This facile catalytic reduction of pyrroles was the central feature of convenient, high yield syntheses of 2-acylpyrrolidines and 5-substituted proline derivatives.

It became necessary, in connection with several research programs, to devise syntheses of 2-(1-hydroxyalkyl)-5-substituted pyrrolidines 1 of a nature such that stereochemical control could be exercised in the side chain as well as at positions 2 and 5 of the heterocyclic ring. It was obvious that this objective was reducible to the development of a synthesis of *cis*-2-acyl-5-alkylpyrrolidines 2 which ought to be available by catalytic reduction of the corresponding pyrroles 3. Such reductions are known to be difficult[3,4] but facilitation of this process might be antic-



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