The Formation of Complexes between Aza-derivatives of Crown Ethers and Primary Alkylammonium Salts. Part 5.[1] Chiral Macrocyclic Diamines

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Syntheses of three types of chiral macrocyclic diamines, analogous to crown ethers, are described. The chirality of these systems is based, in one case, upon the plane of chirality of paracyclophane systems and, in the other two cases, upon the axis of chirality of bridged biphenyls. Two methods are described for the measurement of chiral selectivity in the formation of complexes between these chiral macrocyclic host molecules and chiral guest primary alkylammonium salts. Both methods use n.m.r. spectrometry, a single-phase system, a racemic chiral host and (*R*)- and (*RS*)-guest salts. The first method is suitable for both optically labile and optically stable hosts and the second method is only suitable for optically labile host species.

In previous papers [1] of this series we have discussed the formation of complexes between aza-analogues of crown ethers as host molecules and primary alkylammonium salts as guest molecules. In all the cases discussed the macrocyclic host was an achiral system and, although some selectivity was observed in complex formation, the guest–host interactions did not differentiate between the two enanantiomeric forms of a chiral guest molecule. Chiral recognition by hosts of the crown ether type requires a chiral host molecule and this approach to chiral recognition has been extensively and elegantly developed by Professor Cram and his co-workers using hosts incorporating one or more chiral 2,2′-dioxy-1,1′-binaphthyl units.[2] Other chiral crown ethers have been synthesised based upon carbohydrates,[3] tartaric acid,[4] and suitably substituted glycerol [5] as sources of chirality. In some cases it has been shown that these systems also show chiral selectivity in complex formation.

Chiral recognition has usually been studied using a procedure based upon the distribution of a racemic guest ammonium salt between an aqueous phase and an organic phase containing the chiral host molecule. The enantiomer distribution constant (EDC) may then be calculated using an n.m.r. method or from the specific rotation of the guest in the aqueous and organic phases. Using the binaphthyl derivative (1) as a host molecule EDC values of 12 and 18 have been reported for the hexafluorophosphate salts of the methyl esters of phenylglycine and *p*-hydroxyphenylglycine.[6] The EDC value varies in a complex way with changes of counter-ion and solvent [7] and it is clear that chiral recognition cannot be predicted with confidence from simple considerations of non-bonded interactions between host and guest components.

In this paper we discuss alternative procedures for assessing chiral selectivity using racemic host molecules, and single-phase rather than two-phase systems. For this study we have synthesised chiral paracyclophanes and chiral bridged biphenyls, using the methods outlined below. In the final section of the paper we discuss the methods used to measure chiral selectivity.

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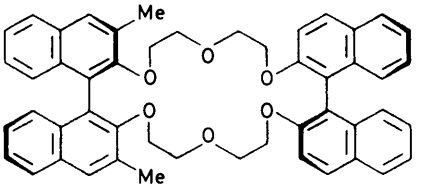
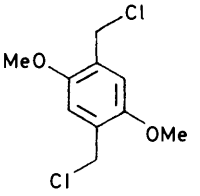
RESULTS AND DISCUSSION

Host Syntheses.—The first chiral systems to be examined were paracyclophanes, since the paracyclophane system could be located within the macrocycle of a crown ether analogue, and the chirality of paracyclophanes with suitably substituted aromatic rings is well established.[8] Reaction of the readily available bis-chloromethyl compound (2) with the dianion from the biscarbamate (3a) gave the paracyclophane (4a) in moderate yield. The product (4a) was reduced with



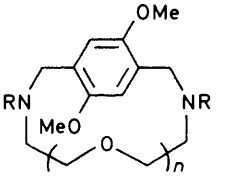
(1)



(2)

$EtO_2CNHCH_2[CH_2OCH_2]_nCH_2NHCO_2Et$

(3)



(4) R = CO_2Et

(5) R = Me

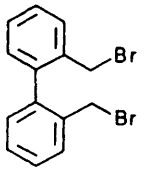
(3)–(5) a; *n* = 3

b; *n* = 2

lithium aluminium hydride giving the diamine (5a). Due to the presence of some triethylene glycol as an impurity in the tetraethylene glycol used for the synthesis of (3a) the cyclization reaction gave the paracyclophane (4b), in addition to (4a). Reduction of (4b) gave (5b).

The second type of chiral system to be examined was the bridged biphenyl system. The chirality of bridged biphenyl systems has been investigated in some detail,[9] and by analogy with known results for the energy

barrier to the conformational inversion of such systems it was possible to design systems with high and moderate energy barriers. Thus reaction of the dibromide (6) with the dianions from the biscarbamates (3) gave the bridged biphenyls (7) which were reduced with lithium aluminium hydride to give the diamines (8). The inversion of (8) was highly hindered ($\Delta G^{\ddagger} > 25$ kcal mol^{-1}) and in order to prepare a system undergoing more rapid conformational inversion the 2,2′-dioxybiphenyl unit was investigated. 2,2′-Dihydroxybiphenyl was readily converted into the bistoluene-*p*-sulphonate (9d) by the reaction sequence (9a)→(9b)→(9c)→(9d) (see Experimental section). The reaction of the toluenesulphonate (9d) with the dianion from the biscarbamate (10a) gave the biphenylophane (11a), which yielded the diamine (11b) on reduction with lithium aluminium hydride. The corresponding bisbenzylcarbamate (10b) gave the biphenylophane (11c) which gave the bis-secondary amine (11d) on debenzylation (HBr–acetic acid), and hence the possibility of preparing derivatives of the biphenylophane system (11) having functional groups in the side chain, as for example the diol (11e). The biphenylophanes (12), (13), and (14) were prepared by analogous methods from the bistoluene-*p*-sulphonate (9d) with the appropriate biscarbamate.



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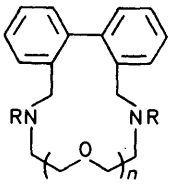
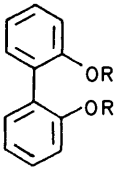


(7) R = CO_2Et
(8) R = Me
a; *n* = 2
b; *n* = 3



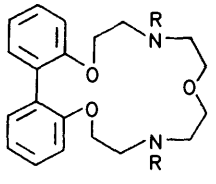
(9)
a; R = H
b; R = CH_2CO_2Et
c; R = CH_2CH_2OH
d; R = $CH_2CH_2OSO_2C_6H_4Me$-*p*
e; R = $CH_2CH{=}CH_2$

$RO_2CNHCH_2[CH_2OCH_2]_nCH_2NHCO_2R$

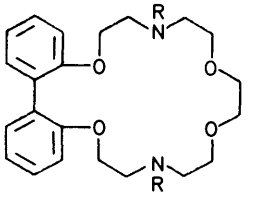
(10)
a; *n* = 1, R = Et
b; *n* = 1, R = CH_2Ph
c; *n* = 2, R = CH_2Ph

An extension of these syntheses to 3,3′-disubstituted biphenyl systems was also investigated since the additional substituents could potentially increase the chiral barriers in the host macrocycles, hence achieving greater chiral selectivity. The bisallyl ether (9e) rearranged thermally when heated under reflux in diethylaniline but the product (16) had undergone cyclization of one of the *o*-hydroxyallylbenzene systems. This cyclization was readily avoided by carrying out the Claisen rearrangement of (9e) in the presence of acetic anhydride,[10] giving initially the diacetate (15a) which was readily hydrolysed to the phenol (15b). The bistoluene-*p*-sulphonate (15e) of the diol (15d) was then synthesised by the conventional sequence (15b)→(15c)→(15d)→(15e) (see Experimental section).

The bistoluene-*p*-sulphonate (15e) reacted with the dianion from the biscarbamate (10a) to give a moderate yield of the biphenylophane (17a). Unfortunately under the strongly basic reaction conditions the double bonds of the allyl side chains moved into conjugation with the aromatic rings giving the propenyl derivative (17a) rather than the required allyl derivative. The biscarbamate (17a) could be reduced in the usual way with lithium aluminium hydride giving the diamine (17b) and further reduction (H_2,Pd–C) gave the propyl-substituted biphenylophane (17c).

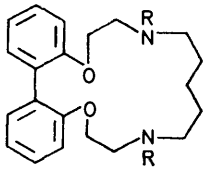


(11)
a; R = CO_2Et
b; R = Me
c; R = CO_2CH_2Ph
d; R = H
e; R = CH_2CH_2OH



(12)

The introduction of functional groups, having potential hydrogen bonding interactions with guest molecules, into the side chains R^2 of the host system (17) was also investigated. Thus ozonolysis of the propenyl derivative (17b), followed by reduction of the ozonide, gave the diol (17d) but the usual reduction of the ethoxycarbonyl substituents of (17d) failed to give the pure *NN*′-dimethyl derivative. An alternative procedure involved ozonolysis of the allyl side chains of the biphenyl derivative (15e) and protection of the resulting di-aldehyde (18a) as its bisacetal derivative (18b). The bisacetal (18b) could be used successfully in a cyclization reaction to give (17e) and subsequent reduction with lithium aluminium hydride gave the functionalised macrocycle (17f).



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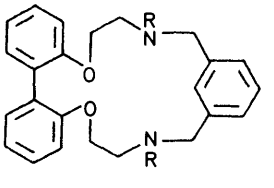
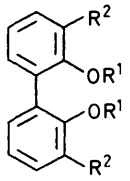


(14)

(12)—(14) a; R = CO_2CH_2Ph
b; R = Me

Complexes.—The formation of a complex between a racemic chiral host molecule and a racemic chiral guest molecule gives the four complexes (19a—d). The pair of complexes (19a) and (19d) are related as enantiomers, as



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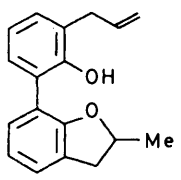


(16)

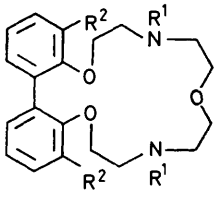
a; R^1 = Ac, R^2 = $CH_2CH{=}CH_2$

b; R^1 = H, R^2 = $CH_2CH{=}CH_2$

c; R^1 = CH_2CO_2Et, R^2 = $CH_2CH{=}CH_2$

d; R^1 = CH_2CH_2OH, R^2 = $CH_2CH{=}CH_2$

e; R^1 = $CH_2CH_2OSO_2C_6H_4Me$-*p*, R_2 = $CH_2CH{=}CH_2$



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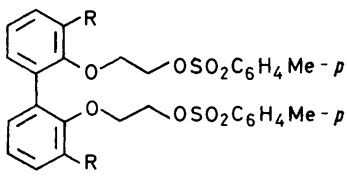


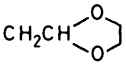
(18)

a; R^1 = CO_2Et, R^2 = (*E*)-CH=CHMe

b; R^1 = Me, R^2 = (*E*)-CH=CHMe

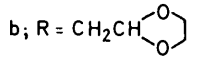
c; R^1 = Me, R^2 = CH_2CH_2Me

d; R^1 = CO_2Et, R^2 = CH_2OH

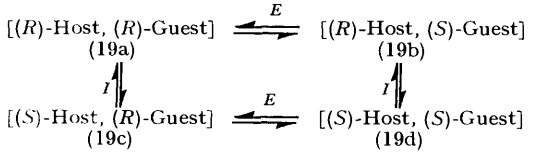
e; R^1 = CO_2Et, R^2 = 

f; R^1 = Me, R^2 = 

a; R = CH_2CHO

b; R = 

are the pair of complexes (19b) and (19c); also each pair has a diastereoisomeric relationship with the other pair. In the system containing the racemic host and racemic guest the two diastereoisomeric complexes are interconverted by process E (Scheme 1) which involves



SCHEME 1

exchange of guest molecules of opposite chirality; this process is normally fast on the n.m.r. time scale at normal probe temperatures (25—35 °C) for complexes of primary alkylammonium salts with macrocyclic diamines [1,13] and other crown ether analogues.[14] The n.m.r. spectrum under these conditions will therefore be the time-averaged spectrum of an *equilibrium mixture* of the diastereoisomers. If only the (*R*)-configuration of the guest is present, but the host molecule is racemic, process *E* (Scheme 1) is no longer possible and the two diastereoisomeric complexes can only be equilibrated by process *I* which involves inversion of the configuration of the host molecule. In some cases process *I* may be rapid on the n.m.r. time scale as, for example, the interconversion of two enantiomeric conformations of a monoaza- or diaza-15-crown-5 host system. Two other situations are possible that permit the evaluation of chiral selectivity, using a racemic host system, by two different methods.

Method 1.—For optically labile * host molecules ($\Delta G^{\ddagger}$ for process 1 *ca.* 15—20 kcal mol^{-1}), such as the bridged biphenyls (11)—(14) and (17), the equilibrium may be slow on the n.m.r. time scale but relatively fast on the laboratory time scale. Under these conditions the species (19a) and (19c) give distinct n.m.r. spectra and the equilibrium (19a) ⇌ (19c) is attained in the solution during the period of observation. The position of equilibrium can then be measured by, for example, integration of the n.m.r. signals associated with each of the diastereoisomers (19a) and (19c).

Method 2.—If the chiral host system is optically stable, as for example the binaphthyl derivative (1), the paracyclophanes (5), and the bridged biphenyls (8), it is still, in principle, possible to measure the position of the equilibrium for the fast process E shown in Scheme 1. Thus the spectra of the diastereoisomers (19a) and (19c) can be separately observed using a racemic host and the optically active (*R*)-guest salt. The position of equilibrium may then be obtained from the chemical shifts observed from a 1 : 1 mixture of racemic host and racemic guest, since under these conditions a rapid equilibrium is established between the two diastereoisomers and the n.m.r. chemical shifts will correspond to the time-averaged signals of the equilibrium composition. This is also applicable for optically labile hosts and in this case the results may be compared with those obtained using Method 1.

The investigation of the formation of complexes by the chiral host systems (5), (8), (11)—(14), and (17) will be discussed in the following three sections of this paper.

Paracyclophanes as Host Molecules.—The signals assignable to the benzylic protons in the n.m.r. spectrum of the [15]*paracyclophane* (5a) in perdeuteronitrobenzene appeared as an AB system ($\nu_A - \nu_B$ 66 Hz, J_{AB} 13 Hz) which remained sharp as the temperature of the solution was increased to 180 °C. This lack of line-broadening due to site exchange indicates that the inversion process *I* (*cf.* Scheme 1) interconverting the enantiomeric conformations (20a) and (20b) remains slow on the n.m.r. time scale up to 180 °C ($\Delta G^{\ddagger} \geqslant 24$ kcal mol^{-1}). Method 2 is

* The terms 'optically labile' and 'optically stable' will be used because of their wide use in other contexts; in this paper optically labile systems refer to those with inversion barriers in the range $\Delta G^{\ddagger}$ 15—20 kcal mol^{-1} and optically stable systems have inversion barriers with $\Delta G^{\ddagger} \geqslant 22$ kcal mol^{-1}.

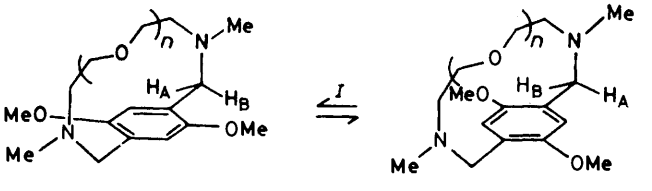
TABLE 1

N.m.r. spectra [a] of complexes of diazaparacyclophanes (5a) and (5b) [b] with primary alkylammonium thiocyanates.

Host	Guest	Temperature (°C)	Aryl-H	$ArCH_AH_BN$ [c]	OMe	NMe
(5a)		35	6.96	3.85, 3.23	3.79	2.43
(5a)	$PhCH_2NH_3^+NCS^-$	35	7.15		3.92	2.59
(5a)	(*R*)-$PhCHMeNH_3^+NCS^-$	50	7.09		3.86, 3.89	2.63, 2.59
		20				2.58, 2.52
		−20				2.50, 2.44
(5a)	(*RS*)-$PhCHMeNH_3^+NCS^-$	50	7.09	4.04, 3.46	3.86	2.60
		20				2.54
		−20				2.46
(5a)	$PhNH_3^+NCS^-$	35	7.19	4.12, 3.69	3.85	2.69
		−80	7.38, 6.92			*ca.* 3.22, 2.44
(5a)	H^+NCS^-	35	7.24	4.18, 3.78	3.88	2.76
		−80	7.42, 6.92			3.24, 2.43
(5b)		35	6.96	3.84, 3.22	3.84	2.49
(5b)	$PhCH_2NH_3^+NCS^-$	35	7.05	4.01, 3.40	3.89	2.57
(5b)	(*R*)-$PhCHMeNH_3^+NCS^-$	20	7.05		3.96	2.64, 2.55
		−20				2.63, 2.43
(5b)	(*RS*)-$PhCHMeNH_3^+NCS^-$	20	7.05		3.96	2.60
		−20				2.52

[a] Recorded at 100 MHz for solutions in CD_2Cl_2 or $CDCl_3$; chemical shifts in δ (±0.01) relative to $SiMe_4$. [b] Assignable signals only, the OCH_2CH_2O and NCH_2CH_2O systems generally gave complex multiplets. [c] AB system, J_{AB} 12 Hz.

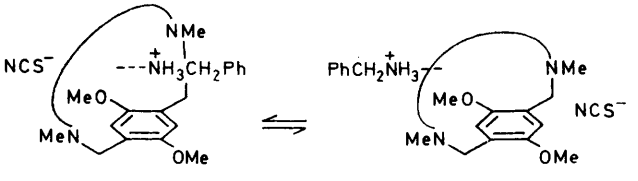
therefore appropriate for the assessment of chiral selectivity.



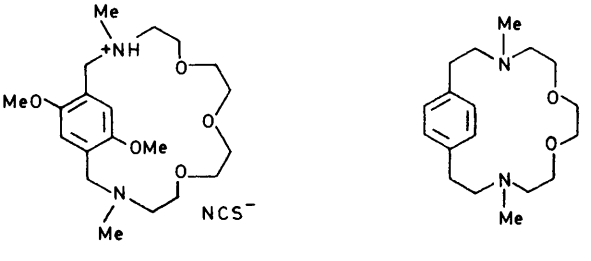
(20a) (20b)

The chemical shifts of the signals associated with the OMe, NMe, and $ArCH_2N$ protons of the paracyclophanes (5a) and (5b) moved downfield on the addition of 1 equiv. of benzylammonium thiocyanate (Table 1), these downfield shifts contrasting with the shifts to both higher and lower fields usually observed for other aza-crown ether systems.[1,11,13] At low temperatures the signals in the spectrum of the complex of the [12]paracyclophane (5b) broadened but did not separate into sets of signals assignable to a complex in which face-to-face guest exchange (21a) ⇌ (21b) was slow on the n.m.r. time scale. The spectrum of the complex of the [15]paracyclophane (5a) showed some evidence for signal separation at low temperatures, but it was rather poorly defined. We conclude that the complexes are in both cases rather weakly bound as compared with other diaza-crown ethers in which guest-exchange processes usually become slow on the n.m.r. time scale at low temperatures. The n.m.r. spectrum of the monothiocyanate of host (5a) shows a temperature dependence at low temperatures that appears to be associated with slow intramolecular proton exchange (see Table 1),* thus at −80 °C two signals are observable for the NMe protons and the aryl protons corresponding to the monoprotonated structure (22). The chemical shifts of these signals are, however, quite distinct from those observed in the spectrum of the benzylammonium thiocyanate complex of (5a). We note that attempts to form a complex between (5a) and anilinium thiocyanate appear to result in the formation of the monothiocyanate of (5a) and free aniline (see Table 1).

The spectra of both (5a) and (5b) in the presence of one equivalent of (*R*)-phenylethylammonium thiocyanate showed doubling of the NMe signal, whereas in the presence of the (*RS*)-guest the NMe signal was observed as a singlet (Table 1). These observations are in accord with expectations based upon Scheme 1 (*I* slow and *E* fast). Comparisons of the chemical shifts for the two cases, as required by Method 2, indicated that the ratio of the diastereoisomeric complexes was not experimentally distinguishable from a 1 : 1 ratio, but because



(21a) (21b)



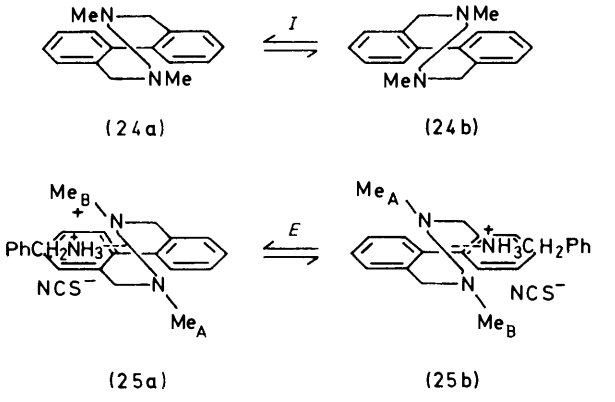
(22) (23)

the separation of the two NMe signals was small in both cases the accuracy of the assessment was limited. The results were therefore unsatisfactory in that no evidence for chiral selectivity could be obtained and this is probably a consequence, at least in part, of the weak binding

* The results could also be explained in the terms of slow proton exchange between the free base and a doubly protonated species but this seems unlikely.

between guest and host components. It has recently been reported,[15] however, that the [14]paracyclophane system (23) forms strong complexes with alkylammonium salts.

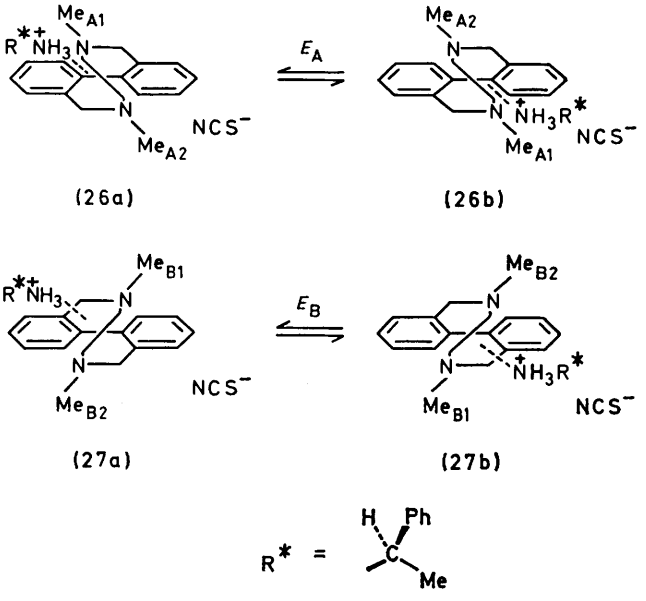
Optically Stable Bridged Biphenyls as Host Molecules.— The bridged biphenyls (8) were expected to have high barriers ($\Delta G^{\ddagger} \geqslant 22$ kcal mol^{-1}) to conformational inversion, by analogy with the known inversion barriers for a wide range of bridged biphenyl systems.[9] In accord with this expectation the benzylic methylene protons of both (8a) and (8b) are observable as AB systems in their n.m.r. spectra, recorded for solutions at 35 °C. The AB system for (8b) in perdeuterionitrobenzene remains unchanged



as the temperature is increased to 200 °C, indicating that the energy barrier to conformational invesion (24a) ⇌ (24b) * is high ($\Delta G^{\ddagger} \geqslant 24$ kcal mol^{-1}).

The n.m.r. spectra of both (8a) and (8b) were changed by the addition of one mol equiv. of benzylammonium thiocyanate (Table 2). The n.m.r. spectrum of the complex of (8a) showed no effects other than line-broadening as the temperature was lowered but the n.m.r. spectrum of the complex of (8b) showed two NMe signals at low temperatures (<−80 °C) consistent with a slow rate, on the n.m.r. time scale, for the guest exchange process (*E*) (25a) ⇌ (25b). This result indicates that the guest is more strongly bound to the larger ring system of (8b), with its additional binding site, with a free-energy barrier of *ca.* 9.4 kcal mol^{-1} for the exchange process *E* (based upon the coalescence of the NMe signals).

The two complexes (25a) and (25b) are actually identical, although their interconversion may be studied because of the diastereotopicity of the two NMe groups. The situation for a chiral guest is more complex since, as indicated in Scheme 1, two diastereoisomeric complexes are formed. Each diastereoisomer will give two NMe signals if the exchange process analogous to (25a) ⇌ (25b) is slow on the n.m.r. time scale.



SCHEME 2 Exchange of (*R*)-phenylethylammonium thiocyanate between the two faces of host (8) in two diastereoisomeric complexes. The assignment of the labels A and B to the two diastereoisomers is arbitrary (*cf.* Figure 1 and Discussion)

TABLE 2

N.m.r. spectra [a] of complexes of bridged biphenyls (8a) and (8b) with primary alkylammonium thiocyanates

		Spectrum of host [b]					Spectrum of guest		
		ArCH$_2$N [c]							
Host	Guest	H$_A$	H$_B$	OCH$_2$ [d]	OCH$_2$CH$_2$O	NMe	CH [e]	CH$_2$	CH$_3$ [e]
(8a)		3.92	2.81	3.50	3.43	2.04			
(8a)	PhCH$_2$NH$_3$$^+NCS^-$	4.16	3.10	3.60	3.46	2.16		3.88	
(8a)	(*R*)-PhCHMeNH$_3$$^+NCS^-$	4.16	3.07	3.59	3.45	2.15	4.12		1.43
(8a)	(*RS*)-PhCHMeNH$_3$$^+NCS^-$	4.15	3.07	3.57	3.43	2.13	4.12		1.41
(8b)		3.62	3.02			2.08			
(8b)	PhCH$_2$NH$_3$$^+NCS^-$	3.92	3.28	3.52	3.52	2.15		3.73	
(8b)	(*R*)-PhCHMeNH$_3$$^+NCS^-$	3.81	3.25	3.52	3.52	2.21 2.16	4.12		1.43
(8b)	(*RS*)-PhCHMeNH$_3$$^+NCS^-$	3.82	3.28	3.52	3.52	2.19	4.11		1.44

[a] Recorded at 100 MHz for solutions in CD_2Cl_2, chemical shifts in δ (±0.01) relative to $SiMe_4$. [b] Assignable signals only. The aryl and NC*H*$_2$CH$_2$O protons generally give complex multiplets. [c] AB system, J_{AB} *ca.* 14 Hz. [d] Triplet, *J ca.* 5 Hz. [e] Quartet and doublet, *J ca.* 7 Hz.

Thus if (*R*)-phenylethylammonium thiocyanate is used as the guest molecule the spectrum of the complex of (8b) shows two NMe signals at +35 °C, corresponding to the two diastereoisomeric complexes (Table 2). As the temperature of the solution is lowered the separation of these two signals changes and the high-field signal (diastereoisomer A) broadens and appears as two signals

* In formulae (24)—(27) the line linking the two nitrogen atoms represents the $CH_2(CH_2OCH_2)_nCH_2$ moiety.

below −80 °C. The low-field NMe signal (diastereoisomer B) broadens at very low temperatures but does not separate into two signals. The CMe signal of the guest molecule also broadens and at temperatures below −90 °C it is observable as two distinct signals corresponding to the two diastereoisomeric complexes (Figure 1). This behaviour can be associated with the guest–host exchange process outlined in Scheme 2; two

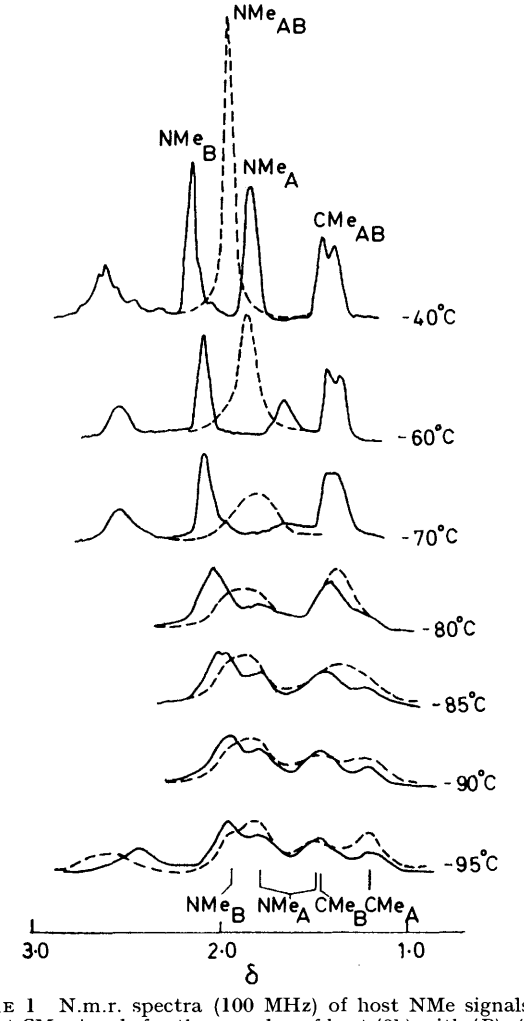


FIGURE 1 N.m.r. spectra (100 MHz) of host NMe signals and guest CMe signals for the complex of host (8b) with (*R*)- (——) and (*RS*)- (– – – –) phenylethylammonium thiocyanate

of these processes, E_A and E_B involve exchange of guest between the two equivalent faces of the host in the two diastereoisomeric complexes (26) and (27). Clearly in the case of diastereoisomer A which gives the high-field methyl signal this exchange may be a slower process than it is for the diastereoisomer B, suggesting that guest–host binding is stronger in diastereoisomer A.

The spectrum of the complex formed between the host (8b) and (*RS*)-phenylethylammonium thiocyanate (Table 2) shows interesting differences (Figure 1). Thus at 35 °C the signals corresponding to the two diastereoisomeric complexes are averaged with the observed signal positions corresponding to the weighted mean of the

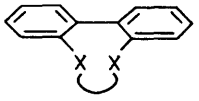
TABLE 3

Chemical shifts of NMe protons for complexes of the bridged biphenyl (8b) with (*R*)- and (*RS*)-phenylethylammonium thiocyanate and chiral selectivity

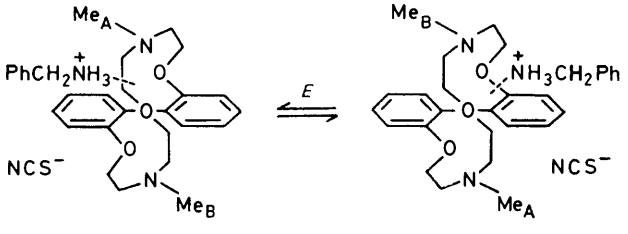
Temperature (°C)	NMe chemical shifts [a] (*R*)-guest NMe$_B$	NMe$_A$	(*RS*)-guest NMe$_{AB}$	$P_A/P_B = K$ [b]	ΔG_{AB} [c] / kcal mol^{-1}
+14	221.8	216.5	220.0	0.5	−0.37
+4	221.3	213.0	217.7	0.8	−0.13
−7	220.2	209.0	214.9	0.9	−0.06
−16	219.3	203.8	211.3	1.06	0.03
−25	218.0	197.3	207.1	1.1	0.05
−34	216.5	190.9	201.6	1.4	0.16
−42	215.0	183.6	195.5	1.7	0.23
−50	213.5	176.7	188.8	2.0	0.31
−58	211.8	171.6	182.9	2.5	0.39

[a] Spectra recorded using a Varian HA100 spectrometer, chemical shifts (±0.2) in Hz relative to SiMe$_4$. [b] Calculated using the formula $k = (\nu_B - \nu_{AB})/(\nu_{AB} - \nu_A)$ where ν_A, ν_B, and ν_{AB} are the chemical shifts of NMe$_A$, NMe$_B$, and NMe$_{AB}$ respectively. [c] Corresponding to ΔS_{AB} +9.5 cal K^{-1} mol^{-1} and ΔH_{AB} +2.4 kcal mol^{-1}; probable errors in these values are difficult to assess.

chemical shifts of the two diastereoisomers. As the temperature is lowered the NMe and CMe signals broaden, but at −95 °C the spectrum is significantly different from the spectrum of the (*R*)-guest with the host (8b). Thus the signal associated with diastereoisomer A giving the high-field NMe and CMe signals appear to be of higher intensity than the NMe and CMe signals assignable to diastereoisomer B. Unfortunately the signals at these very low temperatures are too broad to be used in other than a qualitative fashion. The ratio of the two diastereomeric complexes can be obtained at higher temperatures (>−50 °C) using method 2 and the results are shown in Table 3. In view of the indirect nature of the method the calculated diastereoisomer ratios are subject to uncertainty and the derived figures for ΔH and ΔS must be regarded as approximate; it appears, however, that both entropy and enthalpy differences are important in determining chiral selectivity.



(28)



(29a) (29b)

These results indicate that the bridged biphenyl (8b) shows significant chiral selectivity for binding between the crown system and a chiral alkylammonium thiocyanate. This difference presumably results from dif-

ferent non-bonded interactions between the Ph, Me, and H substituents of an (*R*)-guest with the (*R*)- and (*S*)-host molecules, but it is not possible to assign structures (26) and (27) to the diastereoisomers A and B.

The bridged biphenyl (8a), having a smaller host macrocycle, does not give doubling of the NMe signals when (*R*)-phenylethylammonium thiocyanate is used as the guest molecule, neither is any temperature dependence observable in the n.m.r. spectra of the complexes which may be assigned to processes of the type shown in Scheme 2.

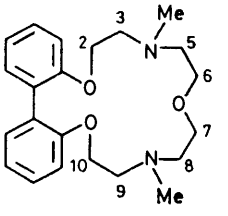
Optically Labile Bridged Biphenyls as Host Molecules.— Consideration of the transition state (28) for the inversion of a bridged biphenyl [*e.g.* (24a) ⇌ (24b)] suggested that a bridged 2,2′-dioxybiphenyl system (28, X = O) would be optically labile, having an inversion barrier within the range 15—20 kcal mol^{-1}. Accordingly the crown ether analogue (11b) was synthesised and its ^{1}H n.m.r. spectrum examined. As anticipated the spectrum of a solution of (11b) in perdeuterionitrobenzene showed ABCD systems for the OCH_2CH_2N units at 35 °C, which collapsed to give an AA′BB′ system at temperatures above 100 °C. Due to the complexity of the spectral changes only an approximate energy barrier ($\Delta G^{\ddagger}$ 18 ± 1 kcal mol^{-1}) for the inversion process could be obtained, but the value for this energy barrier indicated that the crown ether analogues (11) and related compounds would be optically labile systems of the type required for the assessment of chiral selectivity by Method 1.

The n.m.r. spectrum of a 1 : 1 mixture of the host (11b) and benzylammonium thiocyanate in dideuteriomethylene chloride showed significant shifts in the signals as compared with the spectrum of the free host (Table 4), suggesting the formation of a complex. Further evidence for complex formation was obtained from the temperature dependence of the n.m.r. spectrum. Thus at very low temperatures the host signals separated into two sets as expected for a complex having the structure (29a) ≡ (29b) with face-to-face exchange of the guest cation (Process *E*) slow on the n.m.r. time scale. In particular the NMe group of the host gave two widely separated signals at low temperatures (δ 1.27 and 2.35), similar to those observed, for example, for the NMe group of the achiral diaza-15-crown-5 hosts with phenylethylammonium thiocyanate as the guest molecule. The energy barrier for the guest exchange process *E* ($\Delta G^{\ddagger}$ 9.9 kcal mol^{-1}), based upon the coalescence of the two NMe signals, indicated reasonably strong guest–host binding, comparable with other diaza-crown ether systems, and fast guest-exchange down to reasonably low temperatures as required for the assessment of chiral selectivity by Method 1.

The n.m.r. spectra of the host (11b) with (*R*)- and

TABLE 4

N.m.r. spectra of the complexes of host (11b) with primary alkylammonium thiocyanates



(11b)

Guest	Temp. (°C)	Spectrum of host: 2-H_2 + 10-H_2	3-H_2 + 9-H_2	5-H_2 + 8-H_2	6-H_2 + 7-H_2	NMe	Spectrum of guest
a	25	4.02 (t, *J* 7 Hz)	2.98 (dt, *J* 13 and 7 Hz) 2.53 (dt, *J* 13 and 7 Hz)	2.58 (t, *J* 5 Hz)	3.55 (dt, *J* 11 and 5 Hz) 3.42 (dt, *J* 11 and 5 Hz)	2.26	
$PhCH_2NH_3^+NCS^-$ [a]	25	4.11 (*J* 11, 7, and 4.5 Hz) 3.91 (*J* 11, 4.5, and 5.5 Hz)	2.77 (*J* 13, 5.5, and 4.5 Hz) 2.60 (m)	2.61 (t, *J* 4.5 Hz)	3.45 (t, *J* 4.5 Hz)	2.08	3.73
	−90	4.20, 4.03 (br m) 3.85 (br m)				2.35, 1.27	
(*R*)-$PhCHMeNH_3^+NCS^-$ [b]	30	4.10 (m) 3.90 (m)	*ca.* 2.8 (m)	*ca.* 2.7 (m)	3.47 (t, *J* 5 Hz) 3.57 (t, *J* 5 Hz)	2.25, 2.06	1.49 (d, *J* 7 Hz)
(*RS*)-$PhCHMeNH_3^+NCS^-$ [b]	30	4.10 (m) 3.90 (m)	2.77 (t, *J* 5 Hz)	2.65 (t, *J* 5 Hz)	3.51 (t, *J* 5 Hz)	2.13	1.49 (d, *J* 7 Hz)

[a] At 220 MHz using a Perkin-Elmer R34 spectrometer. [b] At 100 MHz using JEOL PS100 FT spectrometer.

TABLE 5

Chiral selectivity for complex formation between host (11b) and phenylethylammonium thiocyanate

Temperature (°C)	P_A/P_B (method 1) [a]	ΔG_{AB} [d] (method 1)	P_A/P_B (method 2) [a]	ΔG_{AB} [e] (method 2)
30	1.70	0.32	1.44	0.22
20	1.69	0.30	1.41	0.20
11	1.87	0.35	1.57	0.26
1	1.97	0.37	1.79	0.32
−9	2.16	0.40	1.97	0.36
−18	2.26[b]	0.41[b]	1.94	0.34
−28	c	c	2.62	0.47

[a] Spectra recorded for CD_2Cl_2 solutions in the Fourier-transform mode using a JEOL PFT100 spectrometer. [b] One NMe signal becomes broad at this temperature and accurate integration is not possible; furthermore host inversion becomes relatively slow ($t_{\frac{1}{2}}$ *ca.* 460 s at −20 °C) so that the equilibrium between the two diastereoisomers is attained only slowly. [c] Broadening of the high field signal (NMe_A) makes accurate integration difficult below −18 °C. [d] Corresponding to ΔS_{AB} 3.3 kcal K^{-1} mol^{-1} and ΔH_{AB} 1.28 kcal mol^{-1}. [e] Corresponding to ΔS_{AB} 5.5 cal K^{-1} mol^{-1} and ΔH_{AB} 1.82 kcal mol^{-1}.

(*RS*)-phenylethylammonium thiocyanate as the guest species were particularly informative (Tables 4 and 5). Thus with the (*R*)-guest salt two NMe signals were observable at 30 °C (δ 2.24 and 2.05) having an intensity ratio of 1 : 1.7 and indicative of moderate chiral selectivity by the host molecule (Scheme 1). The spectrum of the complex of the (*RS*)-guest salt showed, as expected, only a single NMe signal (δ 2.13) * and comparison with the chemical shifts of the two diastereoisomeric species indicated a ratio of 1 : 1.44 in reasonable agreement with the previous result. Thus both Method 1 and Method 2 could be used for the assessment of chiral slectivity over a moderately wide temperature range and the results obtained by the two methods were in reasonable agreement (Table 5); this agreement between results supports the validity of both approaches. The more direct approach of Method 1 should be more accurate, since Method 2 depends, for example, upon the 1 : 1 stoicheiometry of complex formation and the relative insensivity of chemical shifts to changes in the composition of the mixture of complexes. Both procedures have the advantages that they can be used for a single-phase system, do not require the resolution of the host molecule, and give data for a wide range of temperatures.

The NMe signals of the host (11b) in the complex with (*R*)-phenylethylammonium thiocyanate exhibit temperature dependence at low temperatures associated with guest–host exchange processes becoming slow on the n.m.r. time scale. Thus the high-field signal, due to NMe_A of the major diastereoisomer A, broadens and separates into two signals at significantly higher temperatures than the low field signal, NMe_B associated with the minor diastereoisomer B. At very low temperatures diastereoisomer A gives a well defined high-field NMe signal (δ 1.16) but the low field signal (δ *ca.* 2.4) is obscured by other signals in the same region of the spectrum (see Figure 2). The NMe signal due to diastereoisomer B broadens and disappears at very low temperatures but separation into two signals is not observable. This suggests that the exchange process corresponding to (29a) ⇌ (29b) (*cf.* Scheme 2) is slower for the major, more strongly bound diastereoisomer A, as might be expected from consideration of the relationship between binding energy and the energy barrier for guest exchange (see refs. 13—16 for discussions).

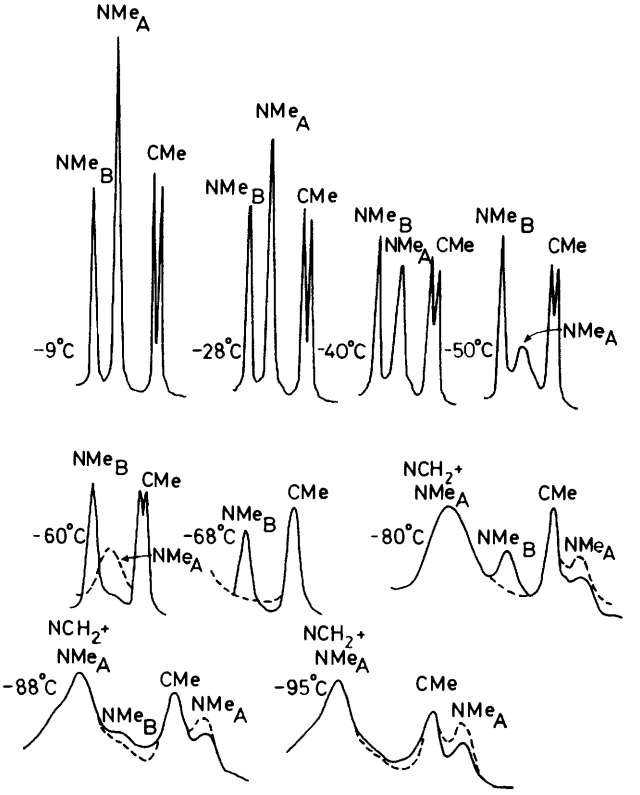


FIGURE 2 N.m.r. spectra (100 MHz, Fourier-transform mode) of host NMe signals and guest CMe signals for the complex of host (11b) with (*R*)- (——) and (*RS*)- (– – – –) phenylethylammonium thiocyanate. The equilibrium between diastereoisomers A and B is not fully established for the complex of the (*R*)- salt at temperatures below −40 °C. The low field NMe_A signal from diastereoisomer A is obscured by broad signals from the NCH_2 groups of the macrocycle in the spectra run at or below −80 °C

The chiral selectivity shown by the host (11b) is only moderate and the investigation was therefore extended to systems related to (11b), having additional substituents on the biphenyl system and different macrocyclic ring systems. Examination of the n.m.r. spectra of the complexes between (*R*)-phenylethylammonium thiocyanate and the macrocycles (12b), (13b), and (14b) proved to be disappointing. Thus the complex of (12b) showed only a single NMe signal in its n.m.r. spectrum, but a singlet from the OCH_2CH_2O system of the macrocycle appeared as two signals of nearly equal intensity in the n.m.r. spectrum of the complex with the (*R*)-ammonium salt indicating little or no chiral selectivity. In the cases of the hosts (13b) and (14b), the NMe signal was

* These chemical shifts and signal intensities were obtained using Fourier-transform n.m.r. whereas results for the biphenyl (8b) were obtained using continuous-wave n.m.r. The greater confidence in chemical shift information obtained by the Fourier-transform method is important when Method 2 is used.

doubled in the spectrum of the complex with (*R*)-phenylethylammonium thiocyanate, but in both cases the signal intensities were approximately 1 : 1 even after prolonged standing (Figure 3). It appears that modifications of the macrocycle do not enhance chiral selectivity in complex formation for a guest such as phenylethylammonium thiocyanate.

The substituted analogues of the host (11b) were examined using similar methods, again with disappointing results. Thus the bispropenyl system (17b) showed two NMe signals in the spectrum of the complex with (*R*)-phenylethylammonium thiocyanate (Figure 4) but the ratio of signal intensities indicated a lower chiral selectivity than that shown by the unsubstituted host (11b); furthermore at low temperatures the olefinic CMe signals obscured the high field NMe signal preventing the use of Method 1. The propyl-substituted system (17c) (Figure 4) showed even lower chiral selectivity and it appears that the introduction of groups on the biphenyl system adjacent to the aryl oxygen atoms decreases, rather than increases, chiral selectivity for guests such as phenylethylammonium thiocyanate. Increased steric interactions in the macrocycle system (11b) do not therefore appear to enhance chiral selectivity and future investigations will be based upon the introduction of bonding, rather than non-bonding interactions.

The synthesis of host molecules, such as (17f), having additional binding sites for polyfunctional guest molecules is described in the first section of this paper. An examination of chiral selectivity in complex formation by hosts of this type will be described in a future paper. The results described above establish the methods that may be used for single phase systems and racemic host molecules, particularly those which are optically labile such as the bridged biphenyls (11b), (12b), (13b), (14b), (17b), and (17c).

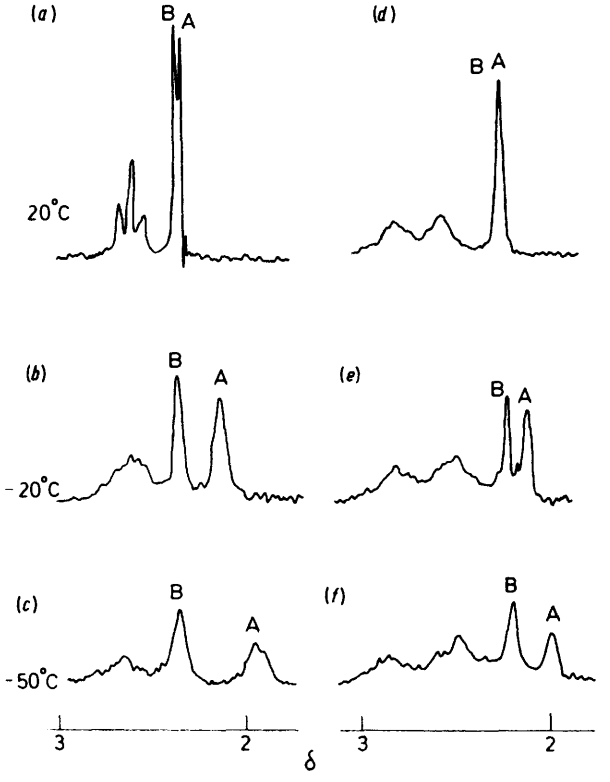


FIGURE 3 N.m.r. spectra (100 MHz) of the NMe signals (A and B) of the complexes of hosts (14b) [(*a*), (*b*), and (*c*)] and (13b) [(*d*), (*e*), and (*f*)] with (*R*)-phenylethylammonium thiocyanate

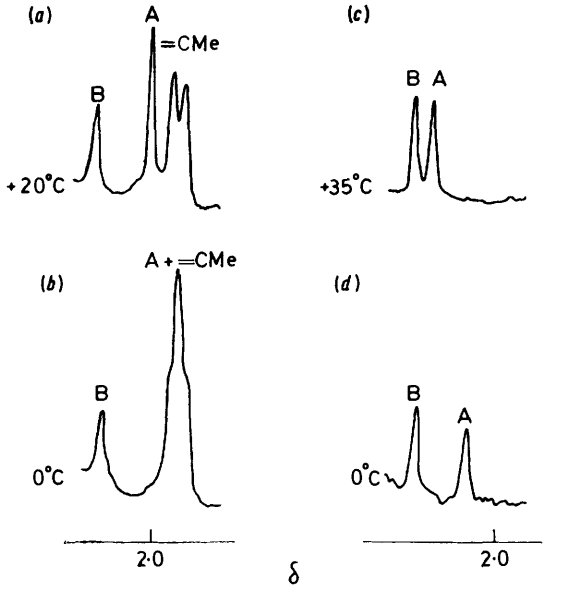


FIGURE 4 N.m.r. spectra (100 MHz) of the NMe signals (A and B) of the complexes of hosts (17b) [(*a*) and (*b*)] and (17c) [(*c*) and (*d*)] with (*R*)-phenylethylammoniun thiocyanate

EXPERIMENTAL

See Part 2 of this series [11] for general methods. N.m.r. spectra were determined using either a Varian HA100 (100 MHz) or a Perkin-Elmer R34 (220 MHz) spectrometer (^{1}H continuous-wave spectra), or a JEOL PFT100 spectrometer (^{1}H and ^{13}C Fourier-transform spectra). Spectra were recorded for *ca.* 0.1M solutions in either deuteriochloroform or dideuteriomethylene chloride; temperatures were varied in the range −110 to +50 °C and were calibrated using either a methanol sample or a thermocouple. Spectra run at higher temperatures (+50 to +200 °C) were recorded for approximately 0.1M solutions in perdeuterionitrobenzene and temperatures were calibrated using an ethylene glycol sample. Solutions of complexes were prepared by dissolving the appropriate amounts of the two components in the solvent immediately prior to running the spectra. Thiocyanate salts of primary amines were prepared as described in earlier papers of this series.

NN′-*Bisethoxycarbonyl*-17,20-*dimethoxy*-2,14-*diaza*-5,8,11-*trioxa*[15]*paracyclophane* (4a) *and* NN′-*Bisethoxycarbonyl*-14,17-*dimethoxy*-2,11-*diaza*-5,8-*dioxa*[12]*paracyclophane* (4b).*—Sodium hydride (1.0 g, 0.042 mol) was added in portions during 45 min to a stirred solution of the biscarbamate (3a) † (6.6 g, 0.0197 mol) in dry dimethyl

* This procedure describes a typical preparation of a macrocycle; other similar preparations will be described in outline only.

† This carbamate (3a) was prepared from a commercial sample of tetraethylene glycol which contained *ca.* 15% triethylene glycol as an impurity. The carbamate (3a) therefore contained *ca.* 15% of the carbamate (3b).

sulphoxide (70 ml) and the resulting suspension left at room temperature for 2 h. This solution and a solution of 1,4-bischloromethyl-2,5-dimethoxybenzene (2) [12] (4.5 g, 0.0192 mol) in dimethyl sulphoxide (70 ml) were added dropwise and simultaneously over 1 h to stirred dimethyl sulphoxide (50 ml). The mixture was left for several days until t.l.c. analysis showed that reaction was complete. The solution was diluted with water (100 ml) and hydrochloric acid (100 ml, 2N), extracted with chloroform (3 × 75 ml) and the combined extracts were washed with water, dried, filtered, and evaporated to give the crude product as an orange oil (11.8 g). Column chromatography [silica, chloroform–ethyl acetate (40 : 60)] gave a mixture of the cyclophanes (4a) and (4b) (3.27 g, 32%). The first few fractions yielded the [12]*paracyclophane* (4b) which was purified by short-path distillation (230 °C, 0.01 Torr) to give a colourless oil (Found: *M*, 454.2309. $C_{22}H_{34}O_8N_2$ requires *M*, 454.2315); $\nu_{max.}$ ($CHCl_3$) 1685 cm^{-1}; δ ($CDCl_3$), 6.87 (aryl-H), 6.77 (aryl-H), 4.53 (br s, 2 × CH_2Ar), 4.16 (q, *J* 7 Hz, 2 × OCH_2Me), 3.77 (s, 2 × OMe), 3.8—3.0 (m, 2 × OCH_2CH_2N + OCH_2CH_2O), and 1.3 (t, *J* 7 Hz, OCH_2Me). The later fractions yielded the [15] *paracyclophane* (4a) which crystallised from ether as colourless crystals m.p. 84—85 °C. (Found: C, 57.7; H, 7.5; N, 5.35. $C_{24}H_{38}O_9N_2$ requires C, 57.8; H, 7.7; N, 5.6%); $\nu_{max.}$ ($CHCl_3$) 1685 cm^{-1}; δ ($C_6D_5NO_2$, 80 °C) 6.78 2 × aryl-H), δ_A 4.58, δ_B 4.30 (AB system, J_{AB} 15.5 Hz, 2 × $ArCH_AH_B$), 4.06 (q, *J* 7 Hz, 2 × OCH_2Me), 3.58 (s, 2 × OMe), 3.4—3.0 (m, 2 × OCH_2CH_2N + 2 × OCH_2CH_2-O), and 1.08 (t, *J* 7 Hz, 2 × OCH_2Me).

NN′-*Dimethyl*-17,20-*dimethoxy*-2,14-*diaza*-5,8,11-*trioxa*-[15]*paracyclophane* (5a).—Lithium aluminium hydride (180 mg, 4.7 mmol) was added in portions to a stirred solution of the paracyclophane (4a) (293 mg, 0.59 mmol) in ether (20 ml). The resulting mixture was stirred at room temperature for 2 h, excess of hydride destroyed by the careful addition of water, and the resulting suspension was filtered. The filtrate and washings of the residual alumina were evaporated to dryness to give the required [15]*paracyclophane* (5a) as a colourless oil, (222 mg, 99%). A sample was purified by short-path distillation at 250 °C, 0.01 Torr (Found: *M*, 382.2465. $C_{20}H_{34}O_5N_2$ requires *M*, 382.2467); δ ($C_6D_5NO_2$, 40 °C), 6.93 (s, 2 × aryl-H), 3.75 (H_A of AB system, J_{AB} 13 Hz, 2 × $ArCH_AH_B$), 3.58 (s, 2 × OMe), 3.7—2.0 (m, 2 × $ArCH_AH_B$ + 2 × OCH_2CH_2N + 2 × OCH_2CH_2O), and 2.75 (s, 2 × NMe).

NN′-*Dimethyl*-14,17-*dimethoxy*-2,11-*diaza*-5,8-*dioxa*[12]-*paracyclophane* (5b).—A solution of the paracyclophane (4b) (133 mg, 0.293 mmol) in ether (15 ml) and lithium aluminium hydride (90 mg, 2.37 mmol) gave the required [12]*paracyclophane* (5b) (98 mg, 99%) as a colourless oil. A sample was purified by short-path distillation at 230 °C, 0.01 Torr (Found: *M*, 338.2214. $C_{18}H_{30}O_4N_2$ requires *M*, 338.2205); δ ($CDCl_3$) 6.96 (s, 2 × aryl-H), 3.84 (s, 2 × OMe), δ_A 3.82, δ_B 3.22 (AB system, J_{AB} 12 Hz, $ArCH_AH_B$), 4.0—2.1 (m, 2 × OCH_2CH_2N + OCH_2CH_2O), and 2.49 (s, 2 × NMe).

NN′-*Bisethyoxycarbonyl*-2,11-*diaza*-5,8-*dioxa*[12](2,2′)-*biphenylophane* (7b).—A solution of the biscarbamate (3b) (5.4 g, 0.018 mol) in dimethyl sulphoxide (50 ml), sodium hydride (0.98 g, 0.041 mol), and a solution of 2,2′-bis(bromomethyl)biphenyl (6) (6.3 g, 0.018 mol) in dimethyl sulphoxide (50 ml) gave the crude product as an orange oil (10.3 g). Purification by column chromatography [silica, chloroform–ethyl acetate (40 : 60)] gave the *biphenylophane* (7b), (3.19 g, 36%) as a colourless oil. A sample was purified by short-path distillation at 280 °C, 0.01 Torr (Found: C, 66.4; H, 7.3; N, 5.8. $C_{26}H_{34}O_6N_4$ requires C, 66.4; H, 7.3; N, 5.95%); $\nu_{max.}$ ($CHCl_3$) 1 675 cm^{-1}; δ ($CDCl_3$, 40 °C), 7.4—7.0 (m, 8 aryl-H), δ_A 4.76, δ_B 4.00 (AB system, J_{AB} 17 Hz, 2 × $ArCH_AH_BN$), 4.15 (q, *J* 7 Hz, 2 × OCH_2Me), 3.7—3.3 (m, 2 × OCH_2CH_2N), 3.31 (s, OCH_2CH_2O), and 1.21 (t, *J* 7 Hz, 2 × OCH_2Me).

NN′-*Dimethyl*-2,11-*diaza*-5,8-*dioxa*[12](2,2′)*biphenylophane* (8b).—A solution of the biscarbamate (7b) (1.387 g, 2.95 mmol) in ether (15 ml) and lithium aluminium hydride (900 mg, 24 mmol) gave the *biphenylophane* (8b) (1.043 g, 99%) as a colourless crystalline solid. A sample purified by short-path distillation at 200 °C, 0.05 Torr had m.p. 81—90 °C (Found: C, 74.3; H, 8.6; N, 7.6. $C_{22}H_{30}O_2N_2$ requires C, 74.5; H, 8.5; N, 7.9%); δ (CD_2Cl_2), 7.7—7.0 (m, 8 aryl-H), δ_A 3.92, δ_B 2.81 (AB system, J_{AB} 14 Hz, 2 × $ArCH_AH_BN$), 3.50 (t, *J* 5 Hz, 2 × OCH_2CH_2N), 3.43 (s, OCH_2CH_2O), 2.6—2.3 (m, 2 × NCH_2CH_2O), and 2.04 (s, 2 × NMe).

NN′-*Bisethoxycarbonyl*-2,14-*diaza*-5,8,11-*trioxa*[15](2,2′)-*biphenylophane* (7a).—A solution of the biscarbamate (3a) (5.9 g, 0.018 mol) in dimethyl sulphoxide (50 ml), sodium hydride (0.85 g, 0.037 mol) and a solution of 2,2′-bis(bromomethyl)biphenyl (6) (6.0 g, 0.018 mol) in dimethyl sulphoxide (50 ml) gave the crude product as an orange oil (13.1 g). Purification by column chromatography [silica, chloroform–ethyl acetate (20 : 80)] gave the *biphenylophane* (7a) (3.57 g, 40%) as a colourless oil. A sample was purified by short-path distillation at 250 °C, 0.03 Torr (Found: C, 65.2; H, 7.5; N, 5.6. $C_{28}H_{38}O_7N_2$ requires C, 65.35; H, 7.4; N, 5.4%); $\nu_{max.}$ ($CHCl_3$) 1 680 cm^{-1}; δ ($CDCl_3$), 7.5—7.0 (m, 8 aryl-H), 4.60 (d, J_{AB} 17 Hz, 2 × H_A of AB system, $ArCH_AH_B$), 4.4—3.1 (m, 2 × $ArCH_AH_B$ + 2 × NCH_2CH_2O + OCH_2CH_2O + 2 × CH_2Me), and 1.4—0.9 (m, 2 × CH_2Me).

NN′-*Dimethyl*-2,14-*diaza*-5,8-11-*trioxa*[15](2,2′)*biphenylophane* (8a).—A solution of the biscarbamate (7a) (1.081 g, 2.1 mmol) in ether (15 ml) and lithium aluminium hydride (650 mg, 17 mmol) gave the *biphenylophane* (8a) (830 mg, 99%) as a colourless oil. A sample was purified by short-path distillation at 180 °C, 0.04 Torr (Found: C, 72.2; H, 8.6; N, 6.8. $C_{24}H_{34}O_3N_2$ requires C, 72.3; H, 8.6; N, 7.0%); δ ($CDCl_3$), 7.7—7.0 (m, 8 aryl-H), δ_A 3.63, δ_B 3.02 (AB system, J_{AB} 14 Hz, 2 × $ArCH_AH_B$), 3.6—3.4 (m, 4 × OCH_2), 2.47 (t, *J* 7 Hz, 2 × NCH_2), and 2.08 (s, 2 × NMe); δ ($C_6D_5NO_2$, 200 °C) δ_A 3.33, δ_B 3.07 (AB system, J_{AB} 14 Hz, 2 × $ArCH_AH_B$) (the line-widths in the AB system at 200 °C indicate that $k_{inv.} \leqslant 5$ sec^{-1}).

Diethyl Biphenyl-2,2′-*bis*(*oxyacetate* (9b).—Biphenyl-2,2′-diol (37 g, 0.2 mol), ethyl bromoacetate (74 g, 0.44 mol) and potassium carbonate (250 g) were stirred in dry acetone (600 ml) and heated under reflux for 18 h. The mixture was cooled and filtered, the solid washed with acetone, and the combined filtrate and washings evaporated giving the *diester* (9b) (62 g, 86%) as colourless crystals, m.p. 63—67 °C after crystallisation from ether–light petroleum (Found: C, 66.75; H, 6.3. $C_{20}H_{22}O_6$ requires C, 67.0; H, 6.1%); $\nu_{max.}$ (Nujol) 1 750 cm^{-1}; δ ($CDCl_3$), 7.1 (m, 8 aryl-H), 4.46 (s, 2 × $ArOCH_2$), 4.09 (q, *J* 7 Hz, 2 × OCH_2Me), and 1.12 (t, *J* 7 Hz, 2 × OCH_2Me).

2,2′-*Bis*(2-*hydroxyethoxy*(*biphenyl* (9c).—The diester (9b) (36 g, 0.1 mol) in ether (100 ml) was added dropwise during 30 min to a stirred suspension of lithium aluminium hydride (5 g, 0.13 mol) in dry ether (100 ml). The mixture was stirred for 2 h and carefully poured onto crushed ice (500 g), hydrochloric acid (200 ml, 2N) was added, the ether layer separated, and the aqueous layer extracted with chloroform

(3 × 100 ml). The combined extracts and ethereal solution were dried ($MgSO_4$) and evaporated giving the *diol* (9c) as a colourless crystalline solid, m.p. 56—69 °C (24.8 g, 90%). A sample was purified by short-path distillation at 200 °C, 0.1 Torr (Found: C, 70.1; H, 6.8. $C_{16}H_{18}O_4$ requires C, 70.1; H, 6.6%); $\nu_{max.}$ (liquid film) 3 400 cm^{-1}; δ ($CDCl_3$), 7.2 (m, 4 aryl-H), 6.95 (m, 4 aryl-H), 3.94 (t, *J* 4 Hz, 2 × $ArOCH_2$), and 3.60 (t, *J* 4 Hz, 2 × CH_2OH), 3.25 (br s, 2 × OH).

*2,2′-Bis(2-hydroxyethoxy)biphenyl Bistoluene-*p*-sulphonate* (9d).—The diol (9c) (24 g, 0.088 mol) in dry pyridine (65 ml) was stirred at 0—5 °C and toluene-*p*-sulphonyl chloride (38 g 0.2 mol) added in portions during 30 min. The mixture was allowed to warm to room temperature and stirred for a further 3 h before being poured into ice–water (500 g) containing hydrochloric acid (50 ml, 11N). The product was extracted into chloroform (3 × 150 ml) and the extracts washed with hydrochloric acid (2 × 250 ml, 2N) and water (250 ml), dried ($MgSO_4$), and evaporated giving the *bistoluene-*p*-sulphonate*(9d) (20.5 g, 40%), m.p. 103.5—105 °C after crystallization from methanol (Found: C, 61.9; H, 5.4; S, 11.2. $C_{30}H_{30}S_2O_8$ requires C, 61.9; H, 5.15; S, 11.0%); δ ($CDCl_3$), δ_A 7.39, δ_B 7.10 (2 × AA′BB′ system, 8 aryl-H), 6.9 (m, 8 aryl-H), 3.93 (s, 2 × OCH_2CH_2O), and 2.18 (s, 2 × ArMe).

NN′-*Bisethoxycarbonyl*-4,10-*diaza*-1,7,13-*trioxa*[13](2,2′)-*biphenylophane* (11a).—A solution of the biscarbamate (10a) (2.48 g, 0.01 mol) in dimethyl sulphoxide (25 ml), sodium hydride (0.6 g, 0.025 mol), and a solution of the bistoluene-*p*-sulphonate (9d) (5.82 g, 0.01 mol) in dimethyl sulphoxide (50 ml) gave the crude product as a dark oil. Purification by column chromatography [silica, chloroform–ethyl acetate (4 : 3)] gave the *biphenylophane* (11a) (2.1 g, 43%) as a colourless oil (Found: C, 64.4; H, 7.15; N, 5.6. $C_{26}H_{34}N_2O_7$ requires C, 64.2; H, 7.0; N, 5.8%); $\nu_{max.}$ (liquid film) 1 700 cm^{-1}; δ ($CDCl_3$), 7.2 (m, 8 aryl-H), 4.2 (m, 4 × OCH_2 + 2 × OCH_2Me), 3.5 (m, 4 × NCH_2), and 1.2 (t, *J* 7 Hz, 2 × OCH_2Me).

NN′-*Bisbenzyloxycarbonyl*-4,10-*diaza*-1,7,13-*trioxa*[13]-(2,2′)*biphenylophane* (11c). This was prepared in an analogous manner from the bistoluene-*p*-sulphonate (9d) and the biscarbamate (10b). The product was purified by column chromatography [silica, ether–light petroleum (3 : 1)] giving the *biphenylophane* (11c) as a colourless oil (48%) (Found: *M*, 610.2 656. $C_{36}H_{38}N_2O_7$ requires *M*, 610.2 679); $\nu_{max.}$ (liquid film) 1 705 cm^{-1}; δ ($CDCl_3$), 7.31 (m, 2 × Ph), 7.1 (m, 8 aryl-H), 5.09 (s, 2 × OCH_2Ph), and 4.1—3.5 (m, 4 × OCH_2CH_2N).

NN′-*Bisbenzyloxycarbonyl*-4,13-*diaza*-1,7,10,16-tetraoxa-[16](2,2′)*biphenylophane* (12a). This was prepared in an analogous manner from the bistoluene-*p*-sulphonate (9d) and the biscarbamate (10c). The product was purified by column chromatography [silica, ether–light petroleum (4 : 1)] giving the *biphenylophane* (12a) as a colourless oil (40%) (Found: *M*, 654.2 927. $C_{38}H_{42}N_2O_8$ requires *M*, 654.2 941); $\nu_{max.}$ (liquid film) 1 700 cm^{-1}; δ ($CDCl_3$), 7.18 (m, 2 × Ph), 7.00 (m, 8 aryl-H), 5.07 (s, 2 × OCH_2Ph), 4.1 (m, 2 × CCH_2), and 3.5 (m, 4 × CCH_2 + 4 × NCH_2).

NN′-*Bisbenzyloxycarbonyl*-4,10-*diaza*-1,13-*dioxa*[13] (2,2′)-*biphenylophane* (13a). This was prepared in an analogous manner from the bistoluene-*p*-sulphonate (9d) and NN′-bisbenzyloxycarbonyl-1,5-diaminopentane. The product was purified by column chromatography [silica, ether–light petroleum (1 : 1)] giving the *biphenylophane* (13a) as a colourless oil (39%) (Found: *M*, 608.2 880. $C_{37}H_{40}N_2O_6$ requires *M*, 608.2 886); $\nu_{max.}$ (liquid film) 1 695 cm^{-1}; δ ($CDCl_3$), 7.2 (m, 2 × Ph + 4 aryl-H), 6.93 (m, 4 aryl-H), 5.08 (s, 2 × OCH_2Ph), 4.0—2.9 (br m, 2 × OCH_2 + 4 × NCH_2), and *ca.* 1.2 (br m, $CH_2CH_2CH_2$).

NN′-*Bisbenzyloxycarbonyl*-2,13-*diaza*-5,10-*dioxa*[5.5]-*metacyclo*(2,2′)*biphenylophane* (14a). This was prepared in a similar manner from the bistoluene-*p*-sulphonate (9d) and NN′-bisbenzyloxycarbonylmetaxylylenediamine. The product was purified by column chromatography [silica, ether–light petroleum (1 : 1)] giving the *metacyclophane* (14a) (25%) as a colourless oil which slowly crystallized (Found: *M*, 642.2 729. $C_{40}H_{38}N_2O_6$ requires *M*, 642.2 730); $\nu_{max.}$ (liquid film) 1 695 cm^{-1}; δ ($CDCl_3$), 7.30—7.1 (m, 22 aryl-H), 5.06 (br s, 2 × OCH_2Ph), and 4.7—3.3 (br m, 4 × NCH_2 + 2 × OCH_2).

NN′-*Dimethyl*-4,10-*diaza*-1,7,13-*trioxa*[13](2,2′)*biphenylophane* (11b). The biscarbamate (11a) (1.0 g, 2.7 mmol) in dry ether (25 ml) was added dropwise to a stirred suspension of lithium aluminium hydride (0.2 g, 5.3 mmol) in dry ether (25 ml). The mixture was stirred overnight, ethyl acetate (10 ml) added, and after a further 1 h water was added. The mixture was filtered and the filtrate dried ($MgSO_4$) and evaporated giving the *diamine* (11b), (0.5 g, 66%) as a colourless oil. A sample was purified by short-path distillation at 200 °C, 1 Torr (Found: C, 71.45; H, 8.3; N, 7.7. $C_{22}H_{30}N_2O_3$ requires C, 71.35; H, 8.1; N, 7.6%); δ ($CDCl_3$, 220 MHz) 7.16 (dd, *J* 8 and 2 Hz, 18-H + 21-H), 6.97 (br t, *J* 8 Hz, 17-H + 22-H), 7.16 (dt, *J* 2 and 8 Hz, 16-H + 23-H), 6.95 (br d, *J* 8 Hz, 15-H + 24-H), 4.02 (t, *J* 7 Hz, 2 × $ArOCH_2$), 3.55 (dt, *J* 11 and 5 Hz, 2 × OCH_AH_B), 3.42 (dt, *J* 11 and 5 Hz, 2 × OCH_AH_B), 2.98 (dt, *J* 13 and 7 Hz, 2 × NCH_AH_B), 2.53 (dt, *J* 13 and 7 Hz, 2 × NCH_AH_B), 2.58 (t, *J* 5 Hz, 2 × NCH_2), and 2.26 (s, 2 × NMe).

NN′-*Dimethyl*-4,13-*diaza*-1,7,10,16-*tetraoxa*[16](2,2′)*biphenylophane* (12b). This was prepared in a similar manner by the reduction of the biscarbamate (12a) with lithium aluminium hydride. The *diamine* (12b) was obtained as a colourless oil (84% yield) purified by short-path distillation at 180 °C, 0.2 Torr (Found: C, 69.5; H, 8.1; N, 6.8%; *M*, 414.2 513. $C_{24}H_{34}N_2O_4$ requires C, 69.5; H, 8.3; N, 6.8%; *M*, 414.2 518); δ (CD_2Cl_2), 6.7—7.3 (m, 8 aryl-H), 3.92 (t, *J* 6 Hz, 2 × $ArOCH_2$), 3.40 (s, OCH_2CH_2O), *ca.* 3.4 (m, 2 × OCH_2), *ca.* 2.6 (m, 2 × NCH_2), *ca.* 2.45 (m, 2 × NCH_2), and 2.12 (s, 2 × NMe).

NN′-*Dimethyl*-4,10-*diaza*-1,13-*dioxa*[13](2,2′)*biphenylophane* (13b). This was prepared in a similar manner by reduction of the biscarbamate (13a) with lithium aluminium hydride. The *diamine* (13b) was obtained as a colourless oil (55% yield) (Found: C, 75.1; H, 8.8; N, 7.7. $C_{23}H_{32}N_2O_2$ requires C, 75.0; H, 8.75; N, 7.6%); δ ($CDCl_3$) 6.9—7.3 (m, 8 aryl-H), 3.98 (t, *J* 6 Hz, 2 × $ArOCH_2$), *ca.* 2.6 (m, 2 × NCH_2), *ca.* 2.3 (m, 2 × NCH_2), 2.17 (s, 2 × NMe), and *ca.* 1.35 (m, $CH_2CH_2CH_2$).

NN′-*Dimethyl*-2,13-*diaza*-5,10-*dioxa*[5.5.]*metacyclo*(2,2′)-*biphenylophane* (14b). This was prepared in a similar manner by reduction of the biscarbamate (14a) with lithium aluminium hydride. The *diamine* (14b) was obtained as a colourless oil (69% yield) which slowly crystallized to give colourless crystals m.p. 110—125 °C (Found: C, 77.5; H, 7.4; N, 7.15. $C_{26}H_{30}N_2O_2$ requires C, 77.6; H, 7.5; N, 7.0%); δ ($CDCl_3$), 7.2—6.6 (m, 12 aryl-H), 4.1—3.5 (m, 2 × $ArOCH_2$), δ_A 3.65, δ_B 3.35 (AB system, J_{AB} 13 Hz, 2 × $ArCH_AH_BN$), 2.7—2.2 (m, 2 × NCH_2), and 2.40 (s, 2 × NMe).

4,10-*Diaza*-1,7,13-*trioxa*[13](2,2′)*biphenylophane* (11d).—A solution of the biscarbamate (11c), (235 mg, 0.385 mmol) in 48% hydrobromic acid in acetic acid (3 ml) was heated on a steam-bath for 3 min. Water (25 ml) was added and the aqueous solution extracted with chloroform (2 × 20 ml). The aqueous layer was made basic (10N NaOH) and extracted with chloroform (2 × 25 ml) and this second chloroform extract was dried and evaporated to give the *diamine* (11d) as a pale yellow oil (120 mg, 91%) which could be used without further purification, or purified by short-path distillation at 190 °C, 1 Torr; $\nu_{max.}$ (liquid film) 3 320 cm^{-1}; δ ($CDCl_3$), 7.3—6.8 (m, 8 aryl-H), 4.23 (ddd, *J* 4, 8, and 9.5 Hz, 2 × $ArOCH_AH_B$), 3.84 (dt, *J* 9.5 and 4 Hz, 2 × $ArOCH_AH_B$), 3.55 (t, *J* 5 Hz, 2 × OCH_2), 3.1—2.6 (m, 4 × NCH_2), and 2.57 (s, 2 × NH); *m/e* 342 (M^+).

NN′-*Bis*-(2-*hydroxyethyl*)-4,10-*diaza*-5,11,17-*trioxa*[13]-(2,2′)-*biphenylophane* (11e).—Ethylene oxide (2 ml), was added to a solution of the diamine (11d) (302 mg, 0.88 mmol) in ethanol (3 ml) containing 1 drop of water. The solution was left overnight, evaporated to dryness, and the oily residue purified by column chromatography (alumina, 8% ethanol in ether) giving the *diol* (11e) (180 mg, 47%) as a colourless oil purified by short-path distillation at 250 °C, 1 Torr (Found: C, 67.3; H, 7.9; N, 6.5. $C_{24}H_{34}N_2O_5$ requires C, 67.0; H, 7.9; N, 6.5%); $\nu_{max.}$ (liquid film) 3 330 cm^{-1}; δ ($CDCl_3$), 7.4–6.9 (m, 8 aryl-H), 4.2—3.8 (m, 2 × $ArOCH_2$), 3.40 (br t, *J ca.* 4.5 Hz, 4 × OCH_2), *ca.* 3.40 (s, 2 × OH), and 2.9—2.5 (m, 6 × NCH_2).

2,2′-*Bis*(*allyloxy*)*biphenyl* (9e).—A solution of biphenyl-2,2′diol (18.6 g, 0.1 mol) and allyl bromide (27 g, 0.22 mol) in acetone (150 ml) containing anhydrous potassium carbonate (35 g) was heated under reflux for 18 h. The mixture was cooled, filtered, and the filtrate evaporated to give the required *allyl ether* (9e) as a colourless oil (21 g, 78%) (Found: C, 81.0; H, 6.8 $C_{18}H_{18}O_2$ requires C, 81.2; H, 6.8%); δ ($CDCl_3$), 7.5—6.7 (m, 8 aryl-H), 5.76 (ddt, *J* 17, 10, and 5 Hz, 2 × CH_2–CH=CH_2), 5.09 (dq, *J* 17 and 2 Hz, 2 × CH=CH_AH_B), 4.99 (dq, *J* 10 and 2 Hz, 2 × CH=CH_AH_B), and 4.34 (dt, *J* 5 and 2 Hz, 2 × OCH_2).

2,2′-*Dihydroxy*-3,3′-*diallylbiphenyl Diacetate* (15a).—The allyl ether (9e) 41 g, 0.154 mol) was heated under reflux (N_2 atmosphere) for 120 h in diethylaniline (400 ml) containing acetic anhydride (41 g, 0.4 mol). The reaction mixture was added to hydrochloric acid (2N, 2 l) and extracted with chloroform (2 × 500 ml). The extracts were washed with hydrochloric acid (2N, 3 × 1 l) and water (500 ml), dried, and evaporated to yield the *diacetate* (15a) as a golden-yellow oil (54 g, 68%). A sample was purified by distillation at 180 °C, 0.1 Torr (Found: C, 75.1; H, 6.2. $C_{22}H_{22}O_4$ requires C, 75.4; H, 6.3); $\nu_{max.}$ (liquid film) 1 760 cm^{-1}; δ ($CDCl_3$), 7.15 (m, 6 aryl-H), 5.89 (ddt, *J* 17, 10, and 7 Hz, 2 × CH_2CH=CH_2), 5.05 (m, 2 × CH=CH_2), 3.26 (br d, *J* 7 Hz, 2 × $ArCH_2$), and 1.90 (s, 2 × OCOMe).

2,2′-*Dihydroxy*-3,3′-*diallylbiphenyl* (15b). This was obtained from the diacetate (92% yield) by heating under reflux for 2 h in methanolic potassium hydroxide (3% w/v). The *phenol* (15b) was obtained as an oil, which slowly crystallized to give colourless crystals, m.p. 35—38 °C (Found: C, 80.8; H, 7.0. $C_{18}H_{18}O_2$ requires C, 81.2; H, 6.8%); $\nu_{max.}$ 3 530 cm^{-1}, δ ($CDCl_3$) 7.3—6.8 (m, 6 aryl-H), 6.04 (ddt, *J* 17, 10, and 7 Hz, 2 × CH_2CH=CH_2), 5.42 (br s, 2 × OH), 5.12 (br d, *J* 17 Hz, 2 × CH=CH_AH_B), 5.10 (br d, *J* 10 Hz, 2 × CH=CH_AH_B), and 3.46 (br d, *J* 7 Hz, 2 × $ArCH_2$).

Diethyl 3,3′-*Diallylbiphenyl*-2,2′-*bis*(*oxyacetate*) (15c).—A solution of the phenol (15b) (25 g, 0.094 mol) in acetone (300 ml) containing ethyl bromoacetate (33.4 g, 0.2 mol) and anhydrous potassium carbonate (100 g, 0.72 mol) was heated under reflux for 18 h. The mixture was filtered and the filtrate evaporated giving the *diester* (15c) as a pale yellow oil (28.3 g, 69%), used without further purification for the preparation of the diol (15d); $\nu_{max.}$ (liquid film) 1 754 cm^{-1}; δ ($CDCl_3$), 7.3—7.1 (m, 6 aryl-H), 6.00 (ddt, *J* 17, 10, and 7 Hz, 2 × CH_2CH=CH_2), 5.06 (br d, *J* 17 Hz, 2 × CH=CH_AH_B), 5.03 (br d, *J* 10 Hz, 2 × CH=CH_AH_B), 4.11 (s, 2 × OCH_2), 4.07 (q, *J* 7 Hz, 2 × OCH_2Me), 3.54 (br d, *J* 7 Hz, 2 × $ArCH_2$), and 1.16 (t, *J* 7 Hz, 2 × OCH_2Me).

3,3′-*Diallyl*-2,2′-*bis*-(2-*hydroxyethoxy*)*biphenyl* (15d).—The diester (15c) (9.6 g, 22 mmol) in ether (100 ml) was added dropwise to a stirred suspension of lithium aluminium hydride (1.7 g, 44 mmol) in ether (100 ml). The mixture was stirred overnight, and excess hydride was then hydrolysed by the cautious addition of water. The solution was filtered and the solid washed with ethyl acetate (2 × 50 ml). The combined filtrate and washings were dried and evaporated giving the *diol* (15d) as an oil which slowly crystallized (7.3 g, 94%), giving colourless crystals, m.p. 92—96 °C after crystallization from ether–light petroleum (Found: C, 74.5; H, 7.7. $C_{22}H_{26}O_4$ requires C, 74.55; H, 7.4%); $\nu_{max.}$ (Nujol) 3 460 cm^{-1}; δ ($CDCl_3$), 7.2—7.0 (m, 6 aryl-H), 5.97 (ddt, *J* 17, 10, and 7 Hz, 2 × CH_2CH=CH_2), 5.04 (d, *J* 10 Hz, 2 × CH=CH_AH_B), 5.02 (d, *J* 17 Hz, 2 × CH=CH_AH_B), 3.50 (m, 2 × OCH_2CH_2O + 2 × $ArCH_2$), 3.00 (br s, 2 × OH).

3,3′-*Diallyl*-2,2′-*bis*-(2-*hydroxyethoxy*)*biphenyl Bis-toluene*-p-*sulphonate* (15e).—Toluene-*p*-sulphonyl chloride (7.57 g, 40 mmol) was added in portions over 30 min to a stirred solution of the diol (15d) (6.5 g, 18.4 mmol) in pyridine (50 ml) at 0.5 °C. The mixture was stirred for a further 2.5 h at room temperature and poured into water (500 ml) containing hydrochloric acid (11N, 75 ml). The product was extracted into chloroform (2 × 150 ml) and the extract dried and evaporated giving the *toluene*-p-*sulphonate* (15e) as colourless crystals m.p. 87—90 °C (9.3 g, 76%) after crystallization from methanol (Found: C, 65.3; H, 5.9; S, 9.5%. $C_{36}H_{38}O_8S_2$ requires C, 65.2; H, 5.8; S, 9.7%); δ ($CDCl_3$, 220 MHz), 7.71 (d, *J* 8.5 Hz, 4 aryl-H), 7.32 (d, *J* 8.5 Hz, 4 aryl-H), 7.0—7.2 (m, 6-aryl H), 5.92 (ddt, *J* 17, 11, and 7 Hz, 2 × CH_2CH=CH_2), 5.04 (d, *J* 11 Hz, CH=CH_AH_B), 5.01 (d, *J* 17 Hz, 2 × CH=CH_AH_B), 3.90 (t, *J* 5 Hz, 2 × CH_2O), 3.59 (t, *J* 5 Hz, 2 × OCH_2), 3.36 (d, *J* 5 Hz, 2 × $ArCH_2$), and 2.42 (s, 2 × $ArMe$).

NN′-*Bisethoxycarbonyl*-15,24-*di*(*prop*-1-*enyl*)-4,10-*diaza*-1,7,13-*trioxa*[13](2,2′)*biphenylophane* (17a).—The biscarbamate (10a) (1.24 g, 5 mmol) in dimethyl sulphoxide (25 ml) was treated with sodium hydride (0.275 g, 11 mmol) and stirred for 2 h (N_2 atmosphere). The resulting solution was added to a solution of the bistoluene-*p*-sulphonate (15e) (3.31 g, 5 mmol) in dimethyl sulphoxide (25 ml) and the mixture stirred for 60 h. The reaction mixture was poured into water (1 l) containing hydrochloric acid (100 ml, 2N) and the product extracted into chloroform (2 × 250 ml). The extracts were dried and evaporated and the residual oil purified by column chromatography [silica, ether–light petroleum (2 : 1)] giving the *biphenylophane* (17a) as an oil which slowly crystallized (1.2 g, 43%) (Found: *M*, 566.2 991. $C_{32}H_{42}N_2O_7$ requires *M*, 566.2 992); $\nu_{max.}$ (liquid film) 1 698 cm^{-1}; δ ($CDCl_3$), 7.43 (dd, *J* 8 and 2 Hz, 2-aryl-H),

7.20 (m, 2-aryl-H), 7.11 (t, *J* 8 Hz, 2-aryl-H), 6.72 (br d, *J* 16 Hz, 2 × ArC*H*=CH), 6.22 (dq, *J* 16 and 6 Hz, 2 × CH=C*H*Me), 4.10 (q, *J* 7 Hz, 2 × OC*H*$_2$Me), 4.0—3.2 (br m, 4 × OCH$_2$ + 2 × NCH$_2$), 3.0—2.5 (br m, 2 × NCH$_2$), 1.89 (d, *J* 6 Hz, 2 × CHMe), and 1.19 (t, *J* 7 Hz, 2 × OCH$_2$Me).

NN′-*Dimethyl*-15,24-*di*(*prop*-1-*enyl*)-4,10-*diaza*-1,7,13-*trioxa*[13](2,2′)*biphenylophane* (17b).—The biphenylophane (17a) (283 mg, 0.5 mmol) in ether (25 ml) was stirred with lithium aluminium hydride (100 mg, 3 mmol) for 18 h. Excess of hydride was destroyed by the dropwise addition of ethyl acetate (5 ml) followed by water (3 drops). The solution was filtered and the filtrate combined with the ethyl acetate (2 × 25 ml) washings of the solid. The combined extracts were dried and evaporated giving the *biphenylophane* (17b) as an oil which slowly crystallized (209 mg, 93%) (Found: *M*, 450.2 882. $C_{28}H_{38}N_2O_3$ requires *M*, 450.2 873); δ (CDCl$_3$), 7.39 (dd, *J* 8 and 2 Hz, 2-aryl-H), 7.16 (dd, *J* 8 and 2 Hz, 2-aryl-H), 7.00 (t, *J* 8 Hz, 2-aryl-H), 6.80 (d, *J* 16 Hz, 2 × ArC*H*=CH), 6.19 (dq, *J* 16 and 6 Hz, 2 × CH=C*H*Me), 3.9—3.3 (m, 4 × OCH$_2$), 2.6—2.3 (m, 4 × NCH$_2$), 2.19 (s, 2 × NMe), and 1.88 (d, *J* 6 Hz, 2 × CH*Me*).

NN′-*Dimethyl*-15,24-*dipropyl*-4,10-*diaza*-1,7,13-*trioxa*[13]-(2,2′)-*biphenylophane* (17c).—The dipropenyl-biphenylophane (17b) (160 mg, 0.356 mmol) in ethanol (20 ml) was hydrogenated using a 10% Pd–C catalyst (1 mg) (1 atm H$_2$) for 18 h. The solution was filtered (Celite) and evaporated giving the *dipropyl-biphenylophane* (17c) as an oil. A sample was purified by short-path distillation at 240 °C, 0.4 Torr (Found: *M*, 454.3 120. $C_{28}H_{42}N_2O_3$ requires *M*, 454.3 195); δ (CDCl$_3$), 7.0—7.2 (m, 6-aryl-H), 3.9—3.4 (m, 4 × OCH$_2$), 2.8—2.5 (m, 4 × NCH$_2$ + 2 × ArCH$_2$), 2.25 (s, 2 × NMe), 1.69 (sextet, *J* 7 Hz, 2 × CH$_2$C*H*$_2$Me) 1.00 (t, *J* 7 Hz, 2 × CH$_2$*Me*).

NN′-*Bisethoxycarbonyl*-15,24-*dihydroxymethyl*-4,10-*diaza*-1,7,13-*trioxa*[13](2,2′)*biphenylophane* (17d).—A stream of ozonised oxygen was passed into a stirred solution of the biphenylophane (17a) (200 mg, 0.353 mmol) in dichloromethane (100 ml) at −78 °C. After 20 min the solution became blue and excess of ozone was removed by flushing the solution with oxygen. The solution was allowed to warm to 0 °C, methanolic sodium borohydride (0.2 g in 10 ml) was added, and the solution stirred for 1 h. Hydrochloric acid (5 ml, 2N) was added, the solution was evaporated, the residual solid was extracted with boiling chloroform (20 ml), and the extracts filtered and evaporated yielding the *dihydroxymethyl-biphenylophane* (17d) (108 mg, 56%). A sample, recrystallized from chloroform–light petroleum, had m.p. 163—166 °C (Found: C, 61.3; H, 7.0; N, 5.1. $C_{28}H_{38}N_2O_9$ requires C, 61.5; H, 7.0; N, 5.1%); ν$_{max.}$ (Nujol), 3 455, 1 680 cm^{-1}; δ (CDCl$_3$), 220 MHz), 7.40 (dd, *J* 2 and 8 Hz, 2-aryl-H), 7.29 (br m, 2-aryl-H), 7.14 (t, *J* 8 Hz, 2-aryl-H), 4.75 (br s, 2 × ArC*H*$_2$O), 4.11 (q, *J* 7 Hz, 2 × OCH$_2$), 4.0—3.3 (br m, 4 × OCH$_2$ + 2 × OH), 3.2—2.7 (br m, 4 × NCH$_2$), and 1.20 (t, *J* 7 Hz, 2 × OCH$_2$*Me*).

3,3′-*Bis*(2,2-*ethylenedioxyethyl*-2,2′-*bis*-(2-*hydroxyethoxy*)*biphenyl Bistoluene*-p-*sulphonate* (18b).—A stream of ozonised oxygen was passed into a solution of the toluene-*p*-sulphonate (15e) (6.0 g, 9.1 mmol) in dry methylene chloride (150 ml) at −78 °C. When the solution turned blue the ozone supply was removed and the solution was flushed with oxygen until colourless. The colourless solution was allowed to warm to −10 °C, and zinc dust (12 g) was added followed by acetic acid (50 ml). The suspension was stirred at 0 °C for 1 h and allowed to come to room temperature. The solution was washed successively with water (2 × 500 ml), saturated aqueous sodium bicarbonate (2 × 300 ml), and water (500 ml), dried, and evaporated. The residual oil consisted of the crude dialdehyde (18a), (5.9 g, 98%); ν$_{max.}$ 1 722 cm^{-1}, δ (CDCl$_3$, 220 MHz), 9.72 (s, 2 × CHO), 7.73 (d, *J* 9 Hz, 4-aryl-H), 7.34 (d, *J* 9 Hz, 4-aryl-H), 7.3—7.1 (m, 6-aryl-H), 3.94 (t, *J* 5 Hz, 2 × OCH$_2$), 3.78 (s, 2 × ArCH$_2$), 3.55 (t, *J* 5 Hz, 2 × OCH$_2$), and 2.43 (s, 2 × ArMe); *m/e* 666 (*M*$^+$). The dialdehyde prepared as above (7.4 g, 11.1 mmol) was heated under reflux in dry toluene (100 ml) containing ethylene glycol (1.55 g, 25 mmol) and toluene-*p*-sulphonic acid (5 mg). Evolved water was collected in a Dean–Stark apparatus and after water formation had ceased the solution was cooled and evaporated to leave the *bis-acetal* (18b) (6.9 g, 82%) as a golden-yellow oil (Found: C, 60.3; H, 5.8; S, 8.4. $C_{38}H_{42}O_{12}S_2$ requires C, 60.5; H, 5.6; S, 8.5%); δ (CDCl$_3$), 7.72 (d, *J* 9 Hz, 4-aryl-H), 7.30 (d, *J* 9 Hz, 4-aryl-H), 7.3—7.0 (m, 6-aryl-H), 5.07 (t, *J* 5 Hz, 2 × CH$_2$C*H*), 4.0—3.8 (m, 6 × OCH$_2$), 3.5—3.8 (m, 2 × OCH$_2$), 2.96 (d, *J* 5 Hz, 2 × ArC*H*$_2$CH), and 2.31 (s, 2 × ArMe).

NN′-*Bisethoxycarbonyl*-15,24-*bis*-(2,2-*ethylenedioxyethyl*)-4,10-*diaza*-1,7,13-*trioxa*[13](2,2)*biphenylophane* (17e).—The bistoluene-*p*-sulphonate (18b) (3.77 g, 5 mmol) in dimethylsulphoxide (50 ml) was added to a stirred solution of the dianion prepared from the biscarbamate (10a) 1.24 g, 5 mmol) and sodium hydride (0.275 g, 11 mmol) in dimethylsulphoxide (50 ml). The mixture was stirred overnight at room temperature, poured into water (1 l) containing hydrochloric acid (2N, 100 ml) and the product extracted into chloroform (2 × 250 ml). The extract was washed with water (2 × 250 ml), dried, evaporated, and the residual golden-yellow oil purified by column chromatography (silica, 40% ethyl acetate–60% chloroform) to give the *biphenylophane* (17e) as a colourless oil (1.4 g, 42%) (Found: *M*, 658.3 084. $C_{34}H_{46}N_2O_{11}$ requires *M*, 658.3 102); ν$_{max.}$ 1 700 cm^{-1}; δ (CDCl$_3$, 220 MHz), 7.31 (d, *J* 8 Hz, 18-H + 21-H), 7.2 (br d, *J* 8 Hz, 16-H + 23-H), 7.08 (t, *J* 8 Hz, 17-H + 22-H), 5.13 (t, *J* 5 Hz, 2 × CH$_2$C*H*), 4.12 (q, *J* 7 Hz, 2 × OC*H*$_2$Me), 4.2—3.3 (m, 8 × OCH$_2$), 3.1—2.6 (m, 4 × NCH$_2$), and 1.2 (2 t, *J* 7 Hz, 2 × OCH$_2$*Me*).

NN′-*Dimethyl*-15,24-*bis*-(2,2-*ethylenedioxyethyl*)-4,10-*diaza*-1,7,13-*trioxa*[13](2,2′)*biphenylophane* (17f).—The biscarbamate (17e) (230 mg, 0.35 mmol) was stirred with lithium aluminium hydride (200 mg) in ether (10 ml) for 18 h. Excess of hydride was destroyed by the addition of water, the solution was filtered, and the filtrate combined with ether washings of the solid. The combined ethereal solutions were dried and evaporated to yield the biphenylophane (17f) as a colourless oil (161 mg, 85%). A sample was purified by short-path distillation at 220 °C, 0.005 Torr (Found: C, 66.5; H, 8.0; N, 5.2. $C_{30}H_{42}N_2O_7$ requires C, 66.4; H, 7.8; N, 5.2%); δ (CDCl$_3$, 220 MHz), 7.3 (m, 4-aryl-H), 7.06 (t, *J* 8 Hz, 2-aryl-H), 5.20 (t, *J* 5 Hz, 2 × C*H*CH$_2$), 4.2—3.6 (m, 6 × OCH$_2$), 6.68 (m, 2 × OCH$_2$ + 2 × ArC*H*$_A$H$_B$), 2.94 (dd, *J* 14 and 5 Hz, 2 × ArCH$_A$*H*$_B$), 2.7—2.2 (m, 4 × NCH$_2$), and 2.23 (s, 2 × NMe).

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