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1,4,7-Trioxa-10-azacyclododecane and Some *N*-Substituted Derivatives; Synthesis and Cation Complexing

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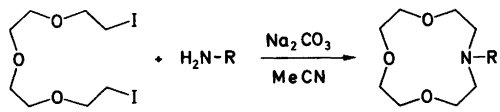
Primary amines condense with 1,11-diiodo-3,6,9-trioxaundecane in acetonitrile solution containing dispersed Na_2CO_3 to give *N*-substituted derivatives of monoaza-12-crown-4, including several directly appended with an additional donor group. The unsubstituted azacrown and the *N*-methyl derivative were obtained from the *N*-benzyl derivative.

The alkali cation complexing properties were studied by ^{13}C NMR spectroscopy. It was found that the presence of an additional donor atom in the side-chain suppresses the formation of 2:1 in favour of 1:1 complexes.

Whereas monoaza-18-crown-6,[1-3] monoaza-15-crown-5,[3] and their variously *N*-substituted derivatives[1-4] have been known for several years, and new methods for preparing monoaza-crown ethers continue to appear,[5,6] only an *N*-aryl derivative of the 12-ring analogue has been reported.[7] Significantly, attempts to prepare non-aromatic monoaza-12-crown-4 derivatives by closing a C – O bond in the cyclization step by analogy with the reactions used for the synthesis of the larger-ring azacrowns have failed.[4,8,9] A recent report[10] on the preparation of a macrocyclic diazaoligoether *via* direct double *N*-alkylation of a diaminoether with a diiodoether promoted by alkali cations led us to consider the possibility that a corresponding C – N bond-forming reaction may generate the monoaza-12-crown-4 system. Accordingly, the condensation of primary amines with 1,11-diiodo-3,6,9-trioxaundecane (*1*) was investigated.

Heating of this diiodide (*1*), as the crude product prepared from the corresponding dichloride of tetraethylene glycol, with benzylamine in moderately dilute acetonitrile solution (0.07 M) containing dispersed Na_2CO_3 resulted in the complete consumption of the dihalide and the formation of one new compound detectable by gas chromatography. Distillation from co-polymeric material allowed the isolation of a colourless oil of narrow boiling range. This was readily shown to be *N*-benzyl-monoaza-12-crown-4 (*3a*). The isolated yield was 54 % and could be improved, as shown by GLC, by higher dilution of the reactants (>90 % in 0.02 M solution), but not by replacing the Na_2CO_3 with Li_2CO_3 (*cf.* Ref. 10). Several other derivatives of monoaza-12-crown-4 were similarly prepared from the corresponding primary amines, and details are presented in Table 1. The volatility of ammonia and methylamine precluded their use, but the *N*-benzyl derivative could be converted into the parent azacrown (*3*, R = H) by hydrogenolysis over 10 % Pd – C in 85 % yield and to the *N*-methyl derivative (*3*, $R = CH_3$) *via* the urethane (*3*, R = COOPh) by successive reaction in THF with phenyl chloroformate and $LiAlH_4$ in 74 % yield.



1 *2* *3*

Finally, coupling of the *N*-phenyl derivative with *p*-nitrophenyldiazonium chloride gave the azo-dye (*3*, $R = -C_6H_4-p-N_2-C_6H_4-p-NO_2$), m.p. 166 °C. This latter preparation complements those reported by Dix and Vögtle[11] of the corresponding *N*-aryl-monoaza derivatives of 21-crown-7, 18-crown-6 and 15-crown-5. However, whereas the position of the UV-absorption around 475 nm suffers a marked hypsochromic shift on the addition

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Table 1. Reaction of primary amines with 1,11-diiodo-3,6,9-trioxaundecane.[a]

	R in substrate (*2*) and product (*3*)	Initial conc. of *1* (M)	Reaction time (h)	Yield[b] of *3* (%)	b.p. (m.p.) (°C/mmHg)	*m/e* (M^+)
a	$-CH_2Ph$	0.07	18	54	140–143/0.05	265
b	$-CH_2CH_2OMe$	0.08	18	51	100–102/0.005	233
c	$-CH_2CH_2OH$	0.08	18	48	106–108/0.01	219
d	$-CH_2CO_2Et$[c]	0.09	48	30	118–122/0.01	261
e	$-CH_2CONH_2$[c]	0.06	48	24	(106–108)	232
f	$-Ph$	0.06	120	51	150–152/0.005	251

[a] Reactions were run under N_2 in MeCN under reflux using per eq. diiodide 1.05 eq. amine and in the presence of *ca.* 4 molar eq. anhydrous Na_2CO_3. [b] Isolated yield based on 1,11-dichloro-3,6,9-trioxaundecane taken (see Experimental). [c] Substrate used as hydrochloride.

of alkali metal salts to acetonitrile solutions of these crowns,[11] no such shift could be detected during experiments on the new azo-dye using either LiSCN or NaSCN.

An important feature of the present method is that azacrown ethers can be prepared with a side-chain providing secondary binding sites directly in place (Table 1). Such compounds are commonly prepared using an *N*-protecting group, removing it after cyclization,[12] and introducing the desired sidechain in a separate reaction.[10,12,13] The term "lariat ether" has been coined to describe this type of macrocyclic polyether, and some 18-crown-6 and 15-crown-5 lariats having either a carbon or nitrogen atom of the ring as a pivot point, have very recently been prepared and the effect of "axial solvation" of a cation on the *strength* of the complexes studied.[6,13,14]

An effect on the *stoichiometry* has been observed when two ligating side-chains are present in a 12-crown-4 system; the formation of a 2:1 sandwich complex with sodium, which is particularly strong for the tetraether,[15,16] is suppressed completely for the 4,10-bis(2-hydroxyethyl) derivative of 1,7-dioxa-4,10-diazacyclododecane.[12]

It was now of interest to examine whether a single ligating sidechain would be sufficient to suppress the formation of a sandwich complex with sodium and other cations. The complexing properties in methanol solution of some of the *N*-substituted 1,4,7-trioxa-10-azacyclododecanes were therefore studied by titration with solid alkali salts monitored by the upfield shift of the averaged ^{13}C NMR resonance lines (fast exchange). Assuming that the limiting chemical shift of a given ligand is the same in 1:1 as in 2:1 complexes of the same cation, the position of the curve bend would then give the *stoichiometry*, and the deviation from a sharp bend a qualitative idea of the *strength* when the complexation is not too strong.[12,16]

The *N*-methyl derivative served as a reference compound and gave, like 12-crown-4,[15,16] a weak 1:1 complex with Li and somewhat stronger 2:1 complexes (sandwich) with Na and K (Fig. 1).* The Na complex is the strongest of these, as was also observed[15] for 12-crown-4, although the replacement of one ether oxygen by a tertiary amino nitrogen has led to the expected general weakening.

The *N*-(2-methoxyethyl) derivative formed a 1:1 complex not only with Li, but also with Na (Fig. 2). The strength of the Li complex is practically unchanged when compared qualitatively with the *N*-methyl derivative, suggesting that the side-arm is not used in coordination to Li. In sharp contrast, the Na complex has become very much stronger even than the sandwich complex of the *N*-methyl derivative. With K (as well as with Rb) the titration curve (Fig. 2) is of a more complicated nature. After the addition of one equivalent of KSCN a constant chemical shift is reached quickly (Fig. 2), which means that the final complex must be quite strong. Its stoichiometry cannot however be 2:1 since the

* Strictly, the curves of Fig. 1 can also be interpreted on the basis of mixtures of weak complexes with various stoichiometries. However, the geometry of the 12-membered ring limits the realistic possibilities to a 1:1 complex for Li and to 1:1 and 2:1 complexes for Na and K. Since the curve for the stronger Na complex is clearly best interpreted on the basis of a dominating 2:1 stoichiometry, it seems unlikely that the larger K cation should not also bias a 2:1 stoichiometry, although its being weaker leads to a curve permitting a wider range of interpretations.

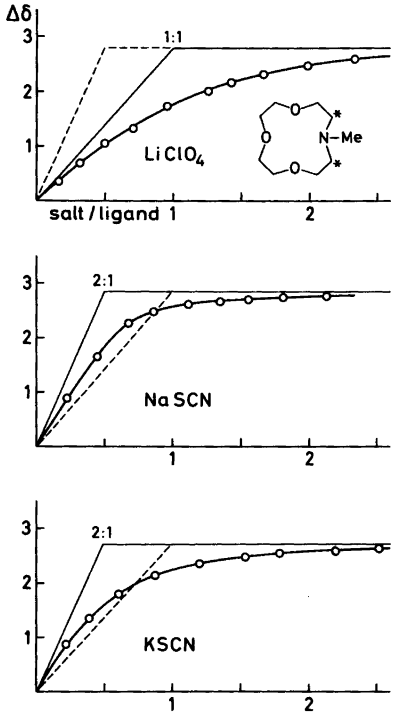

Fig. 1. ^{13}C NMR upfield chemical shift displacement ($\Delta\delta$) for the ring NCH_2 carbon of 10-methyl-1,4,7-trioxa-10-azacyclododecane (*3*, $R=CH_3$) in methanol solution on portionwise addition of solid $LiClO_4$, NaSCN and KSCN (molar ratio as abscissa). The sharp-bend curves are those expected for very strong complexing with limiting chemical shift fitted visually to the experimental curve.

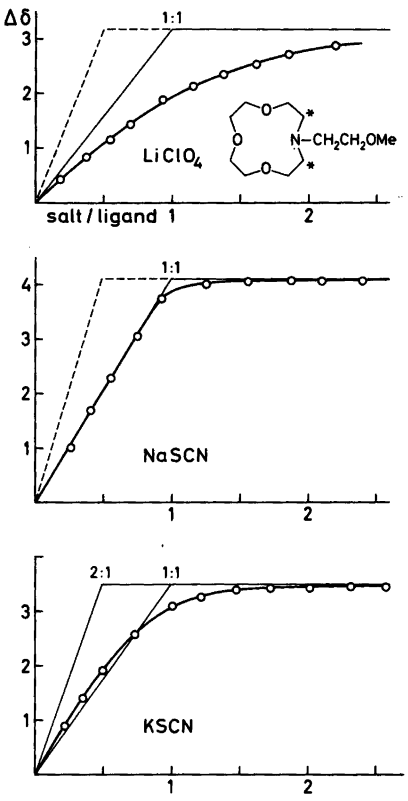

Fig. 2. ^{13}C NMR upfield chemical shift displacement ($\Delta\delta$) for the ring NCH_2 carbon of 10-(2-methoxyethyl)-1,4,7-trioxa-10-azacyclododecane (*3b*) in methanol solution on portionwise addition of solid $LiClO_4$, NaSCN and KSCN (molar ratio as abscissa). With RbSCN the titration curve resembles that of KSCN. The sharp-bend curves are those expected for very strong complexing with limiting chemical shift fitted visually to the experimental curve.

corresponding straight curve at low salt concentrations is not equally closely followed (Fig. 2). The most likely explanation is that the stoichiometry of the strong complex is 1:1 and that in the early phase of the titration a weaker 2:1 complex is present to some extent and only as long as there is an excess of ligand.

The *N*-ethoxycarbonylmethyl derivative also gave a relatively strong Na complex with 1:1 stoichiometry.

Since no seriously increased steric hindrance to sandwich complexation, involving two 12-membered rings, would be expected on passing from the *N*-methyl to the *N*-(2-methoxyethyl) derivative, we conclude that a fifth ligating oxygen atom, covalently bonded and correctly positioned 1,4 to a heteroatom of the ring, is more advantageous for Na and K cation complexing than the four ligating atoms of a second macrocycle. Of course, the loss of the second ring may in part be balanced by reestablishment of a contact ion-pair structure of the salt, since sandwiching of the cation requires its complete separation from the anion.[15]

A quantitative evaluation of the stability constants by computer analysis[12] of the titration curves was not considered justified since the results would be accurate only for the weaker 1:1 complexes among those studied here. Also, a comparison of

complexation constants is difficult when various stoichiometries are involved. We plan instead more elaborate ^{13}C NMR studies at temperatures low enough to freeze ligand exchange. The stoichiometries and the limiting chemical shifts of the complexed ligands, which must be guessed in the computer analysis, can thereby be obtained experimentally, as can the activation free energy for ligand exchange (by DNMR). The latter allows an independent estimate of the complexation constant to be made,[17] which is particularly useful in the case of strong complexing when the titration curve analysis fails.

EXPERIMENTAL

Melting points were determined on a Kofler hot stage apparatus and are uncorrected. GLC analyses were performed on a Hewlett-Packard 5700 A Gas Chromatograph equipped with a flame ionization detector and a 2 m × 2 mm 10 % SP 2100 on Chromosorb W AW DMCS 80/100 column. TLC analyses were performed on Merck plates precoated with Kieselgel 60 F−254. Elemental analyses were carried out at Microanalytisches Laboratorium Ilse Beetz, 8640 Kronach, West Germany. IR spectra were recorded on a Jasco IRA-1 spectrophotometer. ^1H NMR spectra (normally in $CDCl_3$) were recorded on a Varian HA 100 instrument, and ^{13}C NMR spectra (normally in CH_3CN) on a JEOL JNM-FX60 instrument. Mass spectra were recorded on a Micromass 7070 F spectrometer either with electron impact (70 eV) or with chemical ionization using isobutane.

1,11-Dichloro-3,6,9-trioxaundecane. Thionyl chloride (195 g, 1.64 mol) was added to a mechanically stirred and ice-cooled solution of tetraethylene glycol (150 g, 0.77 mol) in dry pyridine (135 g, 1.71 mol) at a rate such that the temperature of the reaction mixture remained below 50 °C. Stirring was then continued at room temperature overnight (during which time the initially-formed precipitate had largely redissolved) before adding water (20 ml) and extracting with ether (5 × 100 ml), adding a further 20 ml of water before each subsequent extraction. The ether layers were combined, washed with water (100 ml), brine (100 ml), dried ($MgSO_4$) and concentrated *in vacuo*. Distillation of the residue through a short Vigreux column gave the *dichloride* (148 g, 83 %) as a colourless liquid, b.p. 106−108 °C/0.1 mmHg. ^1H NMR ($CDCl_3$): δ 3.43−3.77 (complex sym. m, OCH_2CH_2Cl) and 3.56 (sharp s, OCH_2CH_2O).

1,11-Diiodo-3,6,9-trioxaundecane. 1. Powdered sodium iodide (100 g, 0.67 mol) was added to a solution of 1,11-dichloro-3,6,9-trioxaundecane (65.0 g, 0.28 mol) in acetone (150 ml), and the stirred mixture heated under reflux for 70 h. After cooling, the reaction mixture was filtered (washing with acetone), and the filtrate concentrated *in vacuo*, diluted with ethyl acetate (200 ml) and extracted with 20 % sodium thiosulphate solution (50 ml). The organic layer was washed with water (100 ml), brine (100 ml) and dried ($MgSO_4$). Removal of the solvent *in vacuo* gave the *diiodide 1* (115.5 g) as a very pale yellow oil, which was used directly in the following preparations. ^1H NMR ($CDCl_3$): δ 3.19 (4H, t, *J* 7, OCH_2CH_2I), 3.58 (8H, s, OCH_2CH_2O) and 3.70 (4H, t, *J* 7, OCH_2CH_2I). GLC showed the presence of *ca.* 2 % of 1-chloro-11-iodo-3,6,9-trioxaundecane as the only significant impurity. Crystallization of the oil from ether solution gave the *diiodide 1* as needles, m.p. 92−93 °C initially colourless but soon becoming yellow on storage.

10-Benzyl-1,4,7-trioxa-10-azacyclododecane 3a. A stirred solution of 1,11-diiodo-3,6,9-trioxaundecane (30.0 g, 0.073 mol) and benzylamine (8.2 g, 0.077 mol) in dry acetonitrile (1 l) containing suspended powdered anhydrous sodium carbonate (30 g) was heated under reflux under an atmosphere of nitrogen for 18 h. The cooled solution was decanted from most of the solid and concentrated *in vacuo*. The residues from decantation and concentration were combined and partitioned between water (600 ml) and ether (300 ml). The aqueous layer was re-extracted with ether (2 × 200 ml), and the combined organic layers washed with water (200 ml), brine (200 ml) and dried (Na_2SO_4). After removing the ether *in vacuo*, the residue was distilled through a short path, collecting material volatile at 0.05 mmHg with a bath temperature up to 200 °C. The distillate was redistilled through a short Vigreux column to give the pure *aza-crown 3a* (10.5 g, 54 %) as a colourless oil, b.p. 140−143 °C/0.05 mmHg. Found: C 67.8; H 8.7; N 5.2. Calc. for $C_{15}H_{23}NO_3$: C 67.9; H 8.7; N 5.3. ^1H NMR ($CDCl_3$) δ 2.69 (4H, t, *J* 5, OCH_2CH_2N), 3.55 (4H, t, *J* 5, OCH_2CH_2N), 3.60 (10H, s, OCH_2CH_2O and $PhCH_2N$) and 7.02−7.30 (5H, m, Ar*H*). ^{13}C NMR (CH_3CN) δ 55.7 (N−*C* (ring)), 61.4 (N−*C*−Ph), 70.6, 71.0 and 71.8 (O−*C*), 127.6, 129.0 and 129.8 (tert. arom. *C*) and 141.1 (quatern. arom. *C*), MS, *m/e* (% rel. int.) 265 (M^+, 2) and 91 (100).

10-(2-Methoxyethyl)-1,4,7-trioxa-10-azacyclododecane 3b. A stirred solution of 1,11-diiodo-3,6,9-trioxaundecane (15.4 g, 0.038 mol) and 2-methoxyethylamine (2.9 g, 0.039 mol) in dry acetonitrile (0.5 l) containing suspended powdered anhydrous sodium carbonate (15 g) was heated under reflux under an atmosphere of nitrogen for 18 h. The cooled suspension was filtered and the filtrate concentrated *in vacuo* to give a semi-solid. This was

extracted with chloroform (3 × 50 ml), each time decanting the clear solution from the crystalline residue. After filtration, the combined extracts were concentrated *in vacuo* and the residue was distilled through a short path, collecting material volatile at 0.01 mm with a bath temperature up to 250 °C. (No distillation was observed before the bath temperature reached *ca.* 180 °C, although the main fraction subsequently distilled steadily at 110–115 °C.) The distillate was redistilled through a short Vigreux column to give the pure *aza-crown 3b* (4.5 g, 51 %), as a colourless oil, b.p. 100–102 °C/0.005 mmHg. Found: C 56.5; H 9.9; N 6.1. Calc. for $C_{11}H_{23}NO_4$: C 56.6; H 9.9; N 6.0. ^{1}H NMR ($CDCl_3$) δ 2.69 (2H, t, *J* 6, $CH_3OCH_2CH_2N$), 2.73 (4H, t, *J* 4.5, $CH_2OCH_2CH_2N$), 3.27 (3H, s, CH_3O), 3.43 (2H, t, *J* 6, $CH_3OCH_2CH_2N$), 3.58 (t*, *J* 4.5, $CH_2OCH_2CH_2N$) and 3.60 (s*, OCH_2CH_2O) (* these signals together integrate for 12 H). ^{13}C NMR (CH_3CN) δ 56.6 [N–*C* (ring)], 56.9 [N–*C* (side chain)], 58.9 (O–CH_3), 71.0, 71.0 and 71.9 [O–*C* (ring) (obscuring CH_3OC)]; with excess NaSCN: δ 65.6, 66.4 and 66.9 (O–*C* (ring)) and 69.2 (CH_3OC). MS, *m/e* (% rel. int.) 233 (M^+, 0.5) and 188 (100).

10-(2-Hydroxyethyl)-1,4,7-trioxa-10-azacyclododecane 3c. Ethanolamine (2.4 g, 0.039 mol) was used instead of 2-methoxyethylamine as substrate in the immediately preceding preparation. The first distillation commenced when the bath temperature was over 200 °C, the main fraction distilling at *ca.* 130 °C/0.1 mmHg. Redistillation gave the *aza-crown 3c* (3.9 g, 48 %) as a very pale yellow oil, b.p. 106–108 °C/0.01 mmHg. Found: C 54.5; H 9.5; N 6.1. Calc. for $C_{10}H_{21}NO_4$: C 54.8; H 9.7; N 6.4. IR ν_{max} 3300 (broad, OH). ^{1}H NMR (CD_3CN) δ 2.53 (2H, t, *J* 5.5, $HOCH_2CH_2N$), 2.60 (4H, t, *J* 4.5, $CH_2OCH_2CH_2N$), 3.36 (t*, *J* 5.5, $HOCH_2CH_2N$), 3.45 (t*, *J* 4.5, $CH_2OCH_2CH_2N$) and 3.52 (s*, OCH_2CH_2O) (* these signals together integrate for 15 H, and obscure $HOCH_2CH_2N$). ^{13}C NMR (CH_3CN) δ 55.8 (N–*C* (ring)), 57.5 [N–*C* (side chain)], 59.9 (O–*C* (side chain)), 69.9, 71.1 and 71.2 [O–*C* (ring)]. MS, *m/e* (% rel. int.) 219 (M^+, 1.6) and 188 (100); CIMS 220 $(M+1)^+$.

10-Ethoxycarbonylmethyl-1,4,7-trioxa-10-azacyclododecane 3d. Glycine ethyl ester hydrochloride (6.5 g, 0.047 mol) was used instead of 2-methoxyethylamine as substrate in the procedure for the preparation of the *aza-crown 3b*, but using 18.5 g (0.045 mol) diiodide *1* and 18 g sodium carbonate, and heating under reflux for 48 h. The first distillation commenced when the bath temperature was over 200 °C, the main fraction then distilling at 138–140 °C/0.05 mmHg. Considerable darkening of the residue occurred during this distillation. Redistillation gave the *aza-crown 3d* (3.5 g, 30 %) as a colourless oil, b.p. 118–122 °C/0.01 mmHg. IR ν_{max} 1725 (C=O). ^{1}H NMR ($CDCl_3$) δ 1.24 (3H, t, *J* 7, OCH_2CH_3), 2.88 (4H, t, *J* 5, OCH_2CH_2N), 3.43 (2H, s, NCH_2CO_2), 3.56 (t*, *J* 5, OCH_2CH_2N), 3.60 (s*, OCH_2CH_2O) and 4.07 (2H, q, *J* 7, OCH_2CH_3) (* these signals together integrate for 12 H). ^{13}C NMR (CH_3CN) δ 14.6 (CO_2–C–*C*), 55.5 [N–*C* (ring)], 57.3 (CO_2–*C*–C), 60.7 [N–*C* (side chain)], 70.8, 70.8 and 71.5 [O–*C* (ring)] and 172.4 (O=*C*). MS, *m/e* (% rel. int.) 261 (M^+, 1.0) and 188 (100).

10-Carbamoylmethyl-1,4,7-trioxa-10-azacyclododecane 3e. The use of glycinamide hydrochloride (1.25 g, 0.011 mol) instead of glycine ester hydrochloride as substrate in the preceding preparation, except using 4.5 g (0.011 mol) diiodide *1*, 5 g sodium carbonate and 200 ml acetonitrile, gave a residue, after concentration of the chloroform solution, from which the *aza-crown 3e* (0.60 g, 24 %) was sublimed at 250 °C/0.01 mmHg as needles, m.p. 106–108 °C. IR ν_{max} (nujol mull) 3330, 3130 (NH_2) and 1680 (C=O). ^{1}H NMR (CD_3CN) δ 2.60 (4H, t, *J* 4.5, OCH_2CH_2N), 3.00 (2H, s, NCH_2CONH_2), 3.40 (4H, t, *J* 4.5, OCH_2CH_2N), 3.53 (8H, s, OCH_2CH_2O) and 5.77 (br, NH_2). ^{13}C NMR (CH_3CN) δ 56.4 [N–*C* (ring)], 59.8 [N–*C* (side chain)], 69.2, 70.7 and 71.5 [O–*C* (ring)]. MS, *m/e* (% rel. int.) 232 (M^+, 0.3) and 188 (100).

10-Phenyl-1,4,7-trioxa-10-azacyclododecane 3f. Aniline (1.9 g, 0.020 mol) was used instead of benzylamine as substrate in the procedure for the preparation of the *N*-benzyl derivative *3a*, but using 8.0 g (0.019 mol) diiodide *1*, 8 g sodium carbonate and 300 ml acetonitrile, and heating under reflux for 5 days. The extractions were performed using 1/4 of the described quantities. After removing the ether *in vacuo* the residue was distilled through a short path, collecting the *aza-crown 3f* (2.5 g, 51 %) at 150–152 °C/0.005 mmHg as a pale yellow viscous oil. Considerable darkening of the residue occurred during this distillation. ^{1}H NMR ($CDCl_3$) δ 3.47 (4H, t, *J* 5, OCH_2CH_2N), 3.54 (8H, s, OCH_2CH_2O), 3.76 (4H, t, *J* 5, OCH_2CH_2N), 6.42–6.66 (3H, unsymm. m, N–Ar–*o,p*–H) and 6.91–7.14 (2H, m, N–Ar–*m*–*H*). ^{13}C NMR (CH_3CN) δ 52.7 (N–*C* (ring)), 70.1, 70.6 and 72.0 (O–*C*), 113.2, 116.7 and 129.9 (tert. arom. *C*) and 149.7 (quatern. arom. *C*). MS, *m/e* (% rel. int.) 251 (M^+, 19) and 105 (100).

1,4,7-Trioxa-10-azacyclododecane. A solution of the *N*-benzyl-aza-crown *3a* (3.5 g, 0.013 mol) in acetic acid (10 ml) containing suspended 10% palladium on activated carbon catalyst (0.5 g) was stirred at 60 °C under 3 atmospheres of hydrogen for 15 h. The cooled mixture was filtered through a bed of celite, using ethanol for washing. The solution was concentrated *in vacuo* and the residue dissolved in water (10 ml). After basification with 30 % potassium carbonate solution (20 ml), the

solution was extracted with chloroform (4 × 25 ml) and the combined organic layers washed with 10 % potassium carbonate solution (10 ml), brine (20 ml) and dried (Na_2SO_4). The solvent was removed *in vacuo* and the residue distilled (air condenser) to give the unsubstituted *aza-crown* (*3*, R = H) (2.3 g, 85 %), b.p. 72 – 74 °C/0.01 mmHg, m.p. 59 – 60 °C. Sublimation at 60 °C/0.01 mmHg gave needles of unchanged m.p. Found: C 54.7; H 9.6; N 8.0. Calc. for $C_8H_{17}NO_3$: C 54.8; H 9.8; N 8.0. IR ν_{max} (nujol mull) 3300 (NH). ^{1}H NMR ($CDCl_3$) δ 2.70 (5 H, symm. m with t structure, "*J*" 5, OCH_2CH_2NH*) and 3.44 – 3.72 (12H, unsymm. m OCH_2) (* exchanges with D_2O, after which the m integrates for 4H). ^{13}C NMR (CH_3CN) δ 48.7 (N – *C*), 69.2, 69.8 and 71.1 (O – *C*). MS, *m/e* (% rel. int.) 175 (M^+, 0.9) and 57 (100); CIMS 176 $(M+1)^+$.

10-Methyl-1,4,7-trioxa-10-azacyclododecane. Redistilled phenyl chloroformate (3.0 g, 0.019 mol), was added to a stirred solution of the *N*-benzyl-aza-crown *3a* (4.0 g, 0.015 mol) in dry tetrahydrofuran (50 ml) containing suspended anhydrous potassium carbonate (2 g) and stirring continued overnight.

The reaction mixture was shaken well with 10 % potassium hydroxide solution (50 ml) and extracted with ethyl acetate (3 × 50 ml). The combined organic layers were washed with water (30 ml), brine (30 ml) and dried ($MgSO_4$). Removal of the solvents *in vacuo* gave an equimolar mixture of 10-phenoxy-carbonyl-1,4,7-trioxa-10-azacyclododecane (*3*, R = – COOPh) and benzyl chloride as an oil. IR ν_{max} 1720 (urethane C = O). ^{1}H NMR ($CDCl_3$) δ 3.40 – 3.98 (16H, m, crown ring protons), 4.45 (2H, s, $PhCH_2Cl$) and 6.88 – 7.20 (10H, m, Ar*H*). MS, *m/e* (% rel. int.) 202 (M^+ crown-OPh, 27) and 114 (100).

This mixture was dissolved in dry tetrahydrofuran (200 ml) and the stirred solution cooled to 0 °C. Lithium aluminium hydride (2.5 g, 0.066 mol) was added in one portion, and stirring was continued at room temperature for 18 h. Excess metal hydride was destroyed by the careful addition of a mixture of water (5 ml) and tetrahydrofuran (20 ml) to the ice-cooled suspension, which was then stirred for an additional 30 min before filtering on a sintered glass funnel, the residue being well washed with tetrahydrofuran. The filtrate was concentrated *in vacuo*, dissolved in water (50 ml) and extracted with ether (3 × 20 ml). The ether extracts (containing phenol) were discarded, and the aqueous layer concentrated *in vacuo*. After removal of the last traces of water by concentration of an absolute ethanolic solution, the residue was distilled through a short Vigreux column to give the *N*-methylated *aza-crown* (*3* R = CH_3) (2.1 g, 74 %) as a colourless oil, b.p. 65 – 67 °C/0.1 mmHg. Found: C 57.4; H 10.1; N 7.2. Calc. for $C_9H_{19}NO_3$: C 57.1; H 10.1; N 7.4. ^{1}H NMR ($CDCl_3$) δ 2.29 (3H, s, NCH_3), 2.58 (4H, t, *J* 4.5, OCH_2CH_2N), 3.58 (4H, t, *J* 4.5, OCH_2CH_2N) and 3.60 (8H, s, OCH_2CH_2O). ^{13}C NMR (CH_3CN) δ 44.8 (N – CH_3), 58.3 (N – *C* (ring)), 70.2, 71.0 and 71.5 (O – *C*). MS, *m/e* (% rel. int.) 189 (M^+, 4) and 71 (100); CIMS 190 $(M+1)^+$.

10-[4-(4-Nitrophenylazo)-phenyl]-1,4,7-trioxa-10-azacyclododecane. 4-Nitroaniline (6.50 g, 0.047 mol) was dissolved with warming in a mixture of water (15 ml) and hydrochloric acid (36 %, 10.5 ml, 0.104 mol). The stirred solution was cooled in ice while a solution of potassium nitrite (4.1 g, 0.048 mol) in water (7 ml) was added slowly enough to keep the temperature below 5 °C. The resulting solution of 4-nitrophenyldiazonium chloride was diluted to 250 ml with iced water.

An aliquot (17 ml) of the diluted solution was withdrawn and the N-phenyl-aza-crown *3f* (0.80 g, 3.2 mmol) was added to it with stirring at 0 °C. A solution of potassium acetate (0.38 g, 3.9 mmol) in water (3 ml) was added and stirring continued for 30 min at 5 °C. The precipitated dye was filtered off, washed consecutively with water, 10 % acetic acid, water and ethanol, and dried in air. Recrystallization from toluene (50 ml) gave the *azo-dye* (*3*, R = $-C_6H_4-N_2-C_6H_4NO_2$) (0.65 g, 51 %) as orange-red needles, m.p. 166 °C. Found: C 60.8; H 6.0; N 13.7. Calc. for $C_{20}H_{24}N_4O_5$: C 60.0; H 6.0; N 14.0. ^{1}H NMR ($CDCl_3$) δ 3.54 (8H, s, OCH_2CH_2O), 3.61 (4H, t, *J* 5, OCH_2CH_2N), 3.83 (4H, t, *J* 5, OCH_2CH_2N), 6.67 (2H, d, *J* 9, $CH_2N-Ar-o-H$), 7.68 (2H, d, *J* 9, $CH_2N-Ar-m-H$), 7.71 (2H, d, *J* 9, $O_2N-Ar-m-H$) and 8.11 (2H, d, *J* 9, $O_2N-Ar-o-H$). MS, *m/e* (% rel. int.) 400 (M^+, 100). UV λ_{max} (CH_3CN) 479 nm (unchanged on the addition of either Li-, Na- or K-SCN).

Titration curves. The ligand solutions in CD_3OD (2 ml) were ~0.5 *M*. After each addition of solid alkali salt the ^{13}C NMR chemical shift (rel. to TMS) was measured at room temperature in a Bruker CXP-200 instrument operating at 50 MHz. The four signals for the ring carbons underwent the strongest upfield displacement; the one for the ring NCH_2 carbons was best resolved and selected for plotting the curves in Figs. 1 and 2.

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