MACROHETEROCYCLES WITH AN ENDOCYCLIC AZO-GROUP.

1. TETRAAZAMACROCYCLES OBTAINED FROM RESORCINOL

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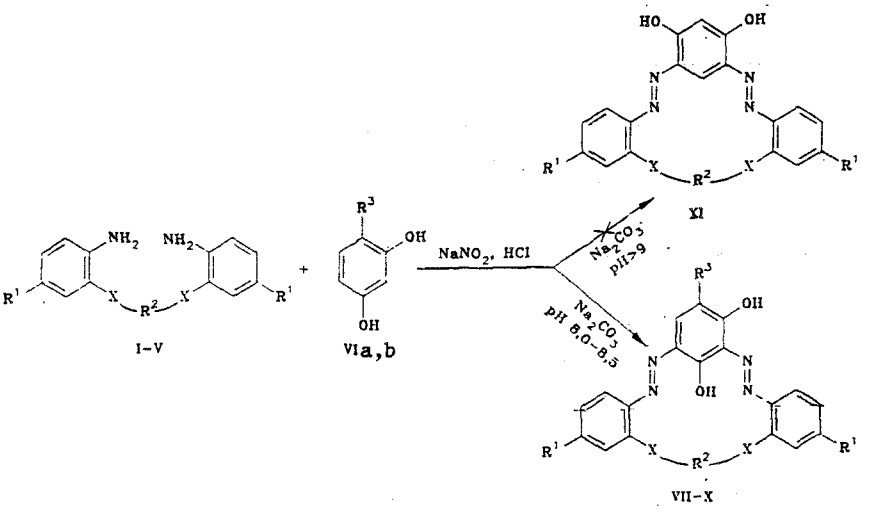
High-dilution azocoupling of bisdiazotized bis-(2-aminophenyl)oligooxa (or thia)alkanes with resorcinol gives tetraazamacrocycles with two endocyclic azo-groups. It is shown that azocoupling occurs exclusively at the 2- and 4-positions of the resorcinol ring.

It was in 1977 that the first report appeared on chromophoric crown ethers [1], and this was followed in a short time by the synthesis of over a hundred colored crown ethers and many other macroheterocyclic dyes, which have found wide application as organic reagents and extractants in analytical chemistry, and as ligands in the preparation of new coordination compounds [2]. One method of obtaining chromogenic crown ethers is to introduce into the molecule azo-groups, which can be either exocyclic, or form part of the coordination contour of the macrocycle (endocyclic azo-group). In the first case, the azo group simply confers color on the crown ether, but does not participate in complex formation, while in the second case it interacts directly with metal ions.

As was first shown by Japanese workers [3], endocyclic azo-groups not only affect adversely the extractant properties, but also confer new properties on the molecule, namely rigidity of the cyclic skeleton, and the possibility of varying the extractant capacity by light irradiation, as a result of cis–trans isomerization. Crown ethers containing an endocyclic azo-group have hitherto been obtained for the most part from already-synthesized azo-dyes, by alkylating azophenols with bishalooligooxaalkanes [2, 3].



I R^2=—CH_2—; II, VII R^2=—CH_2CH_2—; III, VIII R^2=—$CH_2CH_2CH_2$—; IV, IX R^2= =—$CH_2CH_2OCH_2CH_2$—; V, X R^2=—$CH_2CH_2OCH_2CH_2OCH_2CH_2$— IIb, VIIb X=S; IVb, IXb R^1=NO_2; VIb, IXc R^3=SO_3Na; when not given R=H, when not given X=O

This report describes the synthesis of crown-like macroheterocycles with two endocyclic azo-groups, by azo-coupling. The azo-component chosen was highly reactive towards resorcinol, enabling high-dilution conditions to be used for azo-coupling.

To obtain the starting bis-(2-aminophenyl)oligooxaalkanes, a method has been developed involving the alkylation of o-nitrophenol with the appropriate bishalooligooxaalkanes in DMSO, followed by reduction of the resulting nitro compounds with hydrazine hydrate.

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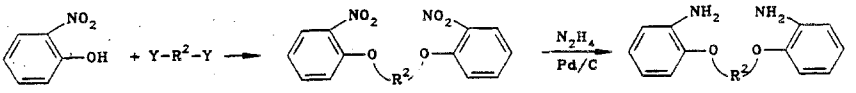
TABLE 1. Properties of Tetraazamacrocycles (VII-X) and the Acyclic Analog (XII)

Compound	mp, °C	M^+	Found, %			Empirical formula	Calculated, %			Yield, %
			C	H	N(S)		C	H	N(S)	
VII[a]	272—274 (разл.)	376	63,9	4,2	14,4	$C_{20}H_{16}N_4O_4$	63,8	4,3	14,9	3
VII[b]	275—277 (разл.)	408	58,9	3,9	13,7 (15,7)	$C_{20}H_{16}N_4O_2S_2$	58,8	3,9	13,7 (15,7)	20
VIII	247—248	390	64,5	4,7	14,4	$C_{21}H_{18}N_4O_4$	64,6	4,6	14,3	13
IX[a]	278—279	420	62,7	4,8	13,2	$C_{22}H_{20}N_4O_5$	62,8	4,8	13,3	52
IX[b]	>300	510	51,7	3,8	15,9	$C_{22}H_{18}N_6O_9$	51,8	3,5	16,2	35
IX[c]	>300	—	49,2	3,8	10,7 (5,7)	$C_{22}H_{19}N_4NaO_8S\times H_2O$	48,9	3,9	10,4 (5,9)	56
X	208—209	464	62,1	5,3	12,1	$C_{24}H_{24}N_4O_6$	62,1	5,2	12,1	54
XII	200—201	406	65,1	5,4	13,7	$C_{22}H_{22}N_4O_4$	65,0	5,5	13,8	40



XIII-XVII XVIII a-e I, II a III, IV a,V

XIII, XVIIIa R^2=—CH_2—; XIV, XVIIIb R^2=—$(CH_2)_2$—; XV, XVIIIe R^2=—$(CH_2)_3$—; XVI, XVIIId R^2=—$(CH_2)_2$—O—$(CH_2)_2$—; XVII, XVIIIe R^2=—$(CH_2)_2$—O—$(CH_2)_2$—O—$(CH_2)_2$—; XIII Y=I; XIV, XV Y=Br; XVI, XVII Y=Cl

It is known [4] that azo-coupling of resorcinol with an excess of the diazo-component can, depending on the acidity of the medium give a principal product either 2,4- (pH ~ 8, compounds (VII-X)), or 4,6-bis(phenylazo)-substituted (pH ~ 12), (XI) resorcinols. It is interesting that azocoupling of bisdiazotized diamines (I-V) with resorcinol (VIa) and its sulfo-derivative (VIb) gives only the macrocyclic 2,4-bis(arylazo)resorcinols (VII-X). When the pH is increased, however, i.e., under conditions favoring the formation of the 4,6-bis-arylazo-compounds (XI), the yields of macrocyclic compounds fall sharply, only polymeric products being obtained. The absence from the reaction products of tetraazamacrocycles of general formula (XI) may be due to steric hindrance to exocyclic hydrogen bonding in (XI).

The yields of macrocycles are also highly dependent on the size of the ring formed. For instance, no 14-membered heterocycle was obtained from the diamine (I), and 15- (VIIa) and 16-membered (VIII) oxygen-containing macrocycles were obtained in only low yield. The difficulty of formation of small rings in this macrocyclic system is clearly due to increased strain and rigidity, as is readily apparent from their Stuart—Briegleb molecular models. The instability of the smallest of the rings obtained, the 15-membered rings (VIIa) and (VIIb), is apparent on heating, since these compounds decompose at their melting points.

The sites of azo-coupling in positions 2 and 4 of the resorcinol ring has been proved by direct synthesis in the reaction of bisdiazotized 1,7-bis(2-aminophenyl)-1,4,7-trioxaheptane (IVa) with 4-sulforesorcinol (VIb). Desulfonation of the product (IXc) by heating in phosphoric acid gave the same product (IXa) as was obtained by azo-coupling bisdiazotized (IVa) with resorcinol (VIa).

In order to establish the optimum conditions for the synthesis of the tetraazamacrocycles, and to compare the properties of the cyclic compounds with an acyclic analog with the same system of chromophores, 2,4-bis-(2-ethoxyphenylazo)resorcinol (XII) was obtained under similar conditions.

The tetraazamacrocycles (VII-X) (Table 1) were deep-colored crystalline solids which were soluble in most organic solvents.

The UV spectra of (VII-X) showed absorption maxima characteristic of 2,4-bis(phenylazo)-substituted resorcinols at 410-470 nm [5], which were shifted to shorter wavelengths by 40-50 nm as compared with the acyclic analog (XII). Unlike the acyclic analog (XII), on changing from a polar solvent (ethanol) to a nonpolar solvent (chloroform), there was observed a slight hypsochromic shift and the appearance of a second long-wavelength maximum at 510-540 nm. It is clear that in the macrocyclic bis(arylazo)resorcinols (VII-X), the influence of the solvent on the shift in the azoquinone hydrazone equilibrium is more pronounced than in the acyclic analog (XII).

TABLE 2. Spectral Properties of Tetraazamacrocycles (VII-X) and the Acyclic Analog (XII)

Compound*	UV spectrum, λ_{max}, nm (lg ε)		IR spectrum, ν, cm^{-1}			PMR spectrum, δ, ppm		
	in alcohol	in $CHCl_3$	aryl	—N=N—	C—X—C	CH_2—X	aryl (m)	NH/OH(s)
VIIa	416,1 (4,38)	413,3 (4,51), 513,5 пл.	1640, 1600	1408	1270, 1108	4,39 m	6,32—7,92	15,25; 16,07
VIIb	411,3 (4,48)	411,3 (4,51), 523,2 (4,04)	1640, 1600	1401	1250, 1120	3,08 s	6,43—8,10	15,86; 16,56
VIII	426,7 (4,54)	424,6 (4,56), 534,4 (4,16)	1640	1408	1261, 1247, 1110	3,52t; 3,97q	6,21—7,87	15,64; 16,55
IXa	430,4 (4,49)	426,0 (4,60), 531,0 (4,25)	1630	1409	1266, 1113	4,18m	6,35—8,09	15,39; 16,48
IXb	—	426,7 (4,66), 536,7 (4,38)	1640	1417	1260, 1122	4,30 m	6,42—8,04	15,18; 16,04
X	417,5 (4,55)	412,6 (4,57), 513,5 (4,29)	1637	1408	1260, 1111	3,89s; 4,17m	6,32—8,04	14,13; 15,17
XII	466,5 (4,63)	469,2 (4,65)	1610	1400	1255, 1119	1,43t; 4,05q	6,27—7,65	15,94; 16,67

*Compound (IXb) was insoluble in alcohol; ν_{-NO_2} 1513, 1347 cm^{-1}.

In the IR spectra of both the acyclic (XII) and the cyclic (VII-X) bis(arylazo)resorcinols (Table 2), absorption is present at 1400-1417 cm^{-1} characteristic of azo-group vibrations [6], together with bands at 1108-1122 and 1247-1270 cm^{-1} characteristic of the asymmetrical and symmetrical stretching vibrations of the C—O—C group, and strong absorption at 1600-1640 cm^{-1} characteristic of the skeletal vibrations of the aromatic ring.

In the PMR spectra of the tetraazamacrocycles (VII-X) (Table 2), singlets are seen for the equivalent protons of the methylene groups in the X—CH_2—CH_2—X group at 3.08 ppm (α-CH_2S, X = S, VIIb) and 3.89 ppm (γ=CH_2O, X = O, X), and in the other cases the spectra contain multiplets for the methylene group protons at 4.02-4.50 ppm, and for the aromatic ring protons at 6.21-8.09 ppm. In the acyclic compound (XII), signals are present for the ether ethyl group at 1.43 ppm (3H, t, CH_3C) and 4.05 ppm (2H, q, α-CH_2O). The singlets for the hydroxyl protons in all the bis(arylazo)-resorcinols except (X) are seen at 15 and 16 ppm, probably indicating the quinone hydrazone structure, as shown by the PMR spectra of acyclic 2,4-bis-(phenylazo)resorcinols [7]. In the case of (X), the azoquinonehydrazone equilibrium is apparently shifted more towards the azo-form, since the chemical shifts of the corresponding protons are to higher field by ~1.5 ppm as compared with those of the protons in 2,4-bis-(2-ethoxyphenylazo)resorcinol (XII).

EXPERIMENTAL

UV spectra were obtained on a Specord M-40 UV-VIS in ethanol and chloroform. IR spectra were recorded on a UR-20 spectrophotometer in KBr disks. PMR spectra were obtained on a Bruker AC-250 in $CDCl_3$, internal standard TMS. The progress of the reactions was followed and the purity of the products established by TLC on Silufol UV-254 plates. The azocoupling products were separated by column chromatography on silica gel L 40/100, eluent chloroform. Molecular masses were measured by mass spectrometry on an AEI MS-30 mass spectrometer, ionizing voltage 70 eV.

The resorcinol-4-sulfonic acid salt (VIb) used as starting material was obtained as described in [8], and amines (IIb) and (IVb) as described in [9] and [10].

Bis-(2-nitrophenyl)oligooxaalkanes (XVIIIa-e). To a solution of 0.3 mole of 2-nitrophenol in 150 ml of DMSO was added with stirring 60 g of finely ground, freshly-calcined potassium carbonate and 0.2 mole of the dihaloalkane (XIII-XV) or the dihalooligooxaalkane (XVI, XVII). The mixture was heated with stirring for 6 h at 130°C, poured into water, filtered, washed with a small amount of cold alcohol, dried, and crystallized from alcohol.

1,3-Bis-(2-nitrophenyl)-1,3-dioxapropane (XVIIIa), yield 85%, mp 129-130°C [11]; 1,4-bis-(2-nitrophenyl)-1,4-dioxabutane (XVIIIb), yield 75%, mp 167-168°C [12]; 1,5-bis-(2-nitrophenyl)-1,5-dioxapentane (XVIIIc), yield 75%, mp 106-107°C [13]; 1,7-bis-(2-nitrophenyl)-1,4,7-trioxaheptane (XVIIId), yield 85%, mp 69°C [14]; 1,10-bis-(2-nitrophenyl)-1,4,7,10-tetraoxadecane (XVIIIe), yield 77%, mp 63-64°C (according to [13], mp 47-50°C).

Bis-(2-aminophenyl)oligooxaalkanes (I, IIa, III, IVa, V). To a solution of 10 mmole of bis-(2-nitrophenyl)oligooxaalkane (XVIIIa-e) in 300 ml of alcohol, heated to 75°C, was added 10 ml of 85% hydrazine hydrate, followed by the portionwise addition over 1 h of 0.5

g of 5% palladium on charcoal. When all the catalyst had been added, the mixture was boiled for a further 2 h, then the catalyst was filtered off, the solvent evaporated to 50 ml, and the filtrate diluted with water. The oil which separated was triturated with cooling until it solidified, then the solid was filtered off, washed with water, dried, and crystallized from alcohol.

1,3-Bis-(2-aminophenyl)-1,3-dioxapropane (I), yield 87%, mp 79-81°C [11]; 1,4-bis-(2-aminophenyl)-1,4-dioxabutane (IIa), yield 91%, mp 130-131°C [9], 1,5-bis-(2-aminophenyl)-1,5-dioxapentane (III), yield 88%, mp 50-51°C (according to [15], mp 42-48°C); 1,7-bis-(2-aminophenyl)-1,4,7-trioxaheptane (IVa), yield 93%, mp 64-66°C [14]; 1,10-bis-(2-aminophenyl)-1,4,7,10-tetraoxadecane (V), yield 62%, mp 54-56°C (according to [13], mp 48-49°C).

Tetraazamacrocycles (VII-X). A suspension of 1 mmole of the bis-(2-aminophenyl)oligooxaalkane (I, IIa, III, IVa, or V) in 10 ml of 2.5 M HCl was diazotized with 1 ml of a 5 M solution of sodium nitrite at 0°C, stirred for 30 min, and the excess nitrous acid destroyed with sulfamic acid. To 500 ml of soda solution at 5°C were added simultaneously, dropwise, a solution of the diazonium salt diluted to 50 ml, and a solution of 1 mmole of resorcinol in 50 ml of water the pH of the solution being kept at 8.0-8.5. The solid was filtered off, dried, extracted with chloroform, and the extract chromatographed on a column of silica gel, eluent chloroform.

The acyclic analog, 2,4-bis-(2-ethoxyphenylazo)resorcinol (XII) was obtained similarly. The diazo-component was o-phenetidine.

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