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SYNTHESIS OF NEW MACROCYCLIC POLYETHER DI- OR TETRAESTER LIGANDS CONTAINING PYRAZOLE UNITS

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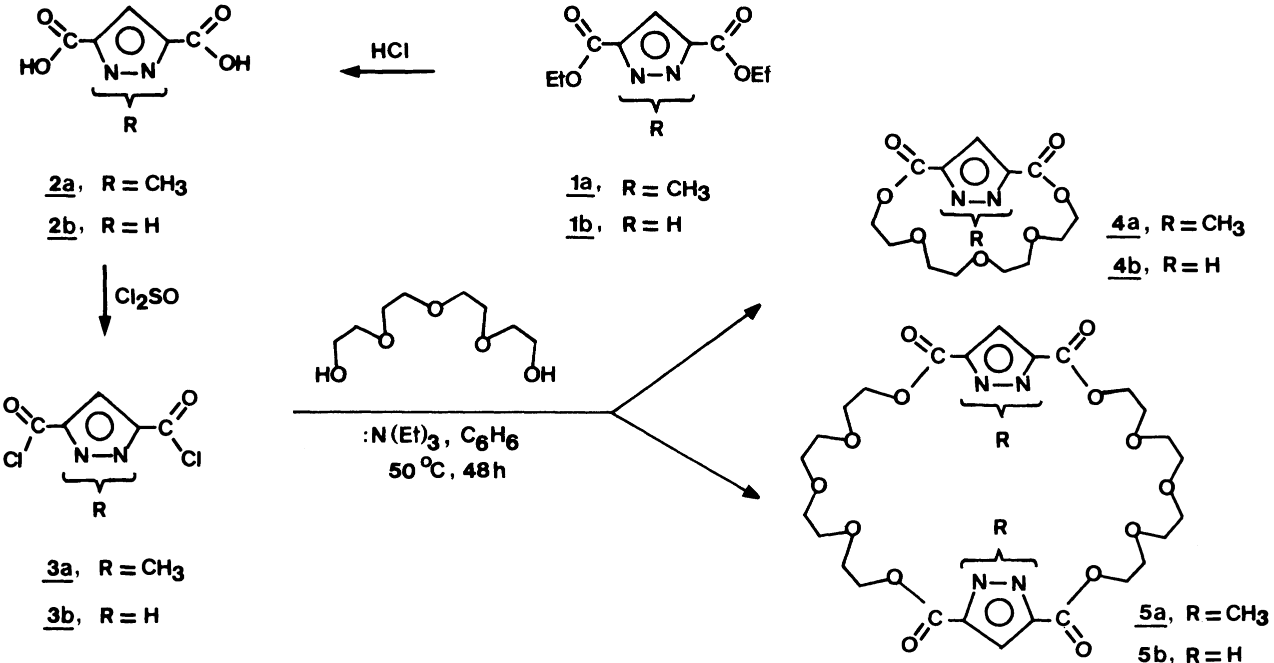
A new series of macrocyclic polyether - diester compounds containing one or two pyrazole rings (NH or N-methyl substituted) have been prepared by treating 3,5-pyrazolyldicarbonyl chlorides with tetraethylene glycol in the presence of triethylamine. Their complexation abilities towards the shift reagent Eu(Fod)$_3$ have been studied by ^{1}H NMR in Cl$_3$CD solution.

In order to compare the metal complexation properties of synthetic macrocyclic multidentate compounds containing ester functions with those naturally occurring macrocyclic antibiotics[1,2] a number of heterocyclic crowns with pyridine,[3] furan,[4] and isoxazole[5] units have been recently obtained. Considering the excellent complexing properties of the pyrazole nucleus,[6] we report in this paper the synthesis of macrocyclic polyether di- or tetraester derivatives containing one or two pyrazole units 4a-b and 5a-b, respectively (Scheme 1). These compounds were prepared from the 3,5-pyrazolyldicarbonyl chlorides 3a-b[7] with tetraethylene glycol (TEG), molar ratio 1:1 in the presence of triethylamine (TEA), molar ratio



Scheme 1.

1:3, using benzene as solvent and high dilution conditions.[8)]

Crowns 4a and 5a[9)] were formed in the same reaction as the result of 1:1 or 2:2 cyclization of 3a and TEG, respectively. Analogously, 4b and 5b were obtained from 3b and TEG. It is to be noted that in the absence of TEA the larger crowns 5a-b and the smaller one 4b have not been isolated and only crown 4a was obtained in much lower yield (2.5 %). Physical and analytical data are shown in Table 1. The molecular weights of 4a-b and 5a-b were determined first by osmometry (Osm.), in Cl_3CH solution with an error of about 10%, and then confirmed by mass spectrometry.[10)]

Table 1. Physical and experimental data of compounds 4a-b and 5a-b

Compound	4a	5a	4b	5b
Mp	143-144 °C (Acetone)	90-91 °C (Acetone/n-hexane)	144-145 °C (AcOEt)	171-172 °C (Chromatographied)
Mw (theoretical)	328	656	314	628
Mw (Osm.)	309	720	340	621
Ms : m/e	328 (M^+)	657 (M^++1)	314 (M^+)	-
Analytical data	Calcd for $C_{14}H_{20}N_2O_7$ C% H% N% 51.22 6.10 8.45 Found: 51.35 6.38 8.97	Calcd for $C_{28}H_{40}N_4O_{14}$ C% H% N% 51.22 6.10 8.45 Found: 50.92 6.19 8.81	Calcd for $C_{13}H_{18}N_2O_7$ C% H% N% 49.68 5.73 8.92 Found: 49.83 5.87 9.16	Calcd for $C_{26}H_{36}N_4O_{14}\cdot 2H_2O$ C% H% N% 46.98 6.02 8.43 Found: 46.83 5.81 8.03
Chromatographic conditions	On silica gel Toluene, chloroform, acetone (1:1:1) Rf 0.58	Rf 0.36	On silica gel Toluene, ether, ethanol (1:2:2) Rf 0.69	Rf 0.45
Yield/%	54	23	12	10

Table 2. ^1H NMR data of 4a-b and 5a-b (Cl_3CD)

Compound		4a	5a	4b	5b
Pyrazole ring	$\underline{H}$-C≪	7.52 s(1 H)	7.32 s(2 H)	7.50 s (1 H)	7.32 s(2H)
	>N-CH_3	4.23 s(3 H)	4.20 s(6 H)	-	-
	>N$\underline{H}$	-	-	9.65^e b(1 H)	7.9^e b(2H)
-$\underline{CH_2}$-OCO-	Next to >N	4.28 - 4.53 m (2H)	4.33 - 4.50 m (8H)	4.37 - 4.52 m (4H)	4.33 - 4.57 m (8H)
	Next to >NR	4.33 - 4.38 m (2H)			
-O-$\underline{CH_2}$-CH_2-OCO-		3.63 - 3.90 m (12 H)	3.66 - 3.85 m (8H)	3.60 - 3.90 m (12H)	3.70 - 3.87 m (8H)
-O-$\underline{CH_2}$-$\underline{CH_2}$-O-			3.63 m (16H)		3.62 m (16H)

(s=singlet; d=doublet; m=multiplet; b=broad; e=disappear by exchange with D_2O).

The proposed structures are consistent with their ir spectra (carbonyl bands at 1730-1750 cm^{-1} as expected for lactones and NH bands at 3200-3480 cm^{-1} for 4b and 5b) as well as with their ^1H NMR data (Table 2).

In order to study further the complexation ability of the new crowns here prepared and their coordination sites with shift reagents, increasing amounts of $Eu(Fod)_3$ (Fod = 6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octandionate) were added to a Cl_3CD solution of 4a-b and 5a-b, and their ^1H NMR spectra recorded. The results are shown in Figs. 1-4. [Δδ(ppm) observed in ^1H NMR vs. [L]/[S_n] ratio being

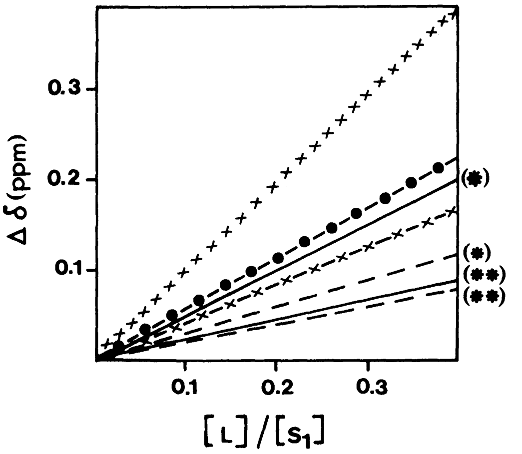


Fig. 1.

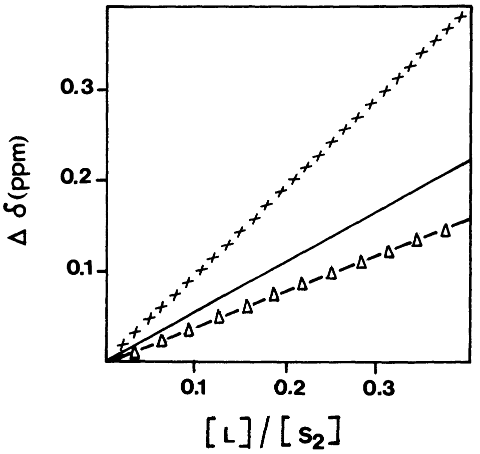


Fig. 2.

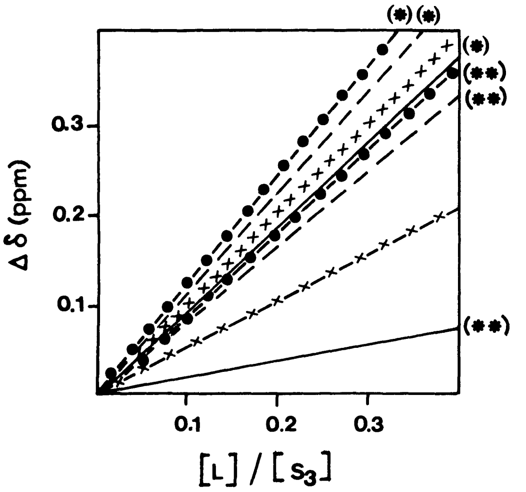


Fig. 3.

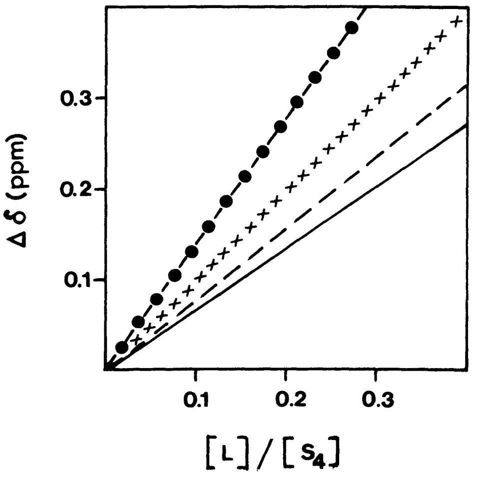


Fig. 4.

x x x x x x x $\underline{H}$-arom

●-●-●-●-● $O-C\underline{H}_2-C\underline{H}_2-O$

———— $-C\underline{H}_2-OCO-$ (*) Next to N:

– – – – – $-O-C\underline{H}_2-CH_2-OCO-$ (**) Next to CH_3-N

-x-x-x-x- CH_3N

-Δ-Δ-Δ-Δ- $-O-C\underline{H}_2-C\underline{H}_2-O-C\underline{H}_2-CH_2-O-CO-$

$[L] = [Eu(Fod)_3]$ and $[S_n] = [Crown]$, n = 1 (4a), n = 2 (4b), n = 3 (5a), and n = 4 (5b), respectively].11)

All of these crown compounds were found to interact with the shift reagent through the pyrazole pyridinic nitrogens as demonstrated by the considerable induced shift, not only on the pyrazole aromatic protons and the methyl groups (in 4a and 5a)12) but also on the oxygens belonging to the polyethylenic chains.

References

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7) Compounds 3a-b which had not been described before, were obtained as indicated in Scheme 1.
8) B. Dietrich, J.M. Lehn, J.P. Sauvage, and J. Blanzat, Tetrahedron, 29, 1629 (1973).
9) Crown 5a probably is a mixture of isomers N-R depending on cyclization step.
10) Mass spectra of the large crown 5a has been determined by chemical ionization using ammonia as gas ($M^{+}+1$, molecular peak of the protonated species).
11) In all the plots, the slopes are referred to the pyrazole aromatic protons which have been taken equal to 1 by definition.
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