Seven-co-ordination in Metal Complexes of Quinquedentate Macrocyclic Ligands. Part 6.† Magnesium Complexes of Macrocyclic Ligands containing Nitrogen and Oxygen Donor Atoms

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Reaction of 2,6-diacetylpyridine or 2,6-diformylpyridine with 3,6-dioxaoctane-1,8-diamine in methanol in the presence of $MgCl_2 \cdot 6H_2O$ gves complexes $[MgL(OH_2)_2]Cl_2 \cdot H_2O$ of 15-membered quinquedentate N_3O_2 macrocycles (L) in high yield. Simple metathetical reactions lead to derivatives containing other anions including neutral complexes having axially co-ordinated thiocyanate. On the basis of various physical properties, the complexes are assigned seven-co-ordinate, probably pentagonal-bipyramidal, structures. Control experiments show that in the absence of a salt of Mg^{2+} the macrocycles are formed in only small yield or not at all. The Ca^{2+} ion is ineffective in promoting the synthesis of these macrocycles, as is Mg^{2+} in the synthesis of three related quadridentate N_4 and N_3O macrocycles.

WE recently reported [1] briefly the template synthesis of magnesium complexes of two N_5 quinquedentate macrocycles (L^1 and L^2). From the results of a single-crystal X-structure determination of one of these, $[MgL^1(OH_2)_2]Cl_2 \cdot 4H_2O$, it was shown that the metal ion is co-ordinated in a pentagonal-bipyramidal arrangement, the N_5 macrocycle defining the equatorial plane with water molecules occupying the axial positions. These results are of interest, first because of the unusual co-ordination geometry and secondly because of the apparent template action of Mg^{2+}. Since this ion occurs in relatively high abundance in intracellular tissue, there is the possibility that it might be implicated in the biosynthesis of naturally occurring macrocycles. We now describe the results of an extension of the investigation to the Mg^{2+}-promoted synthesis of the macrocycles L^3 and L^4 which contain both nitrogen and oxygen donor atoms and to the related quadridentate N_4 and N_3O macrocycles L^5, L^6, and L^7.

RESULTS AND DISCUSSION

Reaction of 2,6-diacetylpyridine with 3,6-dioxaoctane-1,8-diamine in the presence of $MgCl_2 \cdot 6H_2O$ in 1 : 1 : 1

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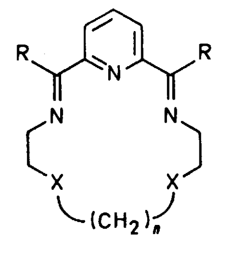
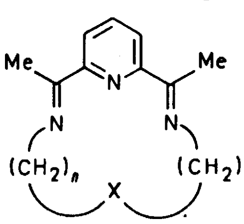
† Part 5 is ref. 3.

[1] M. G. B. Drew, A. H. Othman, S. G. McFall, and S. M. Nelson, *J.C.S. Chem. Comm.*, 1975, 818.

molar ratio in refluxing methanol for 3 h yielded $[MgL^3(OH_2)_2]Cl_2{\cdot}H_2O$ in >75% yield. The preparation of $[MgL^4(OH_2)_2]Cl_2{\cdot}H_2O$, from 2,6-diformylpyridine, required a much shorter reaction time (*ca.* 15 min) for maximum yield (40—50%) (see Experimental section for details). In the case of the complex of L^3, simple metathetical reactions led to the isolation of perchlorate, tetraphenylborate, and thiocyanate derivatives. The perchlorate and thiocyanate complexes of the macrocycle L^4 were prepared as for the chloride salt, while the tetraphenylborate was prepared by metathesis. Mull i.r. spectra revealed the presence of bound water in the crystalline complexes except in the case of the thiocyanates; the formulations given in the Table represent the best fit to the analytical data. The distinction, implied by the formulae of the chloride salts, of water bound in two ways is supported by the results of a thermogravimetric analysis of $[MgL^3(OH_2)_2]Cl_2{\cdot}H_2O$ which showed the loss of one molecule of water at 80—100 °C and two molecules of water at 120—180 °C. The anhydrous complex showed remarkable thermal stability, there being no further weight loss below 300 °C. The thermal stability of the complex is paralleled by its stability in solution towards reagents potentially capable of dislodging the metal from the macrocycle. Thus, treatment with quinolin-8-ol, sodium hydroxide, or aqueous ammonia caused no decomposition. Attempts to exchange the bound magnesium using manganese(II) and nickel(II) salts were also unsuccessful.



	X	R	*n*
L^1	NH	Me	2
L^2	NH	Me	3
L^3	O	Me	2
L^4	O	H	2



	X	*n*
L^5	NH	2
L^6	NH	3
L^7	O	2

Analytical and electrical-conductance data for the complexes

	Analysis (%)									
	Found				Calc.				Λ [a]/S cm^2 mol^{-1}	
Complex	C	H	N	Halogen	C	H	N	Halogen	Water	MeCN
$[MgL^3(OH_2)_2]Cl_2{\cdot}H_2O$	42.7	6.6	10.1	16.7	42.4	6.4	9.9	16.7	256	*b*
$[MgL^3(OH_2)_2][ClO_4]_2$	34.2	4.8	7.2		33.7	4.7	7.9		228	279
$[MgL^3(OH_2)_2][BPh_4]_2$	76.9	6.8	4.1		77.7	6.7	4.3		*b*	224
$[MgL^3(NCS)_2]$	49.0	5.1	16.9	15.4 [c]	49.1	5.1	16.8	15.4 [c]	221	79
$[MgL^4(OH_2)_2]Cl_2{\cdot}H_2O$	39.1	5.7	10.4	17.0	39.4	5.8	10.6	17.9	284	*b*
$[MgL^4(OH_2)_2][ClO_4]_2$	30.4	4.2	7.9		30.8	4.2	8.3		264	228
$[MgL^4(OH_2)_2][BPh_4]_2$	76.1	6.7	4.8		77.5	6.5	4.4		*b*	214
$[MgL^4(NCS)_2]$	46.6	4.6	18.2	16.7 [c]	46.5	4.4	18.1	16.5 [c]	256	59

[a] For 10^{-3} mol dm^{-3} solutions at 25 °C; see W. J. Geary, *Co-ordination Chem. Rev.*, 1971, **7**, 81 for typical molar conductances for different electrolyte types. [b] Insoluble. [c] Sulphur analysis.

Parent-ion peaks were not observed in the mass spectra, although the chloride salts showed peaks at, respectively, *m/e* 275 and 247 corresponding to $[L^3]^+$ and $[L^4]^+$. In the spectrum of the thiocyanate of macrocycle L^3 the highest mass peaks were at *m/e* 357 and 275 corresponding to $[MgL^3(NCS)]^+$ and $[L^3]^+$, respectively.

The i.r. spectra are closely similar to one another when allowance is made for variations in the nature of the anions present and in the water content. An important feature common to all the complexes is the occurrence of a strong absorption at 1 650—1 655 cm^{-1} attributable to the imino-linkage, ν(C=N). None of the spectra showed any absorption at *ca.* 1 700 cm^{-1} which could arise from the presence of unchanged carbonyl groups, nor at 3 100—3 300 cm^{-1} attributable to unchanged primary amine groups, although the latter region was partly obscured by OH absorption in a few cases. Mull spectra of the perchlorate salts indicated that this anion is unco-ordinated (unsplit bands at 1 085 and 620 cm^{-1}). The asymmetric stretch, the symmetric stretch, and the bending vibration of the thiocyanate ion are assigned to absorptions at 2 070s, 790w, and 480m cm^{-1}, respectively, consistent with co-ordination *via* the nitrogen atom. The hydrates displayed strong broad absorption at 3 200—3 500 cm^{-1} and a weaker band at 1 620—1 630 cm^{-1}, attributable to the stretching and bending vibrations of water; in the $[BPh_4]^-$ salts the latter mode was unusually strong. In addition, all the hydrates showed a broad medium-intensity band at *ca.* 550 cm^{-1} (460 cm^{-1} in the case of the $[BPh_4]^-$ salt) which we assign to a rocking or wagging mode of co-ordinated water.

All the complexes are 2 : 1 electrolytes in water except the $[BPh_4]^-$ salts which are insoluble (see Table). In acetonitrile the $[ClO_4]^-$ and $[BPh_4]^-$ salts are 2 : 1 electrolytes, whereas the thiocyanates are intermediate in behaviour, in 10^{-3} mol dm^{-3} solution, between a 1 : 1 electrolyte and a non-electrolyte; the chlorides are insoluble in this solvent.

Measurements of the electronic spectra of solutions of the complexes in water and in acetonitrile in the range 12 000—50 000 cm^{-1} were made. All the complexes gave very similar spectra in water. These consisted of two regions of absorption, a multicomponent band at *ca.* 45 000 cm^{-1} ($\varepsilon \simeq$ 20 000 dm^3 mol^{-1} cm^{-1}) and another centred at *ca.* 33 500 cm^{-1} ($\varepsilon \simeq$ 6 000 dm^3 mol^{-1} cm^{-1}) for complexes of macrocycle L^3 and at *ca.* 46 000 cm^{-1} ($\varepsilon \simeq$ 19 000 dm^3 mol^{-1} cm^{-1}) and *ca.* 33 000 cm^{-1} ($\varepsilon \simeq$ 8 000 dm^3 mol^{-1} cm^{-1}) for complexes of macrocycle L^4. The spectra of the acetonitrile solutions were essentially the same as were the spectra of the solids, although the latter were less well resolved. The solid-state spectra of the thiocyanates were exceptional, however, in showing a weaker band, appearing as a shoulder at *ca.* 21 000 cm^{-1}. This absorption also appeared weakly in the spectra of the acetonitrile solutions, but not in those of the aqueous solutions. These observations are in complete accord with the conductance data and confirm the conclusion that the chloride, perchlorate, and tetraphenylborate complexes are salts of the diaqua-cations both in the solid state and in aqueous solution, and that the thiocyanates are neutral complexes in the solid state but with the anions partially (in MeCN) or completely (in water) displaced by solvent molecules in solution.

The ^1H and ^{13}C n.m.r. spectra of the complexes $[MgL^3(OH_2)_2]Cl_2 \cdot H_2O$, $[MgL^4(OH_2)_2]Cl_2 \cdot H_2O$, and $[MgL^4(NCS)_2]$ in D_2O were recorded; the data are given in the Experimental section. The chemical shifts and integrated relative intensities (proton spectra) are fully consistent with the proposed ligand structures.

Finally, we note that $[MgL^3(NCS)_2]$ is isostructural with the corresponding complexes of Fe^{II}, Co^{II}, and Zn^{II} for which, on the evidence of a range of properties, a seven-co-ordinate structure seems certain.[2] It has a somewhat different powder-diffraction pattern from that of the manganese(II) analogue, known [3] from a single-crystal *X*-ray structure determination to be pentagonal bipyramidal. Despite the different unit cells we consider that the complexes of Mg^{2+} are also pentagonal bipyramidal as are the complexes of Mg^{2+} of the N_5 macrocycle L^1.[1] Information gained from the study of macrocycles L^1 and L^2, as well as of a 17-membered macrocycle (L^3 of the preceding paper), with different metal ions suggests that the macrocycle conformation as well as the overall co-ordination geometry is governed largely by the nature of the macrocycle rather than by the nature of the metal ion.[2,4]

The template action of the Mg^{2+} ion in the synthesis of the co-ordinated macrocycles was demonstrated by control experiments in which the diketone (or dialdehyde) and the diamine were allowed to react in the absence of metal ion under the same conditions as in the preparations described in the Experimental section, and also under conditions of high dilution. In these experiments yellow amorphous solids of low solubility were obtained from reactions involving 2,6-diacetylpyridine. These materials gave variable analyses in different preparations. However, they showed a peak at *m/e* 275 in the mass spectra, with no significant higher mass peaks, suggesting the presence of some macrocyclic product. It is also possible that cyclisation may have occurred in the mass spectrometer source. Infrared spectra of these products showed absorption at *ca.* 1 650 cm^{-1} indicating that some Schiff base had formed, but they also showed strong absorption at *ca.* 1 700 cm^{-1} due to carbonyl groups. Extraction of the yellow solid with diethyl ether, in which 2,6-diacetylpyridine is very soluble, did not reduce the intensity of the carbonyl band and we conclude, therefore, that it is due to an unchanged carbonyl function in an open-chain oligomer or mixture of oligomers. The yellow solid was heated under reflux in methanol containing $MgCl_2 \cdot 6H_2O$ for several hours. The sparingly soluble solid eventually dissolved and from the solution a small yield (*ca.* 5%) of a white solid was obtained. This had the same chemical analyses and i.r. spectrum as $[MgL^3(OH_2)_2]Cl_2 \cdot H_2O$. The origin of this complex is uncertain. It could be the result of reaction of Mg^{2+} with free monomeric macrocycle already present in the yellow solid, or it could have been formed by a template action of Mg^{2+} on hydrolysis products of the oligomeric species.

The reaction of 2,6-diformylpyridine and the diamine in the absence of Mg^{2+} afforded only orange-brown oils. A low intensity peak at *m/e* 247, together with others at higher mass numbers, was observed in the mass spectrum. Again the i.r. spectra indicated the presence of both C=N and C=O groups. No identifiable product was recovered on reaction of this oil with $MgCl_2 \cdot 6H_2O$. The results demonstrate clearly that the Mg^{2+} ion is effective in organising the reactant molecules in the 1 : 1 : 1 reaction in a manner which leads to the formation of the cyclic Schiff base in high yield and/or in stabilising the cyclic product once formed. In one case at least, however, it is possible that the cyclic product may be obtained in much reduced yield in the absence of Mg^{2+}.

The possibility that the Ca^{2+} ion might similarly function as a template for the macrocycle synthesis was briefly investigated. Using the same experimental conditions, but replacing $MgCl_2 \cdot 6H_2O$ by $CaCl_2 \cdot 6H_2O$, we obtained only a dark tarry material from which we failed to obtain a significantly cleaner product on extraction with, and attempted recrystallisation from, different

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[2] M. G. B. Drew, A. H. Othman, and S. M. Nelson, *J.C.S. Dalton*, 1976, 1394; M. G. B. Drew, S. G. McFall, and S. M. Nelson, unpublished work.

[3] M. G. B. Drew, A. H. Othman, S. G. McFall, P. D. A. McIlroy, and S. M. Nelson, preceding paper.

[4] M. G. B. Drew, A. H. Othman, P. D. A. McIlroy, and S. M. Nelson, *J.C.S. Dalton*, 1975, 2507; M. G. B. Drew, A. H. Othman, W. E. Hill, P. D. A. McIlroy, and S. M. Nelson, *Inorg. Chim. Acta*, 1975, **12**, L25.

solvents. Infrared spectra of the tar were broad and poorly resolved and they indicated the presence of residual carbonyl and primary-amine functions.

In view of the fact that naturally occurring macrocycles are quadridentate, the template action of $\mathrm{Mg^{2+}}$ in the synthesis of macrocycles $\mathrm{L^5}$, $\mathrm{L^6}$, and $\mathrm{L^7}$ was examined. Once again, similar reaction conditions yielded only gummy or tarry materials having properties similar to those obtained in the experiments with $\mathrm{Ca^{2+}}$. The failure of the template synthesis in these cases is a little surprising, particularly in the case of the 14-membered $\mathrm{N_4}$ macrocycle $\mathrm{L^6}$ which has been successfully prepared in the presence of salts of $\mathrm{Co^{II}}$, $\mathrm{Ni^{II}}$, $\mathrm{Cu^{II}}$, and $\mathrm{Zn^{II}}$.[5] Arguments based on the slightly smaller ionic radius of $\mathrm{Mg^{2+}}$ are unconvincing in view of the stability of the magnesium(II) complexes of the 15- and 16-membered $\mathrm{N_3O_2}$ and $\mathrm{N_5}$ mocrocycles. Clearly, the precise nature of the template process is not yet understood.

EXPERIMENTAL

2,6-Diacetylpyridine, 3-azapentane-1,5-diamine, and 4-azaheptane-1,7-diamine were used as supplied (Aldrich). 2,6-Diformylpyridine was prepared by the method of Papadoupoulous *et al.*,[6] 3,6-dioxaoctane-1,8-diamine by the method of Dwyer *et al.*,[7] and 3-oxapentane-1,5-diamine by a slight modification of the method of Dietrich *et al.*[8]

Preparation of the Complexes.—*Diaqua*{2,13-*dimethyl*-6,9-*dioxa*-3,12,18-*triazabicyclo*[12.3.1]*octadeca*-1(18),2,12,14,16-*pentaene*}*magnesium*(II) *dichloride hydrate*, $\mathrm{[MgL^3(OH_2)_2]Cl_2{\cdot}H_2O}$. 2,6-Diacetylpyridine (0.01 mol, 1.63 g), 3,6-dioxaoctane-1,8-diamine (0.01 mol, 1.48 g), and $\mathrm{MgCl_2{\cdot}6H_2O}$ (0.01 mol, 2.03 g) were gently heated under reflux in methanol (300 $\mathrm{cm^3}$) for 3 h. The almost colourless solution was filtered while hot and the filtrate was evaporated to dryness to leave a white powder. This was recrystallised from n-butanol. Yields were 75—80% in different preparations. Longer reflux periods resulted in lower yields and the formation of some tarry by-product. The ^{1}H n.m.r. spectrum in $\mathrm{D_2O}$ showed the pyridine protons at δ 8.36(m), the $\mathrm{CH_2}$ protons of the $\mathrm{OCH_2CH_2O}$ group at δ 4.10(s), the remaining $\mathrm{CH_2}$ protons at δ 4.05(m), and the methyl group resonance at δ 2.55 p.p.m., relative to dss (sodium 3,3-dimethyl-3-silabutanesulphonate) internal standard. Integrated intensities were in the ratio 3 : 4 : 8 : 6, respectively. The ^{13}C spectrum in $\mathrm{D_2O}$ showed the $\mathrm{C^2}$, $\mathrm{C^6}$, the $\mathrm{C^3}$, $\mathrm{C^5}$, and the $\mathrm{C^4}$ pyridine resonances at δ 169.82, 145.51, and 152.86 p.p.m., respectively. The C=N resonance occurred at δ 127.12, the four methylene carbons adjacent to oxygen at 71.10, the two methylene carbons adjacent to nitrogen at 50.69, and the methyl groups at 17.22 p.p.m., relative to external $\mathrm{SiMe_4}$.

The following *complexes* were prepared from the chloride salt: $\mathrm{[MgL^3(OH_2)_2][ClO_4]_2}$, from an ethanol solution of the chloride salt and ethanol solution of an excess of $\mathrm{Na[ClO_4]{\cdot}H_2O}$, separated on standing, recrystallised from ethanol; $\mathrm{[MgL^3(OH_2)_2][BPh_4]_2}$, precipitated immediately on addition of an aqueous solution of a slight excess of $\mathrm{Na[BPh_4]}$ to a methanol solution of the chloride, washed with water and then with methanol; $\mathrm{[MgL^3(NCS)_2]}$ from a hot ethanolic solution of a slight excess of Na[NCS] and a hot ethanolic solution of the chloride, separated on cooling.

Diaqua{6,9-*dioxa*-3,12,18-*triazabicyclo*[12.3.1]*octadeca*-1(18),2,12,14,16-*pentaene*}*magnesium*(II) *dichloride hydrate*, $\mathrm{[MgL^4(OH_2)_2]Cl_2{\cdot}H_2O}$. 2,6-Diformylpyridine (0.002 mol, 0.27 g), 3,6-diazaoctane-1,8-diamine (0.002 mol, 0.296 g), and $\mathrm{MgCl_2{\cdot}6H_2O}$ (0.002 mol, 0.406 g) were gently warmed in methanol on a steam-bath for 15 min. The resulting light yellow solution was filtered while hot and the filtrate was evaporated to dryness. The crude off-white solid was recrystallised from n-butanol to give a white product. Yields were 40—50% in different preparations. When longer reaction times were employed red-brown tarry products were obtained. The ^{1}H n.m.r. spectrum in $\mathrm{D_2O}$ showed the imine protons at δ 8.80(s), the pyridine protons at 8.15(m), the $\mathrm{CH_2}$ protons adjacent to the oxygen atoms at 4.10(s), and the remaining $\mathrm{CH_2}$ protons at 3.90(m) p.p.m., relative to dss as internal standard. The integrated intensities were in the ratio 2 : 3 : 8 : 4. The ^{13}C spectrum in $\mathrm{D_2O}$ showed the $\mathrm{C^2}$,$\mathrm{C^6}$, the $\mathrm{C^3}$,$\mathrm{C^5}$, and the $\mathrm{C^4}$ resonances of the pyridine ring at δ 161.14, 144.09, and 149.85 p.p.m., respectively. The C=N resonance occurred at δ 128.12, the methylene carbons adjacent to oxygen at 70.74 and 69.71, and those adjacent to nitrogen at 52.54 p.p.m., relative to external $\mathrm{SiMe_4}$.

The *complex* $\mathrm{[MgL^4(OH_2)_2][BPh_4]}$ was prepared as for the diacetyl analogue. The *complexes* $\mathrm{[MgL^4(OH_2)_2][ClO_4]_2}$ and $\mathrm{[MgL^4(NCS)_2]}$ were prepared in the same manner as the chloride complex. In the case of the perchlorate evaporation of the filtrate from the reaction mixture to dryness gave an oil which slowly crystallised on standing. It was washed with n-butanol. The ^{1}H n.m.r. spectrum of the thiocyanate in $\mathrm{D_2O}$ showed the imino-protons at δ 8.60(s), the pyridine protons at 8.15(m), the $\mathrm{CH_2}$ protons adjacent to oxygen at 4.00(s), and the remaining $\mathrm{CH_2}$ protons at 3.75(m) p.p.m. The integrated intensities were in the ratio 2 : 3 : 8 : 4.

Reactions at High Dilution.—To 2,6-diacetyl- or 2,6-diformyl-pyridine (0.008 ml) in n-butanol (900 $\mathrm{cm^3}$) were added four drops of 5N $\mathrm{H_2SO_4}$. The solution was stirred vigorously and brought to reflux at which stage 3,6-dioxaoctane-1,8-diamine (0.008 mol) in n-butanol (100 $\mathrm{cm^3}$) was added dropwise. The mixture was heated under reflux overnight and then cooled and evaporated to dryness. The yellow residue was examined as described in the text.

Physical measurements were carried out as described in earlier papers in this series.

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