Macrocyclic Schiff Base Complexes of Lanthanides and Actinides

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1 Introduction

It would not be a total exaggeration to state that macrocyclic complexes lie at the centre of life, particularly when regarding the roles of such systems as the iron–porphyrin core in haemoglobin, the cobalt–corrin of vitamin B_{12} and the magnesium–hydroporphyrin in chlorophylls.[1] Recognition of the importance of complexes containing macrocyclic ligands, where a macrocycle is defined as a cyclic compound having nine, or more, heteroatomic members and with three, or more, ligating atoms,[2] has led to a considerable effort being invested in developing reliable syntheses for these compounds. Ideally the complex is formed by adding the required metal ion to a preformed macrocycle but there are potential disadvantages to this approach: the synthesis of the macrocycle often results in a low yield of the desired product with side reactions such as polymerization predominating. In order to circumvent this problem the ring-closure step in the synthesis may be carried out under conditions of 'high dilution',[3] or 'rigid groups' may be introduced to restrict rotation and internal entropy losses in the open-chain precursors[4–6] and so facilitate cyclization.

One effective method for the synthesis of macrocyclic complexes involves an *in situ* approach wherein the presence of a metal ion in the cyclization reaction markedly increases the yield of the cyclic product. The metal ion plays an important role in directing the steric course of the reaction and this effect has been termed the metal-template effect.[7] The first example of a deliberate synthesis of a macrocycle using this procedure was described by Thompson and Busch (Scheme 1),[8] although Curtis had previously demonstrated the potential of template assembly through his observations that the reaction of $Ni(en)_3(ClO_4)_2$ (en = 1,2-diaminoethane) and acetone yields isomeric tetra-azamacrocyclic complexes of

[1] M. N. Hughes, 'The Inorganic Chemistry of Biological Processes', 2nd edn., Wiley, N.Y., 1981.
[2] 'Co-ordination Chemistry of Macrocyclic Compounds', ed. G. A. Melson, Plenum, N.Y., 1979.
[3] K. Ziegler, H. Eberle, and H. Ohlinger, *Liebigs Annalen*, 1933, **504**, 94.
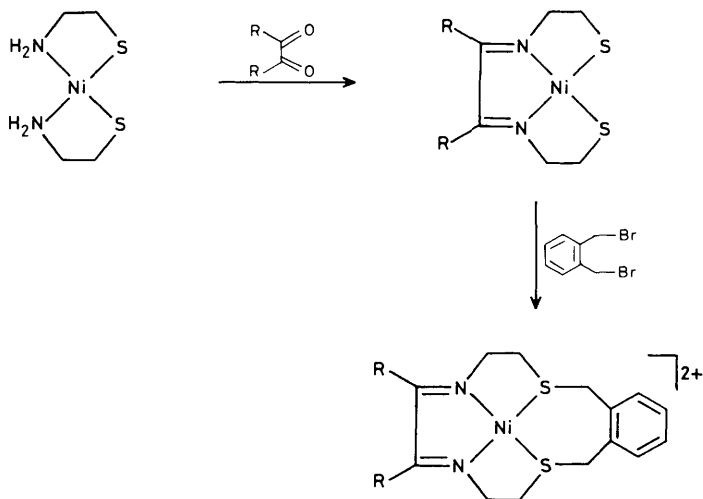[4] W. Baker, J. W. F. McOmie, and W. D. Ollis, *J. Chem. Soc.*, 1951, 200.
[5] E. L. Eliel, 'Stereochemistry of Carbon Compounds', McGraw-Hill, N.Y., 1962.
[6] B. L. Shaw, *J. Am. Chem. Soc.*, 1975, **97**, 3856.
[7] L. F. Lindoy and D. H. Busch in 'Preparative Inorganic Reactions', ed. W. L. Jolly, Wiley-Interscience, N.Y., Vol. 6, 1971, p. 1.
[8] M. C. Thompson and D. H. Busch. *J. Am. Chem. Soc.*, 1964, **86**, 3651.
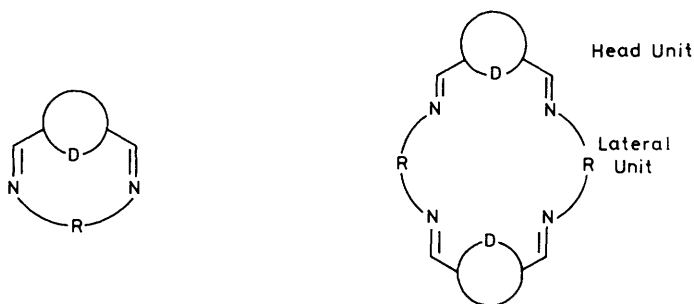
Scheme 1

Figure 1 *Schematic representations of the '1 + 1' and '2 + 2' Schiff base macrocycles*

nickel(II) (Scheme 2),[9] and metal salts had been shown to facilitate the self-condensation of *o*-phthalonitrile to give metal–phthalocyanine complexes (Scheme 3).[10]

Much of the early work featured the use of transition metal ions in the template syntheses of tetradentate macrocycles: the directional influence of the orthogonal *d*-orbitals was regarded as instrumental in guiding the synthetic pathway. The last decade has seen an extension of this technique to include the use of organo-transition metal derivatives to generate tridentate cyclononane complexes[11,12]

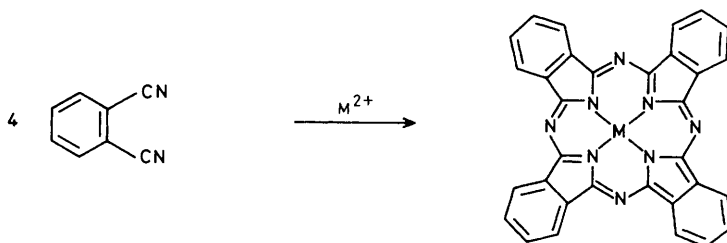[9] D. A. House and N. F. Curtis, *Chem. Ind.*, 1961, 1708.

[10] R. P. Linstead and A. R. Lowe, *J. Chem. Soc.*, 1934, 1022.

[11] D. Sellman and L. Zapf. *Angew. Chem., Int. Edn. Engl.*, 1984, **23**, 807.

[12] B. N. Diel, R. C. Haltiwanger, and A. D. Norman, *J. Am. Chem. Soc.*, 1982, **104**, 4700.
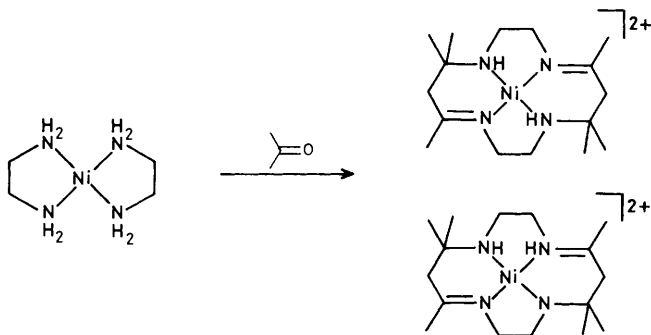
Scheme 2

Scheme 3

and an expansion to the *s*- and *p*-block cations which guide the synthesis of penta- and hexa-dentate Schiff base macrocycles[13,14] and a range of tetraimine Schiff base macrocycles.[15,16] The smaller Schiff base macrocycles have been termed '1 + 1' macrocycles and the tetraimine derivatives '2 + 2' macrocycles as a consequence of the number of head and lateral units present (Figure 1).[15] The metal complexes of the '2 + 2' macrocycles may be mono- or di-nuclear in nature.

It has been generally found that for the larger Schiff base macrocycles the transition metal cations are ineffective as templates.[13] Consequently the kinetic lability of the metals present in the generation of macrocyclic complexes derived from the use of alkaline earth and main group templating agents has enabled the generation of the corresponding transition metal complexes through trans-metallation reactions (Figure 2).[13–16] This approach has been particularly successful when applied to the generation of dinuclear copper(II) complexes of

[13] S. M. Nelson, S. G. McFall, M. G. B. Drew, and A. H. Othman, *Proc. R. Ir. Acad., Sect. B*, 1977, **77**, 523.

[14] (*a*) D. H. Cook and D. E. Fenton, *J. Chem. Soc., Dalton Trans.*, 1979; 266; (*b*) D. H. Cook and D. E. Fenton, *J. Chem. Soc., Dalton Trans.*, 1979, 810.

[15] S. M. Nelson, *Pure Appl. Chem.*, 1980, **52**, 2461.

[16] D. E. Fenton, *Pure Appl. Chem.*, 1986, **58**, 1437.

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tetraimine Schiff base macrocycles which have then been used as speculative models for the bimetallobiosites in cupro-proteins such as haemocyanin and tyrosinase.[17]

The size of the cation used as a template has proved to be of importance in directing the synthetic pathway in the Schiff base systems (Figure 3). Of the alkaline earth cations only magnesium generates the pentadentate '1 + 1' macrocycle but it is ineffective in generating the hexadentate '1 + 1' macrocycle which is readily synthesized in the presence of the larger cations calcium, strontium, barium, and lead(II). These cations, however, generate the '2 + 2' macrocycle derived from the components giving the '1 + 1' macrocycle with magnesium.[14a,b,18]

A further size-related effect is metal-induced ring-contraction whereby if the metal ion is too small for the macrocyclic cavity and there is a functional group (=NH or –OH) available for addition to the imine bond then this can add to produce a smaller, more accommodating cavity for the available metal (Figure 4).[19,20]

The similarity in ionic radii between the alkaline earth metal cations and the lanthanide(III) cations suggested that the latter should also be efficient templating devices (Table 1). Furthermore the steady diminution in ionic radius in the lanthanide series (the 'lanthanide contraction') could perhaps facilitate a fine control in the synthetic pathway. This article reviews the progress made in the development of lanthanide and actinide complexes of Schiff base macrocycles through application of the above techniques.

## 2 Lanthanide Complexes

(1)   (2)   (3)
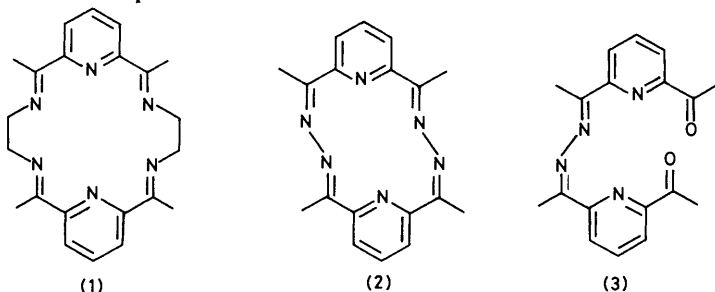
A. '2 + 2' Macrocycles derived from Pyridine Head Units.—(i) *Aliphatic Lateral Units.* The early work concerning the use of lanthanide templates in the synthesis of '2 + 2' tetraimine Schiff base macrocycles suggested that the potential application was limited. The reaction of hydrated lanthanide nitrates, 1,2-diaminoethane, and 2,6-diacetylpyridine in 1:2:2 molar ratio in alcohol gave the macrocyclic

[17] S. M. Nelson, J. Trocha-Grimshaw, A. Lavery, K. P. McKillop, and M. G. B. Drew, in 'Biological and Inorganic Copper Chemistry, Vol. II.' ed. K. D. Karlin and J. Zubieta, Adenine Press, N.Y., 1986, p. 27.
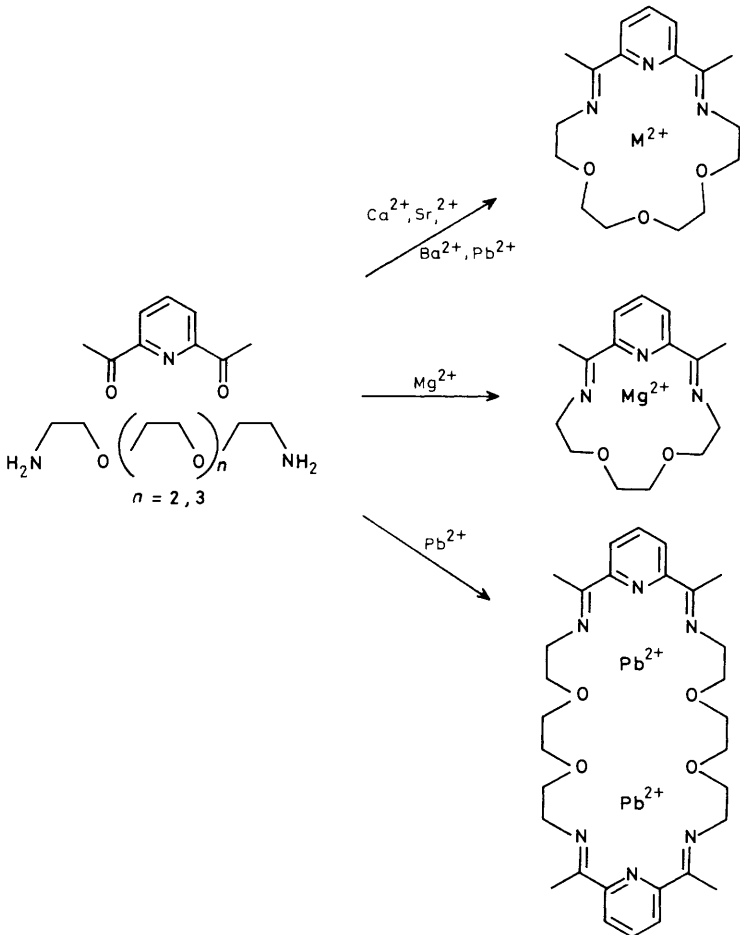
[18] D. H. Cook, D. E. Fenton, M. G. B. Drew, A. Rodgers, M. McCann, and S. M. Nelson, *J. Chem. Soc., Dalton Trans.,* 1979, 414.

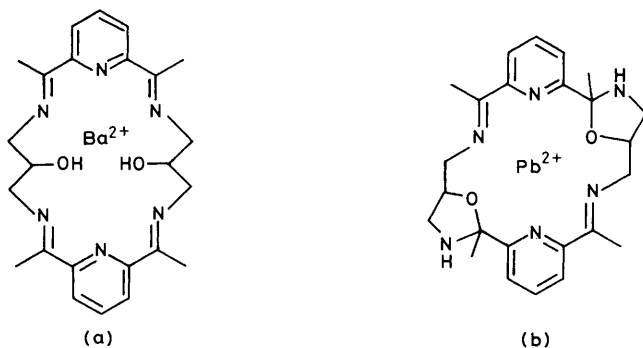[19] M. G. B. Drew, J. Nelson, and S. M. Nelson, *J. Chem. Soc., Dalton Trans.,* 1981, 1678.

[20] N. A. Bailey, D. E. Fenton, R. J. Good, R. Moody, and C. O. Rodriguez de Barbarin, *J. Chem. Soc., Dalton Trans.,* 1987, 207.
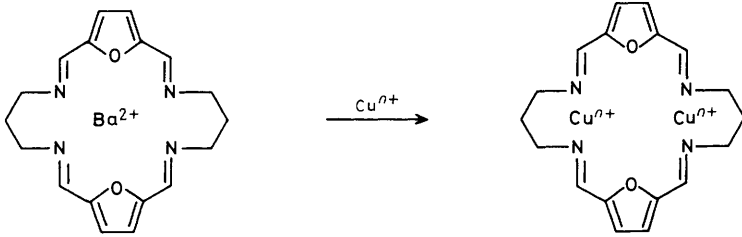
Figure 2 *Transmetallation reaction*

Figure 3 *Schiff base macrocycle synthesis in the presence of non-transition metal templates*

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(a)   (b)

Figure 4 *Metal-induced ring contraction. The larger barium cation gives (a) as the product from the reaction of 2,6-diacetylpyridine and 1,3-diamino-2-hydroxypropane, whereas the smaller lead(II) cation gives (b)*

Table 1 *Ionic radii of alkaline earth metals and lanthanides* (Å)

Mg^{2+}	0.72	Pr^{3+}	1.013	Dy^{3+}	0.908
Ca^{2+}	1.00	Nd^{3+}	0.995	Ho^{3+}	0.894
Sr^{2+}	1.16	Sm^{3+}	0.964	Er^{3+}	0.881
Ba^{2+}	1.36	Eu^{3+}	0.950	Tm^{3+}	0.869
La^{3+}	1.061	Gd^{3+}	0.938	Yb^{3+}	0.859
Ce^{3+}	1.034	Tb^{3+}	0.923	Lu^{3+}	0.848

(Compiled from R. D. Shannon and C. T. Prewitt, *Acta Crystallogr.. Sect. B*, 1969, **25**, 925)

complexes $[Ln(1)](NO_3)_3$ only for lanthanum and cerium.[21] The heavier lanthanides were not found to be effective templating agents in the formation of this 18-membered ring, perhaps due to their smaller size.[21-23] They were effective, however, as templating agents in the synthesis of the 14-membered ring (2) in which hydrazine provides the lateral units;[24] the complexes $[Ln(2)(H_2O)_2](ClO_4)_3,4H_2O$ are recovered when Ln = Tb, Dy, Ho, Er, Tm, Yb, or Lu. Employment of the lighter lanthanides as templates gave complexes of the acyclic derivative (3) and, in some experiments, lanthanide complexes of 2,6-diacetylpyridine.

The discrete nature of $[Ln(1)](NO_3)_3$ was confirmed by *X*-ray crystallography, and conductivity studies showed that the complexes of (1) existed mainly as $[Ln(1)(H_2O)_n]^{3+}$ in aqueous solution. The macrocycles were resistant to hydrolysis, and ^1H n.m.r. experiments showed that the complexes were remarkably stable to dissociation in D_2O, unlike the corresponding complexes of cyclic

[21] J. D. J. Backer-Dirks, C. J. Gray, F. A. Hart, M. B. Hursthouse, and B. C. Schoop, *J. Chem. Soc., Chem. Commun.*, 1979, 774.

[22] W. Radecka-Paryzek, *Inorg. Chim. Acta*, 1980, **45**, L147.

[23] G. Wang and L. Miao, *Guodeng. Xuexiao HuaXua Xuebao*. 1984, **5**, 28; *Chem. Abstr.*, 1984, **101**, 182591c.

[24] W. Radecka-Paryzek, *Inorg. Chim. Acta*, 1981, **52**, 261.

(4)   (5)
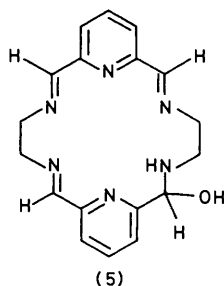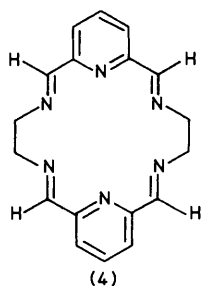
polyethers. No precipitation of the cation was detected on treatment of the complex with aqueous solutions of KF or KOH. In contrast, the complexes of (2) ring-opened on reaction with water to give the acyclic complexes $[Ln(3)(H_2O)_2]$-$(ClO_4)_2,2H_2O$, and in some experiments lanthanide complexes of 2,6-diacetyl-pyridine were also recovered.

More recent surveys of the template potential of the lanthanides have indicated a greater breadth to the reactions. Using 2,6-diformylpyridine as the dicarbonyl precursor, complexes of macrocycle (4) were recovered for all of the lanthanides save promethium.[25] The i.r. spectra of the complexes of the heavier lanthanides (Nd—Lu, except Pm and Eu) were different from those for the lighter lanthanides (La—Pr and Eu) in that the former group exhibited a distinctive sharp band at *ca.* 3 220 cm^{-1}, assigned to a secondary amine group. Addition of a water molecule across an imine double bond leads to the formation of a carbinolamine species (5), as has previously been noted for some macrocyclic complexes of transition metals.[26] This is accompanied by an increase in the flexibility of the macrocycle, making it capable of accommodating the smaller lanthanide cations. Such a process could provide fine-tuning of lanthanide complexation. The carbinolamine complex may be shown to exist in solution by ^{13}C and ^1H n.m.r. studies on the lutetium derivative. A significant change occurred on recrystallization of the samarium complex of (5). The i.r. now showed that the amine band had been replaced by a new band at 3 560 cm^{-1} ascribable to a Sm–OH group, and the X-ray structure of the product was found to consist of the discrete complex cation $[Sm(4)(NO_3)(OH)$-$(H_2O)]^+$, a nitrate anion, and clathrated methanol molecules.[27]
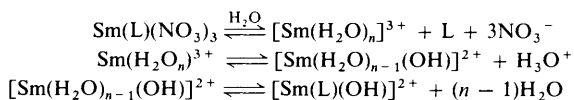
During the course of the recrystallization there has been a reversion of the macrocycle to the tetraimine form. It is possible to consider that optimal cavity–cation criteria have been met and that the samarium can actually be accommodated by either form of the macrocycle. An alternative explanation is that the bulk product isolated is a complex of a carbinolamine precursor to the tetraimine Schiff base, with the former being the kinetically-favoured product and

[25] K. K. Abid and D. E. Fenton, *Inorg. Chim. Acta*, 1984, **95**, 119.
[26] (*a*) Z. P. Haque, M. McPartlin, and P. A. Tasker, *Inorg. Chem.*, 1979, **18**, 2920. (*b*) C. Cairns, S. G. McFall, S. M. Nelson, and M. G. B. Drew, *J. Chem. Soc., Dalton Trans.*, 1979, 446.
[27] K. K. Abid, D. E. Fenton, U. Casellato, P. A. Vigato, and R. Graziani, *J. Chem. Soc., Dalton Trans.*, 1984, 351.

the latter being the thermodynamically-favoured product. The carbinolamine complex would represent the stabilization of a reaction intermediate *via* the facile co-ordination of that species to the smaller lanthanide cations. On dissolution in water and recrystallization a higher temperature is reached than in the original reaction in alcohol, and this helps the reaction move to completion. The samarium complex is also hydrolysed during the recrystallization process from $Sm[(4)](NO_3)_3$ to $[Sm(4)(NO_3)(OH)(H_2O)]NO_3$. It is plausible that on prolonged exposure to water the following sequence occurs:

$$Sm(L)(NO_3)_3 \xrightleftharpoons{H_2O} [Sm(H_2O)_n]^{3+} + L + 3NO_3^-$$
$$Sm(H_2O_n)^{3+} \rightleftharpoons [Sm(H_2O)_{n-1}(OH)]^{2+} + H_3O^+$$
$$[Sm(H_2O)_{n-1}(OH)]^{2+} \rightleftharpoons [Sm(L)(OH)]^{2+} + (n-1)H_2O$$

This seemingly facile hydrolysis of lanthanide complexes has been observed in related systems bearing compartmental ligands[28] and is also noted in macrocyclic complexes derived from 2,6-diacetylpyridine.[29]

Tetraimine Schiff bases derived from 2,6-diformylpyridine and 1,2-diamino-propane, and from 2,6-diformylpyridine and 1,3-diaminopropane have been isolated for the lanthanides (except promethium).[25] With the latter complexes no evidence for carbinolamine intermediates was found.

More recently the template procedures have been used to extend the range of complexes available from 2,6-diacetylpyridine.[29,30] Complexes of the general formulae $Ln(1)(MeCOO)_2Cl,nH_2O$ ($n = 3$—6) and $Ln(1)(ClO_4)_2OH,nH_2O$ ($n = 0$—2) have been recovered for all of the lanthanides except promethium.[29] This contrasts with the earlier results; the ease and yield of the reaction depends on the counterion present. Good oxygen-donor anionic ligands such as $MeCOO^-$ favour the reaction more than Cl^- or ClO_4^-. Once the complex is formed, then an appropriate combination of anions (*e.g.* $MeCOO^-$ and Cl^-, or ClO_4^- and OH^-) favours isolation in a crystalline form. In this work it was not found possible to reproduce the preparation of $La(1)(ClO_4)_3,2H_2O$; instead the compound $La(1)(ClO_4)_2OH,nH_2O$ was isolated consistently.

Lanthanide complexes of some of the heavier lanthanides have also been prepared by a transmetallation reaction in which the alkaline earth complex $Ba(1)(ClO_4)_2$ exchanges metal with the appropriate lanthanide to give two types of complexes: $[Ln(1)(NO_3)_2(H_2O)]NO_3,H_2O$ (Ln = La, Ce, or Pr) and $[\{Ln(1)-(NO_3)(H_2O)_2\}_2]NO_3[ClO_4]_3,4H_2O$ (Ln = Nd, Sm, Eu, Gd, Tb, Dy, Ho, or Er).[30] The smaller lanthanides appear to have too small an ionic radius to co-ordinate effectively with the macrocycle in competition with barium.

The large ionic radii of the lanthanide ions, together with the electrostatic nature of the metal–ligand bonding in their complexes, leads to the generation of high

[28] K. K. Abid, *Inorg. Chim. Acta*, 1985, **109**, L5.

[29] L. De Cola, D. L. Smailes, and L. M. Vallarino, *Inorg. Chem.*, 1986, **25**, 1729.

[30] A. M. Arif, J. D. J. Backer-Dirks, C. J. Gray, F. A. Hart, and M. B. Hursthouse, *J. Chem. Soc., Dalton Trans.*, 1987, 1665.

co-ordination numbers.[31b] The use of macrocyclic ligands such as cyclic polyethers has been said to have brought a new dimension to lanthanide chemistry as it allows study of highly co-ordinated compounds.[31a] X-Ray crystal structural information is available for the complexes $[Ce(1)(NO_3)_2(H_2O)]NO_3,H_2O$,[30] $[\{Nd(1)(NO_3)-(H_2O)_2\}_2]NO_3[ClO_4]_3,4H_2O$,[30] and $[Lu(1)(MeCOO)(OH)(ClO_4)],MeOH$, nH_2O[32] (Figure 5), as well as for the Ln(1) and Sm(4) complexes previously mentioned. The structures of the complexes derived from (1) show a decreasing coordination number for the metal from La—Lu: La = 12, Ce = 11, Nd = 10, and Lu = 9. The samarium complex derived from (4) has the samarium present with co-ordination number 10.

For descriptive purposes the macrocyclic plane may be viewed as generating two hemispheres, one above and one below the donor atom plane (Figure 5a), and the anions or accompanying ligands will occupy sites within these hemispheres. The lanthanum ion in $[La(1)][NO_3]_3$ has the uncommon co-ordination number of 12.[21] Although the icosahedron is generally regarded as the most favoured polyhedron for 12-co-ordination,[33] the co-ordination environment here consists of the six nitrogen donors in a girdle around the metal with two bidentate nitrates on one side of the macrocycle and the other bidentate nitrate on the opposite site, as has been found in the hexaoxamacrocyclic complex $[Ln(18\text{-}crown\text{-}6)](NO_3)_3$.[34] The ligand is folded away from the hemisphere containing the extra nitrate anion.

In the cerium complex the unusual co-ordination number of 11 is noted for the metal ion which is co-ordinated as follows: to the six nitrogen atoms of the macrocycle, to one bidentate nitrate anion on one side of the ligand plane, and to the remaining nitrate and the water molecule on the other side of the plane.[30] The macrocycle is folded away from the hemisphere containing the extra water molecule. With a single exception, all lanthanide complexes known to have 11-co-ordination contain the bidentate nitrate anion, and so a distorted polyhedral structure is the rule and not the exception. It has been remarked that it is futile to try to define such complexes in terms of a particular polyhedron.[33]

The co-ordination numbers 9 and 10 are more commonly observed in lanthanide complexes and have previously been reported for 18-crown-6 complexes of neodymium and gadolinium.[31a] In the neodymium complex the metal is 10-co-ordinated by the six macrocyclic nitrogen atoms, one bidentate nitrate anion on one side of the macrocyclic plane and to two water molecules on the other side. The ligand is folded away from the hemisphere containing the two water molecules, clearly illustrating the smaller steric requirement of the nitrate to the two monodentate ligands.

[31] (a) J. C. G. Bunzli and D. Wessner, *Coord. Chem. Rev.*, 1984, **60**, 191; (b) F. A. Hart, in 'Comprehensive Co-ordination Chemistry', ed. G. Wilkinson, R. D. Gillard, and J. A. McCleverty, Pergamon Press, Oxford, 1987, Chap. 39.

[32] G. Bombieri, F. Benetollo, A. Polo, L. De Cola, D. L. Smailes, and L. M. Vallarino, *Inorg. Chem.*, 1986, **25**, 1127.

[33] G. J. Palenik, in 'Systematics and the Properties of the Lanthanides', ed. S. P. Sinha, NATO ASI Series C NO.109, D. Reidel Publishing Co., Dordrecht, 1983, Chap. 5.

[34] J. D. J. Backer-Dirks, J. E. Cooke, A. M. R. Galas, J. S. Ghotra, C. J. Gray, F. A. Hart, and M. B. Hursthouse, *J. Chem. Soc., Dalton Trans.*, 1980, 2191.
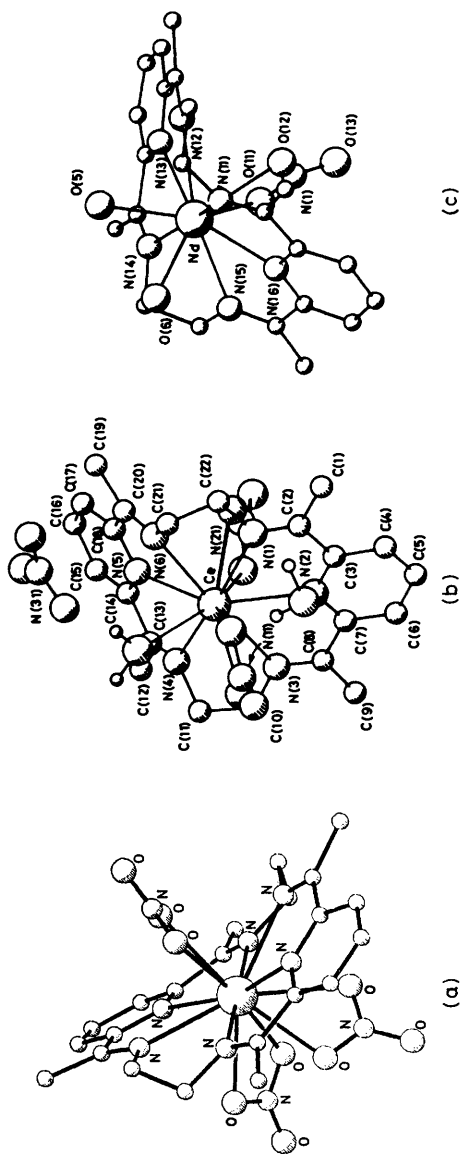
Figure 5 *The X-ray structures of (a),* [La(1)](NO₃)₃; *(b),* [Ce(1)(NO₃)₂(H₂O)]NO₃.H₂O; *(c),* [Nd(1)(NO₃)(H₂O)₂]²⁺ (Reproduced by permission from references 21 and 30)

Folding of the macrocycle towards the hemisphere containing the nitrate anion has also been detected in the samarium complex,[26] in which the metal is 10-co-ordinated with a chelating nitrate anion on one side of the macrocyclic plane and the hydroxyl anion and water molecule on the other.

In the lutetium complex two species are shown to be present in 1:1 ratio, $[Lu(1)(MeCOO)(H_2O)](OH)(ClO_4)(MeOH)$ and $[Lu(1)(MeCOO)(MeOH)]$-$(OH)(ClO_4)$.[32] The complex cations contain 9-co-ordinated lutetium which is linked to the six nitrogen atoms of the macrocycle, a bidentate acetate anion, and a molecule of solvation (water or methanol). The macrocycle is in a 'folded butterfly' arrangement and is folded away from the hemisphere containing the acetate anion. It is proposed that this relieves strain in the macrocycle and minimizes repulsion between the heteroatoms, and thus allows optimum co-ordination at the metal. As there are non-co-ordinated but potentially strong oxygen-donor ligands present it is also suggested that nine-co-ordination is the limit in such species. There remains the question of whether the folding of the macrocycle is indeed governed by the size of the metal or by the steric requirement of the ligands. In general the non-coplanarity of the macrocycle increases in the same sequence as does the co-ordination number and appears to be a consequence of the ligand buckling to accommodate and maintain hexadentate contact with the smaller cations; the folding is always in the direction of the hemisphere containing the single counter-ligand.

The complex $Eu(1)(NCS)_3$ is a solitary example of a macrocyclic complex bearing only monodentate ligands.[35] The europium is nine-co-ordinated by the six nitrogen donors from the macrocycle and by three nitrogen atoms from monodentate thiocyanate anions, two on one side and one on the other side of the macrocyclic plane. The above trend is followed as the macrocycle is bent towards the single thiocyanate.

The lanthanide complexes of (1) have been found to undergo reversible dehydration in the crystalline state and anion loss through hydrolysis, but the macrocyclic entity is stable to 240 °C—an unusually high temperature for lanthanide-bound nitrogen-donor ligands. It must be noted that the praseodymium and europium nitrate complexes both decomposed violently at 300 °C.[30] In solution the macrocycle remains intact in the presence of H_2O and di-methylsulphoxide (dmso) and this is evidenced by the n.m.r. spectra recorded in these solvents. Typical precipitating agents such as F^-, OH^-, and $C_2O_4^{2-}$ do not remove the lanthanide ions readily. For example the complex $[Pr(1)$-$(NO_3)_2(H_2O)]NO_3,H_2O$ is stable for some time in KOH solution before $Pr(OH)_3$ is precipitated, and with KF no ready precipitation occurs. This may be contrasted with the behaviour of $Pr(18$-crown-$6)(NO_3)_3$ which gave instant precipitation with both reagents.[30] The complexes of (1) may be compared with lanthanum cryptates, edta complexes, and complexes of substituted phthalocyanines and porphyrins which are stable in water and, for the last two ligands, stable to base.

A [1]H n.m.r. study of the nitrate complexes of (1) has revealed fairly considerable contact shifts.[30] However, it is likely that for the smaller lanthanides (Tb—Er)

[35] G. Bombieri, *Inorg. Chim. Acta*, 1987, **139**, 21.

structural changes are occurring in solution. It cannot be ascertained whether this is by means of an n.m.r.-rapid equilibrium between two or more discrete structures which changes as the series is traversed or whether one structure is present for each metal but progressively alters with ionic radius. The crystal structures must be treated with caution as predictors of the structures in solution; this is reinforced by the observations on the samarium complex of (4).
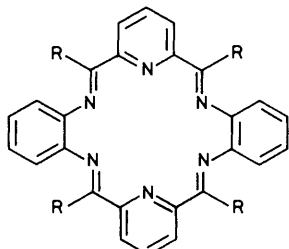
(6)

a ; R = Me
b ; R = H
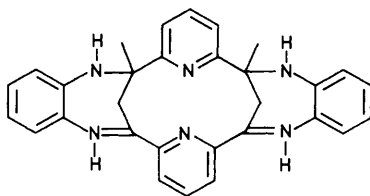
(7)

(ii) *Aromatic Lateral Units.* The condensation of 1,2-diaminobenzene with 2,6-diacetylpyridine in the presence of lanthanide nitrates (La, Ce, Pr, Nd) has been reported to give $[Ln(6a)(NO_3)_3],2H_2O$. The presence of a peak corresponding to the free macrocycle in the m.s. and the interpretation of the i.r. spectrum led to the proposal that the complexes contained 12-co-ordinated lanthanide cations; the three nitrate anions were predicted to be bidentate.[23,36,37] During attempts to repeat and extend this work a yellow crystalline product, having the same molecular mass peak as (6a), was consistently obtained as the major product.[38] This compound was shown to be identical to the tricyclic product (7) obtained by direct reaction of the organic precursors in the absence of metal ions. The nature of (7) had remained an enigma from its first appearance[39] until the solution of the X-ray crystal structure[40] and its facile recovery during attempts to obtain transition metal complexes of (6a) by template procedures led to the conclusion that steric crowding inhibited the formation of (6a). This could arise *via* interaction of the methyl groups with proximal aromatic hydrogen atoms. In contrast, the related condensation of 1,2-diaminobenzene with 2,6-diformylpyridine in the presence of Ca^{II}, Sr^{II}, Ba^{II}, and Pb^{II} templates readily gives complexes of the hexa-azamacrocycle (6b),[41] bearing out the predictions made for this [18]-annulene

[36] W. Racecka-Paryzek, *Inorg. Chim. Acta*, 1981, **54**, L251.
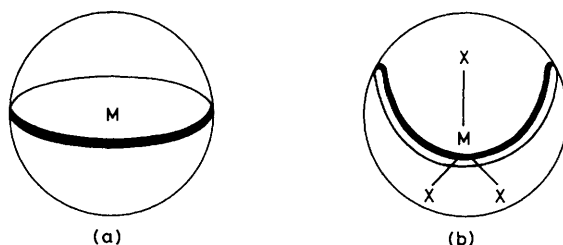
[37] W. Radecka-Paryzek, *Inorg. Chim. Acta*, 1985, **109**, L21.

[38] L. M. Vallarino, personal communication.

[39] R. W. Stotz and R. C. Stoufer, *Chem. Comm.*, 1970, 1682.

[40] J. de O. Cabral, M. F. Cabral, M. G. B. Drew, F. S. Esho, O. Haas, and S. M. Nelson, *J. Chem. Soc., Chem. Commun.*, 1982, 1066.

[41] M. G. B. Drew, J. de O. Cabral, M. F. Cabral, F. S. Esho, and S. M. Nelson, *J Chem. Soc., Chem. Commun.*, 1979, 1033.

Figure 6 (*a*) *The generation of hemispheres by the macrocyclic ligand;* (*b*) *the folding of the macrocycle to accommodate counter-ligand presence*

analogue *via* theoretical calculations.[42]

In a recent preliminary communication[35] the structure of [Pr(6a)(NO$_3$)$_2$-MeOH]ClO$_4$,0.5MeOH has been reported, revealing the reality of the formation of macrocyclic complexes of (6a). No experimental details have been released as yet. The praseodymium is 11-co-ordinated to the six nitrogen donors from the macrocycle, with one bidentate nitrate anion on one side of the macrocycle plane and the remaining bidentate nitrate and the methanol on the other side; the macrocycle is reported as being folded.

B. '2 + 2' Macrocycles derived from Furan-2,5-dialdehyde.—The metal template procedure has been used to prepare complexes of the macrocycles (8)—(10).[43] For the lighter lanthanides the following complexes were reported: [Ln(8)(NO$_3$)$_3$],*n*-H$_2$O (*n* = 0—2), Ln = La—Eu except Pm; [Ln(9)(NO$_3$)$_3$,*n*H$_2$O (*n* = 0—2), Ln = La, Ce, Pr, and [Ln(10)(NO$_3$)$_3$],*n*H$_2$O (*n* = 0, 1), Ln = La, Ce, Pr. When the heavier lanthanides (Gd—Lu) were used with ethylenediamine as the lateral unit, analyses corresponding to a ratio of three metal cations to two macrocyclic units were obtained, [Ln$_3$(8)$_2$(NO$_3$)$_9$],4H$_2$O. The presence of the discrete macrocycle is indicated by m.s. and the observation of this unexpected stoicheiometry may be related to decreased cation size. In the corresponding reactions with diaminopropanes intractable materials were recovered. In contrast to the pyridine-based macrocycles, but in keeping with the lanthanide complexes of the cyclic polyethers,[44] the complexes of (8)—(10) decompose in water. This may be attributed to a deviation from the 'best-fit' criterion, leading to reduced ion–dipole interactions and so giving a more labile system. In addition, the weakly donating furan head-group would help in labilizing the system. The ^{1}H n.m.r. spectrum of [La(8)(NO$_3$)$_3$], in [^{2}H$_6$]dmso, obtained immediately on dissolution gave two sets of signals; after *ca.* one hour only one set remained and it was proposed that this was due to the free macrocycle. Attempts to isolate the free macrocycle were unsuccessful.

[42] C. L. Honeybourne, *Tetrahedron*, 1973, **29**, 1549.

[43] K. K. Abid and D. E. Fenton, *Inorg. Chim. Acta*, 1984, **82**, 223.

[44] (*a*) J. C. G. Bunzli and A. Wessner, *Helv. Chim. Acta*, 1981, **64**, 582; (*b*) A. Musumeci, *Inorg. Chim. Acta*, 1981, **53**, L249.

The kinetic lability of the alkaline earth metal cations in the Schiff base macrocyclic complexes generated by template procedures has provided a synthetic pathway to otherwise inaccessible transition metal complexes.[15,16] The lability of the lanthanide cation has also been explored in such transmetallation reactions.[43] For example, the reaction of $[La(10)(NO_3)_3]$ with copper(II) perchlorate gave the homodinuclear complex $[Cu_2(10)(OH)_2(ClO_4)_2],3H_2O$, which differs only in the hydration number from the analogous complex derived by transmetallation from $[Ba(10)(ClO_4)_2]$.[45] The general applicability of this reaction is further indicated by the ability of the lanthanum complexes of the '2 + 2' macrocycles derived from 2,6-diformylpyridine and 1,2-diaminoethane or 1,2-diaminopropane, to transmetallate with copper(II).[25]


	R
(8)	$-CH_2CH_2-$
(9)	$-CH_2CH(Me)-$
(10)	$-CH_2CH_2CH_2-$

(11)
(12)
(13)
(14)
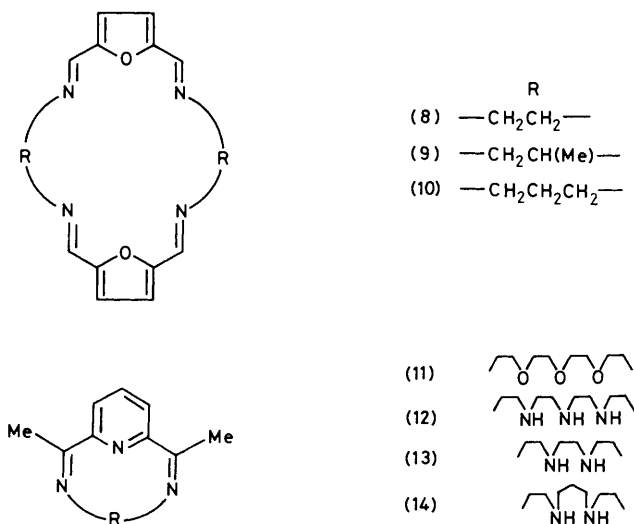
C. '1 + 1' Macrocycles derived from Pyridine Units.

—Transition metal complexes of '1 + 1' Schiff base macrocycles containing pyridinyl head-units have been well studied with particular reference being made to their capability for generating high co-ordination geometries at the metal centres.[15,16] Alkaline earth metals have been used as templates to prepare Schiff base macrocycles derived from facultative diamines,[14a,b] and as precursors for transmetallation reactions to synthesize otherwise inaccessible transition metal complexes.[13] For the lanthanides, use of the template procedure has given the complexes $[La(m/c)(NO_3)_3],nH_2O$ for (11) and (12), and $[La(m/c)(NO_3)_2OH],nH_2O$, for (13) and (14).[23,46,47] If $La(NCS)_3$ is used as the template, mixed OH–NCS complexes are obtained throughout:

[45] S. M. Nelson and F. S. Esho, *J. Chem. Soc., Chem. Commun.*, 1981, 388.

[46] A. M. Arif, C. J. Gray, F. A. Hart, and M. B. Hursthouse, *Inorg. Chim. Acta*, 1985, **109**, 179.

[47] D. E. Fenton and S. J. Kitchen, unpublished results.
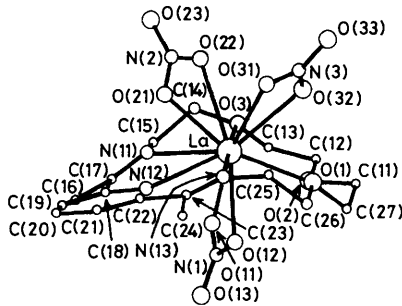
Figure 7 *The X-ray structure of* [La(11)](NO$_3$)$_3$
(Reproduced by permission from *Inorg. Chim. Acta*, 1985, **109**, 179).

[La(m/c)(NCS)(OH)$_2$], [m/c = (12), (14)] and [La(m/c)(NCS)$_2$(OH)], [m/c = (11), (12)].[47] It was, however, necessary to use transmetallation from the barium complex of (1) in order to prepare the cerium and samarium complexes of (11).[46] The presence of the macrocycle may be confirmed by i.r. and ^{1}H n.m.r. studies, and for [La(11)(NO$_3$)$_3$] an *X*-ray crystal structure is available to confirm the assignment (Figure 7). The lanthanum is centred in the macrocyclic ring. It is 12-co-ordinated by the six heteroatoms from the ring and the three bidentate nitrate anions, one on one side of the macrocyclic plane and two on the other side;[46] such an arrangement was also noted for [La(18-crown-6)(NO$_3$)$_3$][34] and [La(1)(NO$_3$)$_3$].[21] The lanthanum is equally disposed towards the oxygen and nitrogen donors of the ring, as has been found for the alkaline earth metal complexes [Ca(11)](NCS)$_2$ and [Sr(11)](NCS)$_2$,H$_2$O[48]—in contrast to the preferential disposition of the lead cation towards the nitrogen donors in [Pb(11)](NCS)(SCN).[49] In this last case the affinity of the metal for the 'softer' ligand environment is evidenced. There appears to be a consistency in the 12-co-ordination of lanthanum in the presence of 18-membered rings bearing six donor atoms and three potentially bidentate ligands. In [La(11)(NO$_3$)$_3$] the macrocycle is quite bent, folding away from the hemisphere containing the two nitrate anions towards that containing the single nitrate, exactly as found for the '2 + 2' tetraimine Schiff base complexes.

The lanthanide complexes are considerably less stable in water than are the analogous complexes of (1); they are more similar in behaviour to the complexes of (8) and of cyclic polyethers. Metal hydroxide is readily precipitated on dissolution in H$_2$O and it is probable that this reaction begins with the breaking of the three adjacent ether–lanthanum bonds. The ^{1}H n.m.r. spectra of the complexes [Ln(11)(NO$_3$)$_3$] have been recorded in acetonitrile solution and indicate the integrity of the macrocycle in that medium.[46]

[48] D. E. Fenton, D. H. Cook, and I. W. Nowell, *J. Chem. Soc., Chem. Commun.*, 1978, 279.
[49] D. E. Fenton, D. H. Cook, and I. W. Nowell, *J. Chem. Soc., Chem. Commun.*, 1977, 274.

Scheme 4

*(when X = NH a ring contraction occurs in the free compartment)

D. '2 + 2' Macrocycles derived from Phenols.—The first defined binucleating ligands were prepared from 2,6-diformyl-4-methylphenol and 1,*n*-diamino-alkanes.[50] The co-ordination chemistry of transition metal complexes of these ligands has been much explored and has been reviewed.[51]

The reaction of 2,6-diformyl-4-chlorophenol, polyamines, and the appropriate lanthanum nitrate gave the macrocyclic complexes depicted in Scheme 4.[52] The application of the template procedure is erratic in result and so use of preformed ligands is preferred. The best route is not to isolate these ligands but to prepare the requisite one *in situ* and to follow the appropriate lanthanide addition sequence. The presence of a base (LiOH, NaOH) promotes formation of the monocationic species (15), whereas an absence of base leads to the tricationic species (16). In the complexes derived from X = NH, one NH is non-co-ordinated and so available for further reaction. A ring contraction is found to occur in the presence of the smaller lanthanides; this allows a diminution of the macrocyclic cavity and reduction in ligand denticity (Figure 8).[52] Similar contractions generating oxazolidine- or imidazoline-bearing macrocycles have been noted in the presence of main group or alkaline earth templates for the related '2 + 2' tetraimine Schiff base macrocycles derived from pyridinyl head-units and the appropriate functionalized diamine.[19,53]

The *X*-ray structure of the terbium complex of the contracted macrocycle (and of the isostructural europium analogue) has been solved and shows the cation to be nine-co-ordinated and sitting in the lateral compartment of the macrocycle derived from the open-chain amine. The co-ordination environment is completed by two bidentate nitrate anions. The third nitrate is ionic and the imidazoline-ring containing compartment is empty.[53]

The synthesis of homodinuclear complexes of Schiff base macrocycles was first accomplished through the use of a lead(II) template in the condensation reaction of 2,6-diacetylpyridine and 3,6-dioxaoctane-1,8-diamine.[54,55] The dinuclear nature of the product of the reaction, $[Pb_2(17)](NCS)_4$, was confirmed by *X*-ray crystal structure analysis.[50] Both the di-lead and corresponding mononuclear Ba^{II} complexes underwent facile transmetallation reactions to generate homodinuclear copper(II) complexes. These complexes are of interest as speculative models for the dinuclear copper sites in copper-containing proteins and enzymes such as haemocyanins and tyrosinase.[17] The synthesis of homodinuclear macrocyclic complexes of lanthanides has been achieved through the condensation of 2,6-diformyl-4-cresol and triethylenetetramine in the presence of $Ln(NO_3)_3$ or $Ln(ClO_4)_3$ (Ln = La—Gd).[56] Complexes of the general formula $[Ln_2(18)$-

[50] N. H. Pilkington and R. Robson, *Aust. J. Chem.*, 1970, **23**, 2225.

[51] (*a*) S. Groh, *Israel J. Chem.*, 1976 –77, **15**, 277; (*b*) D. E. Fenton, *Adv. Inorg. Bioinorg. Mech.*, 1983, **2**, 187; (*c*) P. Zanella, S. Tamburini, P. A. Vigato, and G. Mazzocchin, *Coord. Chem. Rev.*, 1987, **77**, 165.

[52] P. Guerriero, U. Casellato, S. Tamburini, P. A. Vigato, and R. Graziani, *Inorg. Chim. Acta*, 1987, **129**, 127.

[53] N. A. Bailey, D. E. Fenton, I. T. Jackson, R. Moody, and C. O. Rodriguez de Barbarin, *J. Chem. Soc., Chem. Commun.*, 1983, 1463.

[54] M. G. B. Drew, A. Rodgers, M. McCann, and S. M. Nelson, *J. Chem. Soc., Chem. Commun.*, 1978, 415.

[55] D. H. Cook, D. E. Fenton, M. G. B. Drew, A. Rodgers, M. McCann, and S. M. Nelson, *J. Chem. Soc., Dalton Trans.*, 1979, 414.

[56] I. A. Kahwa, J. Selbin, T. C. Y. Hasieh, and R. A. Lane, *Inorg. Chim. Acta*, 1986, **118**, 179.
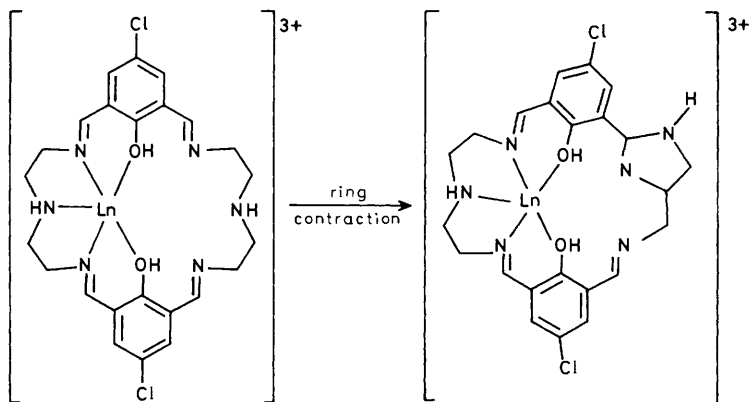
Figure 8 *Ring contraction in the lanthanide complexes* (15)

$(NO_3)_{4-x}(OH)_x]$, ($x = 0$—2) were recovered on concentration of the methanolic solution; diluted solutions deposited $[Ln_2(18)(NO_3)_4],nH_2O$. The hydroxyl-containing complexes could be converted into the latter by reflux in methanol containing the tetramine and a threefold excess of $Ln(NO_3)_3$. The dinuclear nature of the complexes was established by positive-ion fast atom bombardment m.s.; the interesting, mostly new, polyatomic oxo-clusters $Ln_2O_2{}^+$, $Ln_3O_4{}^+$, $Ln_4O_6{}^+$, and $Ln_5O_7{}^+$ were dominant in the mass spectrum.

The organizational role of the lanthanide cations in the assembly of the binucleating macrocycle was evidenced by the recovery of intractable materials when Ca^{II}, Sr^{II}, Ba^{II}, and Pb^{II} were used as putative templates. The condensation of 2,6-diformyl-*p*-cresol with triethylenetetramine in the absence of the lanthanide templates gave only intractable materials.

3 Actinide Complexes

Interest in generating Schiff base macrocycles around an actinide template was stimulated by the formation of the so-called 'superphthalocyanine', formed by the reaction of 1,2-dicyanobenzene with anhydrous dioxouranium(VI) dichloride in dimethylformamide solution,[57] in which the uranium is equatorially bonded to five nitrogen atoms of the ring. The intermediate size of the cation (1.00 Å for eight-co-ordination) and preference for equatorially directed bonding suggest that the trans-dioxouranium(VI) ions should promote the formation of flat macrocyclic systems.

In the presence of $UO_2{}^{2+}$ the condensation of 2,6-dicarbonylpyridines and 1,2-diaminoethane proceeds smoothly to yield the complexes $[UO_2(1)]X_2$ and $[UO_2(4)]X_2$, $X = ClO_4$, NO_3, or I.[58,59] The i.r. and ^1H n.m.r. of these complexes suggest that all six aza-donor atoms are co-ordinated to the uranium and that there

[57] V. W. Day, T. J. Marks, and W. A. Wachter, *J. Am. Chem. Soc.*, 1975, **97**, 4519.
[58] K. K. Abid, M.Sc. Thesis (University of Sheffield) 1982.
[59] L. De Cola, D. L. Smailes, and L. M. Vallarino, *Inorg. Chim. Acta*, 1985, L1.

(17)

H₂- (18)
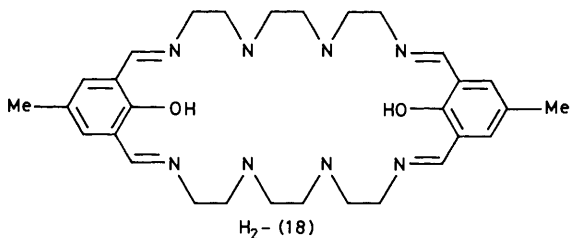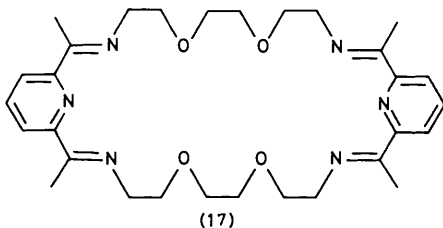
is an effective D_{6h} site symmetry. There is an exceptional inertness towards the release of UO_2^{2+} in solution, even towards strong acids or strongly competing ligands, which suggests that systems of this type may be of value when efficient sequestering of actinide ions is necessitated.

'*After last returns the first*':[60] the reaction of 2,6-diformyl-4-chlorophenyl with diethylenetriamine gave on addition of a dioxouranium(VI) salt mononuclear acyclic complexes which could be cyclized on further addition of di- or tri-amines to give the mononuclear macrocyclic complexes (19)—(22).[61] These cyclic complexes were found to act as ligands towards transition metals and so give some of the first examples of compounds in which a heterodinuclear fragment was held within a dinucleating macrocyclic periphery (23).

Recent adaptation of the synthetic procedure has given the symmetric and non-symmetric macrocycles (23)—(25) and these have also been used to prepare mononuclear dioxouranium(VI) complexes $[UO_2(m/c)]$.[62] An X-ray crystal structure of $[UO_2(26)]$ confirms that the UO_2^{2+} is equatorially co-ordinated by the N_2O_2S donor atoms from one of the two identical compartments with the second remaining empty; a 'butterfly-fold' occurs in the ligand.[63] The site occupancy in the non-symmetric macrocyclic complex $[UO_2(25)]$ is believed to be in the 'harder' compartment, although this has yet to be verified by crystallography.

Although it has not yet been possible to add a second UO_2^{2+} to these systems to give homodinuclear complexes, the heterodinuclear complex $[UO_2(24)Cu]$-$ClO_4,2EtOH$ has been reported.[64] Cyclic voltammetric studies on this compound show that two successive one-electron reactions occur; a reoxidation peak

[60] Robert Browning, 'Apparent Failure', in 'The Poetical Works of Robert Browning, Vol. VII, Smith, Elder, and Co., London, 1902.

[61] (*a*) U. Casellato, M. Vidali, and P. A. Vigato, *Inorg. Nucl. Chem. Lett.*, 1974, **10**, 437; (*b*) M. Vidali, P. A. Vigato, U. Casellato, E. Tondello, and O. Traverso, *J. Inorg. Nucl. Chem.*, 1975, **37**, 1715.

[62] U. Casallato, D. Fregona, S. Sitran, S. Tamburini, P. A. Vigato, and D. E. Fenton, *Inorg. Chim. Acta*, 1985, **110**, 181.
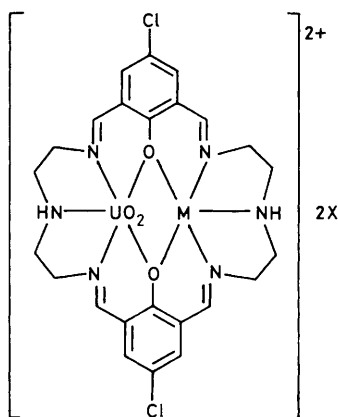
[63] U. Casellato, S. Sitran, S. Tamburini, P. A. Vigato, and R. Graziani, *Inorg. Chim. Acta*, 1986, **114**, 111.

[64] U. Casellato, P. Guerriero, S. Tamburini, P. A. Vigato, and R. Graziani, *Inorg. Chim. Acta*, 1986, **119**, 215.
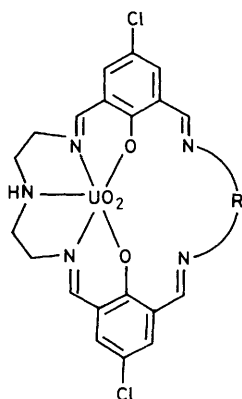
$$R_2$$
(19) —CH_2CH_2—
(20) —$CH_2CH_2CH_2$—
(21) —$CH_2CH(Me)$—
(22) —$CH_2CH_2NHCH_2CH_2$—
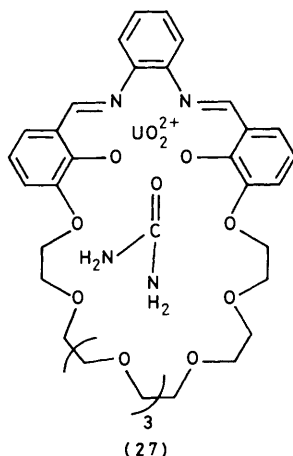
(M = Cu, Co, Ni)
(X = ClO_4^-)

(23)
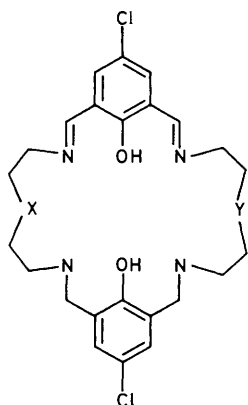
H_2 − (24) (X = Y = NH)
H_2 − (25) (X = NH, Y = S)
H_2 − (26) (X = Y = S)

(27)

attributable to free copper(I) ions produced by decomplexation of the mixed-valence Cu^IU^{VI} species is noted, as is a peak attributed to the U^V/U^{VI} redox couple.[65]

An interesting application of a macrocyclic complex of dioxouranium(VI) has recently been reported.[66] The co-complexation of a neutral guest molecule by both hydrogen bonding and co-ordination with a metal ion is proposed for metalloenzymes, such as urease, where urea is believed to bind at the active site *via* hydrogen bonding to the peptide chain and co-ordination to a nickel ion.[67] Mimicry of such an event has been achieved by co-complexing urea and the dioxouranium(VI) cation within the macrocyclic cavity in the complex (27). The X-ray structure shows the cation to be held in the Schiff base compartment and the urea in the polyether compartment. The urea is co-ordinated to the cation *via* a lone pair from the carbonyl oxygen, advantage being taken of the capacity of the uranium to receive a fifth equatorial donor atom. The urea is also hydrogen bonded to five oxygen atoms of the polyether chain and one phenolic oxygen. These interactions lead to a highly structured ternary complex.

4 Concluding Remarks

The lanthanide(III) cations have been found to act as template reagents, generating Schiff base macrocycles in the same manner as do the larger alkaline earth metals and lead(II). Although 18-membered hexa-azamacrocycles are found in the presence of all the lanthanide ions, there is a noticeable cation–cavity control exercised in the formation of 14-membered macrocycles, where the larger radius lanthanides are ineffective as templates, and also in the 20-membered macrocycles, where the smaller radius lanthanides are excluded. Within the series of complexes

[65] P. Zanello, A. Cinquantini, P. Guerriero, S. Tamburini, and P. A. Vigato, *Inorg. Chim. Acta*, 1986, **117**, 91.
[66] C. J. van Staveren, D. E. Fenton, D. N. Reinhoudt, J. van Eerden, and S. Harkema, *J. Am. Chem. Soc.*, 1987, **109**, 3456.
[67] R. K. Andrews, R. L. Blakeley, and B. Zerner, *Adv. Inorg. Biochem.*, 1984, **6**, 245.

derived from the 18-membered macrocycles there does not appear to be any significant fine control exercised in the template synthesis, even though more flexible carbinolamine macrocycles were obtained in some instances. The introduction of oxygen donors restricted complex formation to the lighter lanthanides.

There is a current paucity of actinide-containing Schiff base macrocycles. It has, however, proved possible to prepare heterodinuclear complexes involving uranium; the only homodinuclear complexes prepared to date in this area are restricted to those of the lanthanides.

X-Ray crystal structures of the '2 + 2' hexa-azamacrocycles reveal that there is a steady decrease in co-ordination number of the metal within a given series of macrocycle as the series moves from La to Lu; a similar effect has also been noted with complexes of cyclic polyethers.[31] Many of the structures contain bidentate nitrates and these are less strongly bound to the metal than in the corresponding cyclic polyether complexes. Generally the accompanying ligands are bound to the metal, with two on one side of the macrocyclic plane and one on the other side with the macrocycle folding in the direction of the single ligand. This folding about the lateral-unit appears to relieve steric strain and also minimizes repulsions between the accompanying ligands.

In aqueous solution there is a remarkable kinetic stability of the hexa-azamacrocyclic complexes of the lanthanides relative to the corresponding cyclic polyether complexes. Given that the bonding is predominately electrostatic, this may be compared with the enhanced stability of potassium complexes of (1) relative to potassium complexes of 18-crown-6 which has been attributed to a stronger ion–dipole interaction being made available in the hexa-azamacrocycle—potassium.[68] The triazatrioxamacrocyclic complexes are less stable in water, as are the furan-derived species, and so are intermediate in character between the hexa-aza and hexa-oxa-species.

The inertness of the dioxouranium complexes of (1) and (4) towards the release of UO_2^{2+} in solution has suggested the use of such systems as effective sequestrants for the actinide ions.[59] N.m.r. studies on the water-stable lanthanide complexes have indicated a possible application of the complexes as shift reagents.[29,30] The time frame of metal exchange and ligand exchange kinetics is important when considering the use of lanthanide ions in such a way and as probes for biological systems.[29] In the dilute aqueous, or aqueous organic, solutions required for such studies even a complex that is stable towards hydrolysis may be sufficiently labile towards exchange to give unreliable results. The systematic study of macrocyclic Schiff base complexes of the lanthanides has revealed a unique inertness of the complexes which, together with their solubility in both water and organic solvents, may prove to be of potential value in any application of these complexes as shift reagents or fluorescent probes.

[68] T. W. Bell and F. Guzzo, *J. Am. Chem. Soc.*, 1984, **106**, 6111.