Complexes of Ligands providing Endogenous Bridges. Part 5.[1] Solution Studies on a Novel '3 + 3' Hexamine Schiff-base Macrocyclic Complex of Lanthanum

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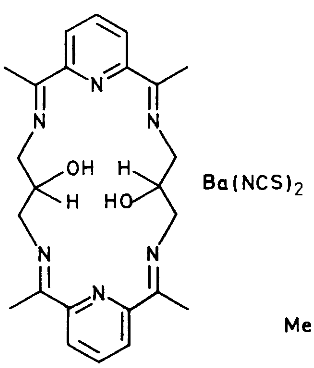
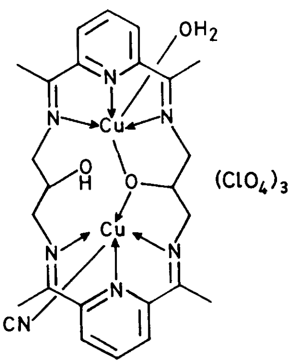
Structural studies in solution show that when lanthanum nitrate is used as a template in the reaction of 2,6-diacetylpyridine and 1,3-diamino-2-hydroxypropane a '3 + 3' macrocycle containing three lanthanum ions is the predominant species formed. Hydrogen-1 n.m.r. decoupling and n.O.e. difference spectroscopy confirms the presence of a two-fold axis of symmetry where two 'sides' of the macrocycle are identical and different from the third.

2,6-Diacetylpyridine (dap) and 1,3-diamino-2-hydroxypropane (dahp) form macrocyclic compounds when a metal template is used. The form and size of the resultant macrocycle appears to be determined by the metal used. When $Ba(SCN)_2$ is employed, a '2 + 2' macrocycle incorporating one barium predominates; the OH groups on the macrocycle remain intact and the two thiocyanate ligands balance the positive charge on the barium, compound (**1**).[2,3] A transmetallation reaction with this species using $Cu(ClO_4)_2$ produces the bimetallic copper complex (**2**).[1,2,4] A proton is lost from one OH group and the alkoxide bridges both copper ions. In the crystal, the intact OH group hydrogen bonds to a molecule stacked below. When $Pb(ClO_4)_2$ is invoked as the metal template, complete rearrangement of the ligands occurs to form compound (**3**),[2,3] containing oxazolidine rings.

It has been shown[4] that when $Mn(ClO_4)_2$ is used in a transmetallation reaction of the barium '2 + 2' macrocycle, a '4 + 4' macrocycle with four Mn^{2+} ions is formed as a minor product, compound (**4**); see Figure 1. McKee and Shephard[4] indicate that this probably is a result of a '4 + 4' macrocycle with two barium ions being present as an impurity in the barium '2 + 2' macrocycle. Further investigations using fast atom bombardment (f.a.b.) mass spectrometry have shown that a '4 + 4' macrocycle with two barium ions is indeed present in a sample of the barium '2 + 2' macrocycle.[5] It is with the versatility of these two ligands in mind that we examined the product of the condensation of dap with dahp in the presence of lanthanum nitrate as a templating device.



(**1**)



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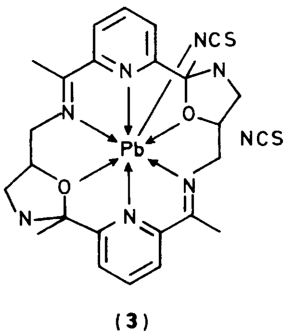
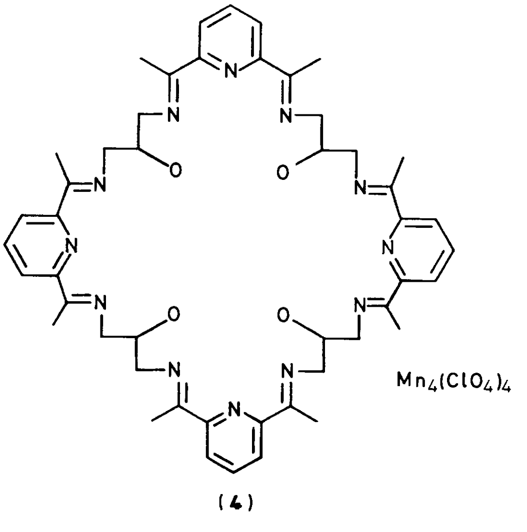


(**3**)



(**4**)

Results and Discussion

The reaction of dap with dahp in the presence of $La(NO_3)_3$ gave a yellow product (**5**). The ^1H n.m.r. spectrum of this product was more complex than that previously noted for '2 + 2' macrocycles[1,2] and the microanalytical data were imprecise for such a species; therefore a more detailed study was undertaken.

With precedence for '2 + 2', '4 + 4', and oxazolidine type of macrocycles established, these possibilities were first investigated and rejected on the following grounds. The complexity of the methyl region in the ^1H n.m.r. spectrum precludes the assignment of the reaction product to a '2 + 2' macrocycle and the integration (2:2:1:2) of the four methyl signals eliminates the possibility of a '4 + 4' macrocycle. Oxazolidine formation can be ruled out on chemical shift arguments. The CH_3 signals in the spectrum are at too high frequency for protons on an sp^3 carbon with oxygen and nitrogen substituents.

The product is considered to be a '3 + 3' macrocycle containing three lanthanum ions, (**5a**), together with a minor species, (**5b**). The ^1H n.m.r. spectroscopic results supporting this

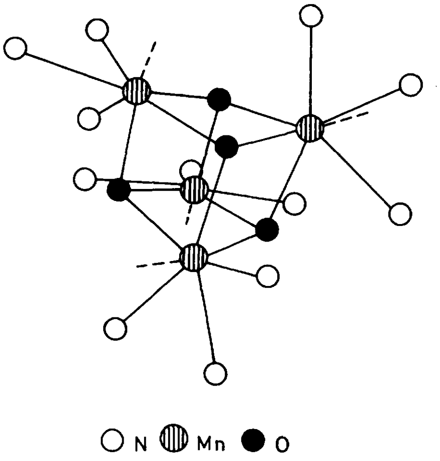


Figure 1. The '4 + 4' macrocycle formed in a transmetallation reaction of the barium complex with manganese perchlorate

Table. Chemical shifts and coupling constants for both (**5a**) and (**5b**)

Major species δ/p.p.m.	Integral	Assignment	*J*/Hz
8.450	2 H	2 H^{11}	$J(H^1H^2) = 8$
8.445	1 H	H^1	$J(H^{10}H^{11}) = 8$
8.348	2 H	2 H^{10}	$J(H^{11}H^{12}) = 8$
8.324	2 H	2 H^{12}	$J(H^6H^5) = 2$
8.260	2 H	2 H^2	$J(H^6H^4) = 12$
4.97	2 H	2 H^6	$J(H^6H^8) = 5.5$
4.75	1 H	H^{16}	$J(H^4H^5) = 12$
4.32	2 H	2 H^7	$J(H^7H^8) = 14$
4.25	2 H	2 H^8	$J(H^{16}H^{15}) = 3$
4.16	2 H	2 H^{15} (*cis*)	$J(H^{16}H^{14}) = 11$
3.96	2 H	2 H^5	$J(H^{15}H^{14}) = 13$
3.62	2 H	2 H^{14} (*trans*)	
3.49	2 H	2 H^4	
2.74	6 H	2 $CH^9{}_3$	
2.68	6 H	2 $CH^{13}{}_3$	
2.57	6 H	2 $CH^3{}_3$	
Minor species			
8.435	*n*	*n* H^1	$J(H^1H^2) = 8$
8.288	2*n*	2*n* H^2	$J(H^6H^5) = 3.5$
4.83	*n*	*n* H^6	$J(H^6H^4) = 5$
4.11	2*n*	2*n* H^5	$J(H^4H^5) = 16$
3.89	2*n*	2*n* H^4	
2.64	6*n*	2*n* $CH^3{}_3$	

* Reference: external $(SiMe_3)CD_2CD_2CO_2H$.

postulation are presented and discussed below. The data were obtained with ^2H_2O as solvent since the macrocycle was virtually insoluble in all non-oxidising organic solvents. Even in ^2H_2O a solution formed very slowly but heating was avoided as this accelerated breakdown of the complex; the stability in water was monitored with respect to concentration and time.

This secondary reaction may be due to oxazolidine formation but a more likely explanation is that it represents the initial stages of hydrolysis since dap is also formed with time. The dap formation was at first undetected but close examination revealed that the methyl group of dap appears briefly after *ca.* 30 min but rapidly disappears with concurrent growth of signals for CH_2D and CHD_2. Further studies showed that deuteriation of the methyl protons in dap occurs rapidly under basic conditions. These findings contrast markedly with the lanthanide complexes of related '2 + 2' Schiff-base macrocycles which have been shown to be quite robust in water.[6,7]

The ^1H n.m.r. spectrum of (**5**) in ^2H_2O is shown in Figure 2 (ambient temperature). Irradiation of the signal at 4.75 p.p.m. (Table) which integrates for one proton and is a triplet of triplets (J = 3 and 11 Hz) causes a large coupling to vanish in the multiplet at 3.62 p.p.m. and a small coupling to disappear in the signal at 4.16 p.p.m. This is consistent with the signals at 3.62 and 4.16 p.p.m. each consisting of two protons and allows the integral of the multiplet partially overlapping the signal at 4.16 p.p.m. to be ascertained. These three signals at 4.75, 4.16, and 3.62 p.p.m. (integrating in the ratio 1:2:2) may be assigned to one side of a 'triangle' formed in the '3 + 3' macrocycle, see Figure 3[(**5a**)]. The multiplet, a triplet of triplets at 4.75 p.p.m., is assigned to H^{16} in the centre of the diaminopropane chain attached to the carbon bearing the oxygen. The two protons at 3.62 p.p.m. are attributed to the two H^{14} protons at either side of H^{16} and *trans* to it [$J(H^{14}H^{16}) = 11$ Hz] while those at 4.16 p.p.m. are due to the two H^{15} protons *cis* to H^{16} [$J(H^{15}H^{16} = 3$ Hz].

Irradiation at 3.96 p.p.m. causes a large coupling of 12 Hz in the multiplet at 3.49 p.p.m. to collapse. Decoupling at 3.49 p.p.m. confirms this but although it is a triplet no other change is detected. The similarity of the patterns of the multiplets at 3.62 and 4.16 p.p.m. to those at 3.96 and 3.49 p.p.m. prompted the idea that the missing proton was close to 4.75 p.p.m. but obscured by the residual H_2O in the solvent. To investigate this possibility arbitrary points under the water envelope were irradiated and protons were located at 4.97 and 4.83 p.p.m. Since it was not possible to integrate or observe the coupling patterns of these protons the temperature of the sample was dropped from 20 to 8 °C in order to shift the water signal to high frequency and clear of the signals of interest. This revealed a multiplet which integrated for two protons at 4.97 p.p.m. and one which integrated for 0.5 protons at 4.83 p.p.m., see Figure 4. The latter integral is not unexpected in view of the fact that the product is considered as consisting of two species. Decoupling experiments reveal that the multiplets at 4.11 and 3.89 p.p.m. are coupled to each other (J = 16 Hz) and to the signal at 4.83 p.p.m. with J = 3.5 and 5 Hz, respectively. There is also a small (< 1 Hz) coupling of the signal at 3.89 p.p.m. through the CH_3 signal at 2.64 p.p.m. (see below). The relative intensities of these signals at 4.83, 4.11, 3.89, and 2.64 p.p.m. are 1*n*:2*n*:2*n*:6*n* which is consistent with an '*n* + *n*' macrocycle. If *n* = 3 then this minor species has three-fold symmetry and is present in one sixth the amount of the major species.

Having accounted for the minor species in the aliphatic region of the spectrum attention was again focused on the major species. Saturation of the signal at 4.97 p.p.m. which integrates for two protons and has a chemical shift appropriate for a proton on an sp^3 carbon bearing an oxygen causes couplings of 2, 5.5, and 12 Hz to vanish in the multiplets at 3.96, 4.25, and 3.49 p.p.m. respectively. The coupling pattern of the signal at 4.97 p.p.m., see Figure 4, is only consistent with the other two diamino chains being equivalent as shown in Figure 3[(**5a**)]. (In the diagram the macrocycle is drawn flat for clarity.) The signals at 4.32 and 4.25 p.p.m. form the AB part of an ABX system with X (H^6) already located at 4.97 p.p.m. Therefore the signals at 4.32 and 4.25 p.p.m. may be assigned to either H^7 and H^8 on both of the equal sides of the isosceles triangle in Figure 3[(**5a**)] or to the two H^5 and two H^4 protons. In accord with this the signals at 3.96 and 3.49 p.p.m. may be assigned to either the four H^5 and H^4 protons or H^7 and H^8 protons.

In order to resolve this situation and further unravel the remaining unassigned protons in the spectrum, nuclear Overhauser enhancement (n.O.e.) and decoupling difference experiments were performed and the results are illustrated in Figures 5—7. As stated earlier a small long-range coupling from the diaminopropane chain to the CH_3 group was observed for

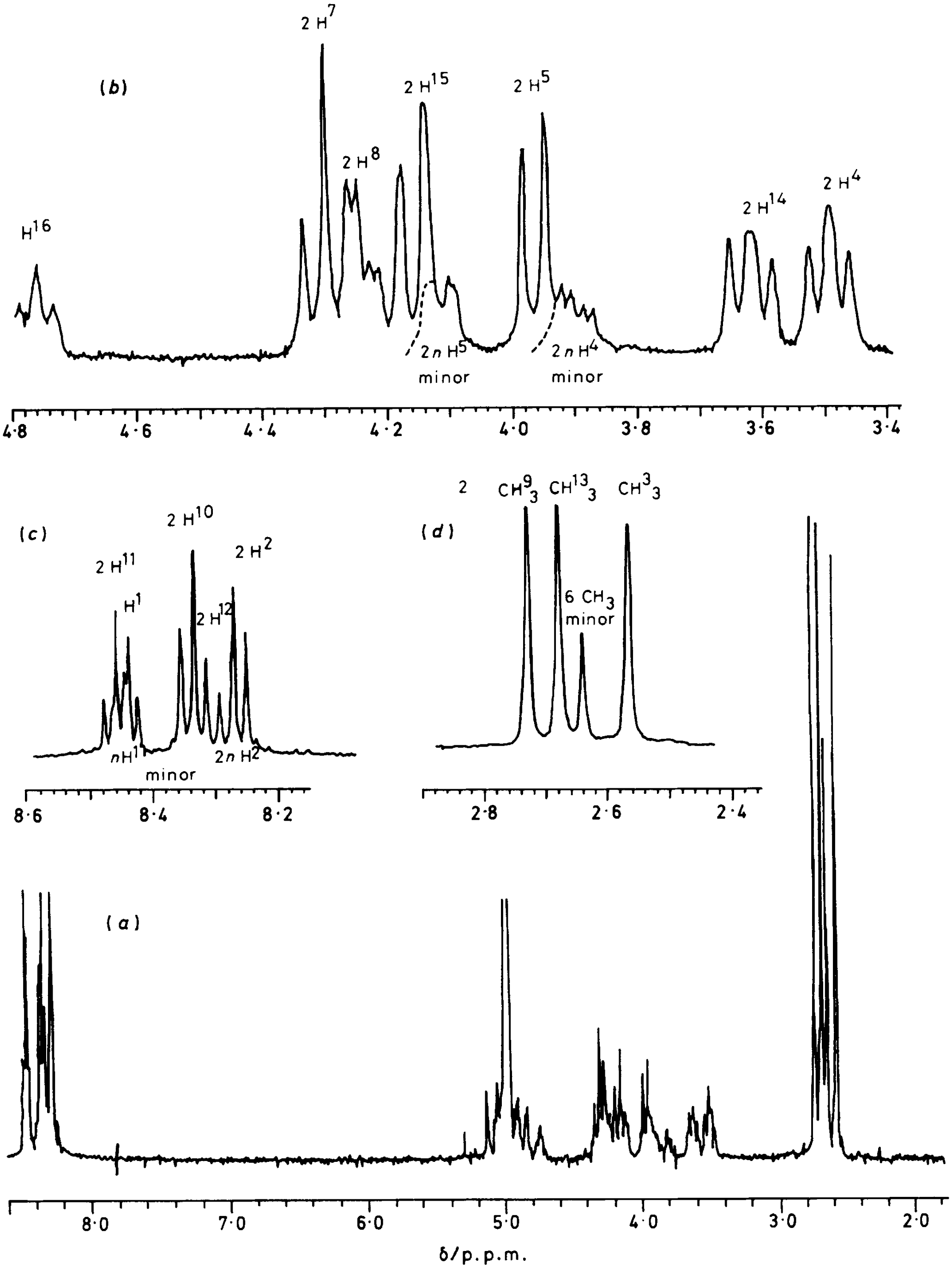
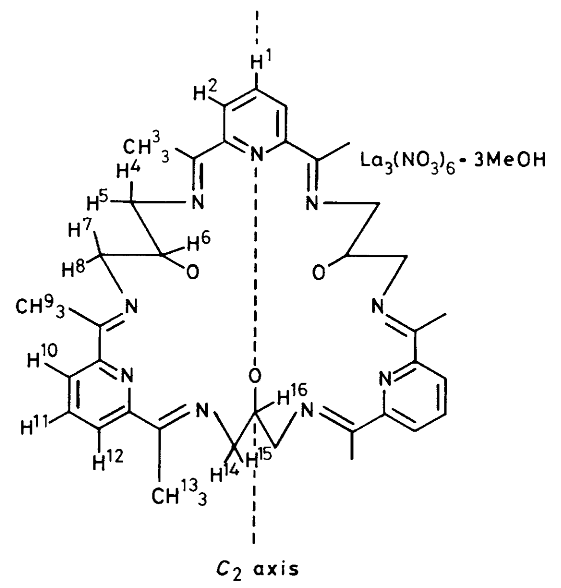
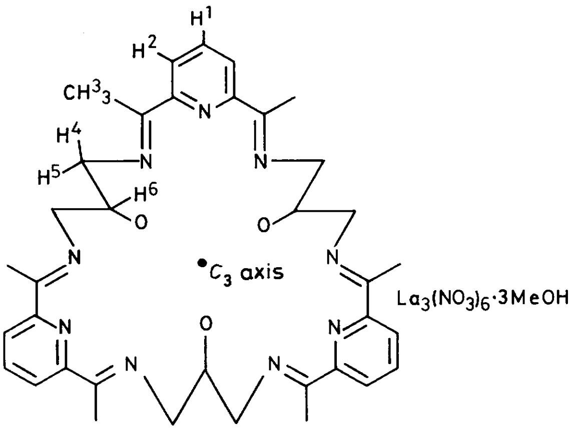


Figure 2. The ^{1}H n.m.r. spectrum in ^2H_2O at 20 °C of the product, (5), of the template reaction of lanthanum nitrate with 2,6-diacetylpyridine and 1,3-diamino-2-hydroxypropane: (*a*) full spectrum; (*b*), (*c*), (*d*) expansions

the minor species. Due to the presence of this small coupling, also present in the major species, complete assignment of the compound was possible. Decoupling difference experiments irradiating the H^{14} protons at 3.62 p.p.m. revealed a small (< 1 Hz) five-bond coupling to the CH_3 group at 2.68 p.p.m., see Figure 5(*c*), thus allowing the methyl group to be assigned to 2 $CH^{13}{}_3$. A n.O.e. experiment irradiating this methyl in turn identified two H^{12} protons in the aromatic region as a doublet at 8.324 p.p.m., see Figure 6(*c*). Decoupling difference spectra at this signal located the triplet attributable to two H^{11} protons at 8.450 p.p.m., Figure 7(*c*). When the doublet at 8.348 p.p.m. was irradiated the two H^{11} protons were again detected in the difference spectra [Figure 7(*d*)] indicating that the doublet being irradiated was due to the two H^{10} protons. Continuing in this fashion the n.O.e. experiments identified $CH^9{}_3$ at 2.74 p.p.m. [Figure 6(*b*)] and decoupling difference studies (Figure 5(*d*)] showed coupling to this signal from that at 4.25 p.p.m. This permitted the assignment of the signal at 4.25 p.p.m. to the two H^8 and that a 4.32 p.p.m. to the two H^7 protons and consequently the multiplets at 3.96 and 3.49 p.p.m. to the two H^5 and two H^4 protons respectively. For completeness, decoupling difference experiments on H^4 at 3.49 p.p.m. [Figure



(5a)



(5b)

Figure 3. Structures of the '3 + 3' macrocycles [major product (**5a**) and minor product (**5b**)] showing the proton numbering (assignments in the Table)

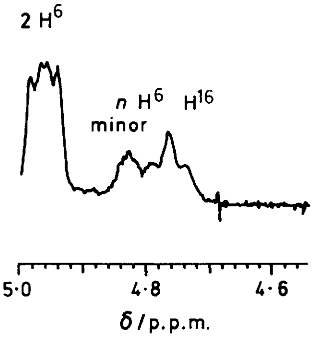


Figure 4. The ^1H n.m.r. spectrum (4.6—5.0 p.p.m.) in ^2H_2O at 8 °C of the '3 + 3' macrocycle

Figure 5. The ^1H decoupling difference spectra in the region 2.8—2.5 p.p.m.: irradiating at (*a*) 3.89 p.p.m. (H^4 of minor species), (*b*) 3.49 p.p.m. (H^4 of major species), (*c*) 3.62 p.p.m. (H^{14} of major species), and (*d*) 4.25 p.p.m. (H^8 of major species), (*e*) normal spectrum for reference

5(*b*)] confirmed the remaining CH_3 group as $CH^3{}_3$ and the n.O.e. from this located the two H^2 protons at 8.260 p.p.m., Figure 6(*e*). Decoupling difference spectra [Figure 7(*a*)] of the two H^2 protons identified the triplet at 8.445 p.p.m. as H^1. The outstanding irradiations shown in Figures 5—7 are due to the minor component and may be followed in an analogous manner.

The f.a.b. positive ion mass spectrum is consistent with a '3 + 3' macrocycle deprotonated on each OH site with three lanthanide ions, each having two nitrate ions to balance the charge and one of these being lost to form the 1 375 positive ion peak detected. The pool of evidence from ^1H n.m.r., C, H, and N analyses, and mass spectral data confirms that the major species is a '3 + 3' macrocycle with C_{2v} symmetry. The minor species is a '*n* + *n*' macrocycle and the lack of evidence for other peaks in the mass spectrum supports the postulation that it too is a '3 + 3' entity. If indeed it is '3 + 3' then it has three-fold symmetry.

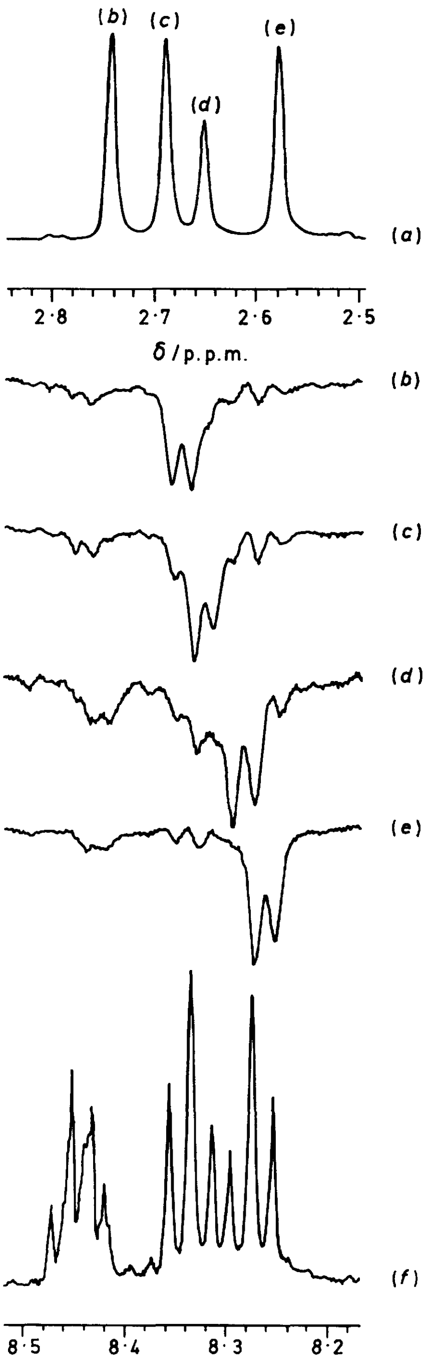


Figure 6. The n.O.e. difference spectra: (*a*) shows the irradiation points (*b*)—(*e*), with n.O.e. observed at (*b*) 8.348 p.p.m. (2 H^{10}, irradiating 2 $CH^9{}_3$), (*c*) 8.324 p.p.m., (2 H^{12}, irradiating 2 $CH^{13}{}_3$), (*d*) 8.288 p.p.m. (2*n* H^2, irradiating 2*n* CH_3 of minor product), (*e*) 8.260 p.p.m. (2 H^2, irradiating 2 $CH^3{}_3$), and (*f*) no irradiation

Preliminary crystal structure data indicated an arrangement of three lanthanum ions in an isosceles triangle. Unfortunately problems with the crystals prevented a full solid-state structural analysis for direct comparison with the solution studies.

Experimental

A methanolic solution (3 cm^3) of $La(NO_3)_3 \cdot 6H_2O$ (1 mmol) was added dropwise to a solution of 1,3-diamino-2-hydroxypropane (1 mmol) in methanol (3 cm^3). The white cloudy precipitate cleared on shaking after each addition. 2,6-Diacetylpyridine (1 mmol), also in methanol (3 cm^3), was added to the resulting clear solution, which turned yellow immediately. This was shaken well and heated to boiling. It was covered and placed in an oven at 50 °C and allowed to stand; crystallisation started to occur after 2 h. The solution was left untouched for 24 h. The supernatant liquid was then decanted and the crystals washed several times in hot methanol and dried *in vacuo* at 50 °C for 6 h [Found: C, 30.6; H, 4.05; N, 13.3.

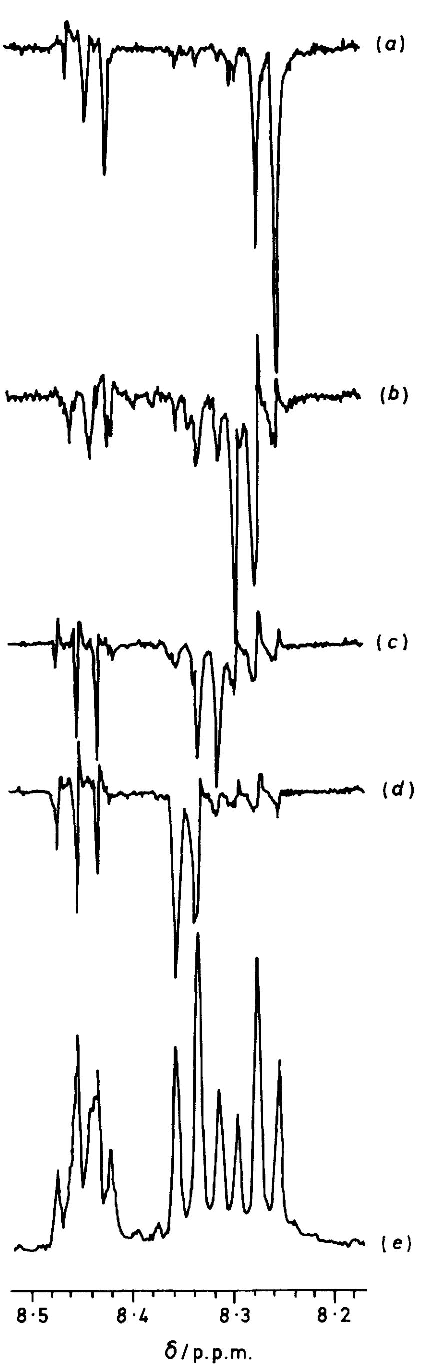


Figure 7. The ^1H decoupling difference spectra in the region 8.5—8.2 p.p.m.: irradiating at (*a*) 8.260 p.p.m. (2 H^2 locating H^1 at 8.445 p.p.m.), (*b*) 8.288 p.p.m. (2*n* H^2 of minor species, locating *n* H^1 at 8.435 p.p.m.), (*c*) 8.324 p.p.m. (2 H^{12} locating H^{11} at 8.450 p.p.m.), (*d*) 8.348 p.p.m. (2 H^{10} locating H^{11} at 8.450 p.p.m.), and (*e*) no irradiation

$C_{36}H_{42}La_3N_{15}O_{21}\cdot3MeOH$ (**5**) requires C, 30.55; H, 3.55; N, 13.7%]. Mass spectrum (f.a.b., using xenon gas as the primary beam): positive ion observed at *m*/*e* 1 375 [(**5**) – (NO_3 + 3MeOH)]. (In the spectrum shown in Figure 2 the complex was made using ethanol instead of methanol so as to avoid obscuring the two H^4 protons with overlap from the CH_3 signal of the co-ordinated methanol.)

Spectroscopy.—All the experiments were carried out on a Bruker WH400 spectrometer equipped with an aspect 2000 computer. ^2H_2O was used as solvent in all cases and the concentration was 5 mg of complex in 0.5 cm^3 of solvent, at 20 °C, unless otherwise stated. Decoupling difference spectra were recorded with a decoupling power of 16-dB attenuation from 0.5 W; the n.O.e. data were acquired with 40-dB attenuation. Fresh samples were made up for each series of experiments to avoid further complications from decomposition products.

References

1 Part 4, N. A. Bailey, D. E. Fenton, R. Moody, C. O. Rodriguez de Barbarin, I. N. Sciambarella, J. M. Latour, D. Limosin, and V. McKee, *J. Chem. Soc., Dalton Trans.*, 1987, 2519.

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

3 H. Adams, N. A. Bailey, D. E. Fenton, R. J. Good, R. Moody, and C. O. Rodriguez de Barbarin, *J. Chem. Soc., Dalton Trans.*, 1987, 207.

4 V. McKee and W. B. Shephard, *J. Chem. Soc., Chem. Commun.*, 1985, 158.

5 P. R. Ashton, W. D. Carlisle, and D. E. Fenton, unpublished work.

6 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.

7 L. deCola, D. L. Smailes, and L. M. Vallarino, *Inorg. Chem.*, 1986, **25**, 1729.

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