Inorganica Chimica Acta, 154 (1988) 229–238

The Stereochemical Activity or Non-activity of the 'Inert' Pair of Electrons on Lead(II) in Relation to its Complex Stability and Structural Properties. Some Considerations in Ligand Design

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(Received December 29, 1987; revised June 1, 1988)

Abstract

The role of the lone pair of electrons on Pb(II) in its coordination geometry and complex stability is examined. In a series of macrocyclic ligands where oxygen donors are successively replaced by nitrogen donors, it is found that when three or four nitrogens are present, there is a sudden marked increase in the rate of change of complex stability per nitrogen donor added. This is attributed to a change from a stereochemically inactive lone pair with approximately two or fewer nitrogen donors present, to an active lone pair. Below the transition point, the Pb(II) ion behaves as a large metal ion with rather ionic M–L bonding. In this state it responds to added oxygen donor bearing groups as expected for such a metal ion. Thus, the size-related selectivity patterns of Pb(II) with the ligand DAK-22 (4,7,13,16-tetraoxa-1,10-diazacyclooctadecane-*N*,*N*′-diacetate) are as expected for its size. The protonation constants and formation constants of DAK-22 with several metal ions are reported. For the complexes formed by 12-aneN_4 (1,4,7,10-tetraazacyclododecane) and 12-aneN_3O (1-oxa-4,7,10-triazacyclododecane) the Pb(II) appears to have a stereochemically active lone pair. Thus, when *N*-(2-hydroxypropyl) groups are added to 12-aneN_4 and 12-aneN_3O to give the ligands THP-12-aneN_4 and THP-12-aneN_3O, the Pb(II) ion does not respond to the added hydroxyalkyl groups as might have been expected. It behaves as a smaller more covalent ion, and a study of the formation constants of THP-12-aneN_4 and THP-12-aneN_3O with Cu(II), Zn(II), Cd(II), Pb(II), Ca(II), Sr(II) and Ba(II) reveals lower than anticipated Pb/Zn selectivities. A crystallographic study of $[Pb(C_{20}H_{44}N_4O_4)](NO_3)_2\cdot C_3H_8O$ reveals that there is space between the O donors for a stereochemically active lone pair, but the lack of shortening of the Pb–N bonds suggests that the lone pair is not active. The complex crystallizes in the orthorhombic system, space group *Pnma*, with cell dimensions $a = 10.352(8)$, $b = 14.781(2)$, and $c = 21.850(4)$ Å, $Z = 4$. A final conventional $R = 0.056$ was obtained. Although the ligand THP-12-aneN_4 has four chiral carbon atoms, the crystal structure suggests that only the *RRRR* and *SSSS* enantiomers of the free ligand are obtained after recrystallisation from n-hexane. The structure indicates that the $[Pb(\text{THP-12-ane}N_4)]^{2+}$ cations are disordered, with 50% site occupancy by the *RRRR* and by the *SSSS* conformer.

Introduction

In a recent paper [1] it was pointed out that the presence of neutral oxygen donors could be used to control selectivity for large metal ions over small metal ions. This factor is of considerable importance in attempts to design ligands which can be used in cases of lead intoxication, where selectivity is required [2] for the large Pb(II) ion over the small Zn(II) ion. Thus, the addition of chelating groups bearing oxygen donors generally leads to an increase in selectivity for the large Pb(II) ion over the small Zn(II) ion, as shown in the following examples (Scheme 1). (Pb/Zn is log K_1 for the Pb(II) complex minus log K_1 for the Zn(II) complex.)

It is noteworthy that similar increases in selectivity can be produced by addition of oxygen donor groups so as to form either an open-chain ligand (THPED) or macrocycles (12-aneN_2O_2 and 18-aneN_2O_4). It might therefore seem that in order to generate ligands selective for Pb(II), all that is necessary is to add groups bearing oxygen donors. Following this line of reasoning, the effect of adding hydroxyethyl groups to cyclam produces a large increase in Pb/Zn selectivity. The formation constants of 12-aneN_4 therefore suggested that addition here of *N*-(2-hydroxyethyl) groups would lead to a ligand with high Pb(II) formation constants and high Pb/Zn selectivity (Scheme 2). (The selectivity for Pb(II) over Zn(II) is indicated as Pb/Zn, and is log K_1 for the Pb(II) complex minus log K_1 for the Zn(II) complex.)

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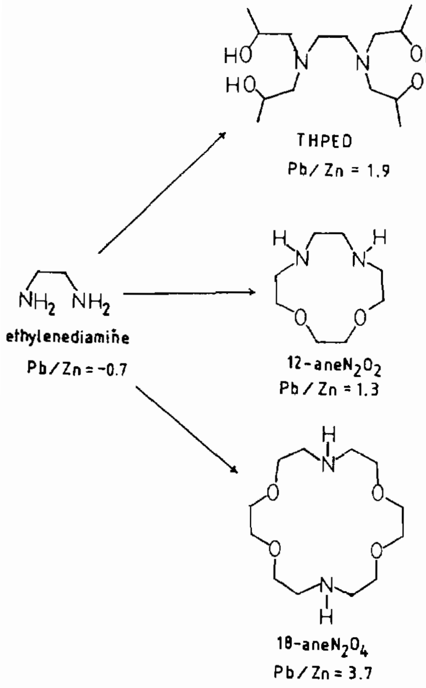
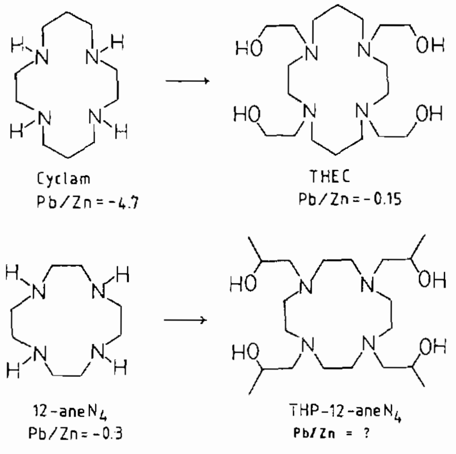


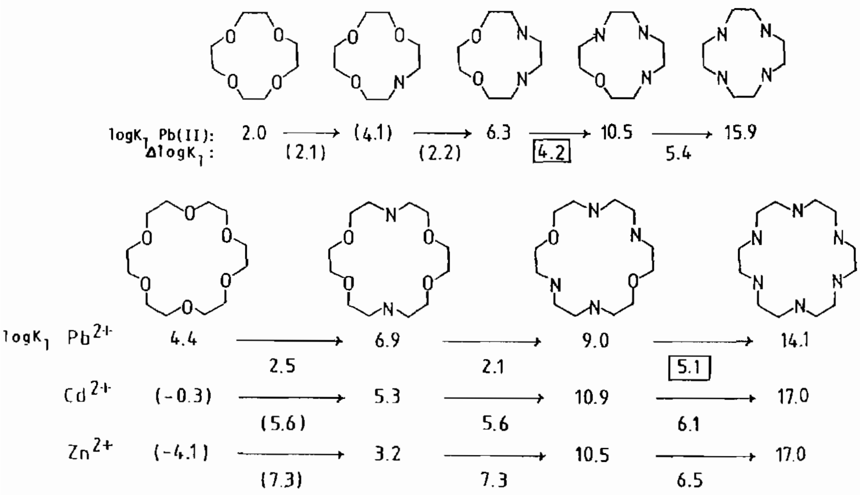
Scheme 1.



Scheme 2.

As seen in this work, the complex stability of THP-12-aneN_4 with Pb(II), and its Pb/Zn selectivity are much lower than might be expected from the general observation of what happens when oxygen donor bearing groups are added. Thus, a Pb/Zn selectivity of some 4.2 log units might have been anticipated for THP-12-aneN_4 by comparison with THEC, whereas that found is only some 1.6 log units. Closer examination of the stability of the complexes of Pb(II) with nitrogen donors indicated a discontinuity in behaviour as more nitrogen donors were present. This can be illustrated by considering the formation constants of a series of macrocycles of Pb(II), and also of Cd(II), as oxygen donors are successively replaced by nitrogen donors (Scheme 3). (Incremental changes in $\log K_1$ as oxygen donors are replaced by nitrogens, where it is considered that the activity of the inert pair on Pb(II) changes, are denoted in square brackets, as [ ].)

It is seen that both Cd(II) and Zn(II) show equal sized increases in $\log K_1$, the formation constant of the ML complex, as nitrogen donors replace oxygens in passing from 18-aneN_2O_4 to 18-aneN_4O_2, and then to 18-aneN_6. However, the Pb(II) ion shows a discontinuity between 18-aneN_4O_2 and 18-aneN_6, where the increase in $\log K_1$ is 5.1 log units, as compared with only about 2 log units for the other members of the series. This is found to occur generally in such series, as, for example the series 12-ane-$N_{(4-n)}O_n$ (n = 0 to 4) or 15-ane-$N_{(5-n)}O_n$ (n = 0 to 5). It is almost as if at some point in the series the character of the Pb(II) ion changes, with a sudden increase in affinity



Scheme 3.

for the nitrogen donor atom. A possible explanation which springs to mind is the change in stereochemical activity of the lone pair of electrons on the Pb(II) ion. This lone pair may reside in the spherically symmetric 6s orbital, or may exhibit stereochemical activity, in accord with the Gillespie–Nyholm [3] or Sidgwick–Powell [4] valence shell electron-pair repulsion (VSEPR) model, in a hybrid sp^n or sp^nd^m orbital. This explanation has already been tentatively advanced [5] by us to explain the unusually high $\log K_1$ for the 9-aneN_3 complex (see Fig. 1 for key to ligand abbreviations) of Pb(II) as compared with the complexes with 9-aneN_2O and 9-aneN_2S.

The effect of the stereochemically active lone pair of Pb(II) on the structure of its complexes has been demonstrated crystallographically [6, 7]. There are two pronounced effects:

(i) The stereochemical lone pair can be detected by its apparent occupation of a coordination site on the Pb(II), *i.e.* there will be a 'gap' in the coordination geometry.

(ii) There will be a shortening of the Pb–L bonds on the side of the Pb(II) ion opposite to the position of the lone pair, which is accompanied by a decrease in coordination number.

Effect number two obviously indicates a change in the nature of the Pb–L bonding, with an increase in covalency. It seemed likely that it was this effect which produced the discontinuity in complex stability in each of the series discussed above. The Pb(II) ion thus might undergo a change, which can be likened to spin-pairing in metal ions such as Ni(II) or Fe(II), which is accompanied by a dramatic decrease in size and change in the nature of the M–L bonding. The dependence of the transitions, from high-spin to low-spin in Ni(II), or from stereochemically inactive to active lone-pair on Pb(II), is dependent on the covalence of the M–L bonds formed, *i.e.* the relative numbers of N *versus* O donor atoms. Thus, complexes of Ni(II) with 13-aneN_2O_2 or 13-aneN_3O are [8] completely high-spin, whereas the 13-aneN_4 complex is largely low-spin.

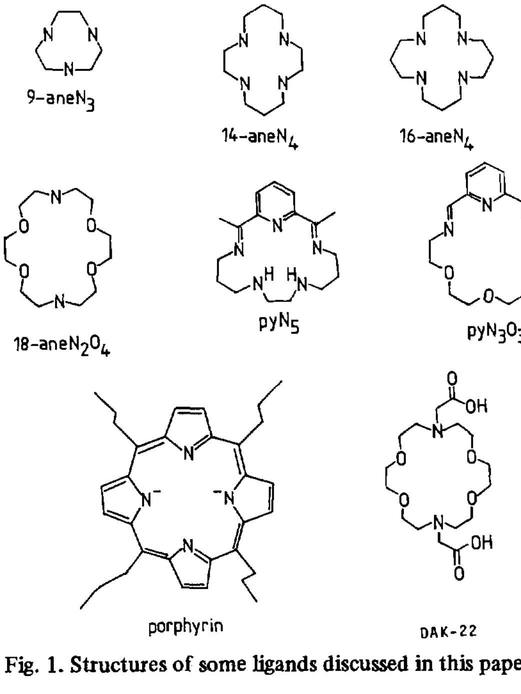


Fig. 1. Structures of some ligands discussed in this paper.

The indication for Pb/Zn selectivity is therefore that if the selectivity for the large Pb(II) ion over the small Zn(II) ion is to be maximized, the Pb(II) ion must be prevented from becoming 'active', *i.e.* from having a stereochemically active lone pair, where the Pb(II) will shrink in size and become more like Zn(II). In its active form, the Pb(II) will behave as a much smaller ion (the change from active to inactive Pb is accompanied by a shortening of Pb–N bonds by about 0.3 Å [7]) and would therefore not show the expected response to added groups bearing neutral oxygen donor atoms.

In this paper the formation constants of the complexes of THP-12-aneN_4 and THP-12-aneN_3O are reported with Cu^{2+}, Zn^{2+}, Cd^{2+} Pb^{2+}, Ca^{2+}, Sr^{2+} and Ba^{2+}, determined at 25 °C in 0.1 M $NaNO_3$. The formation constants with the ligand DAK-22 are also reported. The interest here was to see whether the presence of acetate groups would affect the selectivity patterns of Pb(II) with ligands containing neutral oxygen donors in the same way as nitrogen donor groups do. Chang and Rowland [9] have previously reported $\log K_1$ values for DAK-22 complexes, which are compared with those reported here. At the same time, in order to see whether the lone pair was stereochemically active on the Pb in its complex with THP-12-aneN_4, a crystallographic study of $[Pb(THP\text{-}12\text{-}aneN_4)](NO_3)_2 \cdot C_3H_8O$ was carried out, and is reported here.

Experimental

Synthesis of Ligands

1,4,7,10-Tetra-(2-hydroxypropyl)-1,4,7,10-tetraazacyclododecane (THP-12-aneN_4)

The free base of 12-aneN_4 (Parish Chemicals, 2 g, 0.01 mol) was dissolved in ethanol (50 ml, 96%) and 4 ml propylene oxide (0.06 mol) added. This was left for two days, when a white solid was obtained on evaporation of the ethanol. This solid was boiled in hexane, which was decanted from a sticky solid residue. White crystals were obtained from the cooled hexane solution by filtration. Yield of recrystallized material, 50%, melting point 115.5 to 117.5 °C. NMR ($CDCl_3$): 1.13 ppm (12H, d, CH_3–CHOH–), 2.23 ppm (8H, d, N–CH_2CHOH–), 2.25 ppm (16H, d, –CH_2–N), 2.6 ppm (8H, m, –CH_2N), 3.3 ppm (4H, s, O–*H*), 3.8 ppm (4H, m, –C*H*). *Anal.* Found: C, 59.43; H, 10.68; N, 13.72. Calc. for $C_{20}H_{44}N_4O_4$: C, 59.37; H, 10.96; N, 13.85%.

4,7,10-Tri-(2-hydroxypropyl)-1-oxa-4,7,10-triazacyclododecane (THP-12-aneN$_3$O)

The synthetic procedure was similar to that for THP-12-aneN$_4$, except that the starting amine was 12-aneN$_3$O, synthesized as described previously [8, 10]. NMR: 1.1 ppm (9H, d, C*H*$_3$CHOH), 2.5 ppm (22H, m, C*H*$_2$), 3.6 ppm (3H, m, –C*H*OH), 5.1 ppm (3H, s, br, –OH). *Anal.* Found: C, 56.74; H, 10.53; N, 11.70. Calc. for $C_{17}H_{37}N_3O_4$: C, 58.76; H, 10.73; N, 12.09%.

1,4,10,13-Tetraoxa-7,16-diazacyclooctadecane-7,16-diacetate (DAK-22)

This was synthesized by the method of Kulstad and Malmsten [11].

Determination of Stability Constants

These were carried out mainly by potentiometry using glass electrodes as described previously [12]. The rate of equilibration of Zn^{2+} with THP-12-aneN$_4$ was slow, so that an out-of-cell technique [13] was used where a set of Zn^{2+}/THP-12-aneN$_4$ solutions with varying amounts of added acid were allowed to equilibrate in a water bath at 25 °C for one week. The Cu(II) complex did not break up in acid appreciably above pH 2, so that for the determination of $\log K_1$ for this complex, a spectrophotometric technique was used to monitor the extent of complex formation as a function of pH in the pH range 1 to 2. A similar difficulty existed with the Cd(II) complex, and its formation constant with THP-12-aneN$_4$ was determined spectrophotometrically in a competition experiment with Cu(II), where the Cu(II)/Cd(II) ratios were varied, with the extent of complex formation of the Cu(II) complex being followed spectrophotometrically.

X-ray Crystallographic Studies

Evaporation of a 1:1 solution of $Pb(NO_3)_2$ plus THP-12-aneN$_4$ in water gave a white solid, which was recrystallized from n-propanol. A single crystal suitable for diffraction analysis was selected by Weissenberg and standard oscillation techniques using Cu Kα radiation. Diffraction data collection was carried out at room temperature using an Enraf-Nonius CAD-4 diffractometer, with Mo Kα graphite monochromated radiation. Cell dimensions and orientation matrix were determined by least-squares refinement of 25 reflections ($18 \leqslant \theta \leqslant 20°$). The intensity of the standard reflections was measured every hour, and the data was corrected for Lorentz and polarization effects, for crystal decay, and for absorption using the empirical absorption correction of North *et al.* [14]. The crystal data and details of the data collection are seen in Table I.

TABLE I. Details of the Crystallographic Analysis

	[Pb(THP-12-aneN$_4$)]-(NO$_3$)$_2$·C$_3$H$_8$O
Formula	$PbC_{23}H_{52}N_6O_{11}$
Molecular weight (g mol^{-1})	795.89
Crystal system	orthorhombic
Space group	*Pnma*
Cell dimensions	
a (Å)	14.781(2)
b (Å)	10.354(8)
c (Å)	21.852(4)
V (Å^3)	3344.3
Z	4
d_{obs} (g cm^{-3})	1.61(1)
d_{calc} (g cm^{-3})	1.58
F(000)	1600
Crystal colour	white
Crystal dimenions (mm)	0.23 × 0.24 × 0.90
Radiation (Å)	λ(Mo Kα) 0.71073
Data collection	$\omega-2\theta$
Theta range	$3 < \theta < 30$
Range of h, k, l	+14, +20, +30
Scan width (°)	$0.60 + 0.35 \tan \theta$
Scan speed range (° min^{-1})	1.0–5.5
No. reflections measured	5412
No. unique data	4096 (R_{int} = 0.0648)
No. data used	2368 [$F_o \geqslant 4\sigma(F_o)$]
Absorption coefficient (μ_λ) (cm^{-1})	48.89
Range transmission factors (%)	67.9–94.5
Final R	0.056
No. parameters	103
Residual density (e Å^{-3})	1.1

Solution of the structure was first attempted in the non-centrosymmetric space group *Pna*2$_1$. The vectors corresponding to the Pb atom were located on a Patterson map [15], but subsequent difference Fourier synthesis lead to poor convergence. Some disorder was also apparent, and the nitrogen coordinates suggested that a mirror plane could be present. It was then decided, as indicated by Marsh [16] in such cases, to switch to a centrosymmetric space group, *Pnma*. In *Pnma*, half of the molecule was found, and when the atoms (except for the nitrogens) were given a site occupancy factor of one half, the second half of a disordered cation pair was found. It was necessary to refine the cation with fixed bond lengths and angles derived from crystal structures [17] of 12-aneN$_4$ complexes. Further refinement of the lead coordinates and a rigid body macrocycle, but with the isopropanol arms free to rotate about the N–C bond, was carried out. Figure 2 shows the atomic numbering scheme of one cation of a disordered pair. One nitrate was placed in the mirror plane and the other perpendicular to the mirror plane. The n-propanol solvent molecule was restricted by the space group symmetry to have two carbon

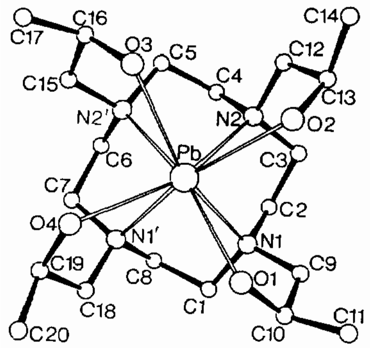


Fig. 2. View of one member of the disordered pair of $[Pb(THP\text{-}12\text{-}aneN_4)]^{2+}$ cations from above, showing the numbering scheme.

TABLE II. Fractional Coordinates ($\times 10^5$) and Common Isotropic Temperature Factors ($Å^2$, $\times 10^3$, $\times 10^4$ for Pb) for the Cation of $[Pb(C_{20}H_{44}N_4O_4)](NO_3)_2 \cdot C_3H_8O$

Atom	*x*/*a*	*y*/*b*	*z*/*c*	*U*(iso)
Pb	15475(5)	25000	19532(3)	611(4)
N(1)	19674(5)	10839(1)	9878(3)	75(6)
N(2)	30082(5)	10866(1)	21405(3)	89(7)
C(1)	19068(5)	18952(1)	4299(3)	73(7)
C(2)	28977(5)	5717(1)	10485(3)	87(8)
C(3)	30341(5)	238(1)	16866(3)	68(6)
C(4)	38244(5)	19024(1)	20715(3)	108(10)
C(5)	37067(5)	31409(1)	24378(3)	84(8)
C(6)	33323(5)	44563(1)	15590(3)	101(9)
C(7)	25520(5)	50129(1)	11904(3)	75(7)
C(8)	24247(5)	31441(1)	5314(3)	89(8)
C(9)	13254(5)	−97(1)	9421(3)	85(8)
C(11)	−2787(5)	−6946(1)	10243(3)	98(12)
O(1)	1634(5)	14714(1)	12863(3)	80(5)
C(12)	29800(5)	5379(1)	27661(3)	118(11)
C(13)	21381(5)	−2435(1)	29152(3)	105(10)
C(14)	20762(5)	−4207(1)	36076(3)	124(13)
O(2)	13462(5)	4403(1)	27088(3)	110(7)
C(15)	27536(5)	50243(1)	25594(3)	111(10)
C(16)	23648(5)	46303(1)	31760(3)	134(13)
C(17)	19995(5)	58314(1)	34989(3)	105(10)
O(3)	16264(5)	37418(1)	30848(3)	130(7)
C(18)	11117(5)	44768(1)	7284(3)	69(6)
C(19)	6071(5)	53589(1)	11663(3)	77(7)

All atoms except N(1) and N(2) have site occupancy factors of 0.5.

atoms in the mirror plane, which is probably not strictly correct, and may be the cause of the high temperature factors and standard deviations of the solvent molecule. The structure was refined with isotropic thermal parameters for all atoms except the lead and nitrogen atoms and the nitrate atoms. Table II and Table III give the final fractional coordinates and isotropic temperature factors for the structure, and in Table IV are listed the important bond angles and bond lengths.

TABLE III. Fractional Coordinates ($\times 10^4$) and Equivalent Isotropic Temperature Factors ($Å^2$, $\times 10^3$) for Nitrate and Solvent of $[Pb(C_{20}H_{44}N_4O_4)](NO_3)_2 \cdot C_3H_8O$

Atom	*x*/*a*	*y*/*b*	*z*/*c*	*U*(eq) [a]
N(3)	−1638(12)	2500	368(6)	102(14)
N(4)	4825(12)	2500	7514(6)	96(13)
O(31)	−1595(12)	2500	942(6)	129(13)
O(32)	−2369(12)	2500	76(10)	193(21)
O(33)	−896(12)	2500	87(8)	131(4)
O(41)	4065(11)	2500	7255(8)	121(13)
O(42)	5128(10)	1421(9)	7677(7)	158(12)
CA	445(38)	2500	5543(25)	287(24)
CB	−204(41)	2500	5004(30)	396(39)
CC	372(33)	1615(53)	4609(22)	216(23)
O	1059(23)	2111(44)	4206(15)	241(18)

All atoms except O(42), CC and O have site occupancy factors of 0.5. [a] $U_{eq} = \frac{1}{3}\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* (a_i a_j)$.

TABLE IV. Bond Lengths and Bond Angles of the Rigid Body of $[Pb(C_{20}H_{44}N_4O_4)](NO_3)_2 \cdot C_3H_8O$

Bond lengths (Å)			
Pb–N1	2.64	C–C	1.52 ± 0.01
Pb–N2	2.64	C–O	1.44 ± 0.01
Pb–O1	2.71	C–N	1.48 ± 0.05
Pb–O2	2.71		
Pb–O3	2.78		
Pb–O4	2.78		
Bond angles (°)			
N1–Pb–N2	67.9	O1–Pb–O2	86.5
N1–Pb–N1'	67.6	O1–Pb–O3	133.2
N1–Pb–N2'	103.6	O1–Pb–O4	80.5
N2–Pb–N1'	103.6	O2–Pb–O3	79.9
N2–Pb–N2'	66.7	O2–Pb–O4	133.1
N1'–Pb–N2'	67.9	O3–Pb–O4	77.2
N1–Pb–O1	62.2	Pb–N–C	109.5 ± 2
N2–Pb–O2	63.9	Pb–O–C	118.1 ± 2
N1'–Pb–O4	62.7	C–N–C	109.5 ± 3
N2'–Pb–O3	64.8	about C	109.5 ± 2

Standard deviations of the shifts of the pivot Pb atom are $x/a = 0.155(01)$ and $z/c = 0.195(01)$, and of the rotation parameters are $\sigma(x) = 0.0001(17)$, $\sigma(y) = 0.0003(17)$, and $\sigma(z) = 0.0006(18)$ radians.

Results and Discussion

In Table V are seen the protonation constants and formation constants for a variety of metal ions with the ligands THP-12-aneN$_4$ and THP-12-aneN$_3$O, at 25 °C in 0.1 M NaNO$_3$. Also included for the purposes of comparison are the formation constants of the complexes with 12-aneN$_4$ and 12-aneN$_3$O. As mentioned above, the Pb/Zn selectivity, and the absolute stability of the Pb(II) complex with the

TABLE V. Formation Constants for THP-12-aneN$_3$O and THP-12-aneN$_4$ at 25 °C and Ionic Strength (NaNO$_3$) 0.1 M

	12-aneN$_4$	12-aneN$_3$O	THP-12-aneN$_4$	THP-12-aneN$_3$O
pK_1	10.6	10.18	9.98(3)	10.14(1)
pK_2	9.6	8.56	8.26(3)	6.46(1)
pK_3		1.43		1.11(4)
Cu^{2+}	23.4	15.85	19.48(4)[a]	13.43(1)
Zn^{2+}	16.2	10.53	13.45(3)	9.92(1)
Cd^{2+}	14.3	10.78	17.46(5)[a]	12.77(2)
Pb^{2+}	15.9	11.54	15.07(1)	12.17(1)
Ca^{2+}	3.12(2)	2.03(2)	5.68(1)	4.60(1)
Sr^{2+}			5.02(3)	3.92(1)
Ba^{2+}			3.74(1)	3.30(1)
Pb/Zn	−0.3	1.01	1.62	2.25

Constants for metal ions, except Ca^{2+}, with 12-aneN$_4$ and 12-aneN$_3$O taken from refs. 8 and 18. Protonation constants have the significance that pK_1 refers to the equilibrium $H^+ + L = HL^+$, pK_2 refers to $H^+ + HL^+ = H_2L^{2+}$, and pK_3 refers to $H^+ + H_2L^{2+} = H_3L^{3+}$.

[a] Ionic strength 0.5 M.

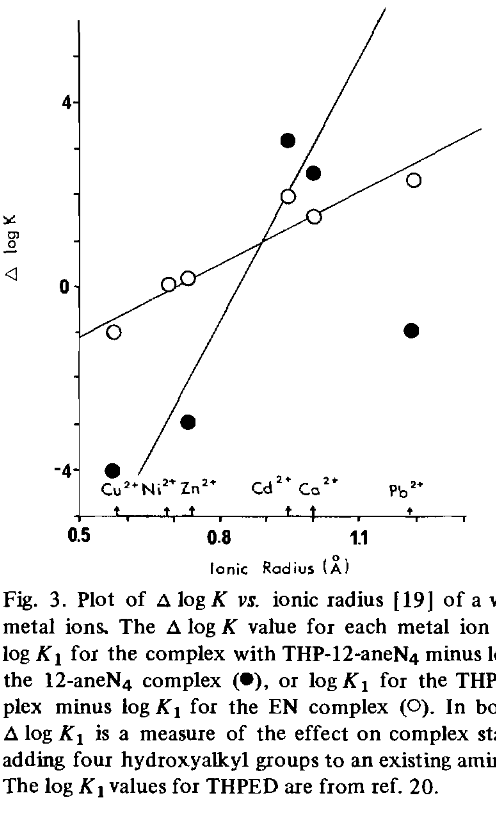


Fig. 3. Plot of Δ log K vs. ionic radius [19] of a variety of metal ions. The Δ log K value for each metal ion is simply log K_1 for the complex with THP-12-aneN$_4$ minus log K_1 for the 12-aneN$_4$ complex (●), or log K_1 for the THPED complex minus log K_1 for the EN complex (○). In both cases, Δ log K_1 is a measure of the effect on complex stability of adding four hydroxyalkyl groups to an existing amine ligand. The log K_1 values for THPED are from ref. 20.

THP-12-aneN$_4$ and THP-12-aneN$_3$O ligands are disappointing. This is illustrated in Fig. 3, where Δ log K, the change in complex stability in passing from the 12-aneN$_4$ to the THP-12-aneN$_4$ complex for each metal ion, is plotted against the ionic radius [19] of the metal ion. Also plotted in Fig. 3 is Δ log K for the ligand THPED *versus* EN, as a function of ionic radius of the metal ion. It is seen that the latter relationship is linear, with the point for the Pb(II) ion falling on the relationship as expected. This is the usual behaviour found where the number of nitrogen donor atoms in the ligand is less than three [1]. On the other hand, the point for Pb(II) on the THP-12-aneN$_4$ *versus* 12-aneN$_4$ relationship is displaced downwards considerably. By extrapolation of the linear relationship which involves the points for Cu(II), Zn(II), Cd(II) and Ca(II) in the relationship of Δ log K *versus* ionic radius for THP-12-aneN$_4$ *versus* 12-aneN$_4$, a log K_1 value for Pb(II) with THP-12-aneN$_4$ of 22.6 would have been expected, instead of the observed value of 15.1 log units.

In Fig. 4 is plotted Δ log K for the pairs of ligands 12-aneN$_3$O and THP-12-aneN$_3$O, and 14-aneN$_4$ and THE-14-aneN$_4$ plotted against ionic radius of the metal ion. Once again, the ligands contain more than two nitrogen donors, and the Pb(II) ion shows a much more unfavourable response to the added oxygen donors than would have been anticipated from its large size. As will be shown below, the change from an inactive to an active pair of electrons on Pb(II) is generally accompanied by a shortening of the Pb–N bond lengths by about 0.3 Å. As shown in Fig. 4, the response of the Pb(II) ion to the added hydroxyalkyl groups corresponds very well to a decrease in the apparent ionic radius of the Pb(II) by about 0.3 Å when the lone pair of electrons becomes stereochemically active.

The results for THP-12-aneN$_4$ and THP-12-aneN$_3$O suggest that in order to produce high Pb/Zn selectivity when O donors are added to existing ligands, the number of nitrogen donor atoms must be kept at less than three. Thus, ligands such as BHP-18-aneN$_2$O$_4$ show high Pb/Zn selectivity because they have a large number of O donor atoms, and only two nitrogen donors. However, the problem with such a ligand is that the actual log K_1 value for Pb(II) at 8.6 is rather low. The next step appeared to be to see

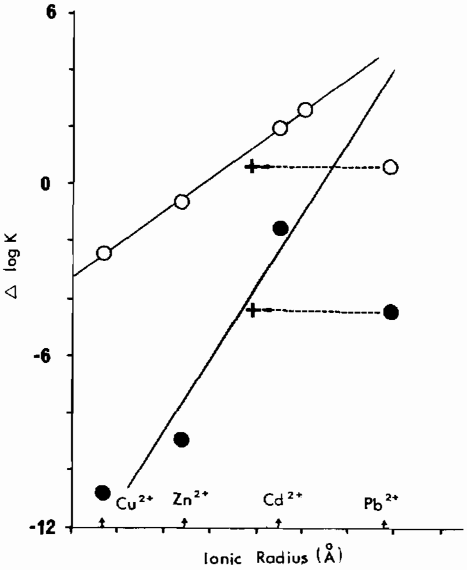


Fig. 4. Plot of log K *vs.* ionic radius [19] of a variety of metal ions. The Δ log K value for each metal ion is simply log K_1 for the complex with THEC minus log K_1 with cyclam (●), or log K_1 with THP-12-aneN$_3$O minus log K_1 with 12-aneN$_3$O (○). The broken lines indicate how the points for Pb(II), where it is thought that the lone pair is stereochemically active (see text), may be made to agree with the linear relationship found for other metal ions by assuming that the ionic radius has decreased by 0.3 Å.

whether the Pb(II) would maintain an inactive lone pair in the presence of two nitrogen donors plus two carboxylate oxygens. The latter should increase the value of log K_1, and in the presence of added oxygen donors, increase greatly the Pb/Zn selectivity provided the Pb(II) lone pair remains inactive. The best way to put together a ligand containing two nitrogen donor atoms, plus two carboxylate groups, plus a number of neutral oxygen donor atoms appeared to be as seen in DAK-22 (Fig. 1). The ligand DAK-22 is formally derived from two glycines by adding bridging oxygen donors. The formation constants for DAK-22 with a variety of metal ions are seen in Table VI, together with those determined by Chang and Rowland [9] It is seen that our reported log K_1 values are generally higher than those of Chang and Rowland, which relates in part to the higher value of pK_1 found here for DAK-22. The log K_1 values found here for Pb(II) and Cd(II) are very much higher than those of Chang and Rowland, which would appear to relate to the presence of 0.1 M Cl^- ion in the background electrolyte of Chang and Rowland. Both Pb(II) and Cd(II) have a high affinity for Cl^- ion, which would thus compete with DAK-22 for complexation to the Pb(II) and Cd(II) ions in 0.1 M Cl^-, and lead to lower log K_1 values.

The results in Table VI show the expected type of behaviour of log K_1 as oxygen donors are added to two glycine molecules to give DAK-22. It is seen that small metal ions such as Cu(II) and Zn(II) show no increase in complex stability as neutral oxygen donors are added to two glycine molecules to give DAK-22, whereas for large metal ions such as Cd(II), La(III), Ca(II), Sr(II), Pb(II) and Ba(II), the change in complex stability on adding oxygen donors to two glycines to give DAK-22 is in the range 5 to 8 log units. Of particular importance is the fact that Pb(II) appears to behave very much like Sr(II), which suggests that the inert pair is inactive when two glycine molecules are coordinated to Pb(II), in that the change in log β_2 for glycine to log K_1 for DAK-22

TABLE VI. Formation Constants for DAK-22 at 25 °C and Ionic Strength 0.1 M

	log K DAK-22		log β_2 glycine[a]	Δ log K [b]	Ionic radius[c]
	this work (0.1 M $NaNO_3$)	Chang and Rowland [9] (0.1 M $(CH_3)_4NCl$))			
pK_1 [d]	9.04(2)	8.45(2)			
pK_2	7.81(8)	7.80(2)			
pK_3	2.08(16)	2.90(10)			
log K_1 Cu^{2+}	14.94(1)	14.49(3)	15.03	−0.1	0.57
Zn^{2+}	8.91(3)	8.42(9)	9.19	−0.3	0.74
Cd^{2+}	12.82(1)	11.07(3)[e]	7.69	+5.1	0.95
Ca^{2+}	8.57(2)	8.39(6)	(2.1)[f]	+6.4	1.00
La^{3+}	12.47(1)	12.21(13)	(6.2)[f]	+6.3	1.03
Sr^{2+}	8.57(4)	8.29(7)	(1.1)[f]	+7.5	1.17
Pb^{2+}	14.54(2)	13.55(6)[e]	7.7	+6.8	1.18
Ba^{2+}	8.46(1)	7.63(2)	(0.9)[f]	+7.6	1.36

[a] From ref. 18, ionic strength 0.1, 25 °C. [b] The difference in log K_1 for DAK-22 and log β_2 for glycine, calculated using log K_1 DAK-22 from this work. [c] From ref. 19. [d] The equilibria referred to are for pK_1, $L^{2-} + H^+ \rightleftharpoons LH^-$; p$K_2$, $LH^- + H^+ \rightleftharpoons LH_2$; p$K_3$, $LH_2 + H^+ \rightleftharpoons LH_3^+$, where L is DAK-22. [e] The large discrepancies in log K_1 with DAK-22 for Cd^{2+} and Pb^{2+} between this work and the work of Chang and Rowland is thought to be due to the presence of chloro complexes in the study of Chang and Rowland, as discussed in the text. [f] Estimated from the reported [18] log K_1 values by comparison with Cd(II).

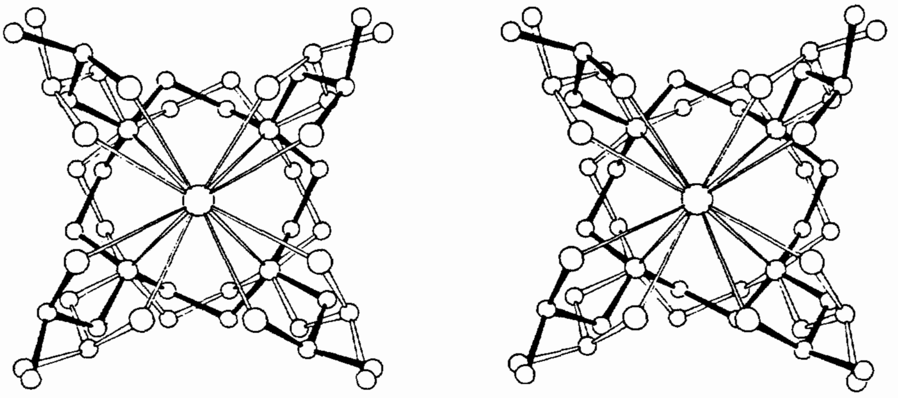


Fig. 5. Stereoview from above of the disordered pair of *RRRR* and *SSSS* $[Pb(THP\text{-}12\text{-}aneN_4)]^{2+}$ cations.

for Pb(II) is similar to that for Sr(II) and other large metal ions.

The Structural Effects of the Stereochemically Active Lone Pair

In Fig. 5 is seen a stereoview of the disordered pair of $[Pb(THP\text{-}12\text{-}aneN_4)]^{2+}$ cations. It is seen that the two disordered cations have opposite chirality, *i.e.* one is the *RRRR* and the other is the *SSSS* conformer. This observation may account for the behavior of the ligand during recrystallization, when part of the crude product dissolved in hexane and crystallized out as needles, while a residue, with an almost identical NMR spectrum, remained undissolved, even in further aliquots of hexane. If one assumes, as seems rather likely for racemization about a carbon atom, that the enantiomer observed in the Pb(II) complex is the same as the hexane-soluble fraction of the crude THP-12-aneN$_4$, *i.e.* racemization does not take place, then it seems likely that the hexane-soluble fraction of THP-12-aneN$_4$ is a mixture of *RRRR* and *SSSS* 12-aneN$_4$, which was the ligand used to prepare the crystals of the Pb(II) complex.

The Pb atom in $[Pb(THP\text{-}12\text{-}aneN_4)]^{2+}$ sits out of the plane of the macrocycle, and is eight coordinate. It forms four bonds to the nitrogens of the macrocycle (2.642(2) and 2.640(1) Å), and four bonds to the oxygens of the hydroxypropyl arms (2.713(1), 2.710(1), 2.783(1) and 2.782(1) Å). No other atoms were found bonded to the Pb atom within 4 Å. The question is whether the Pb(II) has an active lone pair or not. There appears (Fig. 6) to be a vacant site between the oxygen donors, since the O–Pb–O angles are very large, being in the vicinity of 133°. However, one has to examine the structure in the context of other Pb(II) structures to decide whether this represents an active lone pair or not. In Table VII are shown the Pb–N and Pb–O bond lengths of a variety of complexes of Pb(II) where it has been determined that the lone pair is

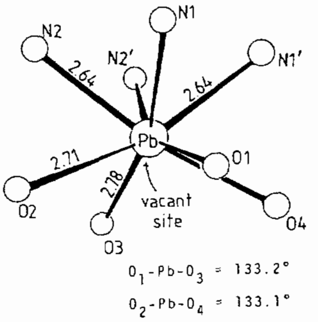


Fig. 6. View of the coordination sphere around the Pb(II) ion in the complex $[Pb(THP\text{-}12\text{-}aneN_4)]^{2+}$, showing the vacant coordination site. As discussed in the text, this vacant site is probably not occupied by a stereochemically active lone pair.

TABLE VII. Summary of Observations from Crystal Structures of some Pb(II) Complexes with Nitrogen and/or Oxygen Donors, Arranged in Increasing Coordination Number

Ligand[a]	Pb–N (Å)	Pb–O (Å)	*CN*[b]	Lone pair	Reference
Porphyrin	2.37	–	4	active[c]	21
9-aneN$_3$	2.44	2.86	6	active	7
pyN$_5$	2.54	–	6	active	22
16-aneN$_4$	2.54	2.86	7	active	23
EDTA	2.56	2.61	7	active	24
14-aneN$_4$	2.49	2.92	8	active	25
pyN$_3$O$_3$	2.62	3.06	8	inactive	26
THP-12-aneN$_4$	2.64	2.75	8	inactive	this work
18-aneN$_2$O$_4$	2.75	2.84	8	inactive[c]	27
Cryptand-222	2.88	2.85	10	inactive	28

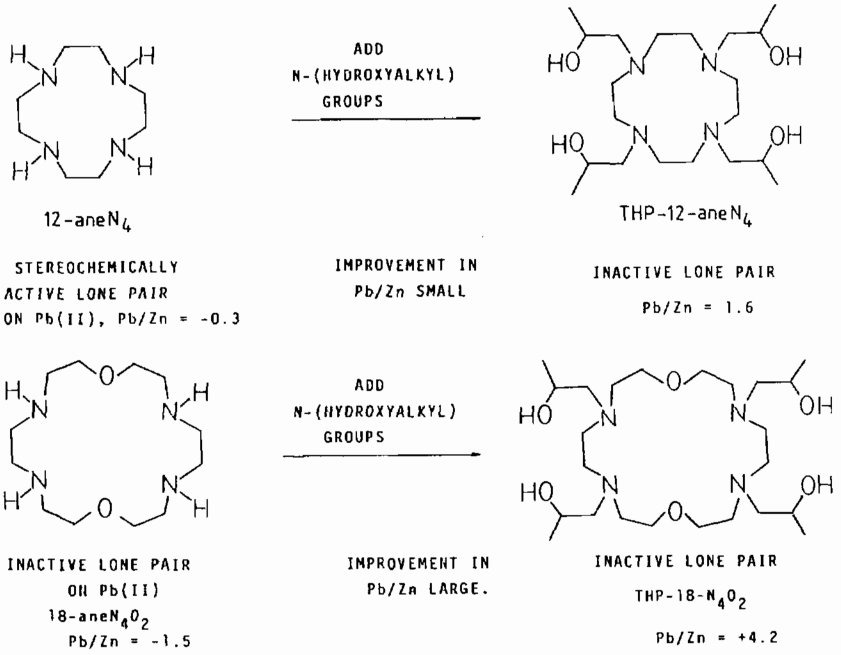
[a] For abbreviations of ligands, see Fig. 1. [b] *CN* = coordination number. [c] In these complexes the decision that the lone pair was either stereochemically active or inactive was taken by the present authors. For the porphyrin complex, the Pb atom is situated some 1.17 Å out of the plane of the ring, but has no donor atoms near it, suggesting an active lone pair. For the 18-aneN$_2$O$_4$ it was proposed [27] that the lone pair was active, but there is no real sign of this in the structure.

either active or inactive. It is seen that where the lone pair is active, the Pb–N bond lengths fall in the range 2.37 to 2.56 Å. On the other hand, for an inactive lone pair, the Pb–N bond lengths fall in the range 2.62 to 2.88 Å. On this basis, we would suggest that the lone pair in $[Pb(THP\text{-}12aneN_4)]^{2+}$ is inactive, since the Pb–N bond lengths at 2.64 Å fall into the bottom of the range for inactive complexes. The coordination numbers for active complexes tend to be 7 or less, and where a coordination number of eight has been found for an active Pb(II) complex, the Pb–N bond length is only 2.49 Å. It would thus seem that the addition of the 2-hydroxypropyl arms to 12-aneN_4 has forced the Pb(II), because of the higher coordination number, to switch from having a stereochemically active lone pair in $[Pb(12\text{-}aneN_4)]^{2+}$ to a stereochemically inactive lone pair in $[Pb(THP\text{-}12\text{-}aneN_4)]^{2+}$. The change of activity of the lone pair from active to inactive must be an energetically unfavourable process, rather like a change from low-spin to high-spin in Ni(II) or Fe(II), with regard to complex stability, and accounts for the much lower complex stability than expected for the Pb(II) complex of THP-12-aneN_4.

The conclusion that one comes to with regard to designing ligands which are selective for Pb(II) is that if the selectivity for Pb(II) over other smaller metal ions such as Zn(II) is to be optimized, when use is being made of the size-selectivity effects of added neutral oxygen donors [1], then cognizance must be made of the effects of the activity or non-activity of the lone pair on Pb(II) with regard to the apparent size of the metal ion. Thus, if a ligand such as 12-aneN_4 is selected as a starting point for ligand design, one must bear in mind that the Pb(II) has probably an active lone pair, and as such behaves as a very much smaller metal ion. Obviously one must select as a starting point a complex where the Pb(II) has not yet passed through the transition to an active lone pair. Thus, for example, the ligand 18-aneN_4O_2 appears from the discussion in the introduction not to have gone through the transition to an active lone pair in its complex with Pb(II). Thus, if hydroxyalkyl groups are added to 18-aneN_4O_2, instead of the drop in complex stability seen for Pb(II), and the modest increase in Pb/Zn selectivity, an increase in complex stability for the Pb(II) complex of THP-18-aneN_4O_2 plus a large increase in Pb/Zn selectivity is observed (Scheme 4). (Pb/Zn is log K_1 for the Pb(II) complex minus log K_1 for the Zn(II) complex.) The application of the idea of control of the apparent size of Pb(II) by whether the lone pair is stereochemically active or not will be more fully discussed in a future paper, where the complexing properties of ligands such as THP-18-aneN_4O_2 will be more fully discussed [29].

Supplementary Material

Tables of anisotropic thermal parameters and observed and calculated structure factors are available from the authors on request (11 pages).



Scheme 4.

Acknowledgements

The authors thank the Council Research Grants Committee of the University of the Witwatersrand, and the Foundation for Research Development, for financial support for this work.

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