

## Conformational Analysis of Macrocyclic Ether Ligands. II. 1,4,7,10,13-Pentaoxacyclopentadecane and 1,4,7,10,13-Pentathiacyclopentadecane

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### Abstract

Crystallographic results retrieved from the Cambridge Structural Database (CSD) have been used to perform a systematic conformational classification of free and metal-coordinated unsaturated 15-membered oxa and thia macrocycles using symmetry-modified Jarvis–Patrick cluster analysis. Relative molecular mechanics energies of the observed conformations are compared with the cluster populations. With oxa donors a uniaxial and a [348] conformer predominate for larger metal ions; these lie above the donor atom plane with 1–6 additional ligands bound on the same side. With smaller cations an anaxial conformer is adopted, the O atoms describing the equatorial plane of a pentagonal bipyramid. Other conformers occur as dictated by the coordination environment, particularly if not all donor atoms are metal-bound; in some cases the conformation is determined by a hydrogen-bonded network. In some thia examples the ligand binds to an axial/apical and four equatorial sites of the coordination polyhedron; in others containing Au<sup>I</sup> or Ag<sup>I</sup> the metal is linearly or tetrahedrally coordinated with additional M–S interactions. With mixed donors, the hard/soft characteristics of the metal determine the coordination mode.

### 1. Introduction

One of the most important areas of coordination chemistry that has developed over the last two decades is the metal-ion and host–guest chemistry of macrocyclic ligands, which now also has considerable biochemical relevance (Cram, 1988; Lehn, 1988; Pedersen, 1988; Lindoy, 1989). The chemistry of metal-ion macrocyclic complexes and the structures they adopt, in the solid state and in solution, are influenced by a variety of factors which include the size and ionic character of the metal ion and the flexibility and cavity size of the macrocycle (Constable, 1990). All these factors must be taken into account when tailoring ligands to recognize particular metal ions. Much research effort has centred on understanding the effect of altering the nature of the metal or the ligand on the stoichiometry and structure of the complexes formed (Blake &

Schröder, 1990). Both molecular mechanics methodologies (Blake, Gould, Halcrow & Schröder, 1993; Hay, Rustad & Hostetler, 1993; Lockhart *et al.*, 1992; Setzer, Tang, Grant & Van Derveer, 1991) and conformational mapping (Fyles & Gandour, 1992) have been applied to metal macrocycle complexes using crystallographic coordinates from the Cambridge Structural Database (CSD: Allen *et al.*, 1991; Allen & Kennard, 1993*a,b*) as the starting point for the analyses. However, the problems of including metals in molecular mechanics calculations have not been fully overcome and an alternative method based on trends observed in a large number of individual structures has been developed. We have successfully applied this technique using the methods of clustering and principal component analysis (PCA: Murray-Rust & Bland, 1978; Chatfield & Collins, 1980; Auf der Heyde, 1990) to the analysis of the conformations adopted by 1,4,7,10-tetraoxacyclododecane and 1,4,7,10-tetrathiadodecane and their derivatives both as free macrocycles and in their coordination complexes (Raithby, Shields & Allen, 1997).

In this paper we apply this methodology to the conformational analysis of 1,4,7,10,13-pentaoxacyclopentadecane and 1,4,7,10,13-pentathiacyclopentadecane, both as free macrocycles and in metal complexes, in order to examine the influence of size and ionic character of the metal ion on the structure adopted by their complexes.

### 2. Methodology

Version 5.09 (April 1995, 146,232 entries) of the Cambridge Structural Database (CSD) was used throughout. The programs *QUEST3D*, *GSTAT* and *VISTA* (Cambridge Structural Database, 1992, 1994, 1995) were employed for substructure search, information retrieval and data analysis.

Initial substructure searches located the required macrocycles (1) and (2) (Fig. 1) and their substituted derivatives. The group 16 atoms and C atoms (constrained to have a total coordination number of four, *i.e.*  $sp^3$  hybridized) were defined as being singly bonded in the search query. Secondary search criteria were used to select only those entries (a) with  $R \leq 0.10$ , (b) error-free

at the 0.02 Å level and (c) with an average e.s.d. of a C—C bond less than 0.03 Å or not specified. Entries with disorder reported in the macrocyclic ring (but not in any other part of the structure) were rejected after manual inspection. The retained CSD refcodes are reported in Table 1 and full literature citations have been deposited as supplementary material.\*

Conformational clustering was performed using the program *GSTAT* (Murray-Rust & Raftery, 1985*a,b*). Cluster analysis was based on the intra-annular torsion angles and the Jarvis–Patrick (Jarvis & Patrick, 1973) algorithm, as modified by Allen, Doyle & Taylor (1991) to take account of the permutational isomerism of the fragments. The data set was expanded to fill the topological symmetry space by the use of bond permutational symmetry operators and the inversion operator (which reverses the sign of every torsion angle). The Jarvis–Patrick procedure employs four user-defined variables: (i) a power factor (PWR) defining the metric to be used in dissimilarity calculations; (ii)  $K_{NN}$ , the maximum length of the nearest-neighbour list for each fragment ( $p$ ); (iii)  $K_{JP}$ , the Jarvis–Patrick clustering criterion, *i.e.* the number of fragments which must be common to the nearest-neighbour lists of fragments  $p_1$  and  $p_2$  such that both fragments may be assigned to the

\* Full literature citations for refcodes and principal component analysis data have been deposited with the IUCr (Reference: HA0153). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

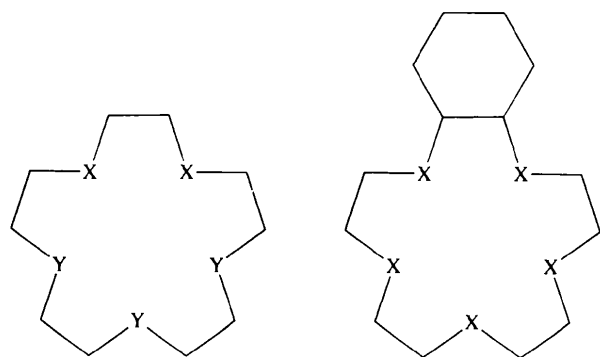
same cluster; (iv)  $D_{max}$ , a maximum dissimilarity above which pairs of fragments may not be nearest neighbours even if the  $K_{NN}$  limit is not exceeded. The values of the user-defined variables were adjusted manually until a chemically sensible set of conformational clusters was obtained. A symmetry-expanded list of torsion angles was generated in *GSTAT* and imported into *VISTA* for further statistical calculations and principal component analysis (PCA).

Molecular mechanics calculations were performed using a modified MM2 force field (Allinger, 1977; Allinger & Yuh, 1981), as implemented in the program *MacroModel*, Version 4.5 (Mohamadi *et al.*, 1990; Columbia University, 1994). Calculations were performed on the free ligands alone with explicit lone pairs on oxygen donor atoms. The initial structures for minimization were imported from the CSD if suitable examples existed; otherwise, the conformation was selected by the temporary imposition of appropriate torsional constraints. No attempt was made to model the behaviour of metal-coordinated species directly.

The conformers are designated in the shorthand notation of Dale (1963, 1973*a*): Two successive *gauche* torsion angles of the same sign are taken to constitute a corner and the number of bonds between corners are listed successively between square brackets. The starting point and direction followed round the ring are chosen so as to give the smallest overall number. Two successive *gauche* torsion angles of opposite signs constitute a pseudo-corner and are neglected in this treatment. An eclipsed bond (such as in a transition state between two conformers) is also taken to represent a side and is identified by an underscore (Dale 1973*b*).

### 3. Results

The ligands (1*a*) and (1*b*) (Fig. 1) have topological  $D_{5h}$  symmetry. The ten COCC torsion angles ( $\tau_1, \tau_3, \tau_4, \tau_6,$



1*a* X = Y = O.  
1*b* X = Y = S.  
1*c* X = S, Y = O.

Atom permutational operators:

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15  
4 5 6 7 8 9 10 11 12 13 14 15 1 2 3  
7 8 9 10 11 12 13 14 15 1 2 3 4 5 6  
10 11 12 13 14 15 1 2 3 4 5 6 7 8 9  
13 14 15 1 2 3 4 5 6 7 8 9 10 11 12  
4 3 2 1 15 14 13 12 11 10 9 8 7 6 5  
7 6 5 4 3 2 1 15 14 13 12 11 10 9 8  
10 9 8 7 6 5 4 3 2 1 15 14 13 12 11  
13 12 11 10 9 8 7 6 5 4 3 2 1 15 14  
1 15 14 13 12 11 10 9 8 7 6 5 4 3 2

Bond permutational operators:

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15  
4 5 6 7 8 9 10 11 12 13 14 15 1 2 3  
7 8 9 10 11 12 13 14 15 1 2 3 4 5 6  
10 11 12 13 14 15 1 2 3 4 5 6 7 8 9  
13 14 15 1 2 3 4 5 6 7 8 9 10 11 12  
3 2 1 15 14 13 12 11 10 9 8 7 6 5 4  
6 5 4 3 2 1 15 14 13 12 11 10 9 8 7  
9 8 7 6 5 4 3 2 1 15 14 13 12 11 10  
12 11 10 9 8 7 6 5 4 3 2 1 15 14 13  
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1

Fig. 1. Chemical substructures (1) and (2).

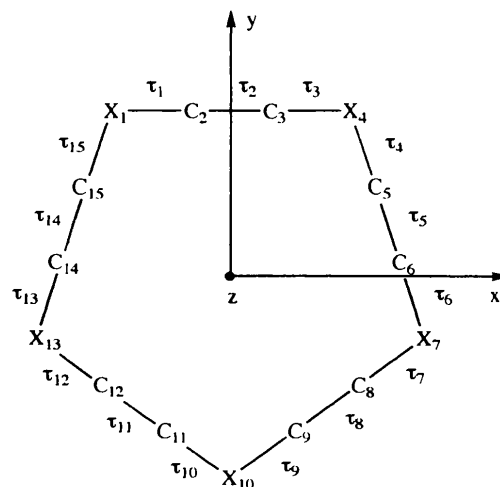


Fig. 2. Atomic and permutational symmetry groups for (1*a*) and (1*b*).

Table 1. CSD refcodes for fragments (1) and (2)

BEKWUJ	GEMXIF	KIPDOC	PASLEA	SOZGOD	VILMOS
BOGKUD	JAFGUS	KOGSII	PEHLOD	SUHCON	VOMWUP
BUTRUD	JAFGUS01	KOJGIZ	PEKWAD	TADFEJ	VUKKOB
CABLAS01	JAKCUT	KOKDIX	PXCDBA	TADLUF	WAHFAM
CABLEW	JAVKAS	KORKUX	PXCDCB	TAGFEM	WAHFOA
CAGTIN	JAZKAW	KOWJOV	SAMCIS	TAGGOX	WANSIN
CUXVIA	JETPAZ	KOYHAH	SAMZUB	TAZYUO	WATJAC
DECVAI01	JIGSUN	KOYZUT	SANBAK	TAZZAV	WATJEG
DUCNEU	JOZSOG	KOZKUF02	SANBEO	VAGFEO	WATJIK
FANRUH	JUSGAF	KUHXOA	SEHFUJ	VAJZAH	YAFYEJ
FAYVEG01	JUWKAN	KUPHEI	SEHHAO	VATLIL	YAFYIN
FAZLIB	KAJTUK	KURLOY	SESBUN	VATLUX	YARSOZ
FETPEZ10	KAPDUA	KUZJEU	SESCAU	VECNIA	YARSUF
FUYCIL	KAPFOW	LADSIJ	SEVXEW01	VEJMAY01	YARTAM
FUYCOR	KAVKAT	LESNEC	SIWHIP	VIFGAS	YATBEA
GAVPEY	KICKUC	PAFHOT	SIXBIK	VIFGEW	YAVCIH

Table 2. Symmetry coordinates for (1)

	IR	K	Co K	Deformation coordinate
$S_1$	$A_1''$	$D_5$	—	$1/10^{1/2}(\tau_1 + \tau_3 + \tau_4 + \tau_6 + \tau_7 + \tau_9 + \tau_{10} + \tau_{12} + \tau_{13} + \tau_{15})$
$S_2$	$A_1''$	$D_5$	—	$1/5^{1/2}(\tau_2 + \tau_5 + \tau_8 + \tau_{11} + \tau_{14})$
$S_3$	$A_2''$	$C_{5v}$	—	$1/10^{1/2}(\tau_1 - \tau_3 + \tau_4 - \tau_6 + \tau_7 - \tau_9 + \tau_{10} - \tau_{12} + \tau_{13} - \tau_{15})$
$S_{4a}$	$E_1''$	$C_1$	$C_2$	$1/5^{1/2}\{(\tau_1 + \tau_3) + \cos(2\pi/5)(\tau_4 + \tau_6 + \tau_{13} + \tau_{15}) + \cos(4\pi/5)(\tau_7 + \tau_9 + \tau_{10} + \tau_{12})\}$
$S_{4b}$	$E_1''$	$C_1$	—	$1/[2(5 - 5^{1/2})]^{1/2}\{(\tau_4 + \tau_6 - \tau_{13} - \tau_{15}) + 2 \cos(2\pi/5)(\tau_7 + \tau_9 - \tau_{10} - \tau_{12})\}$
$S_{5a}$	$E_1''$	$C_1$	$C_5$	$1/5^{1/2}\{(\tau_1 - \tau_3) + \cos(2\pi/5)(\tau_4 - \tau_6 + \tau_{13} - \tau_{15}) + \cos(4\pi/5)(\tau_7 - \tau_9 + \tau_{10} - \tau_{12})\}$
$S_{5b}$	$E_1''$	$C_1$	—	$1/[2(5 - 5^{1/2})]^{1/2}\{(\tau_4 - \tau_6 - \tau_{13} + \tau_{15}) + 2 \cos(2\pi/5)(\tau_7 - \tau_9 - \tau_{10} + \tau_{12})\}$
$S_{6a}$	$E_1''$	$C_1$	$C_2$	$(2/5)^{1/2}\{(\tau_2) + \cos(2\pi/5)(\tau_5 + \tau_{14}) + \cos(4\pi/5)(\tau_8 + \tau_{11})\}$
$S_{6b}$	$E_1''$	$C_1$	—	$1/(5 - 5^{1/2})^{1/2}\{(\tau_5 - \tau_{14}) + 2 \cos(2\pi/5)(\tau_8 - \tau_{11})\}$
$S_{7a}$	$E_2''$	$C_1$	$C_2$	$1/5^{1/2}\{(\tau_1 + \tau_3) + \cos(4\pi/5)(\tau_4 + \tau_6 + \tau_{13} + \tau_{15}) + \cos(2\pi/5)(\tau_7 + \tau_9 + \tau_{10} + \tau_{12})\}$
$S_{7b}$	$E_2''$	$C_1$	—	$1/[2(5 - 5^{1/2})]^{1/2}\{2 \cos(2\pi/5)(\tau_4 + \tau_6 - \tau_{13} - \tau_{15}) - (\tau_7 + \tau_9 - \tau_{10} - \tau_{12})\}$
$S_{8a}$	$E_2''$	$C_1$	$C_5$	$1/5^{1/2}\{(\tau_1 - \tau_3) + \cos(4\pi/5)(\tau_4 - \tau_6 + \tau_{13} - \tau_{15}) + \cos(2\pi/5)(\tau_7 - \tau_9 + \tau_{10} - \tau_{12})\}$
$S_{8b}$	$E_2''$	$C_1$	—	$1/[2(5 - 5^{1/2})]^{1/2}\{2 \cos(2\pi/5)(\tau_4 - \tau_6 - \tau_{13} + \tau_{15}) - (\tau_7 - \tau_9 - \tau_{10} + \tau_{12})\}$
$S_{9a}$	$E_2''$	$C_1$	$C_2$	$(2/5)^{1/2}\{(\tau_2) + \cos(4\pi/5)(\tau_5 + \tau_{14}) + \cos(2\pi/5)(\tau_8 + \tau_{11})\}$
$S_{9b}$	$E_2''$	$C_1$	—	$1/(5 - 5^{1/2})^{1/2}\{2 \cos(2\pi/5)(\tau_5 - \tau_{14}) - (\tau_8 - \tau_{11})\}$

NB  $\cos(2\pi/5) = [(5^{1/2} - 1)/4]$ ;  $\cos(4\pi/5) = -[(1 + 5^{1/2})/4]$ .

$\tau_7, \tau_9, \tau_{10}, \tau_{12}, \tau_{13}, \tau_{15}$ ; Fig. 2) span the representations  $A_1'' \oplus A_2'' \oplus 2E_1'' \oplus 2E_2''$ , whilst the five OCCO torsion angles ( $\tau_2, \tau_5, \tau_8, \tau_{11}, \tau_{14}$ ) span  $A_1'' \oplus E_1'' \oplus E_2''$ . Symmetry-adapted linear combinations, of which three are formally redundant, are detailed in Table 2 with their kernel and co-kernel (McDowell, 1965) symmetries.

The search yielded 96 hits comprising 130 fragments, comprising 117 (1/2a) (99  $\eta^5$ ; 1  $\eta^2, \eta^2$ ; 2  $\eta^2$ ; 15 free), 10 (1/2b) (4  $\eta^5$ ; 4  $\eta^3, \eta^1$ ; 2  $\eta^1, \eta^1$ ) and 3 (1/2c) ( $\eta^2$ -S, S') examples. The most reasonable set of conformational clusters (Table 3) was obtained with  $K_{NN} = 12$ ,  $K_{JP} = 4$ ,  $D_{max} = 0.15$  and PWR = 1. Ideal point-group symmetries are given, corresponding to the symmetry of the special position occupied by the cluster centroid in the 15-dimensional parameter space. It was necessary to reduce the parameter which determines how close a symmetry-generated fragment must be to the original cluster centroid (based on permutations initially matched) for it to be considered equivalent and included in the symmetry-expanded cluster mean to 0.5 (from the default value of 1.0) to prevent inequivalent permuta-

tions from being considered. The symmetry-expanded mean torsion angle sequence (Table 3) corresponds to the final cluster centroid in the conformational space, but may not necessarily represent a realisable geometry in real space given the constraint of ring closure. The most representative fragment (Fig. 3) is that closest to the cluster centroid, the distance being determined according to the value of PWR.

Principal component analysis eigenvalues and eigenvectors for the symmetry-expanded data set (ten atomic permutations plus inversion) have been deposited.  $A_1''$  and  $A_2''$  deformations maintain  $D_5$  and  $C_{5v}$  symmetry, respectively, and an arbitrary deformation along both preserves  $C_5$  symmetry. Whereas the sole  $A_2''$  coordinate  $S_3$  accounts for a significant proportion of the variance (PC<sub>3</sub>, 14.3%),  $A_1''$  distortions are relatively unimportant; most of the variance is described by degenerate  $E_1''$  and  $E_2''$  coordinates. The principal component analysis does not lead to a substantial reduction in dimensionality. Furthermore, since most of the fragments comprise  $C_2$ ,  $C_5$  and  $C_1$  conformers, it is not effective in distinguishing

Table 3. Cluster analysis results for fragments (1) and (2)

Cluster	(1)	(4)	(2)	(5)	(3)	(7)	(6)	(8)	Free(1b)	
Size	33	24	18	14	5	4	4	3		
Conformer	Uniangular	Anangular	[348]	[ <u>1</u> 14]	[339], [23334]	[23343], [3435]	[ <u>1</u> 383]	Uniangular		
Symmetry	$C_1$	$C_2$	$C_1$	$C_s$	$C_1$	$C_1$	$C_s$	$C_1$	$C_1$	
Most representative fragment	KAPDUA	FETPEZ10 (b)	CABLAS01	WATJAC(a)	KOYZUT	PEHLOD	SIXBIK	SAMZUB, SANBAK, SANBEO‡	FOPCES	
Mean or most representative	-179.5 (10)	178.6 (12)	179.9 (23)	-179.7 (14)	-176 (4)	179 (4)	177 (4)	-179.8	-121.9	
(‡) torsion angle sequence/ <sup>o</sup>	61.1 (9)	57.1 (10)	-57.2 (23)	42.9 (39)	-66.8 (16)	-61 (4)	-56 (8)	61.3	91.0	
	-157.9 (11)	-178.6 (12)	-88.0 (19)	-179.0 (18)	-85 (4)	-72 (10)	-95 (9)	-154.2	174.4	
	163.3 (7)	179.9 (11)	171.8 (12)	179.0 (18)	176 (2)	-166 (9)	164 (6)	167.3	82.8	
	-59.8 (7)	-59.0 (14)	-61.7 (19)	-42.9 (39)	-67 (3)	-60 (7)	-52 (13)	-60.7	113.8	
	-177.2 (9)	169.8 (12)	-173.6 (21)	179.7 (14)	-81 (4)	-119 (8)	-156 (10)	-172.9	-63.9	
	-171.1 (12)	-176.9 (11)	167.4 (25)	178.4 (26)	-179 (7)	94 (13)	156 (10)	125.6	-88.5	
	66.1 (6)	48.5 (13)	58.8 (13)	37.6 (32)	-69.7 (10)	70 (4)	52 (13)	90.3	84.3	
	-172.2 (5)	154.5 (12)	-161.0 (18)	174.1 (20)	-142 (20)	-178 (2)	-164 (6)	-131.3	166.6	
	92.4 (23)	154.5 (12)	81.4 (12)	170.1 (22)	116 (26)	74 (6)	95 (9)	165.6	-156.4	
	51.9 (20)	48.5 (13)	58.6 (16)	0.0 (0)	62.1 (13)	66 (4)	56 (8)	-53.7	-78.4	
	-176.1 (16)	-176.9 (11)	-176.3 (15)	-170.1 (22)	-172 (5)	-173 (2)	-177 (4)	-133.8	167.0	
	165.7 (10)	169.8 (12)	-177.6 (13)	-174.1 (20)	180 (2)	172 (4)	133 (7)	180.0	-80.9	
	-64.8 (7)	-59.0 (14)	-56.1 (14)	-37.6 (32)	-58 (2)	-66 (3)	0.0 (0)	-65.4	-76.1	
	172.5 (9)	-179.9 (11)	-96.4 (35)	-178.4 (26)	-73 (5)	-80 (1)	-133 (7)	178.0	-171.9	
Singletons										
1	1	1	1	1	1	2	3	3	2	1
[249]	[2436]	[33333]	[411]	[510]	[357]	[12345]	[12354]	[1284]	[12156]	[121272]
$C_1$	$C_1$	$C_s$	$C_1$	$C_1$	$C_1$	$C_1$	$C_1$	$C_1$	$C_1$	$C_1$
CAGTIN	BEKWUJ	PXCDBA	KOWJOV	TADFEJ	KICKUK	SUHCON	SUHCON	VIFGAS	KURLOY‡	LADSIS
(a)		(b)	(c)			(a‡,b)	(c‡,d)	VIFGEW	CUXVIA	
							PAFHOT	(a‡,b)		
-175.0	-168.7	-179.3	-163.2	178.6	61.0	168.4	167.0	-167.2	66.8	-166.3
45.9	51.9	-57.2	73.6	-56.0	-67.1	-75.1	-78.6	60.2	44.7	50.7
92.7	113.4	-81.6	-156.5	-59.7	167.1	130.5	143.5	79.4	81.2	88.8
-95.9	-159.6	-173.0	156.0	-164.2	-149.8	-77.4	-82.4	42.5	-140.6	-61.0
-50.1	-4.5	-80.9	61.9	-50.2	53.5	-68.2	-72.1	-84.4	55.1	-44.1
-159.8	172.8	-88.8	-169.7	-130.9	88.3	160.5	165.0	-81.0	-151.5	-89.4
161.8	-172.3	-171.8	90.6	73.5	-172.9	-177.0	-82.4	164.8	158.6	81.9
51.4	16.8	-59.6	-75.0	61.2	51.3	61.6	-59.2	-73.6	-37.2	45.4
90.6	112.5	-78.9	177.5	-177.1	86.7	73.6	173.0	-174.8	-100.0	69.2
-139.6	-92.6	163.1	-78.4	164.4	179.8	-165.0	-160.9	-176.8	169.4	-85.8
31.3	-54.5	-33.6	-68.0	-68.9	75.4	71.5	68.6	69.6	-64.3	-46.9
159.9	-167.7	-121.4	176.7	167.7	-76.5	95.3	86.9	-161.3	148.8	151.2
-158.3	169.3	179.6	-174.5	-173.9	114.9	-64.7	-61.5	77.4	-74.6	-162.8
-44.3	55.6	-66.7	53.8	62.5	39.2	-55.4	-51.4	73.1	-42.1	32.3
176.7	86.4	-91.5	81.2	-149.0	177.8	-59.8	-63.5	-54.6	-76.3	112.7

conformations on the basis of symmetry and is thus of limited value in allowing cluster visualization in conformational space.

$PC_1$  and  $PC_2$  (each accounting for 14.8% of the variance) comprise linear combinations of  $S_7$ ,  $S_8$  and  $S_9$  and neither  $C_2$  nor  $C_s$  co-kernel symmetry is conserved along any direction in the arbitrary plane they describe in conformational space (Fig. 4a). Similarly, scatterplots of  $PC_1$  versus  $PC_3$  (Fig. 4b) and  $PC_1$  versus  $PC_4$  (Fig. 4c) do not discriminate between  $C_2$ ,  $C_s$  and  $C_1$  conformers. A scatterplot of  $S_{7a}$  versus  $S_{8a}$ , coordinates contributing to  $PC_1$  and  $PC_2$  (Fig. 4d), does, however, allow  $C_s$  and  $C_2$  to be distinguished from  $C_1$  fragments. Those with apparent  $C_s$  symmetry ( $[114]$ ,  $[1383]$ ) appear along the  $S_{8a}$  axis and those with  $C_2$  symmetry (anangular) along  $S_{7a}$ , with  $C_1$  fragments on neither axis.

## 4. Discussion

### 4.1. 1,4,7,10,13-Pentaoxacyclopentadecane

Dale (1973a) suggested that the quinquangular [33333] conformation of the parent cyclopentadecane has the lowest energy with other less regular quinquangular conformations having slightly higher energies. Triangular [339], [348], [447], [357], [555] and [456] conformers were all predicted to have energies more than 14 kJ mol<sup>-1</sup> higher than [33333]. A CSD search for simple unsaturated 15-membered carbocyclic rings yielded no hits. The lowest-energy conformations for (1a) differ due to the preferences for *anti* COCC and *gauche* OCCO torsion angles (Podo, Némethy, Indovina, Radics & Viti, 1974; Zefirov, 1977; Uiterwijk, Harkema, van der Waal, Göbel & Nibbeling, 1983),

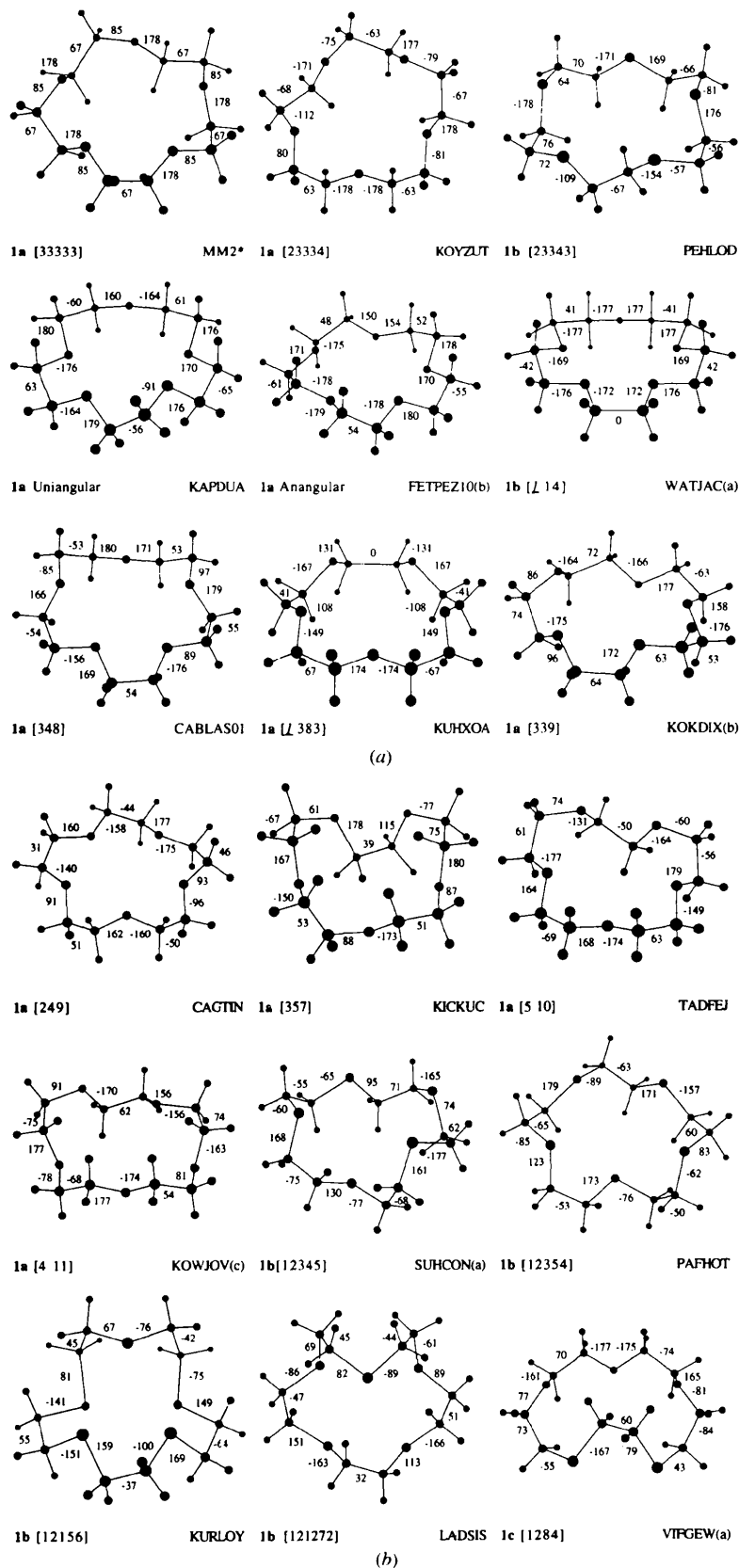


Fig. 3. Perspective views of selected conformers of (1) and (2) from CSD entries and molecular mechanics calculations with torsion angles in degrees.

which are incompatible with fivefold symmetry. We believe that the crystal structure of free (1a) has not been determined: the ligand remains a liquid to very low temperatures (Arte, Feneau-Dupont, Declercq, Germain & Van Meerssche, 1979). The favoured torsion angle placements are achieved in the commonly observed  $D_{3d}$  anangular (A+GAA-GA)<sub>3</sub> conformation of the larger [18]aneO<sub>6</sub> macrocycle (Fyles & Gandour, 1992). Removal of one O(CH<sub>2</sub>)<sub>2</sub> unit produces (1a) with two

successive *gauche* OCCO torsion angles of the same sign. For ring closure either one *anti* COCC torsion angle must be rotated to  $\pm G$  [cluster (1); Arte, Feneau-Dupont, Declercq, Germain & Van Meerssche, 1979], one OCCO torsion angle must become staggered [cluster (5); Wei, Tinant, Declercq, Van Meerssche & Dale, 1988] or there must be a systematic deviation of the torsion angles from their ideal ( $\pm 60, 180^\circ$ ) values in that portion of the ring [cluster (4); Larson, Simonsen, Ramsden & Lagowski,

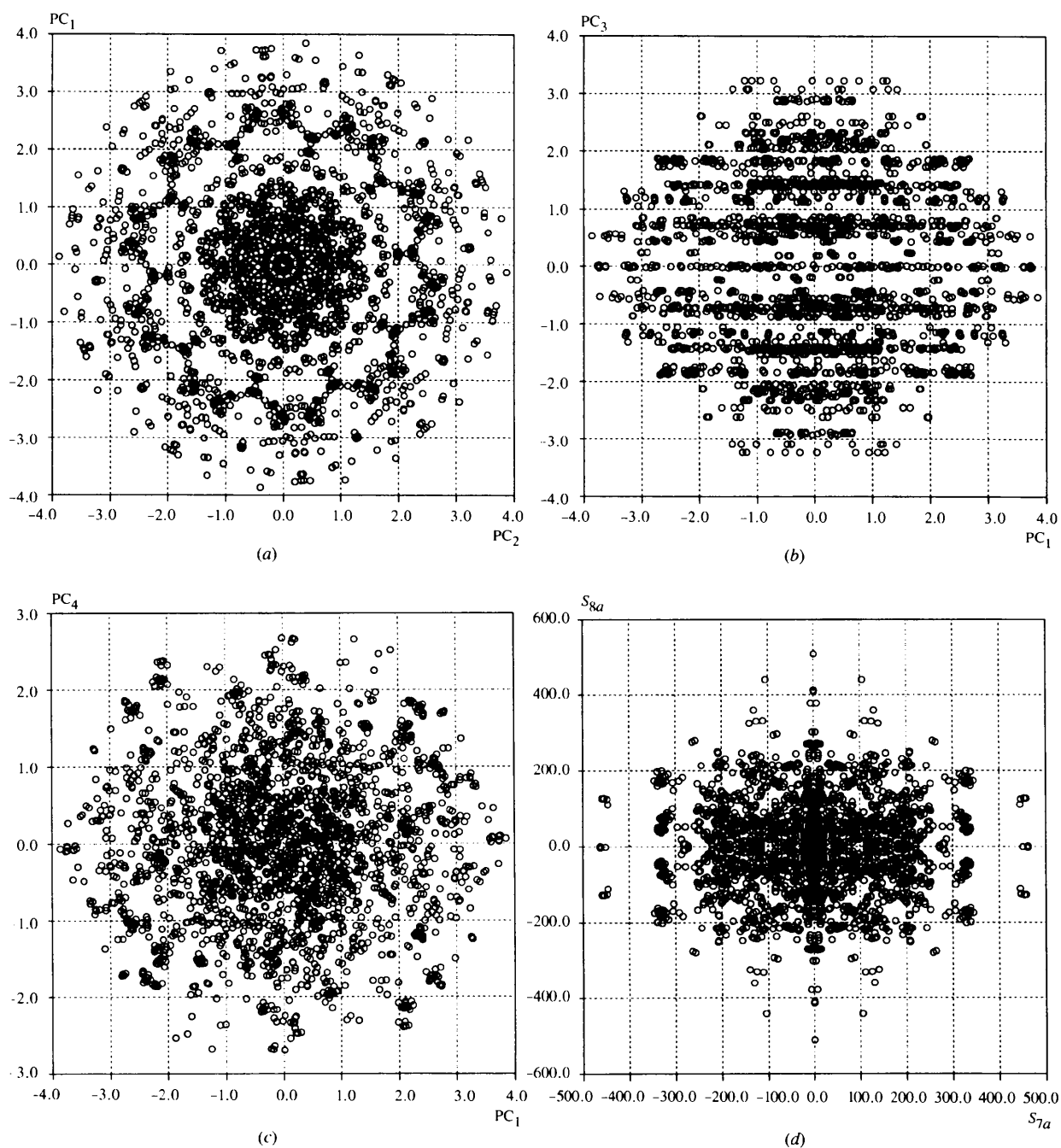


Fig. 4. Scatterplots of principal component scores for fragments (1) and (2).

Table 4. *Molecular mechanics minimized conformations of (1a)*

Conformation	An- angular	Uni- angular	[348]	[339]	[357]	[249]	[3435]	[2436]	[33333]	[23334]	[510]	[411]	[78]	[114]	[1383]
Relative energy (kJ mol <sup>-1</sup> )	1.3	0.0	7.3	9.2	17.9	11.9	19.9	23.5	23.1	21.4	11.6	6.0	13.7	13.6	26.5
Torsion angle sequence	-172	-178	180	-168	7	-179	173	-168	178	-179	179	-159	-168	-163	-176
	65	63	-76	-69	-81	56	-53	54	67	-68	-50	65	-35	65	-44
	-172	-161	-90	-94	165	70	-57	67	85	-89	-53	179	-68	-172	-70
	175	168	167	178	-169	-107	-174	-176	178	178	-170	173	169	171	167
	-66	-60	-70	-73	61	-59	-59	59	67	-60	-57	67	-69	-66	-67
	151	-178	177	-92	82	-172	-145	176	85	-62	-138	-168	173	164	177
	-170	-171	178	161	178	-165	86	170	178	-165	79	101	177	-173	-177
	54	72	67	-71	70	70	66	49	67	-65	54	-69	65	58	66
	165	-169	-159	173	80	82	-167	68	85	-117	-179	180	-164	179	-167
	165	85	83	-179	172	-145	83	-106	178	70	164	-82	76	170	71
	54	57	61	62	78	68	58	-52	67	60	-66	-67	55	0.0*	44
	-170	176	-177	-168	-78	-178	175	-176	85	-178	168	177	162	-170	176
	153	164	-179	178	114	173	175	-166	178	-176	-175	177	176	-179	170
	-66	-69	-61	-50	68	-65	-64	68	67	-57	66	53	-53	58	0.0*
	175	169	-80	-59	171	175	-84	88	85	-78	-159	78	-154	173	-170

\* Angle constrained in minimization.

1990]. Such conformations maximize the number of favourable *anti* COCC torsion angles. In complexes of the uniaxial type the *gauche* COCC angle is generally much larger than 60° [mean 92 (2)° in cluster (1)]. This relieves CH...HC repulsive interactions, whilst allowing the donor atoms to adopt a more planar geometry (Blaschette, Nagel & Jones, 1993).

The uniaxial conformation is the most common and cluster (1) comprises six- (pentagonal pyramidal), seven- and eight-coordinate Na<sup>+</sup> complexes, six-coordinate Li<sup>+</sup> complexes and compounds with (1a) in the second coordination sphere of a metal ion. In alkali-metal complexes the bonding is principally ionic and the cation is bound to five O atoms of the macrocyclic ether and one, two or more additional donor atoms on the same side of the macrocycle. A [6 + 1]-coordination mode is common for Na<sup>+</sup>, with six shorter bonds to the macrocycle and another ligand and a longer bond to the seventh donor atom. On average, the Na ion lies 0.89 (2) Å above the mean plane of the O atoms with a mean Na—O distance of 2.457 (6) Å in cluster (1) complexes, whereas the average distance from the donor atoms to the donor atom centroid is 2.28 (3) Å. This is consistent with the demonstration by Shoham & Cohen (1989) that the van der Waals cavity diameter of 1.21–1.71 Å (Shoham, Lipscomb & Olsher, 1983) is too small for the coplanar coordination of six- and seven-coordinate Na ions. Closely related to these examples are three fragments in cluster (8), which have the same +G,–G,+G,+G,–G OCCO torsion angle sequence as the uniaxial conformer, but three near-eclipsed COCC torsion angles. These contain Na<sup>+</sup> in a pentagonal–pyramidal coordination environment with the sixth contact to a Se atom of a (Se<sub>4</sub>)<sub>2</sub>M unit (M = Zn, Cd, Hg). The Na—O distances were constrained in the refinements of the Zn and Hg structures (Adel, Weller & Dehnicke, 1988), suggesting that it might not have been possible to determine accurate C-atom positions; alternatively they

may be subject to slight thermal disorder. Several other six- and seven-coordinate sodium complexes, which appear as singletons, also adopt distorted variants of the uniaxial conformation.

The O atoms deviate from their mean plane in an up–up–down–up–down manner [two adjacent O atoms must be directed to the same side in an odd-membered ring (Shoham & Cohen, 1989)] with a mean absolute deviation from the plane of 0.305 (4) Å for the 33 fragments in cluster (1). The five O atoms adopt an approximate envelope conformation with one O atom deviating substantially from the plane of the other four (Coleman, Villain, Navaza, Galons & Miocque, 1991; Rubtsova *et al.*, 1992). The low symmetry of the ligand is reflected in the inequivalent Na—O distances; typically there are two shorter and two longer Na—O distances, whilst the fifth is usually similar to the longer pair of distances or is longer still. This pattern is a consequence of the envelope conformation (Coleman, Villain, Navaza, Galons & Miocque, 1991; Blaschette, Nagel & Jones, 1993) of the donor atoms.

The ligand is also found in the second coordination sphere of metal atoms in this conformation. It can act as a hydrogen-bond acceptor to two H atoms on each side of the ring, one of the O atoms remaining uninvolved in the network (Arte, Feneau-Dupont, Declercq, Germain & Van Meerse, 1979). Such bonding leads to dimerization (*e.g.* KOKDIX) or the formation of polymeric chains (DUCNEU, FANRUH, KAPFOW, KUZJEU and PXCDCB). The singletons KUPHEI and VUKKOB also have such a hydrogen-bonding network and a similar, although more distorted, conformation.

The other conformation commonly adopted in complexes in which the metal is not approximately coplanar with the donor atoms is the triangular [348] [cluster (2); Wei, Tinant, Declercq, Van Meerse & Dale, 1988]. The OCCO torsion angle sequence (–G,–G,+G,+G,–G) includes three pairs of adjacent *gauche* OCCO of the

same sign, requiring three unfavourable *gauche* COCC torsion angles. The latter deviate substantially from  $\pm 60^\circ$  towards eclipsed values (Rogers *et al.*, 1991). Molecular mechanics calculations (Table 4) show this conformer to be somewhat higher in energy than the uniangular, chiefly due to the less favourable torsion angles.

The [348] conformation is found with a wider range of metals and coordination numbers than the uniangular conformer, being adopted in six- and seven-coordinate Na, eight-coordinate lanthanide/Ca, ten-coordinate pentagonal anti-prismatic  $(1a)_2M^{2+}$  sandwich complexes (TAGFEM, WAHFOA [ $M = Cs$ ] and YATBEA [Ba]) and eleven-coordinate  $(1a)Ln(\eta^2\text{-NO}_3)_3$  complexes (BUTRUD [Ln = Ce], CABLAS01 [La] and CABLEW [Nd]). The binding to the alkali metal, alkaline earth or lanthanide cations is predominantly electrostatic and interligand repulsions, subject to the restrictions imposed by chelate rings and the macrocyclic backbone, determine the coordination geometry. The eight-coordination polyhedron has been described as 'irregular' (Wei, Tinant, Declercq, Van Meerssche & Dale, 1988) or 'bicapped trigonal prismatic' [SOZGOD (Rogers *et al.*, 1991)]; two of the macrocyclic O atoms are in capping positions and their metal–oxygen distances are 2.630(8) Å, *cf.* 2.55(4) Å for the other three]. The more common dodecahedral ( $D_{2d}$ ) and square-antiprismatic ( $D_{4d}$ ) geometries (Drew, 1977) cannot be attained in the 3:5 coordination mode, given the limited flexibility of the macrocyclic ether.

The  $(1a)$  ligands in [J383] fragments (cluster 6) approach  $C_s$  symmetry with a planar OCCO unit. The [J383] is related to the [348] by the formal replacement of an  $A-G-G$  by an  $+E$ , *syn*,  $-E$  sequence. It represents a saddle point on the conformational energy surface and its apparent existence may be the result of static or dynamic disorder involving two mirror-image [348] conformers with  $A-G-G$  and  $+G+GA$  OCCO sequences. Molecular mechanics minimization (Table 4) with the torsion angle of the *syn*-periplanar C—C bond constrained to 0 gave an energy 19.1 kJ mol<sup>-1</sup> higher than the [348] with the donor atoms describing a pronounced envelope conformation. Subsequent free minimization is accompanied by relaxation to a [78] conformer in which the *syn* OCCO torsion angle becomes *gauche*, but both eclipsed bonds become *anti* (rather than *gauche* as in the [348]) requiring a small ( $-35.5^\circ$ ) OCCO torsion angle in the adjacent  $O(\text{CH}_2)_2$  unit. Since the donor atoms still show a high deviation from planarity, it is unlikely that this conformation is as important as the [348] in these metal-coordinated species. Both  $(1a)\text{AsBr}_3$  JIGSUN and  $(1a)\text{TeCl}_3^+$  KUHXA lie on a crystallographic mirror plane that forces a flat OCCO unit in the absence of disorder. The C—C single bond distance in JIGSUN is 1.143 Å, which seems unrealistic for a static *syn*-periplanar unit. The existence of disorder is also supported by the values of the *anti* torsion angles either

side of the *syn*-periplanar OCCO bond: they are much closer to  $180^\circ$  in the molecular-mechanics minimized structure (Table 4) than in the crystal fragments where they approach eclipsed placements.

Similar disorder, in the absence of crystallographic mirror symmetry, may exist in the structures of the centrosymmetric  $\text{Sr}(1a)_2$  sandwich complex JUWKA and the 11-coordinate  $(2a)\text{La}(\text{NO}_3)_3$  SIXBIK, which both have approximately [J383] conformations. The complex  $(1a)\text{Eu}(\text{NO}_3)_3$  BEKWUJ has a similar stereochemistry to SIXBIK; the coordination polyhedron can be described as a distorted monocapped pentagonal antiprism with a nitrate O atom in the capping position; the ether O atoms in the basal plane adopt an envelope conformation. The macrocycle has two almost *syn*-periplanar OCCO torsion angles, attributed to slight fluxional thermal motion (Bunzli, Klein, Chapuis & Schenk, 1982). The conformation minimized to [2436] (Table 4), although it is likely that the lower-energy [348] conformer is also involved in the dynamic processes. Thus, all fragments of the general formula  $(1/2a)Ln(\text{NO}_3)_3$  essentially adopt conformations based on [348].

JOZGOG is interesting in that both the uniangular and [348] conformers are present in the same structure, which contains two independent pentagonal–pyramidal sodium ions each bonded to one end of a  $S_6^{2-}$  chain. The co-existence of these conformers would seem to indicate that there is little energy difference for coordinated ligands and intermolecular interactions are important in determining the precise conformation in the solid state. The Na—O distance and Na—O mean plane distance for the four Na complexes in cluster (2) do not differ significantly from those of cluster (1), suggesting that both conformations are suited to sodium binding.

The larger lanthanide ions are displaced further from the oxygen plane and oxygen–metal distances are longer than those for  $\text{Na}^+$ . However, the mean hole size in [348] lanthanide complexes [2.218(9) Å] is slightly smaller than for [348] Na examples [2.289(8) Å], since the crown ether occupies a smaller portion of the coordination polyhedron. This indicates a reasonable degree of flexibility in the [348] conformation of  $(1a)$ , explaining its ability to participate in a wide range of coordination geometries. However, in some circumstances other conformations may be more suitable: the nine-coordinate  $(1a)\text{Sm}(\text{H}_2\text{O})_4$  complex CAGTIN has the macrocyclic ligand in a [249] conformation, related to the uniangular by rotation of two adjacent *anti* torsion angles to  $93$  and  $-96^\circ$ , respectively, to give three *gauche* COCC torsion angles in total. The [249] conformation has a slightly higher energy than [348] (Table 4); the donor atoms adopt a twist configuration (mean absolute deviation from planarity 0.366 Å), allowing a more ideal nine-coordination polyhedron around the metal.

The [348] conformer of  $(1a)$  also occurs hydrogen-bonded to the  $\text{H}_3\text{N}^+\text{SO}_3^-$  zwitterion in the host–guest complex KOGSII. The unit cell contains two inde-



pendent complexes and there are five N...O(crown) distances of 2.8–3.0 Å, as well as one short N...O distance (2.9 Å) to a symmetry-related amidosulfuric acid zwitterion in each (Dvorkin *et al.*, 1991). Similar NH<sub>3</sub><sup>+</sup>...O(crown) interactions were reported in inclusion compounds of amidosulfuric acid with [18]aneO<sub>6</sub> (Seel, Klein, Krebs, Dartmann & Henkel, 1985) and a [18]aneO<sub>6</sub> derivative (Fonar *et al.*, 1989). The macrocycle in the latter adopts the archetypal *D*<sub>3d</sub> conformation with NH...O contacts to every alternate ether O atom and similar interactions are probably present in the (1a) structure. Similarly, in CAGTIN, three metal-coordinated water molecules form hydrogen bonds to (1a) in a distorted [348] conformation, which allows four such bonds to the same side of the macrocycle. In contrast, the shortest intermolecular CH...O contacts in VILMOS between the crown ether and Mo( $\eta^2$ -O,O'-Me<sub>2</sub>O(CH<sub>2</sub>)<sub>2</sub>OMe<sub>2</sub>)Cl<sub>4</sub> are at 2.44, 2.52 and 2.56 Å.

The quinquangular [23343] conformer [cluster (7)] exhibited by PXCDBA is related to [348] by the rotation of a pair of anti-periplanar COCC, CCOC torsion angles to *-G* and *+G*, respectively, maintaining the *-G,-G,+G,+G,-G* OCCO torsion angle sequence, but giving five unfavourable COCC torsion angles. The [3435] conformer exhibited by the [6 + 1] Na complex TADLUF is intermediate between the two, having one *+G* rather than an *anti* torsion angle, whilst the other is nearer to *anti* ( $-141^\circ$ ); this requires some systematic deviation of the other torsion angles. Molecular mechanics calculations (Table 4) gave similar torsion angle values and showed it to be higher in energy than [348] as a result of a less favourable bond angle and torsional terms. The donor atoms in the complex are more coplanar than in the [348] conformation (mean absolute deviation 0.066 Å); the average sodium–oxygen bond length is longer than typical [2.63 (11) Å], whilst one of the Na–F bonds is particularly short [2.260 (7) Å].

The additional *gauche* COCC torsion angles in [23343] PXCDBA are much larger than the other three [83.2 (8)°] and are almost eclipsed [117 (2)°], allowing a more coplanar configuration of the donor atoms (mean absolute deviation 0.09 Å from mean plane). The other (1a) ligand in the ten-coordinate sandwich complex adopts the [33333] quinquangular conformation (the only example in the data set) having an all *-G* OCCO sequence. With ideal *C*<sub>5</sub> symmetry the five O atoms are precisely coplanar and directed to the same side of the ring (analogous to the [3333]B conformation of [12]aneO<sub>4</sub>; Raithby, Shields & Allen, 1997). Molecular mechanics calculations showed this conformer to be considerably higher in energy than the uniaxial (Table 4) with systematically larger *gauche* COCC (84.9°) than OCCO (67.3°) torsion angles. Since some of the OCCO torsion angles in the PXCDBA approach *syn* placements, it is possible that the macrocycle is subject to slight thermal disorder. YATBEA contains

another ten-coordinate barium sandwich cation; both macrocycles have the lower energy [348] conformation and slightly longer average Na—O bond distances than in PXCDBA (2.842 *versus* 2.822 Å): the quinquangular conformations may allow stronger binding to the cation at the expense of greater strain in the macrocycle.

The [339] conformation has three unfavourable *gauche* COCC torsion angles, as with [348], but has a *-G,-G,-G,+G,-G* OCCO sequence (Table 4). The [23334] conformation is related to [339] in the same way that [23343] is to [348], *i.e.* by a systematic deviation of two successive *anti* COCC, CCOC torsion angles to *-G* and *+G*, respectively. Both conformers are represented in cluster (3), [339] by KOKDIX in which (1a) is not directly coordinated to the metal and three hydrogen bonds are formed to the same side of the ring. The donor atoms are directed in an up–up–up–down manner with one of the 'up' atoms further above than the others so as to form an approximate envelope. It has a similar energy to the [348] conformation and is probably dictated by the nature of the hydrogen-bonding network: two Y(H<sub>2</sub>O)<sub>3</sub>(NO<sub>3</sub>)<sub>3</sub> molecules form a hydrogen-bonded dimer, one water molecule on each forming two hydrogen bonds on opposite sides of (1a) in the uniaxial conformation and the remaining two water molecules coordinated to each yttrium forming three bonds to the [339] (1a) ligand and to an acetone solvent molecule.

The [23334] conformation is adopted in the eight-coordinate 3:5 complexes (1a)SbCl<sub>3</sub> FAZLIB, (1a)SbBr<sub>3</sub> KOYZUT and (1a)AsCl<sub>3</sub> WANSIN. The stereochemically active lone pair of the pyramidal EHal<sub>3</sub> unit is directed into the centre of the ring so as to interact with the oxygen donor atoms of the crown ether. The oxygen–metalloid distances are much greater than the usual covalent distances and the geometry of the EHal<sub>3</sub> moiety is changed little on complexation (Hough, Nicholson & Vasudevan, 1987). In contrast, although (1a)BiCl<sub>3</sub> KOZKUF is isomorphous (Alcock, Ravindran & Willey, 1993), it has the [348] conformation with the five donor atoms less precisely coplanar, as does the isostructural (1a)BiBr<sub>3</sub> (Rogers, Bond, Aguinaga & Reyes, 1992). This was attributed to the large size of Bi imposing different steric requirements on the ligand atoms. However, (1a)AsBr<sub>3</sub> JIGSUN and (1a)TeCl<sub>3</sub><sup>+</sup> KUHXA also have an essentially [348] conformation. This is another instance where intermolecular forces, as well as subtle differences in geometry around the metalloid, may be instrumental in determining the solid-state conformation. The donor-atom distances are shorter in the Te than in the Sb compound, despite the larger covalent radius of the former, consistent with significantly stronger binding to the cationic EHal<sub>3</sub><sup>+</sup> moiety.

A very different coordination mode is exhibited by (1a) and (2a) in clusters (4) and (5). Cluster (4) represents an angular conformation with ideal *C*<sub>2</sub> symmetry and no *gauche* COCC torsion angles (Larson, Simonsen,

Ramsden & Lagowski, 1990). Molecular mechanics calculations (Table 4) suggest that this conformer is very slightly higher in energy than the uniaxial, principally as a result of greater van der Waals repulsion between the O atoms which are directed in a more endodontate manner. This configuration permits a more coplanar disposition of the five oxygen donor atoms and is particularly suited to the binding of relatively small metal ions, including  $Mn^{II}$ ,  $Fe^{II}$ ,  $Co^{II}$ ,  $Cu^{II}$ ,  $Zn^{II}$ ,  $Ti^{IV}$  and  $Mg^{II}$ , in a pentagonal-bipyramidal coordination geometry [mean cavity size for cluster (4) = 2.230 (6) Å]. The donor atoms adopt a twist conformation (Strel'tsova, Ivanov, Vashchenko, Bel'skii & Kalinichenko, 1991; Belsky, Strel'tsova, Kireeva, Bulychev & Sokolova, 1991) with small mean absolute deviations from the oxygen mean plane [0.132 (9) Å]. The mean displacement of the metal atoms from this plane is 0.033 (8) Å and is necessarily zero if the complex lies on a crystallographic twofold axis (*e.g.* VOMWUP). The planar nature of the conformer allows six hydrogen bonds to be formed to the macrocycle in GEMXIF, one oxygen forming hydrogen bonds to both sides of the ring.

Cluster (5) comprises similar pentagonal bipyramidal complexes with approximate or crystallographic  $C_s$  symmetry, requiring one syn-periplanar OCCO bond and other small *gauche* torsion angles. This has been described as a transition state [ $\bar{1}14$ ] between two uniaxial conformations having a corner at each carbon of the syn-periplanar unit, *i.e.* cluster (1)-type conformations (Dale, 1976). However, the latter is not suited to binding in a coplanar manner. Rather the  $C_s$  conformer could be described in terms of static or dynamic disorder about two anangular conformers with +*G* and -*G* OCCO torsion angles, respectively. Molecular mechanics calculations (Table 4) with one OCCO torsion angle constrained to 0 showed [ $\bar{1}14$ ], with an envelope configuration of donor atoms, to be 12.6 kJ mol<sup>-1</sup> higher than the anangular conformation. Removal of the constraint led to relaxation to the anangular and thus [ $\bar{1}14$ ] probably represents a saddle point on the potential energy surface.

Some deviation towards a more eclipsed OCCO bond might occur in coordinated ligands in order to direct the oxygen orbitals more effectively towards the metal [mean absolute deviation of O atoms from mean plane 0.076 (10) Å in cluster (5) examples], but an exact syn-periplanar bond would seem unlikely. Seven fragments in the data set have crystallographic  $C_s$  symmetry, JUSGAF has crystallographic  $C_2$  symmetry (two almost syn-periplanar units) and the remainder have one almost *syn* unit (although other torsion angles are substantially less than  $\pm 60^\circ$  in some fragments). The local minima corresponding to the mirror-related  $C_2$  conformers will be unequal in energy in these due to the low symmetry of the molecular environment and their relative occupancies will be weighted accordingly. In practice, the disorder is probably more complex, involving subtle displacements

in the rest of the macrocycle. Further evidence for disorder are large thermal parameters (Strel'tsova, Bel'skii, Bulychev & Kireeva, 1992), larger standard deviations of CC and CO bonds (Strel'tsova, Bulychev, Bel'skii & Kireeva, 1991) and unusually long or short apparent CC bond lengths in the syn-periplanar portion of the ring.

The [ $\bar{1}14$ ] conformer is found with the metal cations  $Mg^{II}$ ,  $Co^{II}$ ,  $Yb^{III}$ ,  $Zn^{II}$ ,  $Sc^{III}$  and  $Ti^{III}$  and the mean hole size [2.174 (9) Å] and deviation from the mean plane [0.024 (7) Å] are not significantly different to those for cluster (4). These ions, as in cluster (4) examples, are all hard or intermediate cations with a charge of  $\geq +2$ , hence the bonding is expected to be primarily electrostatic. Although there may be a greater degree of directional covalent interaction than with the uniaxial or [348] structures, the principal factors favouring the anangular conformer are probably the smaller size and greater charge/radius ratio of the ions. Strel'tsova, Bel'skii, Bulychev & Kireeva (1992) suggested that lanthanide ions were too large for the cavity and  $Sc^{III}$  was the upper limit of what would fit. However, Yb resides 0.2 Å from the ether plane in KAVCAT with unusually short Yb—O distances (2.23–2.32 Å) for seven-coordinate Yb, the crown providing a snug fit for the cation even though it is displaced from the ring (Atwood, Bott & Atwood, 1987).

(1a) does not always coordinate in a pentadentate manner in metal complexes. It is limited to an  $\eta^2$ -chelating mode in  $(\eta^2-1a)Cr^{III}Cl_3(H_2O)$  TADFEJ, forming an envelope chelate ring with a 77.35 (7)° O—Cr—O angle. The crown adopts a [510] conformation with two *gauche* COCC torsion angles and some *anti* torsion angles deviating towards eclipsed. The two O atoms adjacent to the chelating atoms are directed to the same side of the ring, allowing two hydrogen bonds to be formed to the coordinated water molecule. KICKUC ( $\eta^2-1a$ )BeCl<sub>2</sub> also has an envelope chelate ring. The ligand has a fairly strained [357] conformation (Table 3), which directs the coordinating donor atoms *exo* whilst retaining approximate coplanarity of the five O atoms. This arrangement allows beryllium to maintain its usual tetrahedral geometry and preferential coordination of chlorine rather than oxygen donor atoms (greater degree of covalency in bonds to the former), whilst minimizing repulsion between the Cl<sup>-</sup> ligands and the non-coordinated ether O atoms. KOWJOV consists of two (1a)Na<sup>+</sup> units joined in an  $\mu^2-\eta^2,\eta^2$  manner by a central crown molecule in a [411] conformation (three *gauche* COCC bonds and one pseudo-corner), the fifth donor atom not being coordinated. This arrangement has been dubbed a club sandwich complex (Getman, Knobler & Hawthorne, 1992).

Whether the crown ether enters the primary coordination sphere of the metal ion depends on many factors as well as the crude size-match criterion (Bulychev, Kireeva, Belsky & Strel'tsova, 1992). The solution behaviour is more complex still and is likely to be

crucial in determining the structure which crystallizes. The electronic configuration of the metal atom, degree of ionization in the solvent chosen, the relative basicities of the solvent and crown ether and the possibility of additional stabilization of the molecule by numerous hydrogen bonds all play a rôle (Strel'tsova, Bel'skii, Bulychev & Kireeva, 1991); thus (1a) or (2a) cannot be guaranteed to complex the metals directly in these systems.

#### 4.2. 1,4,7,10,13-Pentathiacyclopentadecane

Free (1b) adopts an irregular  $C_1$  conformation (Wolf, Hartman, Storey, Foxman & Cooper, 1987) with all five donor atoms exodentate, having seven *gauche*, two nearly eclipsed and one *anti* CCCC and four favourable *gauche* SCCS torsion angles (Table 3). Anomalous torsion angles were attributed to inherent strain in odd-membered rings, although slight disorder was evident in one of the ethylene linkages. Significant reorganization must occur for endodentate chelation to metal centres.

Pentadentate coordination is achieved in the square-based pyramidal  $Cu^{II}$  and  $Ni^{II}$  complexes CUXVIA and KURLOY (Fig. 3), with a [12156] quinqueangular conformation. CCCC torsion angles about the apical S atoms are *gauche* of opposite sign and the S(4/13)CCS(7/10) units have the  $A\pm GA$  torsion angle sequence necessary for the formation of MSCCS five-membered chelate rings. The S(4)CCS(7) and S(10)CCS(13) units are approximately mirror images and the S(7)CCS(10) unit is forced to adopt a SCCS torsion angle approaching syn-periplanar and a CCCC approaching eclipsed (Table 3). The apical S is bent back from the vertical in both the  $Cu^{II}$  and  $Ni^{II}$  complexes due to restrictions imposed by the short  $(CH_2)_2$  linkages. The  $Cu^{II}$  ion in CUXVIA is 0.44 Å from the mean plane of the four basal S atoms (which deviate by  $\pm 0.09$  Å from coplanarity) and the equatorial distances of 2.32 Å are not very different from the apical one of 2.398 (2) Å. The similarity in the axial and equatorial distances was attributed to strain in these bridges compromising the tendency for elongation in  $Cu^{II}$  species; in solution all Cu—S bonds are equivalent, suggesting rapid rearrangement (Corfield *et al.*, 1985). There is a marked inequivalence in the *trans*-basal angles [154.58 (5), 164.36 (5)°], indicating some distortion towards the trigonal bipyramidal geometry. Conversely, the *trans*-basal angles in KURLOY [166.45 (23), 165.82 (25)°] are equivalent within experimental error and were said to be typical for square-based pyramidal high-spin  $Ni^{II}$  complexes (Blake, Halcrow & Schröder, 1992). Interestingly the nickel ion deviates less from the mean basal plane (0.26 Å) and the shorter basal  $M—S$  bond lengths [2.173 (11) Å] are consistent with this. The apical distance of 2.413 (5) Å is significantly longer, in marked contrast to the  $Cu^{II}$  complex.

All five donor atoms of the macrocycle are also coordinated in the distorted octahedral complex (1b) $Ru^{II}PPh_3$

(LADSI). The ligand has a [121272] conformation (Table 3) which places the axial donor atom on the opposite side of the equatorial S plane (from which the Ru atom is displaced by only 0.063 Å) to [12156]. This permits access to the sixth coordination side without hindrance from the  $(CH)_2$  groups of the ring. The conformation also has an all-*gauche* SCCSCCS unit with change of sign at the axial S atom and two AGG chelate rings related by approximate mirror symmetry requiring a small *gauche* angle (32°) in the unique SCCS unit. The apical bond is considerably longer than the equatorial bonds, attributed to the greater *trans*-influence of  $PPh_3$  compared with  $SC_2$  (Blake, Reid & Schröder, 1992), although constraints imposed by the macrocycle may also be responsible. The strained conformation allows the octahedral coordination geometry preferred by the fairly large  $d^6$   $Ru^{II}$  ion to be achieved, but not without significant deviations from ideal S—Ru—S angles.

The (1b) ligand is coordinated in one axial and four equatorial sites of a distorted pentagonal bipyramid in the seven-coordinate  $Cd^{II}$  complex PAFHOT, the coordination sphere being completed by an equatorial perchlorate anion and an axial water molecule. The lack of ligand-field stabilization energy with the  $d^{10}$   $Cd^{II}$  ion allows a higher coordination number and a less strained [12354] conformation to be adopted. However, ligand constraints still cause substantial deviations from ideal coordination geometry. Setzer, Tang, Grant & Van Derveer (1992) performed molecular mechanics calculations on selected (1b) conformers and found [12354] to be 16.7 kJ mol<sup>-1</sup> higher than the free ligand; [12156] was significantly higher than this (by another 16.2 kJ mol<sup>-1</sup>). However, the metal probably dictates the necessary conformation and coordination mode, subject to the limited flexibility of  $(CH_2)_2$  linkages, given the significant directional, covalent, bonding character with these relatively soft transition-metal ions.

In other complexes all five donor atoms are not used in metal coordination, as in the  $Ag^+PF_6^-$  salt SUHCON in which the [12354] conformation is also adopted. Parallel chains are formed in which each silver ion is bonded *via* three short contacts [2.62 (3) Å] and two long contacts [3.15 (7) Å] to the S atoms in one ring and to one sulfur in the next at 2.742 (5) Å, giving a 'four-plus-two' coordination environment with the short bonds defining an approximately tetrahedral geometry. Similar chains run anti-parallel and differ only in that they involve a [12345] conformer (one  $A-G-G$  torsion angle sequence replaced by  $-G-GA$ ). The coordination mode is critically dependent on the counterion: a macrobicyclic structure incorporating two  $Ag^+$  ions is produced with  $BPh_4^-$  and a 1:1 complex with the even larger  $B(C_6F_5)_4^-$  counter-anion, the five Ag—S distances ranging from 2.471 (2) to 2.881 (2) Å. In these complexes the preference of the  $Ag^I$  cation for tetrahedral coordination is compromised by restrictions imposed by the five-membered  $AgSCCS$  chelate

rings (Blake, Collison, Gould, Reid & Schröder, 1993).

Au<sup>I</sup> is coordinated in an approximately linear manner in PEHLOD. Two gold ions are bridged by two (1b) ligands in an  $\eta^1, \eta^1$  manner to form a centrosymmetric macrobicyclic dimer, the remaining thioether donor groups being directed toward the cavity. The ligand has the [23343] conformation (exhibited by 1a in PXCDBA) with all SCCS torsion angles in unfavourable *gauche* placements. This conformation may be adopted because it directs all donors to the same side to provide some additional, albeit weak, stabilization of the Au<sup>I</sup> centres.

#### 4.3. 1,4,7-Trioxa-10,13-dithiacyclopentadecane

The mixed-donor ligand (1c) is coordinated to Pd (VIFGAS) and Ru (VIFGEW) in an  $\eta^2$ -S,S' manner. The O atoms are directed away from the Pd<sup>II</sup> centre and do not interact with it. Spectroscopic evidence suggests that the Pt<sup>II</sup> complex is analogous (Blake, Reid & Schröder, 1990). The Pd atom is on an inversion centre such that the non-coordinated chains are on opposite sides of the square plane (*anti* configuration). The Ru complex is octahedral with *trans*-disposed PPh<sub>3</sub> and Cl<sup>-</sup> ligands; the steric bulk of the former forces the macrocyclic rings towards the face occupied by the chloride ion, *i.e.* a *syn* disposition of chains; some hydrogen-bonding between a solvent water molecule and O atoms of the macrocycle is evident. In both complexes a [1284] conformation is adopted with all-*gauche* OCCO, SCCO and SCCS torsion angles. The chelating SCCS group has the usual AGG conformation, the other CSCC torsion angles are both the favoured *gauche* and six of the eight COCC angles have preferred *anti* placements (Table 3). Thus, the conformation adopted is a compromise between a suitable chelating disposition of the SCCS unit, torsion angle preferences in the non-coordinated part and repulsion between oxygen donor atoms and the metal centre.

### 5. Conclusions

Whilst it is possible to classify successfully the conformations of both free and metal-coordinated unsaturated 15-membered oxa and thia macrocycles, using symmetry-modified Jarvis–Patrick clustering, principal component analysis was less successful in allowing the visualization of these clusters than for 12-membered macrocycles (Raithby, Shields & Allen, 1997). This is a consequence both of the  $D_{5h}$  point group having fewer kernels than  $D_{4h}$  and the incompatibility of the torsional preferences of COCC and OCCO units with conformations having fivefold symmetry. Although there are some  $C_s$  and  $C_2$  conformations,  $C_1$  conformers are more common and thus symmetry is a less useful tool in distinguishing conformations in the parameter space.

With oxa donors the conformations more frequently found are those with lower molecular mechanics ener-

gies, particularly the uniaxial, anangular and [348] and the energy differences are small ( $< 10 \text{ kJ mol}^{-1}$ ). The conformation adopted can be rationalized generally on the basis of the size, coordination number and geometry of the metal ion and considerable flexibility of the macrocycle is evident. These factors dictate the preferred disposition of the donor atoms and hence the conformation of the backbone subject to the torsional preferences of the COCC and OCCO units. In particular, the anangular conformation is ideally suited to coplanar complexation of relatively small main-group or transition-metal ions, whilst the uniaxial and [348] are adopted for larger (typically alkali-metal or lanthanide) cations with the additional ligands directed to the same face of the macrocycle, bonding to the macrocycle being primarily electrostatic in both cases. If the macrocycle does not enter the primary coordination sphere of the metal ion, and in host–guest complexes, the conformation is frequently directed in a similar manner by the nature of the hydrogen-bonding network.

The existence of complexes of the form (1a)EHal<sub>3</sub> (where E = As, Sb, Bi and Hal = Cl, Br) with both the [348] and the higher-energy [23334] conformers in isomorphous structures suggests that intermolecular packing forces, as well as subtle differences in bond lengths and angles around the metalloid, may be instrumental in determining the solid-state conformation. The co-existence of different conformers in similar environments in the same crystal structure also points to the similarity in energy of coordinated conformers and the importance of intermolecular interactions in these structures. In this context molecular mechanics calculations based on metal complexes would not differentiate between the conformations either. The [348] and anangular conformers appear to be particularly subject to static or dynamic order, of which apparent [1383] and [114] configurations, respectively, are probably an artefact. It is possible that other structures are subject to some degree of unresolved thermal disorder, particularly at room temperature.

There are few thia-donor examples and these fall into two classes: those in which the ligand binds in a pentadentate manner to an apical/axial and four equatorial sites of the coordination polyhedron and those in which the donor atoms are not all bound equally strongly to the metal. The former occur with intermediate-to-soft transition-metal ions and the bonding is more directional (covalent) than with the oxa macrocycle; the preferred regular coordination geometries require more strained non-coplanar conformations. The latter are characterized by a mismatch between the metal and ligand coordination preferences. A compromise between the linear and tetrahedral geometries preferred for the Au<sup>I</sup> and Ag<sup>I</sup> cations, respectively, and the pentadentate nature of the ligand results in additional long metal–sulfur interactions. With mixed O/S donors the S atoms coordinate preferentially to the soft transition-metal ions studied

(Ru<sup>II</sup>, Pd<sup>II</sup> and Pt<sup>II</sup>) and the conformer adopted is consistent with expected torsion angle preferences in the non-coordinated part, given the need for a suitable chelating conformation of the SCCS unit.

This study has shown that symmetry-modified cluster analysis is useful in enumerating the conformations adopted by quite complex cyclic ligands where constraints are imposed by coordination to a metal or participation in a hydrogen-bonded network. Whilst results of molecular mechanics calculations on the free ligands do assist with rationalizing the preferred conformations, it is apparent that there are a large number of possible conformers and energy differences between those actually observed in the solid state are of the order 25 kJ mol<sup>-1</sup> or less. Hence, where the metal–ligand binding energies are similar, intermolecular interactions have a strong determinative influence. Furthermore, the macrocyclic ligands are susceptible to disorder which may render precise conformational classification difficult. Despite these difficulties clear patterns do emerge where there are sufficient examples and consideration of the metal size and coordination geometry enables these trends to be explained.

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