Self-assembled trinuclear arsenic and antimony macrobicycles†

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The synthesis of six trinuclear Pn3L2 macrobicycles (Pn = As, Sb) was achieved by self-assembly of a pnictogen trichloride and a 2,4,6-trisubstituted-1,3,5-benzenetrimethanethiol ligand. 1H-NMR spectroscopy reveals self-assembly in 1,1,2,2-tetrachloroethane is dynamic in solution producing two structural isomers. The symmetric and the asymmetric isomers (in which a single chloride ligand is cast in an opposing direction from other chlorides) of the As3L2 complexes exist in a ca. 2:1 distribution, whereas only the symmetric isomer is observed in solution for Sb3L2. Solvent effects appear to influence conformational isomerism and conversion to the final products. Macrobicycles were confirmed by 1H-NMR spectroscopy and X-ray crystallography and further studied by MP2/LANL2DZ optimizations.

Introduction

Supramolecular systems rely on multiple weak interactions to achieve stable, specific coordination to their hosts. Through creative ligand design, one can incorporate binding elements that enable directional self-assembly. Historically, a diversity of self-assembled systems incorporate the predictable coordination geometry of transition metals as a directional tool.1–4 Only recently has more effort been made toward understanding the supramolecular self-assembly of main group elements, including Group 15.5–16 We utilize mercaptomethyl substituents as a preorganizing binding motif to accommodate the pnictogen’s trigonal pyramidal geometry and thiophilicity. In addition to the predictable geometric configuration, electron density from the ligand provides a supporting non-covalent stabilizing force with the Lewis acidic pnictogen, known as a Pn···π interaction.11,12 Further studies by our laboratory have investigated how self-assembly is dictated by the structure of the dithiolate ligand by altering its length, width or the placement of steric bulk (Chart 1).13–16

The 1,3,5-trisubstituted-2,4,6-triethyl benzene scaffold has been exploited in numerous supramolecular hosts since Mislow first demonstrated steric gearing of adjacent substituents, where each substituent is positioned in an alternating up-down arrangement.17 While this preorganization technique has now been readily utilized to form supramolecular structures,18 its use with Group 15 metalloids (As, Sb) has not yet been explored, and led to some surprising structures. In this study, a series of six trinuclear arsenic and antimony supramolecular macrobicycles [Pn3L2Cl3] were synthesized using a trisubstituted, trithiol ligand (Fig. 1). In addition to the syntheses, we address some unusual dynamic solution behaviour that arises from these new ligands that feature this steric gearing component. Typically, steric gearing serves as an effective preorganizational tool for metal–ligand-based supramolecular systems, providing enhanced thermodynamic stability of a complex and/or faster kinetics of formation. In this system we observed a surprising deviation where this gearing effect does not influence the rate of

Chart 1 Selection of dithiol ligands used for Pn-thiolate self-assembly.
self-assembly in mediating thiol reactivity with a pnictogen. Rather, interaction with the solvent and/or other external additives (such as chloride and tetrafluoroborate salts) more directly influences the course of the self-assembly reaction. For instance, a subtle change in solvent or the addition of a salt accelerates the formation of macrobicycles in solution and additionally facilitates or prohibits a change in conformation to favor an unexpected, slightly higher energy asymmetric macrobicycle in tandem with the more stable, symmetric macrobicycle. Furthermore, close Pn···πaryl contacts suggest a Pn···πaryl interaction acts as a stabilizing force during assembly formation. These structures represent the first known trinuclear supramolecular arsenic–antimony–thiolate assemblies.\(^a\)

**Results and discussion**

**Symmetric and asymmetric \(\text{Pn}_3\text{L}_2\text{Cl}_3\) macrobicycles**

To study the steric effect imparted by a trisubstituted benzene in arsenic–thiolate self-assembly, three bridging tridentate 2,4,6-trisubstituted-1,3,5-tris(mercaptomethyl)benzene ligand derivatives \(\text{H}_3\text{L}^R (R = \text{H, Me, Et})\) were synthesized (see ESI\(^f\) for complete experimental details). When treated with a stoichiometric amount of \(\text{AsCl}_3\) in 1,1,2,2-tetrachloroethane (TCE), a discrete trinuclear \(\text{As}_3\text{L}_2\text{Cl}_3\) macrobicycle emerges (Scheme 1). The unsubstituted metallacyclophane \(\text{As}_3\text{L}^\text{H}\text{Cl}_3\) can alternatively be synthesized in a more facile method through the addition of tetrabutylammonium chloride at 0 °C in chloroform. The presence of a chloride guest was initially used to catalyze or template formation of a tetrahedral cage; however, TBA\(^+\text{Cl}^−\) instead induced a rapid precipitation of pure macrobicycles in the form of colorless needles (45% isolated crystalline yield after filtration, see ESI\(^f\)).

Each prepared ligand derivative \(\{\text{H}_3\text{L}^\text{H,Me,Et}\}\) provides quantitative conversion to \(\text{As}_3\text{L}_2\text{Cl}_3\) upon treatment with \(\text{AsCl}_3\) as observed by \(^1\text{H}-\text{NMR}\) spectroscopy. Layering benzene over a solution of \(\text{H}_3\text{L}^\text{H,Me,Et}\) and \(\text{AsCl}_3\) in TCE gave crystals suitable for X-ray diffraction in a 25% yield for \([\text{As}_3\text{L}^\text{H,Me,Et}_2\text{Cl}_3]\) and 15% for \([\text{As}_3\text{L}^\text{H,Me,Et}_3\text{Cl}_3]\) respectively, within one week. Antimony macrobicycles were isolated from a mixture of the corresponding \(\text{H}_3\text{L}\) species and an excess of \(\text{SbCl}_3\) and crystallized by slow evaporation of TCE. The formation of \(\text{Sb}_3\text{L}^\text{Me,Et}_2\text{Cl}_3\) complexes under these conditions could not be observed by \(^1\text{H}-\text{NMR}\) spectroscopy,\(^20\) and only partial conversion to \([\text{Sb}_3\text{L}^\text{H,Et}_2\text{Cl}_3]\) from \(\text{SbCl}_3\) and \(\text{H}_3\text{L}^\text{H}\) was observed when heating the solution to 70 °C (Fig. S18\(^f\)). Nevertheless, crystallization of these solutions appears to induce formation of these macrobicycles, and the structures of each \([\text{Sb}_3\text{L}_2\text{Cl}_3]\) complex were determined by single crystal X-ray diffraction (ESI Table 1\(^f\)). These Sb-macrobicycles are then stable and can be redissolved TCE-\(d_2\) to verify their structure in solution (see Fig. S18, S21 and S24\(^f\)).

By incorporating the 2,4,6-triethyl-substituted benzene scaffold, we envisioned the rate of self-assembly for both arsenic and antimony complexes to be favored over ligands that do not have such steric gearing components. While this organizing element has been successfully utilized to overcome high energy binding conformations or potential unfavorable binding entropies in relation to free host, guest or solvated host–guest complexes,\(^22\) we did not observe steric gearing as the primary driving force by \(^1\text{H}-\text{NMR}\) in the formation of pnictogen–thiolate macrobicycles as expected. The unsubstituted analogue \([\text{As}_3\text{L}^\text{H}_2\text{Cl}_3]\), bearing no steric gearing component, forms faster in solution (1 day) by \(^1\text{H}-\text{NMR}\) than its ethyl-substituted counterpart (4 days) in TCE-\(d_2\) (Fig. S6 and S16\(^f\)).

However, evidence for steric gearing was observed in the crystalline state (single crystal structure data and parameters are shown in ESI Table 1, see ESI\(^f\) for complete details). As anticipated, none of the 2,4,6-triethyl substituents are directed toward the arsenic atoms in the crystal structure of \([\text{As}_3\text{L}^\text{H,Me,Et}_3\text{Cl}_3]\), since the 1,3,5-trimercaptomethyl groups of the ligands are all...
pointed in that direction in order to converge on the three arsenic ions (Fig. 1C and 2). The electron-rich chlorine atoms coordinated to arsenic would also sterically disfavour the presentations of ethyl groups toward the center of the assembly. Interestingly, the increased steric bulk of the ethyl groups appears to affect the flexibility of the molecule to adopt a position that maintains the shortest As⋯πaryl contact. This trend is apparent in both the As and Sb complexes, in which the Pn⋯πaryl contact increases in distance from [Pn,LH₂Cl₂] to [Pn,LMe₂Cl₂] to [Pn,LMe₃Cl₂] (Table 1). As shown in Fig. 2A, each pnictogen atom is positioned endo relative to the aromatic ligand backbone, allowing for the stereochemically active pnictogen lone pairs to be directed inside the cavity of the macrobicycle. This arrangement facilitates an attractive Pn⋯πaryl interaction, which we have observed in many other structures of this type and use as a key design feature. The smallest As⋯πaryl contacts in the As₂L₂Cl₃ macrobicycles range between 3.17 and 3.27 Å, which is shorter than the sum of the van der waals radii for C and As (3.7 Å), suggesting a stabilizing As⋯π interaction (Table 1). The close As⋯πaryl Contacts for the unsubstituted macrobicycle and the faster self-assembly of these congenerers suggest that providing for As⋯π interactions in the ligand design may play a more significant directing role in the self-assembly than steric gearing. Moreover, the less restricted rotation around the Caryl bonds in the less sterically hindered ligand may accelerate self-assembly.

1H-NMR characterization of As macrobicycles was performed in TCE-d₂. The methylene protons in the structure are inequivalent, creating an AB splitting system due to geminal coupling. Interestingly, all As₂L₂Cl₃ derivatives exhibit the presence of an unusual, asymmetric isomer that accompanies the dominant symmetric isomer (sym-As₂LMe₂Cl₂ and asym-As₂LMe₂Cl₂, Fig. 3). The asymmetric conformer exhibits a framework in which a single chloride atom is pointing in the opposite direction relative to the other As–Cl bonds. This results in inequivalent methyl groups giving rise to singlets at 2.58, 2.48, and 2.43 ppm in TCE-d₂. A similar type of symmetric vs. asymmetric isomerism was previously observed in two-fold symmetric, naphthalene-based arsenic–thiolate As₂L₂Cl₂ macrocycles, in which a single ligand “flips” causing the loss of C₂ symmetry of the complex. Fig. 4 shows the mixture of sym- and asym-As₂LMe₂Cl₂ macrocycles obtained from dissolving single crystals of As₂LMe₂Cl₂, and shows the AB splitting pattern observed for the methylene protons (H₄ in figure). From integrating the resonances of each structure, it was determined that the symmetric isomer is favoured over the asymmetric isomer by a 63 : 37 ratio. The relative

Table 1 Select distances and bond angles for As₂L₂Cl₃ and Sb₂L₂Cl₃ macrobicycles

<table>
<thead>
<tr>
<th></th>
<th>As₂LH₂Cl₂</th>
<th>As₂LMe₂Cl₂</th>
<th>As₂LMe₃Cl₂</th>
<th>Sb₂LMe₂Cl₂</th>
<th>Sb₂LMe₃Cl₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pn–S (Å)</td>
<td>2.209(9)</td>
<td>2.197(9)</td>
<td>2.217(2)</td>
<td>2.400(4)</td>
<td>2.403(2)</td>
</tr>
<tr>
<td>Pn⋯Pn (Å)</td>
<td>3.882(13)</td>
<td>4.40(19)</td>
<td>4.110(2)</td>
<td>3.768(34)</td>
<td>4.023(1)</td>
</tr>
<tr>
<td>S–Pn–S (deg)</td>
<td>88.1(9)</td>
<td>88.4(3)</td>
<td>85.73(7)</td>
<td>88.2(2)</td>
<td>81.92(2)</td>
</tr>
<tr>
<td>Pn⋯Caryl (Å)</td>
<td>3.169(8)</td>
<td>3.211(8)</td>
<td>3.269(6)</td>
<td>3.223(7)</td>
<td>3.386(5)</td>
</tr>
</tbody>
</table>

As₂LH₂Cl₂ not included due to significant disorder in structure. Denotes an averaged value. Value provided corresponds to shortest Pn⋯Caryl contact.
stability of the two different isomers was also investigated with
electronic structure calculations. MP2/LANL2DZ geometry
optimizations revealed the symmetry, unsubstituted As macrobi-
cycle to be 3.63 kcal mol$^{-1}$ lower in energy than the asymmetric
isomer (Fig. 3C and D).

While a variation in the dithiolate ligand core appeared to
dictate the isomer ratio in related studies on As$_3$L$_2$Cl$_2$
macrocycles,
 in the case of the macrobicycles the substitution at the 2,4,6 position did not affect the sym : asym ratio between deriv-
atives in solution as estimated by $^1$H NMR spectroscopy: 68 : 32
([As$_3$L$_2$H$^2$Cl$_2$], 63 : 37 ([As$_3$L$_2$Me$_2$Cl$_2$]), and 69 : 31 ([As$_3$L$_2$Et$_2$Cl$_2$]).
Given that the sym-isomers are favoured by this ~2 : 1 ratio in
solution, then at 25 °C these sym-isomers are ca. 0.4 kcal mol$^{-1}$
more stable than the asym-isomers. The difference between the
relative energy of the two isomers in solution versus that calculated
in vacuum presumably reflects the influence of solvation. Addi-
tionally, $^1$H NMR reveals a slow equilibrium between sym-
and asym-As$_3$L$_2$Cl$_2$: each isomer has a distinct NMR spectrum at room
temperature, meaning the equilibration between the two species
is slow on the NMR timescale. However, upon dissolving single
crystals of As$_3$L$_2$Cl$_2$ macrobicycles, the equilibrium mixture of sym-
and asym-isomers is established within minutes, suggesting this equilibration is fast on the seconds to minutes timescale.

Structural characterization using single crystal X-ray diffraction
is in agreement with solution state NMR studies, suggest-
ing the symmetric conformers are again the dominant species.
The preferred $C_{3v}$-symmetric As$_3$L$_2$Me$_2$Cl$_2$ conformer co-crystal-
zizes with the $C_{6v}$ asymmetric complex in a 90 : 10 ratio (Fig. 3A
and B). The opposing chloride in the asymmetric structure
shows a significant amount of disorder. The crystal packing
structures for ethyl- and methyl-substituted macrobicycles
reveal a formation of columns in a herringbone fashion (Fig. S12
and S17†). Discernible stabilizing forces in each As-containing
macrocycle are intermolecular interactions seen in the form of
short S–S contacts between 3.28–3.67 Å. In addition, a single
benzene molecule co-crystallizes orthogonal to the 1D stacks in
the crystal structure of the unsubstituted derivative, [As$_3$L$_2$H$^2$Cl$_2$].

Effect of external additives and solvent dependence
Due to the low energy barrier of conversion from the symmetric
macrocycle to the asymmetric macrocycle, the kinetic
stability of the macrobicycles was tested by heating the solution
to 120 °C over several days. Both -sym and -asym conformers
were kinetically stable under these conditions and showed no
apparent conversion from asym-As$_3$L$_2$Cl$_3$ to the symmetric
complex on the NMR timescale. Interestingly, the self-assem-
bled isomerism was found to be strongly influenced by solvent
effects as revealed by solution studies performed in deuterated chloroform. Reacting unsubstituted ligand H$_3$LH with AsCl$_3$
results in only partial conversion to the macrobicycle after more
than a week in CDCl$_3$; whereas 100% conversion to the macro-
cycle in TCE-d$_3$ is achieved in only one day, suggesting some
unusual solvent effect is at play in TCE that facilitates macro-
 Abrupt precipitation from the reaction solution, resulting in
limited conversion to macrocycle. The degree of solubility for
these oligomeric intermediates also appears to impact the
formation of a single stereoisomer over another. This was most
apparent in tetrahydrofuran where only the symmetric isomer is
formed in solution; whereas, dichloromethane, benzene, and
chloroform hinder the self-assembly of both sym/asym-macro-
 bicycles. Supplementary to solvent effects, tetrabutylammo-
nium tetrafluoroborate increases the relative rate of self-
assembly in TCE giving complete conversion to As$_3$L$_2$Cl$_3$ in
8 minutes without subsequent precipitation of product seen
with TBA$^+$ chloride. This change in reactivity when subjected
to an external agent is another unusual example of a self-
assembly reaction driven by a small molecule that facilitates the
organization process, and augurs well for the formation of
 even greater, more intricate self-assembled systems using
related thiol ligands and main group ion building blocks.

$C_{3v}$-Symmetric Sb$_3$L$_2$Cl$_3$ macrobicycles appear to be more
static in solution when compared to the arsenic-based conge-
ers as only symmetric macrobicycles are present in TCE-d$_3$,
suggesting the asymmetric isomers are much more stable
relatively. Similar to its As counterpart, the Sb$_3$L$_2$H$^2$Cl$_3$-sym
is only 4.46 kcal mol$^{-1}$ lower in energy than the asymmetric
conformer calculated via MP2/LANL2DZ. Single crystal X-ray
diffraction of [Sb$_3$L$_2$Me$_2$Cl$_3$] reveal columnar packing in a
herringbone pattern with short S–S contacts of 3.62 Å
and intramolecular Sb–S contacts ranging between 3.24–3.39 Å
(VDW radii is 3.85 Å for Sb). Similar to As macrobicycles, the
sulfur-sulfur interaction poses as the prominent stabilizing
factor in crystal packing. However, the solid state structure of
Sb$_3$L$_2$Me$_2$Cl$_3$ adopts more sulfur contacts between the layers of
columns than [As$_3$L$_2$H$^2$Cl$_3$] (Fig. S26†). A similar trend in Pn–π
interactions is observed, with the distance in this stabilizing
force increasing with added steric bulk at the ligand core.

Surprisingly, no evidence for asym-Sb$_3$L$_2$Cl$_3$ conformers was
observed in solution, although under certain conditions the
asym-conformer does contribute to a minor disordered
component in single crystal X-ray structures. These disordered
crystals still lead to NMR spectra indicating only the presence
of sym-Sb$_3$L$_2$Cl$_3$ macrobicycles. This is in stark conflict with
previous studies on dinuclear Pn$_2$L$_4$ cryptands, which revealed
added stability in Sb [and Bi] complexes over the As
derivatives.

Conclusion
In conclusion, this is the first report of a series of self-assembled
trinuclear As(III) and Sb(III) coordination complexes, and we
report the syntheses of six such macrobicyclic assemblies. The As-derivatives exist in two different conformations: a slightly more stable \( C_{1,3,5} \)-symmetric structure and an asymmetric conformer that lacks the three-fold symmetry. Steric gearing at the tripodal core of the 1,3,5-trisubstituted benzene ring does not appear to influence the rate of self-assembly in solution nor the equilibrium between different macrobicryclic conformers, negating the presence of any apparent steric gearing effects during self-assembly and dynamic motion in solution. However, X-ray crystallography suggests pnictogen···πaryl interactions may act as a strong directing force in self-assembly complementary to steric gearing. Additionally, the self-assembly of these macrobicycles is sometimes enhanced and/or suppressed by different organic solvents as well as the addition of chloride and tetrafluoroborate salts.

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**Notes and references**