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Secondary Bonding Interactions Observed in Two Arsenic Thiolate Complexes

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Treatment of *N*-(2-mercaptoethyl)-1,8-naphthalimide (H**L**) with stoichiometric amounts of $AsCl_3$ and base affords $As\mathbf{L}_2Cl$ and $As\mathbf{L}_3$ complexes stabilized in part by secondary As···O bonding interactions.

In the process of developing a new supramolecular approach to the design of arsenic(III) coordination complexes, we have begun to explore the role weak attractive forces such as As−π interactions and secondary bonding interactions (SBIs) play in chelator optimization.[1,2] The trigonal-pyramidal coordination geometry of As(III) features a stereochemically active lone pair when coordinated by sulfur-based ligands and is predictable enough to be exploited as a target for specific ligand design.[3−5] Additionally, the use of SBIs[6,7] between As(III) and heteroatoms of appropriate ligands offers a complementary tool for designing ligands specific for this ion. SBIs are observed between main group metals and heteroatoms such as O, N, S, or halogens with interatomic distances less than the sum of the corresponding van der Waals radii.[8−12] These interactions have only recently been systematically studied in the context of supramolecular chemistry,[8] and they offer a potentially useful method toward designing chelators optimized to bind main group metalloids. The β-mercaptoimido ligand described herein represents two examples of SBIs between an imido oxygen of a ligand and the central arsenic atom of the complex.

The characteristic coordination of As(III) by sulfur-containing biological molecules such as glutathione or cysteine has recently been reported in the context of developing a better understanding of arsenic toxicity.[3,13] However, there are relatively few known structures of arsenic thiolate complexes: a search of the Cambridge Structure Database (CSD)[14] reveals only 59 examples of an As(III) ion coordinated by one or more thiolate organic ligands.[15] Of these examples, only three complexes demonstrate As···O SBIs within the range of 2.7−3.2 Å. The use of thiolate ligands optimized for the specific pyramidal coordination geometry of As(III) that possess additional functional groups capable of exhibiting secondary bonding interactions is relevant toward designing specific chelators and sensors for this toxic main group element.

We report the synthesis and crystal structure of a new first-generation sulfur-based ligand—*N*-(2-mercaptoethyl)-1,8-naphthalimide, H**L**—capable of binding As(III) via a thiolate group with complementary SBIs between the imido oxygen and arsenic. The naphthalimide core was chosen as a model for future supramolecluar chelators due to the proximity of its imido oxygens to the thiol and for its well-known electronic absorption and emission properties.

The complexes $[As\mathbf{L}_2Cl]$ and $[As\mathbf{L}_3]$ form by treatment of H**L** with $AsCl_3$. Thiol ligand H**L** was synthesized (Scheme 1) in ca. 85% yield[16,17] and formed light brown single crystals suitable for diffraction analysis from slow diffusion of acetonitrile into a $CHCl_3$ solution of H**L**. The single-crystal X-ray structure of the ligand consisted of two sets of layers of ligands interacting via aromatic face-to-face π−π stacking with an intermolecular distance between adjacent layers of 3.45 Å (Figure 1).[18] The planes formed by these two sets of

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(15) A CSD (Conquest Version 1.7, February 2005 Release) search of compounds that possessed at least one As−S bond (with S also bonded to a C) revealed 59 strucures of which only 45 contained an As ion not also bonded to a carbon atom.

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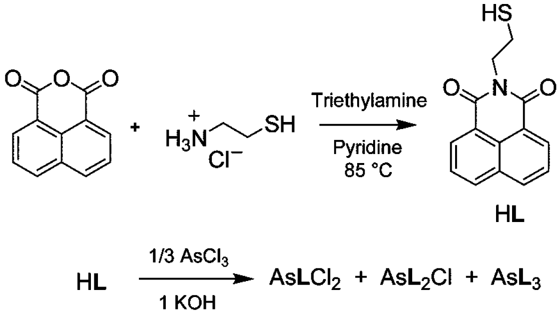
Scheme 1



layers are twisted at an angle of ca. 20°. This nonparallel arrangement is sustained by weak interactions between aromatic CH and oxygen atoms of the imide with *d*(C···O) = 3.21 Å. Furthermore, in the crystalline state, the mercapto-ethylene moiety adopts the expected anti conformation with a dihedral angle between the sulfur atom and the nitrogen atom of the imide of 177°.

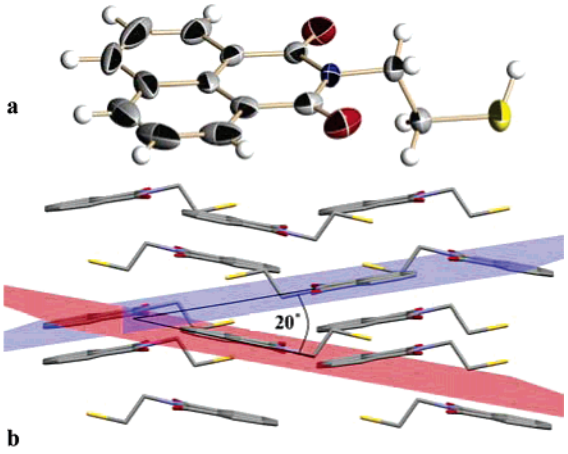


Figure 1. Crystal structure of the ligand H**L**. (a) ORTEP representation with 50% thermal ellipsoids and (b) view of the crystal packing down [101] showing the nonparallel arrangement between the planes of aromatic stacking formed by H**L**.

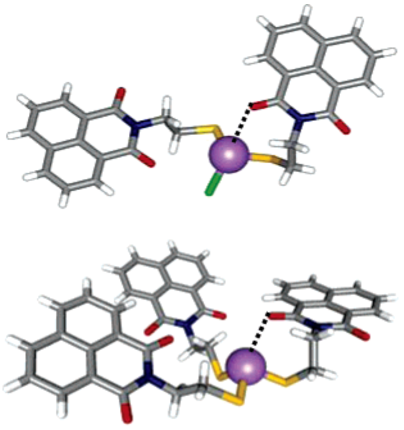


Figure 2. Crystal structures of the two pyramidal complexes $[\mathrm{As}\mathbf{L}_2\mathrm{Cl}]$ (top) and $[\mathrm{As}\mathbf{L}_3]$ (bottom) showing the gauche conformation adopted by the mercapto-ethylene moieties allowing for the secondary As···O bonding interactions of 2.91 and 3.21 Å for $[\mathrm{As}\mathbf{L}_2\mathrm{Cl}]$ and $[\mathrm{As}\mathbf{L}_3]$, respectively.

Treatment of 3 equiv of H**L** with $AsCl_3$ and a stoichiometric amount of KOH as a methanol solution yields a mixture of $[\mathrm{As}\mathbf{L}\mathrm{Cl}_2]$, $[\mathrm{As}\mathbf{L}_2\mathrm{Cl}]$, and $[\mathrm{As}\mathbf{L}_3]$ complexes according to ^{1}H NMR spectroscopy. However, treatment of an excess of H**L** with $AsCl_3$ and KOH reproducibly provides $[\mathrm{As}\mathbf{L}_3]$ in 56% crystalline yield. The single crystals were verified to be $[\mathrm{As}\mathbf{L}_3]$ by single-crystal X-ray diffraction, and ^{1}H NMR spectroscopy shows the bulk crystalline sample to be the same material.[16] Pale yellow crystals suitable for X-ray analysis were obtained for both the $[\mathrm{As}\mathbf{L}_2\mathrm{Cl}]$ and $[\mathrm{As}\mathbf{L}_3]$ complexes (Figure 2).[18] The structure of $[\mathrm{As}\mathbf{L}_2\mathrm{Cl}]\cdot\mathrm{CHCl}_3$ reveals that the complex is stabilized by As···O secondary bonding interactions (*d*(As···O) = 2.91 Å) resulting from one ligand adopting a gauche conformation about the mercapto-ethylene moiety with a dihedral angle between the sulfur and nitrogen atoms of ca. 51°. This SBI is within the range of previously observed As···O secondary interactions,[19] and it suggests that in the crystalline state crystal packing forces and/or the As···O secondary interaction is at least strong enough to compensate for one unfavorable gauche

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(16) Experimental details: *N*-(2-mercaptoethyl)-1,8-naphthalimide, H**L**, was prepared as described by Jankowski et al.[17] with the following modifications: Cysteamine HCl (1.16 g, 10.2 mmol) was activated with triethylamine (1.05 g, 10.4 mmol) and pyridine (20 mL) under a nitrogen atmosphere for 10 min at room temperature while stirring. 1,8-Naphthalic anhydride (0.5 g, 2.5 mmol) was added, and the solution was heated to 125 °C for 20 h. The resulting hite suspension was cooled, filtered to remove unreacted cystamine, and the filtrate concentrated in vacuo to yield crude product as a brown solid. Deionized water was added (30 mL) to suspend solids followed by filtration and washes with water, 1:1 EtOH/water and EtOH. Solids were vacuum-dried to yield 0.547 g (ca. 0.649 g, 84%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62 (dd, 2H, *J* = 7.5, 0.9 Hz), 8.23 (dd, 2H, *J* = 8.4, 0.9 Hz), 7.70 (t, 2H, *J* = 7.5 Hz), 4.38 (t, 2H, *J* = 7.5 Hz), 2.93−2.85 (m, 2H), 1.53 (t, 1H, *J* = 8.7 Hz). $[\mathrm{As}\mathbf{L}_3]$: *N*-(2-mercaptoethyl)-1,8-naphthalimide (49 mg, 190 μmol) was combined with 1 equiv of solid KOH in a 2:1 mixture of CH_2Cl_2/MeOH (1050 μL) and stirred until dissolved. $AsCl_3$ (5 μL in 95 μL of $CHCl_3$, 60 μmol) was carefully layered onto this solution to yield single crystals of $[\mathrm{As}\mathbf{L}_3]$ by slow diffusion. (These crystals diffract to provide a low-resolution data set that confirms the composition of $[\mathrm{As}\mathbf{L}_3]$ in a different crystal form than that reported below.[18]) The crystals were washed sequentially with MeOH, 3:1 MeOH/H_2O, MeOH, and then $CHCl_3$ (yield 56%). Single crystals were also obtained by slow evaporation from an NMR tube containing a mixture of $[\mathrm{As}\mathbf{L}\mathrm{Cl}_2]$, $[\mathrm{As}\mathbf{L}_2\mathrm{Cl}]$, and $[\mathrm{As}\mathbf{L}_3]$ prepared with an excess of KOH (see crystallographic data). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 (dd, 3H, *J* = 7.2, 1.2 Hz), 8.55 (dd, 3H, *J* = 7.2, 1.2 Hz), 8.22 (dd, 3H, *J* = 8.4, 1.2 Hz), 8.14 (dd, 3H, *J* = 8.4, 1.2 Hz), 7.75 (dt, 6H, *J* = 7.5, 0.9), 4.58 (m, 3H), 4.44 (m, 3H), 3.17 (m, 6H).

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(18) Crystallographic data. H**L**: Monoclinic, $P2(1)/c$, $a = 8.1026(11)$ Å, $b = 12.9398(17)$ Å, $c = 11.2969(16)$ Å, $\beta = 91.735(3)°$, $V = 1183.9(3)$ Å^3, $Z = 4$, $D_c = 1.444$ g cm^{-3}, $\mu = 0.265$ mm^{-1}, $F(000) = 536$, $2\theta_{max} = 54.18°$ ($-10 \le h \le 10$, $-16 \le k \le 17$, $-14 \le l \le 14$). Final residuals (163 params) R1 = 0.0614 for 1323 reflns with $I > 2\sigma(I)$, and R1 = 0.1320, wR2 = 0.1827, GOF = 1.008 for all 2604 data. Residual electron density was 0.321 and −0.281 e·A^{-3}; $[\mathrm{As}\mathbf{L}_2\mathrm{Cl}]$: single crystals grown by slow evaporation of $\underline{C}DCl_3$ from a mixture of $[\mathrm{As}\mathbf{L}\mathrm{Cl}_2]$, $[\mathrm{As}\mathbf{L}_2\mathrm{Cl}]$, and $[\mathrm{As}\mathbf{L}_3]$, Triclinic, $P\bar{1}$, $a = 7.9782(7)$ Å, $b = 18.8417(16)$ Å, $c = 20.3116(17)$ Å, $\alpha = 97.856(2)°$, $\beta = 97.098(2)°$, $\gamma = 91.123(2)°$, $V = 2999.4(4)$ Å^3, $Z = 4$, $D_c = 1.644$ g cm^{-3}, $\mu = 1.669$ mm^{-1}, $F(000) = 1496$, $2\theta_{max} = 56.52°$ ($-10 \le h \le 10$, $-24 \le k \le 24$, $-26 \le l \le 26$). Final residuals (757 params) R1 = 0.0706 for 6238 reflns with $I > 2\sigma(I)$, and R1 = 0.1780, wR2 = 0.1428, GOF = 0.943 for all 13 528 data. Residual electron density was 1.083 and −0.557 e·A^{-3}; $[\mathrm{As}\mathbf{L}_3]$: Monoclinic, $P2(1)/n$, $a = 14.8242(19)$ Å, $b = 10.6849(13)$ Å, $c = 24.910(3)$ Å, $\beta = 103.239(4)°$, $V = 3840.8(8)$ Å^3, $Z = 4$, $D_c = 1.570$ g cm^{-3}, $\mu = 1.115$ mm^{-1}, $F(000) = 1856$, $2\theta_{max} = 49.42°$ ($-17 \le h \le 17$, $-12 \le k \le 12$, $-29 \le l \le 29$). Final residuals (508 params) R1 = 0.0931 for 2108 reflns with $I > 2\sigma(I)$, and R1 = 0.2846, wR2 = 0.2456, GOF = 0.941 for all 6518 data. Residual electron density was 0.458 and −0.490 e·A^{-3}.

(19) A CSD search revealed that the few As···O SBIs previously observed are in the range of 2.7−3.2 Å. For a representative example, see: Tani, K.; Hanabusa, S.; Kato, S.; Mutoh, S.; Suzuki, S.; Ishida, M. *J. Chem. Soc., Dalton Trans.* **2001**, 518.

interaction. The other ligand exists in the expected anti conformation with a corresponding dihedral angle of ca. 170°. Presumably, the steric bulk of the ligand prevents additional As···O interactions from forming. The crystal packing of [As**L**$_2$Cl]•$CHCl_3$ is sustained by aromatic stacking similar to that observed for H**L** (Figures 1b, S1), with distances between the centroids of naphthalimide moieties of adjacent arsenic complexes ranging from 3.40 to 3.65 Å.

The crystal structure of [As**L**$_3$] reveals that two of the ligands adopt the expected anti conformation ((S−C−C−N) = 180° and 170°), while the third thiolate again adopts a gauche conformation ((S−C−C−N) = 60°) to allow for one weak As···O interaction (d = 3.21 Å). This distance is 0.3 Å greater than that observed in [As**L**$_2$Cl], presumably due to the steric bulk of the additional third ligand in [As**L**$_3$] (Figure 2). Notably, none of the SBIs in [As**L**$_3$] result in bond elongation of the As−S bonds, and all As−S and As−Cl bonds fall within the range of those reported in the CSD for related arsenic(III) complexes. The crystal packing of [As**L**$_3$] is similar to that of H**L** and [As**L**$_2$Cl] with the two sets of planes sustained by aromatic stacking (d(centroid−centroid) = 3.50−3.56 Å) and twisted at an angle of ca. 37° (Figures 1b, S2).

Despite widespread awareness of the hazards of arsenic contamination in living organisms and the environment, surprisingly few arsenic thiolate complexes are structurally characterized. In fact, although it is well-known that arsenic binds to cysteine sites in proteins[20] (which contain a similar β-mercapto*amido* structure), detailed structural studies of related arsenic thiolate complexes remain lacking. We have presented a β-mercapto*imido* ligand that binds to arsenic through its thiolate with supporting As···O secondary interactions. We are currently exploring the importance of secondary As···O interactions and As−π interactions in preparing specific chelators for arsenic.

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Supporting Information Available: Crystallographic experimental details (cif), packing diagrams of [As**L**$_2$Cl] and [As**L**$_3$] (Figures S1 and S2). This material is available free of charge via the Internet at http://pubs.acs.org.

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