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Solid State and Solution Structural Studies of Chiral Phosphoramide-Tin Complexes Relevant to Lewis Base Catalyzed Aldol Reactions†

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Abstract: Complexes of chiral phosphoramides **4** and **5** with tin-based Lewis acids were studied by both X-ray crystallography and low temperature ^{119}Sn NMR spectroscopy. The structure of a ternary complex between **5**, $SnCl_4$ and benzaldehyde was also obtained and provided a detailed view of the binding of both aldehyde and phosphoramide to Lewis acids. ^{119}Sn NMR, spectroscopy indicated that a 2/1 stoichiometry of phosphoramide to tin is favored in solution as well.

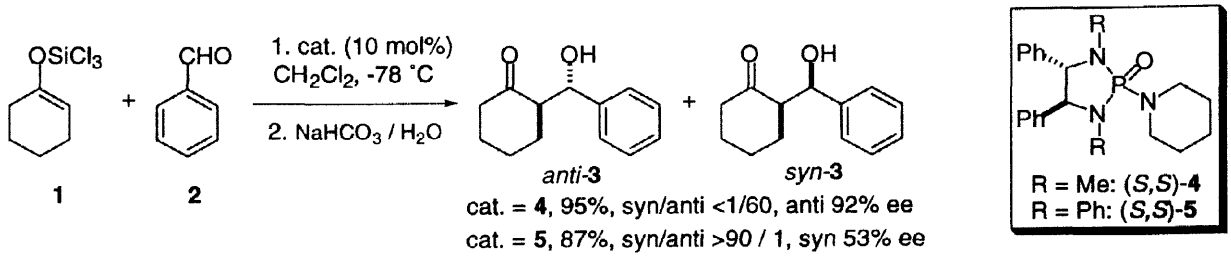
Key Words: Phosphoramides, Tin and Compounds, X-Ray Crystal Structures, Aldol Reactions

Introduction

The interaction of Lewis acids and Lewis bases has profound influence on structure and reactivity in organic chemistry.[1-3] This fundamental interaction is responsible for the activation of organic compounds and the creation of reactive intermediates in ionic and polar reactions. For example, the association of electron rich heteroatoms with electron deficient Lewis acids is responsible for the generation of carbenium ions, oxocarbenium ions and acylium ions by the removal of halogens and oxygens.[4] Furthermore, the coordination of electron rich carbonyl oxygens with Lewis acids is responsible for the polarization of that function and its activation toward nucleophiles.[2,5-7]

Recently we described a Lewis base-catalyzed aldol addition reaction wherein very high enantio- and diastereoselectivities were achieved with a catalytic amount of phosphoramide **4** (Scheme 1).[8] Both diastereo- and enantioselectivities of the reaction were sensitive to modification of the phosphoramide structure. The specific composition of **4** was so important to the reaction that essentially any modification of the structure resulted in inferior results. Moreover, with phosphoramide **5** the reaction became highly syn selective and only moderate enantiomeric excess was obtained.

Scheme 1



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Our basic mechanistic tenet is that the reaction proceeds via a ternary complex of enolate, aldehyde and phosphoramide assembled around the silicon atom.[9] Thus, to understand the origin of the selectivities in these reactions and the unique features of phosphoramides such as **4** and **5**, we initiated studies on the structure of chiral phosphoramide complexes with Lewis acids. A search of the Cambridge Crystallographic Data Base (CCDB) for the substructure HMPA-Si generated only five hits all of which are silylene complexes of iron or chromium.[10] Our own studies also showed that the complexation between silicon tetrachloride or trichlorosilyl enolate **1** and phosphoramides was very weak as judged by ^{1}H and ^{31}P NMR spectroscopy. Therefore, we focused our efforts on tin as a surrogate for silicon and report herein the results of X-ray and ^{119}Sn NMR studies of phosphoramides **4** and **5** with tin-based Lewis acids.

Results

X-Ray Crystallography. The CCDB contains a number of HMPA complexes with tin-containing Lewis acids,[11] including HMPA•Me_3SnCl[12a] and $(HMPA)_2$•$SnCl_4$.[12b] Thus, as point of entry we prepared the complex **4**•Me_3SnCl, and obtained a crystal (benzene/pentane) suitable for X-ray analysis, Figure 1.[13a]

The structure is analogous to that of HMPA•Me_3SnCl reported by Aslanov and coworkers.[12a] The pentacoordinate tin atom adopts a trigonal bipyramidal arrangement with both the chlorine atom and the oxygen of the phosphoramide at the apical positions as expected. The most interesting feature of the structure is in the phosphoramide portion. The 1,3,2-diazaphospholidine ring is highly distorted due to the long P-N bonds leading to an N(1)-P-N(2) angle of 94.3(2)°, much less than the ideal angle 109.5° for sp^3 hybridized atoms.[14] The nitrogens of the five-membered ring are pyramidalized (the sum of the three angles (Σ) around N(1) and N(2) are 353.7° and 344.4° respectively). Thus, the methyl and phenyl substituents in the ring adopt up-down-up-down arrangements creating a highly dissymmetric space around the phosphoramide oxygen atom. The C(10) atom on the piperidinyl group is almost eclipsed with the oxygen of the phosphoramide (torsional angle for O-P-N(3)-C(10) -19.3(5)°). An important consequence of this interaction is the disposition of the Me_3Sn unit. Interestingly, the P-O-Sn unit is not linear, but rather adopts a 148.3(2)° bend. In this structure, the tin atom sits away from the piperidinyl group to

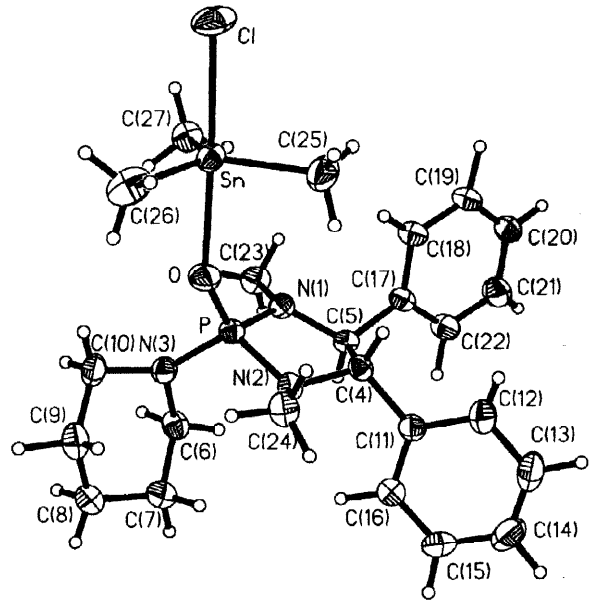


Figure 1. SHELXTL representation of the crystal structure of the **4**•Me_3SnCl complex (**6**) (35% thermal ellipsoids). Selected bond lengths [Å]: Sn-O 2.336(3); Sn-Cl 2.5239(13); P=O 1.490(3); P-N(1) 1.641(4); P-N(2) 1.667(4); P-N(3) 1.637(4); bond angles [°]: Sn-O-P 148.3(2); N(1)-P-N(2) 94.3(2); ΣN(1) 353.7(10); ΣN(2) 344.4(9); ΣN(3) 356.6(10); torsional angles [°]: Sn-O-P-N(1) -10.7(5); Sn-O-P-N(2) 98.9(4); Sn-O-P-N(3) -135.3(4)

avoid the possible steric interactions with the C(10)H_2 group (torsional angle for Sn-O-P-N(3) -135.3(4)°). The tin atom is above the five-membered ring and almost eclipsed with N(1) in the ring (torsional angle Sn-O-P-N(1) -10.7(5)°). Thus, the ligands around tin are located close to the dissymmetric space above the five-membered ring.

A second structure was secured by crystallization of (±)-**4** with $SnCl_4$. Crystals suitable for X-ray analysis (benzene/pentane) were found to constitute a 2/1 complex of the stoichiometry (**4**)$_2$•$SnCl_4$ (Figure 2).[13b]

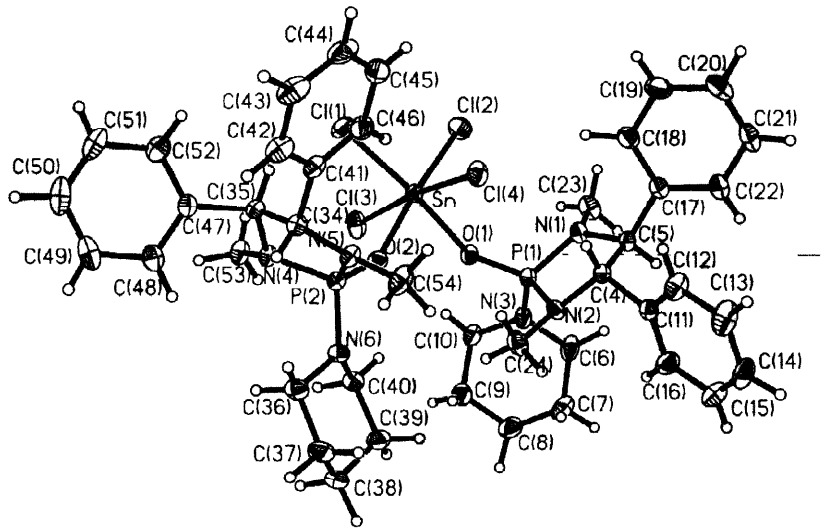


Figure 2. SHELXTL representation of the crystal structure of the (**4**)$_2$•$SnCl_4$ complex (**7**) (35% thermal ellipsoids). Selected bond lengths [Å]: Sn-O(1) 2.076(2); Sn-O(2) 2.085(2); P(1)=O(1) 1.502(2); P(2)=O(2) 1.505(2); Sn-Cl(1) 2.3863(8); Sn-Cl(2) 2.3953(7); Sn-Cl(3) 2.3926(7); Sn-Cl(4), 2.3894(7); bond angles [°]: Sn-O(1)-P(1) 150.05(11); Sn-O(2)-P(2) 148.18(11); N(1)-P(1)-N(2) 95.40(11); N(4)-P(2)-N(5), 95.62(11); O(1)-Sn-O(2) 83.21(7); torsional angles [°]: Sn-O(1)-P(1)-N(3). 158.1(2); Sn-O(2)-P(2)-N(6) -177.9(2).

The tin atom adopts an octahedral geometry with the two phosphoramide molecules cis to each other (at an acute angle, O(1)-Sn-O(2) (83.21(7)°)) in contrast to the (HMPA)$_2$•$SnCl_4$ complex,[12b] but in agreement with (4-*t*-butylbenzaldehyde)$_2$•$SnCl_4$ complex.[15] It is also interesting to note that the two phosphoramides attached to the same central tin atom had the same configuration although the unit cell was centrosymmetric. The Sn-O bonds (2.076(2) Å and 2.085(2) Å) are significantly shorter than that in **4**•Me_3SnCl (2.336(3) Å) while the P=O bonds are longer (1.502(2) Å, 1.505(2) Å vs. 1.490(3) Å in **4**•Me_3SnCl). These bond length changes are presumably due to the stronger complexation of the phosphoramide with the more electron deficient Lewis acid $SnCl_4$. As a consequence, the P-N bonds in the complex are shorter, due to increased hyperconjugation of the nitrogen lone pairs to the phosphorus.[14] The basic conformation of the phosphoramides is similar to that in **4**•Me_3SnCl. The Sn-O(1)-P(1) and Sn-O(2)-P(2) angles are 150.05(11)° and 148.18(11)° respectively, and the torsional angles Sn-O(1)-P(1)-N(3) and Sn-O(2)-P(2)-P(6) are 158.1(2)° and -177.9(2)° respectively. As in **4**•Me_3SnCl, the tin atom is situated above the five-membered rings of the phosphoramides.

In the reactions in Scheme 1, the phosphoramide **5** with phenyl groups on the internal nitrogens gave strikingly different results from those from the sterically less demanding phosphoramide **4**. Accordingly we sought to crystallize a 2/1 complex of **5** with $SnCl_4$ to provide some structural basis for us to understand the origin of the change of selectivities.

The deposition of a single crystal of a 2/1 complex of **5** and $SnCl_4$ turned out to be difficult. Similar conditions as the crystallization of (**4**)$_2$•$SnCl_4$ either resulted amorphous material or co-crystallization with water (*vide infra*). Ultimately, slow evaporation from benzene deposited single crystals suitable for X-ray analysis,

which turned out to be a benzene-solvated complex of $(\mathbf{5})_2$•$SnCl_4$ (Figure 3).[13c] Four molecules of benzene were also found in a unit cell, which implies the importance of solvent benzene in the crystal packing.

Since the complex was centrosymmetric, the two phosphoramides have identical conformation. The trans disposition of the two phosphoramides may be a consequence of the steric bulk of the molecules, in addition to possible crystal packing forces. The disposition of the tin atom relative to the phosphoramide was similar to other complexes discussed; for example, the N(3)-P(1)-O(1)-Sn(1) dihedral angle was 175.3(4)°. The conformation of the four phenyl rings were different. While the two phenyl rings on the backbone were almost perpendicular to the five-membered ring, the phenyl rings on the nitrogens approximately eclipsed the ring C-N bonds. Presumably, the n-π hyperconjugation between the nitrogens and the phenyl rings is still important in the complex. This observation coupled to the slightly longer Sn(1)-O(1) bond (2.100(2) Å, vs 2.076(2) Å and 2.085(2) Å in $(\mathbf{4})_2$•$SnCl_4$) and slightly shorter P(1)-O(1) bond (1.492(3) Å vs 1.505(2) Å and 1.502(2) Å in $(\mathbf{4})_2$•$SnCl_4$) strongly suggests a weaker coordination of phosphoramide **5** compared to **4** with $SnCl_4$. It is also interesting to note that the relative disposition of the piperidinyl ring in **8** is opposite to those in complexes **6** and **7**. Whereas the piperidinyl ring is folded toward the β-pyramidalized nitrogen[16] in **6** and **7**, the piperidinyl ring in **8** is folded away from the β-pyramidalized nitrogen (dihedral angle P(1)-N(3)-C(27)-C(28), 129.8(4)°). This is probably caused by the conformation of phenyl rings on the nitrogens. These conformational differences contribute to the spatial environment for asymmetric induction in Lewis base-catalyzed aldol reactions.

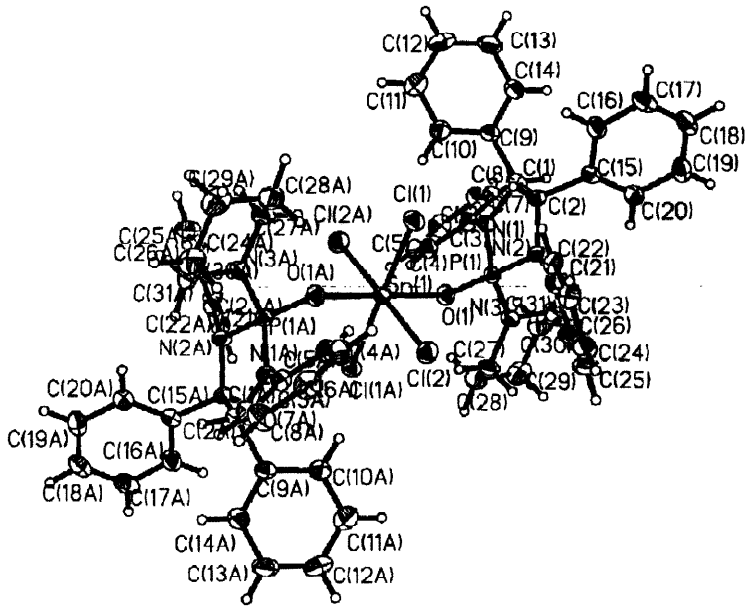


Figure 3. ORTEP representation of $(\mathbf{5})_2$•$SnCl_4$ complex (**8**) (35% thermal ellipsoids) View of the complex (solvents omitted). Selected bond lengths [Å]: Sn(1)-O(1), 2.100(2); Sn(1)-Cl(2), 2.3821(11); Sn(1)-Cl(1), 2.3963(10); P(1)-O(1), 1.492(3); P(1)-N(3), 1.619(3); P(1)-N(1), 1.645(3); P(1)-N(2), 1.651(3); bond angles [°]: P(1)-O(1)-Sn(1), 156.4(2); N(1)-P(1)-N(2), 94.9(2); O(1)-P(1)-N(3), 105.8(2); ΣN1 356.5(8); ΣN2 350.4(8); ΣN3 359.7(9); torsional angles [°]: N(3)-P(1)-O(1)-Sn(1), 175.3(4); N(1)-P(1)-O(1)-Sn(1), -61.5(5); N(2)-P(1)-O(1)-Sn(1), 49.0(5); P(1)-N(3)-C(27)-C(28), 129.8(4); C(1)-N(1)-C(3)-C(8), 24.9(6); C(2)-N(2)-C(21)-C(22), 21.0(5).

Our emerging mechanistic interpretation suggests that the bulkier phosphoramide might be capable of only 1/1 complexation thus promoting a different reaction pathway.[9] Therefore, we investigated the complexation of $SnCl_4$ with **5** in a 1/1 stoichiometry. Indeed, crystallization of **5** with $SnCl_4$ resulted in a 1/1/1 ternary complex (**9**) of $SnCl_4$, **5** and one molecule of water (Figure 4).[13d] It is interesting to note that the crystallization of this ternary complex between **5**, water and $SnCl_4$ is preferred over binary complexes $(\mathbf{5})_2$•$SnCl_4$ and $(H_2O)_2$•$SnCl_4$. The two oxygen ligands are cis to each other and the acute angle O(1)-Sn(1)-O(2) (81.00(13)°) is similar to the angle in $(\mathbf{5})_2$•$SnCl_4$ (83.21(7)°). The conformation of the phosphoramide is very close to that observed in $(\mathbf{5})_2$•$SnCl_4$.

Since water can be regarded as a Lewis base in the complex **9**, the immediate implication of the successful crystallization of H_2O•**5**•$SnCl_4$ was the possibility to substitute water with a chemically more significant Lewis basic ligand, namely benzaldehyde. Thus, from a CH_2Cl_2/hexane (1/2) solution containing equimolar amounts of $SnCl_4$, **5** and benzaldehyde, single crystals of the desired ternary complex (**10**) suitable for X-ray analysis were obtained by slow diffusion (Figure 5).[13e] The formation PhCHO•**5**•$SnCl_4$ is remarkable given the fact that both benzaldehyde[15] and **5** independently form 2/1 complexes with $SnCl_4$. Presumably, the balance between the steric bulk and the Lewis basicity of both ligands is crucial for the successful crystallization of this complex.

In this species as well, the tin atom adopts an octahedral geometry with the oxygen atoms cis to each other. The global conformation of the phosphoramide is similar to that in the two previous complexes. The Sn-O(1) (2.074(2) Å) bond is shorter than the Sn-O(2) bond (2.210(2) Å) and the acute angle of O(1)-Sn-O(2) (78.39(6)°) has already been noted in $(4)_2$•$SnCl_4$. As was seen in the other structures, the P-N(3) bond (1.616(2) Å) is much shorter than the P-N(1) (1.647(2) Å) or P-N(2) (1.650(2) Å) bonds, implying that there is greater degree of double bond character in P-N(3). This is in agreement with the fact that N(3) is

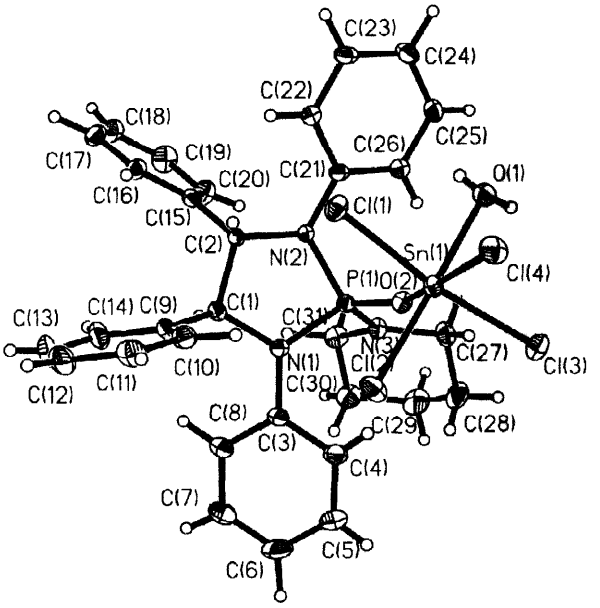


Figure 4. SHELXTL representation of H_2O•**5**•$SnCl_4$ complex (**9**) (35% thermal ellipsoids, solvents omitted for clarity). Selected bond lengths [Å]: Sn(1)-O(2), 2.106(3); Sn(1)-O(1), 2.230(4); Sn(1)-Cl(2), 2.3470(12); Sn(1)-Cl(1), 2.3633(12); Sn(1)-Cl(4), 2.3648(12); P(1)-O(2), 1.506(3); P(1)-N(3), 1.610(4); P(1)-N(1), 1.646(4); P(1)-N(2), 1.659(4); bond angles: [°] O(2)-Sn(1)-O(1), 81.00(13); P(1)-O(2)-Sn(1), 146.6(2); N(1)-P(1)-N(2), 95.2(2); ΣN1 355.2(10); ΣN2 354.6(9); ΣN3 359.2(10); torsional angles [°]: N(3)-P(1)-O(2)-Sn(1), -173.8(3); N(1)-P(1)-O(2)-Sn(1), -50.8(4); N(2)-P(1)-O(2)-Sn(1), 59.0(4); O(1)-Sn(1)-O(2)-P(1), -112.0(4); P(1)-N(3)-C(27)-C(28), 134.2(5).

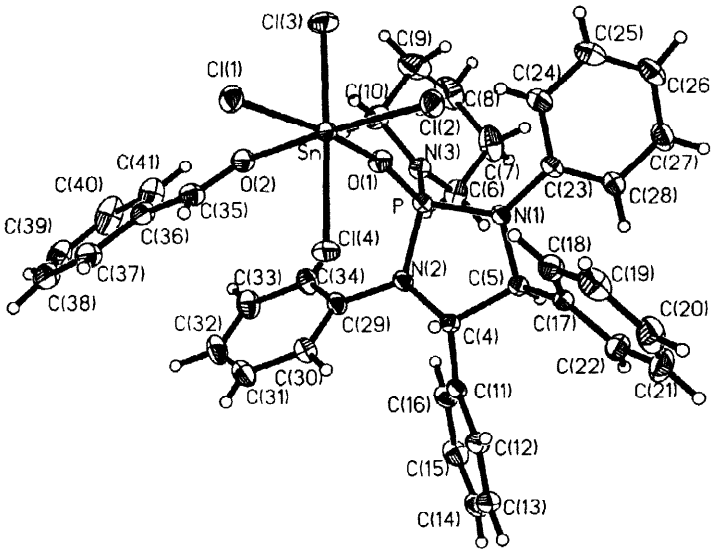


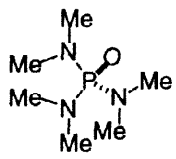
Figure 5. SHELXTL representation of the crystal structure of the PhCHO•**5**•$SnCl_4$ complex (**10**) (35% thermal ellipsoids). Selected bond lengths [Å]: Sn-O(1), 2.074(2); Sn-O(2), 2.210(2); P=O(1), 1.500(2); P-N(1), 1.647(2); P-N(2), 1.650(2); P-N(3), 1.616(2); bond angles [°]: O(1)-Sn-O(2), 78.39(6); Sn-O(1)-P, 158.20(11); torsional angles [°]: Sn-O(1)-P-N(3), 173.3(3); O(1)-P-N(3)-C(6), 177.2(2); O(1)-P-N(3)-C(10), -11.3(2).

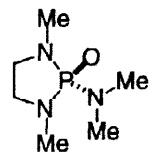
almost perfectly sp^2 hybridized (ΣN(3) is 359.5°), and is capable of more effective hyperconjugation with phosphorus.[14] Again the C(3) atom of the piperidinyl group is almost eclipsed with the oxygen of the phosphoramide (O(1)-P-N(3)-C(10): -11.3(2)°) and the tin atom is directly above the 1,3,2-diazaphospholidine ring.

NMR Spectroscopy. Although X-ray crystallography provided detailed structural information about the phosphoramide-tin complexes, the influence of crystal packing forces cannot be ignored. Accordingly, a solution NMR investigation (^{119}Sn, ^{31}P, ^{1}H) into the complexation behavior of these ligands with $SnCl_4$ was undertaken.

Chiral phosphoramides **4** and **5** as well as achiral phosphoramides HMPA and **11** were employed in the NMR studies (Table 1). In general, a 2/1 stoichiometry of phosphoramide to $SnCl_4$ gave much cleaner spectra than a 1/1 ratio of the two reagents. The ^{119}Sn NMR spectrum of the 2/1, HMPA/$SnCl_4$ combination displayed two triplets with coupling constants of 102 and 168 Hz. Clearly two species were present in solution and in the two complexes each tin atom is coupled to two phosphorus atoms, implying a stoichiometry of $(HMPA)_2$•$SnCl_4$. This is supported by the ^{31}P NMR spectra wherein two signals displaying ^{119}Sn satellites with the corresponding coupling constants were present. In addition, the chemical shifts of the ^{119}Sn resonances were in agreement with hexacoordinate species.[17] The complexation of chiral phosphoramides and $SnCl_4$ was also detectable in solution. At -80°C (0.1 M in CH_2Cl_2) a mixture of $SnCl_4$ with two equivalents of **4** displayed a triplet at -713 ppm (J = 115 Hz) in the ^{119}Sn NMR spectrum (Figure 6). The triplet most likely arises from coupling to two equivalent

Table 1. NMR Studies of Phosphoramide-Tin Complexation.[a]


HMPA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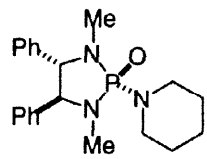
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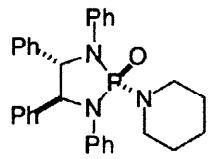
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entry	phosphoramide	ratio (phosphoramide/$SnCl_4$)	^{119}Sn NMR, ppm (J, Hz)	^{31}P NMR, ppm (J, Hz)
1	HMPA	1/1	−455(d, J=167)*, −720, −239	21.6*, 24.0-20.2(m)
2[b]	HMPA	2/1	−719(t, J=102)*, −727(t, J=168)	20.9(s)*, 21.2(s)
3	**11**	1/1	−696(t, J=102)*, −480, −720	25.1(s)*, 27-19(m)
4[c]	**11**	2/1	−721(t, J=105)*, −725(t, J=156)	25.1(s)*, 27-24.5(m)
5	(−)-**4**	1/1	−452(br)*, −692, −714	23.5(br)*, 27-19(m)
6[d]	(−)-**4**	2/1	−713(t, J=115)*, −662(br)	23.2(br)
7	(±)-**5**	1/1	−445(d, J=205)*, −657	9.2(br)*, 11.2(br)
8	(±)-**5**	2/1	−711(t, J=137)*, −724, 725(t, J=200), −671, −706	10.7(br)*, 9.8(br), 15.2(br)

[a] All the studies were conducted in CD_2Cl_2 at 0.1 M concentration in $SnCl_4$. A * designates the major peaks observed in the spectra. [b] The ratio of the two peaks in ^{119}Sn NMR are 2.3/1 (−719 and −727 ppm) at −90 °C and 1/1.4 (δ −721 (t, J=120), −733 (t, J=188)) at 20 °C. Satellites in ^{31}P NMR were clearly seen: at 20.9 (ca. 100 Hz) and 21.2 ppm (ca. 170 Hz). [c] The ratio of the two peaks in ^{119}Sn NMR was 3.5/1, satellites in ^{31}P NMR not clear due to overlap. [d] The ratio of the two peaks was >10/1. When racemic **4** was used, white precipitates were observed in solution.

phosphorus atoms and thus represents a 2/1 complex in solution.[17-19] An equimolar solution of $SnCl_4$ and **4** was more complicated; the major signal appeared at -452 ppm and was broad. This chemical shift region is ascribed to pentacoordinate tin[17] and thus it appears that only one molecule of **4** was bound to $SnCl_4$ and this species was in rapid equilibrium with other species including 2/1 complexes (d, –692, –713 ppm) (Figure 6).

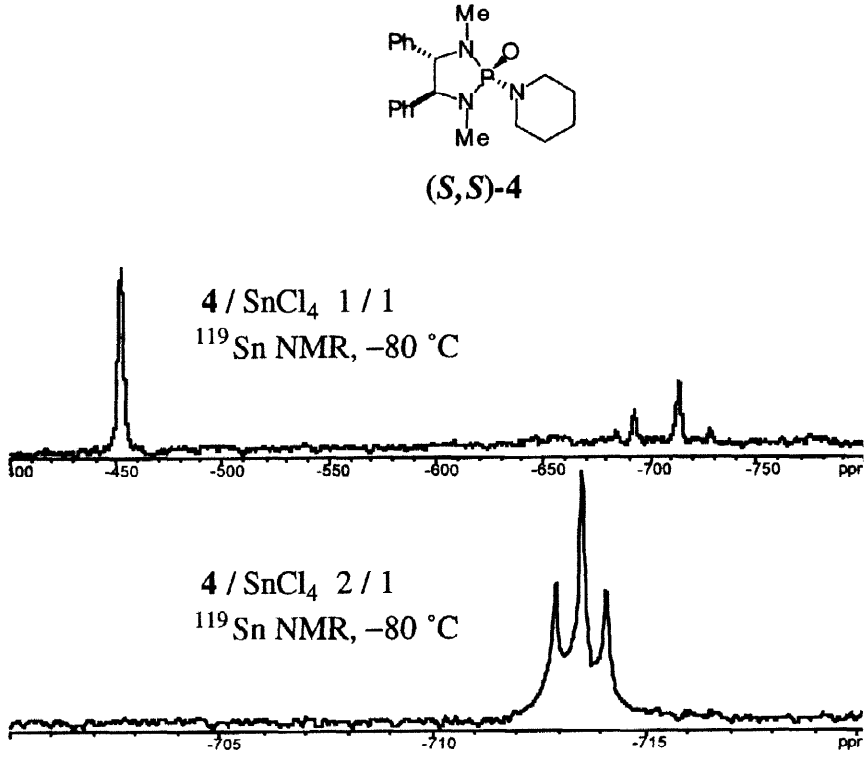

Figure 6. ^{119}Sn NMR spectra of **4** / $SnCl_4$ complexes.

Several general trends can be summarized from the NMR data. (1) Usually the NMR spectra were complicated, implying the presence of a number of species and dynamic process in the solution even at –80 °C. (2) A 2/1 stoichiometry of phosphoramide to $SnCl_4$ showed only hexacoordinate species (δ ~– 700 ppm), but 1/1 stoichiometry gave both pentacoordinate (δ ~–460 ppm) and hexacoordinate complexes. In the case of HMPA, the signal at –239 ppm may be assigned to free $SnCl_4$, but in other spectra, no peaks corresponding to $SnCl_4$ could be found, presumably due to broad lines caused by the interaction of $SnCl_4$ with the complexes. (3) In the case of 2/1 stoichiometry, mainly two complexes, presumably cis and trans isomers, were found in the ^{119}Sn NMR spectra except for the **5**/$SnCl_4$ complexes, where at least 5 species were present in solution, perhaps arising from rotamers. (4) The pentacoordinate complexes were more labile and broad lines were seen in both ^{119}Sn and ^{31}P NMR spectra. Only in the pentacoordinate complexes with HMPA and phosphoramide **5** could the coupling constants be extracted. The magnitude of the coupling constants, 167 and 205 Hz, imply an averaged coupling constants with the phosphoramide located at the apical and the basal positions, thus also indicating the lability of the trigonal bipyramidal geometry of the central tin atom.

Discussion

These studies provide vital information about the structural features of phosphoramides and their complexes with tin-based Lewis acids. To correlate these results to the reactivity and selectivity of phosphoramides **4** and **5** in

the Lewis base-catalyzed aldol reaction, it is important to understand the structures of the complexes in solution. Thus, the following discussion will begin with the NMR studies.

Assignment of Complex Geometry from the NMR Studies. For the hexacoordinate complexes of $SnCl_4$ with two molecules of a phosphoramide, both cis and trans isomers are possible. In the solid state, the HMPA complex with $SnCl_4$ showed a trans geometry.[12b] In solution, complexes of the general formula $L_2{\bullet}SnCl_4$ exists as a mixture of both cis and trans isomers.[20] The determination of cis/trans isomer ratio in solution turned out to be difficult and often conflicting results are encountered in the literature.[20] The most compelling studies for the isomers of the complex $(HMPA)_2{\bullet}SnCl_4$ was presented by Ruzicka and Merbach.[21] By consideration of the different symmetry of *cis*- and *trans*-$(HMPA)_2{\bullet}SnCl_4$, the authors were able to assign the IR and Raman spectroscopy signals of two isomers in a solution of the complex in dibromomethane. The authors then correlated these data with ^1H NMR and ^{31}P NMR studies and showed that the trans/cis ratio was 1.33 in CH_2Cl_2 at 20 °C. This result is in agreement with our observation of a 1/1.4 ratio by ^{119}Sn NMR analysis at 20 °C. Furthermore, the authors have shown that the coupling constants $^2J(^{31}P\text{-}^{119}Sn)$ were different for *cis*- and *trans*-isomers in the complexes of $SnCl_4$ with $(MeO)_3PO$ and $Me_2N(MeO)_2PO$. At 203 K the cis isomers of the two complexes had the coupling constants $^2J(^{31}P\text{-}^{119}Sn)$ of 146 and 141 Hz respectively, and the coupling constants for the trans isomers were 195 and 194 Hz respectively. These results are in agreement with the coupling constants 102 and 168 Hz observed with $(HMPA)_2{\bullet}SnCl_4$ at 183K in our case. With this information, it is possible to assign the major isomer of $(HMPA)_2{\bullet}SnCl_4$ at 183K as the cis isomer (δ –719 (t, J=102)). By comparing the coupling constants, the isomers of the other complexes in Table 1 could be assigned by analogy, i.e., all of the complexes which have smaller $^2J(^{31}P\text{-}^{119}Sn)$ coupling constants can be assigned to the cis isomers.

Complexation of Phosphoramides to $SnCl_4$. From the above assignments and the NMR data in Table 1, several trends for the complexation of phosphoramides to $SnCl_4$ can be summarized. (1) The hexacoordinate complexes are easily accessible in CD_2Cl_2 solution, even in the presence of less than two equivalents of Lewis bases. This fact supports the accessibility of hexacoordinate silicon with two phosphoramides. (2) The cis isomers of the complexes are preferred in solution at low temperature. Even with sterically hindered phosphoramide **5**, cis isomer coexists with the trans one. Caution must be taken when this is extrapolated to the transition structure geometry in the Lewis base-catalyzed aldol reaction because of the difference in the bond lengths and the type of ligands involved in the trichlorosilyl enolate complex from those of $SnCl_4$ complexes. (3) Phosphoramide **4** is unique in that it forms almost exclusively the cis complex with $SnCl_4$ in solution. The exact reason for this preference is not clear because both sterically more hindered and less hindered phosphoramides form trans complexes in solution. (4) With phosphoramide **5**, five peaks were observed in the ^{119}Sn NMR spectra when a 2/1 mixture of **5** / $SnCl_4$ was present in solution. This may be caused by conformers due to restricted rotation of the hindered phosphoramide. (5) At a 1/1 ratio of phosphoramide to $SnCl_4$, pentacoordinate species is favored except for **11**, which showed largely the hexacoordinate species. This result indicates that in addition to stoichiometry, steric effects contribute to the equilibrium between hexacoordinate and pentacoordinate complexes.

Conformational Information from X-Ray Structures of Complexes of Phosphoramides to Tin Lewis Acids. The interpretation of solid state structures must be carried out with caution due to crystal

packing forces. Nevertheless, some intrinsic preferences of a molecule should be maintained in the solid state as well. Thus, analysis of a number of structures is necessary to arrive at meaningful conclusions.[22]

From the five structures of phosphoramide-tin complexes, it is notable that several conformational preferences were maintained (Figure 7). The binding of the tin atom to the phosphoramide is not linear; the Sn-O-P angle of 146 to 158° agrees well with that in $(HMPA)_2 \cdot SnCl_4$ (148°). This nonlinear binding has important consequences for the position of tin relative to the phosphoramides. The five phosphoramides studied all have piperidinyl and the diazaphospholidine ring systems. The tin atom always turns away from the piperidinyl group (dihedral angles for Sn-O-P-N (piperidinyl) ranged from −135 to +157°. This conformation puts the tin atom directly above the five-membered ring, and may have important implications for asymmetric induction. The piperidinyl nitrogen is close to planar (ΣN ranged from 357° to 360°, except in one case it was 352°), which is most likely a consequence of overlap of the nitrogen lone pairs with the phosphorus anti bonding orbitals.[14c,d] Because the donation of the lone pair electron on the nitrogens is important for the stabilization of the complex, the piperidinyl nitrogen, which is free of ring strain as compared to the nitrogens in the diazaphospholidine ring, will maximize the electron-donating potential by adopting sp^2 hybridization. The torsion around the P-N(piperidinyl) bond is biased due to this overlap (dihedral angles for O-P-N-C ranged from 173° to −177°). This unique conformation of the piperidinyl ring may explain why the change of this achiral group to other dialkylamino groups resulted in the dramatic decrease in selectivities in the Lewis base-catalyzed aldol reaction.[23] Other dialkylamino groups may have different conformational preferences thus resulting in a change of coordination geometry of phosphoramides with the Lewis acid. On the other hand, the nitrogen atoms in the five-membered ring are pyramidalized. As a result, the substituents on the ring atoms adopt an up-down-up-down arrangement, creating a highly dissymmetric space in which to accommodate the reacting components in the aldol addition.

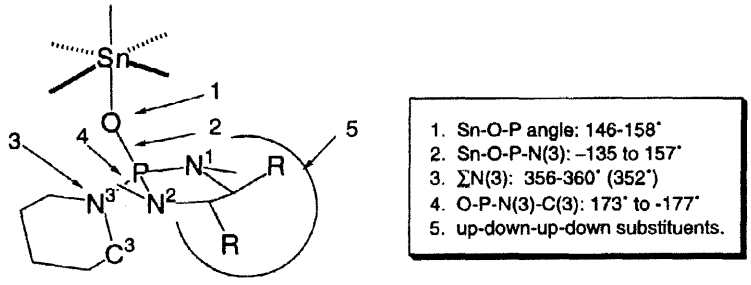

Figure 7. Important conformational features in phosphoramide-tin complexes.

Conclusion

In summary, X-ray and NMR studies have provided useful structural details for the complexation of chiral phosphoramides **4**, and **5** to tin-based Lewis acids. This information provides a firm foundation for understanding the origin of catalysis and selectivity in the Lewis base-catalyzed aldol reactions with chiral phosphoramides. These insights, together with computational analyses, will assist our development of proposals for transition structure assemblies and guide the rational design of better catalysts for the reaction.

Experimental Section

X-Ray Crystal Structure Analyses. All of the data were collected on a Siemens three-circle platform diffractometer with Mo irradiation ($Mo_{K\alpha}$ = 0.71073 Å) and a CCD area detector, T = 198 K; programs used: SHELXS-86, SHELXL-93. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication nos. CCDC-103025 (**6**), CCDC-103026 (**7**), CCDC-113722 (**8**), CCDC-113721 (**9**), CCDC-103027 (**10**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

4•Me_3SnCl (**6**). To a solution of trimethyltin chloride in hexane was added an equal molar amount (*S,S*)-**4** in a 1/1 mixture of benzene-hexane and white crystals were generated instantly. The crystals were collected, washed with fresh hexane and then (about 30 mg) were dissolved in 0.5 mL of benzene in a small test tube (1 X 5 mm) under nitrogen. Freshly distilled pentane (2 mL) was slowly added along the side wall of the test tube to create two layers in the solution. The test tube was then placed in an Erlenmeyer flask (125 mL) and capped with a rubber stopper. Single crystals suitable for X-ray analysis were obtained after two days.

$(\mathbf{4})_2$•$SnCl_4$ (**7**). The crystals of this complex were prepared essentially the same way from (±)-**4** and $SnCl_4$ above in 1/1 benzene/hexane solution.

$(\mathbf{5})_2$•$SnCl_4$ (**8**). Attempted co-crystallization of (±)-**5** with $SnCl_4$, benzaldehyde and a phenoxide in a benzene/hexane mixed solvent system deposited crystals, which were redissolved in benzene. Slow evaporation of the solvent benzene deposited single crystals suitable for X-ray analysis, which turned out to be a benzene-solvated complex of $(\mathbf{5})_2$•$SnCl_4$ (**8**).

(H_2O)•**5**•$SnCl_4$ (**9**). To a solution of an equimolar amount of (±)-**5** and $SnCl_4$ in CH_2Cl_2 in a test tube was added equal volume of hexane on top of the CH_2Cl_2 solution. The test tube with the mixture was then placed in an Erlenmeyer flask and capped with a rubber stopper. Crystals suitable for X-ray analysis were obtained after the solvents were slowly evaporated.

(PhCHO)•**5**•$SnCl_4$ (**10**). To a solution of (±)-**5** (12.3 mg, 0.025 mmol) in CH_2Cl_2 (1.5 mL) were added $SnCl_4$ (3 μL, 0.025 mmol) and benzaldehyde (2.4 μL, 0.025 mmol). Hexane (1.5 mL) was then added slowly on top of the solution via a syringe. The mixture was then allowed to slowly evaporate at rt inside an Erlenmeyer flask capped with a rubber stopper. The oily residue obtained was redissolved in 2 mL of CH_2Cl_2 and 0.5 mL of the solution was transferred to another test tube and 1 mL of fresh hexane was added. The mixture was again allowed to slowly evaporate and single crystals were obtained after two days at rt.

NMR Spectroscopy. ^1H-, ^{31}P- and ^{119}Sn-NMR spectra were recorded on a Varian Unity 500 spectrometer. The frequency of the spectrometer was calibrated against residual $CDHCl_2$ (4.32 ppm) in the solvent. The ^{31}P- and ^{119}Sn-NMR chemical shifts were then referenced to the spectrometer. The temperature of the probe was calibrated using methanol.

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(13) (a) X-ray crystal structure analysis of **4**•Me_3SnCl (**6**): formula: $C_{24}H_{37}ClN_3OPSn$, M_r = 568.68, crystal size 0.12 X 0.4 X 0.8 mm, a = 10.1751(2) Å, b = 14.5451(3) Å, c = 10.5454(2) Å, β = 116.3310(10)°, V = 1398.77(5) Å^3, ρ_{calcd} = 1.350 gcm^{-3}, m = 1.085 mm^{-1}, empirical absorption correction, Z = 2, monoclinic, space group, $P2_1$; of 9023 reflections measured ($\pm h$, $\pm k$, $\pm l$), 5344 were independent and 4970 observed with I > 2 σ(I); 351 parameters refined in full matrix, *R*1 = 0.0387, *wR*2 = 0.0992 (against F^2), residual electron density -0.837/1.314 e.Å^{-3}. (b) X-ray crystal structure analysis of $(\mathbf{4})_2$•$SnCl_4$•$(CH_2Cl_2)_{1.5}$ (**7**): formula: $C_{43.5}H_{59}Cl_7N_6O_2P_2Sn$, M_r = 1126.75, crystal size 0.50 X 0.20 X 0.20 mm, a = 13.2996(2) Å, b = 14.2280(2) Å, c = 16.0325(2) Å, α = 67.1790(10)°, β = 85.2970(10)°, γ = 68.2820(10)°, V = 2591.09(6) Å^3, ρ_{calcd} = 1.444 gcm^{-3}, μ = 0.957 mm^{-1}, empirical absorption correction, Z = 2, triclinic, space group, *P*-1; of 17014 reflections measured ($\pm h$, $\pm k$, $\pm l$), 11810 were independent and 8675 observed with I > 2 σ(I); 596 parameters refined in full matrix, *R*1 = 0.0388, *wR*2 = 0.0902 (against F^2), residual electron density -1.015/0.903 e.Å^{-3}. (c) X-ray crystal structure analysis of $(\mathbf{5})_2$•$SnCl_4$•$(C_6H_6)_4$ (**8**): formula: $C_{86}H_{88}Cl_4N_3O_2P_2Sn$, M_r = 1529.18, crystal size 0.07 X

0.12 X 0.32 mm, a = 10.6411(2) Å, b = 12.9718(3) Å, c = 16.2842(2) Å, α = 102.7590(10)°, β = 102.1010(10)°, γ = 111.0640(10)°, V = 1939.90(6) Å^3, ρ_{calcd} = 1.335 g/cm^3, μ = 0.560 mm^{-1}, empirical absorption correction, Z = 2, triclinic, space group, *P*-1; of 12695 reflections measured (±*h*, ±*k*, ±*l*), 8804 were independent and 5072 observed with I > 2 σ(I); 457 parameters refined in full matrix, *R*1 = 0.0570, *wR*2 = 0.1322 (against 'F^2'), residual electron density 0.541 and -0.789 e.Å^{-3}. (d) X-ray crystal structure analysis of H_2O•**5**•$SnCl_4$•(CH_2Cl_2) (**9**): formula: $C_{32}H_{36}Cl_6N_3O_2PSn$, M_r = 857.00, crystal size 0.14 X 0.17 X 0.36 mm, a = 9.7858(2) Å, b = 13.9330(3) Å, c = 14.1430(3) Å, α = 78.1050(10)°, β = 82.7510(10)°, γ = 73.8200(10)°, V = 1807.33(7) Å^3, ρ_{calcd} = 1.575 g/cm^3, μ = 1.229 mm^{-1}, empirical absorption correction, Z = 2, triclinic, space group, *P*-1; of 11815 reflections measured (±*h*, ±*k*, ±*l*), 8269 were independent and 6883 observed with I > 2 σ(I); 536 parameters refined in full matrix, *R*1 = 0.0537, *wR*2 = 0.1245 (against 'F^2'), residual electron density 0.924 and -1.208 e.Å^{-3}. (e) X-ray crystal structure analysis of PhCHO•**5**•$SnCl_4$ (**10**): formula: $C_{38}H_{38}Cl_4N_3O_2PSn$, M_r = 860.17, crystal size 0.16 X 0.20 X 0.37 mm, a = 17.2934(2) Å, b = 17.3585(2) Å, c = 13.02570(10) Å, β = 95.63°, V = 3891.30(7) Å^3, ρ_{calcd} = 1.468 gcm^{-3}, μ = 1.009 mm^{-1}, empirical absorption correction, Z = 4, monoclinic, space group, $P2_1/c$; of 25037 reflections measured (±*h*, ±*k*, ±*l*), 9341 were independent and 8100 observed with I > 2 σ(I); 557 parameters refined in full matrix, *R*1 = 0.0316, *wR*2 = 0.0743 (against 'F^2'), residual electron density -0.477/0.423 and e.Å^{-3}.

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