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Unusual Conformational Effect in α-Aminoorganostannanes

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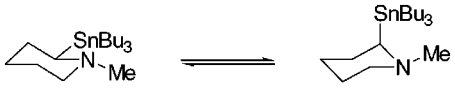
ABSTRACT



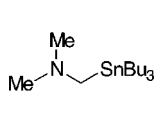
ΔG° = 73 cal/mole at −70°

Dynamic NMR analysis of conformationally mobile and rigid 2-tributylstannyl-*N*-methylpiperidines revealed an unexpected conformational effect that is manifested in a small energy difference between conformers in which the tin is equatorial and axial. The major reason appears to be a distortion of the conformer in which the C-2–Sn bond is synclinal to the nitrogen lone pair.

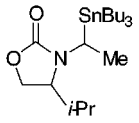
In the last 20 years, α-aminoorganolithiums have become important reagents in organic synthesis because of their versatility and configurational stability.[1−7] From a stereochemical standpoint, two of the more useful methods used to access α-aminoorganolithiums are deprotonation and transmetalation by tin−lithium exchange. The two methods are complementary: deprotonation can be stereoselective, whereas tin−lithium exchange provides access to compounds that are not accessible by deprotonation due to a kinetic barrier. Furthermore, since metal exchange usually proceeds with retention of configuration at a stereogenic metal-bearing carbon, tin−lithium exchange can afford organolithiums of known absolute configuration.

Unfortunately, metal exchange in α-aminoorganostannanes is characterized by anomalies. Although α-aminoorganostannanes first became precursors to α-aminoorganolithiums nearly 30 years ago,[8] transmetalation can be capricious. Several examples of α-aminoorganostannanes for which transmetalation attempts have been reported are shown below.[9−16] In particular, note the effects of rings on the success or failure of the transmetalation reaction. At a position where the metal-bearing carbon is secondary, tin-lithium exchange fails when the metal-bearing carbon is acyclic, unless there is a chelating atom available. Clearly, there are very subtle factors at work here, and structural studies of α-aminoorganostannanes are warranted.

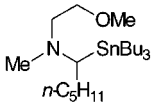
Successfully transmetalate:



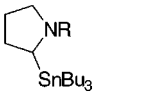
Peterson, 1970[8]



Pearson, 1991[9]

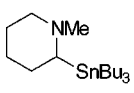


Chong, 1993[10]



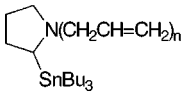
R = Me, $CH_2CH_2OCH_3$

Gawley, 1993[11] 1994[12]



1

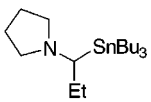
1993[11]



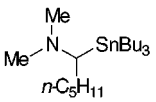
n = 1,2

1995[13] 1996[14]

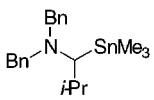
Fail to transmetalate:



Tsunoda, 1991[15]



Chong, 1993[10]



Pearson, 1996[16]

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Recently, as part of an NMR investigation of heterocyclic α-aminoorganometallics, we examined the carbon-13 NMR spectra of *N*-methyl-2-tributylstannylpiperidine (**1**) at low temperature. We were surprised to find evidence of two nearly equally populated conformers, suggesting that there is a stereoelectronic effect that influences the solution structure of α-aminoorganostannaes.

Partial ^{13}C spectra (C-2, C-6, and the *N*-methyl region) of *N*-methyl-2-tributylstannylpiperidine and the same region (now including C-4) of *cis*-*N*-methyl-4-*tert*-butyl-2-tributylstannylpiperidine, **2**, at various temperatures, are shown in Figure 1. The absence of any dynamic phenomena in the

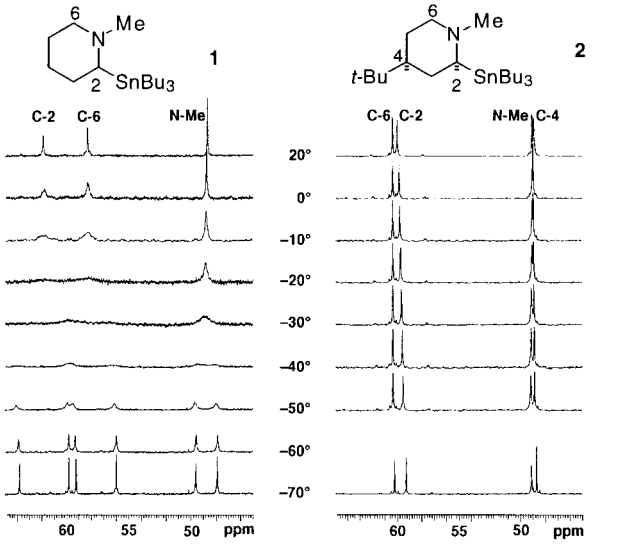
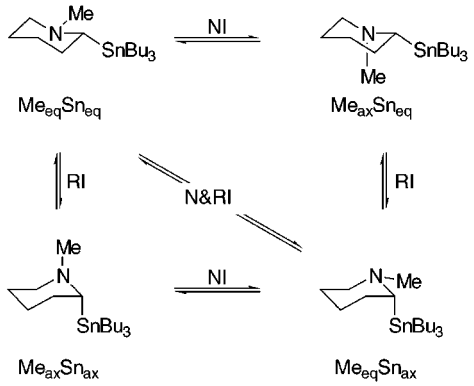


Figure 1. Partial ^{13}C NMR spectra (100 MHz, THF-d_8) of *N*-methyl-2-tributylstannylpiperidine and *cis*-*N*-methyl-4-*tert*-butyl-2-tributylstannylpiperidine.

spectra of **2** fix the dynamic phenomena of **1** as ring inversions. The coalescence temperature for the *N*-methyl signal of **1** is near −30° and corresponds to an energy of activation of approximately 11 kcal/mol. In comparison, the barrier to ring inversion for *N*-methylpiperidine (in methanol) is 14.4 kcal/mol.[17]

Only two species are observed in the DNMR spectra at slow exchange. There are four possible chair conformations for *N*-methyl-2-tributylstannylpiperidine, as shown in Scheme 1, resulting from ring inversion (RI, vertical arrows) and

Scheme 1[a]



[a] NI = nitrogen inversion; RI = ring inversion. N&RI = simultaneous nitrogen and ring inversion.

nitrogen inversion (NI, horizontal arrows). From the $Me_{eq}Sn_{eq}$ conformer, RI gives the high-energy $Me_{ax}Sn_{ax}$ conformer and then NI affords the $Me_{eq}Sn_{ax}$ conformer. The latter is more easily accessed via the $Me_{ax}Sn_{eq}$ conformer by a sequential NI−RI sequence from the $Me_{eq}Sn_{eq}$ conformer. It has also been suggested that these individual motions could be coupled such that conversion of the $Me_{eq}Sn_{eq}$ to the $Me_{eq}Sn_{ax}$ conformer takes place directly (N&RI).[18] The energetic preference for the *N*-methyl of *N*-methylpiperidine for the equatorial orientation is 2.41 kcal/mol (chloroform solution),[19] so the two Me_{ax} conformers are unlikely contributors, leaving the $Me_{eq}Sn_{eq}$ and $Me_{eq}Sn_{ax}$ as the two species observed by NMR.

The free energy difference for a methyl in the 2-position of *N*-methylpiperidine is 1.7 kcal/mol,[20] the same as its *A* value in methylcyclohexane. The *A* values for several trialkylstannyl groups (Me_3Sn, i-Pr_3Sn, Me_2PhSn) range from 1 to 1.1 kcal/mol in substituted cyclohexanes,[21] and those for tributylstannyl should be similar. Since the free energy differences for a methyl in cyclohexane and *N*-methylpiperidine are the same, it is reasonable to assume similar energy differences for stannyl groups in cyclohexanes and *N*-methylpiperidine. Therefore, one might expect $\Delta G° = 1.0-1.1$ kcal/mol for the $Me_{eq}Sn_{eq} \rightleftarrows Me_{eq}Sn_{ax}$ equilibrium at low temperature (the Me_3Sn value was determined at low temperature). This would correspond to an equilibrium constant of ∼1/14, reflecting an 7:93 mixture. The ratio of peaks in the low-temperature NMR of **1** is 55:45 favoring the diequatorial isomer (vide infra), corresponding to $\Delta G° = 73$ cal/mol at −70 °C. To compensate for the expected

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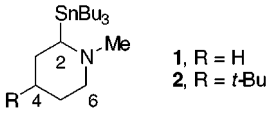
equatorial preference of 1.0−1.1 kcal/mol, there must be a compensating force reminiscent of the anomeric effect in carbohydrates, and its value must be approximately 0.9−1.0 kcal/mol. However, as explained below, this effect is *not* due to a stabilization of the axial conformer.

A Karplus relationship has been observed for the $^3J_{Sn-C}$ couplings in a number of rigid bicyclic and tricyclic organostannanes.[22] Synclinal torsions afford $^3J_{Sn-C}$ couplings of 14 Hz, whereas antiperiplanar $^3J_{Sn-C}$ couplings are 63 Hz. Substituted cyclohexylstannanes, such as *cis*- and *trans*-4-*tert*-butylcylohexyltrimethylstannane show couplings from tin to the C-3 and C-5 ring carbons that are entirely consistent with the Karplus relationship: in the *cis* isomer, the synclinal coupling is 12.0 Hz, whereas the coupling is 67.1 Hz in the *trans* isomer, which has an antiperiplanar torsion angle.[23] The chemical shifts and coupling constants for **2** are listed in Table 1. Couplings to C-4 and C-6 correspond to torsion angles of ~125°. This anticlinal angle requires that the C-2−Sn bond must nearly eclipse the C-3−H bond. A small (<9 Hz) coupling is evident in the *N*-methyl carbon, but it is difficult to quantitate because of line broadening by the nitrogen. Nevertheless, this value is near the minimum possible coupling on the Karplus curve and corresponds to a torsion angle of approximately 70°. Taken together, these features are consistent with a half-chair conformation for **2**, with a nearly planar, sp^2-hybridized nitrogen atom.

Table 1. Chemical Shifts and $^3J_{Sn-C}$ Coupling Constants for **1** and **2**[a]



1, R = H
2, R = *t*-Bu

	$Me_{eq}Sn_{eq}$ **1**	$Me_{eq}Sn_{ax}$ **1**	**2**
N-Me	49.9[b](≤8.8)[c]	48.2[b] (8.8)	49.1 (5.3)[c]
C-2	59.6	64.2	59.6
	(202, 214)[d]	(139, 145)[d]	(204, 213)[d]
C-4	26.2[e] (20.3)		49.0 (25.5)
C-6	60.2 (24.6)	56.3 (11.8)	60.5 (27.5)

[a] Chemical shifts in ppm, relative to TMS; reference line THF-d_8 at 67.4 ppm. Coupling constants in parentheses. All spectra recorded at 100 MHz, at −70 °C, unless otherwise noted. [b] Conformational isomers assigned by comparison of the chemical shifts and the coupling constants with **2**. [c] Coupling constant is approximate due to line broadening. The satellite appeared as an unresolved shoulder. [d] Couplings to ^{117}Sn and ^{119}Sn nuclides. [e] Room-temperature value. At −70 °C, the lines are obscured by the THF signal.

At the slow exchange limit, the two conformations of **1** can be analyzed independently, with the couplings summarized in Table 1. The $Me_{eq}Sn_{eq}$ conformer has couplings to the *N*-methyl and C-6 that indicate a half-chair conformation similar to that observed for **1**, while the $Me_{eq}Sn_{ax}$ conformation shows couplings indicative of a normal, undistorted chair.

The Karplus relationship for couplings to the *N*-methyl and C-6 go through a nitrogen atom and therefore may not strictly adhere to the Karplus curve derived from carbocycles. Nevertheless, there appear to be no inconsistencies in the data, so we assume the relationship is valid for ^{119}Sn−C−N−^{13}C.

The reasons for the conformational distortions in the diequatorial isomers are not obvious. No such distortions are evident in *cis*-2-methylcyclohexyltrimethylstannane, which exhibits couplings to the C-3 and C-5 carbons consistent with a 180° torsion angle,[24] so it would seem that the nitrogen is responsible for the ring distortion. Since the diequatorial conformer is the one that is distorted, the small energy difference between the $Me_{eq}Sn_{eq}$ and $Me_{eq}Sn_{ax}$ conformers of **1** appears to be due to a destabilization of the conformer in which the carbon−tin bond is synclinal to the nitrogen lone pair.

It is not clear whether this conformational distortion is relevant to the failure of certain α-aminostannanes to transmetalate, since both **1** and **2** transmetalate in 15 minutes or less at −80°. On the other hand, the effect observed here may manifest itself differently in acyclic systems.

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Supporting Information Available: Details of the synthesis of stannane **2** from 4-*tert*-butylpyridine. This material is available free of charge via the Internet at http://pubs.acs.org.

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