6196 *J. Org. Chem.* **2000,** *65,* 6196−6201

Synthesis and Reactivity of Dipole-Stabilized but Unchelated α-Aminoorganolithiums

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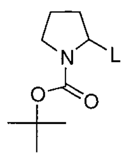
Received May 22, 2000

Two *N*-methyl-5-lithio-2-pyrrolidinones have been prepared by tin−lithium exchange. These two α-aminoorganolithium compounds that are stabilized by an amide dipole, but not by chelation to the amide carbonyl. Both constitute test cases for comparing the stability and reactivity of "dipole-stabilized" and "unstabilized" α-aminoorganolithiums. We find that active methylene protons interfere with the reaction, so geminal disubstitution α to the amide carbonyl was necessary to supress side reactions. These species do not react as efficiently as unstabilized α-aminoorganolithiums, or even as well as chelated dipole-stabilized α-aminoorganolithiums, toward typical electrophiles. The tin−lithium exchange to form these species was also not as facile as with other α-aminoorganostannanes.

Introduction

The study of α-aminoorganolithium compounds over the past 35 years has not only left us richer in our repertoire of synthetic methods (for reviews, see refs 1−13) but also hungry to develop a unifying theory to rationalize the behavior of these species. α-Aminoorganolithium compounds in which the metal-bearing carbon is sp^3 can be classified as either dipole-stabilized (such as carbamate **1**) or unstabilized (such as amine **2**). Although one might take issue with the nomenclature,[14] there are clear and distinct differences in the chemical properties of these two types of functionalized organolithiums (drawn for convenience in this paper as covalent). For example, both types react with carbonyl electrophiles in good to excellent yield. On the other hand, organolithium **2** shows greater resistance to racemization than **1**.[15] In addition, the dipole-stabilized systems such as **1** do not react well with alkyl halides while their unstabilized counterparts (e.g., **2**) do so with high yields and invertive stereoselectivities, a property that makes them unique among nonmesomerically stabilized organolithiums.[16] Last, addition of scalemic **1** to benzophenone occurs stereospecifically with retention,[17,18] whereas enantiopure **2** (or its pyrrolidine analog) adds to benzophenone in a stereorandom fashion;[16] this difference may reflect a difference in oxidation potential of the organolithium, with more easily reduced electrophiles reacting by single electron transfer (SET).[12,19] A third class of sp^3 α-aminoorganolithium compounds (**3**) is one which is dipole-stabilized but lacks the possibility of internal chelation such as that seen with compounds such as **1**.



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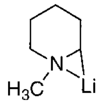

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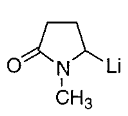

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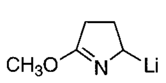

4

One obvious structural difference between **1** and **2** is that, in **1**, the lithium is probably coordinated to the carbonyl oxygen but not the nitrogen, whereas in **2**, the lithium bridges the carbon−nitrogen bond.[20a] These structural features are observed in crystal structures of similar compounds[20b,21] and may contribute to the observed differences in chemical behavior. Recent evidence shows that amide nitrogens may participate as acceptors in hydrogen bonds.[22,23] Would the amide nitrogen of a species such as **3** coordinate the lithium and render its reactivity similar to **2**, or would the reactivity of **3** be more similar to that of **1**? To our knowledge, dipole-stabilized but unchelated organolithiums such as **3** are unprecedented, although the constitutional isomer of **3**,

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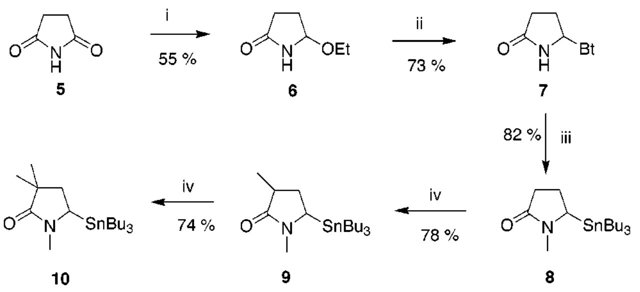
Scheme 1^a



i) $NaBH_4$, HCl, EtOH; ii) Bt-H, AcOH; iii) a) Bu_3SnLi, b) MeI, THF; iv) a) LDA, b) MeI, THF.

azaallyl anion **4**, was reported by Pearson and Stevens shortly after we began our work.[24] Herein, we wish to report the results of our investigation into this new type of α-aminoorganolithium. Because deprotonation is not a viable route to such a compound, tin−lithium exchange was planned. The questions we sought to answer were as follows:

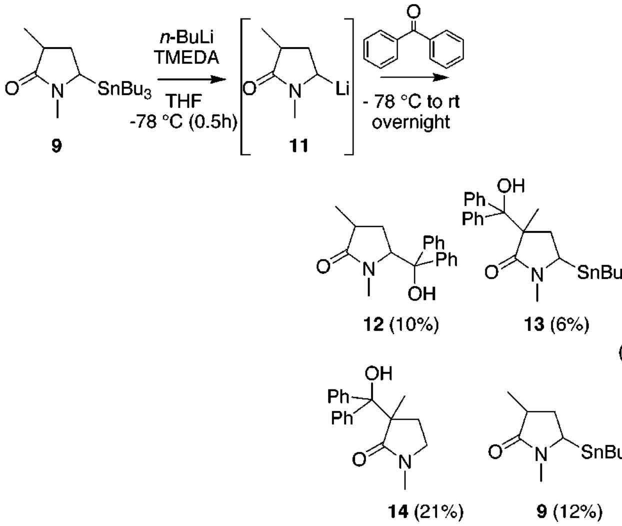
(1) Could such a species be synthesized via tin−lithium exchange? Transmetalation is sometimes problematic in α-aminoorganostannanes.[25−29]

(2) How would the organolithium react with a variety of electrophiles: would it behave more like chelated dipole stabilized α-aminoorganolithiums (e.g., **1**) or unstabilized α-aminoorganolithiums (e.g., **2**)?

Results

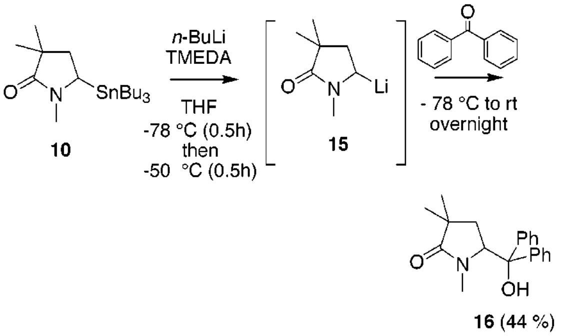
The stannylated lactams used in this study were synthesized as shown in Scheme 1. Starting from succinimide, ethoxy lactam **6** was prepared by careful $NaBH_4$ reduction according to Speckamp's procedure.[30] Treatment of **6** with benzotriazole in acetic acid leads to benzotriazole adduct **7**, which is then treated with 2 equiv of tri-*n*-butyltinlithium according to Pearson's procedure.[24] Quenching of the stannylation reaction with methyl iodide affords 1-methyl-5-tri-*n*-butylstannyl-2-pyrrolidinone **8** in good yield. Monomethyl and dimethyl analogues **9** and **10** were prepared by successive LDA deprotonation followed by methyl iodide quenching.

To minimize possible competition of the lactam's acidic α-protons for the *n*-BuLi, we began our studies using lactam **9**. Thus, a solution of stannane **9** with 1.3 equiv of TMEDA was treated with 1.3 equiv of *n*-BuLi at −78 °C. The reaction was monitored by TLC for the disappearance of starting material and quenched with benzophenone after 30 min at −78 °C. TLC revealed the presence of tetrabutyltin (the byproduct of transmetalation), some unreacted starting material, benzophenone, and three new products. After isolation, analysis of the products by NMR and FAB-MS revealed that transmetalation had indeed occurred, although it had not gone to completion, and three benzophenone adducts were found, as shown in eq 1. As we had anticipated, deprotonation of the lactam's acidic proton is a competing side-reaction as we observed two C-3 benzophenone adducts (**13** and **14**) in addition to the desired C-5 adduct **12**. Clearly if we were to study the reactivity of such a system, it would have to be done in the absence of any acidic protons so that we could concentrate on adducts resulting exclusively from metalation at the 5-position of the pyrrolidinone.



(1)

Therefore, *n*-BuLi-mediated tin−lithium exchange of *gem*-dimethyl lactam **10** in the presence of TMEDA was carried out at −78 °C as shown in eq 2. The reaction was monitored by TLC for the disappearance of starting material and quenched with benzophenone after 1.3 h at −78 °C giving 14% of the desired product along with 34% of unreacted starting material. This yield was improved to 30% by raising the transmetalation temperature to −25 °C for 1.3 h to ensure complete transmetalation. The best results, however, were obtained when the transmetalation mixture was maintained at −78 °C for 30 min and then placed in a bath at −50 °C for an additional 30 min. Under these conditions, we could isolate a 90% yield of tetrabutyltin, the byproduct of transmetalation. The isolated yield of benzophenone adduct **16** under these conditions was 44%.



(2)

To further explore the scope of **10**'s reactivity, other electrophiles were employed (eq 3). Trimethylsilyl chloride also couples effectively with the organolithium as trimethylsilyl adduct **17** was isolated in 46% yield. Under the same reaction conditions however, benzyl bromide

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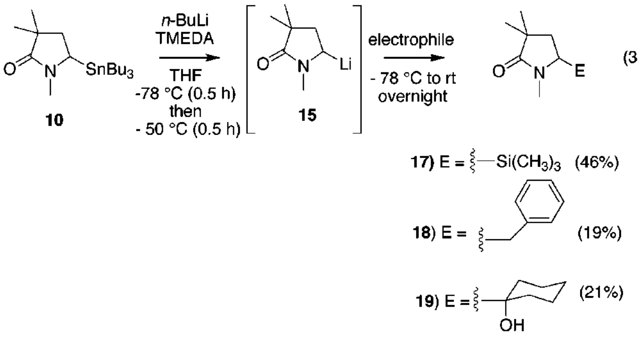
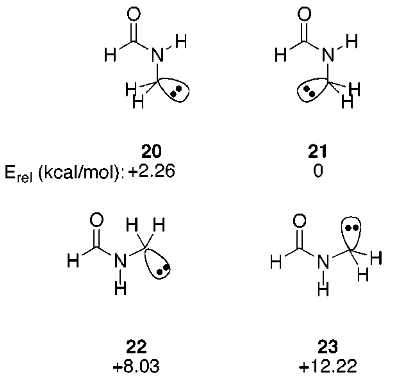
and cyclohexanone gave yields of only 19 and 21% respectively.



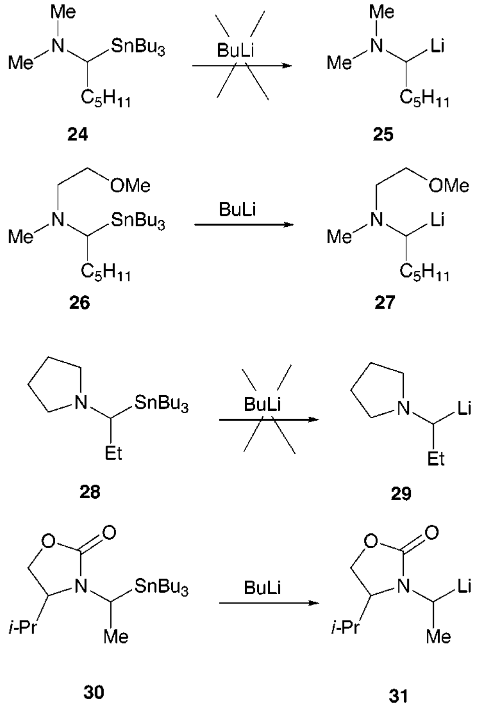
(3)

Discussion

Several theoretical studies have been conducted over the years in an effort to understand the behavior of α-aminocarbanions and α-aminoorganolithiums. In 1981, single-point calculations using the 4-31+G basis set on STO-3G-optimized geometries showed that formylating the nitrogen of $H_2NCH_2^-$ provided 28 kcal/mol stabilization.[31] In this and a subsequent study,[32] it was found that the anionic lone pair of a dipole stabilized anion preferably occupies the nodal plane of the amide π system, a feature that is now well documented in reactions of dipole-stabilized α-aminoorganolithiums,[31,33–35] and confirmed in the solid state.[14,20] In 1989, our group showed that, of the four possible orientations of the anionic lone pair, illustrated as **20**–**23**, the most stable was **21**, the least stable **23**.[36] Interestingly, it is the latter anion that most closely resembles **1**, absent the lithium ion. In the presence of a lithium ion, **23** is stabilized significantly, and becomes the most stable (6-31G* basis set).[36] The free anion that most closely resembles **3** is **20**, 10 kcal/mol more stable than **23**. Since unstabilized α-aminoorganolithiums such as **2**, modeled by $^-CH_2NH_2$[37] and its lithium counterpart $LiCH_2NH_2$,[20,38] have proven to be an extraordinarily versatile species,[10] and since dipole stabilization of α-aminoorganolithiums afford species, modeled by **23** and its lithium counterpart, with significantly different properties, exploring other types of dipole-stabilized species, such as typified by **20** and its lithium counterpart, is worthwhile. Because of kinetic barriers and competing sites for deprotonation, tin–lithium exchange was chosen to access these species.



The first report of tin–lithium exchange in α-aminoorganostannanes, to make dimethylaminomethyllithium, appeared 30 years ago.[39,40] More recently, several examples have been reported where transmetalation fails,[25–29] although minor structure modifications often facilitate the tin–lithium exchange. For example, Chong found that whereas secondary stannane **24** would not transmetalate to **25**, the derivative **26**, in which a chelating methoxy ligand is present, transmetalates smoothly to **27**.[26,27] In 1991, Tsunoda reported the failure of **28** to transmetalate to **29**, whereas Pearson showed that either diastereomer of **30** transmetalated to **31** smoothly.[41] In these examples, transmetalation appears to depend on the presence of an oxygen capable of chelation.



In THF, the mechanism of tin–lithium exchange involves oxidative addition of BuLi to a tetraalkyltin, producing a tin ate-complex, which then reductively eliminates an alkyllithium to regenerate a tetraalkyltin and an alkyllithium.[42] It is thought that the reaction is thermodynamically controlled, with the most stable alkyllithium being formed.[43] There are two possible explanations for the failure of tin–lithium exchange: one is the failure to produce the ate-complex, possibly due to steric

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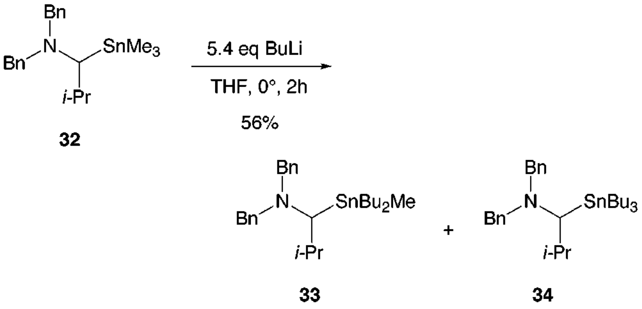
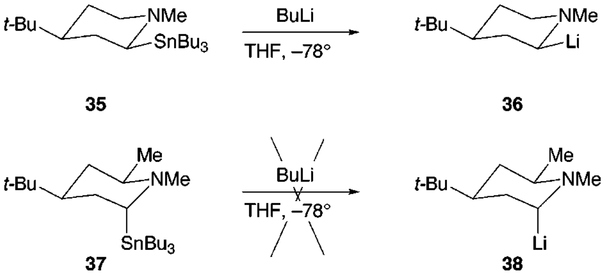
hindrance by the butyl groups, the other is that reductive elimination produces a different alkyllithium than the one you want. Pearson showed that failure of the transmetalation of compounds similar to **24** was not due to steric hindrance around tin, as shown by the example below, wherein transmetalation of **32** is achieved under forcing conditions, but not in the desired way.[28] Instead of producing an α-aminoorganolithium by reductive elimination, methyllithium is eliminated. Successive cycles produce **33** and **34** in a 1:2 ratio.



In our laboratories, we have found that rigid stannylpiperidines transmetalate readily when the tin is in an equatorial configuration (**35** → **36**), but fail to transmetalate at all when the tin is axial (**37** → **38**).[29] In this case, the availability of the lone pair of a basic nitrogen, in a synclinal relationship to the tin, is a requirement.



Based on these precedents, we were interested in evaluating the facility by which compounds of general structure **3** could be made by tin–lithium exchange, since a chelating atom is absent, and the nitrogen lone pair is tied up by delocalization into the amide carbonyl. In the first experiments with **9**, our fears of complications from proton transfers from the active methylene protons were confirmed. The desired adduct **12** was only isolated in 14% yield, along with aldol adduct **13** in 6% yield. Destannylated aldol adduct **14** was obtained in 21% yield, indicating that a complex sequence of deprotonations and destannylations must have occurred. The isolation of 12% yield of recovered **9** gave us our first indication that this type of stannane might be less susceptible to tin–lithium exchange than the stannane precursors to either **1** or **2**.

To avoid the complications of proton transfer, we continued our investigation with trimethylpyrrolidinone **10**. The yield of tetrabutyltin, the byproduct of tin–lithium exchange, was judged to be the most reliable indicator of the efficiency of the transmetalation, and treatment of **10** for 30 min at −78 °C and 30 min at −50 °C, gave a 90% yield of tetrabutyltin. This rather lengthy treatment is considerably more vigorous than that required to produce organolithiums such as **2**, which are formed by tin–lithium exchange after only 5–10 min at −78 °C. As outlined above, successes and failures of tin–lithium transmetalations depend on subtle structural differences. Here, we have a subtle structural difference that does not produce a failure, but does attenuate the proclivity of a reaction. Stannanes **24**, **26**, **28**, and **30** are all acyclic, so the relevant comparison is to cyclic α-aminostannanes **35** and **37**, which require the synclinal lone pair for successful transmetalation. While speculative, the successful transmetalation of **9** and **10** may mean that, in reacting with the stannane, the butyllithium is able to substitute the π-system of an amide (or the lone pair of an amide nitrogen) for the synclinal lone pair of a basic nitrogen in the transmetalation.

After cooling the THF solution of **15** back down to −78 °C, it was quenched with a variety of electrophiles. With benzophenone and trimethylsilyl chloride, moderate yields of coupling products **16** and **17** were obtained. An interesting point is the mechanism of coupling with benzophenone. Dipole-stabilized organolithium **1** adds to benzophenone by a polar mechanism with retention of configuration, affording enantiopure adduct (≥99.5% ee) in 73–74% yield.[17] In contrast, enantiopure lithiopiperidine **2**, or its pyrrolidine analogue, add to benzophenone in 50% and 70% yields, respectively, but the products are racemic.[16] Mechanistic studies suggest that the reason for the stereorandom additions of **2** is the intervention of a SET process.[19] A question that could be posed is whether **15** adds by SET. Since all compounds in this study are racemic, we cannot use the steric course as an indicator. A qualitative observation we have made over the years is that stereorandom additions of α-aminoorganolithiums to benzophenone are accompanied by an intense blue color that has been identified as the benzophenone ketyl.[16,44] In the present instance, we saw a green color, which could have arisen from some ketyl (blue) and the organolithium (pale yellow). Although inconclusive, this could mean that some SET had occurred.

The other two electrophiles tested, benzyl bromide and cyclohexanone gave only about 20% yield of coupling product, for reasons that are not clear. We did not find any of stannane **10** in the product mixture, indicating that there are pathways other than those producing substitution products in operation. These could include removal of a proton from the electrophile or the solvent, fragmentation of the heterocycle, or in the case of benzyl bromide, SET pathways. However, adducts **18** and **19** were the only identifiable products we could find. Note that if protonation of **15** occurred, the lactam produced would probably be very volatile and difficult to isolate after rotary evaporation or even atmospheric distillation. Attempts to find other products by GC–MS were unsuccessful due to the large amounts of tetrabutyltin in the product mixture.

Conclusion

We have found that α-aminoorganostannanes such as **9** and **10** undergo transmetalation with *n*-BuLi to yield the corresponding dipole-stabilized organolithium which then reacts with electrophiles in 20–50% yields. The organolithium coupled best with benzophenone and TMSCl but less well with benzyl bromide and cyclohexanone. On the basis of these studies, it appears that dipole-

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stabilized, but unchelated, α-aminoorganolithiums do not behave as well toward electrophiles as their nonstabilized counterparts.

Experimental Section

General Methods. ^{1}H NMR and ^{13}C NMR spectra were recorded on either a 300 or a 400 MHz spectrometer. Elemental analyses were performed at Atlantic Microlab, Inc. (Norcross, GA). FAB mass spectra were recorded on a single-stage quadropole mass spectrometer. HRMS were recorded at the University of California (Riverside) Mass Spectroscopy Facility. IR spectra were recorded on a FT-IR instrument. Column chromatography was performed on silica gel 60 (230−400 mesh) while TLC was carried out using on aluminum backed plates coated with 0.25 mm silica gel 60 (F-254). Solvents were freshly distilled prior to use: THF and diethyl ether from sodium-benzophenone ketyl, while CH_2Cl_2, DMF, TMEDA, and diisopropylamine were distilled from CaH_2. All reagents were obtained commercially and used as received. The *n*-BuLi and *s*-BuLi were titrated using 1,3-diphenylacetone *p*-tosylhydrazone as acid and indicator.

1-Methyl-5-(tri-*n*-butylstannyl)-2-pyrrolidinone (8). To a 0 °C-cooled solution of diisopropylamine (4.6 mL, 32.64 mmol) in THF (100 mL) was added *n*-BuLi (25.90 mL, $c = 1.26$ M, 32.6 mmol) dropwise via syringe over a 20 min period under N_2. After the solution was stirred for 30 min, tributyltin hydride (9.17 mL, 34.1 mmol) was added dropwise via syringe over a 20-min period. The reaction mixture turned a turbid yellow color. After 40 min, the benzotriazole-lactam **7** (3.00 g, 14.8 mmol) was added as a solid portionwise. The reaction turned orange as the lactam was being added. After 2 h at 0 °C, iodomethane (4.62 mL, 74.2 mmol) was added and the reaction mixture was allowed to warm to room temperature overnight. Note: the addition of the iodomethane caused the reaction mixture to turn opaque and pink colored, which eventually turned yellow with white precipitate. The mixture was diluted with diethyl ether (200 mL), and water (50 mL) was added. The organic phase was then washed with 10% NaOH (2 × 25 mL), satd NH_4Cl (25 mL), and brine (25 mL) and then dried over $MgSO_4$. Column chromatography (silica gel, gradient: 100% Hex to 5:1 Hex/EA to 1:1 Hex/EA) afforded the desired product as a yellow oil (4.71 g, 82%): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.89−0.98 (15H, m), 1.29−1.37 (6H, m), 1.48−1.52 (6H, m), 2.08 (1H, m), 2.29−2.38 (3H, s), 3.53−3.58 (1H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.5, 14.0, 24.2, 27.8, 29.5, 30.8, 32.2, 51.0, 174.9; IR (neat) 1656 cm^{-1}; MS (FAB) $MH^+ = 390$.

1,3-Dimethyl-5-(tri-*n*-butylstannyl)-2-pyrrolidinone (9). To a 0 °C-cooled solution of diisopropylamine (2.21 mL, 15.8 mmol) in THF (30 mL) was added *n*-BuLi (14.36 mL, $c = 1.1$ M, 15.8 mmol) dropwise via syringe over a 10-minute period. After stirring for an additional 20 min, the reaction mixture was cooled to −78 °C. A solution of lactam **8** (4.71, 12 mmol) in THF (30 mL) was then added dropwise over a 20-minute period. This caused the reaction to turn a dark olive-green color. Iodomethane (1.5 mL, 24 mmol) was added via syringe and the mixture allowed to stir for 1.5−2 h. The reaction was then diluted with diethyl ether (100 mL), washed with sat. NH_4Cl (2 × 30 mL), treated with brine (15 mL), and dried over $MgSO_4$. The crude product was then purified by column chromatography (silica gel, gradient: 5:1 to 3:1 to 2:1 to 1:1 Hex/EA) to afford **9** (3.75 g, 78%) as a light yellow oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.87−0.94 (15H, m), 1.19 (3H, d, $J = 6.8$ Hz), 1.27−1.36 (6H, m), 1.43−1.53 (6H, m), 1.95−2.00 (1H, m), 2.23−2.31 (2H, m), 2.80 (3H, s), 3.44−3.48 (1H, dd, $J = 9.4$, 3 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.7, 14.0, 16.3, 27.8, 29.5, 30.7, 33.2, 37.6, 48.9, 176.4; IR (neat) 1685 cm^{-1}; MS (FAB) $MH^+ = 404$. Anal. Calcd for $C_{18}H_{37}NOSn$: C, 53.57; H, 9.27. Found: C, 53.81; H, 9.23.

1,3,3-Trimethyl-5-(tri-*n*-butylstannyl)-2-pyrrolidinone (10). To a 0 °C-cooled solution of diisopropylamine (0.95 mL, 6.76 mmol) in THF (20 mL) was added *n*-BuLi (5.0 mL, c=1.35M, 6.76 mmol) dropwise via syringe over a 5-minute period. After stirring for an additional 30 min, the reaction mixture was cooled to −78 °C. A solution of lactam **9** (2.1 g, 5.2 mmol) in THF (15 mL) was then added dropwise over a 5-minute period. This caused the reaction to turn a dark yellow color. Iodomethane (0.65 mL, 10.4 mmol) was added via syringe and the mixture allowed to stir for 1 h. The reaction was then diluted with diethyl ether (150 mL), washed with aqueous NH_4Cl (2 × 20 mL), treated with brine (20 mL), and dried over $MgSO_4$. Column chromatography (silica gel, gradient: 100% Hex to 5:1 to 1:1 Hex/EA) afforded **10** (1.60 g, 74%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.88−0.97 (15H, m), 1.09 (3H, s), 1.16 (3H, s), 1.29−1.38 (6H, m), 1.46−1.54 (6H, m), 1.88−2.10 (3H, m), 3.45 (1H, t, $J = 7.5$ Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.3, 14.0, 23.9, 25.6, 27.8, 27.8, 29.5, 31.4, 40.2, 40.9, 46.4, 180.1; IR (neat) 1688 cm^{-1}; MS (FAB) $MH^+ = 418$. Anal. Calcd for $C_{19}H_{39}NOSn$: C, 54.83; H, 9.44. Found: C, 54.86; H, 9.42.

General Procedure for Transmetalation and Electrophile Quench. To a stirring solution of lactam (490 mg, 1.18 mmol) and TMEDA (0.267 mL, 1.77 mmol) in THF was added *n*-BuLi (1.6 mL, $c = 1.1$ M, 1.77 mmol) at −78 °C or −82 °C under Ar or N_2. After 30 min at this temperature the reaction vessel was placed in a bath maintained at − 50 °C where it remained for an additional 30 min. The reaction was then cooled back to −78 °C and after a short while (10−30 min) is quenched with the given electrophile (2.36 mmol) and allowed to warm to room-temperature overnight. The reaction mixture was then diluted with diethyl ether (100 mL), washed with water (2 × 15 mL) then brine (15 mL) and dried over $MgSO_4$. Careful column chromatography (solvent gradient: 100% Hex to 10:1 to 5:1 to 3:1 to 1:1 Hex/EA) afforded the desired coupling products.

1,3-Dimethyl-5-(diphenylhydroxymethyl)-2-pyrrolidinone (12). According to the general procedure for transmetalation and electrophilic quench, **12** was isolated as a yellow solid: ^{1}H NMR ($CDCl_3$, 300 MHz) [diastereomeric mixture] δ [1.07 and 1.14] (3H, d, 7 Hz), [1.47−1.55 and 1.77−1.81 and 2.14−2.27] (3H, m), [4.59 (d, $J = 8.5$ Hz) and 4.74 (t, $J = 7{,}6$ Hz)] (1H), 7.25−7.68 (10H, m); HRMS calcd for $C_{19}H_{22}NO_2$ (MH^+) 296.1651, found 296.1657.

1,3-Dimethyl-3-(diphenylhydroxymethyl)-5-(tri-*n*-butylstannyl)-2-pyrrolidinone (13). According to the general procedure for transmetalation and electrophilic quench, **13** was isolated as a light yellow oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.90 (15H, t, $J = 7.1$ Hz), 1.25−1.32 (6H, st, $J = 7.1$ Hz), 1.40−1.48 (9H, m), 2.05−2.13 (1H, dd, $J = 13.5$, 7.3 Hz), 2.30−2.36 (1H, dd, $J = 9.6$, 7.3 Hz), 2.68 (3H, s), 3.00−3.06 (1H, dd, $J = 13.5$, 9.6 Hz), 6.77 (bs, 1H), 7.20−7.78 (10H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.6, 14.0, 23.6, 27.7, 29.3, 31.0, 36.0, 47.2, 50.6, 82.0, 127.3, 127.3, 127.8, 127.9, 128.1, 128.2, 144.2, 146.4, 179.3; IR (neat) 3342 and 1655 cm^{-1}; MS (FAB) $MH^+ = 569$.

1,3-Dimethyl-3-(diphenylhydroxymethyl)-2-pyrrolidinone (14). According to the general procedure for transmetalation and electrophilic quench, **14** was isolated as a colorless oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.36 (3H, s), 1.91−1.98 (1H, m), 2.67−2.78 (2H, m), 2.82 (3H, m), 3.22−3.29 (1H, m), 6.83 (1H, bs), 7.20−7.53 (10H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.0, 30.3, 30.6, 46.7, 50.4, 82.0, 127.3, 127.3, 128.0, 128.1, 128.3, 144.3, 146.3, 180.5; IR (neat) 3314 and 1659 cm^{-1}; HRMS calcd for $C_{19}H_{22}NO_2$ (MH^+) 296.1651, found 296.1642.

1,3,3-Trimethyl-5-(diphenylhydroxymethyl)-2-pyrrolidinone (16). According to the general procedure for transmetalation and electrophilic quench, **16** was isolated as a white solid: mp = 210−211 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.13 (6H, s), 1.24−1.29 (1H, m), 2.38 (3H, s), 2.71 (1H, bs), 4.75 (1H, t, $J = 7.6$ Hz), 7.20−7.70 (10H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.8, 27.0, 32.1, 37.4, 39.9, 64.1, [125.6 and 125.7], [127.3 and 127.6], [128.8 and 129.0], 144.9 and 146.4], 183.0; IR (neat) 3300 and 1685 cm^{-1}; HRMS calcd for $C_{20}H_{24}NO_2$ (MH^+) 310.1807, found 310.1810. Anal. Calcd for $C_{20}H_{23}NO_2$: C, 77.64; H, 7.49. Found: C, 77.90; H, 7.72

1-Methyl-3,3-dimethyl-5-trimethylsilyl-2-pyrrolidinone (17). According to the general procedure for transmetalation and electrophilic quench, **17** was isolated as a colorless oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.10 (9H, s), 1.07 (3H, s), 1.17 (3H, s), 1.61 (1H, dd, $J = 12$ Hz), 1.85 (1H, dd, $J = 12.5$, 7 Hz), 2.85 (3H, s), 2.93 (1H, dd, $J = 11.4$, 7 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −2.9, 23.7, 25.8, 30.8, 37.6, 40.4, 47.0, 181.2; IR (neat) 1685 cm^{-1}; HRMS calcd for $C_{10}H_{21}NOSi$ (M^+) 199.1392, found 199.1400.

1-Methyl-3,3-dimethyl-5-benzyl-2-pyrrolidinone (18). According to the general procedure for transmetalation and electrophilic quench, **18** was isolated as a colorless oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.06 (3H, s), 1.14 (3H, s), 1.55 (1H, dd, $J = 27$, 7 Hz), 1.81 (1H, dd, $J = 24$, 7 Hz), 2.52 (1H, dd, $J = 9$, 5.5 Hz), 2.89 (3H, s), 3.24 (1H, dd, $J = 8.7$, 4.5 Hz), 3.65 (1H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.7, 26.3, 28.8, 40.5, 40.7, 41.0, 58.2, 127.1, 129.1, 129.6, 137.5, 180.5; IR (neat) 1684 cm^{-1}; HRMS calcd for $C_{14}H_{20}NO$ (MH^+) 218.1545, found 218.1542.

1-Methyl-3,3-dimethyl-5-(1′-hydroxycyclohexyl)-2-pyrrolidinone (19). According to the general procedure for transmetalation and electrophilic quench, **19** was isolated as a white solid: mp = 120−122 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.10 (3H, s), 1.20 (3H, s), 1.33−1.92 (13H, m), 3.00 (3H, s), 3.39 (1H, t, $J = 8$ Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.2, 21.4, 26.0, 27.7, 28.9, 29.5, 32.3, 35.0, 37.3, 40.1, 66.3, 74.3, 181.8; IR (neat) 3421 and 1668 cm^{-1}; MS (FAB) $MH^+ = 226$ m/z. Anal. Calcd for $C_{13}H_{22}NO_2$: C, 69.29; H, 10.29. Found: C, 69.00; H, 10.31.

Acknowledgment. We are grateful to the National Institutes of Health for generous financial support (GM-56271). Early exploratory work on this project was performed by Professor Leonard Kellar, Florida International University, with support from the Petroleum Research Fund. We also thank NIH and NSF for shared instrumentation grants for the purchase of the NMR and MS instruments used in this work.

Supporting Information Available: Copies of ^{1}H NMR and ^{13}C NMR for compounds **8**−**10**, **13**, **14**, and **16**−**19**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO000786J