Aza-Wittig Rearrangements and Cyclizations by Transmetallation of *N*-Benzylaminomethylstannanes

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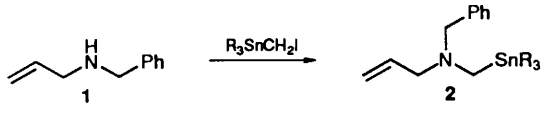
Transmetallation of *N*-allyl-*N*-benzylaminomethylstannanes with butyllithium or methyllithium allows carbon–carbon bond formation by a [1,2]-rearrangement. Substantial amounts of the protodestannylated product are also produced. Transmetallation of the corresponding α-methyl substituted allylic amine or homoallylic amine gives an overall rearrangement by cyclization onto the olefin followed by recapture of the new carbanion by tetramethyltin.

The Wittig rearrangement (Scheme 1, X = O) is a useful

Scheme 1

carbon–carbon bond-forming reaction which has received much attention for the stereocontrolled synthesis of oxygen-containing natural products.[1] The scope of this reaction has been widened by the use of tin-lithium exchange in order to prepare unstabilized α-alkoxy carbanions which rearrange by a [2,3]-sigmatropic shift.[2] Despite this, the corresponding aza-Wittig rearrangement (in which the oxygen atom is replaced by a nitrogen atom) (Scheme 1, X = NR), has received very little study[3–6] and there are no reports of the use of tin-lithium exchange to effect this rearrangement. This communication outlines initial studies on this reaction.

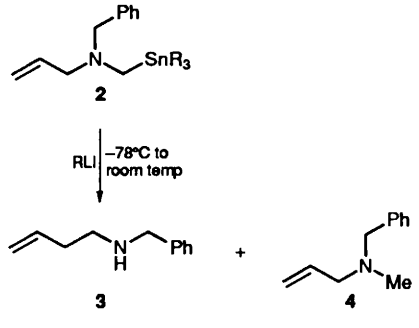
The aminomethylstannanes **2** (R = Me, Bu) were prepared by alkylation of the allylic amine **1** using iodomethyltrialkylstannane[7] in $MeCN/K_2CO_3$. Transmetallation of tin for



1 2

lithium was accomplished with either methyllithium or butyllithium. The subsequent aza-Wittig rearrangement was investigated using a range of solvents and the results are shown in Table 1.

Transmetallation of the tributylstannane **2** (R = Bu) with butyllithium gave some rearranged product **3**, together with substantial amounts of the protodestannylated compound **4**. More promising results were observed with the trimethylstannane **2** (R = Me) and methyllithium, the homoallylic amine **3** being formed in *ca.* 50% yield. These results were surprising



2 3 4

Table 1 Rearrangement of the aminomethylstannane **2**

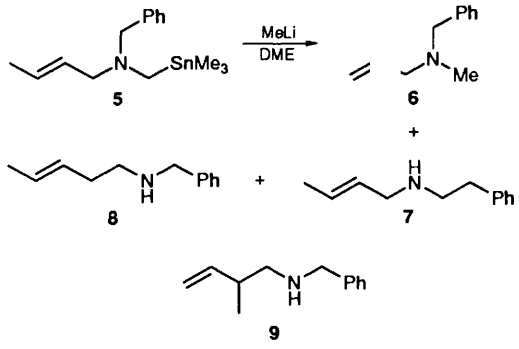
R	RLi	Solvent	Yield (%)	3	4
Bu	1.2	DME	60[a]	18	82
	1.2	THF	65	17	83
	2	Hexane	—	—	—
	1.2[b]	DME	61	60	40
Me	1.5	DME	73	67	33
	1.1	THF	61	75	25
	1.2	THF/BF_3	73[a]	75	25
	2	PhMe	80	30	70
	2	Hexane	—	—	—

[a] Trace amounts of the [1,2]-rearranged product $H_2C{=}CHCH_2NHCH_2CH_2Ph$ were also observed. [b] RLi = Methyllithium.

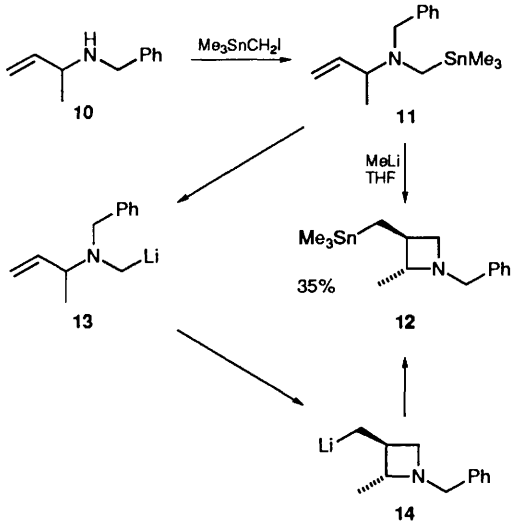
when considering that both reactions should proceed through the same organolithium intermediate. The difference may arise from a slight change in the lithium aggregate structure when using methyllithium (possibly as this contains small amounts of lithium chloride). This was verified by performing the transmetallation of the amine **2** (R = Bu) in 1,2-dimethoxyethane (DME) with methyllithium, which now gave more of the desired homoallylic amine **3** by rearrangement rather than protodestannylation.

The question arises as to the source of the proton in the protodestannylation. Transmetallation of the amine **2** (R = Bu) with butyllithium in DME at −78 °C and quenching the reaction after 20 min with D_2O gave the deuteriodestannylated product. Quenching with D_2O after the mixture had warmed to 0 °C gave the amine **4** with no deuterium incorporation. This suggests that the hydrogen is abstracted from the solvent on warming,[8] a process that is likely to involve radical intermediates.

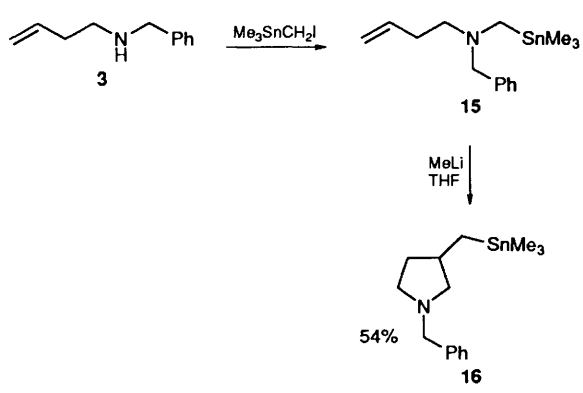
Of particular interest and importance in testing the scope and mechanism of the reaction is the rearrangement of an allylic amine in which a regiochemical marker is present in the allyl group. Transmetallation of the allylic amine **5** (10:1 *trans*:*cis*) which has a methyl group γ- to the nitrogen atom, gave a mixture of products **6**, **7** and **8** (62%, 47:43:10). The absence of any [2,3]-rearranged product **9** clearly demonstrates that this reaction proceeds by a [1,2]-rearrangement rather than a [2,3]-rearrangement. With the incorporation of a regiochemical marker in the α-position rather than the γ-position of the allyl chain a similar [1,2]-shift was expected. Rather surprisingly, however, transmetallation of the amine **11** gave a small amount of the [2,3]-product (< 10%), some of the amine **10** (*ca.* 15%) and a significant amount of the azetidine **12** (35%) as a single geometrical isomer (assigned *trans* from nOe studies). This must arise by cyclization of the resulting aminomethyllithium **13** onto the terminal olefin. This generates a new organolithium



14 which presumably exchanges with tin from the tetramethyltin present after the initial transmetallation. This novel transformation is an overall rearrangement of the aminomethylstannane **11** and gives access to a cyclic amine with a handle for further elaboration.



Cyclization of a homoallylic amine to a five-membered ring should be more favourable than that of an allylic amine to a four-membered ring. This was tested with the aminomethylstannane **15** prepared from the homoallylic amine **3**. Transmetallation of **15** with methyllithium (2 equiv.) gave a respectable yield of the pyrrolidine **16**. Broka[5,9] has shown that a similar homoallylic stannylmethyl ether cyclizes to the tetrahydrofuran on transmetallation, however re-incorporation of the tin group was only observed as a by-product. As the transformation of **15** into **16** is an overall rearrangement, there is the potential for using a catalytic amount of methyllithium to promote the reaction. Indeed, with only 0.4 equiv. of methyllithium the pyrrolidine **16** was isolated in the same yield (54%).



Further work on promoting the aza-Wittig rearrangement and on cyclization of various substituted aminomethylstannanes is in progress and will be reported in due course.

Experimental

Transmetallation of the Aminomethylstannane **15**.—Methyllithium (1.4 mol dm^{-3} in diethyl ether; 0.044 cm^3, 0.061 mmol) was added to the amine **15** (52 mg, 0.154 mmol) in dry THF (1.5 cm^3) under argon at −78 °C. The mixture was allowed to warm slowly to 0 °C over 3 h and was quenched with EtOH (0.1 cm^3). The solvent was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel, eluting with hexane–ethyl acetate (10:1) to give the pyrrolidine **16** (28 mg, 54%).

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