α-Amino carbene or carbenoid formation in the reaction of a tertiary amide with $PhMe_2SiLi$ and its insertion into the Si–Li bond of a second equivalent

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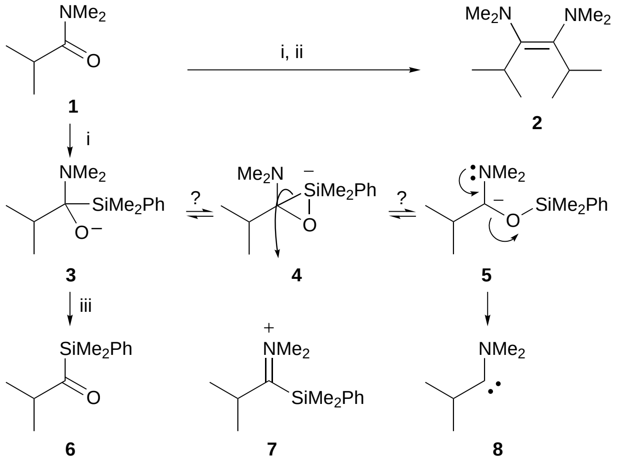
$PhMe_2SiLi$ reacts with tertiary amides, $RCONMe_2$, to give a carbene, $RCNMe_2$, or an equivalent carbenoid, which gives enediamines, $R(Me_2N)C{=}C(NMe_2)R$, in the absence of a strong nucleophile, but is attacked by strong nucleophiles, NuLi, to give lithium reagents $R(Me_2N)CLiNu$.

In the preceding paper[1] and its predecessor,[2] we described the reaction between 1 equiv. of $PhMe_2SiLi$ and the amide **1** giving the acylsilane **6** when the mixture was quenched at −78 °C, but giving the enediamine **2** when the mixture was warmed to −20 °C before quenching. Neither in those papers, nor in the paper describing the one precedent for this type of reaction,[3] has there been any discussion of the mechanism of the formation of the enediamine.

Among other possibilities, such reductive coupling implies that a species electrophilic at the carbonyl carbon has been attacked by an umpolung species nucleophilic at the carbonyl carbon. The latter is easily identified as the consequence of a Brook rearrangement,[4] which can be formulated as an equilibrium between an *α*-silyl alkoxide **3** and the *α*-silyloxy anion **5**,[5] with the latter the umpolung species (Scheme 1). Alternatively, it can be formulated as a single hypervalent species **4**,[6] which can react as an oxygen or a carbon (**4** arrow) nucleophile, depending upon the circumstances. It is, however, much less easy to identify the electrophilic species. Several candidates present themselves: the amide **1**, the acylsilane **6**, an iminium ion **7**, and a carbene **8**. We now report that all the evidence suggests that the carbene is the electrophile.

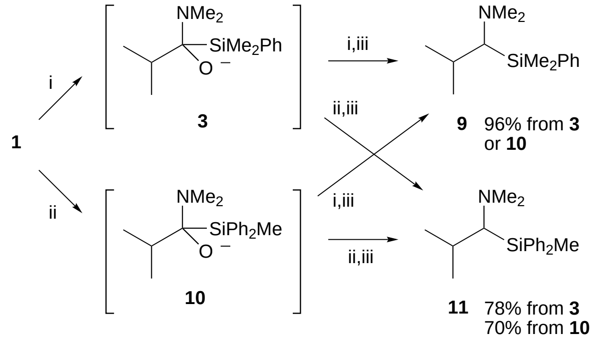
The amide itself cannot have been the electrophile—if we simply warmed the solution of the tetrahedral intermediate **3** from −78 to −20 °C, and then quenched the mixture, we obtained the enediamine **2** in good yield. The tetrahedral intermediate **3** was fully formed at the lower temperature, since on quenching it, the acylsilane **6** was obtained in reasonably good yield. It does not revert to amide and the silyllithium reagent, since adding *N*,*N*-dimethylcyclohexanecarboxamide before warming up from −78 °C gave only the homo-coupled product **2**.[7] The tetrahedral intermediate must have provided both the nucleophilic and the electrophilic species for the coupling reaction.



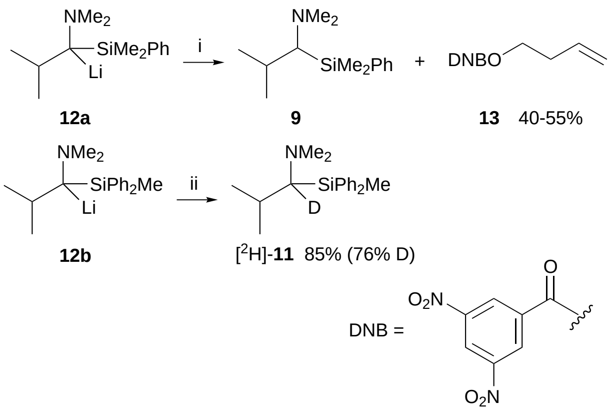
Scheme 1 *Reagents and conditions*: i, $PhMe_2SiLi$ (1.2 equiv.) THF, −78 °C, 1.5 h; ii, −20 °C, then $NaHCO_3$, H_2O; iii, NH_4Cl, H_2O, −78 °C → room temp.

To trap the electrophile, we carried out the same reaction as before but with rather more than 2 equiv. of the silyllithium reagent, in the hope that the intermediate would be trapped by the second equivalent of nucleophile. The product was the *α*-silyl amine **9** (Scheme 2), analogous to a minor product in the Russian work.[3] If the iminium ion **7** had been an intermediate, it ought to have led to a product with two silyl groups, not just one, and the easy loss of one seems unlikely. We showed that this was not the case, by treating the tetrahedral intermediate **3** with $Ph_2MeSiLi$, and obtained this time only the *α*-silyl amine **11** having the Ph_2MeSi group rather than the original $PhMe_2Si$ group. We also carried out the experiment the other way round, adding $Ph_2MeSiLi$ to the amide **1** at −100 °C to give the tetrahedral intermediate **10**. This then reacted with $PhMe_2SiLi$ on warming to −20 °C to give the *α*-silyl amine **9**, showing that neither an *α*,*α*-disilyl amine nor the iminium ion **7** could have been intermediates—only the silyl group from the second silyllithium reagent delivered was incorporated into the product.

The formation of the products **9** and **11** was, however, compatible with the carbene **8** being an intermediate—it could be expected to insert into the Si–Li bond of the second lithium reagent to give an intermediate lithium reagent **12**, which would be protonated before or during the workup. Our attempts to detect the intermediate **12a** were thwarted by its evident strong basicity—it did not incorporate a deuterium label when quenched with D_2O, having already found a proton somewhere else. Nor were we at first successful in finding where that proton came from, but eventually we showed that an organolithium intermediate had been involved by trapping the corresponding Ph_2MeSi intermediate **12b** at −78 °C (Scheme 3). It is known that the more phenyl groups there are on a silyl group, effectively the faster the Brook rearrangement takes place.[8] In consequence, the intermediate **12b** was formed between −100



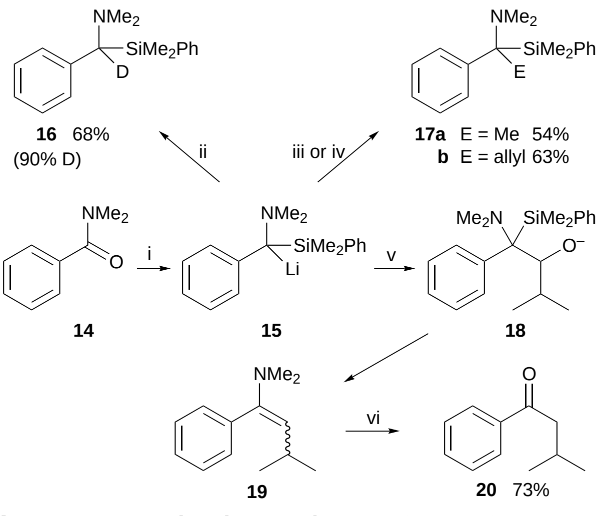
Scheme 2 *Reagents and conditions*: i, $PhMe_2SiLi$ (1.2 equiv.) THF, −78 °C, 1.5 h; ii, $Ph_2MeSiLi$ (1.2 equiv.) THF, −100 °C, 1.5 h; iii, −20 °C, then $NaHCO_3$, H_2O



Scheme 3 *Reagents and conditions*: i, 3,5-$(O_2N)_2C_6H_3COCl$; ii, D_2O

and -78 °C, at which temperature it survived long enough to be quenched with D_2O to give the deuterated α-silyl amine $[^2H]$**11**. The $PhMe_2Si$ intermediate **12a**, having been formed at higher temperature, somewhere between -78 and -20 °C, evidently found a proton before it could be quenched with D_2O. The source of that proton appears to be, at least in part, THF, which is known to react with strong bases like BuLi, losing the proton on C-2 and undergoing a retro-cycloaddition to give the enolate of acetaldehyde.[9] We detected a low level of deuterium incorporation when the reaction was carried out in $[^2H_8]$THF, and, expecting to trap the enolate of acetaldehyde, we added 3,5-dinitrobenzoyl chloride, and obtained instead the 3,5-dinitrobenzoate **13** in yields of 40–55%, with no trace of the expected product. As far as we are aware, the apparently simple E2 elimination from THF losing the proton from C-3 has not been seen before in solution chemistry, although it is thoroughly established with hydroxide ion and amide ion as bases in the gas phase,[10] and the formation of but-3-enol from the reaction between sodium and 3-chlorotetrahydrofuran is also known.[11] It is presumably unfavourable because the elimination is a retro-5-*endo-trig* reaction.

We also found that the presence of a phenyl group in the *N*,*N*-dimethylbenzamide **14** stabilised the corresponding intermediate **15**, which survived even at -20 °C, and gave a deuterated α-silyl amine **16** on quenching with D_2O (Scheme 4). The intermediate **15** also reacted with alkyl halides giving the amines **17a** and **17b**, and with isobutyraldehyde giving, initially, an alkoxide **18** that undergoes a Peterson elimination giving the enamine **19**, which is easily hydrolysed to the ketone **20**. These reactions illustrate an umpolung of reactivity in the amide **14**.



Scheme 4 *Reagents and conditions*: i, $PhMe_2SiLi$ (2.4 equiv.) THF, $-78 \rightarrow -20$ °C, 1.5 h; ii, D_2O; iii, MeI; iv, allylBr; v, Pr^iCHO; vi, HCl, H_2O

The carbene intermediate **8** could be formed by Brook rearrangement, followed by or concerted with the elimination of silane oxide (Scheme 1). This pathway is, as far as we are aware, a new one for reactions taking place within the Brook rearrangement manifold, and is a new route to carbene or carbene-like intermediates. The nearest analogy is the formation of an oxygen-stabilised carbene when the acetals of acylsilanes are heated to 190 °C.[12] Our reaction takes place, presumably, because of the extra electronic push (**5**, arrows) from the Me_2N lone pair. It could equally be derived by cheletropic extrusion of $PhMe_2SiO^-$ directly from the intermediate **4**. It is not clear what the structure of the carbene is in detail—it could be the carbene itself **8**, as we have drawn it here for simplicity, or it could be an equivalent species such as an α-lithio iminium ion. A carbene was also invoked by Ogawa and Sonoda in their work using samarium iodide induced coupling of amides.[13] Whatever its nature, our carbene was not trapped by a silicon hydride—only the enediamine **2** was formed, and not the silyl amine **9**, when the tetrahedral intermediate **3** was warmed to -20 °C in the presence of $PhMe_2SiH$, nor have we found at any stage products that might have been derived by insertion of the carbene into the neighbouring C–H bond, nor into a well-placed C=C bond, as described in the following paper. The enediamine could be produced from the carbene or carbenoid by dimerisation, or, more likely in view of the probable low concentration of such a species, by attack upon it by the *C*-nucleophilic intermediate **4** or **5** of the Brook rearrangement, followed by β-elimination of a second silyloxy anion.

The following paper describes some other remarkable reactions that can be ascribed to the presence of intermediate lithium reagents like **12** and **15**. They add further support to this being the correct mechanism, at least in outline.

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Notes and References

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