Novel Oxidative Generation of Ammonium Ylides and the Subsequent Silicon Polonovski Reaction

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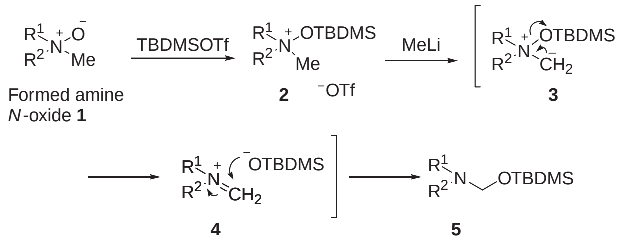
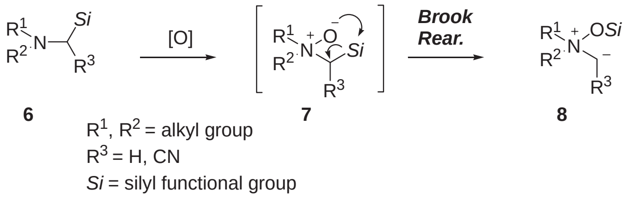
We have demonstrated a novel oxidative generation of ammonium ylides by employing allylic amines having a silyl group. Treatment of *N*-(α-silylmethyl)-*N*-allylic amines with an oxidant, followed by acetic anhydride, brought about a tandem Brook rearrangement/silicon Polonovski reaction via the generation of ammonium ylides to give the corresponding amides, whereas the reaction of *N*-(α-cyano-α-silylmethyl)-*N*-allylic amines with an oxidant afforded the corresponding formamides.

Amine *N*-oxides are readily available compounds by oxidation of *tert*-amines, and the functionalization of amines taking advantage of amine *N*-oxides is used in the syntheses of N-containing natural products such as alkaloids. Actually, the reaction of *tert*-amine *N*-oxides with acid anhydrides is well-known as the Polonovski reaction and is used as a useful dealkylation method for *tert*-amines. After the original work by the Polonovski's group using bicyclic tropane *N*-oxide derivatives,[1] several variations have appeared in the literature.[2,3] The silicon Polonovski variant shows that *tert*-butyldimethylsilyl triflate as the activator promotes the rearrangement of *tert*-amine *N*-oxides **1** to α-siloxy amines **5** via siloxyammonium ions **2**. However, very strong bases such as methyllithium or butyllithium are required to promote the transformation of ammonium ylides **3** and the successive rearrangement to iminium ions **4** (Scheme 1).[2] Although this reaction is useful for functional conversions in *tert*-amines, the use of strong bases may bring about undesirable side reactions, including Hofmann elimination and [1,2]rearrangement.[4] Thus, weaker bases or mild reaction conditions, compatible with many functional groups, might be necessary for regioselective generation of ammonium ylides.

We previously reported regioselective generation of ammonium ylides by the reaction of quaternary ammonium salts having a trimethylsilyl group with fluoride ion.[5a] This prompted us to examine the silicon Polonovski reaction. Now, we wish to report here a novel oxidative generation of the ammonium ylide and the successive silicon Polonovski reaction. Regioselective generation of ammonium ylide was achieved in one-pot by the Brook rearrangement[6] of *tert*-amine *N*-oxides having a silyl group[7] (Scheme 2). To the best of our knowledge, studies of silicon Polonovski reaction were rather confined to symmetrical benzyl or cyclic amines.[1–3] Thus, there are few reports on silicon Polonovski reactions with regard to dissymmetrical acyclic amines.

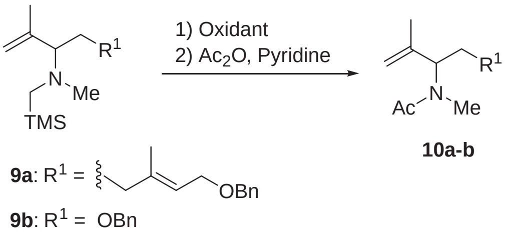


Scheme 1. Silicon Polonovski reaction.



Scheme 2.

Table 1. Oxidation of *N*-(α-silylmethyl)-*N*-allylic amines[a]

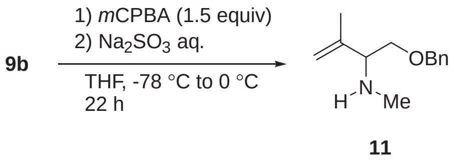


Entry	Amine	Oxidant	Solvent	Time/h	Yield/%
1	**9a**	*m*CPBA	THF	9	64
2	**9b**	*m*CPBA	THF	10	58
3	**9b**	*m*CPBA	DMF	12	60
4	**9b**	AcO_2H	DCM	8	99

[a]Amines **9a** and **9b** were treated with 1 molar equivalent of oxidant at −78 °C (Entries 1, 2, and 4) or −50 °C (Entry 3). After the reaction mixture was stirred for 2–6 h, the reaction mixture was warmed slowly to 0 °C and stirred for 3 h. Then Ac_2O and pyridine were added. The reaction mixture was stirred for 3 h at ambient temperature.

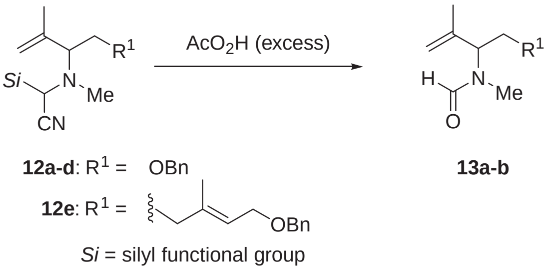
At first, the reaction was carried out by using allylic amine **9a** and **9b** with an oxidant (Table 1). When amine **9a** was oxidized with *m*CPBA at −78 °C in THF, followed by successive treatment with acetic anhydride as an electrophilic reagent, product **10a** was obtained in 64% yield (Entry 1). Similarly, when **9b** was used, product **10b** was obtained in 58–60% yield (Entries 2 and 3). Notably, reaction of **9b** with peracetic acid in dichloromethane furnished the product **10b** quantitatively (Entry 4). After the reaction of **9b** with *m*CPBA, the reaction mixture was subjected to half saturated aqueous sodium sulfite instead of acetic anhydride to give the corresponding *sec*-amine **11** in a 46% yield (Scheme 3).

We next examined the reaction of *N*-(α-cyano-α-silylmethyl)-*N*-allylic amines having various silyl groups in order to investigate the influence of stability of the ammonium ylide



Scheme 3.

Table 2. Oxidation of *N*-(α-cyano-α-silylmethyl)-*N*-allylic amines[a]



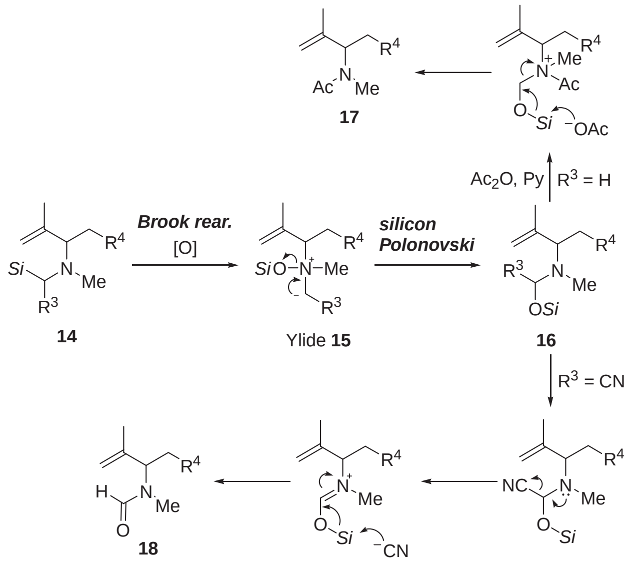
Entry	Amine	Silyl group (*Si*)	Product	Yield/%
1	**12a**	TMS	**13a**	25
2	**12b**	TES	**13a**	37
3	**12c**	TBDMS	**13a**	44
4	**12d**	TIPS	**13a**	61
5	**12e**	TBDMS	**13b**	50

[a]The amines **12a**–**12e** were treated with excess peracetic acid in DCM at −78 °C. After the reaction mixture was stirred for 12 h, the reaction mixture was warmed slowly to 0 °C and stirred for 12 h.

due to an adjacent cyano group. It should be noted that *N*-(α-cyano-α-silylmethyl)-*N*-allylic amines afforded formamides directly without any electrophilic reagent (Table 2). Although some allylic amine *N*-oxides induced from *N*-(α-cyano-α-silylmethyl)-*N*-allylic amines **12a** and **12b** having relatively small silyl groups underwent [2,3]sigmatropic rearrangement[8] to give (*E*)-allyloxyamines concomitantly (Entries 1 and 2), we found that the reaction occurred more readily by using **12c**–**12e** possessing bulky silyl groups (Entries 3–5). When the reaction was carried out by using **12d** and peracetic acid, the product **13a** was given in a 61% yield (Entry 4).

As for a silyl group, TBDMS or TIPS was more effective than TMS. This is most likely due to the steric protection of the silicon atom by *tert*-butyl or isopropyl group which makes the expected Brook rearrangement preferable to the undesirable nucleophilic attack to the silicon atom by peracetic acid. Notably, the present method affords formamides **13** in contrast to the standard base-promoted silicon Polonovski reaction[2] of *tert*-amine *N*-oxide which gives a complex mixture. A likely mechanism for such a process involves the generation of ammonium ylides **15** as a transient intermediate which undergoes the silicon Polonovski reaction to give the corresponding *tert*-amines **16** (Scheme 4).

We investigated the ammonium ylide **15** to know whether the [2,3]sigmatropic rearrangement[5] would occur or not. However, [2,3]sigmatropic rearrangement did not occur owing to unstability of the ylide **15**, and the silicon Polonovski reaction took place predominantly. Thus, reaction of *N*-(α-silylmethyl)-*N*-allylic amines **14** ($R^3 = H$) with an oxidant, followed by



Scheme 4. Plausible reaction mechanism.

treatment with acetic anhydride, gave amides **17**, whereas treatment of *N*-(α-cyano-α-silylmethyl)-*N*-allylic amines **14** ($R^3 = CN$) with an oxidant underwent the tandem Brook rearrangement/silicon Polonovski reaction/fragmentation reaction almost exclusively to afford formamides **18** or the generated cyano anion might attack the silyl group of **16** directly to give **18**.

In summary, we have demonstrated a novel oxidative generation of an ammonium ylide and the subsequent silicon Polonovski reaction. The present method does not require any bases in contrast to the necessity of very strong bases in the standard silicon Polonovski reaction, and will be used in the syntheses of N-containing compounds.

References and Notes

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