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Lewis acid-catalyzed three-component condensation reactions of aldehydes, *N*-silylcarbamates, and allylsilane: synthesis of *N*-homoallylcarbamates

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Abstract

For simultaneous construction of the polyurethane backbone and the allyl side chains, Lewis acid-catalyzed three-component condensation reactions of carbonyl compounds, *N*-trimethylsilylcarbamates, and allyltrimethylsilane are studied. The reaction of these three compounds took place in the presence of a catalytic amount of $TrClO_4$ at 0°C to yield the corresponding *N*-homoallylcarbamates in good yields. This reaction was also applied to the synthesis of a polyurethane having the allyl side chains.

Keywords: *N*-homoallylcarbamate; Lewis acid; allylsilane; polyurethane.

Three-component condensation reactions are interesting and important, not only because two bonds are formed in one pot, but also because the methodology would be useful for making a broad variety of compound libraries. It has been reported that the three-component condensation reactions of aldehydes, alkoxysilanes and silyl nucleophiles such as trialkylsilanes,[1a] allyltrimethylsilane,[1b,c] cyanotrimethylsilane,[1d] and silyl enol ethers[1e,f] take place with a catalytic amount of a Lewis acid to yield ethers, homoallyl ethers, α-alkoxynitriles, and β-alkoxyketones, respectively. We have applied these reactions to polycondensations, which simultaneously construct both the polyether backbone and functional side chains containing the allyl,[2a] cyano,[1d] and keto groups.[1e,2b] However, it would be difficult to extend the Lewis acid-catalyzed three-component condensation to the synthesis of amine derivatives by using *N*-silyl nucleophiles instead of alkoxysilanes, because the strong affinity of Lewis acids for the amino groups does not regenerate the Lewis acid in the reaction. In general, the synthesis of amine derivatives from three compounds is attained by the use of a stoichiometric amount of a Lewis acid in the three-component condensation[3] or by the reaction of organometallic nucleophiles with imines and acylimines prepared from aldehydes and amino derivatives in advance.[4] To the best of our knowledge, there are a few reports of the catalytic systems of three-component condensations for

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amine derivatives, which need a particular Lewis acid stable enough in water[5] or a Brønsted acid–surfactant–combined catalyst in water.[6] We have found that *N*-silyl nucleophiles having an alkoxycarbonyl group adjacent to the amino group undergo three-component condensation reactions by a catalytic amount of ordinary Lewis acids. In this paper, we report the condensation reactions of aldehydes **1**, *N*-silylcarbamates **2**, and allylsilane **3** by a catalytic amount of triphenylmethyl perchlorate ($TrClO_4$), which yield *N*-homoallylcarbamates **4** in a one-pot procedure. Furthermore, the reaction mechanism and the application to polymer synthesis are also described.

1 **2** **3** **4**

In order to establish the optimal conditions for the reactions of **1**, **2**, and **3**, we first studied the reaction of benzaldehyde **1a**, ethyl *N*-trimethylsilylcarbamate **2a**, and **3** by various Lewis acids. The results are shown in Table 1. The reaction was found to proceed with a catalytic amount of Me_3SiOTf and $TrClO_4$. In particular, $TrClO_4$ afforded *N*-homoallylcarbamate **4** in the highest yield at 0°C. However, $ZnCl_2$ was not effective for this reaction even when using an excess amount.

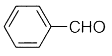
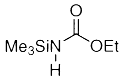
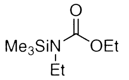
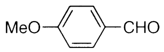
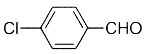
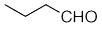
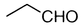
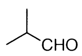
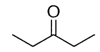
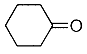
Table 1
Three-component condensation of **1a**, **2a**, and **3**[a]

Lewis Acid[b]	Temp (°C)	Yield (%)[c]
$TrClO_4$	25	92
	0	96
	-20	49
Me_3SiOTf	0	72
$ZnCl_2$[d]	0	8

[a] The reaction was carried out in CH_2Cl_2 ($[\mathbf{1a}]_0 = [\mathbf{2a}]_0 = [\mathbf{3}]_0 =$ 0.5 M) for 24 h. [b] 5 mol% to **1a**. [c] Determined by GC.
[d] 110 mol% to **1a**.

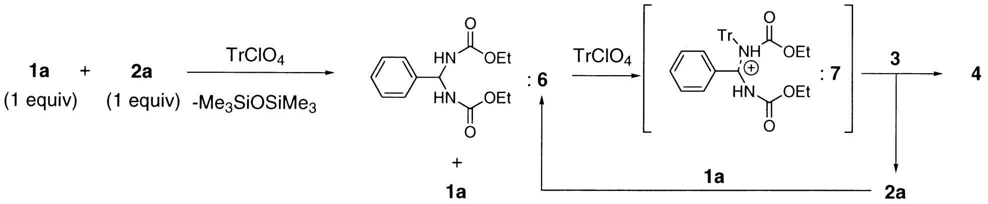
With the optimized conditions in hand, we next carried out the reactions of a variety of **1**, **2**, and **3**. Thus, a round-bottomed flask, equipped with a three-way stopcock, was charged with $TrClO_4$ (0.017 g, 0.05 mmol) and purged with argon. Dry dichloromethane (1.0 ml) was added to the flask, followed by cooling the solution to 0°C. A solution of **1** (1.0 mmol) and **2** (1.0 mmol) in dichloromethane (0.5 ml) was added at 0°C. After 5 min, a solution of **3** (1.0 mmol) in dichloromethane (0.5 ml) was added. The solution was stirred at 0°C for 24 h. The reaction mixture was quenched with a few drops of ammoniacal methanol. The solvent was evaporated and the residue was purified by column chromatography on silica gel to afford the corresponding *N*-homoallylcarbamates **4**. The results are summarized in Table 2. Aromatic and aliphatic aldehydes reacted with **2a** and **3** to yield the corresponding **4** in good yields (entries 1 and 3–7). The electron-donating and electron-withdrawing groups on the benzene ring of aromatic aldehydes did not affect the yields of **4** (entries 3 and 4). Ketones resulted in low yield of **4** for the same reaction time (24 h), but the yield increased up to 97% in 96 h (entry 9 versus 10). *N*-Alkylated **2b** afforded **4** in poor yield (entry 2).

Table 2
Three-component condensation of various **1**, **2**, and **3**[a]

Entry	Carbonyl compound	Silylcarbamate	Yield of **4** (%)[b]
1	 : **1a**	 : **2a**	88[c]
2	**1a**	 : **2b**	14
3		**2a**	79
4		**2a**	83
5		**2a**	79
6		**2a**	67
7		**2a**	56
8		**2a**	15
9	 : **1b**	**2a**	23
10	**1b**	**2a**	97[c,d]

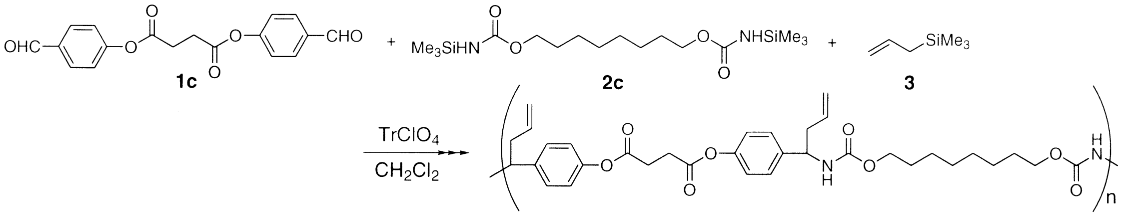
[a] The reaction was carried out with 5 mol% of $TrClO_4$ in CH_2Cl_2 ($[\mathbf{1}]_0 = [\mathbf{2}]_0 = [\mathbf{3}]_0 = 0.5$ M) at 0 °C for 24 h. [b] Isolated yield. [c] Determined by GC.
[d] The reaction was carried out with 5 mol% of $TrClO_4$ in CH_2Cl_2 ($[\mathbf{1}]_0 = [\mathbf{2}]_0 = [\mathbf{3}]_0 = 0.25$ M) at 0 °C for 96 h.

To discuss the reaction mechanism, the reaction of **1a** with **2a** was carried out in the presence of 5 mol% of $TrClO_4$ in $CDCl_3$ at ambient temperature, and then the reaction mixture was directly observed by ^1H NMR. The spectrum showed the signal of the aldehyde proton of **1a** at δ 10.00 and a broad signal of the benzylic proton at δ 6.45–6.11, with a signal intensity ratio of 1:1. At this point, the reaction was quenched to afford **1a** and bisurethane **6**,[3a] the benzylic proton signal of which appeared at δ 6.23 in $CDCl_3$. However, when a catalytic amount of $TrClO_4$ was added to a solution of **6** in $CDCl_3$, the benzylic proton signal of **6** was changed to a broad signal, which was identical with the broad signal of the above reaction mixture. Accordingly, the broad signal at δ 6.45–6.11 would be assigned to a fast equilibrium mixture of **6** and cationic intermediate **7** generated by the coordination of $TrClO_4$ to **6**. On the basis of the above results and the reported mechanism of a similar reaction using 1 equiv. of Lewis acid,[3a] a proposed mechanism is shown in Scheme 1. A half-amount of **1a** reacts with all of **2a** to yield **6**; **1a** and **6** are in the reaction mixture in the ratio 1:1. When **3** is added to this reaction mixture, **3** reacts with **7**, which is generated by the activation of **6** with $TrClO_4$, to yield **4** and **2a**. Regenerated **2a** reacts with **1a** to supply **6**. The fact that no homoallyl alcohols were produced as a result of a direct attack of **3** on **1a** shows that the reaction of **3** with **6** proceeds selectively even in the presence of **1a** in the reaction mixture. It should also be noted that hexamethyldisiloxane as a byproduct in this condensation reaction does not quench the Lewis acid catalyst, and this enables the reaction to proceed in a catalytic fashion.



Scheme 1.

This reaction was also applied to polycondensation. Thus, bis(4-formylphenyl) succinate **1c**, octamethylene *N*,*N*′-bis(trimethylsilyl)carbamate **2c**, and **3** were reacted with 10 mol% of $TrClO_4$ in CH_2Cl_2 at 0°C for 24 h to yield a polyurethane having the allyl side chains with a number-averaged molecular weight (*Mn*) of 12,000.



In summary, the present work has demonstrated that *N*-trimethylsilylcarbamates are available for Lewis acid-catalyzed three-component condensation reactions for *N*-homoallylcarbamates. Furthermore, the three-component polycondensation using bifunctional *N*,*N*′-bistrimethylsilylcarbamate yielded a functional polyurethane with allyl side chains.

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