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A CONVENIENT SYNTHETIC METHOD FOR SCHIFF BASES. THE TRIMETHYLSILYL TRIFLUOROMETHANESULFONATE-CATALYZED REACTION OF N,N-BIS(TRIMETHYLSILYL)AMINES WITH ALDEHYDES AND KETONES

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N,N-Bis(trimethylsilyl)amines react with aldehydes or ketones in the presence of trimethylsilyl trifluoromethanesulfonate to give Schiff bases in high yields. In situ utilization of the reaction solution as the Schiff base is also demonstrated.

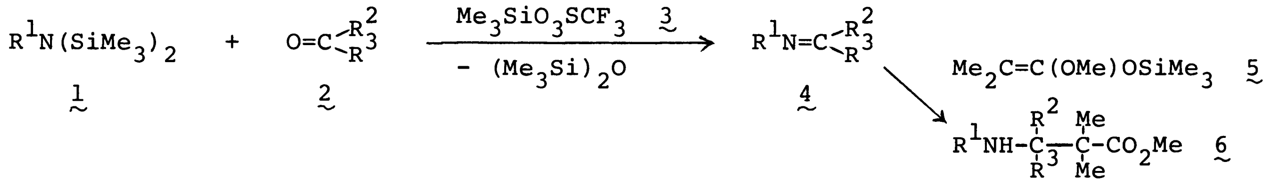
Acid- or non-catalyzed reaction of primary amines with aldehydes or ketones yielding Schiff bases$^{1)}$ is often cumbersome, particularly in the use of carbonyl compounds of low reactivity or volatile amines. The removal of forming water is necessary to complete this reversible reaction, and the reaction of low reactive ones such as diaryl ketones with amines requires higher temperatures and longer reaction times,$^{2)}$ or strong dehydrating agents.$^{3)}$

As an alternative method for Schiff bases, a reaction of N,N-bis(silyl)amines with carbonyl compounds catalyzed by zinc-cadmium couple (or zinc chloride) has appeared in the literature,$^{4)}$ but this reaction is so far from practical use because of its drastic conditions (165 °C, 40 h).

We now report a mild, simple, and high-yield preparation of Schiff bases (4) by trimethylsilyl trifluoromethanesulfonate (TMS triflate) (3)-catalyzed reaction of N,N-bis(trimethylsilyl)amines (1)$^{5)}$ with aldehydes and ketones (2). In addition, utilization of the reaction solution in situ as a Schiff base solution is described.

The reaction was carried out simply by allowing the solution of 1, 2, and a small amount of 3 in dichloromethane or dichloroethane to stand at room temperature or to reflux. A typical example is as follows. The triflate (3) (0.15 mmol) was added to the stirred solution of N,N-bis(trimethylsilyl)amine (1) (3 mmol) and benzophenone (2) (3 mmol) in dichloroethane (6 ml) and the mixture was heated under reflux for 2 h. Usual work-up and distillation gave N-(diphenylmethylene)amine (4) almost quantitatively. In the case of benzaldehyde (2) (3 mmol), the reaction with 1 (3 mmol) in the presence of 3 (0.06 mmol) proceeded exothermically in dichloromethane (6 ml) at room temperature. The production of a variety of Schiff bases (4) in a similar manner is summarized in Table 1.

Advantages of the present method are the mild conditions, simplicity of the procedure, high yields of the products, and no trouble in the use of volatile amines. Moreover, the reaction solution can be securely utilized in situ as an anhydrous state of Schiff base, since hexamethyldisiloxane formed simultaneously is innert to common reagents and, if necessary, a catalytic amount of 3 can be removed by brief treatment with magnesium oxide.



$$\underset{1}{R^1N(SiMe_3)_2} + \underset{2}{O{=}C\begin{smallmatrix}R^2\\R^3\end{smallmatrix}} \xrightarrow[-\ (Me_3Si)_2O]{Me_3SiO_3SCF_3\ \ 3} \underset{4}{R^1N{=}C\begin{smallmatrix}R^2\\R^3\end{smallmatrix}} \xrightarrow{Me_2C{=}C(OMe)OSiMe_3\ \ 5} R^1NH-\underset{R^3}{\overset{R^2}{C}}-\underset{Me}{\overset{Me}{C}}-CO_2Me\ \ 6$$

Table 1. The silyl triflate (3)-catalyzed reaction of 1 with 2

N,N-Bis(silyl)amine (1)	Carbonyl compound (2)		Schiff base (4)[a)]	
R^1	R^2	R^3	Bp[b)]/°C (Torr)	Yield/%[c)]
$PhCH_2$	Ph	H	170 (1.5)	97
$PhCH_2$	Ph	Ph	220 (0.5)	97
(2-thienyl)CH_2	Ph	H	190 (2)	95
(2-thienyl)CH_2	Ph	Ph	240 (3)	96
(9-fluorenyl)CH_2	Ph	H	———	98
$CH_2{=}CH(CH_2)_2$	Ph	H	170 (16)	95
Me	Ph	H	120 (20)	98
Me	2-thienyl	H	120 (20)	99
Me	Ph	Ph	150 (1)	98
Me	Ph	PhCO	160 (1)	88
$(EtO)_2P(O)CH_2$	Ph	H	170 (0.5)	80

a) GLPC analytically and ^1H NMR spectroscopically pure.
b) Bps refer to the bath temperatures in a "Kugelrohr" short-path apparatus.
c) Yields refer to the isolated products.

A typical example of the in situ utilization is as follows. To a N-(benzylidene)methylamine (4) solution, formed from benzaldehyde (2) and N,N-bis(trimethylsilyl)methylamine (1) in the presence of 3 (5 mol%), a ketene silyl acetal (5) was added. The reaction proceeded at room temperature to give β-aminocarboxylic ester (6: R^1=Me, R^2=Ph, R^3=H) in 84% yield, where the remaining triflate (3) functioned as a catalyst. This methodology provides a simple and versatile procedure for synthesizing various β-aminocarboxylic esters, which are useful synthetic intermediates for β-lactams.

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