# Lewis Base-catalyzed Alkynylation of Carbonyl Compounds with Trimethylsilylacetylenes

Takayuki Kitazawa, Tomofumi Minowa, and Teruaki Mukaiyama*
*Center for Basic Research, The Kitasato Institute, 6-15-5 (TCI) Toshima, Kita-ku, Tokyo 114-0003*
*Kitasato Institute for Life Sciences, Kitasato University, 5-9-1 Shirokane, Minato-ku, Tokyo 108-8641*

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Alkynylation of carbonyl compounds with trimethylsilylacetylenes in the presence of a catalytic amount of Lewis bases such as acetate or phenoxide anion is described. The alkynylation proceeded under mild conditions and afforded the corresponding propargyl alcohols in good to excellent yields.

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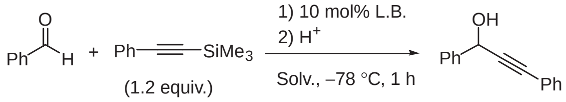
Addition of acetylenes to carbonyl compounds in the formation of propargyl alcohols is one of the most important processes in carbon–carbon bond-forming reactions in organic synthesis.[1] Of the several alkynylation reactions promoted by Lewis acid catalysts reported, examples that involve Lewis base-catalyzed reactions are very few. The fluoride anion-catalyzed alkynylation was first reported by Kuwajima and Nakamura and the corresponding propargyl alcohols were obtained in high yields.[2] Recently, Shioiri and Yoshizawa also reported the similar alkynylation reactions using fluoride anion to give the desired propargylic alcohols with $\beta$-branched Morita–Baylis–Hillman-type adduct as a side product.[3] Also, Sheidt and Lettan, II reported the KOEt-catalyzed alkynylation of carbonyl compounds, but their examples were limited to a case using triethoxysilylacetylenes.[4] Recently, it was reported from our laboratory that the use of Lewis base catalysts was found effective for the activation of silicon–carbon bond which was then employed with success in such as trifluoromethylation,[5] cyanomethylation[6] and Srecker-type reaction.[7] It was therefore planned to use trimethylsilylacetylenes in Lewis base activation of other carbon–silicon bonds. In the present communication, we would like to report on the activation of simple trimethylsilylacetylenes that are catalyzed by the Lewis base catalysts, especially by the phenoxide anion.

**Table 1.** Effect of Lewis base (L.B.) catalysts on the reaction between benzaldehyde and 1-phenyl-2-(trimethylsilyl)acetylene



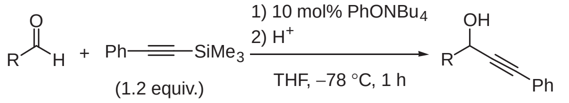
| Entry | L. B. | Solv. | Yield/% | Entry | L. B. | Solv. | Yield/% |
|---|---|---|---|---|---|---|---|
| 1 | AcOLi | DMF | N.R.[a] | 7 | $PhONBu_4$ | DMF | 88 |
| 2 | $AcONBu_4$ | DMF | 62[a] | 8 | $PhONBu_4$ | THF | quant. |
| 3 | $AcONBu_4$ | THF | 54[a] | 9 | $PhONBu_4$ | THF | 95[b] |
| 4 | PhOLi | DMF | 39 | 10 | $PhONBu_4$ | toluene | 97 |
| 5 | PhONa | DMF | 42 | 11 | $PhONBu_4$ | $CH_2Cl_2$ | 96 |
| 6 | PhOK | DMF | 53 | 12 | $PhONBu_4$ | $Et_2O$ | 92 |

[a]The reaction was carried out at 0 °C. [b]1 mol% of the catalyst was used.

In the first place, a reaction between benzaldehyde and 1-phenyl-2-(trimethylsilyl)acetylene was chosen as a model to carefully screen effects of various Lewis base catalysts and reaction conditions (Table 1).[8].When an acetate anion was used, the trimethylsilylacetylene was not effectively activated and the yields turned out to be very low. On the other hand, Lewis base catalysts prepared from phenol proved to be effective and the corresponding propargyl alcohols were obtained in high yields, especially when the ammonium phenoxide was used. The reaction proceeded as smoothly as well in other various solvents when ammonium phenoxide was used as a catalyst under the same conditions.

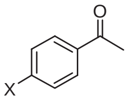
Next, various carbonyl compounds were tried in this ammonium phenoxide-catalyzed alkynylation reaction. (Table 2). Aromatic aldehydes with electron-withdrawing or -donating sub-

**Table 2.** Tetrabutylammonium phenoxide-catalyzed alkynylation reaction of various carbonyl compounds with 1-phenyl-2-(trimethylsilyl)acetylene

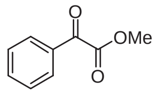


| Entry | R | Yield/% | Entry | R | Yield/% |
|---|---|---|---|---|---|
| 1 | Ph | quant. | 10 | $Ph(CH_2)_2$ | 80[a,b] |
| 2 | $2\text{-}ClC_6H_4$ | quant. | 11 | *c*-Hex | 79[a,b] |
| 3 | $2\text{-}MeOC_6H_4$ | 99 | 12 | $^t$Bu | 55[a,b] |
| 4 | $2\text{-}MeC_6H_4$ | 99 | 13 | (*E*)-PhCH=CH | 57 |
| 5 | $4\text{-}MeOC_6H_4$ | 87 | 14 | $TBDMSOCH_2$ | 83[c] |
| 6 | $4\text{-}MeC_6H_4$ | quant. | 15 | **1a** | trace |
| 7 | $4\text{-}Me_2NC_6H_4$ | 84[a] | 16 | **1b** | 10 |
| 8 | 2-Furyl | 92 | 17 | **2** | 55 |
| 9 | 2-Thienyl | 87 | 18 | **3** | 68 |

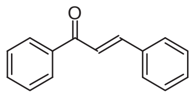
[a]1.5 equiv. of 1-phenyl-2-(trimethylsilyl)acetylene was used. [b]The reaction was carried out at −45 °C for 6 h. [c]The reaction was carried out at −45 °C for 4 h.



**1a** : X = H
**1b** : x = Br

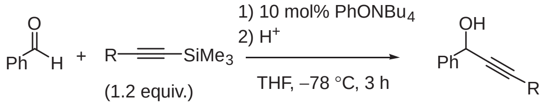


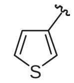
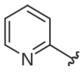
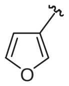
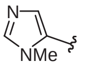
**2**



**3**

**Table 3.** Tetrabutylammonium phenoxide-catalyzed alkynylation reactions of benzaldehyde with various trimethylsilylacetylenes



| Entry | R | Yield | Entry | R | Yield |
|---|---|---|---|---|---|
| 1 | H | 62[a] | 5 |  | 98 |
| 2 | H | 54[b] | | | |
| 3 | $CH_3(CH_2)_3$ | N.R. | 6 |  | 80 |
| 4 |  | quant. | 7 |  | 80[c] |

[a]The reaction was carried out at −45 °C for 6 h. [b]1-Phenylpropan-2-one was used instead of benzaldehyde. [c]Yield determined by $^1H$ NMR because the product was unstable.

stituents reacted smoothly under the above conditions, and the corresponding propargyl alcohols were obtained in excellent yields. Aldehydes having a Lewis basic moiety also reacted equally (Entry 7), and heteroaromatic aldehydes also gave good results (Entries 8 and 9). Aliphatic aldehydes including primary, secondary and tertiary aldehydes worked successfully when the reactions were carried out at −45 °C (Entries 10–12). When simple ketones such as acetophenone and its derivatives were used, the yields of the adduct remained very low whereas ketones with electron-withdrawing groups gave the corresponding tertiary alcohols in moderate yields. When $\alpha,\beta$-unsaturated carbonyl compounds were used, the major products were 1,2-adducts (Entry 18). It is noteworthy that aldehyde with *t*-butyldimethylsilyloxy (TBDMSO) group also reacted under this condition without loss of TBDMS group (Entry 14). This example shows that TBDMS group, which would be inapplicable to fluoride anion-mediated alkynylation reactions, was tolerant toward the reaction condition to give the corresponding propargyl alcohol in 83% yield.

Next, this alkynylation reaction was examined by using other trimethylsilylacetylenes (Table 3). Although 1-alkyl-2-(trimethylsilyl)acetylene did not react under the optimized conditions (Entry 3), various 1-aryl-2-(trimethylsilyl)acetylenes reacted smoothly to afford the corresponding 3-arylpropargyl alcohols in excellent yields. Similarly, the reaction of the substrate having Lewis basic moiety gave the desired adduct in high yield (Entry 7).

It is noted that the ammonium phenoxide-catalyzed alkynylation reactions of both aromatic and aliphatic aldehydes proceeded smoothly under mild conditions. The substrates having Lewis basic moieties also reacted smoothly with trimethylsilylacetylenes and the corresponding propargyl alcohols were obtained in excellent yields. Since reactions of these substrates generally interact with Lewis acids, the present reaction provides effective ways for the preparation of various propargyl alcohols having Lewis basic moieties. Further study on this type of reaction is now in progress.

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## References and Notes

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8 Typical experimental procedure is as follows (Table 1, Entry 8): To a stirred solution of $PhONBu_4$ (0.5 mL of 0.1 M solution, 0.0500 mmol) was added a solution of 1-phenyl-2-trimethylsilylacetylene (105.4 mg, 0.605 mmol) in THF (1.0 mL) and a solution of benzaldehyde (53.3 mg, 0.502 mmol) in THF (1.0 mL) at −78 °C under argon atmosphere. The mixture was stirred for 1 h at the same temperature and 1 M HCl (2 mL) was added to quench the reaction. The mixture was extracted with EtOAc and the combined organic layer was washed with water and brine, dried over anhydrous $Na_2SO_4$, and evaporated. The crude product was purified by preparative TLC (hexane/EtOAc = 4/1) to give the corresponding propargyl alcohol (104.6 mg, quant.) as a light yellow oil.

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