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The Use of α-Trimethylsilyl-α,β-Unsaturated Ketones as 1-Acylethenyl Anion Synthon

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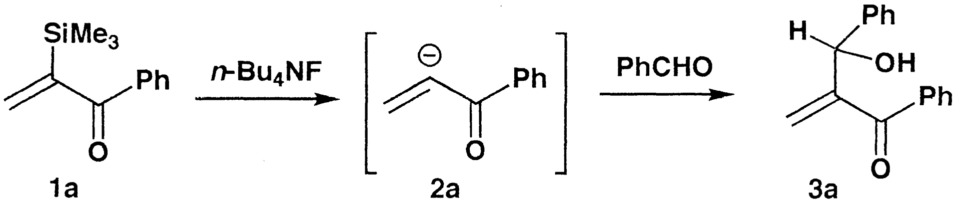
Treatment of α-trimethylsilyl-α,β-unsaturated ketones with tetrabutylammonium fluoride in the presence of aldehydes provided α-(1-hydroxyalkyl)-α,β-unsaturated ketones in good yields. The reaction proceeded via allenolate. The new method was successfully applied to a synthesis of α-(1-hydroxyalkyl)-α,β-unsaturated esters from α-trimethylsilyl-α,β-unsaturated esters.

1-Acylethenyl anion is a versatile synthon in organic synthesis and several indirect methods1) which take a roundabout route to such anion have been reported. Desilylation of α-silyl-α,β-unsaturated ketone is one of the most direct and effective routes to 1-acylethenyl anion. Few attempts to trap an alkenyl anion intermediate derived from alkenyltrimethylsilane by electrophiles such as aldehydes have been reported,2) although protodesilylation of alkenylsilanes has been widely studied.3) Here we wish to report that treatment of α-trimethylsilyl-α,β-unsaturated ketone with tetrabutylammonium fluoride provides 1-acylethenyl anion which gives the corresponding adducts upon addition of electrophiles such as aldehydes.

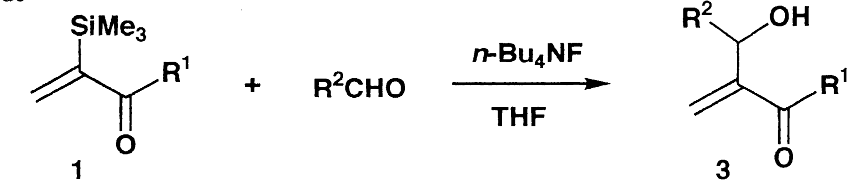
An addition of tetrabutylammonium fluoride4) to a solution of α-trimethylsilylethenyl phenyl ketone **1a**5) and benzaldehyde in tetrahydrofuran (THF) at –78 °C provided α-hydroxybenzylethenyl phenyl ketone **3a** in 76% yield (Scheme 1). The representative results are shown in Table 1.



Scheme 1.

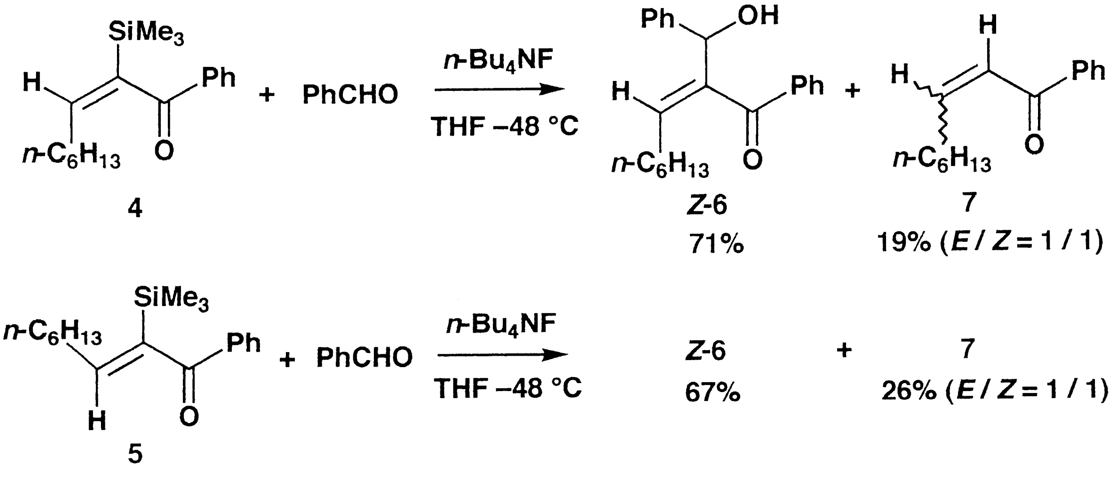
The use of ketone such as acetophenone or benzophenone in place of aldehyde resulted in a formation of complex mixture and the desired adduct could not be obtained. The amount of tetrabutylammonium fluoride could be reduced to a catalytic amount without decrease of the yield of adduct. For instance, treatment of a solution of **1a** (1.0 mmol) and benzaldehyde (2.0 mmol) with 0.3 equivalent of tetrabutylammonium fluoride (0.3 mmol) afforded **3a** in 73% yield. In the case of the reaction of α-trimethylsilylethenyl butyl ketone **1b**, the reaction did not proceed at –78 °C and higher reaction temperature (–48 °C) was required to complete the reaction. By-products derived from aldol reaction were formed in the reaction of **1a** or **1b** with valeraldehyde and the yields of desired adducts decreased.

Table 1. Tetrabutylammonium fluoride induced reaction of α-trimethylsilyl-α,β-unsaturated ketone with aldehyde

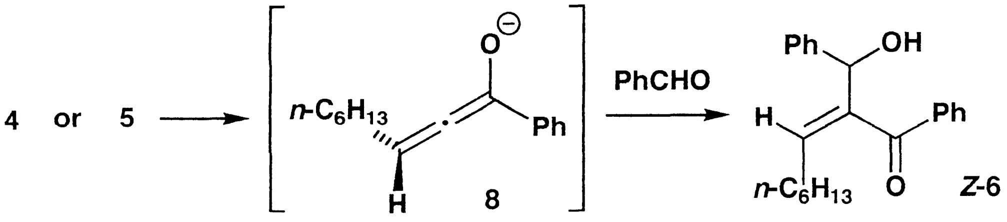


	1	Aldehyde	Reaction Conditions		Yield of **3**
Entry	R^1	R^2CHO	Temp / °C	Time / min	/ %
1	**1a**: Ph	PhCHO	–78	30	**3a** : 76
2	**1a**: Ph	*n*-BuCHO	–78	30	**3b** : 48
3	**1a**: Ph	PhCH=CHCHO	–78	30	**3c** : 58
4	**1b**: *n*-Bu	PHCHO	–48	30	**3d** : 70
5	**1b**: *n*-Bu	*n*-BuCHO	–48	30	**3e** : 39
6	**1b**: *n*-Bu	PhCH=CHCHO	–48	30	**3f** : 40

In order to examine the stereochemistry of the reaction, (*E*)- and (*Z*)-1-trimethylsilylalkenyl phenyl ketone (**4** and **5**) were prepared.6) Treatment of (*E*)-isomer with tetrabutylammonium fluoride in the presence of benzaldehyde provided α-hydroxybenzyl-α,β-unsaturated ketone *Z*-**6**7) in 71% yield along with protodesilylation product **7** (*E*/*Z* = 1/1, 19% yield). Meantime, an addition of tetrabutylammonium fluoride to a solution of *Z*-isomer **5** and benzaldehyde afforded the adduct **6** with the same configuration as the adduct derived from *E*-isomer **4**. Moreover, the by-product **7** (26%) also consists of the same isomeric mixture of (*E*)- and (*Z*)-1-octenyl phenyl ketone (*E*/*Z* = 1/1) as the by-product in the reaction of **4** (Scheme 2). These facts might be explained as follows. Desilylation of **4** or **5** with tetrabutylammonium fluoride would afford the same allenolate8) **8** in which stereochemistry of the starting materials is lost. An attack of benzaldehyde on the allenolate from the less hindered side gives *Z*-enone **6** exclusively (Scheme 3).



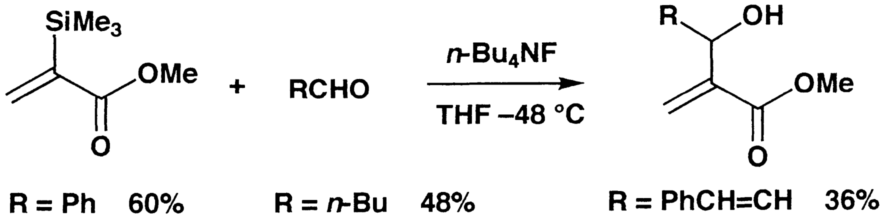
Scheme 2.



Scheme 3.

The reaction of 2-trimethylsilyl-2-cyclohexenone, which can not take an allenolate form, with tetrabutylammonium fluoride in the presence of benzaldehyde resulted in a recovery of 2-trimethylsilyl-2-cyclohexenone and no adduct was obtained. This result does not contradict the assumption of the intermediacy of allenolate in the reaction of **1**,**4**, or **5** with tetrabutylammonium fluoride.

Treatment of α-trimethylsilylacrylate[9) with tetrabutylammonium fluoride in the presence of aldehydes provided α-(1-hydroxyalkyl)-α,β-unsaturated esters (Scheme 4).



Scheme 4.

A typical experimental procedure is as follows. A THF solution of tetrabutylammonium fluoride (1.0 M, 2.0 ml, 2.0 mmol) was added to a solution of α-trimethylsilyl-α,β-unsaturated ketone **1a** (0.42 g, 2.0 mmol) and benzaldehyde (0.42 g, 4.0 mmol) in THF (20 ml) at −78 °C under argon atmosphere. After stirring for 30 min at −78 °C, the mixture was warmed to room temperature. The resulting mixture was poured into saturated ammonium chloride and extracted with ethyl acetate (30 ml x 3). Combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. Purification by silica-gel column chromatography gave α-hydroxybenzyl-α,β-unsaturated ketone **3a** (0.36 g) in 76% yield.10)

References

1) S. J. Branca and A. B. Smith, III, *J. Am. Chem. Soc.*, **100**, 7767 (1978); M. A. Guaciaro, P. M. Wovkulich, and A. B. Smith, III, *Tetrahedron Lett.*, **1978**, 4661; T. Shono, Y. Matsumura, S. Kashimura, and K. Hatanaka, *J. Am. Chem. Soc.*, **101**, 4752 (1979); T. Mukaiyama, K. Inomata, and M. Muraki, *ibid.*, **95**, 967 (1973); A. Itoh, S. Ozawa, K. Oshima, and H. Nozaki, *Bull. Chem. Soc. Jpn.*, **54**, 274 (1981). DABCO-catalyzed reaction of methyl vinyl ketone with aldehyde has been reported: D. Basavaiah and V.V.L. Gowriswari, *Tetrahedron Lett.*, **27**, 2031 (1986).

2) H. Oda, M. Sato, Y. Morizawa, K. Oshima, and H. Nozaki, *Tetrahedron Lett.*, **24**, 2877 (1983); Y. Sato and K. Hitomi, *J. Chem. Soc., Chem. Commun.*, **1983**, 170.

3) K. E. Koenig and W. P. Weber, *J. Am. Chem. Soc.*, **95**, 3416 (1973); K. Utimoto, M. Kitai, and H. Nozaki, *Tetrahedron Lett.* **1975**, 2825; S. Fujikura, M. Inoue, K. Utimoto, and H. Nozaki, *ibid.*, **25**, 1999 (1984); T. H. Chan and W. Mychajlowskij, *ibid.*, **1974**, 3479; H. Oda, M. Sato, Y. Morizawa,

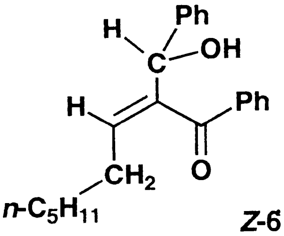
K. Oshima, and H. Nozaki, *Tetrahedron*, **41**, 3257 (1985).

4) A THF solution of tetrabutylammonium fluoride was purchased from Aldrich Chemical Company and used without further purification.

5) R. K. Boecman, Jr., D. M. Blum, B. Ganem, and N. Halvey, *Organic Synthesis,* Coll. Vol. 6, 1033.

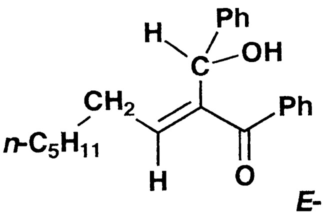
6) The enones **4** and **5** were generated starting from (*E*)-1-iodo-1-trimethylsilyl-1-octene and (*Z*)-1-iodo-1-trimethylsilyl-1-octene, respectively, in similar fashion to the preparation of α-trimethylsilylethenyl phenyl ketone (Ref 5). (*E*)-1-Iodo-1-trimethylsilyl-1-octene was prepared by hydroalumination of 1-trimethylsilyl-1-octyne followed by iodination. (*Z*)-Isomer was obtained by isomerization of (*E*)-isomer with a catalytic amount of triethylborane according to a literature (Y. Ichinose, S. Matsunaga, K. Fugami, K. Oshima, and K. Utimoto, *Tetrahedron Lett.*, **30**, 3155 (1989)).

7) The stereochemistries of *Z*-**6** and *E*-**6** were confirmed by ^{1}H NMR (NOE) experiment. Whereas the compound *E*-**6** showed NOE (13%) between allylic methylene protons and the methine proton on carbon bearing hydroxy group, the isomer *Z*-**6** showed only negligible NOE (<3%). Examination of infrared spectra of *Z*-**6** and *E*-**6** supported these assignments. Steric hindrance in *Z*-**6**, which reduces the coplanarity of the conjugated system, reduces the effect of conjugation, causing C=O stretching absorption at higher wavenumber. Stereoisomeric compound *E*-**6** was prepared as shown below. Deprotection of acetal by $(COOH)_2$ caused isomerization of *Z*-alkene to thermodynamically stable *E*-isomer.



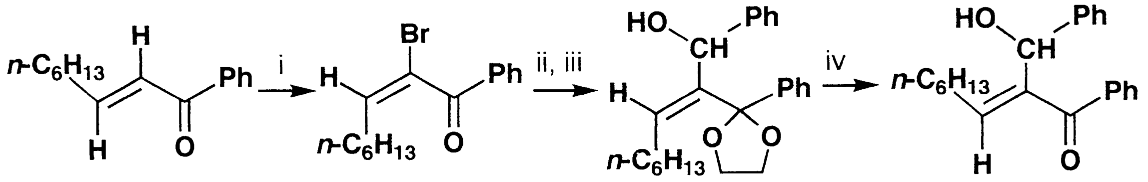
IR: 1654 cm^{-1}
NOE (<3%)

***Z*-6**



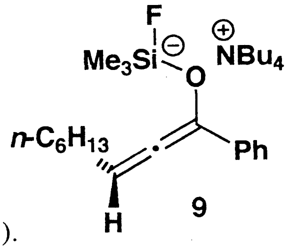
IR: 1637cm^{-1}
NOE (13%)

***E*-6**



i) 1) Br_2, 2) Et_3N. ii) $HOCH_2CH_2OH$ / TsOH. iii) 1) *n*-BuLi / THF, −78 °C, 2) PhCHO.
iv) $(COOH)_2$ / $CHCl_3$ - H_2O, 50 °C, 12 h.

8) T. Tsuda, T. Yoshida, and T. Saegusa, *J. Org. Chem.*, **53**, 1037 (1988); J. P. Marino, and R. J. Linderman, *ibid.*, **46**, 3696 (1981). Referee suggested that an allenolate equivalent such as allenolsilicate **9** instead of **8** might be an intermediate.



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9) A. Ottolenghi, M. Fridkin, and A. Zilkha, *Can. J. Chem.*, **41**, 2977 (1963).

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