

The Boron Trifluoride Catalyzed Aldol Reaction of Methyl 2-(Trimethylsiloxy)acrylate with Aldehydes in the Presence of Alcohols

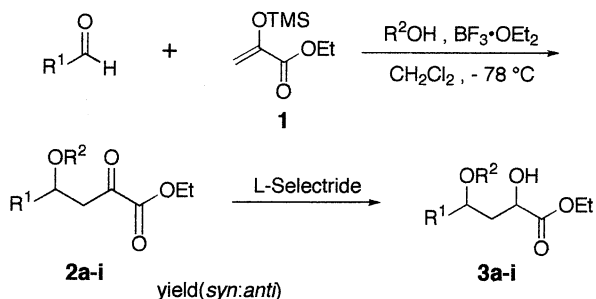
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The boron trifluoride etherate catalyzed aldol reaction of methyl 2-(trimethylsiloxy)acrylate with aldehydes proceeded smoothly in the presence of primary, secondary and tertiary alcohol to give corresponding γ -alkoxy- α -ketoesters.

It is well known as the Mukaiyama-aldol reaction that the reactions of carbonyl compounds with silyl enol ethers catalyzed by Lewis acid such as titanium tetrachloride give aldol adducts.¹ However, methyl 2-(trimethylsiloxy)acrylate (**1**)² does not react smoothly with aldehyde because **1** is sensitive to the Lewis acid. Sugimura *et al.* have reported that the reaction of **1** with acetals in the presence of boron trifluoride etherate gave corresponding γ -alkoxy- α -ketoesters.^{3,4}

We now herein describe the aldol reaction of **1** with aldehyde promoted by boron trifluoride in the presence of various kinds of alcohol. To the mixture of benzaldehyde and two equivalents of methanol, 2-propanol or *t*-butanol in dichloromethane was added boron trifluoride etherate at -78 °C and stirred for 20 min. **1** was added dropwise to this mixture and stirred for 1 h. The reaction mixture was warmed to -30 °C over a period of 1 h and stirred for additional 2 h at -30 °C. Work-up afforded crude ethyl 4-phenyl-4-alkoxy-2-oxo-butanoate (**2a-c**).⁵ Without further purification, **2a** was reduced by L-Selectride in THF at -78 °C to give diastereo mixture of *syn* and *anti* ethyl 4-phenyl-4-alkoxy-2-hydroxybutanoate (**3a-c**) in good yield.



3a : R ¹ , R ² =Ph, Me; 83%(70:30)	3f : R ¹ , R ² =Pr, <i>t</i> -Bu; 65%(38:62)
3b : R ¹ , R ² =Ph, <i>i</i> -Pr; 72%(28:72)	3g : R ¹ , R ² = <i>i</i> -Pr, Me; 73%(73:27)
3c : R ¹ , R ² =Ph, <i>t</i> -Bu; 73%(32:68)	3h : R ¹ , R ² = <i>i</i> -Pr, <i>i</i> -Pr; 71%(33:67)
3d : R ¹ , R ² =Pr, Me; 73%(58:42)	3i : R ¹ , R ² = <i>i</i> -Pr, <i>t</i> -Bu; 71%(28:72)
3e : R ¹ , R ² =Pr, <i>i</i> -Pr; 64%(44:56)	

Scheme 1.

In the similar manner, when butanal and 2-methylpropanal were employed instead of benzaldehyde, corresponding γ -alkoxy- α -ketoesters (**2d-i**) were obtained. Further, L-Selectride reduction gave **3d-i**.⁵ The diastereo ratio of *syn* and *anti* were measured by ¹H-NMR of **3a-i** and determined by *t*-butyldimethylsilylated products which were prepared from **3a-i** by *t*-butyldimethylsilyl chloride and imidazole.⁶

References and Notes

- 1 T. Mukaiyama and M. Murakami, *Synthesis*, **1987**, 1043.
- 2 M. Sekine, T. Futatsugi, K. Yamada, and T. Hata, *J. Chem. Soc., Perkin Trans. 1*, **1982**, 2509.
- 3 H. Sugimura, Y. Shigekawa, and M. Uematsu, *Synlett*, **1991**, 153.
- 4 R. Metternich and W. Lüdi, *Tetrahedron Lett.*, **1988**, 3923.
- 5 The ¹H-NMR(300 MHz, CDCl₃) data of **2a-i** are as follows. **2a**: 1.40(t, 3H, J=7.2 Hz), 2.98(dd, J=16.8, 4.5 Hz), 3.20(s, 3H), 3.41(dd, 1H, J=16.8, 9.0 Hz), 4.31(q, 2H, J=7.2 Hz), 4.73(dd, 1H, 9.0, 4.5 Hz) 7.45-7.89(m, 5H) **2b**: 1.02(d, 3H, J=6.0 Hz), 1.11(d, 3H, J=6.0 Hz), 1.37(t, 3H, J=7.2 Hz), 2.93(dd, 1H, J=16.2, 4.2 Hz), 3.37(dd, 1H, J=16.2, 9.0 Hz), 3.48(sept, 1H, J=6.0 Hz), 4.31(q, 2H, J=7.2 Hz), 4.96(dd, 1H, J=9.0, 4.2 Hz), 7.24-7.40(m, 5H) **2c**: 1.06(s, 9H), 1.37(t, 3H, J=7.2 Hz), 2.89(dd, 1H, J=16.8, 4.5 Hz), 3.32(dd, 1H, J=16.8, 9.0 Hz), 4.31(q, 2H, J=7.2 Hz), 5.06(dd, 1H, J=9.0, 4.5 Hz), 7.23-7.38(m, 5H), **2d**: 0.93(t, 3H, J=7.2 Hz), 1.34(t, 3H, J=7.2 Hz), 1.38-1.72(m, 4H), 2.88(dd, 1H, 16.8, 4.5 Hz), 3.08(dd, 1H, J=16.8, 7.6 Hz), 3.32(s, 3H), 3.68-3.78(m, 1H), 4.33(q, 2H, J=7.2 Hz), **2e**: 0.92(t, 3H, J=7.2 Hz), 1.08(d, 3H, J=6.0 Hz), 1.11(d, 3H, J=6.0 Hz), 1.37(t, 3H, J=7.2 Hz), 1.42-1.54(m, 4H), 2.89(dd, 1H, J=16.2, 4.8 Hz), 3.05(dd, 1H, J=16.2, 7.2 Hz), 3.65(sept, 1H, J=6.0 Hz), 3.88(m, 1H), 4.31(q, 2H, J=7.2 Hz), **2f**: 0.91(t, 3H, J=6.9 Hz), 1.17(s, 9H), 1.37(t, 3H, J=7.2 Hz), 1.42-1.58(m, 4H), 2.95(dd, 1H, J=15.6, 5.7 Hz), 3.01(dd, 1H, J=15.6, 6.3 Hz) 4.03(quint, 1H, J=6.3 Hz), 4.31(q, 2H, J=6.9 Hz), **2g**: 0.87(d, 3H, J=6.6 Hz), 0.89(d, 3H, J=7.2 Hz), 1.36(t, 3H, J=6.9 Hz), 1.93(m, 1H), 2.76(dd, 1H, J=16.2, 3.9 Hz), 3.03(dd, 1H, J=16.2, 8.4 Hz), 3.31(s, 3H), 3.57(ddd, 1H, J=8.7, 8.7, 3.9 Hz), 4.32(q, 2H, J=6.9 Hz), **2h**: 0.89(d, 3H, J=6.9 Hz), 0.91(d, 3H, J=6.6 Hz), 1.06(d, 3H, J=6.3 Hz), 1.10(d, 3H, J=6.3 Hz), 1.37(t, 3H, J=6.9 Hz), 1.89(m, 1H), 2.80(dd, 1H, J=15.9, 3.9 Hz), 3.00(dd, J=15.6, 8.1 Hz), 3.60(sept, 1H, J=6.3), 3.76(dt, 1H, J=8.1, 3.9 Hz), 4.32(q, 2H, J=6.9 Hz), **2i**: 0.86(d, 3H, J=7.2 Hz), 0.90(d, 3H, J=6.6 Hz), 1.16(s, 9H), 1.37(t, 3H, J=6.9 Hz), 1.80(m, 1H), 2.90(dd, 1H, J=15.6, 5.7 Hz), 2.96(dd, 1H, J=15.6, 6.0 Hz), 3.93(bq, 1H, J=5.7 Hz), 4.32(q, 2H, J=6.9 Hz)
- 6 In the silylated product of *anti* **3a**, the coupling constants of Ha, Hb and Hd, Hc were measured as follows. The differences of chemical shift of two methyl groups at silicon for *syn* derivatives were larger than *anti* form.

