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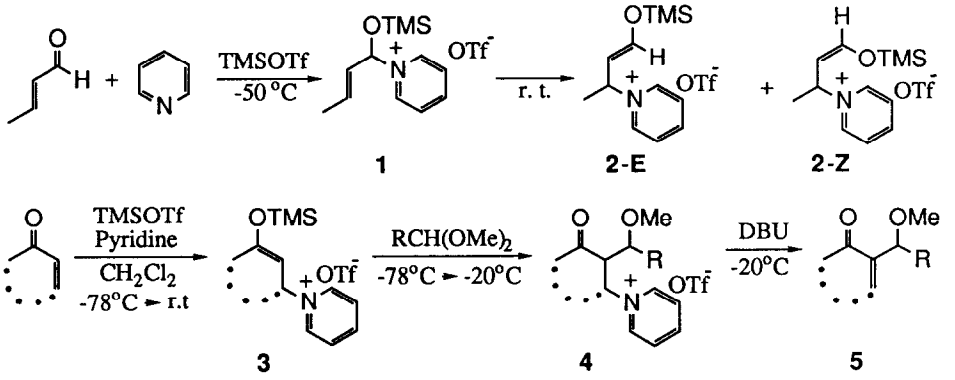
A SIMPLE PROCEDURE FOR α-ALKOXYALKYLATION OF α, β-ENONES via PYRIDINIOSILYLATION

Sunggak Kim*, Yong Gil Kim and Jung Ho Park
Department of Chemistry
Korea Advanced Institute of Science and Technology, Seoul 130-012, Korea

Summary : A one-pot, three-step procedure for α-alkoxyalkylation of α,β-enones utilizing a new pyridiniosilylation reaction is described.

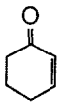
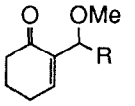
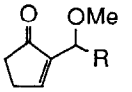
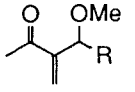
In connection with our ongoing research for the functionalization of α,β-unsaturated carbonyl compounds,[1] we have had an occasion to study a pyridiniosilylation reaction and it has been found that TMSOTf promoted conjugate addition of pyridine to α,β-enals and α,β-enones occurred cleanly. As far as we are aware, this is the first example in which pyridine added to α,β-enals and α,β-enones, although conjugate addition of pyridines and quinolines to acrylic acid, acrylamide, and vinyl sulfone under forcing conditions was previously reported.[2]



The pyridiniosilylation of crotonaldehyde in $CDCl_3$ at -50 °C afforded 1-silyloxyallylpyridinium salt(1)[3] and allylic 1,3-rearrangement to 3-silyloxyallylpyridinium salt(2)[4] has been observed, upon warming to room temperature. This rearrangement was complete within 1 h at room temperature. According to the low temperature ^{1}H-NMR spectroscopy, the pyridiniosilylation of 4-hexene-3-one in d_8-THF at -80 °C occurred to some extent (30%) via the 1,4-addition mode and the reaction was almost instantly complete at room temperature.[5]

α-Alkoxyalkylation of α,β-enones[6] can be conveniently carried out with pyridinium salts(3). The present method is based on (i) TMSOTf promoted addition of pyridine to enones (ii) the aldol-type reaction of silyl enol ethers with acetals in the presence of TMSOTf as a catalyst[7] and (iii) facile β-elimination of pyridine.

Table 1. α–Alkoxyalkylation of α,β–Enones via Pyridiniosilylation

α,β–enone	acetal	product		yield, %
	$PhCH(OMe)_2$		R = Ph	91
	$PhCH=CHCH(OMe)_2$		= CH=CHPh	84
	$CH_3CH_2CH_2CH(OMe)_2$		= $CH_2CH_2CH_3$	60
	$PhCH(OMe)_2$		R = Ph	75
	$PhCH=CHCH(OMe)_2$		= CH=CHPh	74
	$CH_3CH_2CH_2CH(OMe)_2$		= $CH_2CH_2CH_3$	61
	$PhCH(OMe)_2$		R = Ph	86
	$PhCH=CHCH(OMe)_2$		= CH=CHPh	90
	$PhCH_2CH(OMe)_2$		= CH_2Ph	59

The pyridiniosilylation of α,β-enones was initially carried out with 1.1 equiv of pyridine and 1.3 equiv of TMSOTf in dichloromethane at -78 °C and allowed to warm to room temperature. It is noteworthy that the order of mixing the reagents is not important. Thus, an active species for the pyridiniosilylation of α,β-enones is regarded as N-trimethylsilylpyridinium triflate. A slightly excess amount of TMSOTf was added to utilize as a catalyst in the aldol-type reaction. The aldol-type reaction of pyridinium salts(3) with acetals at -78 °C ~ -20 °C for 2 h followed by elimination of pyridine in pyridinium salts(4) with DBU afforded α-alkoxyalkylated enones(5) in high yields. As shown in Table 1, the present method works well with both acyclic and cyclic enones. It is noteworthy that the aldol-type reaction with pyridinium salts(2) derived from α,β-enals did not take place under the present conditions.[8]

References and notes

1. Kim, S.; Lee, P. H. *Tetrahedron Lett.* **1988**, *29*, 5413. Kim, S.; Kim, Y. C. *Synlett*, **1990**,115. *Tetrahedron lett.* **1990**, *31*, 2901.
2. Johns, G. in " *The Chemistry of Heterocyclic Compound* ", Eds. Weissberger, A.; Taylor, E. C.; J. Wiely and Sons Inc. **1977** and references cited therein. Futhermore, the possibility of conjugate addition of pyridine to α,β-enones was suggested in the prepartion of 2-phenylselenylenones. Zima, G.; Liotta, D. *Synthetic Comm.* **1979**, *9*, 697.
3. ^{1}H-NMR(300MHz, $CDCl_3$, -50 °C) δ 0.27 (s, 9H), 1.82 (d, J=6.6Hz, 3H), 5.60 (d,d, J=7.1Hz, 15.2Hz, 1H), 6.53 (m, 1H), 6.79 (d, J=7.1Hz, 1H), 8.00-9.00 (m, 5H).
4. ^{1}H-NMR(300MHz, $CDCl_3$) δ 0.27 (m, 9H), 1.86 (d,d, J=2.9Hz, 6.8Hz, 3H), 5.09(cis) (d,d, J=5.5Hz, 7.3Hz, 0.2H), 5.36(trans) (d,d, J=9.0Hz, 11.7Hz, 0.8H), 5.64(cis) (m, 0.2H), 5.66(trans) (m, 0.8H), 6.96(cis) (d, J=1.3Hz, 0.2H), 7.01(trans) (d, J=11.7Hz, 0.8H), 8.00-9.00 (m, 5H).
5. ^{1}H-NMR(300MHz, d_8-THF) δ 0.18 (s, 9H), 1.04 (t, J=7.2Hz, 3H), 1.75 (d, J=6.8Hz, 3H), 2.18 (q, J=7.2Hz, 2H), 5.19 (d, J=7.7Hz, 1H), 5.77 (m, 1H), 8.10-9.00 (m, 5H).
6. Suzuki, M.; Kawagishi, T.; Noyori, R. *Tetrahedron Lett.* **1981**, *22*, 1809.
7. Murata, S.; Suzuki, M.; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 3248.
8. We thank KOSEF and OCRC for financial support.

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