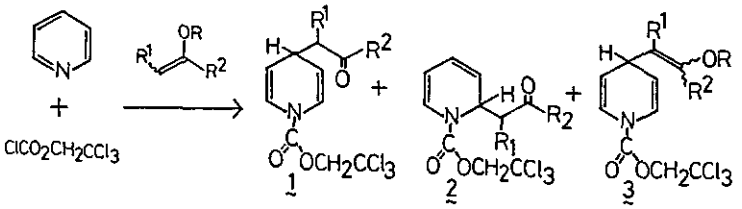
INTRODUCTION OF β-KETOALKYL GROUPS AT 4-POSITION OF PYRIDINE USING SILYL ENOL ETHERS

Kin-ya Akiba, Yoshihiro Nishihara, and Makoto Wada

Department of Chemistry, Faculty of Science, Hiroshima University

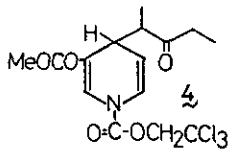
Higashisenda-machi, Hiroshima 730, Japan

Recently we reported three new methods to introduce alkyl and aryl substituents at 4-position of pyridine with better than 99% selectivity.[1] Here we describe further approach to this problem using silyl enol ethers in order to introduce β-keto alkyl groups at 4-position of pyridine with almost complete selectivity. When pyridine is quaternized with ethyl chloroformate in dichloromethane and trimethylsilyl enol ethers of acetone and acetophenone were added, the corresponding 1, 4- (1') and 1, 2-dihydropyridines (2') were obtained in 54, 37% and 69, 21% yields, respectively. The same type of reaction was carried out using β, β, β-trichloroethyl chloroformate as quaternizing reagent to give better yields and almost complete regioselectivity as shown below. When t-butyldimethylsilyl enol ether of acetophenone was used, 3 was obtained quantitatively and was converted to 1 in high yield. Furthermore, methyl nicotinate and trimethylsilyl enol ether of 3-pentanone gave 4 in 71% yield.



Entry	R	R^1	R^2	Solvent	Yield[a] (%) 1	2[b]	3
1	Me_3Si	Me	Ph	CH_3CN	quant.	0	0
2		Me	Et		83	0	0
3		$-(CH_2)_4-$			83	0	6
4		Ph	OMe		quant.	0	0
5		H	Ph		65	22	4
6	t-$BuMe_2Si$	H	Ph	CH_2Cl_2	trace		quant.

a) Isolated yield by flash column chromatography
b) Product ratio(1:2) was determined by ^{1}H-NMR



1. K. Akiba, H. Matsuoka, and M. Wada, Tetrahedron Lett., 22, 4093 (1981); K. Akiba, Y. Iseki, and M. Wada, ibid., 23, 429 (1982); ibid., 23, 3935 (1982).