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A NEW METHOD FOR THE DIRECT INTRODUCTION OF ALKOXYL GROUP TO SILYL ENOL ETHER WITH ALKYL HYPOCHLORITE CATALYZED BY PALLADIUM(0)

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α-Alkoxyketones and α-ketoacetals are prepared in good yields from silyl enol ethers and alkyl hypochlorites catalyzed by tetrakis-(triphenylphosphine)palladium(0).

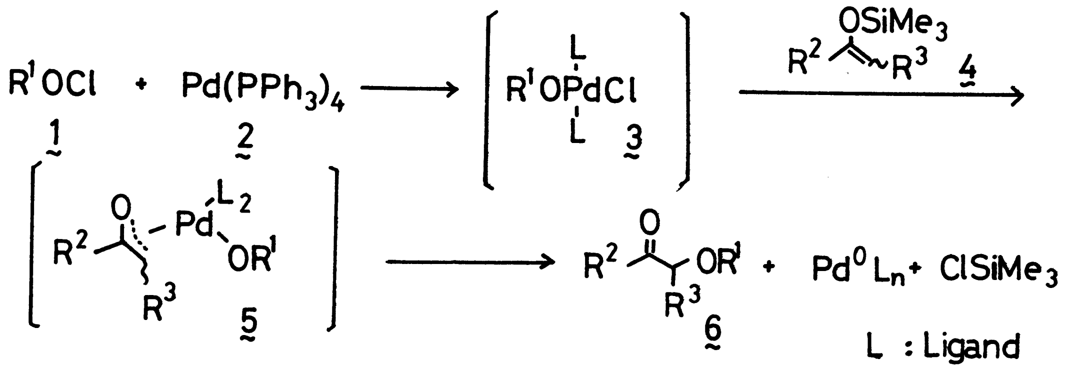
The oxidation reaction of carbonyl compounds to introduce hydroxyl group or its derivatives on carbon adjacent to carbonyl group is a very important process in organic synthesis, and several methods for the preparation of α-hydroxy1)2), α-trimethylsilyloxy2), and α-acyloxyketones4) are known. However, there is no report for the synthesis of α-alkoxyketones by direct oxidative alkoxylation of ketones or their derivatives.

Here we wish to describe a new and efficient method for the preparation of α-alkoxyketones by the reaction of silyl enol ethers5) with alkyl hypochlorites6) catalyzed by tetrakis(triphenylphosphine)palladium(0).

In general, silyl enol ethers react with electrophiles4), for example, halogens, acyl halides, or sulfenyl chlorides to give α-halo, α-acyl, or α-alkylthioketones, respectively. On the other hand, alkyl hypochlorites, polarized as $RO^{\delta-}-Cl^{\delta+}$, generally react with silyl enol ethers to give α-chloroketones.

It is expected that, in the presence of palladium(0), hypochlorite 1 initially reacts with palladium(0) 2 to give alkoxychloropalladium(II) 3 and this unstable intermediate would react with silyl enol ether 4 to form oxo-π-allylpalladium 5.8) Then alkoxyl group migrates to carbon to afford α-alkoxyketone 6 and palladium(0) as shown in Scheme 1.

Scheme 1



Indeed, successful results are obtained after screening conditions for the reaction of tert-butyl hypochlorite with silyl enol ether derived from acetophenone as a model and the results are shown in Table 1-3.

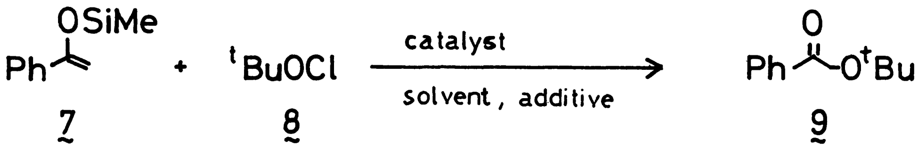


Table 1 Solvent effect

Solvent	Yield of 9(%)
Toluene	55
CH_2Cl_2	50
Et_2O	0

$Pd(PPh_3)_4$ was used as a a catalyst.

Table 2 Effect of catalyst

Catalyst	Yield of 9(%)
$Pd(PPh_3)_4$	55
$PdCl_2(PPh_3)_2$	0
$RhCl(PPh_3)_3$	20
$Ni(PPh_3)_4$	0

Toluene was used as a solvent.

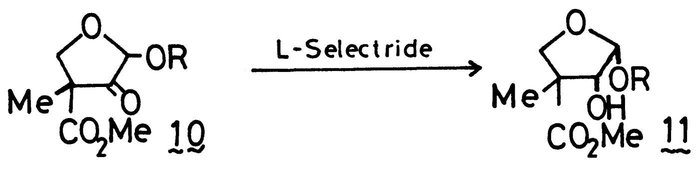
Table 3 Effect of additive

Additive	Yield of 9(%)
None	55
HgO	64
Bu_4NF	50

$Pd(PPh_3)_4$ as a catalyst and toluene as a solvent were used.

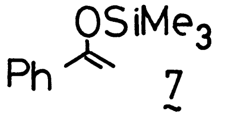
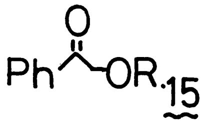
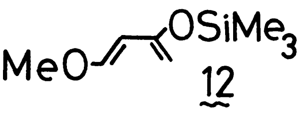
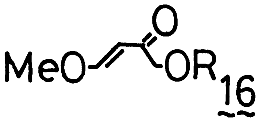
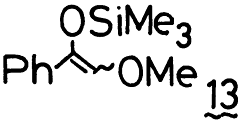
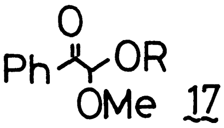
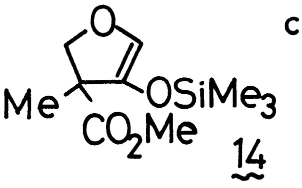
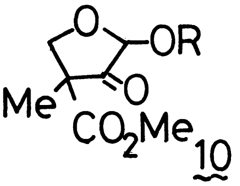
Typical procedure for the preparation of α-tert-butoxyacetophenone was as follows: Under an argon atmosphere, protecting from light, to a toluene (0.5ml) suspension of tetrakis(triphenylphosphine)palladium (0.02mmol) and mercuric oxide (yellow) (0.5mmol) was added dropwise 1-phenyl-1-trimethylsilyloxy ethylene (0.5mmol) in toluene (1 ml) at -78°C, and then was added tert-butyl hypochlorite (0.5mmol) in toluene (1 ml) and the reaction mixture was stirred for 1 hour at this temperature. To this reaction mixture, ether (10 ml) was added and insoluble materials were filtered off. After the removal of the solvents, the residue was purified by preparative TLC (CH_2Cl_2:hexane=1:2) to give α-tert-butoxyacetophenone (0.32mmol, 64%: bp 100°C/0.8mmHg, bulb to bulb distillation). Other results were summarized in Table 4.

It is noted that, according to the present method, α-alkoxyketones and α-ketoacetals are easily prepared in good yields from silyl enol ethers and alkyl hypochlorites and this method is applied to a new glycosidation reaction, that is, compound 10 was reduced by lithium tri-sec-butylborohydride in THF at -78°C to give 1,2-cis alcohol 11[9] stereoselectively as shown in Scheme 2.



Scheme 2

Table 4 Synthesis of α-alkoxyketones and α-ketoacetals

Silyl enol ether	ROCl	Product a)	Yield(%)
 7	^{t}Bu	 15	64
	^{i}Pr		56
 12 b)	^{t}Bu	 16	45
 13 c)	^{t}Bu	 17	85
 14 c)	^{t}Bu	 10	73 d)e)
	^{i}Pr		77 e)f)
	Et		88 e)f)
	$Cl(CH_2)_3$		82 e)f)
	cyclo-C_6H_{11}		89 e)g)

a) Satisfactory spectral and analytical data were obtained for all new compounds.

b) S. Danishefsky and T. Kitahara, J. Am. Chem. Soc., 96, 7807 (1974).

c) The method for the preparation of these silyl enol ethers is described in Ref. 4.

d) Only one isomer was detected by NMR spectrum.

e) The stereochemistry of these compounds was not determined.

f) Two isomers were obtained and the ratio was 3:1 by NMR analysis.

g) Two isomers were obtained and the ratio was 6:1 by NMR analysis.

References

1) A. J. Warning, "Comprehensive Organic Chemistry," ed. by J. F. Stoddart, Pergamon Press (1979), Vol. 1, pp 1065-1066.

2) G. M. Rubottom, M. A. Vazquez, and D. R. Pelegrina, Tetrahedron Lett., 1974, 4319, and references cited therein.

3) G. M. Rubottom, J. M. Gruber, R. K. Boeckman, Jr., M. Ramaiah, and J. B. Medwid, Tetrahedron Lett., 1978, 4603, and references cited therein.

4) G. M. Rubottom, R. C. Mott, and H. D. Juve, Jr., J. Org. Chem., 46, 2717 (1981), and references cited therein.

5) Silyl enol ethers 13 and 14 were prepared as follows; under an argon atmosphere, to a THF solution of LDA (1.05 equiv.) was added α-alkoxyketone (1.00 equiv.) in THF at -78°C. After 5 min, was added a THF solution of chlorotrimethylsilane (1.5 equiv.) and the resulting solution was stirred for 15 min, then was warmed to room temperature. After the removal of the solvents, silyl enol ether was distilled.
13; bp 120 °C/8 mmHg, NMR (CCl_4) $\delta = 0.10$(s.9H), 3.50(s.3H), 6.00(s,1H).7.1(m,5H).
14; bp 76 °C/0.1 mmHg, NMR (CCl_4) $\delta = 0.15$(s.9H), 1.32(s.3H), 3.65(s.3H), 3.80(d,1H, 8Hz), 4.50(d,1H,8Hz), 5.86(s.1H).

6) tert-Butyl and iso-propyl hypochlorite are prepared according to the known method, Org. Syn. Coll. Vol., 5, pp 184-187. Other alkyl hypochlorites were prepared as follows; to a aqueous solution of sodium hypochlorite, was added equimolar amount of acetic acid at 0°C and the resulting solution was shaked for 1 min. Then crushed ice and equimolar amount of corresponding alcohol in CH_2Cl_2 was added and the mixture was shaking vigorously for 2 min. The organic layer was separated and dried over molecular sieves (4A) at -40°C for 1 hour under argon. Prior to use, the concentration of alkyl hypochlorite was titrated by iodometry.

7) E. Negishi, "Organometallics in Organic Synthesis," John Wiley and Sons (1980), Vol. 1, pp 431-432.

8) Y. Ito, H. Aoyama, T. Hirao, A. Mochizuki, and T. Saegusa, J. Am. Chem. Soc., 101, 494 (1979). Y. Ito, T. Hirao, and T. Saegusa, J. Org. Chem., 43, 1011 (1978).

9) Coupling constants $J_{1,2}$ of 11 and its O-benzoylated product are 4.5 Hz (R=^{t}Bu, and ^{i}Pr). Fletcher et al. reported that coupling constants $J_{1,2}$ of pentofuranose derivatives are 4.3-4.6 Hz for 1,2-cis and $<$1.5 Hz for 1,2-trans: J. D. Stevens and H. G. Fletcher, Jr., J. Org. Chem., 33, 1799 (1968).

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