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Oxygenation of Silyl Enol Ethers and Silyl Ketene Acetals with Molecular Oxygen and Aldehyde Catalyzed by Nickel(II) Complex. A Convenient Method for the Preparation of α-Hydroxy Carbonyl Compounds

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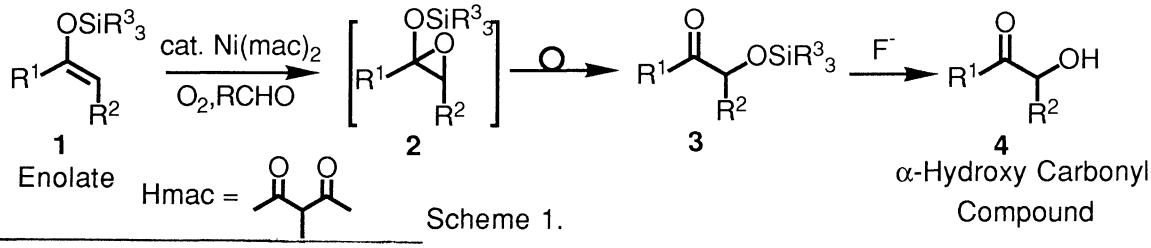
In the presence of a catalytic amount of nickel(II) complex, silyl enol ethers and silyl ketene acetals are smoothly oxygenated by the combined use of molecular oxygen and aldehyde to afford α-siloxy carbonyl compounds *via* possible intermediates, siloxy epoxides. And on treatment of the α-siloxy carbonyl compounds with potassium fluoride α-hydroxy carbonyl compounds are obtained in good to high yields.

One oxygen transfer from molecular oxygen into organic compounds to form the mono-oxygenated compounds is one of the important synthetic methods. It was already reported from our laboratory that nickel(II) complexes coordinated by 1,3-diketones have a notable catalytic activity for monooxygenation of olefins into the corresponding epoxides by the combined use of molecular oxygen (as a safe, inexpensive and the most available **oxidant**) and aldehyde (**reductant**).[1)]

α-Hydroxy carbonyl compounds are the potential intermediates for the synthesis of various natural products including sugars, β-hydroxy-α-amino acids,[2)] and biologically active compounds. For the preparation of these compounds, monooxygenation of enolates could be accounted for the reasonable synthetic route, therefore, many kinds of oxygenation methods have been reported; for example, *m*CPBA in the presence of bases,[3)] triphenylphosphineozonide,[4)] CrO_2Cl_2,[5)] OsO_4/*N*-methylmorphorine *N*-oxide,[6)] PhIO/BF_3-Et_2O,[7)] 2-sulfonyloxazilidine,[8)] dimethyldioxirane,[9)] or $Pd(PPh_3)_4$/*t*-BuOCl.[10)]

In this communication, we would like to describe a novel and convenient monooxygenation method for the preparation of α-hydroxy carbonyl compounds **4**. By the oxygenation of enolates **1** (silyl enol ethers or silyl ketene acetals) with the combined use of molecular oxygen and aldehyde in the presence of nickel(II) complex, α-siloxy carbonyl compounds **3** were obtained *via* possible silyl rearrangement[3)] of siloxy epoxides **2**. And α-hydroxy carbonyl compounds **4** were obtained in good to high yields by successive desilylation of **3**



Scheme 1.

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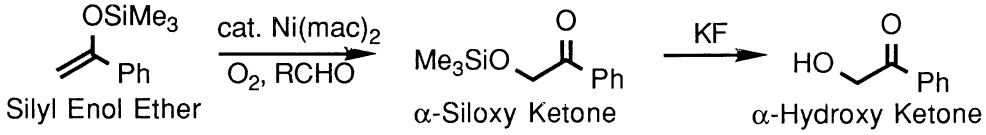
with potassium fluoride.

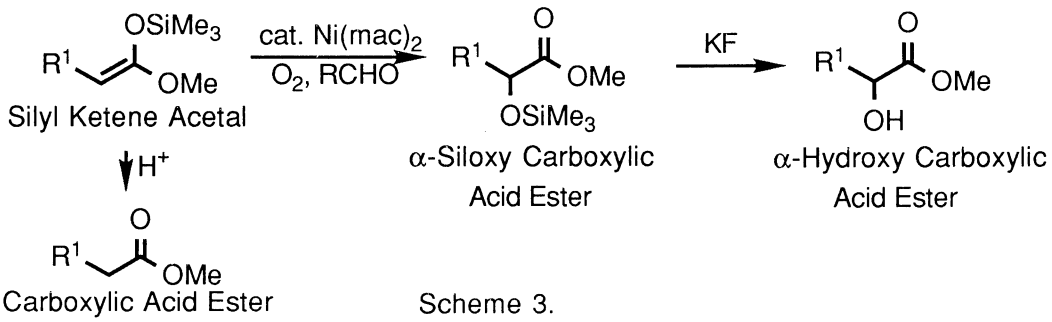
In the first place, oxygenation of acetophenone trimethylsilyl enol ether was tried in the presence of isobutyraldehyde (6 equiv.) and a catalytic amount of bis(3-methyl-2,4-pentanedionato)nickel(II) ($Ni(mac)_2$)[11] in 1,2-dichloroethane (EDC) under an atmospheric pressure of oxygen at room temperature. After 6 h, trimethylsilyl enol ether was completely consumed and purification by column chromatography afforded α-siloxy ketone, 2-trimethylsiloxyacetophenone, along with α-hydroxy ketone, 2-hydroxyacetophenone, in 60% and 25% yields, respectively. Successive treatment of α-siloxy ketone with potassium fluoride gave 2-hydroxyacetophenone (Scheme 2).



Scheme 2.

The present procedure was applied to several trimethylsilyl enol ethers and, in all cases, the corresponding α-hydroxy ketones were obtained in good yields (see Entries 1-3 in Table 1).

Next, oxygenation of trimethylsilyl ketene acetal of methyl undecanoate was tried under similar reaction conditions. Successive treatment of the oxygenated products with potassium fluoride afforded α-hydroxy carboxylic acid ester, methyl 2-hydroxyundecanoate, in 70% yield along with methyl undecanoate in 19% yield (see Entry 4 in Table 1). In the present oxygenation, it was confirmed that aldehyde (**reductant**) accepted one oxygen to form the corresponding carboxylic acid which would cause the decomposition of silyl ketene acetals to yield the carboxylic acid ester, methyl undecanoate (Scheme 3).

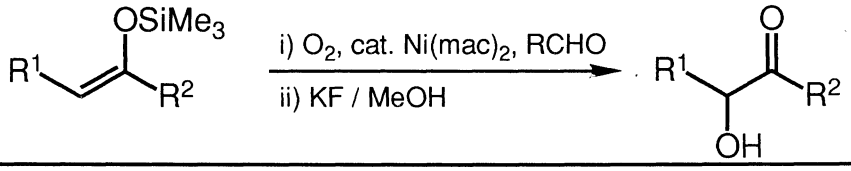


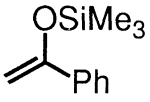
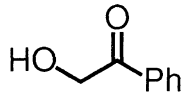
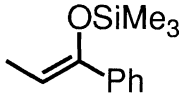
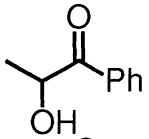
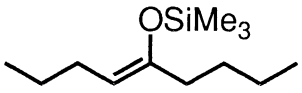
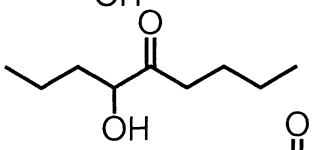
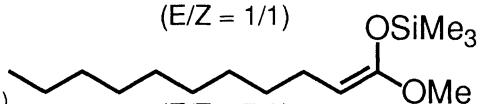
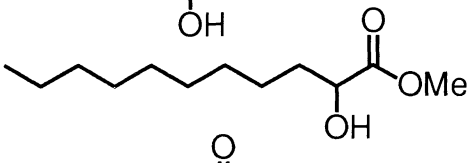
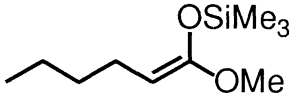
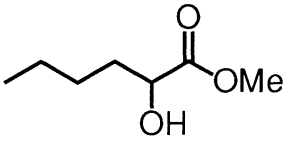
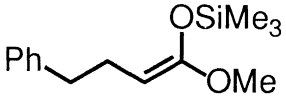
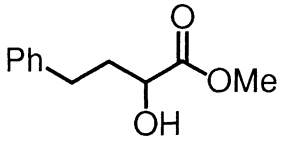
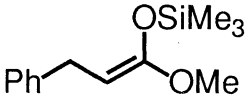
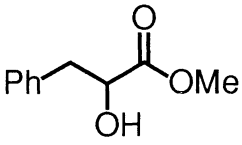
Scheme 3.

In order to suppress the undesirable decomposition of starting silyl ketene acetals, oxygenation was carried out in the coexistence of equimolar amount of silylating reagent (*N*-methyl-*N*-trimethylsilylacetamide) against aldehyde in expectation that carboxylic acid would be trapped as the corresponding trimethylsilyl ester. As shown in Entry 5, yield of methyl 2-hydroxyundecanoate was improved up to 88% and formation of methyl undecanoate was decreased down to 5%. The above procedure was applied to several silyl ketene acetals and it was found that, in the coexistence of *N*-methyl-*N*-trimethylsilylacetamide (Entries 5, 7 and 8) or *N*-methyl-*N*-trimethylsilyltrifluoroacetamide (Entry 6), all the silyl ketene actals afforded the corresponding α-hydroxy carboxylic acid esters in good to high yields.

Based on these results, it is clear that the oxygenation of enolates and the decomposition of starting enolates take place competitively, therefore, the yields of oxygenated products were improved by eliminating the influence of carboxylic acids. Thus, oxygenation of *t*-butyldimethylsilyl (TBDMS) enol ethers which are expected to be more stable under acidic conditions than trimethylsilyl enol ethers was carried out without using

Table 1. Synthesis of α-Hydroxy Carbonyl Compounds[a)]



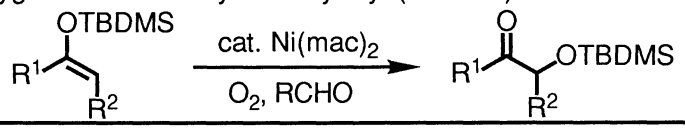
Entry	Enolate	Time /h	α-Hydroxy carbonyl compound	Yield /%[b)]
1		6		76[c)]
2		6		75[c)]
3	 (E/Z = 1/1)	6		79[c)]
4[e)]	 (E/Z = 7/3)	13		70[d)]
5[e,f)]		13		88[d)]
6[e,g)]	 (E/Z = 7/3)	13		78[d)]
7[e,f)]	 (E/Z = 7/3)	13		82[c)]
8[e,f,h)]	 (E/Z = 2/1)	13		77[d)]

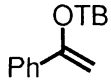
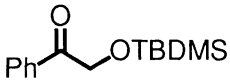
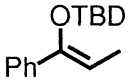
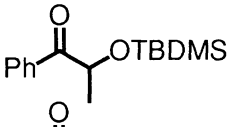
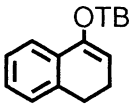
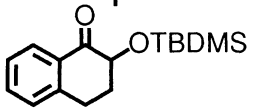
a) Reaction conditions: Enolate 1.0 mmol, $Ni(mac)_2$ 0.016 mmol (1.6 mol%), isobutyraldehyde 6.0 mmol, 1,2-dichloroethane (DCE) 5.0 ml, r.t., 1 atm O_2. b) Yield was caluculated based on starting enolate. c) Isolated yield. d) GC yield. e) Ethyl acetate (5.0 ml) was used as a reaction solvent. f) *N*-methyl-*N*-trimethylsilylacetamide (6.0 mmol) was used. g) *N*-methyl-*N*-trimethylsilyltrifluoroacetamide (6.0 mmol) was used. h) 2-Ethylbutyraldehyde (6.0 mmol) was used instead of isobutyraldehyde.

any silylating reagent (see Table 2). In the case of TBDMS enol ether of acetophenone, propiophenone or 1-tetralone, the corresponding α-*t*-butyldimethylsiloxy ketone was obtained in 93%, 91%, or 82% yield, respectively (Entries 1-3).

A typical procedure for the synthesis of methyl 2-hydroxy-4-phenylbutanoate is described as follows; trimethylsilyl ketene acetal of methyl 4-phenylbutanoate[12)] (1.0 mmol), $Ni(mac)_2$ (0.016 mmol, 1.6 mol%), isobutyraldehyde (6.0 mmol) and *N*-methyl-*N*-trimethylsilylacetamide (6.0 mmol) in ethyl acetate (10.0 ml) were stirred under an atmospheric pressure of oxygen at room temperature for 13 h. Then, reaction mixture was poured into methanol solution of potassium fluoride and stirred at room temperature for 2 h. After desilylation the crude product was extracted with ether, and purified by column chromatography (*n*-hexane/ethyl

Table 2. Oxygenation of *t*-Butyldimethylsilyl (TBDMS) Enol Ethers[a)]



Entry	Silyl Enol Ether	Time /h	Product	Yield /%[b)]
1		4		93
2		6		91
3[c)]		8		82

a) Reaction conditions; TBDMS enol ether 1.0 mmol, $Ni(mac)_2$ 0.016 mmol (1.6 mol%), isobutyraldehyde 6.0 mmol, DCE 5.0 ml, r.t., 1 atm O_2. b) Isolated yield. c) Acetone (5.0 ml) was used as a solvent.

acetate) to afford methyl 2-hydroxy-4-phenylbutanoate (159 mg, 82% yield).

It is noted that, in the presence of a catalytic amount of $Ni(mac)_2$, silyl enol ethers or silyl ketene acetals are smoothly oxygenated by the combined use of molecular oxygen and aldehyde to yield α-siloxy carbonyl compounds. Successive desilylation affords α-hydroxy ketones or α-hydroxy carboxylic acid esters in good to high yields. Thus, the present nickel(II)-catalyzed monooxygenation procedure provides a convenient method for the preparation of α-hydroxy carbonyl compounds.

References

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