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Epoxidation of Olefinic Compounds with Combined Use of Molecular Oxygen and Propionaldehyde Diethyl Acetal Catalyzed by Cobalt(II) Complex. Efficient Method for the Preparation of Acid-sensitive Epoxides

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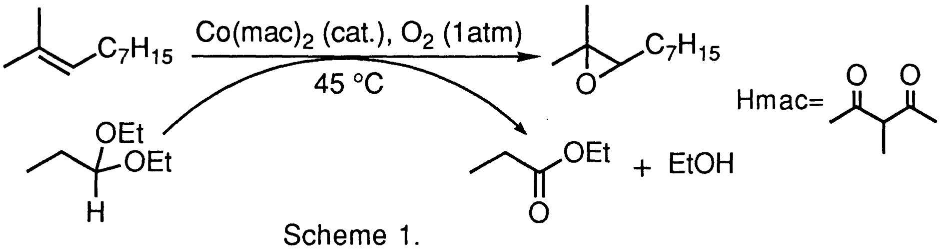
Synthesis of acid-sensitive epoxides such as epoxide of bishomoallyl alcohol or chromene oxide was achieved by the epoxidation of corresponding olefins with combined use of molecular oxygen and propionaldehyde diethyl acetal catalyzed by cobalt(II) complex. Various silyl enol ethers and silyl ketene acetals, acid-sensitive compounds, were also smoothly monooxygenated into the corresponding α-hydroxy carbonyl compounds.

Epoxidation of olefins is one of the most important reactions in organic synthesis because the formed epoxides, useful synthetic intermediates, can be regio- and stereoselectively converted into various oxygen-containing compounds.1) Peroxycarboxylic acids are often employed in the epoxidation of olefins as convenient oxidants,2a) and all possible efforts have been made to develop epoxidation of olefins under neutral conditions in order to avoid undesirable decomposition or rearrangement of the formed epoxides by the co-produced carboxylic acids.2b) On the other hand, vanadium catalyzed epoxidation of allylic alcohols with *tert*-butyl hydroperoxide was performed under acid-free conditions because only *tert*-butyl alcohol was its co-product.3) Recently, it was reported that dimethyldioxirane and its derivatives, prepared from corresponding ketones and potassium peroxymonosulfate, were also useful reagents for epoxidation because non-acidic compounds were formed along with the desired epoxides.4)

Our continuous study was focused on the development of a useful method for monooxygenation of olefinic compounds with combined use of molecular oxygen and a suitable reductant which would accept the other oxygen atom from molecular oxygen to perform the reaction. In our previous communication, it was



Scheme 1.

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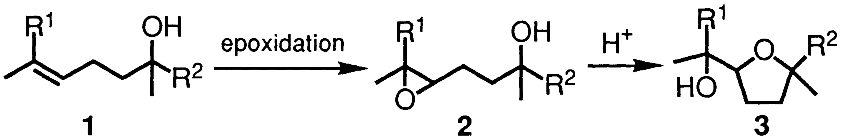
shown that when propionaldehyde diethyl acetal was employed as a reductant, aerobic epoxidation of trisubstituted olefins smoothly proceeded to afford the corresponding epoxides in good to high yields using cobalt(II) complex catalyst. Since the acetal was converted into the non-acidic compounds, corresponding ester and alcohol, the above epoxidation proceeded under neutral conditions (Scheme 1).(5) In this communication, we would like to describe the practical procedure for the synthesis of acid-sensitive epoxides by using molecular oxygen and propionaldehyde diethyl acetal catalyzed by cobalt(II) complex. The epoxidation method was also applied to oxygenation of silyl enol ether and silyl ketene acetal which are sensitive to acid.

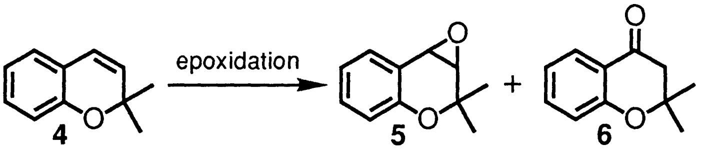
It was reported that when the epoxidation of bishomoallyl alcohol **1** was carried out by using *m*-chloroperbenzoic acid (*m*CPBA) as an oxidant, 2-(hydroxymethyl)tetrahydrofuran **3** was obtained in 84% yield as a major product *via* acid-catalyzed intramolecular cyclization of initially formed epoxide **2**.(6a) On the other hand, it was found by the present experiment that aerobic oxygenation of bishomoallyl alcohol **1** with propionaldehyde diethyl acetal in the presence of Co(mac)$_2$ catalyst afforded the corresponding epoxide **2** in 76% yield without accompanying any cyclized products (Scheme 2).(6b)



	1 → **2**	**3**
O$_2$, Acetal, Co(mac)$_2$ (cat.)	76%	0%
*m*CPBA	0%	84%

Scheme 2.

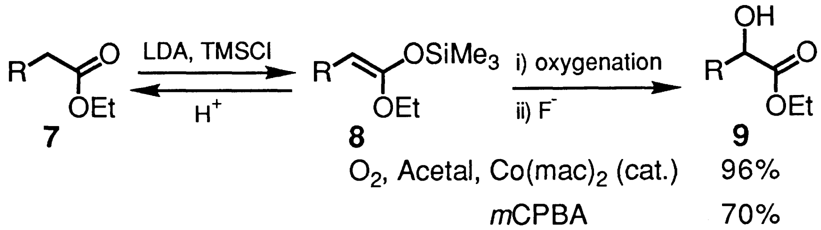
Since much interest has been recently focused on 3,4-epoxy-2,2-dimethylchromane derivatives which have cytotoxic activity, oxygenation of 2,2-dimethylchromene (**4**) was tried. In spite of all efforts to synthesize the chromene oxide, the conventional preparative method with *m*CPBA was not suitable for this purpose.(7a) When *m*CPBA was employed even under buffered conditions by sodium hydrogen carbonate, the corresponding epoxide **5** was obtained in 46% yield along with ketone **6** (33% yield). Whereas chromene oxide **5** was obtained selectively in 77% yield without accompanying ketone **6** according to the present procedure (Scheme 3).(7b)



	5	**6**
O$_2$, Acetal, Co(mac)$_2$ (cat.)	77%	0%
*m*CPBA	46%	33%

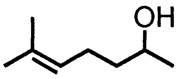
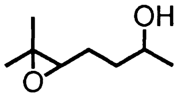
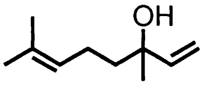
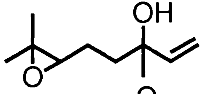
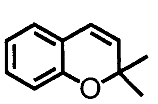
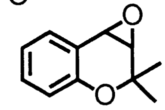
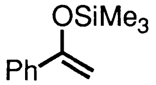
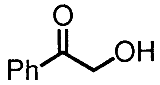
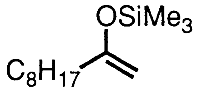
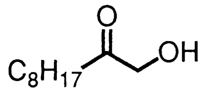
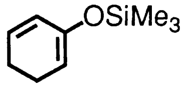
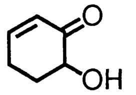
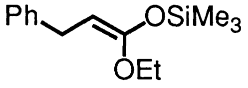
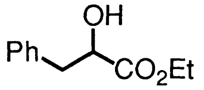
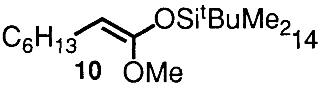
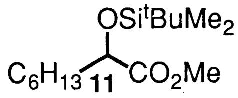
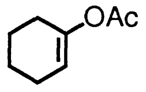
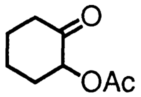
Scheme 3.

It was also expected that monooxygenation of silyl enol ethers or silyl ketene acetals, derived from the corresponding ketones or carboxylic acid esters respectively, and successive desilylation would afford α-hydroxy carbonyl compounds,(8a) useful intermediates for the synthesis of biologically active or natural products.(8b) Especially, silyl ketene acetal **8** is rather sensitive to the acidic compounds to form the starting carboxylic acid ester; for example, when *m*CPBA was employed as an oxidant in dichloromethane solution, desired α-hydroxy carboxylic ester **9** was not obtained at all. Only when *n*-hexane was used as a solvent, α-hydroxy carboxylic ester **9** was obtained in 70% yield.(8c) It was found by the present experiment that aerobic monooxygenation of silyl ketene acetal **8** smoothly proceeded to afford the corresponding α-hydroxy carbonyl compound **9** in 96%



Scheme 4.

Table 1. Synthesis of Acid-sensitive Epoxides and Oxygenation of Acid-sensitive Compounds[a)]

Entry	Olefinic Compound	Time /h	Product	Yield /%[b)]
1		8		76[c, d)]
2		8		78[c)]
3		11		77[c)]
4		9		83[e)]
5		10		77[e)]
6		10		87[e)]
7		10		96[e)]
8		14		95
9		14		89

a) Reaction conditions; substrate 3.2 mmol, propionaldehyde diehtyl acetal 20 ml, Co(mac)2 0.065 mmol (2 mol%), MS 4A 500 mg, 45 °C. b) Isolated yield. c) 2,6-Lutidine 1.28 mmol was used (Ref. 9), and purified by column chromatography on aluminum oxide. d) Diastereomer ratio 76:24. e) After the oxygenation, tetrabutylammonium fluoride treatment was carried out and yield was based on starting silyl enol ether or silyl ketene acetal.

yield, since decomposition of silyl ketene acetal **8** did not occur at all under neutral conditions (Scheme 4).

According to the present epoxidation, various acid-sensitive epoxides were successfully synthesized from bishomoallyl alcohols (Entries 1 and 2) and 2,2-dimethylchromene (Entry 3) in good yields. Silyl enol ethers or silyl ketene acetals were also smoothly oxygenated into the corresponding α-hydroxy ketones or α-hydroxy carboxylic acid esters in good to high yields (Entries 4, 5, 7, and 8). Similarly, α'-hydroxy-α,β-unsaturated ketone was selectively obtained in 87% yield from the silyl enol ether of α,β-unsaturated ketone which has two carbon-carbon double bonds (Entry 6)[8d)] and monooxygenation of enol ester such as 1-acetoxycyclohexene also proceeded easily to afford the corresponding acetate of α-hydroxy ketone in 89% yield (Entry 9).

A typical procedure for epoxidation of silyl ketene acetal (Entry 8 in Table 1) is described as follows; silyl ketene acetal **10** (847 mg, 3.1 mmol), Co(mac)$_2$ (18 mg, 0.063 mmol, 2.0 mol%) and Molecular Sieves 4A (500 mg) in propionaldehyde diethyl acetal (20 ml) was stirred at 45 °C under an atmospheric pressure of oxygen. After stirring for 10 h, solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel (Hexane/AcOEt=10/1) to afford the corresponding silyl ether of α-hydroxy carboxylic acid ester **11** (852 mg, 95% yield).

It is noted that, by the combined use of molecular oxygen and propionaldehyde diethyl acetal, various olefinic compounds are smoothly converted into the monooxygenated products under neutral conditions by using Co(mac)$_2$ catalyst. Thus, the present aerobic procedure provides an effective method for the preparation of acid-sensitive epoxides.

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9) When bishomoallyl alcohol shown in Entry 1 was oxygenated in the absence of 2,6-lutidine, the corresponding epoxide was obtained in 52% yield without accompanying any cyclized products.

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