

Oxygenation of Tetrahydrofurans with Combined Use of Molecular Oxygen
and α -Diketone Catalyzed by Cobalt(III) ComplexEiichiro HATA, Toshihiro TAKAI, and Teruaki MUKAIYAMA[†]Basic Research Laboratories for Organic Synthesis, Mitsui Petrochemical Industries, Ltd.,
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In the presence of a catalytic amount of cobalt(III) complex such as tris(acetylacetonato)cobalt(III), tetrahydrofurans are oxygenated into the corresponding γ -butyrolactones under mild conditions on treatment with an atmospheric pressure of molecular oxygen and α -diketones having hydrogen atom next to the carbonyl carbon.

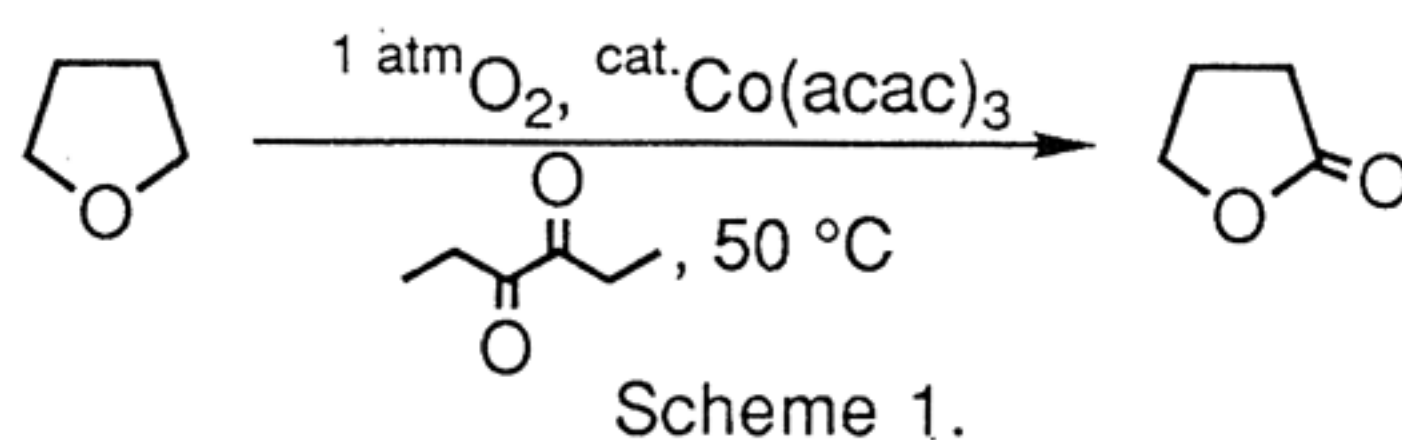
Lactones are one of the most important oxygen-containing compounds in organic chemistry, and many research works have been done to develop practical preparative methods of lactones, for example, the Baeyer-Villiger type oxidation of cyclic ketones with organic peracids¹⁾ or even with molecular oxygen.²⁾

Monooxygenation of cyclic ethers is also considered as a promising route to yield the corresponding lactones. Actually, prostaglandins are successfully synthesized by the oxidation of cyclic ethers.³⁾ Concerning preparative procedure of lactones, stoichiometric amount of metal oxide such as RuO_4 ,^{4a)} ZnCr_2O_7 ,^{4b)} or $\text{Zn}(\text{MnO}_4)_2$ ^{4c)} is conventionally employed as an oxidation agent. Catalytic amount of RuO_4 ^{4d)} or $\text{RuCl}_2(\text{Me}_2\text{SO})_4$ complex^{4e)} also promotes the above oxidation reaction in the presence of NaIO_4 or LiClO , respectively. On the other hand, molecular oxygen, safe and clean oxidant, was utilized in the oxygenation of benzyl ethers into the corresponding benzoate esters catalyzed by cobalt(II) chloride, while oxidation of aliphatic cyclic ethers still remains some difficult problems because C-C bond cleavage of carbon skeleton competitively took place to result in the formation of formate acetals as major products.^{5a)} Recently, aerobic oxygenation of tetrahydrofuran in the presence of carbon dioxide catalyzed by rhodium(I) complex^{5b)} or iron(II) chloride^{5c)} was reported.

In previous papers, aerobic monooxygenation reactions of olefins in the presence of an organic reducing agent catalyzed by transition metal complexes were reported. For example, by the combined use of molecular oxygen and secondary alcohols such as 2-propanol, various olefins were smoothly oxygenated into the corresponding alcohols, hydrated products, by using bis(1,3-diketonato)cobalt(II) complexes under neutral conditions.⁶⁾ When aldehydes were employed as reductants, the corresponding epoxides were also effectively prepared by oxygenation of olefins catalyzed with bis(1,3-diketonato)nickel(II) complexes^{7a)} or tris(1,3-diketonato)iron(III) complexes^{7b)} under an atmospheric pressure of molecular oxygen at room temperature. Recently, cyclic ketones^{8a)} or acetals of aldehydes^{8b)} were successfully employed as reductants in aerobic

epoxidation of olefins by employing cobalt(II)-Schiff base complexes or bis(1,3-diketonato)cobalt(II) complexes as catalysts, respectively. In these reactions, reductants behaved as acceptors of one oxygen atom of molecular oxygen to promote the introduction of the other oxygen atom into the olefins. Considering these results, choice of suitable combination of organic reductant and transition metal catalyst would be crucial in developing the selective aerobic oxygenation reaction. During our continuous study to find a new reductant, it was shown that α -diketones gave rather good results, however, some limitations remain in their utilization in aerobic oxidation reaction because α -diketones themselves are generally oxidized easily.

In this communication, we would like to describe a synthetic method for the preparation of γ -butyrolactones by oxygenation of tetrahydrofurans with combined use of an atmospheric pressure of molecular oxygen and α -diketones catalyzed by tris(1,3-diketonato)cobalt(III) complex (Scheme 1).



First, aerobic oxygenation of tetrahydrofuran was tried as a model reaction by using various α -diketones in the presence of a catalytic amount of tris(acetylacetonato)cobalt(III) ($\text{Co}(\text{acac})_3$). When reaction was carried out in 3,4-hexanedione, γ -butyrolactone was obtained in 60% yield (see Entry 1 in Table 1). γ -Butyrolactone was also yielded when 2,3-butanedione or 1-phenyl-1,2-propanedione was employed (Entries 2 and 3), while the desired lactone was not obtained at all in 2,2,5,5-tetramethyl-3,4-hexanedione (Entry 4) or in the absence of any α -diketone (Entry 5). These results indicated that γ -butyrolactone was obtained only when α -diketones having hydrogen atom next to the carbonyl carbon were employed. In the case of 3,4-hexanedione, the formation of propionic acid and propionic anhydride was observed along with the consumption of 3,4-hexanedione and the conversion of tetrahydrofuran into γ -butyrolactone. It was already reported that aerobic oxygenation of α -diketones afforded the corresponding carboxylic acids or carboxylic anhydrides *via* C-C bond cleavage between two carbonyl carbons.⁹⁾ Thus, it is reasonable to assume that α -diketone behaves as a reductant to accept one oxygen atom of molecular oxygen during the above oxygenation of tetrahydrofuran, however, details are now

Table 1. Aerobic Oxygenation of Tetrahydrofuran Using Various α -Diketones^{a)}

Entry	α -Diketone R^1 R^2		Conversion /% ^{b)}	Yield /% ^{b)}
1	$-\text{CH}_2\text{CH}_3$	$-\text{CH}_2\text{CH}_3$	100	60
2	$-\text{CH}_3$	$-\text{CH}_3$	70	37
3	$-\text{CH}_3$	$-\text{Ph}$	37	7
4	$-\text{C}(\text{CH}_3)_3$	$-\text{C}(\text{CH}_3)_3$	39	0
5 ^{c)}	none		29	0

a) Reaction conditions; tetrahydrofuran 3 mmol, α -diketone 2 ml, $\text{Co}(\text{acac})_3$ 0.35 mol%, 50 °C, 1 atm O_2 , 6 h. b) Determined by GC analysis. c) Benzene (2 ml) was used as a solvent.

Table 2. Aerobic Oxygenation of Tetrahydrofuran Using Various Catalysts^{a)}

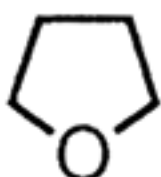
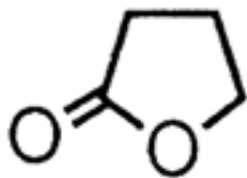
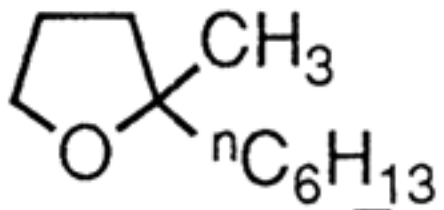
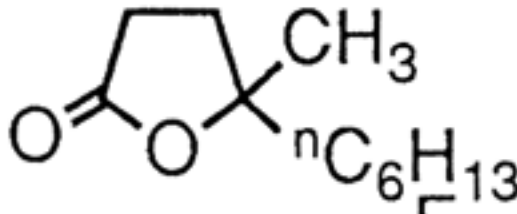
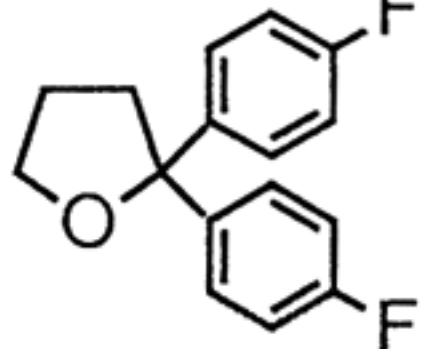
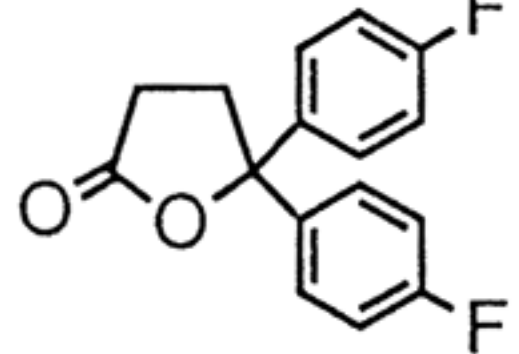
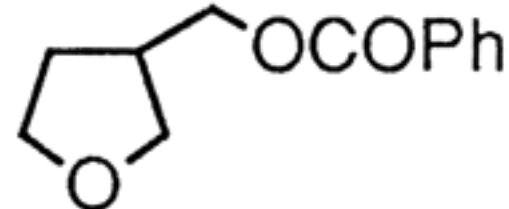
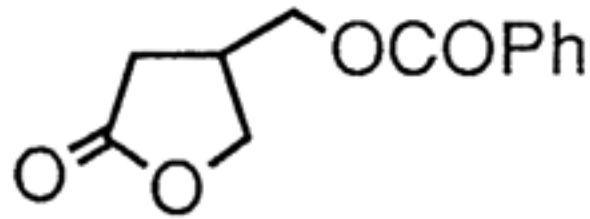
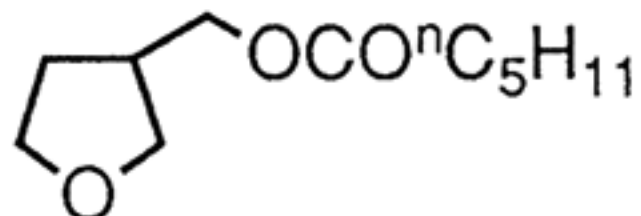
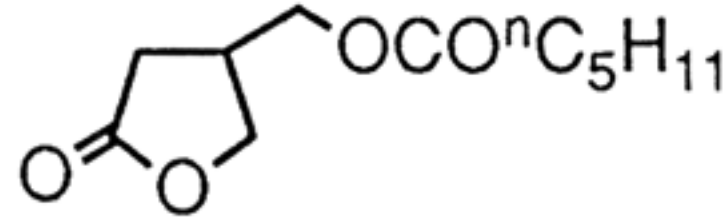
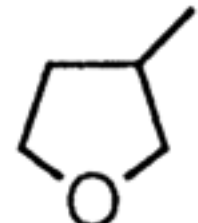
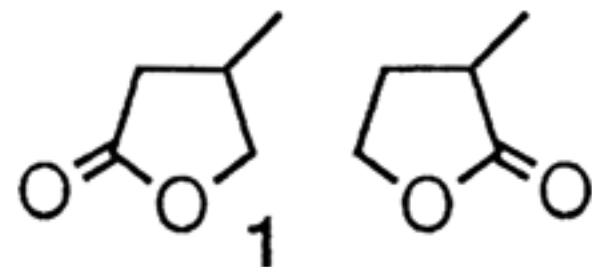
Entry	M(acac) _n	Conversion /% ^{b)}	Yield /% ^{b)}
1 ^{c)}	Co(III)(acac) ₃	100	60
2	Co(II)(acac) ₂	63	40
3	Fe(III)(acac) ₃	30	10
4	Ni(II)(acac) ₂	28	6

a) Reaction conditions; tetrahydrofuran 3 mmol, 3,4-hexanedione 2 ml, catalyst 0.7 mol%, 50 °C, 1 atm O₂, 6 h. b) Determined by GC analysis. c) Catalyst 0.35 mol%.

under investigation.

Next, various metal complexes were examined in the oxygenation of tetrahydrofuran using 3,4-hexanedione as an α -diketone. As shown in Table 2, it was found that cobalt complex, particularly cobalt(III) complex was the suitable catalyst to afford γ -butyrolactone in 60% yield (Entry 1), but iron(III) and nickel(II) complexes were not effective in the present reaction (Entries 3 and 4). The above procedure was successfully applied to various tetrahydrofurans as shown in Table 3. 2-Hexyl-2-methyltetrahydrofuran afforded the corresponding γ -butyrolactone in 76% yield (Entry 2). Tetrahydrofurans having benzoyloxymethyl or *n*-hexanoyloxymethyl group were also oxygenated into the corresponding γ -butyrolactones in 60% or 64% yield, respectively, without accompanying undesirable decomposition of ester groups (Entries 4 and 5). Single regio isomers were obtained by oxygenation of tetrahydrofurans having ester groups on 3-position as shown in Entries 4 and 5, while oxygenation of 3-methyltetrahydrofuran afforded two regio isomers (Entry 6). These results can

Table 3. Synthesis of Various γ -Butyrolactones^{a)}

Entry	Tetrahydrofurans	γ -Butyrolactones	Yield /%
1			60 ^{b)}
2			76 ^{c)}
3			54 ^{c)}
4			60 ^{c)}
5			64 ^{c)}
6			56 ^{b)} (1 : 2 = 59 : 41)

a) Reaction conditions; tetrahydrofuran derivative 3 mmol, 3,4-hexanedione 2 ml, Co(acac)₃ 0.35 mol%, 50 °C, 1 atm O₂. b) Determined by GC analysis. c) Isolated yield.

be explained by considering the possible steric repulsion between bulky ester groups and active oxidant. Oxygenation of cyclic ethers other than tetrahydrofurans also afforded the corresponding lactones, though both conversions of ethers and yields of lactones were not so high.¹⁰⁾

A typical procedure is described for the oxygenation of 2-hexyl-2-methyltetrahydrofuran; a mixture of 2-hexyl-2-methyltetrahydrofuran (510 mg, 3 mmol), 3,4-hexanedione (2 ml), and Co(III)(acac)₃ (3.7 mg, 0.010 mmol, 0.35 mol%) was stirred at 50 °C under an atmospheric pressure of oxygen for 6 h. Then solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel (hexane / ethyl acetate = 5 / 1) to afford tetrahydro-5-hexyl-5-methylfuran-2-one (420 mg, 76% yield).

It is noted that, in the presence of a catalytic amount of tris(acetylacetonato)cobalt(III) complex, tetrahydrofurans are monooxygenated into the corresponding lactones in fairly good yields by combined use of molecular oxygen and α -diketones under mild conditions.

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- 10) According to the present procedure, isochroman was converted into the corresponding lactone, 1-isocromanone, in 66% yield.