Synthesis of γ-Hydroperoxy-α,β-unsaturated Carbonyl Compounds from α,β,γ,δ-Unsaturated Carbonyl Compounds by Cobalt(II) Porphyrin-catalysed Hydroperoxygenation

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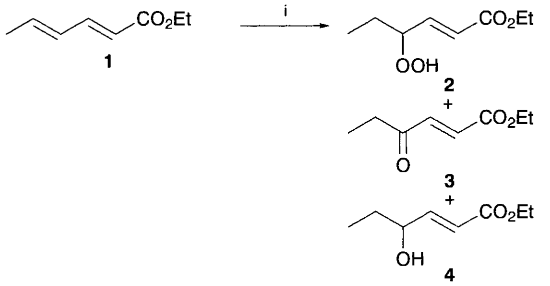
γ-Hydroperoxy-α,β-unsaturated carbonyl compounds are prepared in good yields by the regioselective hydroperoxygenation of α,β,γ,δ-unsaturated carbonyl compounds with molecular oxygen and triethylsilane in the presence of cobalt(II) porphyrin as a catalyst.

Alkyl hydroperoxides have been prepared by various methods.[1] Recently, Dussault and coworker(s) reported an efficient method for the preparation of unsaturated hydroperoxides *via* Wittig or Horner–Emmons olefination of peroxy-substituted aldehydes which are obtained by photochemical oxygenation of dec-5-ene or lipoxygenase-catalysed aerobic oxygenation of linoleic acid followed by acetal protection and ozonolysis.[2,3] However, the olefins used therein are limited to symmetrical olefins in the chemical method and naturally occurring unsaturated fatty acids in the enzymatic method. Therefore, more general methods are desirable for the preparation of the unsaturated hydroperoxides.

We have previously reported that conjugated olefins are oxidized to the corresponding ketones with oxygen and triethylsilane in the presence of [5,10,15,20-tetrakis(2,6-dichlorophenyl)porphinato]cobalt(II) complex [$\mathrm{Co^{II}}$(tdcpp)] as a catalyst followed by treatment with acetic anhydride and 4-(*N*,*N*-dimethylamino)pyridine (dmap), and the unstable hydroperoxide is considered to be formed as an intermediate of this reaction.[4–6] We herein report a successful attempt to isolate the unstable hydroperoxide under appropriate conditions.

In order to examine the effect of reductant, the reaction of ethyl (2*E*,4*E*)octa-2,4-dienoate **1** with 1 atm of oxygen and 1.2 equiv. of substituted silane in the presence of 0.001 equiv. of [$\mathrm{Co^{II}}$(tdcpp)]† in dichloromethane–propan-2-ol (1 : 1) was carried out at 28 °C for 40 min followed by evaporation *in vacuo* at room temperature, and then the mixture was fractionated by flash column chromatography (Scheme 1); the reaction mixture needed to be post-treated as rapidly as possible after the completion of the reaction because the ketone **3** was produced increasingly by degradation of the hydroperoxide **2** under the reaction conditions. The results are summarized in Table 1. The hydroperoxygenation of **1** proceeded smoothly for triethylsilane, ethoxydimethylsilane, methylphenylsilane and *n*-hexylsilane, to give **2** as a major product. However, over-reduction of **2** into the corresponding alcohol **4** was observed for phenylsilane. When using triethoxysilane and triphenylsilane, the reaction did not take place due to their weak reducibility. Triethylsilane was found to be the most effective among the silanes used in formation of hydroperoxide **2**.



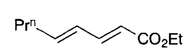
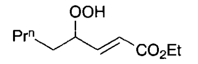
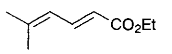
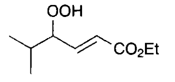
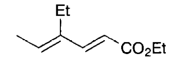
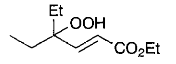
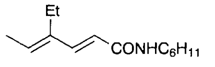
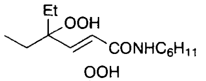
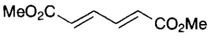
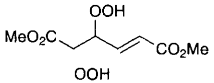
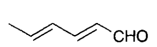
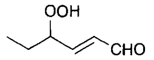
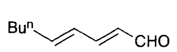
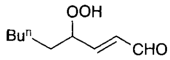
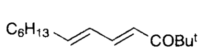
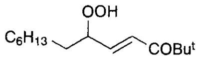
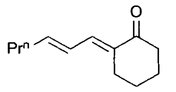
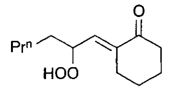
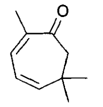
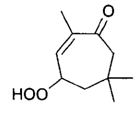
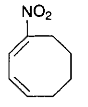
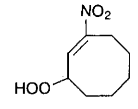
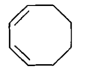
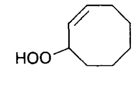
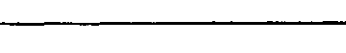
Scheme 1 *Reagents and conditions*: i, [$\mathrm{Co^{II}}$(tdcpp)] (0.001 equiv.), substituted silane (1.2 equiv.), O_2 (1 atm), CH_2Cl_2–Pr^iOH (1 : 1), 28 °C, 40 min

Table 1 Effect of substituted silane on the hydroperoxygenation of ethyl (2*E*,4*E*)hexa-2,4-dienoate **1**

	Isolated yield (%)		
Substituted silane	**2**	**3**	**4**
Et_3SiH	76.4	Trace	0
$Me_2(EtO)SiH$	55.6	22.0	0
$MePhSiH_2$	68.8	6.8	0
$C_6H_{13}SiH_3$	64.5	19.7	0
$PhSiH_3$	13.7	22.0	35.3
$(EtO)_3SiH$	No reaction		
Ph_3SiH	No reaction		

The procedure of hydroperoxygenation using triethylsilane as the reductant‡ was successfully applied to various substituted dienes as shown in Table 2. Both dienoic esters and amide gave

Table 2 Hydroperoxygenation of substituted dienes[a]

Entry	Diene	*t* / h	Product	Yield (%)
1		1		68
2		1		70
3		2		74
4		2		90
5[b]		3		65
6		1.5		49
7		1.5		54
8		1		55
9		1		61
10		0.5		67
11		1		50
12		1		92
13		2	Inseparable mixture	

[a] *Conditions*: diene (1 mmol), [$\mathrm{Co^{II}}$(tdcpp)] (0.001 equiv.), O_2 (1 atm), Et_3SiH (1.1 equiv.), CH_2Cl_2– Pr^iOH (5 cm^3, 1 : 1), 28 °C. [b] 0.005 equiv. of [$\mathrm{Co^{II}}$(tdcpp)] were used.

γ-hydroperoxy-α,β-unsaturated esters and amide in good yields independent of alkyl substituents (entries 1–4). For entry 5, an increase of [Co^{II}(tdcpp)] was required in order to accelerate the reaction. When dienals and dienones were employed as starting materials, the γ-hydroperoxy-α,β-unsaturated carbonyl compounds could be also obtained in moderate yields (entries 6–10). In addition, the reaction of 1-nitrocycloocta-1,3-diene was found to afford the corresponding hydroperoxide (entry 11). It is interesting to point out that the reaction conditions are mild enough to permit the presence of labile groups such as aldehyde, ketone and nitro groups on the substrates. The reaction of cycloocta-1,3-diene gave the allyl hydroperoxide in a high yield (entry 12), while that of 6-phenylhexa-1,3-diene resulted in an inseparable mixture of regioisomeric hydroperoxides (entry 13).§ These results suggest that the substitution of an electron-withdrawing group on the diene is important for γ-selective hydroperoxygenation. Although the reaction mechanism is not yet clear, it is assumed that a σ-alkylcobalt complex is initially generated from the α,β,γ,δ-unsaturated carbonyl compound, triethylsilane, and [Co^{II}(tdcpp)] followed by reaction with molecular oxygen, to produce the hydroperoxide.

It is noted that the present reaction provides a novel and general method for the preparation of unsaturated hydroperoxides from substituted dienes by using molecular oxygen and triethylsilane under neutral and very mild conditions.

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Footnotes

† [Co^{II}(tdcpp)] prepared from the corresponding porphyrin[7] obtained from cobalt(II) in dmf,[8] was used as the catalyst.

‡ *Typical experimental procedure*: A mixture of substituted diene (1.0 mmol), [Co^{II}(tdcpp)] (0.001 mmol), and triethylsilane (1.1 mmol) in 5 cm^3 of dichloromethane–propan-2-ol (1 : 1) was stirred at 28 °C under an oxygen atmosphere. The solvent was removed *in vacuo* at room temp. as soon as the diene was consumed completely as detected by thin layer chromatography. The residue was purified by flash column chromatography on silica gel BW-300 (Fuji-Silysia Chemical Ltd., Japan) using a mixture of hexane and ethyl acetate as eluent, to give the unsaturated hydroperoxide, which was identified by IR, ^{1}H and ^{13}C NMR spectra.

§ When the resultant mixture was treated with acetic anhydride and dmap in dichloromethane followed by chromatography on silica gel,[5] (3*E*)-6-phenylhex-3-en-2-one, (2*E*)-6-phenylhex-2-en-4-one, and (2*E*)-6-phenylhex-2-en-1-al were obtained in 37, 28 and 8% yields, respectively.

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