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A Facile Method for the Oxidation of Aldehydes to Carboxylic Acids via Acetal-type Diperoxides

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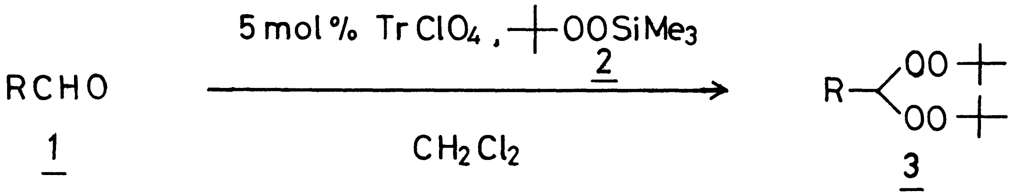
In the presence of a catalytic amount of trityl perchlorate, aldehydes smoothly react with *t*-butyl trimethylsilyl peroxide to give the acetal-type diperoxides in good yields. Treatment of these diperoxides with piperidine at 90 °C or the aqueous solution of $CuSO_4$ and L-ascorbic acid at room temperature gave the corresponding carboxylic acids in good yields.

The oxidation of aldehydes to carboxylic acids is one of important functional group interconversion reactions frequently employed in organic synthesis. Many methods have been reported concerning this reaction,1) however, the conventional methods generally required the oxidants containing hazardous or expensive heavy metals, such as $KMnO_4$, CrO_3, Ag_2O. Some methods are reported on the oxidation of aldehydes by the use of the oxidants free from heavy metals, for example, hydrogen peroxide,2) sodium chlorite,3) calcium hypochlorite.4) Since some of these reactions are applicable to the limited substrates, the novel and useful methods for the oxidation of aldehydes are still desired.

In the previous paper, it was reported that, in the presence of a catalytic amount of trityl perchlorate, dimethylacetals of aldehydes reacted with *t*-butyl trimethylsilyl peroxide to afford the acetal-type peroxides, and further treatment of the peroxides with piperidine in methanol at 60 °C gave the corresponding methyl esters in good yields.5) So we next tried the oxidation of free aldehydes, and in our continuous investigation, the oxidation of aldehydes to the corresponding carboxylic acids was achieved by the two-step procedure including (I) the addition of *t*-butyl trimethylsilyl peroxide to aldehydes catalyzed by trityl perchlorate and (II) the conversion of the acetal-type diperoxides to carboxylic acids.

First, we examined the reaction conditions for the addition of *t*-butyl trimethylsilyl peroxide (2) to aldehydes (1), and it was found that, in the presence of 5 mol% trityl perchlorate, the reaction proceeded smoothly in CH_2Cl_2 even at -78 °C to afford the acetal-type diperoxides (3) in good yields. The results are shown in Table 1.



Scheme 1.

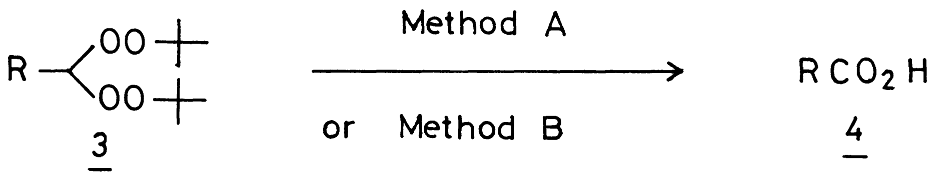
Table 1. The synthesis of acetal-type diperoxides[a)]

Entry	R-	Reaction conditions		Yield/%[b)]
		Temp/ °C	Time/h	
1	$PhCH_2CH_2$-	-45	0.15	95
2	Ph-	-78	12	88
3	$PhCH_2OCH_2CH_2$-	0	0.15	72
4	$CH_2=CH(CH_2)_8$-	-45	3	92
5	*o*-Br-C_6H_4-	-45	2.5	89
6	*p*-CH_3S-C_6H_4-	-78	12	78

a) Molar ratio of 1 : 2 is 1 : 3.

b) Isolated yields. All the products gave satisfactory spectral data (NMR and IR).

Next, the reaction conditions for the conversion of the diperoxides to the corresponding carboxylic acids were investigated, and it was found that the carboxylic acids (4) were obtained in good yields when the diperoxides (3) were heated with piperidine[6)] in water at 90 °C (Method A). Further investigation made it possible to convert the diperoxides to the carboxylic acids under milder conditions. That is, the diperoxides (3) were treated with the aqueous solution of $CuSO_4$ and L-ascorbic acid[7)] at room temperature, and the carboxylic acids (4) were obtained in good yields. Nearly the same results were obtained by the use of a catalytic amount of $CuSO_4$ in the above reaction (Method B). Based on this observation, the synthesis of the various carboxylic acids was tried and the results are summarized in Table 2. According to this method, the carboxylic acids with various functional groups, such as olefin, benzyl ether, halide, sulfide, are easily prepared under mild conditions (entries 3-6). And it is noted that the sulfide group, which is easily oxidized to sulfoxide by the conventional oxidation methods of aldehydes,[3)] was left intact under the reaction conditions.



Method A : piperidine / H_2O, 90 °C
Method B : $CuSO_4$, L-ascorbic acid / THF-H_2O, r.t.
Scheme 2.

Table 2. The synthesis of carboxylic acids

Entry	R-	Yield/% (Method A)[a]	Yield/% (Method B)[a]
1	$PhCH_2CH_2$-	88	77 (68)[b]
2	Ph-	76	99 (75)[b]
3	$PhCH_2OCH_2CH_2$-	80	52
4	$CH_2=CH(CH_2)_8$-	76	59[c]
5	*o*-Br-C_6H_4-	76	70
6	*p*-CH_3S-C_6H_4	78	88

a) Isolated yields. All the products gave satisfactory spectral data (NMR and IR data).

b) The reaction was carried out by the use of a catalytic amount of $CuSO_4$.

c) The reaction was carried out in THF-H_2O-HMPA (2:2:1).

A typical procedure is described for the oxidation reaction of 3-phenylpropanal; To a CH_2Cl_2 solution (2 ml) of trityl perchlorate (9 mg, 0.003 mmol) were added 3-phenylpropanal (67 mg, 0.5 mmol) and *t*-butyl trimethylsilyl peroxide (1.5 mmol)[8)] in CH_2Cl_2 (3 ml) at -45 °C (acetonitrile - dry ice bath) under argon atmosphere. The reaction mixture was stirred for 10 min, then quenched with pH 7 phosphate buffer. The organic materials were extracted with ether three times, and the combined extracts were washed with a saturated aqueous solution of NaCl and was dried over Na_2SO_4. The solvent was evaporated and the residue was purified by preparative TLC (silica gel) to afford 1,1-bis(*t*-butyldioxy)-3-phenylpropane (140 mg, 95% yield).

The methods for the synthesis of the carboxylic acid from the acetal-type diperoxide are as follows; (Method A) 1,1-Bis(*t*-butyldioxy)-3-phenylpropane (105 mg, 0.35 mmol) was dissolved in a mixture of piperidine (1 ml) and water (1 ml) and heated at 90 °C (bath temp) for 3 h. Then the reaction was quenched with 2 $mol \cdot dm^{-3}$ HCl. After stirring for 30 min, the organic materials were extracted with CH_2Cl_2 seven times, and the combined extracts were dried over Na_2SO_4. After evaporation of the solvent, the crude product was purified by preparative TLC (silica gel) to afford 3-phenylpropionic acid (47 mg, 88%). (Method B); To a THF solution (1 ml) of 1,1-bis(*t*-butyldioxy)-3-phenylpropane (76 mg, 0.26 mmol) was added a solution of $CuSO_4$ (59 mg, 0.37 mmol) and L-ascorbic acid (67 mg, 0.38 mmol) in water (1 ml) at room temperature, and the reaction mixture was stirred for 8 h. After the usual work-up, 3-phenylpropionic acid was obtained in 77% yield.

Thus, the addition of *t*-butyl trimethylsilyl peroxide to aldehydes was smoothly promoted by a catalytic amount of trityl perchlorate to afford the acetal-type diperoxides, and the acetal-type diperoxides were converted to the corresponding carboxylic acids in good yields under mild conditions. It is noted that the acetal-type diperoxides can be easily obtained according to the present reaction and it is expected that these interesting intermediates are applicable to various useful synthetic reactions. Further investigation is now in progress.

References

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7) It has been reported that the reactions of cupric salts with L-ascorbic acid in water generate the free radicals such as $O_2^{\bullet -}$ and $OH^{\bullet}$. For example, see for; J. M. C. Gutteridge and S. Wilkins, FEBS Lett., 137, 327 (1982). However, the application of these results to synthetic reactions was not made, and moreover the reactions of peroxides with cupric salts and L-ascorbic acid have been hitherto unknown.

8) *t*-Butyl trimethylsilyl peroxide was synthesized according to the procedure in Ref. 9 and was used as a stock solution in toluene (4.0 mol kg^{-1}).

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