

Syntheses and Crystalline Structures of Several Aldehyde Peroxides as New Flavor Compounds

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Bis(1,1'-hydroxyalkyl) peroxide, which is known as an important aroma constituent in citrus peel oil, can be easily prepared from the corresponding aldehyde by treating it with hydrogen peroxide; however, the α -substituted or α -unsaturated aldehyde is not oxidized to the peroxide dimer under the same conditions. The odor character of the aldehyde peroxide dimer is the same as that of the starting aldehyde, and on a gas chromatogram, it appears as 2 mol of the aldehyde. These results suggest that the peroxide dimer is easily decomposed to the corresponding aldehyde monomer in a dilute solution or by heating to show its characteristic aldehyde odor. On the other hand, the peroxide is very stable in the crystalline state. The contrast between the stability of the crystalline peroxide and its instability under gas chromatographic or dilute conditions has been explained from the crystalline structure estimated by an X-ray crystallographic analysis.

In a preceding paper (Kobayashi *et al.*, 1990), we demonstrated that bis(1,1'-hydroxyalkyl) peroxides are present in the essential oil of *Citrus iyo* and were flavor impact compounds for citrus fruit. In particular, bis(1,1'-hydroxydecyl) peroxide was the main component among the peroxides and showed a characteristic aroma the same as that of decanal, a flavor impact compound for citrus peel oil (Uchida *et al.*, 1983) giving the sweet aroma characteristic of *C. iyo*. The peroxide dimer was easily prepared by oxidizing decanal with hydrogen peroxide to form a very stable crystalline material; however, on the gas chromatogram, both the natural and synthetic compounds showed only one peak of decanal, and an organoleptic evaluation of the aqueous solution indicated that the aldehyde and peroxide had approximately the same threshold value ($5-9 \times 10^{-9}$ w/w in water) and odor character. This implies that, at a high temperature such as that used in gas chromatography or in the dilute water solution applied for sensory analyses, the peroxide decomposed to the corresponding aldehyde, and as far as the contribution to citrus flavor, the peroxide could be treated as 2 mol of aldehyde. On the other hand, synthesized bis(1,1'-hydroxydecyl) peroxide was a very stable crystalline product that could be applied as a new flavoring material because of its easy handling and long-term stability.

This paper describes the scope and limitation of simple hydrogen peroxide oxidation of some volatile aldehydes to the corresponding peroxides. The stability of the crystalline peroxide was confirmed from an X-ray crystallographic analysis of the structure of bis(1,1'-hydroxy-2,2'-phenylethyl) peroxide.

MATERIALS AND METHODS

Aldehydes. Hexanal, dodecanal, 2-phenylethanal, and citronellal were commercially available. (Z)-11-Hexadecanal was purchased from Shin-etsu Kagaku Co., Japan. As the starting materials for peroxide syntheses, all aldehydes were redistilled and their purity was checked by gas chromatography.

Oxidation to the Peroxide (General Method). Three milliliters of a 35% H_2O_2 water solution was added dropwise to

an ethereal solution (50 mL) of 0.02 mol of aldehyde with stirring at room temperature. Stirring was continued for 5 h, and the ethereal layer was separated, washed with 5% $NaHCO_3$ and water, and dried over $MgSO_4$. The filtrate was concentrated *in vacuo* at under 0 °C, and the solid residue was recrystallized from ethyl acetate. The yield was over 65% when the crystalline peroxide was obtained.

The aldehydes used for this oxidation and the identification method and melting point of the peroxides are summarized in Table I. An elemental analysis for the two typical peroxides is as follows. Bis(1,1'-hydroxydecanyl) peroxide: Found: C, 69.19; H, 12.18. Calcd for $C_{20}H_{42}O_4$: C, 69.32; H, 12.22 (%). Bis(1,1'-hydroxy-2,2'-phenylethyl) peroxide: Found: C, 69.30; H, 6.50. Calcd for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61 (%).

X-ray Crystal Structure Determination. Bis(1,1'-dihydroxy-2,2'-phenylethyl) peroxide was repeatedly recrystallized from ethyl acetate. Large platelike crystals were obtained at -20 °C from which a sample $0.5 \times 0.5 \times 0.2$ mm in size was placed on a Rigaku AFC-4 diffractometer with graphite-monochromatized $Cu K\alpha$ radiation. Systematic absences were $h + l = 2n + 1$ for $h00$ and $k = 2n + 1$ for $0k0$. The unit cell dimensions were obtained by the least-squares of 11 independent 2θ values ($42^\circ < 2\theta < 56^\circ$). Crystal data: $M_r = 274.32$, monoclinic, $P2_1/n$, $a = 31.061$ Å, $b = 8.838$ Å, $c = 5.332$ Å, $\beta = 93.77^\circ$, $V = 1460.56$ Å³, $Z = 4$, $d_x = 1.248$ g cm⁻³.

Intensity measurement was performed up to $2\theta = 125^\circ$ ($h = -37$ to 37 , $k = -11$ to 0 , $l = 0$ to 6) by using the $\omega - 2\theta$ scanning technique, with a scanning speed of 4° min⁻¹ for θ and a scanning width of $(1.0 + 0.15 \tan \theta)^\circ$. The background was measured 5 s before and after each scan. During data collection, two standard reflections ($15\ 1\ 0$, $-4\ -3\ -2$), which were monitored every 50 reflections, showed no significant variation in intensity. The data were corrected for Lorentz and polarization factors but not for absorption. Among the 2273 reflections collected, 1202 ($|F_o| > 3\sigma(|F_c|)$) were considered as observed and used for the structural determination.

The structure was solved by the direct method, using MULTAN78 and subsequent difference Fourier syntheses, and refined by full-matrix least-squares with anisotropic thermal parameters for the non-H atoms. All of the H atoms were located on difference Fourier maps and refined with isotropic thermal parameters. The weighting scheme at the final stage was $w = [\sigma^2(F_o) + 0.000696|F_o|^2]^{-1}$. The final R value became 0.095 for 1202 observed reflections ($R_w = 0.098$). No peaks higher than 0.3 e Å⁻³ were found on the final difference map, and the maximum Δ/σ was 0.30. The atomic scattering factors were taken from the *International Tables for X-ray Crystallography* (1974). Calculations were carried out on a HITAC M-680 computer at the Computer Center of the University of Tokyo.

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Table I. Peroxide Products Obtained by H₂O₂ Oxidation from Aldehydes

R of peroxide dimer R-CH(OH)OOCH(OH)-R	starting aldehyde	mp, °C	identification
CH ₃ (CH ₂) ₄ -	hexanal	59	IR, NMR, elem anal. ^a
CH ₃ (CH ₂) ₁₀ -	dodecanal	80	IR, NMR
CH ₃ (CH ₂) ₈ CH=CH(CH ₂) ₉ -	(Z)-11-hexadecanal	58	IR, NMR
C ₆ H ₅ CH ₂ -	2-phenylethanal	92	IR, NMR, elem anal. ^a
(CH ₃) ₂ C=CH(CH ₂) ₂ CH(CH ₃)CH ₂ -	citronellal	liq	IR, NMR

^a The results of elemental analyses are described in the text.

**Figure 1.** Preparation of aldehyde peroxide dimer.

Instrumental Analysis. Gas chromatographic conditions were as follows: column, 35 m × 0.25 mm (i.d.) PEG.20M chemically bonded fused silica WCOT type; carrier gas, N₂ at 1 mL/min; oven temperature, 100 or 150 °C isothermal; injection and detector temperature, 200 °C. Infrared (IR) spectra of the crystalline peroxide were measured as KBr pellets with a Jasco IRA-1 instrument. Proton magnetic resonance (¹H NMR) spectra were recorded on a JEOL JN-GX 270 (270 MHz) instrument. Each sample was dissolved in CDCl₃ with tetramethylsilane as an internal standard.

RESULTS AND DISCUSSION

Hydrogen Peroxide Oxidation. The oxidation of nonanal with hydrogen peroxide has been reported earlier (King, 1942); however, this reaction process had limited application because of the high concentration of hydrogen peroxide that was used (more than 90%). In the earlier stage of this experiment, we used hexane as a solvent for the heterogeneous reaction between the hydrogen peroxide water solution and aldehyde dissolved in an organic solvent to avoid peroxidation of the solvent; however, the yield of peroxide was higher when ether was used as a solvent, and no explosive decomposition of ether peroxide appeared while the ether was being distilled off under reduced pressure at below 0 °C. While a large amount of a sample could be applied, it is recommended to use other organic solvents resisting peroxidation of ethyl ether. The straight chain and β-phenyl-substituted aldehyde yields of the crystalline peroxide are shown in Table I; however, the α-substituted and α,β-unsaturated aldehydes were not oxidized under the same conditions and resulted in recovery of the starting aldehyde. On the other hand, if the double bond was situated far from the functional group, the same peroxide could be prepared as a stable crystalline product. Citronellal, methyl substituted at the β-position, was also oxidized to a peroxide but did not crystallize even at under -10 °C. These results suggest that the stable crystalline form might have resulted from the mutual interaction of the polar hydroxyperoxy functional group among the molecules. An α-substituted bulky structure prevents such an interaction, and the α,β-unsaturated bond is not rotated adjacent to the polar hydroxyperoxy group, resulting in an interruption to the stable crystalline structure. This hypothesis will be discussed later from the results of the X-ray crystallographic analysis.

Molecular Structure and Stability. All IR spectra of the peroxides showed their characteristic absorption bands at 3400 cm⁻¹ (ν_{OH}, s) and 870 cm⁻¹ (ν_{O-O}, s). In the NMR spectra of all aliphatic peroxides, peaks appeared at δ values of 0.85–0.90 (CH₃, t, *J* = 6.4–7.1), 1.26–1.63 (CH₂, m), and 5.20–5.24 (OCHO, t, *J* = 5.4–5.9). These data suggest a dimeric structure for the corresponding aldehyde peroxide, bis(1,1'-hydroxyalkyl) peroxide (Figure 1).

Table II. Selected Bond Distances and Angles for Bis(1,1'-hydroxy-2,2'-phenylethyl) Peroxide

bond distance, Å		angle, deg	
O(1)-O(2)	1.480(8)	O(2)-O(1)-C(1)	105.2(6)
O(1)-C(1)	1.411(11)	O(1)-O(2)-C(2)	106.6(6)
O(2)-C(2)	1.443(11)	O(1)-C(1)-C(3)	105.4(8)
O(3)-C(1)	1.391(12)	O(1)-C(1)-O(3)	110.9(8)
O(4)-C(2)	1.400(12)	O(3)-C(1)-C(3)	111.9(9)
C(2)-C(4)	1.453(16)	O(2)-C(2)-O(4)	108.7(7)
C(3)-C(1)	1.483(16)	O(2)-C(2)-C(4)	105.9(8)
		O(4)-C(2)-C(4)	112.1(9)
		C(5)-C(3)-C(1)	113.0(10)
		C(2)-C(4)-C(6)	112.2(9)

While the crystalline peroxides were very stable and can be preserved for years at room temperature, neither destruction of crystalline form nor hygroscopic feature was observed during preservation in a screw-cocked transparent glass bottle. On thin-layer chromatogram (silica gel, developed with hexane/ether 3:2), the main spot of a peroxide accompanies a faint spot which was identified as the corresponding aldehyde. This means that the peroxides are more unstable in solution. On the other hand, the peroxides gave one peak on the gas chromatogram at the same retention time as that of the original aldehyde and with the same peak area as that of the same amount of aldehyde (Kobayashi *et al.*, 1990). GC-MS or directly injected MS results also gave the same MS pattern for the aldehyde. From these results, we had to apply a nondestructive method. X-ray crystal structure analysis, to analyze the structure of the peroxide homologues.

X-ray Crystal Structure Analysis (See Supplementary Material). The aliphatic peroxides crystallized from ethyl acetate in a silky stringlike form, which was unsuitable for X-ray analysis. On the other hand, the peroxide of 2-phenylethanal gives single crystals in the form of a flat plate from ethyl acetate at -20 °C.

The molecular structure with the numbering of the atoms is shown in Figure 2. Selected bond distances and angles are listed in Table II. Two molecules of 2-phenylethanal are dimerized by the peroxide linkage at the aldehydic carbon atoms and hydroxy groups on the same carbon atoms, C(1) and C(2) in Figure 2, and situated in opposing positions to form a stable conformation. This molecular structure shows that the newly formed asymmetric carbons, C(1) and C(2), have alternate *S* and *R* configurations, which means that this peroxide has a mesoform and no optical rotation, in spite of the presence of two asymmetric carbons in the molecule.

The crystal structure obtained from the X-ray analysis is shown in Figure 3. The molecules are linked by the hydrogen bonds of O(4)-H-O(3)-H-O(4) along the *c* axis. The distances of O(4)-O(3) and O(3)-O(4) are 2.95(1) and 2.91(1) Å, respectively. This crystal structure shows that an unstable polar group is tightly combined with the hydrogen bonds and concentrated at the center of molecular aggregation. The nonpolar residues are situated in the outer part of the aggregate, resulting in protection of the crystal structure. When this crystal

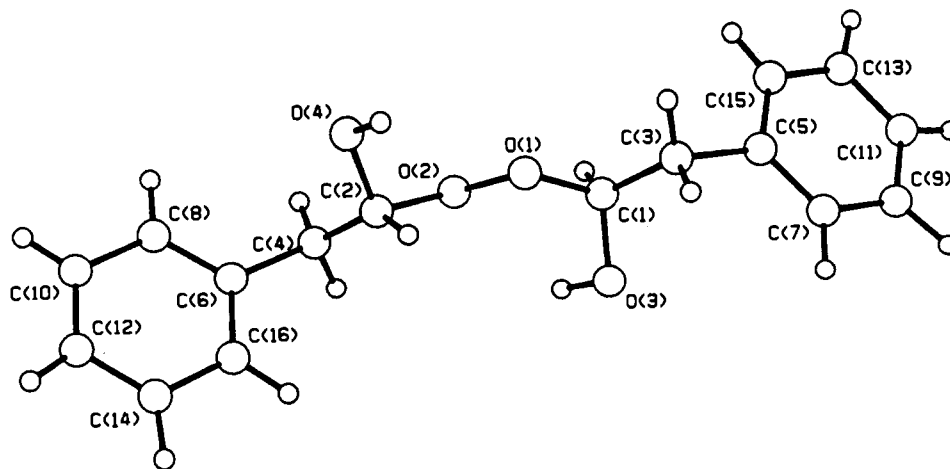


Figure 2. Molecular structure of bis(1,1'-hydroxy-2,2'-phenylethyl) peroxide.

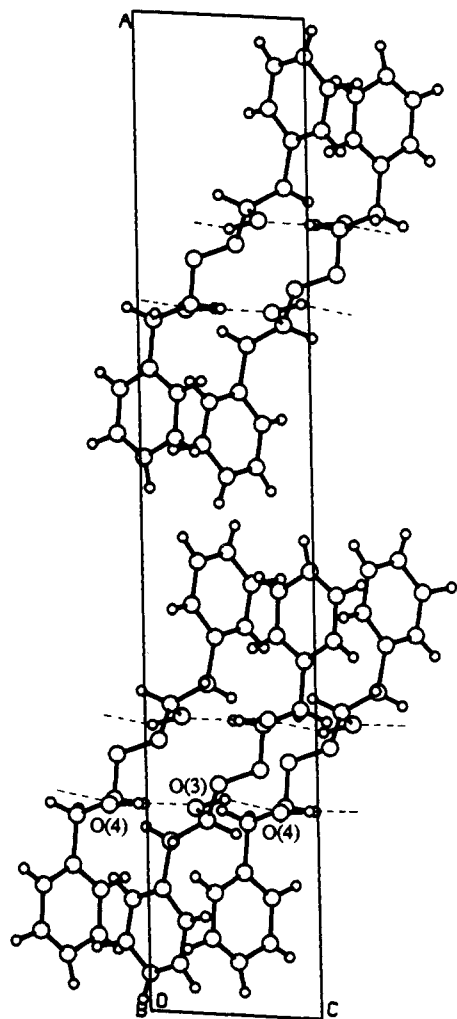


Figure 3. Crystal structure viewed along the *b* axis of bis(1,1'-hydroxy-2,2'-phenylethyl) peroxide.

structure is destroyed by heating or dilution, the unstable hydroxy peroxide linkage seems to be broken to yield aldehydes.

The structure of the dihydroxy peroxide dimer is equivalent to that of hydrated ozonide. The decomposition mechanism for ozonide has long been studied, and hydration is thought to be an important intermediate process to yield an aldehyde as a decomposition product (Bailey, 1958).

It can be reasonably anticipated that other aliphatic peroxides would have the same crystal structure, and the contrast between their stability in crystalline form and their instability under analytical conditions can be explained by the similar characteristics of 2-phenylethanal peroxide.

From a practical viewpoint, the substitution of volatile and odorous aliphatic aldehyde by the corresponding peroxide would result in many economical advantages to the perfumery, flavor, and cosmetics industry because of the easy handling and stable crystalline form of the latter.

Supplementary Material Available: Final atomic coordinates with their estimated standard deviations and final thermal parameters with their estimated standard deviations (2 pages); F_o - F_c tables (15 pages). Ordering information is given on any current masthead page.

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