

# Preparation of 5-Hydroxy 4-Pentanolide and 5-Acetoxy 4-Pentanolide from n-Butyl 4-Pentenoate

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## Summary

The subject of this paper is the preparation of a  $\gamma$ -lactone compound by one step of reaction.

n-Butyl 4-pentenoate (I) was found to react with hydrogen peroxide in acetic acid to afford 5-hydroxy 4-pentanolide (II) and 5-acetoxy 4-pentanolide (III) in the ratio of 4:1 in high yields. The reaction process is a complicated reaction consisted of epoxidation, hydrolysis, acidolysis, lactonization, and acetylation. Various factors affecting the yield were investigated on  $\text{H}_2\text{O}_2$ /(I) mole ratio,  $\text{CH}_3\text{COOH}$ /(I) mol ratio, reaction temperature, and time. The solvent effect using carboxylic acids was also examined and the order of yield was  $\text{HCOOH} > \text{CH}_3\text{COOH} > (\text{CH}_3\text{CO})_2\text{O} > \text{C}_2\text{H}_5\text{COOH}$ .

It is well known that olefinic compounds are oxidized to epoxides or  $\alpha$ -glycols by organic peracids.

Swern<sup>12)</sup> reported that either an epoxide or an  $\alpha$ -glycol containing the mono-acetylated derivatives could be obtained depending upon the peracetic acids employed or operating conditions.

There are many papers on the oxidation of alkene, but few papers on a carboxylic acid having a double bond at  $\gamma$ -position are published. Dangyan and co-workers<sup>3)</sup> reported that 2-alkyl 4-chloro 5-hydroxy pentenoic acid was oxidized with  $\text{H}_2\text{O}_2$  in acetic anhydride to prepare 2-alkyl 4-chloro 5-hydroxy pentanolide. They also studied on a series of 5-pentenoic acid derivatives with  $\text{H}_2\text{O}_2$  in formic acid.<sup>4)5)6)</sup>

However, there is no investigation on the oxidation of the ester derivatives of 4,5-unsaturated carboxylic acid.

This paper deals with the reaction of n-butyl 4-pentenoate (I) with 30%  $\text{H}_2\text{O}_2$ -acetic acid and other various organic acids.

The best yields and operating conditions of temperature, time,  $\text{H}_2\text{O}_2$ /(I) mole

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ratio and  $\text{CH}_3\text{COOH}/(\text{I})$  mole ratio were investigated. The component ratio of 5-hydroxy 4-pentanolide (II) and 5-acetoxy 4-pentanolide (III) in the reaction product was also found by the refractive index measurement.

### Experimental

*Materials:* (I) was chemicals by Towa Gosei Industry Co., Ltd. b.p.  $50^\circ\text{C}/5\text{mmHg}$ ,  $n_D^{20}$  1.4259,  $D_4^{20}$  0.8865. (I) was distilled three times under reduced pressure, using hydroquinone as an antioxidant to remove n-butyl acrylate. Its purity was determined by gas chromatography.

*Gas-chromatography:* Shimazu G.C. 4-AP type gas chromatography with 2m length of column was used. As a stationary phase was used the mixture of Reoplex and Celite 545 (80~120 mesh) in the ratio of 1:4.

*Infrared Spectra:* The IR spectra were measured with Hitachi EPI-2 spectrophotometer. In particular, to observe the absorption band of carbonyl groups in the range of  $1500\text{ cm}^{-1}\sim 2000\text{ cm}^{-1}$ , Perkin-Elmer spectrometer model 337 (grating) was also used in concentration 0.05g/2.5ml of carbon tetrachloride.

*NMR Spectra:* Varian associates A-60 NMR Spectrometer was used and carbon tetrachloride was used as a solvent.

*Measurement of molecular weight:* Molecular weight was measured in methyl ethyl ketone solvent with vapour pressure osmometer 301-A by Mechrolab Co., Ltd. The measurement was accurate to within 3%.

*Refractive index:* Abbe Refractometer by Atago Optical Works Co., Ltd. was employed at  $20^\circ\text{C}$ .

### Procedures

In a 500ml flask were placed 39 g (0.25 moles) of (I) and an excess of 300ml glacial acetic acid (5.25 moles) and then 50 g (0.44 moles) of 30% hydrogen peroxide solution was added dropwise for 30 min. The above reactant was stirred in a water-bath at  $40^\circ\text{C}$  for 6 hr. After acetic acid was removed under reduced pressure, unchanged (I) was distilled at  $45^\circ\text{C}/3\text{mmHg}$ .

The main fraction which was a colorless oily liquid, was collected in the boiling range of  $115\sim 125^\circ\text{C}/3\text{mmHg}$ . It was the mixture of (II) and (III). They could not be isolated by distillation because of the similar boiling points. The distilled residue which was an even more viscous and brownish resin was the dimer or trimer of the lactone.

In order to determine the component ratio of (II) vs (III), pure (II) and (III) were synthesized respectively as described below.

The pure (II) was given by saponifying the above mixture with 10% aqueous alkali solution for 12 hr. A little (II) was obtained by distillation under reduced pressure at  $125^\circ\text{C}/2\text{mmHg}$ ;  $n_D^{20}$  1.4650; Mol. Wt. Found 119, calcd. 116; Analysis Found: C, 51.36; H, 6.99% Calcd. for  $\text{C}_5\text{H}_8\text{O}_3$ : C, 51.72; H, 6.94%.

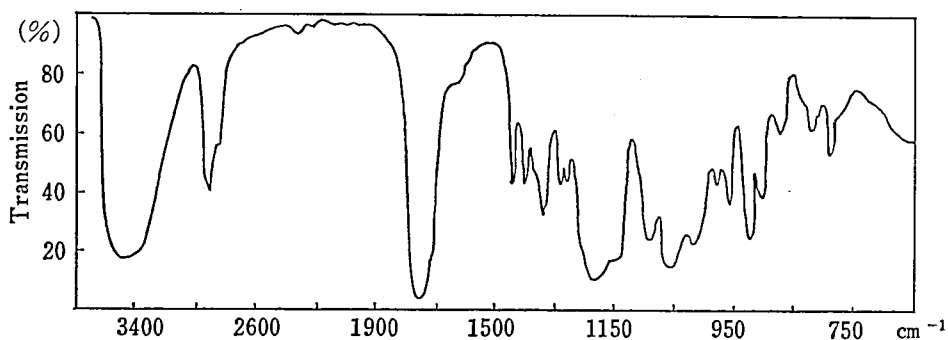


Fig. 1 IR spectrum of 5-hydroxy 4-pentanolide (II)

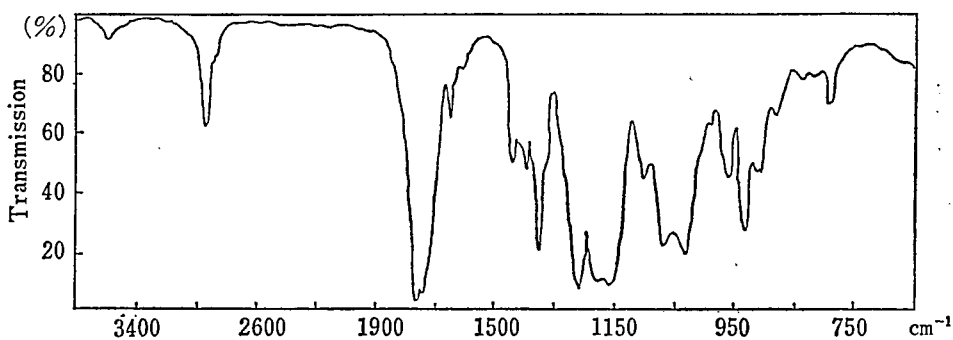


Fig. 2 IR spectrum of 5-acetoxy 4-pentanolide (III)

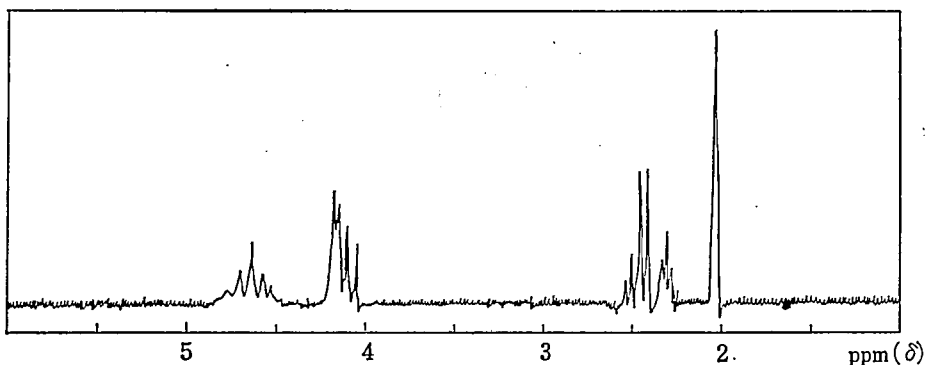
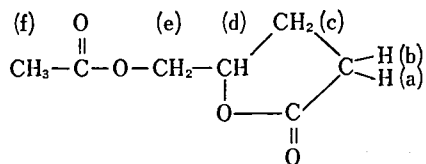


Fig. 3 NMR spectrum of 5-acetoxy 4-pentanolide (III)

While the pure (III) was obtained by the acetylation of the above mixture. It was reacted with acetic anhydride in the presence of sodium acetate as a catalyst. After heating under reflux at 140°C for 2 days, acetic anhydride was evaporated and (III) was distilled *in vacuo* at 114°C/3 mmHg;  $n_D^{20}$  1.4553; Mol. Wt. Found 159 Calcd. 158; Analysis Found : C, 52.81; H, 6.52% Calcd. for  $C_7H_{16}O_4$  : C, 53.15; H, 6.39%.

NMR spectrum of (III) is shown in Fig. 3 and the assignment is as follow. (a) 2.45 (b) 2.40 (c) 2.30 (d) 4.62 (e) 4.07~4.18 (f) 2.05



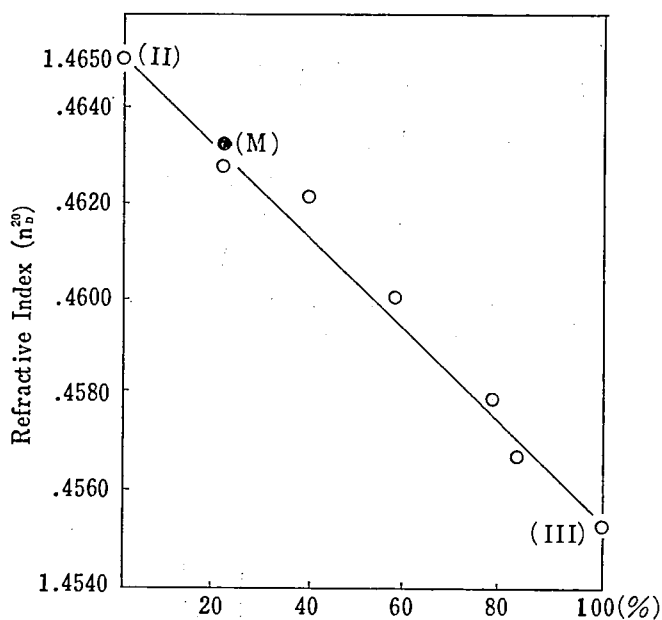


Fig. 4 The ratio of (II) vs (III)

(II)=the refractive index of pure (II)

(III)=the index of pure (III)

(M)=the index of reaction product,  $n_D^{20}=1.4631$

(II) and (III), which were prepared as above-mentioned, were blended in concentrations to find the component ratio of the reaction product by the refractive index measurement. The calibration curve and its result are shown in Fig. 4.

### Results and Discussion

The mixture of (II) and (III) was collected by distillation under reduced pressure in the range of 115~125°C/3 mmHg.

They could not be isolated because of the nearly same boiling points. Pure (II) and (III) were afforded as mentioned in procedures and their IR spectra are shown in Fig. 1. and Fig. 2.

(III) had two absorption bands of a carbonyl group at 1780 $\text{cm}^{-1}$  and 1740 $\text{cm}^{-1}$ . The former was of the carbonyl group of  $\gamma$ -lactone and the latter was of 5-acetoxy group.

While, (II) had the only absorption band (1780 $\text{cm}^{-1}$ ) arising from the carbonyl group of  $\gamma$ -lactone and the band of hydroxy group appeared at 3500 $\text{cm}^{-1}$ . The band of  $\delta$ -lactone was not observed.

Its result agreed with the report that 4-hydroxy acid was ready to form the corresponding lactone rather than 5-hydroxy acid.<sup>1)</sup>

The NMR spectrum of (III) was illustrated in Fig. 3. The sharp singlet band at  $\delta$ -2.05 was of acetoxy group. Although the spectrum of (II) was not presented in this paper, the signal due to the proton of hydroxy group at 5-position appeared

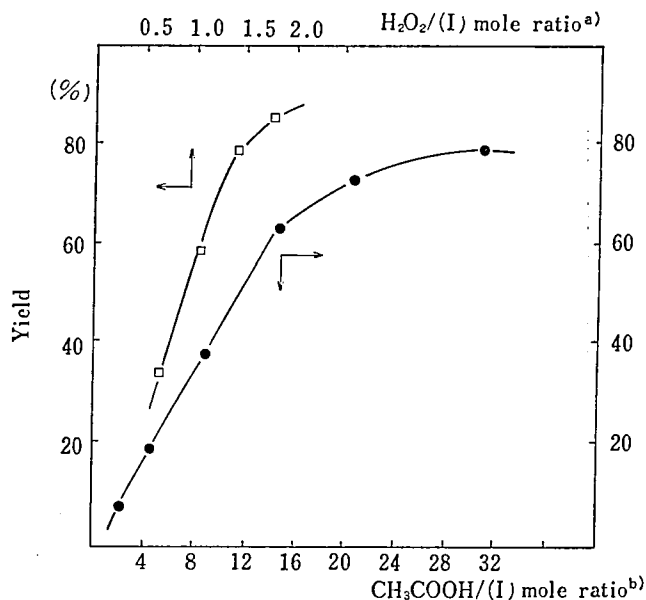


Fig. 5 Yield vs  $CH_3COOH/(I)$  mole ratio and  $H_2O_2/(I)$  mole ratio

React. temp. 40°C, react. time 6 hr

(I)=39.0g (0.25 mole)

a),  $CH_3COOH$  300ml (5.25 mole)

b), 30%  $H_2O_2$  50g (0.44 mole)

at  $\delta$ -3.70. The proton at 4-position in the five membered ring had a multiplet band at  $\delta$ -4.62.

From the above results of IR and NMR, the reaction products were confirmed to be 5-hydroxy 4-pentanolide and 5-acetoxy 4-pentanolide.

The component of (II) and (III) was determined from the caribration curve of refractive index as shown in Fig. 4. The reaction product was found out to be about 80% of (II) and 20% of (III).

The optimum reaction conditions to obtain the highest yield were researched. In Fig. 5 is shown the yield vs  $H_2O_2/(I)$  mole ratio and  $CH_3COOH/(I)$  mole ratio, The yield increased with the incrcseasing  $H_2O_2$  amount. As  $H_2O_2/(I)$  became 1.8, the yield reached 84% of the maximum. Acetic acid inceasing to 20-fold mole ratio to (I), the yield was higher up to 72~78%. The effect of reaction temp. from 10°C to 100°C is illustrated in Fig. 6. The yield was poor at a low temp. but at higher temp., the highest yield (90%) was obtained. As the reaction time was longer, the yield increased as shown in Fig. 6.

The solvent effect was examined by employing various carboxylic acids instead of glacial acetic acid as listed in Table. 1. On the case of formic acid, (II) and 5-formoxy 4-pentanolide which was characterized by IR and NMR was afforded. While, on the case of propionic acid were given (II) and 3.8% of 5-propioxy 4-

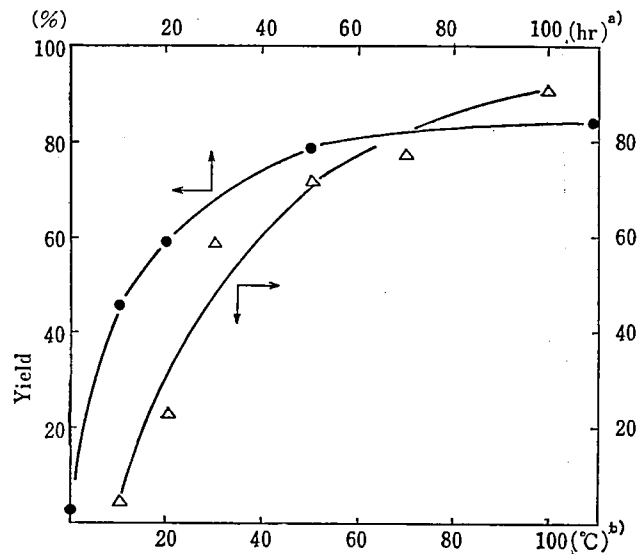


Fig. 6 Yield vs react. temp. and time

(I)=39g (0.25 mole),  $\text{CH}_3\text{COOH}$  300 ml (5.25 mole)  $\text{H}_2\text{O}_2$ /(I)  
mole ratio=1.4

a) react. time 6 hr, b) react. temp. 40°C

solvent ( $\text{pK}_a$ )	(I) g. (mol)	30% $\text{H}_2\text{O}_2$ <sup>b)</sup> g. (mol)	solvent <sup>b)</sup> g. (mol)	Yield g. (%)	Residue g.
$\text{HCOOH}$ (3.77)	39.0 (0.25)	50.0 (0.35)	115 (2.5)	28.2 (97.3)	0.7
$\text{CH}_3\text{COOH}$ (4.76)	39.0 (0.25)	50.0 (0.35)	150 (2.5)	21.1 (72.8)	13.3
$\text{CH}_3\text{CH}_2\text{COOH}$ (4.88)	39.0 (0.25)	50.0 (0.35)	185 (2.5)	3.8 (13.1)	4.2
$\text{CH}_3\text{CO}\rangle\text{O}$ $\text{CH}_3\text{CO}\rangle\text{O}$	39.0 (0.25)	50.0 (0.35)	255 (2.5)	15.9 (54.8)	19.6

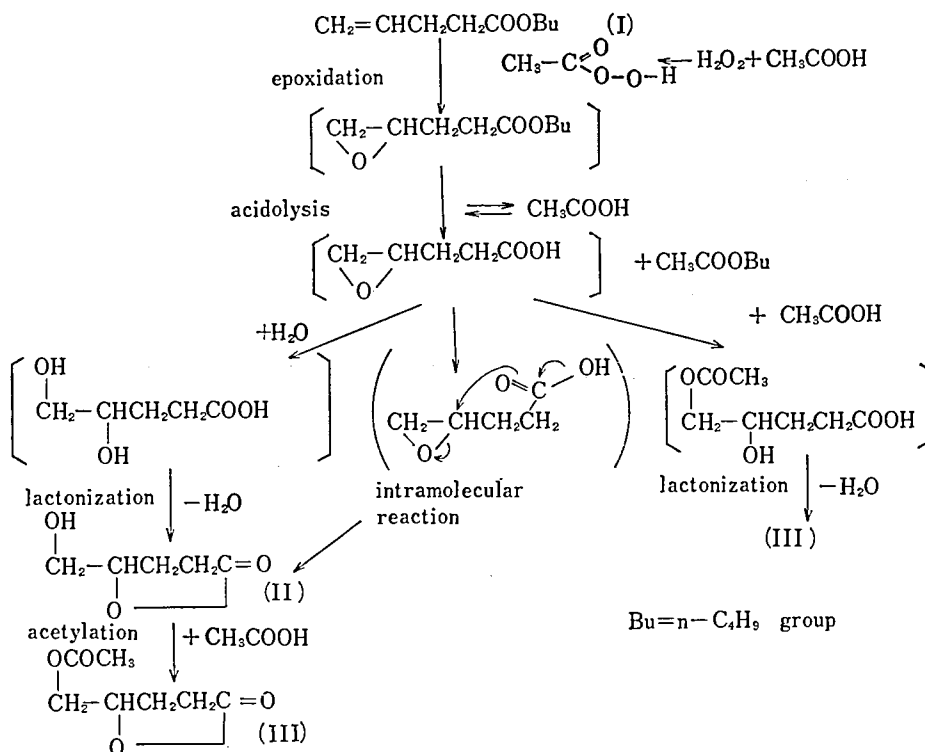
Table. 1 Yield for various carboxylic acid<sup>a)</sup>

a) React. temp. 40°C, React. time. 6 hr.

b)  $\text{H}_2\text{O}_2$ /(I) mole ratio=1.4 Solvent/(I) mole ratio=10.0

pentanolide which was similarly identified. The order of yields was as follow;  
 $\text{HCOOH} > \text{CH}_3\text{COOH} > (\text{CH}_3\text{CO})_2\text{O} > \text{C}_2\text{H}_5\text{COOH}$ .

This order may be closely related to the easiness of the preparation of peracid, which was prepared from  $\text{H}_2\text{O}_2$  and carboxylic acid. When acetic anhydride was used, the distilled residue was in large amount. Probably the lactone was considered to be polymerized. Each residue was regarded as the corresponding trimer of the lactone from the result of molecular weight measurement.



**Chart 1. The conceivable reaction mechanism**

The reaction scheme would be assumed as described in Chart 1. This reaction process consists of five reactions; epoxidation, hydrolysis, acidolysis, lactonization, and acetylation.

(I) was initially epoxidized with peracetic acid which was prepared with hydrogen peroxide and acetic acid.

n-Butyl 4,5-epoxy pentanoate could not be isolated under the above condition.

Though published in our next papers, we succeeded in the isolation of this epoxide compound as an intermediate.

Since the existence of n-butyl acetate was confirmed by gas chromatography, 4,5-epoxy pentanoic acid would be formed by the acidolysis between butyl ester of (I) and acetic acid. But, 4,5-epoxy pentanoic acid was so reactive that it would be easily lactonized to (II) by the intramolecular reaction or the dehydration reaction. (III) was presumed to be prepared by the cleavage of the epoxide with acetic acid or the acetylation of (II). As 4-hydroxy 5-pentanolide and 4-acetoxy 5-pentanolide were not obtained, a five membered lactone was more stable than a six membered lactone. Though the structure of n-butyl 4,5-dihydroxy pentanoate was thought, the quantity of acetic acid was so large that acidolysis would be occurred not to obtain n-butyl 4,5-dihydroxy pentanoate.

The isolation of n-butyl 4,5-epoxy pentanoate will be useful for the explana-

tion of this reaction mechanism.

In any event, the reaction has the characteristics of the preparation of  $\gamma$ -lactone by one step.

### Acknowledgement

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- 1) D. Swern, "Organic Reaction" VII 378 (1957)
- 2) D. Swern, *Chem. Revs.*, **45**, 1 (1949)
- 3) M.T. Dangyan and E.G. Mesropyan, *Izv. Akad. Nauk. Arm. S.S.R. Khim. Nauki*, **15**, 147-50 (1960).  
*ibid* **14**, No. 2 147-9 (1961). *ibid* **12**, 353-6 (1959).
- 4) M.T. Dangyan and S.V. Arakelyan, *Nauch. Trudy Erevan. Gosudarst. Univ., Ser., Khim. Nauk*, **44**, No. 2, 35-9 (1954)
- 5) M.T. Dangyan, M.C. Zalinyan, and A.A. Durgaryan, *ibid* No. **3**, 25-31.
- 6) S.V. Arakelyan and M.T. Dangyan, *ibid* **60**, No. **4** 17-20.