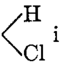
N.m.r.: τ 2.750, 2.938 (C═CH in 1), 3.645, 3.825 (C═CH in 2), 5.608 ($\mathrm{C}{<}^{\mathrm{H}}_{\mathrm{Cl}}$ in 16), 8.996 (CH_3 in 18).

Anal. Calcd. for $C_{18}H_{19}O_4NCl_2$: C, 56.28; H, 4.98; N, 3.64; Cl, 18.46. Found: C, 56.12; H, 4.90; H, 3.59; Cl, 18.54.

2-Chloro-4-aminoestrone (A-XVI).—The residue from the second benzene eluate (150 mg.) in the foregoing experiment was dissolved on the water bath in 7 ml. of acetic acid and 1 g. of zinc dust was added in small portions over a 0.5-hr. period. After further heating for 0.5 hr. under stirring, the solution was decanted and the zinc residue was washed with a small amount of acetic acid and with acetone. The combined solution and washes were neutralized with potassium bicarbonate solution and extracted with chloroform. After washing with water the solvent was distilled *in vacuo* and the brown oily residue was dissolved in water containing 200 mg. of oxalic acid. The hot solution was filtered and neutralized with 10% potassium bicarbonate solution. A white crystalline precipitate was obtained, which was filtered, washed well with water, and then dried *in vacuo* over phosphorus pentoxide. Several recrystallizations were necessary from benzene–hexane to obtain pure material, m.p. 218–222°. In a similar experiment, elimination of the amino group by diazotization gave 2-chloroestrone as reported above. This substance, therefore, must be 2-chloro-4-aminoestrone as confirmed by analysis.

Anal. Calcd. for $C_{18}H_{22}NO_2Cl + {}^1/_2C_6H_6$: C, 70.26; H, 7.02; N, 3.92; Cl, 9.87. Found: C, 70.48; H, 7.41; N, 4.42; Cl, 9.23.

Dehydrogenation of 2,4-Dibromo-10β,16ξ-dichloro-$\Delta^{1,5}$-estradiene-3,17-dione (B-VI).—To 1 g. of B-VI in 20 ml. dimethylformamide was added 2 g. of lithium chloride and the solution was refluxed for 5.5 hr. It soon became red and finally, dark purple. It was poured into ice and water, to which 2 g. of potassium acetate had been added. The blue precipitate was filtered and washed well with water, then dissolved in methanol, and again precipitated as before. This procedure was repeated twice with methanol and three times with acetone as solvent. The last mother liquor was almost colorless. After washing well with water the deep blue powder was dried over phosphorus pentoxide *in vacuo*. It was easily soluble with a deep red color in the usual organic solvents from which it was precipitated by the addition of either pentane or hexane. No way of crystallizing the substance could be found; yield 100 mg., m.p. 116–118°, $\lambda_{\max}$ 224 (27,276), 236 (12,727), 258 (14,090), $\nu_{\max}$ 3445 (H_2O), 2961 (C—H), 1751 (17-keto, Δ^{15}), 1702 (3-keto-$\Delta^{1,4}$-2,4-dichloro), 1620 (C═C) cm.$^{-1}$. N.m.r.: τ 3.875, 4.675 (C═CH in 1 and 6?), 6.108, 7.116, 7.645, 8.811, 8.953 (CH_3 in 18), 9.253.

Anal. Calcd. for $C_{18}H_{12}O_2Cl_2 + {}^1/_2C_3H_6O + H_2O$: C, 61.91; H, 4.53; Cl, 18.75; for $C_{18}H_{14}O_2Cl_2 + {}^1/_2C_3H_6O + H_2O$: C, 61.53; H, 5.03; Cl, 18.63. Found: C, 61.17; H, 4.88; Cl, 18.59.

Acknowledgment.—The authors are grateful to Dr. N. McNiven, Mr. D. F. Horgan, and Mr. T. Wittstruck of this institute for infrared and n.m.r. analyses, to Schering Corporation, Bloomfield, New Jersey, for generous gifts of estrone and estradiol, and to Dr. E. B. Hershberg for useful discussions and help with the manuscript.

The Autoxidation of Nonvicinal Glycols
Ester Formation *via* Cyclic Ethers and Their Peroxides

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Nonvicinal glycols can be readily autoxidized to the keto alcohols; they give high peroxide yields comparable to those obtainable from simpler secondary alcohols when the carbinol groups are separated by more than four carbon atoms. In the case of the 2,5-hexane- and 2,6-heptanediols, the formation of keto alcohols is accompanied by a significant production of 2-acetoxybutanes and -pentanes. The origins of these esters have been traced to a peroxide-consuming reaction sequence proceeding from cyclic hemiketal through tetrahydrofuran or pyran peroxides to the final ester cleavage products. This sequence is supported by syntheses and degradation studies of some cyclic ether peroxides. By analogy with 2,5-dimethylhexane, 2,5-hexanediol might have been expected to be autoxidized by intramolecular peroxy radical attack to the diketone, this reaction occurs to only a minor extent, if at all.

The autoxidation of simple secondary alcohols produces ketones and peroxide as major products and hydrocarbons with two equivalent tertiary hydrogens such as 2,4-dimethylpentane undergo intramolecular oxidation of the order of 90+% to yield principally the 2,4-dihydroperoxide. In contrast, 2,4-pentanediol[1] shows neither high peroxide yields nor evidence of intramolecular oxidation. It was concluded in the latter case that the reactivity of the intermediate peroxy radical was attenuated by internal hydrogen bonding and that the oxidation involved a considerably modified reaction chain.

The effect of interposing additional methylenes between the carbinol groups has now been studied by autoxidizing 2,5-, 2,6-, 2,7-, and 2,8-dihydroxyalkanes. Although Milas, Peeler, and Mageli[2] did not report ring opening by carbon–carbon bond cleavage in their studies of the vapor phase pyrolyses of tetrahydropyran hydroperoxide and *t*-butyl tetrahydropyran peroxide in glass wool packed tubes, such cleavages are postulated here to explain aliphatic ester formation from diols. Accordingly, certain tetrahydrofuran and -pyran peroxides have been synthesized and thermally degraded.

Experimental

Materials.—Unless otherwise noted heart cuts from fractionation through a Piros-Glover spinning band column were used.

2,5-Hexanediol was prepared by hydrogenation of 2,5-hexanedione in isopropyl alcohol over nickel. The yield of product with b.p. 88°/1 mm. and $n^{20}\mathrm{D}$ 1.4470–1.4473 was about 90%.

2-Methyl-2,5-hexanediol was prepared from γ-valerolactone and methyl magnesium bromide; b.p. 107°/4 mm., $n^{19.7}\mathrm{D}$ 1.4500. On standing, this material solidified, m.p. 36–37°.

Anal. Calcd. for $C_6H_{14}O_2$: C, 63.6; H, 12.2. Found: C, 63.5; H, 12.2.

5-Methyl-5-hydroxyhexan-2-one was prepared by oxidation of the glycol with chromic anhydride; b.p. 72–73°/13 mm., $n^{20}\mathrm{D}$ 1.4361; 2,4-dinitrophenylhydrazone, m.p. 106–107°.

Anal. Calcd. for $C_7H_{14}O_2$: C, 64.5; H, 10.8. Found: C, 64.3; H, 10.8.

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[1] F. F. Rust and E. A. Youngman, *J. Org. Chem.*, **27**, 3778 (1962).

[2] N. A. Milas, R. L. Peeler, Jr., and O. L. Mageli, *J. Am. Chem. Soc.*, **76**, 2322 (1954).

Anal. Calcd. for $C_{13}H_{18}O_5N_4$: C, 50.4; H, 5.8; N, 18.0. Found: C, 50.1; H, 5.9; N, 18.4.

2,5-Dimethyl-2,5-hexanediol was obtained by reduction of Air Reduction Co. 2,5-dimethyl-2,5-hexynediol in isopropyl alcohol over nickel and recrystallization from isopropyl alcohol followed by vacuum drying, m.p. 86.5–87.0°.

2,6-Heptanediol was obtained from glutaraldehyde and methylmagnesium bromide (56–59% yield); b.p. 101°/3 mm.; $n^{20.8}$D 1.4515. A heart cut had b.p. 110.5°/4 mm., n^{20}D 1.4512.

2,7-Octanediol was obtained from 1,4-dibromobutane and acetaldehyde *via* the Grignard reagent in 33% yield of crude product, b.p. 110°/2 mm., n^{20}D 1.4529. A heart cut had b.p. 113.5/2 mm., n^{20}D 1.4539.

Anal. Calcd. for $C_8H_{18}O_2$: C, 65.71; H, 12.41. Found: C, 65.73; H, 12.33.

2,8-Nonanediol was prepared by a Grignard synthesis from 1,5-dibromopentane and acetaldehyde. The yield of crude product, b.p. 100–104°/3 mm., was about 25%. Careful rectification afforded material with b.p. 115°/5 mm. or 100°/2 mm.; n^{20}D 1.4522–1.4540. The product was still pale yellow and therefore not completely pure.

Dihydropyran.—Eastman Kodak Co. practical grade. Redistilled heart cut; b.p. 84°, n^{20}D 1.4413.

Isopropyl alcohol, Shell Chemical Co., was dried over calcium hydride and distilled just before use; a heart cut was taken.

***t*-Butyl alcohol**, Shell Chemical Co., was dried over calcium hydride and redistilled before use. A middle cut with b.p. 83.5° was taken.

Hydrogen peroxide was commercial 30% stabilized and 90%.

4-Methyl-2-pentanol, Shell Chemical Co., n^{20}D 1.4113, was used without further purification.

2,5-Dimethylfuran, Eastman Kodak (White Label), was used as such.

Tetrahydrofuran (du Pont) was distilled through a 120-cm. column packed with glass beads; b.p. 88°, n^{20}D 1.4210. Prior to distillation, it was washed with ferrous sulfate solution.

2-*t*-Butylperoxytetrahydropyran.—Using the method of Milas,[2] 69–81% yields of the subject peroxide were obtained from 85% by weight *t*-butyl hydroperoxide and dihydropyran; b.p. 37–38°/~1 mm., n^{20}D 1.4360–1.4372.

Anal. Calcd. for $C_9O_3H_{18}$: C, 62.0; H, 10.4. Found: C, 61.5; H, 10.3.

2-Hydroperoxytetrahydropyran.[2]—This hydroperoxide was prepared at 0° from dihydropyran and 50% hydrogen peroxide (molar ratio of 1:3) in the presence of a catalytic amount of sulfuric acid. The crude hydroperoxide was used as such.

2,5-Dimethyltetrahydrofuran.—2,5-Dimethylfuran was hydrogenated over nickel at 125° and 1000 p.s.i.g. hydrogen. A 74% yield of product, b.p. 91°, n^{20}D 1.4033, was obtained. There was a higher boiling unidentified residue.

The glycols were oxidized in a closed system comprised of a Pyrex reactor, an all-glass pump, a hydraulically pressured steel oxygen reservoir fitted with a sight gage, and Dry Ice-cooled traps in the system immediately following the reactor and the reservoir. Oxygen at 35 p.s.i.g. was circulated through the glycols at 115–120°. The oxygen consumption was measured at constant pressure by following the rising water level in the calibrated reservoir.

The peroxide in the product was determined iodimetrically by reduction with acidified (acetic acid) potassium iodide in isopropyl alcohol solution under reflux for 5 min.

Oxidations and Reactions

Oxidation of 2,5-Hexanediol.—2,5-Hexanediol (400 cc., 375 g., 3.18 moles) containing 14 p.p.m. of phosphoric acid was oxidized at 120° and 35 p.s.i.g. oxygen. Oxygen uptake began after an induction period of about 2.5 hr. After six more hours 0.36 mole of oxygen had been taken up (0.113 mole/mole glycol). The product contained 0.026 mole of peroxide (7.2% yield) and functional group analyses showed the presence of 0.0065, 0.234 and 0.306 equivalents of acid, ester, and aldehyde or ketone carbonyl, respectively, and 0.695 mole of water. The gases from the oxidation contained only traces of carbon monoxide, carbon dioxide, and olefins.

A portion of the crude oxidation product was treated with 2,4-dinitrophenylhydrazine reagent and the mixed derivatives chromatographed on silica gel.

A minor, strongly adsorbed band was taken from the top of the column and the derivative dissolved and crystallized from ethyl acetate. Mixed melting point and elemental analysis showed it to be a derivative of 2,5-hexanedione.

Anal. Calcd. for $C_{18}H_{20}O_8N_8$: C, 45.6; H, 3.8; N, 23.6. Found: C, 45.7; H, 4.1; N, 23.4.

The major band was eluted, concentrated, and crystallized from ethanol–water. Elemental analysis of this derivative melting at 111–112° showed it to be the 2,4-dinitrophenylhydrazone derivative of 5-hydroxy-2-hexanone. Thus, the major product is the hydroxy ketone.

Anal. Calcd. for $C_{12}H_{16}O_5N_4$: C, 48.7; H, 5.4; N, 18.9. Found: C, 48.5; H, 5.4; N, 19.0.

The remaining crude product was distilled to remove all products boiling lower than the glycol. After drying, this material was fractionated and a substantial fraction (16.3 g.) of b.p. 112–113° (n^{20}D 1.3883) was unequivocally identified by infrared spectrum and ester value (0.831 eq./100 g.; calcd. 0.86 eq./100 g.) as 2-butyl acetate. Yield (moles/mole oxygen consumed) of 2-butyl acetate was 39%.

Oxidation of 2-Methyl-2,5-hexanediol.—Oxidation of this glycol (376 g., 2.85 moles) proceeded smoothly at 120° and 35 p.s.i.g. in a well conditioned reactor without added phosphoric acid. After an induction period of about 2 hr., 0.24 mole of oxygen (0.085 mole/mole glycol) was taken up in 5 hr. The total peroxide content was 0.026 mole (10.7% yield).

The greatly preponderant carbonyl compound produced was 5-methyl-5-hydroxy-2-hexanone as shown by quantitative precipitation of 2,4-dinitrophenylhydrazones and chromatography over silica gel (m.p. and m.m.p. with authentic derivative was 106–107°).

The product was concentrated at reduced pressure, the low boiling materials were separated from water, dried, and redistilled through a Piros-Glover column. *t*-Amyl acetate (4 g., 0.03 mole) was obtained (b.p. 124°, n^{20}D 1.3993). Infrared spectra of the product and an authentic sample were indistinguishable.

Anal. Calcd. for $C_7H_{14}O_2$: C, 64.6; H, 10.8; ester value, 0.769 eq./100 g. Found: C, 64.6; H, 11.3; ester value, 0.755 eq./100 g.

Oxidation of 2,6-Heptanediol.—Oxidation of the glycol (289 g., 2.3 moles) proceeded readily at 120° and 35 p.s.i.g. oxygen without added phosphoric acid. After an induction period of about 1 hr., 0.263 mole of oxygen (0.11 mole/mole glycol) was taken up in 14 hr. The total peroxide content was 0.0103 mole (3.9% yield). Gas analysis (Orsat) indicated only traces of carbon monoxide and carbon dioxide. Products with boiling points below that of 2,6-heptanediol were collected at 6 mm., separated from water, dried, and redistilled through a Piros-Glover spinning band column (micro). Although great difficulty was encountered due to dehydration, two constant boiling fractions were obtained.

The first, b.p. 120°, n^{20}D 1.4388, 4.3 g., appeared to be largely 2,6-dimethyl-3,4-dihydro-2H pyran.

Anal. Calcd. for $C_7H_{12}O$: C, 74.9; H, 10.7. Found: C, 73.5; H, 10.8.

The 2,4-dinitrophenylhydrazone of 6-hydroxy-2-heptanone was obtained in good yield, m.p. 96–96.5°.

Anal. Calcd. for $C_{13}H_{18}O_5N_4$: C, 50.3; H, 5.8; N, 18.1. Found: C, 50.2; H, 6.3; N, 18.2.

We conclude that the second fraction, b.p. 130°, n^{20}D 1.4052, 3.9 g., was a mixture of 2-pentyl acetate and 2,6-dimethyl-3,4-dihydro-2*H*-pyran.

Anal. Calcd. for an 80.9–19.2% mixture of ester and pyran: C, 66.7; H, 10.8; ester value, 0.622. Found: C, 66.2; H, 10.8; ester value, 0.622.

The material yielded the same 2,4-dinitrophenylhydrazone as fraction 1. Authentic 2-pentyl acetate, b.p. 134°, n^{20}D 1.3967, was prepared; the alcohol portion was converted to a 3,5-dinitrobenzoate (m.p. 61°). The melting point was undepressed on mixing with the same derivative from the oxidation product.

Only trace amounts of carbonyl products other than 6-hydroxy-2-heptanone (or 2,6-dimethyldihydropyran) were produced in the oxidation of 2,6-heptanediol. This was shown by quantitative preparation of 2,4-dinitrophenylhydrazones from the bulk oxidation product followed by chromatography on silica gel. The preponderant product ($\geq$ 90%) had m.p. 96–97° (m.p. undepressed by the analyzed derivative of 6-hydroxy-2-heptanone). No evidence was found for the diketone, 2,6-heptanedione, or 3-methylcyclohexenone which is readily derived from it.

Oxidation of 2,7-Octanediol.—This diol (47.5 g., 0.33 mole) was oxidized at 118°. After 16 hr., 0.0615 mole of oxygen had been absorbed. Peroxide titration showed that a 13.8% peroxide yield, based on consumed oxygen, had been obtained.

Oxidation of 2,8-Nonanediol.—A 98.5-g. (0.655 mole) quantity of 2,8 nonanediol was oxidized in the usual way at 120°. After 17 hr., 0.042 mole of oxygen had been absorbed. The peroxide titration on the product showed a 60% yield of peroxide.

Reaction of Hydrogen Peroxide with Glycols and Alcohols.—Pyrex reaction tubes (1.5 × 10 cm. with necks of 5-mm. tubing) were cleaned with fuming nitric acid (1 to 2 days at room temperature) and 90% hydrogen peroxide (1 day) with repeated rinsing with distilled water between and after treatments. Finally the tubes filled with distilled water were heated at 100° for about 6 hr. Tubes were used repeatedly after this treatment and reproducibility of results was satisfactory.

Solutions were made up by weighing 30% hydrogen peroxide and the alcohol or glycol into 100-cc. volumetric flasks (cleaned in the same manner as the tubes and containing redistilled *t*-butyl alcohol). The solutions were then made up with *t*-butyl alcohol to be 1.0 *M* in hydrogen peroxide and 1.5 or 3.0 *M* in glycol or alcohol. About 5 cc. of solution was then pipetted into the reaction tubes. The solutions were frozen in isopropyl alcohol–Dry Ice, sealed and placed in a 120° bath for the desired length of time (usually 21 hr.). Analyses before and after heating gave the per cent hydrogen peroxide unchanged. Table I presents the results. The reference compounds, isopropyl alcohol, 5-methyl-5-hydroxy-2-hexanone, and dihydropyran are included for comparison.

TABLE I

REACTION OF HYDROGEN PEROXIDE WITH GLYCOLS[a]

Substrate	% H_2O_2 unchanged
Dihydropyran	0
5-Methyl-5-hydroxy-2-hexanone	0
2-Methyl 2,5-hexanediol	5.0
2,5-Hexanediol	13.0
2,6-Heptanediol	16.0 ± 0.5
2,7-Octanediol	22.5 ± 1.0
Isopropyl alcohol (3.0 mole/l.)	30.5 ± 1.0
2,4-Pentanediol[b]	35.7 ± 2.2
2,5-Dimethyl-2,5-hexanediol	73.0 ± 3.5
t-Butyl alcohol	73.0 ± 2.0

[a] H_2O_2: 1 mole/l. Glycol: 1.5 mole/l. Temperature: 120°. Solvent: *t*-butyl alcohol. Reaction time: 21 hr. [b] Ref. 1.

Table II is a compilation of some products of glycol–peroxide interaction.

TABLE II

PRODUCTS OF GLYCOL–H_2O_2 REACTIONS[a]

Glycol	Products by analyses: mole/mole H_2O_2 Ester	Acid	Carbonyl	Remarks
2,5-Hexanediol	0.32	0.12	0.34	0.21 mole 2-butanol + 2-butyl acetate
2,5-Hexanediol-H^+	0.27	0.12	0.34	0.18 mole 2-butanol + 2-butyl acetate
2-Methyl 2,5-hexanediol	0.28	0.26	0.28	>0.14 mole *t*-butyl alcohol + *t*-butyl acetate
2,6-Heptanediol	0.30	0.16	0.29	2-pentanol + 2-pentyl acetate
2,6-Heptanediol-H^+	0.30	0.18	0.25	2-pentanol + 2-pentyl acetate
2,7-Octanediol	0.12	0.17	0.49	0.04 mole 2-hexanol + 2-hexyl acetate
2,4-Pentanediol	0.11	0.20	0.141	No 2-propanol or isopropyl acetate
1,4-Pentanediol-H^+	0.13	0.16	0.46	No 2-propanol or isopropyl acetate

[a] Temperature, 100°. H_2O_2: glycol, 1.0:1.5.

Reaction of Hydrogen Peroxide and 2,5-Hexanediol at 120°.—Hydrogen peroxide (39 g. 90% H_2O_2,[3] 1.03 moles) was added to stirred 2,5 hexanediol (180 g., 1.5 moles) which had been heated to 120°. The peroxide was added over 15 min. to control the temperature. After 1 hr. at 120°, the peroxide value was 13% of the original. After an additional 2 hr. reflux (112°), reaction was essentially complete. Analyses showed the presence of 0.0445 equiv. total acid, 0.340 equiv. total ester, and 0.326 equiv. total carbonyl.

Rectification afforded 2-butyl acetate (0.214 mole) and small amounts of impure 2,5-hexanedione and a fraction, b.p. 89–91°/10 mm., $n^{20.8}D$ 1.4273, $C_6H_{12.1}O_{2.86}$. Infrared analysis showed the presence of hydroxyl and ester carbonyl groups. The material could be a mixture of 1,3-butanediol monoacetates (4.8 g., 0.036 moles calcd. as monoacetate).

Oxidation of 2,5-Dimethyltetrahydrofuran.—The furan was readily oxidized at 80° by oxygen at 35 p.s.i.g.; a 12% conversion being realized in about 75 min. The oxidation product was concentrated by removal of unchanged starting material through a 12-inch Vigreux column at about 10 mm. Iodometric analysis showed that no peroxide decomposition occurred during oxidation or concentration. The concentrate contained 66% by weight peroxide.

Oxidation of Tetrahydropyran.—In contrast to the behavior of the 2,5-dimethyltetrahydrofuran, the oxidation of purified tetrahydropyran occurred very slowly at 82° (< 0.07 mole of oxygen was absorbed in 15 hr. at 35 p.s.i.g. oxygen; peroxide yield of 53% by iodometric analysis). At 115 ± 2°, an appreciable rate of oxidation (~ 1% conv./hr.) occurred, but the reaction was accompanied by extensive peroxide decomposition. Oxidation was stopped after an uptake of 0.43 mole of oxygen (~ 14% conv.); analyses indicated a 55% yield of formate and a 28% yield of hydroperoxide. Although no attempt was made to isolate and characterize the products completely, the high formate yield is clearly indicative of the carbon–carbon cleavage resulting from decomposition of 2-hydroperoxytetrahydropyran and the 2-tetrahydro*pyranoxy* radical to a formate ester radical.

Thermal Decomposition of 2-Hydroperoxy-2,5-dimethyltetrahydrofuran in 4-Methyl-2-pentanol.—The peroxide (40.0 g. of the 66.0% by weight concentrate; 0.20 mole) in 4-methyl-2-pentanol (200 cc.; 162 g.; peroxide:solvent ratio, 0.20:1.59) was decomposed by simply heating the solution while removing low boiling products through a 12-in. helices-packed column. After 105 min. (kettle temperature 125–131°), the head temperature reached 131°, the solvent boiling point. Distillation was continued until the residue amounted to 21.0 g. The lower boiling products and the concentrate were then redistilled through a Piros-Glover spinning band column. There was obtained 17.8 g. of 2-butyl acetate which represented a 76% yield based upon the peroxide (identification *vide supra*).

Thermal Decomposition of 2-*t*-Butylperoxytetrahydropyran.—The decomposition of 2-*t*-butylperoxytetrahydropyran in the various solvents (4-methyl-2-pentanol, di-*n*-butyl ether and tri-*n*-butylamine) was effected by heating the peroxide in the given solvent and distilling the low boiling products as formed, utilizing a 20-cm. helices-packed column attached to the reaction kettle (e.g., the kettle temperature varied from 125° to 133° with 4-methyl-2-pentanol; 0.20 mole of peroxide:1.57 mole of solvent). After the refractive index of the distillate reached that of the solvent, the total distillate was refractionated in the Piros-Glover column.

n-Butyl formate was isolated and identified by physical properties, ester value, and comparison of its infrared spectrum with that of an authentic sample. Typical physical properties of the isolated *n*-butyl formate samples were b.p. 106–108°, $n^{20}D$ 1.3887–1.3892, ester values of 0.91 to 0.93 eq./100 g. (theory for $C_5H_{10}O_2$ = 0.98 eq./100 g.); (lit.,[4] b.p. 106.6°, $n^{20}D$ 1.3894). Saponification mixtures were demonstrated to give positive tests for formate. *n*-Butyl formate yields were 39%, 44% and ~ 19%, respectively in 4-methyl-2-pentanol, di-*n*-butyl ether and tri-*n*-butylamine (solvent:peroxide molar ratio ≥ 5.4:1).

Reaction of Ferrous Sulfate with 2-Hydroperoxytetrahydropyran.—A solution of 0.25 mole ferrous sulfate heptahydrate in 250 ml. of water was added slowly with stirring to a solution of 0.25 mole of 2-hydroperoxytetrahydropyran in a mixture of 50 ml. of *t*-butyl alcohol and 150 ml. of water at 0–5° (addition time ~ 1 hr.).

The reaction mixture was subjected to liquid–liquid extraction with ether, dried over magnesium sulfate, and distilled. Fraction 1 (b.p. 105–110°, $n^{20}D$ 1.3887) was shown to be principally *n*-butyl formate. Fraction 2 (b.p. 100–106°/1 mm., $n^{20}D$ 1.4410) was shown to be 1,8-octanediformate: calcd. for $C_{10}H_{18}O_4$: C, 59.5; H, 8.9. Found: C, 60.0; H, 9.1. The 1,8-octanediformate was further characterized by conversion to 1,8-octanediol by ester exchange in methanol followed by recrystallization from aqueous methanol, m.p. and m. m.p. 59–60°.

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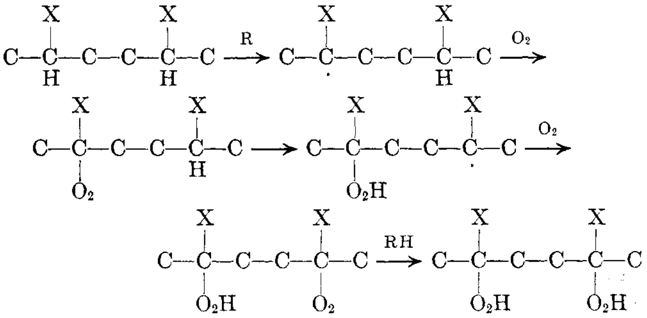
[3] Caution in use is strongly indicated.

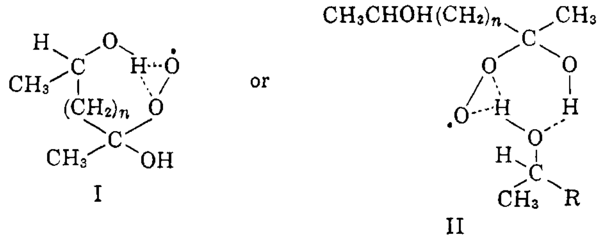
[4] E. H. Huntress and I. P. Mulliken, "Identification of Pure Organic Compounds," John Wiley and Sons, New York, N. Y., 1949, p. 302.

Discussion

In the autoxidation of 2,4-pentanediol the abnormally low peroxide yield and the absence of intramolecular oxidation was ascribed to intramolecular hydrogen bonding of the intermediate peroxy radical.[1] Hydrogen-bonded peroxy radicals must also be affecting the course of reaction in 2,5-hexanediol and to a lesser extent other hydroxy containing molecules. Certainly if no perturbing effects were present, the mechanism of oxidation for 2,5-dimethylhexane and 2,5-hydroxyhexane should be parallel.



When X = CH_3 the preceding sequence of reactions takes place at 100–150° with considerable facility. If, however, one or both CH_3 groups is replaced by —OH, *e.g.*, 5-methyl-2-hexanol or 2,5-dihydroxyhexane, intramolecular reaction is effectively eliminated. This altered reactivity of the peroxy radical is assumed to be a consequence of hydrogen bonding,[1] *e.g.*,



I Intramolecular II Intermolecular

It would seem reasonable that the intramolecular form I should be decreasingly significant and II increasingly so as *n* increases. As discussed in the previous paper[1] intramolecularly hydrogen-bonded peroxy radicals (I) are of increased stability and, as a consequence of increased steady state concentration, should result in increased frequency of radical–radical interaction and low peroxide yields. Low peroxide yields are, in fact, observed in the autoxidation of 2,4-pentanediol and still lower yields are found for the 2,5-, 2,6-, and 2,7-alkanediols (Fig. 1). In these latter cases, however, low yields are additionally, and probably more importantly, a consequence of peroxide consuming reactions leading to ester formation.

The formation of 2-butyl acetate by autoxidation is concluded to occur as shown in col. 2.

In the sequence shown step c leads to peroxide formation, but steps f and g result in its consumption.

In like fashion that part of the 2,6-heptanediol which autoxidizes through a tetrahydropyran intermediate produces 2-acetoxypentane. The same general reaction sequence explains the appearance of *t*-amyl acetate during the oxidation of 2-methyl-2,5-hexanediol.

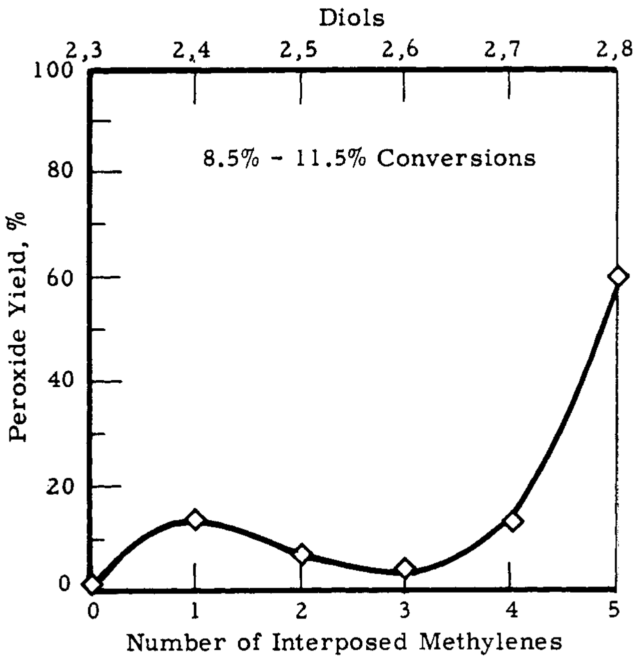
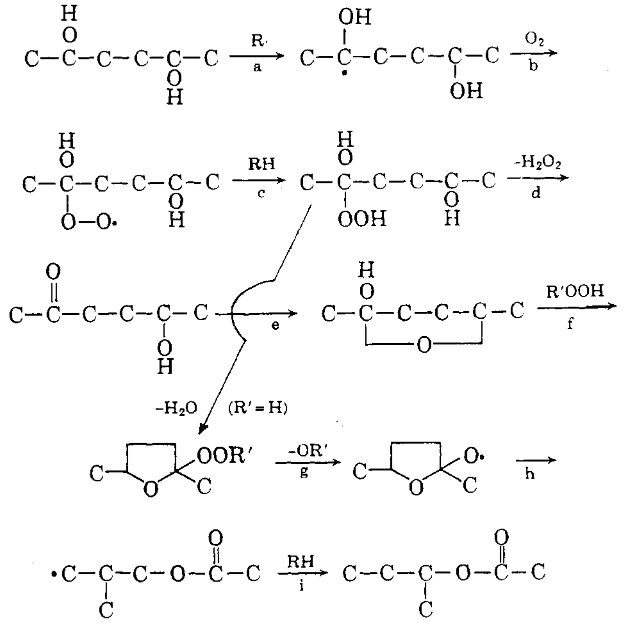


Fig. 1.—The autoxidation of straight chain glycols. Peroxide yield as a function of the number of carbon atoms between carbinol groups.



The autoxidation mechanism for ester formation from 2,5- and 2,6-diols suggests that improved yields of hydrogen peroxide would be obtained if the carbinol groups of the diol were separated sufficiently to minimize cyclic ether formation.

Obviously, as the carbinol groups are further separated, interaction between these polar groups or their reaction intermediates becomes more difficult. Fig. 1 shows that after 2,6-heptanediol there is an increase in peroxide yield in the autoxidation of 2,7-octanediol.[5] Finally, in the case of 2,8-nonanediol intramolecular effects have become so small that peroxide yields approach those obtainable from simple secondary alcohols.

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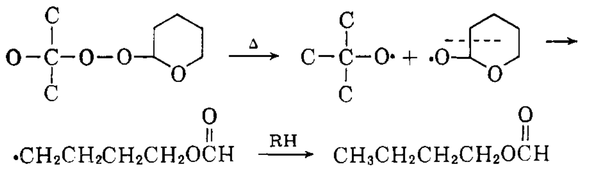
[5] Although only a peroxide determination was made in this instance, one of the oxidation products, when hydrogen peroxide was the chosen oxidant, was 2-acetoxyhexane. Thus, hemiketal formation seems able to contribute to low peroxide yields in this example as well.

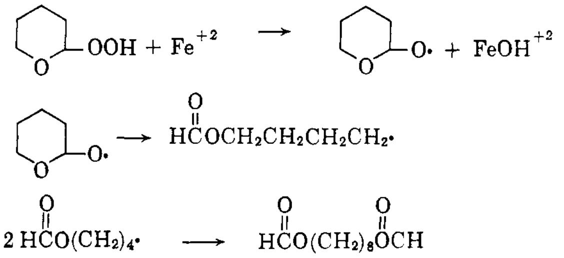
In order to validate further the ester forming steps in the mechanism which require carbon–carbon bond cleavage of a cyclic ether peroxide, the 2-hydroperoxide derivative of 2,5 - dimethyltetrahydrofuran was prepared by autoxidation and decomposed by heating in methyl isobutyl carbinol. The 76% yield of *sec*-butyl acetate supports postulated steps g, h, and i in the reaction sequence.

The methylisobutylcarbinol solvent served as the hydrogen donor to the radicals generated in the decomposition and 0.65 mole of methyl isobutyl ketone per mole of *sec*-butyl acetate formed was actually isolated.

A demonstration that the tetrahydropyran ring can also cleave was shown by the isolation of 39% and 44% yields of *n*-butyl formate when 2-*t*-butylperoxytetrahydropyran was decomposed in methylisobutylcarbinol and di-*n*-butyl ether, respectively. δ-Valerolactone was also produced in *ca.* 15% yield. The extensive ring cleavage observed in the autoxidation of tetrahydropyran is consistent with the same cleavage pattern.



When 2-hydroperoxytetrahydropyran is decomposed by an equivalent amount of ferrous ion in the absence of hydrogen donor—*i.e.*, in aqueous solution, the most important reaction of the intermediate oxy radical is, again, carbon-carbon bond scission with formation of the butyl formate radical. The final product, 1,8-octanediformate has been produced in 50 to 60% yield based on input peroxide. Less important products are *n*-butyl formate and δ-valerolactone[2] in 13 and 3% yields, respectively. This is in distinct contrast with previous descriptions of this system[2] where the major products were reported to be δ-valerolactone and 2-hydroxytetrahydropyran.



Although the actual yields of peroxide are low when 2,5- and 2,6-diols are oxidized, hydroperoxide or hydrogen peroxide is required by the proposed scheme of reaction. Experiments in which hydrogen peroxide replaces oxygen as the oxidizer do, in fact, lead to essentially the same products (Table II). It is further significant that the rate of hydrogen peroxide consumption is greatest in the presence of precisely those glycols, or keto alcohols, where the formation of cyclic hemiketals is most favored (Table I).

Reactions of Methyl-substituted 1,4-Epoxy-1,4-dihydronaphthalenes

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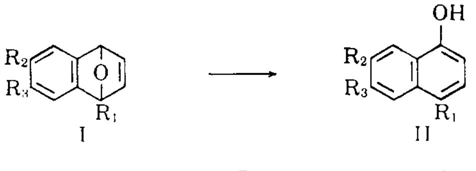
Disruption of the epoxide ring in methyl-substituted 1,4-epoxy-1,4-dihydronaphthalenes by alcohols and a little acid gives alkyl-substituted 1-naphthols when one of the alpha positions contains a hydrogen atom. However, if both the 1- and 4-positions contain methyl groups, the products are substituted 2-naphthols or their derivatives. Furthermore, if the 2- and 3-positions are also occupied by alkyl groups, compounds are formed containing the alkoxymethyl group in the alpha position. Intermolecular condensations also occur under anhydrous conditions.

It has been reported[1] that 1,4-epoxy-1,4-dihydronaphthalene is isomerized nearly quantitatively to 1-naphthol by reaction with methanol containing a little hydrochloric acid. During the course of our work[2] on the synthesis of methyl-substituted anthracenes, a number of methyl-substituted 1,4-epoxy-1,4-dihydronaphthalenes (I) were prepared. The isomerization and other reactions of some of these compounds have now been studied and are reported in this paper.

The first compounds of type I investigated were those in which the 1- and/or 4-positions were occupied by hydrogen. In these cases a little hydrochloric acid in methanol readily caused isomerization to the methyl-substituted 1-naphthols (II) as follows:



Compound no.	R_1	R_2	R_3	Reference
IIa	CH_3	H	H	3
b	H	CH_3	CH_3	4
c	H	CH_3	H	5
d	H	H	CH_3	6

Note: Compounds IIc and d are isomers obtained from the same epoxide.

This method, then, is a fairly convenient one for preparing methyl-substituted 1-naphthols, some of which are otherwise very difficult to prepare.

Naturally the question arose as to what occurs if both the 1- and 4-positions are occupied by methyl or other groups. Such compounds, because of the

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(2) E. Wolthuis, *J. Org. Chem.*, **26**, 2215 (1961).
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