A Free-Radical Reaction of Primary and Secondary Alcohols with Formaldehyde

MINORU OYAMA

Basic Research Laboratories, Toyo Rayon Company, Ltd., Kamakura, Kanagawa, Japan

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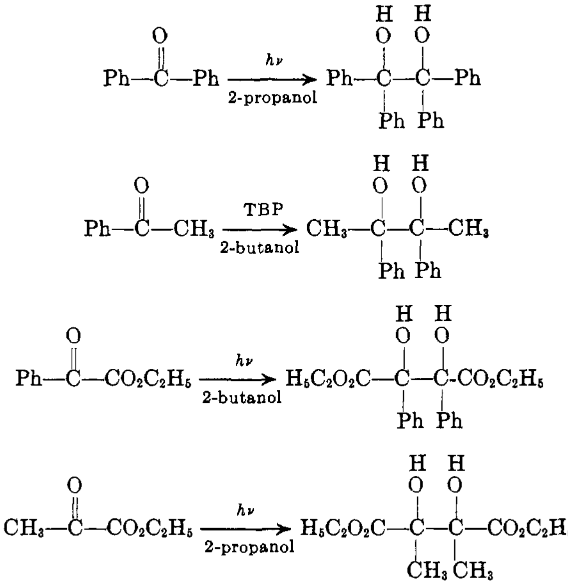
t-Butyl peroxide (TBP) induced free-radical reactions of formaldehyde with some alcohols, such as methanol, ethanol, 2-propanol, 2-butanol, and 3-methyl-2-butanol, were investigated. The reaction of 2-propanol with formaldehyde gave 2-methyl-1,2-propanediol, ethylene glycol, and acetone. The reactions of other alcohols with formaldehyde gave similar results. The results obtained can be explained in terms of addition of a 1-hydroxyalkyl radical to formaldehyde and an oxidation-reduction reaction between formaldehyde and the 1-hydroxyalkyl radical to give a hydroxymethyl radical and ketone or aldehyde derived from the alcohol.

Photochemical reaction[1] and alkyl peroxide induced radical reaction[2] of aromatic ketones in various solvents generally result in reductive dimerization of the ketone to the 1,2-diol and oxidation of the solvents. Photochemical reactions[3,4] of α-keto esters in alcohol also give analogous results.



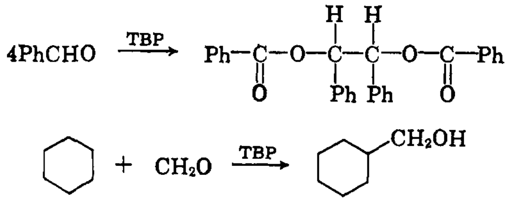
$$\mathrm{Ph{-}C({=}O){-}Ph \xrightarrow[\text{2-propanol}]{h\nu} Ph{-}C(OH)(Ph){-}C(OH)(Ph){-}Ph}$$

$$\mathrm{Ph{-}C({=}O){-}CH_3 \xrightarrow[\text{2-butanol}]{TBP} CH_3{-}C(OH)(Ph){-}C(OH)(Ph){-}CH_3}$$

$$\mathrm{Ph{-}C({=}O){-}CO_2C_2H_5 \xrightarrow[\text{2-butanol}]{h\nu} H_5C_2O_2C{-}C(OH)(Ph){-}C(OH)(Ph){-}CO_2C_2H_5}$$

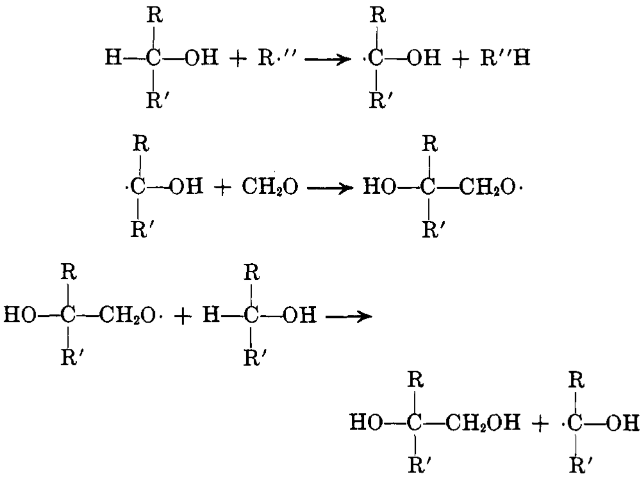
$$\mathrm{CH_3{-}C({=}O){-}CO_2C_2H_5 \xrightarrow[\text{2-propanol}]{h\nu} H_5C_2O_2C{-}C(OH)(CH_3){-}C(OH)(CH_3){-}CO_2C_2H_5}$$

Most free-radical reactions of aldehydes with olefins proceed through hydrogen abstraction from the formyl group to give a carbonyl radical followed by its addition to olefins and result in the formation of ketones, while a few examples[5,6] of radical addition to the carbonyl double bond of aldehydes are reported as follows.



$$\mathrm{4PhCHO \xrightarrow{TBP} Ph{-}C({=}O){-}O{-}CH(Ph){-}CH(Ph){-}O{-}C({=}O){-}Ph}$$

Primary and secondary alcohols easily undergo radical hydrogen abstraction from α-carbon to give a 1-hydroxyalkyl radical, and the addition of alcohols to various olefins is already reported.[7,8] If the radical reaction of formaldehyde is carried out in such alcohols, the addition of a 1-hydroxyalkyl radical to the carbonyl group occurs to form a 1,2-diol according to the following scheme.



$$\mathrm{H{-}C(R)(R'){-}OH + R''\cdot \longrightarrow \cdot C(R)(R'){-}OH + R''H}$$

$$\mathrm{\cdot C(R)(R'){-}OH + CH_2O \longrightarrow HO{-}C(R)(R'){-}CH_2O\cdot}$$

$$\mathrm{HO{-}C(R)(R'){-}CH_2O\cdot + H{-}C(R)(R'){-}OH \longrightarrow HO{-}C(R)(R'){-}CH_2OH + \cdot C(R)(R'){-}OH}$$

The present work is concerned with 1,2-diol formation by *t*-butyl peroxide induced free-radical reactions of formaldehyde with primary and secondary alcohols.

It was found that reaction of formaldehyde with some alcohols in the absence of methanol affords considerable amounts of ethylene glycol and ketones (or aldehyde) in addition to substituted 1,2-diols obtained by the addition of 1-hydroxyalkyl radical to formaldehyde. The experimental results are summarized in Table I.

1,2-Diols were isolated by distillation and identified by converting them into phenylurethans and by the comparison of infrared and n.m.r. spectra with those of authentic samples. Ketones and aldehydes also were identified in the form of their 2,4-dinitrophenylhydrazones and by gas chromatography. The yield of reaction products was determined by gas chromatography.

The formation of 1,2-diols, *t*-butyl alcohol, acetaldehyde, and ketones in these reactions can be explained by the mechanism shown in eq. 1-12.

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(1) J. N. Pitts, R. L. Letsinger, R. P. Taylor, J. M. Patterson, G. Recktenwald, and R. B. Martin, *J. Am. Chem. Soc.*, **81**, 1068 (1959); A. Schoenberg and A. Mustafa, *Chem. Rev.*, **40**, 181 (1947); W. A. Moore, G. S. Hammond, and R. P. Foss, *J. Am. Chem. Soc.*, **83**, 2789 (1961); G. S. Hammond, W. P. Baker, and W. A. Moore, *ibid.*, **83**, 2797 (1961).

(2) E. S. Huyser and D. C. Neckers, *ibid.*, **85**, 3641 (1963).

(3) E. S. Huyser and D. C. Neckers, *J. Org. Chem.*, **29**, 276 (1964).

(4) N. C. Yang and A. Morduchowitz, *ibid.*, **29**, 1654 (1964).

(5) F. F. Rust, F. H. Seubold, and W. E. Vaughan, *J. Am. Chem. Soc.*, **70**, 3258 (1948).

(6) G. Fuller and F. F. Rust, *ibid.*, **80**, 6148 1958).

(7) W. H. Urry, F. W. Stacey, E. S. Huyser, and O. O. Juveland, *ibid.*, **76**, 450 (1954).

(8) F. W. Banes, W. P. Fitzgerald, E. R. Gilliland, and J. P. Nelson, U. S. Patents 2,668,181, 2,671,121 (1954); M. Erchak, Jr., U. S. Patents 2,504,400 (1950), 2,670,386 (1954), 2,712,534, 2,713,071 (1955), 2,779,745 (1957); E. R. Gilliland and R. J. Kallal, *Chem. Eng. Progr.*, **49**, No. 12, 647 (1953); E. V. Kirkland, *Ind. Eng. Chem.*, **52**, 397 (1960).

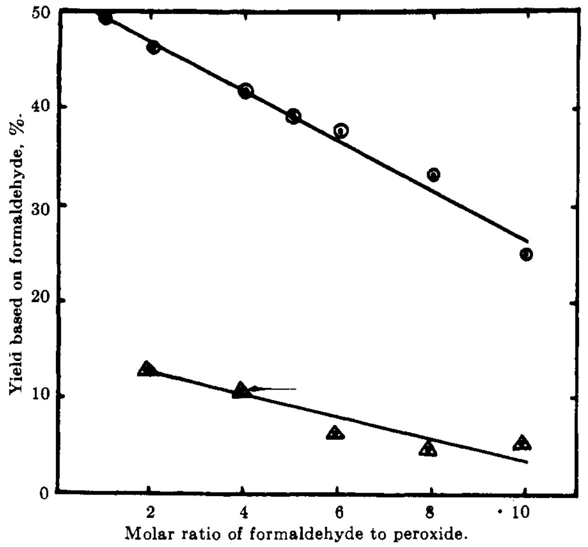


Figure 1a.—The effect of concentration of formaldehyde on the yield of 1,2-diol. 2-Propanol–peroxide = 20:1 at 140° for 12 hr.: ⊙, ethylene glycol; △, 2-methyl-1,2-propanediol.

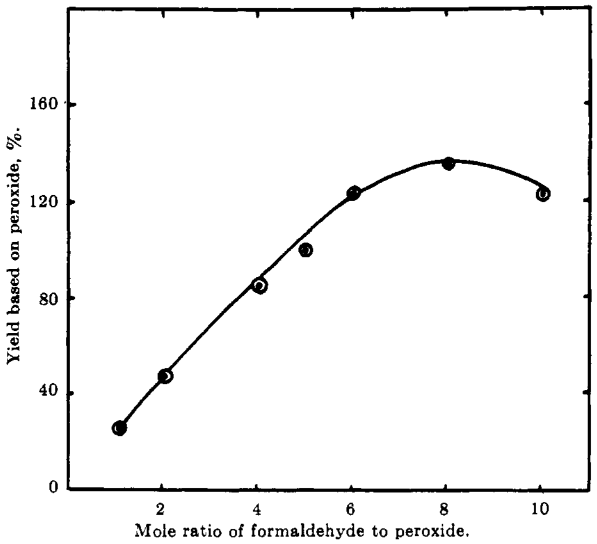


Figure 1b.—The effect of concentration of formaldehyde on the yield of ethylene glycol. 2-Propanol–peroxide = 20:1 at 140° for 12 hr.

First, the formation of 1-hydroxyalkyl radical (A) is essential which is derived from primary or secondary alcohol through hydrogen abstraction by *t*-butoxy radical as shown in eq. 3. 1-Hydroxyalkyl radical (A) reacts with formaldehyde through the two different paths a and b shown in eq. 5 to form two new radicals C and D, respectively. The reaction through path b affords equimolecular amounts of either ketone or aldehyde and hydroxymethyl radical (D). This reaction is analogous to a hydrogen transfer reaction[1-4,7] of 1-hydroxyalkyl radical.

Hydroxymethyl radical (D) is a key intermediate in the formation of ethylene glycol. Coupling of the hydroxymethyl radical (D) itself yields ethylene glycol in eq. 9, and hydroxymethyl radical (D) adds to formaldehyde to form alkoxy radical E. The new radical (E) abstracts another hydrogen from the solvent or other radical having active hydrogen to afford ethylene glycol as shown in eq. 10 and 11.

These reaction schemes of coupling and addition can be reasonably presumed based on these evidences.

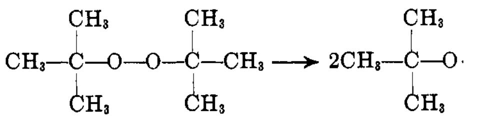
TABLE I

REACTION OF ALCOHOL WITH FORMALDEHYDE INDUCED BY *t*-BUTYL PEROXIDE AT 140° FOR 12 HR.

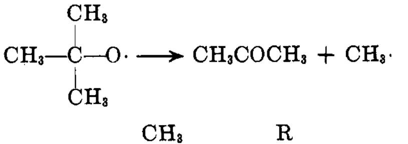
Reactants (moles)	Products (moles)
	Methanol Reaction
Methanol (9)	
Formaldehyde (1.8)	Ethylene glycol (0.21)
t-Butyl peroxide (0.45)	
	2-Propanol Reaction
2-Propanol (7)	Ethylene glycol (0.307, 0.25)
Formaldehyde (1.4)	2-Methyl-1,2-propanediol (0.146, 0.172)
t-Butyl peroxide (0.35)	*t*-Butyl alcohol (0.436, 0.374)
	Acetone (0.930, 0.988)
	Ethanol Reaction
Ethanol (8)	1,2-Propanediol (0.371)
Formaldehyde (1.6)	Ethylene glycol (0.0734)
t-Butyl peroxide (0.4)	*t*-Butyl alcohol (0.435)
	Acetone (0.426)
	Acetaldehyde (0.362)
	2-Butanol Reaction
2-Butanol (6)	2-Methyl-1,2-butanediol (0.091)
Formaldehyde (1.2)	Ethylene glycol (0.206)
t-Butyl peroxide (0.3)	*t*-Butyl alcohol (0.342)
	Acetone (0.200)
	2-Butanone (0.455)
	3-Methyl-2-butanol Reaction
3-Methyl-2-butanol (0.6)	Ethylene glycol (0.0107)
Formaldehyde (0.12)	Diols (0.01)
t-Butyl peroxide (0.03)	*t*-Butyl alcohol (0.0373)
	Acetone (0.01)
	3-Methyl-2-butanone (0.0255)

(1) The yield of ethylene glycol in the reaction of formaldehyde with methanol is higher than that of *t*-butyl peroxide induced dimerization of methanol. This fact suggests that hydroxymethyl radical (D) adds to formaldehyde.

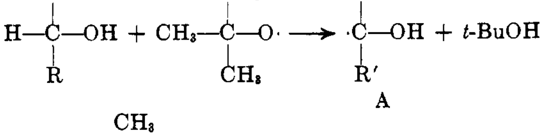
(2) If ethylene glycol is formed only by dimerization of hydroxymethyl radical (D) shown in eq. 9, the yield should be nearly quantitative based on peroxide. However, in the reaction of 2-propanol with formaldehyde, at constant molar ratio (20:1) of 2-propanol to peroxide as shown in Figure 1, the yield of ethylene glycol based on peroxide increases by increasing formaldehyde content. It was found that at molar ratio $[CH_2O]/[TBP] \geqq 5$, the yield was more than 100% based on peroxide.



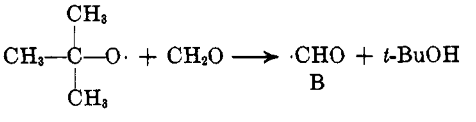
$$CH_3-\overset{CH_3}{\underset{CH_3}{C}}-O-O-\overset{CH_3}{\underset{CH_3}{C}}-CH_3 \longrightarrow 2CH_3-\overset{CH_3}{\underset{CH_3}{C}}-O\cdot \quad (1)$$



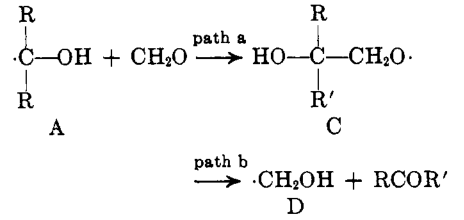
$$CH_3-\overset{CH_3}{\underset{CH_3}{C}}-O\cdot \longrightarrow CH_3COCH_3 + CH_3\cdot \quad (2)$$



$$H-\overset{R}{\underset{R}{C}}-OH + CH_3-\overset{CH_3}{\underset{CH_3}{C}}-O\cdot \longrightarrow \underset{A}{\cdot\overset{R}{\underset{R'}{C}}-OH} + t\text{-BuOH} \quad (3)$$



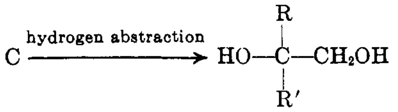
$$CH_3-\overset{CH_3}{\underset{CH_3}{C}}-O\cdot + CH_2O \longrightarrow \underset{B}{\cdot CHO} + t\text{-BuOH} \quad (4)$$



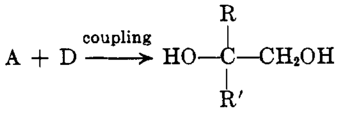
$$\underset{\text{A}}{\cdot\mathrm{C}(\mathrm{R})_2\text{—OH}} + \mathrm{CH_2O} \xrightarrow{\text{path a}} \underset{\text{C}}{\mathrm{HO\text{—}C(R)(R')\text{—}CH_2O\cdot}} \qquad (5)$$

$$\xrightarrow{\text{path b}} \underset{\text{D}}{\cdot\mathrm{CH_2OH}} + \mathrm{RCOR'}$$

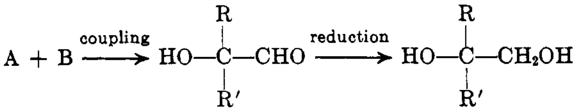
The formation of substituted 1,2-diol



$$\mathrm{C} \xrightarrow{\text{hydrogen abstraction}} \mathrm{HO\text{—}C(R)(R')\text{—}CH_2OH} \qquad (6)$$



$$\mathrm{A} + \mathrm{D} \xrightarrow{\text{coupling}} \mathrm{HO\text{—}C(R)(R')\text{—}CH_2OH} \qquad (7)$$



$$\mathrm{A} + \mathrm{B} \xrightarrow{\text{coupling}} \mathrm{HO\text{—}C(R)(R')\text{—}CHO} \xrightarrow{\text{reduction}} \mathrm{HO\text{—}C(R)(R')\text{—}CH_2OH} \qquad (8)$$

The formation of ethylene glycol

$$2\mathrm{D} \xrightarrow{\text{coupling}} \mathrm{HO\text{—}CH_2\text{—}CH_2OH} \qquad (9)$$

$$\mathrm{D} + \mathrm{CH_2O} \xrightarrow{\text{addition}} \underset{\text{E}}{\mathrm{HO\text{—}CH_2\text{—}CH_2O\cdot}} \qquad (10)$$

$$\mathrm{E} \xrightarrow{\text{hydrogen abstraction}} \mathrm{HOCH_2\text{—}CH_2OH} \qquad (11)$$

$$2\mathrm{B} \xrightarrow{\text{coupling}} \mathrm{OHC\text{—}CHO} \xrightarrow{\text{reduction}} \mathrm{HOCH_2\text{—}CH_2OH} \qquad (12)$$

Since the reaction of 2-propanol with 40% aqueous glyoxal solution does not afford a detectable amount of ethylene glycol by gas chromatography, the coupling–reduction process shown in eq. 12 can be excluded.

Since *t*-butyl peroxide induced reactions of 2-propanol with propionaldehyde and with glycolaldehyde afford only a trace of 1-propanol and 3.5% of ethylene glycol, respectively, it is reasonably presumed that the substituted 1,2-diol is formed by both reactions of eq. 6 and eq. 7 and not by the reaction shown in eq. 8.

Carbon monoxide and methane were detected in the reaction of 2-propanol with formaldehyde. It is reasonably presumed that carbon monoxide is formed by decomposition of formyl radical (B) as shown in eq. 4 and methane is obtained by hydrogen abstraction from the reaction species with methyl radical as shown in eq. 2.

The yields of 1,2-diols at various reaction conditions are shown in Figures 1–3. The yield of 1,2-diol based on formaldehyde decreased when the concentration of formaldehyde increased as shown in Figure 1. This indicates that at higher formaldehyde concentration, another reaction as shown in eq. 4 occurs competitively with the expected reactions. Maximum yield was obtained at 140° as shown in Figure 2, and at higher temperatures it is decreased by further reaction of diols. The yield of ethylene glycol increased with longer periods of reaction time but that of 2-methyl-1,2-propanediol reached a maximum after about 3 hr., and then was decreased by a further reaction as shown in Figure 3.

The rate of decomposition of *t*-butyl peroxide at 140° in the aqueous 2-propanol solution containing of formaldehyde is shown in Figure 4. The value of $k = 1.46 \times 10^{-4}$ sec.$^{-1}$ as the rate constant of the first-order decomposition of the peroxide was obtained. The induced decomposition of peroxide by 1-hydroxyalkyl radical is not likely because formaldehyde can be a radical scavanger as well as olefin.[9] It is fully supported by characterization of reaction products.

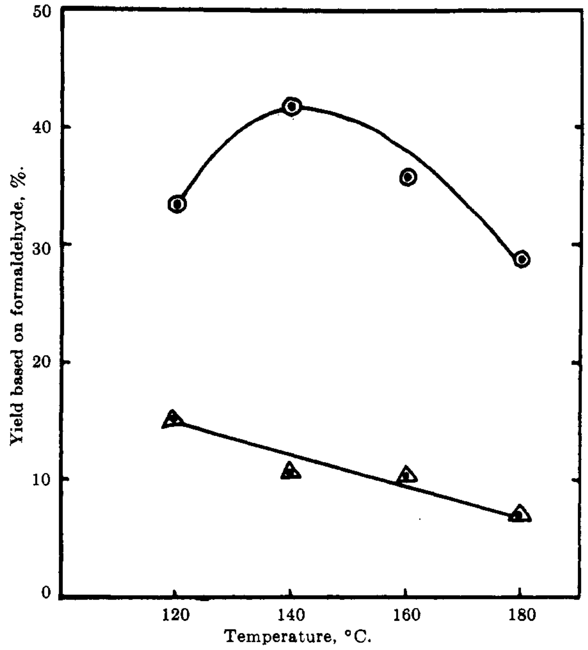


Figure 2.—The effect of reaction temperature. 2-Propanol–CH_2O-peroxide = 20:4:1 for 12 hr: ⊙, ethylene glycol; △, 2-methyl-1,2-propanediol. At 120° a detectable amount of peroxide was found after 12 hr. by gas chromatographic analysis.

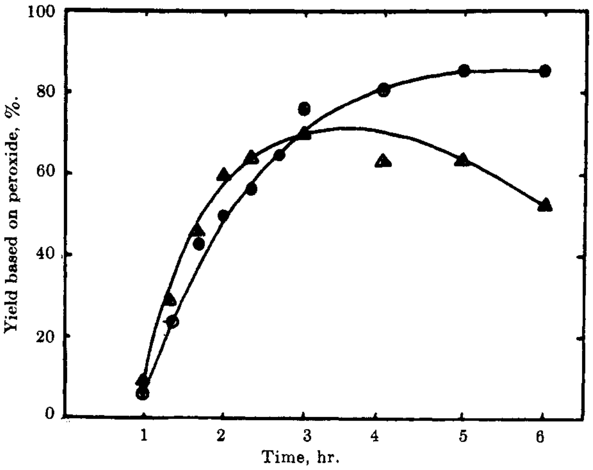


Figure 3.—The effect of reaction time. 2-Propanol–CH_2O-peroxide = 20:4:1 at 140°: ⊙, ethylene glycol; △, 2-methyl-1,2-propanediol.

Experimental

Material.—Formalin (15%) was prepared by the decomposition of commercial G.R.[10] paraformaldehyde with a catalytic amount of 0.1 *N* hydrochloric acid followed by neutralization with 0.1 *N* sodium hydroxide. *t*-Butyl peroxide (Lucidol-Yoshitomi Co. Ltd., purity 97%), methanol, ethanol, 2-propanol, 2-butanol, acetone, 2-butanone, 3-methyl-2-butanone, ethylene glycol, and 1,2-propanediol were commercial materials, purified when necessary by distillation: the materials gave a single peak in gas chromatography before they were used. 3-Methyl-2-

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[9] E. S. Huyser and C. D. Bredeweg, *J. Am. Chem. Soc.*, **86**, 2401 (1964).

[10] Guaranteed reagent.

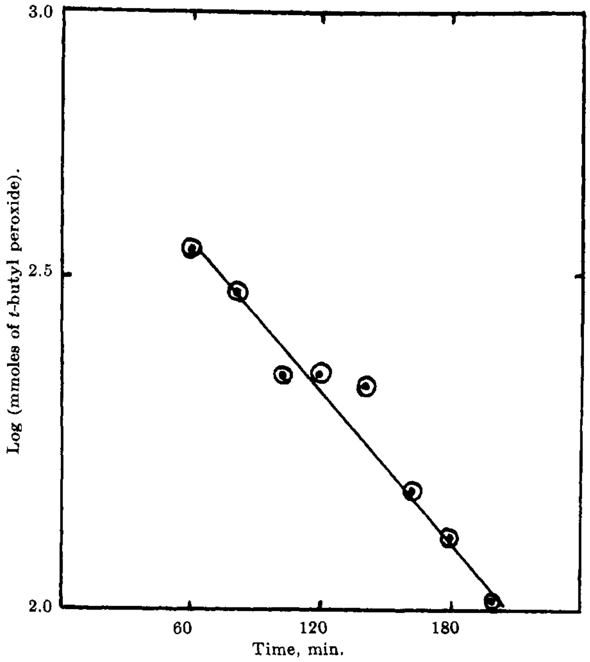

Figure 4.—First-order plots of decomposition of peroxide at 140°. 2-Propanol–CH_2O–peroxide = 20:4:1.

butanol was prepared by reduction of commercial 3-methyl-2-butanone with nickel catalyst. 2-Methyl-1,2-propanediol was prepared by hydrolysis and esterification of acetone cyanohydrin with acidic aqueous methanol solution followed by reduction with lithium aluminum hydride. Similarly, 2-methyl- [b.p. 82° (40 mm.)] and 2,3-dimethyl-1,2-butanediol [b.p. 98° (16 mm.)] were prepared starting with 2-butanone and 3-methyl-2-butanone cyanohydrins.

Apparatus.—The reactions were carried out under a pressure of 10 kg./cm.^{2} of nitrogen in a 200-ml. stainless steel autoclave with magnetic stirrer (Sakashita) or in a 1-l. stainless steel autoclave (Autoclave Engineer). The infrared spectra were recorded on infrared spectrometer IR-27 (Shimazu). The n.m.r. spectra were recorded on a Varian DP-60 n.m.r. spectrometer. In the gas chromatographic analysis the measurement of diol was performed with Yanagimoto GCG-III using a 2 m. × 4 mm. column packed with polyethylene glycol 6000 (Yanagimoto) or silicone DC-550 (Yanagimoto) at 160° and helium (0.7 kg./cm.^{2}) as carrier gas and with Yanagimoto GCG-220 using a 2 m. × 4 mm. column packed with polyethylene glycol 1500 (Yanagimoto) at 130° and helium (0.6 kg./cm.^{2}) as carrier gas. The identification of gaseous products was performed with Molecular Sieve 13X (Yanagimoto) at 82° and helium (80 cc./min.) as carrier gas. Boiling points and melting points are uncorrected.

Reaction of Methanol with Formaldehyde.—A mixture of 289.8 g. (9 moles) of methanol, 360 g. (1.8 moles) of 15% formalin, and 65.7 g. (0.45 mole) of *t*-butyl peroxide was sealed in the autoclave and heated at 150° for 12 hr. After cooling, 649.9 g. of fraction 1, b.p. 50–100°; 12.5 g. of fraction 2, b.p. 94–121° (12 mm.); and 14.78 g. of the residue were obtained by distillation of the reaction mixture. Fraction 2 was identified with ethylene glycol (its phenylurethan had m.p. 164° which showed no depression of the melting point on admixture with authentic sample). The yield amounted to 46.6% based on peroxide.

Fraction 1 was found to be a mixture consisting of methanol, water, *t*-butyl alcohol, acetone, and a small amount of methylal by gas chromatography, and 23.2 g. (0.4 mole) of acetone was obtained.

Dimerization of Methanol.—On heating a solution of 68 g. (2 moles) of methanol containing 14.6 g. (0.1 mole) of *t*-butyl peroxide at 130° for 12 hr., 2.4 g. of ethylene glycol, b.p. 102° (36 mm.), was obtained. The yield was 32.9% based on peroxide.

Reaction of Ethanol with Formaldehyde.—A mixture of 370.4 g. (8 moles) of ethanol, 320 g. (1.6 moles) of 15% formalin, and 54.8 g. (0.4 mole) of *t*-butyl peroxide was heated in an autoclave at 140° for 12 hr. After cooling, 675.2 g. of fraction 1, b.p. 55–100°, 37.16 g. of fraction 2, b.p. 84–94° (12 mm.), and 11.9 g. of the residue were obtained by distillation. Fraction 2 was found to be a mixture of 1,2-propanediol (phenylurethan, m.p. 148°) and ethylene glycol by gas chromatography. The yields of ethylene glycol and 1,2-propanediol amounted to 9.18 and 23.2% based on formaldehyde, respectively.

Fraction 1 was the mixture consisting of ethanol, water, *t*-butyl alcohol, acetone, and acetaldehyde.

Reaction of 2-Propanol with Formaldehyde.—A solution of 445.2 g. (7 moles) of 2-propanol, 280 g. (1.4 moles) of 15% formalin, and 51.1 g. (0.35 mole) of *t*-butyl peroxide was heated at 140° for 12 hr. After the gaseous products were trapped in gas bottle, 686.1 g. of fraction 1, b.p. 55–110°, 35.91 g. of fraction 2, b.p. 90–121° (33 mm.), and 3.7 g. of residue were obtained by distillation of the product. Fraction 1 was found to be the mixture consisting of 2-propanol, water, *t*-butyl alcohol (0.436 mole), and acetone (0.93 mole) by gas chromatography. Ethylene glycol and 2-methyl-1,2-propanediol (phenylurethan, m.p. 137°) were collected by preparative gas chromatography, and identified by infrared and n.m.r. spectroscopy.

The n.m.r. spectrum of 2-methyl-1,2-propanediol showed four absorption peaks, τ 8.82 (singlet) due to methyl, 6.62 (double) due to methylene, 5.45 (singlet) due to tertiary OH, and 5.00 (triplet) due to primary OH. Methylene and primary OH showed the absorption peaks τ 6.57 (singlet) and 5.09 (singlet), respectively, in aqueous solution at room temperature.

Methane and carbon monoxide were detected in the gaseous products by gas chromatography, but ethane was not (using a 2 m. × 4 mm. column packed with DOP–DMF at 5°, helium 70 cc./min.).

Reaction of 2-Butanol with Formaldehyde.—A mixture of 447.2 g. (6 moles) of 2-butanol, 240 g. (1.2 moles) of 15% formalin, and 43.8 g. (0.3 mole) of *t*-butyl peroxide was heated at 140° for 12 hr. Distillation of the reaction mixture gave 670 g. of fraction 1, b.p. 60–120°; 27.3 g. of fraction 2, b.p. 109–110° (14 mm.); and 13.3 g. of residue. Fraction 2 was found to be a mixture of ethylene glycol and 2-methyl-1,2-butanediol by gas chromatography. The yields of ethylene glycol and 2-methyl-1,2-butanediol were 34.2 and 7.5% based on formaldehyde, respectively. Fraction 1 (2-butanol, water, *t*-butyl alcohol, acetone, and 2-butanone) was analyzed by gas chromatography.

Reaction of 3-Methyl-2-butanol with Formaldehyde.—A solution of 52.9 g. (0.6 mole) of 3-methyl-2-butanol, 24 g. (0.12 mole) of 15% formalin, and 4.38 g. (0.03 mole) of *t*-butyl peroxide was heated at 140° for 12 hr. Fraction 1, b.p. 60–130° (60.2 g.), fraction 2, b.p. 97° (13 mm.) (2.37 g.), and a residue (1.58 g.) were obtained by distillation. Fraction 2 was found to be a mixture consisting of ethylene glycol (0.66 g.), 2,3-dimethyl-1,2-butanediol (0.67 g.), and an unidentified product by gas chromatography. Fraction 1 was a mixture of 3-methyl-2-butanol, water, *t*-butyl alcohol, acetone, and 3-methyl-2-butanone (2.19 g.).

Kinetic Measurement.—A mixture of *t*-butyl peroxide (0.35 mole), 2-propanol (7 moles), and 15% formalin (1.4 moles) was sealed under a pressure of 10 kg./cm.^{2} of nitrogen in an autoclave which has an open end of the small stainless steel tube with a bulb. The reaction temperature was measured by an Alumel–Chromel thermocouple and recorded with an automatic recorder. At various intervals, aliquot samples (about 5 ml. each) of the solution were taken from the open end and weighed accurately. Gas chromatographic analysis was performed with a column packed with polyethylene glycol 1500 at 80°, under a pressure of 0.7 kg./cm.^{2} of helium as carrier gas, and the water in formalin was used as internal standard. The amount of *t*-butyl peroxide in the weighed samples was determined from the peak areas of the peroxide and other reactants using the correction factor determined from the standard samples of which the relationship between the peak area ratio and the molar ratio had been established in the gas chromatographic analysis. The logarithms of the concentration of the peroxide were plotted against time and the reaction rate constant was calculated from the slope in Figure 4. The experiments to investigate the effect of reaction time on the yields of diol were also performed with the weighed samples of the reaction mixture containing a known amount of 1,3-propanediol as internal standard for gas chromatographic analysis.

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