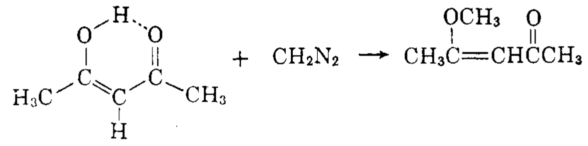
or $CH_3N_2^+ \longrightarrow CH_3^+ + N_2$

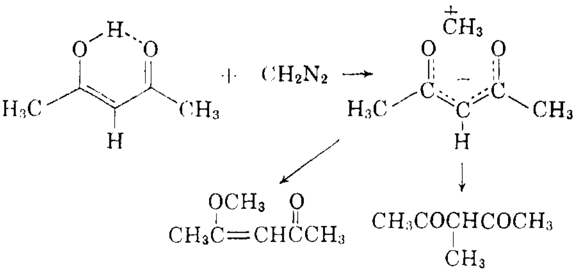
$$CH_3^+ + CH_2N_2 \xrightarrow{-N_2} CH_3CH_2^+ \xrightarrow{CH_2N_2} \longrightarrow \text{polymer}$$

Obviously, the intermediate cations react preferentially with diazomethane rather than acetylacetone. Otherwise, a continuous spectrum of alkyl enol ethers would be produced. Methyl enol ether must be formed by some independent mechanism involving reaction between diazomethane and the diketone. The reaction may involve either a concerted Mechanism A or formation of an ion pair (Mechanism B) with predominant collapse of the ion pair to form alkylated products.



Mechanism A

The fact that small amounts of 3-methylacetylacetone are formed is more easily accommodated by the ion-pair mechanism (Mechanism B). This mechanism also leads easily to an explanation of the fact that trace amounts of polymethylene were formed in all experiments. Separation of a small percentage of the ion pairs would produce a few methyl cations that would react with diazomethane to give high polymer. The stoichiometric relationship in the runs with strong acid present is sufficiently imprecise to allow the assumption that catalysis by strong acid leads only to the formation of polymer.



Mechanism B

# Evidence for Hydrogen Bonding of Peroxy Radicals. The Autoxidation of 2,4-Pentanediol and Related 2,4-Pentanes

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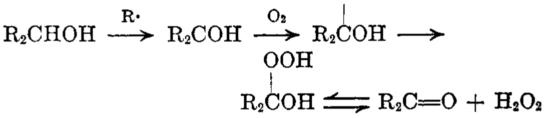
*Received July 19, 1962*

A distinctive characteristic of 2,4-dimethylpentane oxidation is the unusual efficiency with which the two tertiary hydrogen atoms can be replaced in a single reaction sequence (intramolecular oxidation). The same phenomenon is shown by 2,4-dimethoxypentane. However, if either a single methyl or methoxy group is replaced by a hydroxyl group, oxidation is limited to the carbinol moiety and hydrogen peroxide and ketone are formed semiquantitatively. In the case of 2,4-pentanediol, where both substituent groups are hydroxyl, relatively minor amounts of peroxide are produced and no intramolecular oxidation occurs. This absence of intramolecular peroxy radical attack in molecules presumed to be configurationally favorable to such a process is concluded to be a consequence of hydrogen bonding between the peroxy radical and an hydroxyl group with resultant redirection of the point of attack.

When hydrocarbon destruction by oxidation is viewed as a procession of transformations terminating in oxides of carbon and water, it becomes apparent that no real understanding of hydrocarbon oxidation is possible without much greater insight into the reaction characteristics of the many intermediate compounds which are way stations to the end result. Considerable information has been accumulated on the initial sequence of radical reactions involved in the autoxidation of paraffin hydrocarbons, but very little is known concerning subsequent reaction steps which lead to the destruction of primary reaction products. Even such a seemingly simple reaction as hydroperoxide formation can be complicated by the proximity of a second tertiary carbon atom in the molecule. Thus, the finding that 2,4-dimethylpentane can give semiquantitative yields of the dihydroperoxide[1] by an intramolecular process, emphasizes the significance of difunctionality in the over-all oxidation picture.

Inasmuch as a hydroxyl group is essentially equivalent spatially to a methyl group, and since secondary alcohols can give high yields of hydrogen peroxide *via* peroxidation of the "tertiary" carbon atom,[2] the substitution of 2,4-dihydroxypentane for 2,4-dimethylpentane in an autoxidation system could be expected to give a substantial yield of 2,4-pentanedione and hydrogen peroxide. The results are notably otherwise.



$$R_2CHOH \xrightarrow{R\cdot} R_2COH \xrightarrow{O_2} R_2\overset{OO\cdot}{\overset{|}{C}}OH \longrightarrow R_2\overset{OOH}{\overset{|}{C}}OH \rightleftharpoons R_2C{=}O + H_2O_2 \qquad (1)$$

---

[1] F. F. Rust, *J. Am. Chem. Soc.*, **79**, 4000 (1957).

[2] F. F. Rust (to Shell Development Co.), U. S. Patent 2,871,104 (January 27, 1959).

In subsequent discussion, evidence is presented for substantial modification of peroxy radical properties by the proximity of an hydroxyl group.

## Experimental

**4-Methoxy-2-pentanol.**—This ether alcohol was prepared by treating 3-methoxybutyraldehyde with methylmagnesium chloride; yield 65%, $n^{20}\text{D}$ 1.4158, b.p. 77–79° (40 mm.).

*Anal.* Calcd. for $C_6H_{14}O_2$: C, 60.1; H, 11.85. Found: C, 60.5; H, 11.9.

The 3-methoxybutyraldehyde (302 g.) was prepared in 43% yield according to the procedure of Buttner.[3]

**2,4-Dimethoxypentane.**—4-Methoxy-2-pentanol (253 g.) was added dropwise at room temperature to a suspension of 56.5 g. sodium hydride in 500 ml. of ether. The mixture was stirred overnight and the excess sodium hydride then destroyed with methanol. Methyl iodide (335 g., 2.36 moles) was then added and stirring continued for 4 hr. Sodium iodide and ether were removed by filtration and distillation, respectively. The dimethoxypentane fraction was taken overhead in a helices-packed column; yield 204 g. (72%), $n^{25}\text{D}$ 1.3952, b.p. 50–52° (40 mm.).

*Anal.* Calcd. for $C_7H_{16}O_2$: C, 63.75; H, 12.1. Found: C, 63.3; H, 12.2.

**2,4-Pentanediol.**—This glycol was prepared by hydrogenation of acetylacetone in ether over Raney nickel at 129°. The product distilled at 70° (5 mm.), $n^{20}\text{D}$ 1.4345 (lit., b.p. 200°, $n^{20}\text{D}$ 1.4349).

Methylisobutylcarbinol was a product of Shell Chemical used without further purification.

**Oxidation Procedure.**—The materials to be oxidized were charged to 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 reservoir. Oxygen usually at 35 p.s.i.g. was circulated through the organic compound. Oxygen consumption was measured at constant pressure by following the rising water level in the calibrated reservoir. Total oxygen consumption in all cases was held below 15 moles per 100 moles of organic compounds.

**Analytical Procedure.**—Functional group analyses on total oxidation product for acid, ester, and carbonyl and analysis for water were made by standard methods. Peroxide content was determined by reduction with acidified (acetic acid) potassium iodide in isopropyl alcohol under reflux for 5 min. and titration of the iodine formed with thiosulfate.

**Oxidation of 4-Methoxy-2-pentanol.**—A 250-g. charge was oxidized for 5 hr. at 116° and 34 p.s.i.g. of oxygen. 2300-cc. aliquot of oxygen (at 34 p.s.i.g.) was consumed. Titration of the produce (acidified potassium iodide method) showed an 83% yield of peroxide (based on consumed oxygen). Titration for hydrogen peroxide by the ceric sulfate procedure[4] showed that at least 92.5% of the peroxide produced is hydrogen peroxide. Efforts to find acetylacetone by GLC were unsuccessful.

**Oxidation of 2,4-Dimethoxypentane.**—2,4-Dimethoxypentane (148 g.) was autoxidized first at 89° and after reaction was initiated the temperature was dropped to 84°. Oxygen pressure was held at 20 p.s.i.g., 2100 cc. of oxygen at 20 p.s.i.g. were consumed. The yield of peroxide (by titration) was 83% based on consumed oxygen.

A 40-cc. aliquot of the autoxidation product of the dimethoxypentane was topped of all material volatile at *ca.* 35° and 1 mm. pressure. The clear sirupy residue on the basis of titration for active oxygen gave a value of 116 g./mole ROOH. Analysis for carbon and hydrogen and molecular weight showed C, 45.7%, H, 7.5%, and 184 g./mole, respectively.

|  | Calcd. for $C_7H_{16}O_6$ (diperoxide) | Calcd. for $C_7H_{16}O_4$ (monoperoxide) | Found |
|---|---|---|---|
| % C | 42.9 | 51.3 | 45.7 |
| % H | 8.15 | 9.75 | 7.5 |
| Mol. wt. | 196 | 164 | 184 |
| Mol. wt./ROOH | 98 | 164 | 116 |

**Estimation of Ratio of Diperoxide to Monoperoxide.**—From elemental analyses, the empirical formula of the peroxide concentrate is calculated to be $C_7H_{13.8}O_{5.4}$. By interpolation between the theoretical carbon values for the pure mono- and diperoxides and the found value of the mixture, 66.7% is estimated to be the diperoxide. Similarly on the basis of molecular weight determinations an estimate of 62.5% is arrived at and from peroxide titrations 72.5%.

Inspection of infrared absorption curves indicates that less than 1% of carbonylic decomposition products were present. These figures should be conservative because diperoxides should, if anything, be less stable than the corresponding monoperoxides.

As an additional check on the procedures outlined above, 0.082 equivalent of peroxide were present in the aliquot before concentration and 0.076 equivalent after concentration.

**Oxidation of Methylisobutylcarbinol.**—Methylisobutylcarbinol (3.5 moles) containing 25 p.p.m. of phosphoric acid was oxidized at 30 p.s.i.g. oxygen pressure and 117.5°. After 23 hr. 0.457 mole of oxygen had been consumed. Titration showed 0.439 mole peroxide—96% yield based on consumed oxygen.

After treatment with Adams' catalyst and hydrogen, the product was carefully fractionated. A nearly quantitative yield of methyl isobutyl ketone was obtained. Isolation of a single 2,4-dinitrophenylhydrazone (m.p. 79–81°, m.m.p. undepressed on admixture with 2,4-DNP of authentic methyl isobutyl ketone, m.p. 79–81°) and absence of unsaturation in the ketone and recovered alcohol fractions proved that mesityl oxide was not present. Materials boiling [38–86° (10 mm.)] higher than the starting alcohol and distillation residue amounted to only 0.5 g. Even if calculated as pure 2-methyl-1,4-pentanediol or 4-methyl-4-hydroxy-2-pentanone, this amount of material indicates that less than 1% of the oxidation proceeded by way of attack at the tertiary carbon or by an intramolecular path.

**Oxidation of 2,4-Pentanediol.**—The glycol (400 cc.) was oxydized at 120° with 35 p.s.i.g. oxygen circulating through the liquid. An induction period of *ca.* 3 hr. was followed by periods of 6 to 15 hr. during which 0.1 to 0.15 mole of oxygen were taken up per mole of diol. Yields of peroxide were low (15–25%).

Treatment of a portion of the oxidation product with a reagent for quantitative formation of 2,4-dinitrophenylhydrazones[5] significantly afforded none of the highly insoluble, easily isolated derivative of 2,4-pentanedione. The orange-red derivative which formed quite slowly had m.p. 152–154° and 157° after the first and second crystallizations from ethanol. The behavior of authentic 4-hydroxy-2-pentanone was identical. Mixtures of the two derivatives showed no melting point depression and had an analysis for the 2,4-DNP of 2-pentene-4-one (50.3% C, 4.8% H, 21.0% N; calcd. 50.0% C, 4.6% H, 21.2% N).

2-Pentene-4-one is not present as such in the oxidation products since the infrared carbonyl absorption is at 5.83 $\mu$, characteristic of saturated ketones, rather than at 5.92 $\mu$. From this fact, the functional group analyses, and our inability to isolate derivatives of other carbonylic compounds, we conclude that the dominant oxidation product is 4-hydroxy-2-pentanone.

This conclusion is supported by product isolation. Only two product fractions were obtainable by fractional

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[3] F. Buttner, *Ann.*, **583**, 184 (1953).

[4] F. Greenspan and D. MacKellar, *Anal. Chem.*, **20**, 1061 (1948).

[5] H. A. Iddles, A. W. Low, B. D. Rosen, and R. T. Hart, *Ind. Eng. Chem., Anal. Ed.*, **11**, 102 (1939).

distillation. The first was, in part, an azeotrope with water [b.p. 88° (760 mm.)] and in part anhydrous material [b.p. 122° (760 mm.)]. The organic phase contained 0.072 eq./100 g. acid (acetic), 1.036 eq./100 g. carbonyl, and 6.75% water and no ester. On a water and acid free basis the carbonyl is calculated to have an equivalent weight of 85.6 g./eq. (2-pentene-4-one, 84.11). The 2,4-dinitrophenylhydrazine derivative was the same as that obtained directly from the oxidation product. Thus, dehydration occurred during distillation as it did during derivative preparation. The amount of 2-pentene-4-one isolated approached that indicated by functional group analysis.

The second fraction distilled at 79–84° (12 mm.) and was shown by infrared to be principally hydroxy ester with some keto ester—estimated 70 and 30%, respectively. Total ester value was 0.732 eq./100 g. and the formate ester value was 0.108 eq./100 g. (ester equivalent, 137; calcd. for 85.3–14.7% mixture of monoacetate and formate of 2,4-pentanediol, 144). The fraction is most likely an acetic and formic acid monoester mixture of 2,4-pentanediol and 4-hydroxy-2-pentanone (57.88% C, 9.53% H found; calcd. for 85.3–14.7% mixture of acetate and formate esters of the diol as indicated by ester analysis: 57.0% C, 9.6% H.) The distillation residue was pure 2,4-pentanediol (b.p., refractive index, infrared). Thus, essentially all of the ester produced was contained in the second fraction.

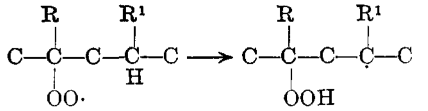
**Reaction of Hydrogen Peroxide with 2,4-Pentanediol and Isopropyl Alcohol.**—Pyrex reaction tubes (1.5 × 10 cm. with necks of 5-mm. tubing) were cleaned with fuming nitric acid (1–2 days at room temperature) and 90% hydrogen peroxide (1 day) with repeated rinsing with distilled water between and after 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 to volume with *t*-butyl alcohol and contained 1.0 mole/l. hydrogen peroxide and 1.5 or 3.0 mole/l. 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 21 hr. Analyses before and after heating gave the per cent hydrogen peroxide reacted.

Under the experimental conditions cited 64.3 ± 2.2% of the hydrogen peroxide reacted with the 2,4-pentanediol and 69.3 ± 1.2% of the peroxide reacted with isopropyl alcohol.

## Discussion of Results

Table I summarizes the experimental results in terms of peroxide yield and frequency of intramolecular hydrogen abstraction by the initially formed peroxy radicals,



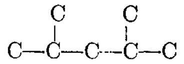
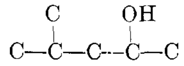
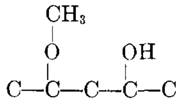
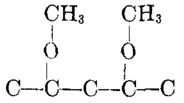
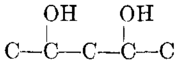
$$C-\underset{OO\cdot}{\overset{R}{C}}-C-\underset{H}{\overset{R^1}{C}}-C \longrightarrow C-\underset{OOH}{\overset{R}{C}}-C-\overset{R^1}{\underset{\cdot}{C}}-C \qquad (2)$$

The frequency of intramolecular attack is very high in 2,4-dimethyl- and dimethoxypentane and very low in all of the molecules containing a carbinol group. In every one of the latter cases the alcohol group has been the focus of attack and, where reactive hydrogen atoms are available elsewhere in the molecule, they have been largely ignored, even when favorably located.

TABLE I

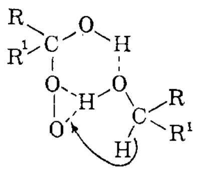
THE AUTOXIDATION OF 2,4-SUBSTITUTED PENTANES

(Less than 15 moles oxygen consumed per 100 moles oxidant)

| | Peroxide yield, % | Intra-molecular[a] oxidation, % |
|---|---|---|
|  $C-\overset{C}{C}-C-\overset{C}{C}-C$ | 89[1] | 95[1] |
|  $C-\overset{C}{C}-C-\overset{OH}{C}-C$ | 96 | <1 |
|  $C-\overset{\overset{CH_3}{O}}{C}-C-\overset{OH}{C}-C$ | 83 | <7.5 |
|  $C-\overset{\overset{CH_3}{O}}{C}-C-\overset{\overset{CH_3}{O}}{C}-C$ | 83 | >60–70 |
|  $C-\overset{OH}{C}-C-\overset{OH}{C}-C$ | 15–25 | <1 |

[a] That part of the consumed oxygen involved in consecutive attacks on the same molecule.

It is concluded that the reactivity of the peroxy radical is both suppressed and directed by hydrogen bonding. In the case of the carbinols (methylisobutylcarbinol and 4-methoxy-2-pentanol) the reactivity of the peroxy radical intermediate is presumably attenuated by intermolecular hydrogen bonding.

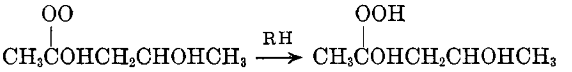


(3)

In any case, the path of reaction is so redirected that the sterically favored intramolecular hydrogen abstraction is eliminated or reduced to insignificance.

Although preference, for example, of the propagating methyl isobutylcarbinol peroxy radical for the carbinol group in another molecule (instead of the nearby tertiary hydrogen in the same molecule) might be ascribed to a polar effect, the fact that the same oxidation path is followed in 4-methoxy-2-pentanol would seem to preclude such an interpretation. On the other hand, the high frequency of consecutive involvement in the propagating chain of the tertiary hydrogen atoms in 2,4-dimethyl- and and 2,4-dimethoxypentane indicates that no steric barriers to intramolecular attack should exist.

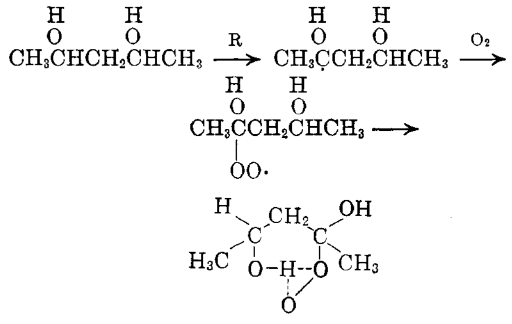
Any remaining possibility that a greater reactivity of the carbinol hydrogen atoms *vis a vis* the other available hydrogens might explain the absence of intramolecular peroxy radical attack, should be dispelled by the results of autoxidizing 2,4-pentanediol. In the case of this diol, where the hydrogen atoms in question are equivalent, only one is attacked and the products are principally 4-hydroxy-2-pentanone and water. Most notable, however, are the very low yields of hydrogen peroxide in contradistinction to the semiquantitative yields obtained from the monohydroxy compounds. These minimal yields indicate that for some reason the usual chain propagation step is taking place only with considerable difficulty. Nor is this reduction in yield a consequence of any unusual instability of hydrogen peroxide in the diol, as comparative peroxide decomposition rates in the diol and in 2-propanol show that hydrogen peroxide is even less stable in 2-propanol from which high peroxide yields are obtainable on autoxidation.



$$CH_3\overset{OO}{C}OHCH_2CHOHCH_3 \xrightarrow{RH} CH_3\overset{OOH}{C}OHCH_2CHOHCH_3$$

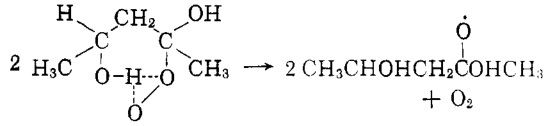
Therefore, the pentanediol peroxy radical must differ markedly from the peroxy radicals derived from the substituted pentanols.

Again, to rationalize these findings, it is concluded that in the case of the mono-ols, chain propagation involves *intermolecularly* bonded peroxy radicals whereas in the case of the 2,4-diol *intramolecularly* hydrogen bonded radicals are the important product determinants.



(4)

Subsequent peroxy radical–peroxy radical interaction should assume increased importance because of the augmented radical stability brought about by hydrogen bonding. The resultant two oxy radicals and oxygen (equation 5) would then lead to the main final products, keto alcohol and water, without formation of peroxide.



(5)

The relatively small amount of peroxide actually found is presumably a consequence of chain propagation by the more conventional intermolecularly hydrogen bonded peroxy groups.

The above conclusions receive support from the work of Denisov[6] which shows that the kinetics of the autoxidation of cyclohexanone can be altered by the presence of water. He concludes that a reduced rate is brought about by hydrogen bonding between the peroxy radicals and water.

**Acknowledgment.**—The authors gratefully acknowledge the assistance of Mr. C. S. Bell who synthesized 4-methoxy-2-pentanol and 2,4-dimethoxypentane, and helpful suggestions of Dr. J. K. Kochi.

[6] E. T. Denisov, *Izv. Akad. Nauk SSSR Otd. Khim. Nauk*, P 53 (1960).

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# Quinazolines and 1,4-Benzodiazepines. V. *o*-Aminobenzophenones[1a,b]

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A series of substituted *o*-aminobenzophenones was prepared. Some of these compounds were converted *via* their tosyl derivatives into N-monosubstituted *o*-aminobenzophenones. These primary and secondary amines were needed as intermediates for the synthesis of 1,3-dihydro-5-phenyl-2*H*-1,4-benzodiazepin-2-ones.[1c]

Several new substituted *o*-aminobenzophenones needed for the synthesis of 1,3-dihydro-5-phenyl-2*H*-1,4-benzodiazepin-2-ones[2] were prepared according to the methods outlined below.

The first method (A) employed was the condensation of a *para*-substituted aniline (I) with benzoyl chloride or a substituted benzoyl chloride (II) using zinc chloride as a catalyst, followed by energetic hydrolysis of the primary reaction product which was not isolated.[3,4] Compounds IIIa–IIIg shown in Table I were obtained by this method.

[1] (a) Paper IV. L. H. Sternbach and E. Reeder, *J. Org. Chem.*, **26**, 4936 (1961). (b) After the manuscript had been prepared, a paper was published by S. C. Bell, T. S. Sulkowski, C. Gochman, and S. J. Childress, *J. Org. Chem.*, **27**, 562 (1962), which contains a few of the compounds described in this paper. (c) The nomenclature for the 1,4-benzodiazepines was adopted after consultation with Dr. L. T. Capell of *Chemical Abstracts*.

[2] L. H. Sternbach, R. Ian Fryer, W. Metlesics, E. Reeder, G. Sach, L. G. Saucy, and A. Stempel, *J. Org. Chem.*, **27**, 3788 (1962).

[3] K. Dziewoński and L. H. Sternbach, *Bull. intern. acad. polon., Classe sci. mat. nath., Ser. A*, 333–348 (1935); *Chem. Abstr.*, **30**, 2972 (1936).

[4] L. H. Sternbach, E. Reeder, O. Keller, and W. Metlesics, *J. Org. Chem.*, **26**, 4488 (1961).