

The Rearrangement of Aliphatic Primary, Secondary, and Tertiary Alkyl Hydroperoxides in Strong Acid

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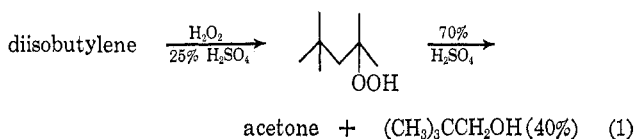
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Aliphatic primary, secondary, and tertiary alkyl hydroperoxides rearrange in 60–98% H_2SO_4 at 25°. With tertiary alcohols, the hydroperoxides can be generated *in situ* and the conversion of tertiary cycloalkanols to ω -hydroxy ketones is an excellent synthetic reaction with yields of >90%. A novel degradation of primary alcohols to their next lower homolog is developed. The migratory aptitudes propyl \approx H > ethyl \gg methyl were found. Solutions of $\text{K}_2\text{S}_2\text{O}_8$ (effectively H_2SO_4) in 20–60% H_2SO_4 are advantageous for the Baeyer–Villiger oxidation of ketones. Yields are quantitative and differences in migratory aptitudes are as large as or larger than those found with other peracids.

Migrations to electron deficient oxygen have been extensively studied in connection with the Criegee solvolysis of peresters,^{1–5} the Baeyer–Villiger oxidation of ketones,^{3–9} and the rearrangement of benzylic hydroperoxides.^{3–5,8} All three of these reactions can be considered as 1,2 alkyl or aryl shifts in RO^+ , though there is ample evidence that the reactions are concerted and that RO^+ is never a true intermediate.

Acid-catalyzed rearrangements of aliphatic alkyl hydroperoxides are less known. The best example is shown in eq 1.¹⁰ The following further rearrange-



ments have been reported. A series of secondary alkyl hydroperoxides were rearranged to ketones in 39–65% yields.¹¹ 1-Methylcyclopentyl hydroperoxide produced 6-hydroxy-2-hexanone in 15% yield.¹² 1-Methylcyclohexyl hydroperoxide formed 7-hydroxy-2-heptanone in unspecified yield.¹¹ Finally, *t*-butyl hydroperoxide formed acetone and methanol in low yield.¹³

It has been well documented that aliphatic alkyl hydroperoxides are far more resistant to acid-catalyzed rearrangement than benzylic or allylic hydroperoxides.^{4,3–6} They are not only generally stable in 5–50% aqueous sulfuric acids, but are usually prepared under such conditions.^{1–6,10,12,14,15} With the exception

of the work in ref 10 (eq 1), the rearrangements of aliphatic alkyl hydroperoxides had been conducted at elevated temperatures in media of relatively low acidity. It was suspected that thermal cleavage competed and made the products unduly complex. This suspicion was confirmed when it was found that 1-methylcyclopentyl, 1-methylcyclohexyl, and *t*-butyl hydroperoxides gave quantitative yields of the rearranged products when higher levels of acidity were employed.

With this result, studies were extended to an examination of propyl, H, ethyl, and methyl migratory aptitudes. Prior work had established that *t*-R > *sec*-R > primary R > methyl in both the Criegee rearrangement² and the Baeyer–Villiger,⁹ but the position of H had not been located and no difference had been noted between propyl and ethyl in the Baeyer–Villiger.⁹

Primary Alkyl Hydroperoxides.—These have become readily available from the treatment of alkyl tosylates with aqueous alkaline hydrogen peroxide.^{16,17} Thermal decomposition forms RCOOH plus H_2 .¹⁶ Acid-catalyzed rearrangement does not seem to have been investigated despite statements that H migration occurs predominantly.^{18,19} It is now found that propyl migrates more than H and ethyl somewhat less.

Addition of propyl hydroperoxide to 98% H_2SO_4 gave $22 \pm 8\%$ ethyl hydrogen sulfate from ethyl migration. A more precise analysis was not possible because of the complexity of products. The product of H migration, propionaldehyde, was shown in independent experiments in 98% H_2SO_4 to form protonated 2-methyl-2-pentenal in >90% yield. However, this pentenal was not a dominant product from the propyl hydroperoxide decomposition. It is presumed that formaldehyde, the coproduct of ethyl migration, interacted to give more complex products than would have arisen from propionaldehyde alone.

Addition of butyl hydroperoxide to 80% H_2SO_4 for 5 min at 55° gave 60% of 1-propanol. The same 60% propyl migration was observed in 98% H_2SO_4 at 25° although in this higher acidity, one observes only isopropyl hydrogen sulfate, the known rearrangement

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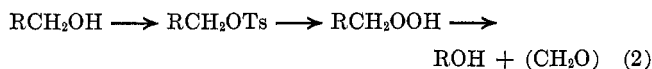
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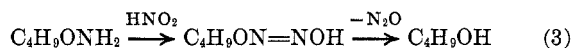
product of 1-propanol.²⁰ These results indicate propyl:H:ethyl migration ratios of 6:2:1 after correcting for the statistical effect of 2 H.

Equation 2 represents a novel method for degrading primary alcohols to their next lower homologs.



It is appropriate to comment on two unsuccessful attempts to produce the BuO^+ moiety from butoxyamine. Addition to 96% H_2SO_4 gave an nmr spectra whose pattern was identical with that of the original butoxyamine but displaced to lower fields. The spectrum was shown to differ from that of BuOSO_3H . It is concluded that butoxyamine simply protonated.

It has been reported that nitrous acid deamination of butoxyamine gave only 1-butanol.²¹ This has been confirmed by monitoring the reaction by nmr. No trace of any product other than 1-butanol could be detected at pH 5 as long as butoxyamine was in excess. The reaction is probably eq 3 though N_2O formation was not investigated.

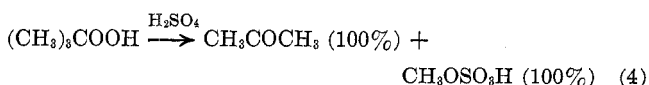


Secondary Alkyl Hydroperoxides.—The acid-catalyzed rearrangement of secondary alkyl hydroperoxides has been reported to produce ketones.¹¹ It is now found that alkyl migration competes significantly so that the generalization that only H migrates¹⁸ must be modified.

2-Pentyl hydroperoxide gave 37% isopropyl hydrogen sulfate (from *n*-propyl migration) and 63% 2-pentanone (from H migration). 3-Pentyl hydroperoxide gave 39% $\text{C}_2\text{H}_5\text{OSO}_3\text{H}$ and 61% 3-pentanone (all percentages are % yields). After the statistical correction for 2 ethyl groups in the 3-pentyl derivative, the migratory ratios of C_3H_7 :H: C_2H_5 were 2:3:1. This differs from the 6:2:1 found in the rearrangement of primary alkyl hydroperoxides.

2-Butyl hydroperoxide gave 78% 2-butanone and 22% $\text{C}_2\text{H}_5\text{OSO}_3\text{H}$. This is a slightly higher H: C_2H_5 ratio than found with 3-pentyl hydroperoxide. 2-Propyl hydroperoxide gave exclusively acetone (100%). Methyl migration of greater than 1% would have been detected. Since ethyl migrates much better than methyl^{2,9} and H better than ethyl, the exclusive formation of acetone was anticipated.

Tertiary Alkyl Hydroperoxides.—The rearrangements of tertiary alkyl hydroperoxides are quantitative. Typical is *t*-butyl hydroperoxide. Addition to 96% H_2SO_4 gave a solution whose nmr showed a 1:1 mixture of protonated acetone and methyl hydrogen sulfate, eq 4. No trace of any other product could be detected.

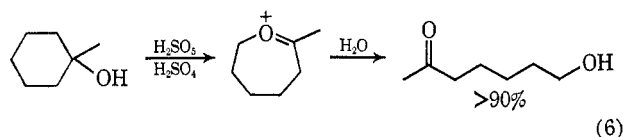
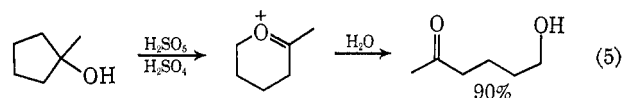


We regard the above result as remarkable since it was feared that ionization of $(\text{CH}_3)_3\text{COOH}$ to $t\text{-C}_4\text{H}_9^+$ would at least compete. The $t\text{-C}_4\text{H}_9^+$ would have yielded the complex mixture of $\text{C}_4\text{--C}_{16}$ alkanes and

$\text{C}_{10}\text{--C}_{16}$ cyclopentenyl cations with great rapidity.²² Even more remarkable, it was found that *t*-butyl alcohol or isobutylene could be added to H_2SO_5 in 96% H_2SO_4 with formation of products entirely derived from 1,2 alkyl shift in RO^+ . The reaction was not as simple as when $t\text{-C}_4\text{H}_9\text{OOH}$ was used because the acetone produced was necessarily in longer contact time with H_2SO_5 and some Baeyer–Villiger oxidation to acetic acid and $\text{CH}_3\text{OSO}_3\text{H}$ occurred.

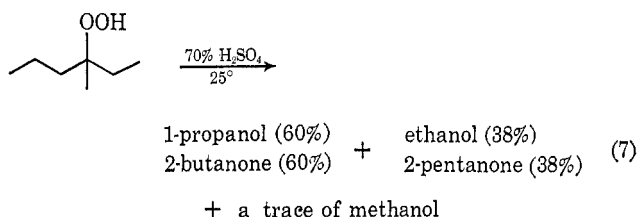
The 2-methyl-2-butyl (*t*-amyl) system also gave nearly as good yields by addition of the alcohol to $\text{K}_2\text{S}_2\text{O}_8$ in sulfuric acid as by addition of the hydroperoxide to sulfuric acid. In 80% H_2SO_4 , the latter reaction gave 100% $\text{C}_2\text{H}_5\text{OSO}_3\text{H}$ and 100% acetone and the former gave 100% $\text{C}_2\text{H}_5\text{OSO}_3\text{H}$, 88% acetone, 6% $\text{CH}_3\text{OSO}_3\text{H}$, and 6% CH_3COOH . Note that ethyl migration occurred exclusively, illustrating the enormous variation in migratory aptitudes which is such a feature of these rearrangements.

The procedure of adding the alcohol directly to solutions of $\text{K}_2\text{S}_2\text{O}_8$ in H_2SO_4 was of particular value with the reactions shown in eq 5 and 6. In both cases, the ketone resisted further attack so that yields were >90%. It has been shown that ω -hydroxy ketones exist as cyclic oxonium ions in sulfuric acid.²³ The nmr of the product from eq 5 and 6 may well be that of the cyclic oxonium ions shown in the equations, and the formation of such species is probably related to their resistance to the Baeyer–Villiger oxidation.



Equation 5 had been reported in 15% yield at lower acidities and higher temperatures,¹² and eq 6 had been reported in unspecified yield.¹¹ Equations 5 and 6 are attractive routes for the preparation of ω -hydroxy ketones.

Treatment of 3-methyl-3-hexyl hydroperoxide for 2 hr at 25° in 70% H_2SO_4 gave the products and yields shown in eq 7. The preference of propyl over ethyl migration was 60:38, comparable to that found in the secondary alkyl hydroperoxides.



Baeyer–Villiger Oxidation of Ketones.—A review of the Baeyer–Villiger reaction⁷ pointed out that only one simple aliphatic ketone had been reported and that other peracids were preferable to H_2SO_5 . It was thus of some interest to find that solutions of $\text{K}_2\text{S}_2\text{O}_8$ in 50% H_2SO_4 gave quantitative yields of the Baeyer–Villiger

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products for a variety of simple aliphatic ketones. The reactions were complete in minutes at 25°, and we cannot understand why this extremely simple procedure has not been utilized. Although K₂S₂O₈ was used to generate H₂SO₄, addition of H₂O₂ would undoubtedly have led to identical results.

The following examples are representative. 2-Butanone gave 100 ± 1% of ethanol (or its hydrogen sulfate above ~70% H₂SO₄) and 100 ± 1% acetic acid from 20% aqueous H₂SO₄ to 10% oleum. These two coproducts arise from ethyl migration. No trace of the coproducts of methyl migration (methanol and propionic acid) could be detected by nmr.

2-Pentanone gave 1-propanol and acetic acid in quantitative yield at 50% H₂SO₄. At higher acidities the 1-propanol became increasingly subject to rearrangement and degradation^{20,22} so that 40–60% H₂SO₄ would be chosen for production of the alcohol. The carboxylic acid fragment could be isolated from any strength of sulfuric acid.²⁴

4-Methyl-2-pentanone gave isobutyl alcohol and acetic acid (isobutyl migration) and 3-methyl-2-butanone gave 2-propanol and acetic acid (isopropyl migration). 3,3-Dimethyl-2-butanone gave acetic acid (100%) and the decomposition products²² of *t*-butyl alcohol.

In these examples, products arose exclusively from migration of the ethyl, propyl, isobutyl, isopropyl, and tertiary butyl groups rather than methyl. An even more dramatic example was 3-hexanone in which the products of propyl migration, 1-propanol and propionic acid, were formed in 75% yield, whereas the products of ethyl migration, ethanol and butyric acid, formed in 25% yield. This is of interest in view of the report that usual Baeyer–Villiger conditions give comparable propyl and ethyl migration.⁹ However, 3-heptanone was reported to give 2:1 butyl to ethyl migration²⁵ using CF₃CO₃H in CHCl₃.

Attempted Alkoxylation with RO⁺.—The most favorable situation for alkoxylation would be internal cyclization. Accordingly, 2-phenylethyl hydroperoxide and 1-phenyl-2-methyl-2-propyl hydroperoxide were added to 96% H₂SO₄. Formaldehyde was produced from the former and acetone from the latter. There was no evidence for the products of cyclization.

Experimental Section

Except for the two cases noted below, products were identified by comparison of nmr spectra with those of authentic samples. This was done by adding the authentic sample to the reaction

mixture and observing exact superposition. For clean spectra with narrow lines, this method is regarded as being of the greatest reliability. This is particularly true in sulfuric acid solutions where protonation equilibria and hydrogen bonding cause the spectra to vary with sulfuric acid concentration.

Yields were computed from nmr band areas.

The primary and secondary alkyl hydroperoxides were prepared from the alkyl tosylates and alkaline aqueous hydrogen peroxide as described.^{16,17} Although the peroxides were not distilled, the nmr spectra of the CH₂Cl₂ solutions were observed and only samples of >90% purity were used. The impurities were the corresponding alcohol and tosylate. Although they give the same nmr pattern, it was sufficiently displaced (different δ values) to allow analysis.

The tertiary alkyl hydroperoxides were prepared in a manner identical with that described for 2,4,4-trimethyl-2-pentyl hydroperoxide.¹⁰

The hydroperoxide rearrangements were conducted by stirring a CH₂Cl₂ solution of the hydroperoxide with the sulfuric acid at –15 to +5°. The initial mixing was generally made at –15–0° and the exothermicity of mixing and the reaction caused the temperature to rise.

Although eq 5 and 6 had been reported,^{11,12} authentic samples of products were not available so that the following additional evidence was used to identify products. In eq 5, the cyclic oxonium ion that is directly produced had the following nmr: singlet at δ 2.48 (C-1 methyl), triplet at 3.53 (C-3 methylene), multiplet centered at 2.05 (C-4 and C-5 methylenes), and triplet at 5.23 (C-6 methylene), with areas within 10% of the calculated 3:2:4:2. Dilution of the reaction mixture to 20% H₂SO₄ and addition to a solution of 2,4-dinitrophenylhydrazine in 20% H₂SO₄ gave an immediate precipitate of the DNP of 6-hydroxy-2-hexanone, mp 95–96° (lit.¹⁰ 97°).

In eq 6, the cyclic oxonium ion derived from 7-hydroxy-2-heptanone was identified on the basis of a singlet at δ 2.88 (C-1 methyl) and multiplets at 1.22–2.20 (C-4, C-5, and C-6 methylenes), 3.27 (C-3 methylene), and 4.7 (C-7 methylene) in the appropriate ratios of band areas. Both cyclic oxonium ions had nmr band positions comparable to others of this type that have been reported.²⁰

In both eq 5 and 6, the absence of the characteristic band of acetic acid or methyl hydrogen sulfate was particularly definitive evidence that methyl migration had not occurred.

Registry No.—Propyl hydroperoxide, 6068-96-8; butyl hydroperoxide, 4813-50-7; 2-pentyl hydroperoxide, 14018-58-7; 2-buthylhydroperoxide, 13020-06-9; 2-methyl-2-butyl hydroperoxide, 3425-61-4; 3-methyl-3-hexyl hydroperoxide, 25237-96-1; *t*-butyl hydroperoxide, 75-91-2.

Acknowledgment.—Grateful acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this work.

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