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

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Aliphatic primary, secondary, and tertiary alkyl hydroperoxides rearrange in 60-95% H2SO4 at 25°. With tertiary alcohols, the hydroperoxides can be generated in situ and the conversion of tertiary cycloalkanols to α-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 > H > ethyl > methyl were found. Solutions of K2SO4 (effectively H2SO4) in 20-60% H2SO4 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,1-4 the Baeyer-Villiger oxidation of ketones,5-7 and the rearrangement of benzylic hydroperoxides.8-10 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 rearrangements have been reported. A series of secondary alkyl hydroperoxides were rearranged to ketones in 39-65% yields.11 1-Methylecyclopentyl hydroperoxide produced 6-hydroxy-2-hexanone in 15% yield.12 1-Pentylmethanol hydroperoxide was rearranged to ketones in 39-65% yields. The following further rearrangements of RO· give 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 R > sec-R > primary R > methyl in both the Criegee rearrangement11 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 H2O. 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% H2SO4 gave 22 ± 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, propionylaldehyde, was shown in independent experiments in 98% H2SO4 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 propionylaldehyde alone.

Addition of butyl hydroperoxide to 80% H2SO4 for 5 min at 55° gave 60% of 1-propanol. The same 60% propyl migration was observed in 98% H2SO4 at 25° although in this higher acidity, one observes only isopropyl hydrogen sulfate, the known rearrangement of the work of 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-methylecyclopentyl, 1-methylecyclohexyl, and t-butyl hydroperoxides gave quantitative yields of the rearranged products when higher levels of acidity were employed.

The following further rearrangements have been 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.

(14) N. A. Miles and D. R. Burgess, ibid., 86, 205, 242, 243 (1944); N. A. Miles and L. H. Perry, ibid., 68, 1938 (1946).
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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.

\[ \text{RCH}_2\text{OH} \rightarrow \text{RCH}_2\text{Ot} \rightarrow \text{RCH}_2\text{OOH} \rightarrow \text{ROH} + (\text{CH}_3 \text{O}) \] (2)

It is appropriate to comment on two unsuccessful at-
ttempts to produce the BuO+ moiety from butoxyamine.
Addition to 96% HSO_4 gave an nmr spectra whose
pattern was identical with that of the original butoxy-
amine but displaced to lower fields. The spectrum
was shown to differ from that of BuOSO_3H. It is con-
cluded 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 de-
tected at pH 5 as long as butoxyamine was in excess.

The reaction is probably eq 3 though N-O formation
was not investigated.

\[ \text{C}_4\text{H}_9\text{ON}=\text{NOH} \rightarrow \text{C}_4\text{H}_9\text{O}^+ + \text{N}_2 \] (3)

Secondary Alkyl Hydroperoxides.—The acid-cata-
yzed 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-Butyl hydroperoxide gave 37% isopropyl hy-
drogen sulfate (from n-propyl migration) and 63% 2-
pentanone (from H migration). 3-Pentyl hydroper-
oxide gave 39% C_3H_7O_SO_3H and 61% 3-pentanone (all
percentages are % yields). After the statistical cor-
rection for 2 ethyl groups in the 3-pentyl derivative, the
migratory ratios of C_3H_7:H:C_3H_4 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-butanon and 22%
C_3H_6O_SO_3H. This is a slightly higher H:C_3H_4 ratio than that 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 methyl14
and H better than ethyl, the exclusive forma-
tion of acetone was anticipated.

Tertiary Alkyl Hydroperoxides.—The rearrangements of
tertiary alkyl hydroperoxides are quantitative. Typ-
ical is t-butyl hydroperoxide. Addition to 96%
HSO_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.

\[ \text{C}_4\text{H}_9\text{COOH} \rightarrow \text{C}_4\text{H}_9\text{COCH}_3 (100\%) + \text{CH}_3\text{OSO}_4\text{H} (100\%) \] (4)

We regard the above result as remarkable since it
was feared that ionization of (CH_3)_2COOH to t-C_4H_9+
would at least compete. The t-C_4H_9+ would have
yielded the complex mixture of C_4-C_8 alkanes and
C_6-C_8 cyclopentenyl cations with great rapidity.22

Even more remarkable, it was found that t-butyl al-
cohol or isobutylene could be added to H_2SO_4 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-C_4H_9OOH was used because the acetone pro-
duced was necessarily in longer contact time with
H_2SO_4 and some Baeyer-Villiger oxidation to acetic
acid and CH_3OSO_2H occurred.

The 2-methyl-2-butyl (t-amyl) system also gave
nearly as good yields by addition of the alcohol to
K_2SO_4 in sulfuric acid as by addition of the hydroper-
oxide to sulfuric acid. In 80% H_2SO_4, the latter reaction
gave 100% C_3H_7OSO_3H and 100% acetone and the
former gave 100% C_3H_6OSO_3H, 88% acetone, 6%
CH_3OSO_3H, and 6% CH_3COOH. Note that ethyl
migration occurred exclusively, illustrating the enor-
rous variation in migratory aptitudes which is such a
feature of these rearrangements.

The procedure of adding the alcohol directly to so-
lutions of K_2SO_4 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 α-hydroxy ketones exist
as cyclic oxonium ions in sulfuric acid.13 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.

\[ \text{H}_2\text{SO}_4 \rightarrow \text{H}_2\text{S}_2\text{O}_8 \rightarrow \text{CH}_3\text{COCH}_3 (100\%) + \text{CH}_3\text{OSO}_4\text{H} (100\%) \] (5)

\[ \text{H}_2\text{SO}_4 \rightarrow \text{H}_2\text{S}_2\text{O}_8 \rightarrow \text{CH}_3\text{COCH}_3 (100\%) + \text{CH}_3\text{OSO}_4\text{H} (100\%) \] (6)

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 α-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.

\[ \text{CH}_3\text{COOH} \rightarrow \text{CH}_3\text{COCH}_3 (100\%) + \text{CH}_3\text{OSO}_4\text{H} (100\%) \] (7)

Baeyer-Villiger Oxidation of Ketones.—A review of
the Baeyer-Villiger reaction1 pointed out that only one
simple aliphatic ketone had been reported and that
other peracids were preferable to H_2SO_4. It was thus of
some interest to find that solutions of K_2SO_4 in 50%
H_2SO_4 gave qualitative yields of the Baeyer-Villiger

(21) J. E. Leffler and A. Bothner-By, ibid., 73, 3473 (1951).
(22) N. Deno, D. B. Boyd, J. D. Hodge, C. U. Pittman, Jr., and J. O.
Turner, ibid., 86, 1745 (1964).
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 K$_2$SO$_4$ was used to generate H$_2$SO$_4$, addition of H$_2$O$_2$ 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% H$_2$SO$_4$) and 100 ± 1% acetic acid from 20% aqueous H$_2$SO$_4$, 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% H$_2$SO$_4$. At higher acidities the 1-propanol became increasingly subject to rearrangement and degradation20,22 so that 40–90% H$_2$SO$_4$ 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 migration22 using CF$_3$CO$_2$H in CHCl$_3$.

**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 90% H$_2$SO$_4$. 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,20,22. Although the peroxides were not distilled, the nmr spectra of the CH$_2$Cl$_2$ 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.20

The hydroperoxide rearrangements were conducted by stirring a CH$_2$Cl$_2$ solution of the hydroperoxide with the sulfuric acid at −15 to −5°. The initial mixing was generally made at −15 to −0° and the exothermicity of mixing and the reaction caused the temperature to rise.

Although eq 5 and 6 had been reported,21,22 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 3.33 (C-3 methylene), multiplet centered at 2.03 (C-4 and C-5 methylene), and triplet at 3.23 (C-6 methylene), with areas within 10% of the calculated 3:2:4:2. Dilution of the reaction mixture to 20% H$_2$SO$_4$ and addition to a solution of 2,4-dinitrophenylhydrazine in 20% H$_2$SO$_4$ gave an immediate precipitate of the DNP of 6-hydroxy-2-heptanone, mp 95–96° (lit.9,97,98).

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), triplet at 3.53 (C-3 methylene), multiplet centered at 2.05 (C-4 and C-5 methylenes), and triplet at 3.37 (C-6 methylene), with areas within 10% of the calculated 1:3:2:2:4:2:4:2:2. Dilution of the reaction mixture to 20% H$_2$SO$_4$ and addition to a solution of 2,4-dinitrophenylhydrazine in 20% H$_2$SO$_4$ gave an immediate precipitate of the DNP of 5-hydroxy-2-heptanone, mp 95–96° (lit.9,97).

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, 6065-96-8; butyl hydroperoxide, 4813-50-7; 2-pentyl hydroperoxide, 14018-58-7; 2-butyhydroperoxide, 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.

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