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THE REARRANGEMENT OF TERTIARY ALICYCLIC HYDROPEROXIDES IN ACID

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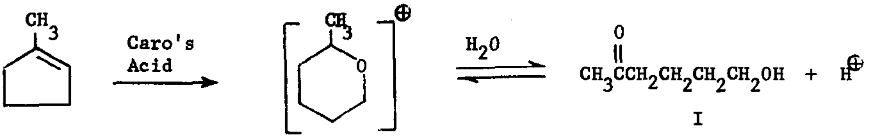
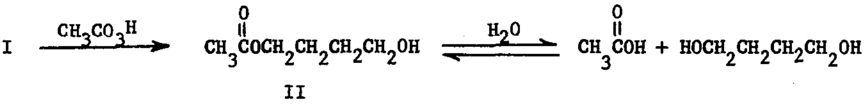
The recent paper by Deno and co-workers[1] has prompted us to report the results obtained some time ago in our laboratory regarding the rearrangement of tertiary alicyclic hydroperoxides. Rearrangements of aliphatic alkyl hydroperoxides have not been explored in much depth. Perhaps the most well-known example of such a rearrangement is exemplified by the studies of Hoffman and Boord.[2] Diisobutylene in the presence of hydrogen peroxide and 25% sulfuric acid formed 2,4,4-trimethyl-2-pentyl hydroperoxide which underwent cleavage in 70% sulfuric acid to yield acetone and 2,2-dimethylpropanol (40%). 1-Methylcyclopentyl hydroperoxide was shown to undergo rearrangement in dilute sulfuric acid at elevated temperature to give an approximately 15% yield of 6-hydroxy-2-hexanone.[3] Other products were also formed as a result of operating for two hours at a temperature between 90-100°. 1-Methylcyclohexyl hydroperoxide was shown to rearrange analogously in the presence of an acid catalyst.[4] It has also been reported[5] that methyl-substituted 1-methylcyclohexyl hydroperoxides will undergo ring opening in acid predominantly to give the corresponding ω-hydroxy ketone after hydrolysis.

Realizing the possibility of either hydroxyl-oxygen or ether-oxygen protonation (or perhaps both) and the subsequent rearrangement of these protonated species, we set out to determine if one path could be made to occur more selectively than another in the presence of strong sulfuric acid or Caro's acid ($K_2S_2O_8$ in 96% H_2SO_4). The tertiary hydroperoxide was generated *in situ* in Caro's acid starting with 1-methylcyclopentene rather than with 1-methylcyclopentanol, as was done by Deno and co-workers.[1] In close agreement with Deno and co-workers[1] the peroxy sulfate ester in Caro's acid was found to have the following nmr spectrum using tetramethylammonium chloride as the reference standard: a singlet at 2.82 δ (C-1 methyl), triplet at 3.34 (C-3 methylene), multiplet centered at 2.00 (C-4 and C-5 methylenes), and a triplet at 5.20 (C-6 methylene). Evidence for ω-hydroxy ketones of this type existing as cyclic oxonium ions in sulfuric acid has already appeared in the literature.[6] α, β-Unsaturated ketones also undergo a similar cyclization in sulfuric acid.[7] In contrast to Deno and co-workers[1], however, our nmr spectrum also contained a singlet at 2.66 δ and a broad band centered at 4.73 characteristic of an acyl methyl group and a methylene group adjacent to an ester group, respectively. This suggests that the initially formed 6-hydroxy-2-hexanone I in equilibrium with its oxonium ion, may be undergoing substantial Baeyer-Villiger oxidation (perhaps as much as 50%) to the ester II (equations 1 and 2). Furthermore, the nmr spectrum of 1-methylcyclopentene (0.2 g.) in 96% sulfuric acid containing 30% hydrogen peroxide (0.13 g.), after ten minutes at room temperature, was similar to what had been observed with the same compound in Caro's acid; in addition, however, this particular nmr spectrum offered strong evidence for the presence of Baeyer-Villiger cleavage products (i.e., acetic acid and 1,4-butanediol). Almost complete cleavage to acetic acid and 1,4-butanediol occurred upon allowing the mixture to stand overnight,[8] Figure 1.



(1)



$$\mathrm{I} \xrightarrow{CH_3CO_3H} \underset{\mathrm{II}}{CH_3\overset{O}{\overset{\|}{C}}OCH_2CH_2CH_2CH_2OH} \overset{H_2O}{\rightleftharpoons} CH_3\overset{O}{\overset{\|}{C}}OH + HOCH_2CH_2CH_2CH_2OH \qquad (2)$$

In agreement with Deno and co-workers[1], we observed no nmr evidence for methyl hydrogen sulfate, which would have been ancicipated if any methyl migration had occurred.

We have also prepared and isolated 1-methylcyclopentyl hydroperoxide and have examined its behavior in sulfuric acid. This compound undergoes a facile rearrangement to 6-hydroxy-2-hexanone, which has an nmr spectrum in 96% sulfuric acid similar to that of the cyclic oxonium ion already described. The area ratios of 3.0:2.0:4.1:1.9 were in good agreement with the calculated ratios of 3.0:2.0:4.0:2.0. The product was further characterized by its 2,4-dinitrophenylhydrazone derivative, m.p. 96-97°, lit.[3] 95-96° (Calculated for $C_{12}H_{16}N_4O_5$: C, 48.65; H, 5.40; N, 18.91. Found: C, 47.45; H, 5.44; N, 19.25).

The oxonium ion precursor, 2-methyl-5,6-dihydro(4H)pyran, was isolated by trapping via VPC from the reaction product of 1-methylcyclopentyl hydroperoxide (2.0 g.) in 25 ml. chloroform containing 1 ml. of 96% sulfuric acid. When acetylated, this pyran underwent ring-opening to give 6-acetoxy-2-hexanone, which was also formed almost quantitatively when 1-methylcyclopentyl

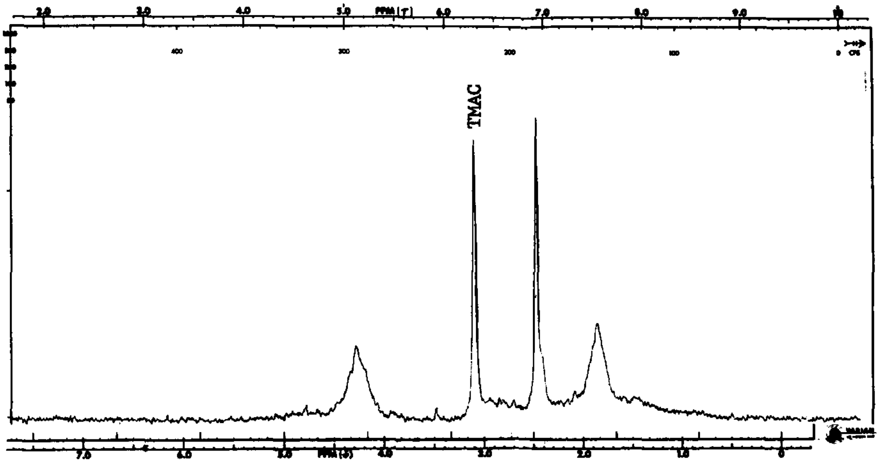


Figure 1 - NMR spectrum of 1-methylcyclopentene in 96% H_2SO_4 and 30% H_2O_2, after standing overnight (TMAC, tetramethylammonium chloride standard).

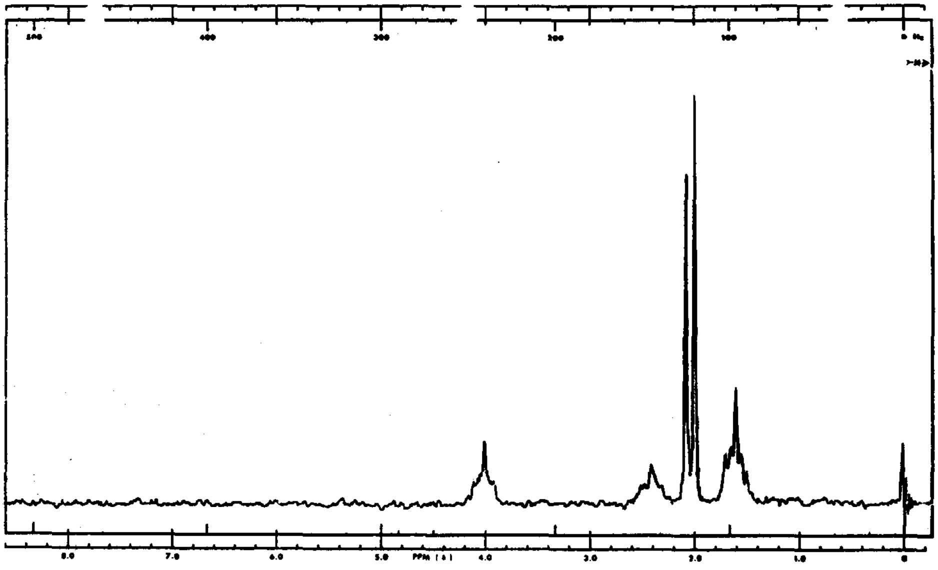


Figure 2 - NMR spectrum of 6-acetoxy-2-hexanone in CCl_4 (TMS, standard).

hydroperoxide (5.0 g.) was rearranged in glacial acetic acid (50 ml.) containing either 96% sulfuric acid (0.5 g.) or 70% perchloric acid (0.2 g.) as catalysts. The nmr spectrum of the acetate derivative in CCl_4, Figure 2, contained a singlet at 2.09 δ (C-1 methyl), triplet at 2.43 (C-3 methylene), multiplet centered at 1.61 (C-4 and C-5 methylenes), triplet at 4.10 (C-6 methylene), and a singlet at 1.98 (C-8 methyl). The area ratios were within 5% of the calculated values of 3:2:4:2:3.

Both 1-methylcyclohexyl hydroperoxide and 1-ethylcyclopentyl hydroperoxide were also shown by nmr to undergo facile rearrangement in acetic acid containing sulfuric acid to give the corresponding ω -acetoxy ketone products.

Acknowledgement

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REFERENCES

1. N. C. Deno, W. E. Billups, K. E. Kramer and R. R. Lastomirsky, J. Org. Chem., 35, 3080 (1970).
2. J. Hoffman and C. Boord, J. Amer. Chem. Soc., 77, 3139 (1955); J. Hoffman, Org. Syn., 40, 76 (1960).
3. E. G. E. Hawkins, J. Chem. Soc., 2801 (1950).
4. W. Pritzkow and K. A. Muller, Chem. Ber., 89, 2321 (1956).
5. F. F. Rust and E. R. Bell, U.S. Pat. 2,717,264 (to Shell Development Co.), Sept. 6, 1955.
6. C. U. Pittman, Jr. and S. P. McManus, J. Amer. Chem. Soc., 91, 5917 (1969).
7. C. U. Pittman, Jr. and S. P. McManus, Chem. Commun., 1479 (1968).
8. R. R. Lastomirsky (Ph.D. Dissertation, Pennsylvania State University, 1969) found by nmr that after one month, 6-hydroxy-2-hexanone had disappeared and acetic acid (36%) and an unknown material (1.0 - 2.3 δ , broad complex, 4.48, broad flat peak) similar to that formed from 1,4-butanediol and H_2SO_5 after standing for one month accounted for the remaining area. Our results with 1,4-butanediol in 96% sulfuric acid indicate that after a period of one week substantial cyclization to tetrahydrofuran occurs, giving an nmr spectrum which includes a multiplet centered at 4.45 δ (C-1 and C-4 methylenes) and another multiplet centered at 2.32 (C-2 and C-4 methylenes). Tetrahydrofuran in 77% sulfuric acid gave an nmr spectrum which contained this same pattern, taking into account the solvent shift.