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THE FACILE AIR OXIDATION OF VIC. CYCLOPROPANEDIOLS

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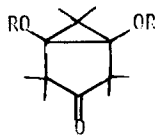
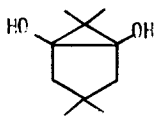
In our preliminary account of the synthesis of vic-cyclopropanediols[1] we noted that these compounds are readily oxidized to diketones by the action of oxygen. DePuy and Gibson have recently reported[2] a similar oxidation of cyclopropanols; and in this light we wish to present additional facts which allow us to rationalize this remarkable reaction.

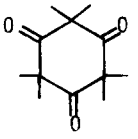
The vic-cyclopropanediols appear to be much more reactive toward oxygen than are cyclopropanols. Thus, an ethyl acetate solution of I absorbed one molar equivalent of oxygen in 30-60 minutes*, giving V as the sole product (ca. 95% yield); and IV was readily oxidized to 2,2,5,5-tetramethylcyclohexane-1,3-dione even in the solid state.



I R = H
II R = CH_3
III R = CH_3CO



IV



V

The absorption of oxygen by solutions of I was easily followed with the aid of a small gas buret, and the formation of a peroxide containing product was determined by iodometry. The results from several dozen experiments show considerable variation: oxygen uptake was 70-95% of theoretical (assuming a 1:1 stoichiometry) and the peroxide concentration always ran a bit lower. Since the gasometric and iodometric measurements correponded more closely during the early stages of the oxidation, it appears that the peroxide suffered a slow decomposition.

*This should be compared with the 24-48 hr. time reported for the oxidation of methyl substituted cyclopropanols in hexane[2].

Other facts germane to this reaction are:

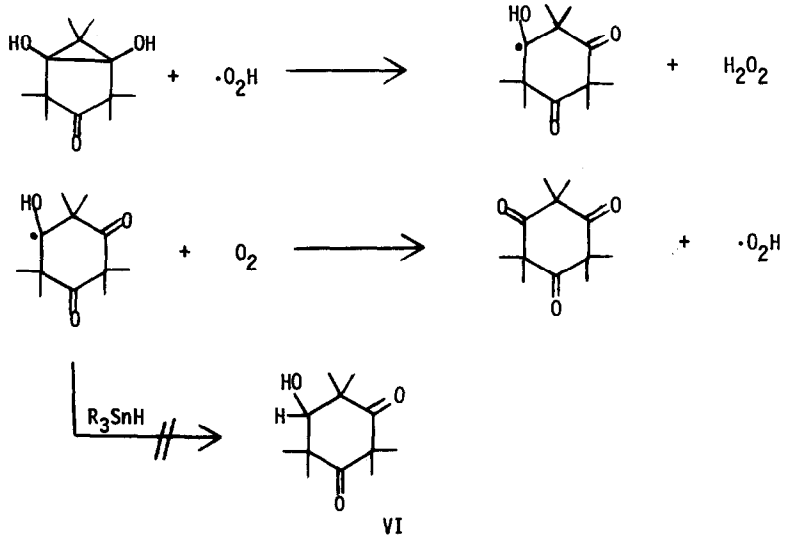
1) A short induction period (ca. 5 min.) was normally observed.

2) The oxidation of I to V could also be effected by nitric oxide; however, the stoichiometry was complex (ca. 1:3.5 respectively). A transient blue color was noted in these reactions, but no intermediates could be isolated.

3) The dimethyl ether (II) and diacetate (III) derivatives of I were not affected by prolonged exposure to oxygen or nitric oxide.

These facts suggest that the reaction of vic. cyclopropanediols with oxygen proceeds by a radical mechanism (equation 1) similar to that proposed by Gibson and DePuy[2]. The opening of the three membered ring is shown to be concerted with hydrogen abstraction in order to rationalize the reactivity order: vic.-cyclopropanediol>cyclopropanol>>other cyclic 3°-alcohols.

(1)

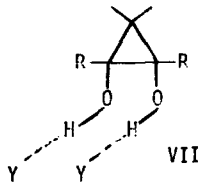


VI

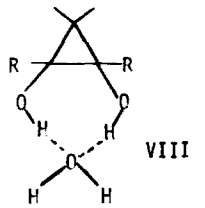
Numerous attempts to trap the intermediate carbinol radical by conducting the oxidation of I in solvent mixtures having large mole excesses of tri-n-butylstannane or triphenylstannane were all unsuccessful. The conversion of I to V proceeded at the customary rate and gave no detectable VI (as little as 0.5% VI could have been detected by our infrared and nmr analysis). These results suggest that carbinol radicals are oxidized by molecular oxygen with extraordinary ease; indeed, a similar oxygen effect was reported by Pitts et.al.[3] in their study of the photoreduction of benzophenone.

When three molar equivalents of p-chlorothiophenol was added to a solution of I in ethyl acetate, the oxidation to V was completely stopped (ie. no change in the concentration of I and no uptake of oxygen was detected over a 24 hr. period). The reasons for this behavior are not clear at this time. It may be that the thiophenol scavanges hydroperoxy radicals so effectively that the chain reaction cannot function (this explanation implies that molecular oxygen does not itself significantly attack cyclopropanols). Alternatively, thiophenol inhibition may be due to the hydrogen bonding effect discussed in the following paragraph.

In the course of these studies we noted a curious solvent effect on the rate of oxidation of I: $CH_3CO_2C_2H_5 > CH_3COCH_3 > C_2H_5OH >> Pyridine, DMSO$.
The time required for a test solution to absorb greater than 90% of the stoichiometric amount of oxygen ranged from 30-60 min. for ethyl acetate and acetone to 24-48 hr. for pyridine and DMSO. A similar reactivity order was observed for nitric oxide oxidations. In addition, small amounts of DMSO were observed to inhibit oxidations in ethyl acetate solution. We suggest that these facts can be explained by hydrogen bonding of the cyclopropanol hydrogen atoms. Since intramolecular hydrogen bonding is precluded by the molecular geometry of the vic.-cyclopropanediols, intermolecular bonding, as in VII, can occur when strong hydrogen bond acceptors (eg Y = DMSO, pyridine) are present in the reaction mixture. These interactions apparently render radical attack at O-H more difficult.



VII



VIII

Compound I also forms a hydrate[4], which we presume has a cyclic hydrogen bonded structure similar to VIII. We find that solutions of this hydrate in ethyl acetate are oxidized much more slowly than pure I.

Acknowledgement: We thank the National Institutes of Health for their support of this work.

References

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(2) D. H. Gibson and C. H. DePuy, Tet. Letters, 2203 (1969).

(3) 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).

(4) W. Reusch and D. B. Priddy, J. Am. Chem. Soc., 91, 7556 (1969).