Tetrahedron Letters,Vol.30,No.41,pp 5567-5570,1989 0040-4039/89 $3.00 + .00
Printed in Great Britain Pergamon Press plc

Dimethyldioxirane: Mechanism of Benzaldehyde Oxidation

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Summary: Under inert atmosphere, dimethyldioxirane **1** converts benzaldehydes solely to the corresponding acids; the reaction is insensitive to electronic effects; yields are limited by the competing decomposition of **1** to acetol; O_2 trapping of free-radical intermediates is observed.

Dioxiranes, three-membered cyclic peroxides, are of interest (in part) because of high reactivity in oxygen-atom transfer chemistry.[1] Based on kinetics, stereochemical and labeling data, Edwards and Curci concluded[2] that dimethyldioxirane was the active oxygen-atom transfer species in the peroxymonosulfate (oxone)/acetone system. Recent work[3] has shown that dioxiranes are isolable by low-temperature distillation. Characterization of dioxiranes has been accomplished[3-5] by physical and spectroscopic methods. Dimethyldioxirane **1** has been shown to be useful for the oxidation of many classes of organic compounds.[1] We have investigated[6] the mechanism of epoxidation by **1**. Oxygen-atom insertion reactions into C-H bonds by dioxirane **1** have been reported.[7] The Baeyer-Villiger type oxidation of acetaldehyde[3] by **1** has been noted. Despite the current interest, relatively few mechanistic investigations have been carried out. We report here a study of the oxidation of benzaldehydes by dimethyldioxirane **1** which provides new insights into the mechanisms of oxidation by **1** and the limitations of stability of this versatile reagent.

The reaction of one equivalent of dimethyldioxirane **1** in acetone with a series of substituted benzaldehydes **2a-f** (at ambient temperature, in the dark, open to the atmosphere) slowly (18 hr) produced the corresponding benzoic acids **3a-f** (reaction 1). For the *p*-anisaldehyde (**2a**) case, ~10% *p*-anisyl formate was found as the minor product. No minor, aldehyde-derived products were detected for reactions of **1** with

(1)

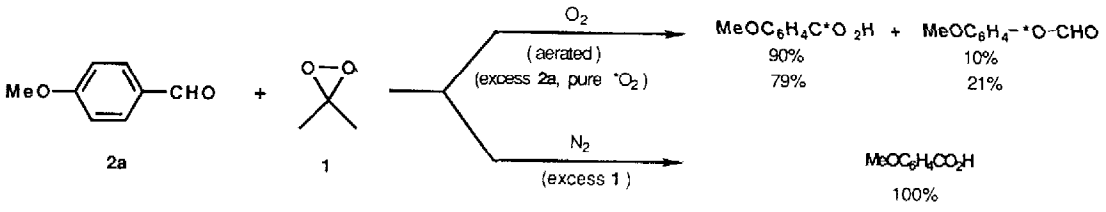
1 **2** **a** = MeO; **b** = Me; **c** = H; **d** = Br; **e** = CN; **f** = NO_2 **3** **a - f**

2b-f. For **2a-c**, 90+% yields of the corresponding acids were obtained. In addition, no starting materials could be detected. For **2d-f** after complete loss of **1**, variable yields of the corresponding acids were obtained (generally 60-70%), with the remaining materials being unreacted aldehydes. However, under inert atmosphere (argon or N_2), the reaction of **1** with **2a, c, d, f** produced the corresponding acids in only 52±8% yield after complete disappearance of dioxirane. When a 3 to 4-fold excess of **1** (argon) was employed, the carboxylic acids were obtained in quantitative yield for all cases.

To maximize the effect of oxygen on reaction 1, the oxidations were carried out under an atmosphere of pure ^{17}O-enriched oxygen. The reactions were faster than those open to the atmosphere and more than

one equivalent of aldehyde could be oxidized. For example, the reaction of **1** with **2a** (2-3 fold excess) carried out under pure ^{17}O-enriched oxygen, resulted in complete conversion of the aldehyde to the acid (79%) and *p*-anisyl formate (21%) (Scheme 1). Furthermore, ^{17}O NMR spectroscopy showed that both the

Scheme 1



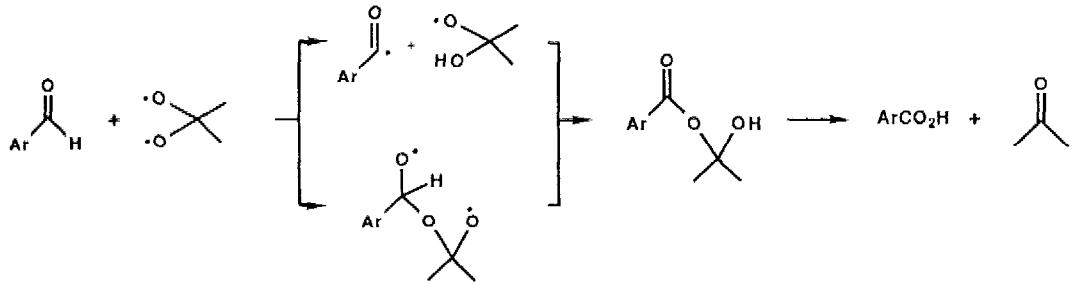
carboxylic acid (δ 246)[8] and the formate contained ^{17}O-enriched oxygen but that the formate was enriched only at single-bonded ester oxygen (δ 198).[9] Oxidation of the other benzaldehydes by **1** in the presence of ^{17}O-enriched oxygen yielded carboxylic acids that contained ^{17}O-enrichment.

In the presence of O_2, aldehydes with electron-donating groups appeared to be more reactive in reaction 1 than those with electron-withdrawing groups. However, under argon, where dioxirane 1 was the sole oxygen-atom source, the yield of carboxylic acid seemed to depend on the stability of dioxirane **1** rather than the electronic nature of the aldehyde. Competitive product studies under argon to 50% conversion gave the following relative reactivity series: *p*-anisaldehyde (**2a**) 1.1 > benzaldehyde (**2c**) 1.0 > *p*-bromobenzaldehyde (**2d**) 0.9, which showed that the reaction is relatively insensitive to electronic effects. Furthermore, the relative reactivity series suggests that reaction 1 would have a small, negative rho value. This result is in the opposite direction from that obtained (rho=+1-2) for oxidation of benzaldehydes by perbenzoic acid.[10] Thus, mechanistically, reaction 1 appears to be unrelated to the Baeyer-Villiger reaction.

For the Baeyer-Villiger oxidation of *p*-anisaldehyde **2a** by perbenzoic acid,[10] *p*-methoxyphenol (from hydrolysis of *p*-anisyl formate) is the major product under neutral or acidic conditions. However, no aryl migration is observed for the oxidation of **2a** by **1** under inert atmosphere. In addition, ^{17}O-labeling experiments showed that molecular oxygen was required for the production of p-anisyl formate in the dioxirane case. The results clearly show that reaction 1 is not a routine Baeyer-Villiger reaction and that at least two pathways are involved.

The unusual characteristics observed in reaction 1 appear indicative of a free-radical process. Under inert atmosphere, abstraction of the aldehyde hydrogen-atom by dioxirane 1,3-diradical would yield a caged radical pair, the combination[1b] of which would produce the unstable "hemi-ketal" of the carboxylic acid and acetone. Likewise, addition of the dioxirane 1,3-diradical to the carbonyl following intramolecular hydrogen-atom abstraction could also produce the unstable "hemi-ketal" intermediate of the observed products. The intermolecular, hydrogen-abstraction route is consistent with the observation[3a] by Murray that ozonide was not produced during the oxidation of acetaldehyde. Direct insertion[1b] of the oxygen-atom from 1 or opening of the dioxirane to the carbonyl oxide can not be ruled out but seems less likely. The diradical pathway proposed for benzaldehyde oxidation under inert atmosphere by 1 is depicted in Scheme 2.

Scheme 2



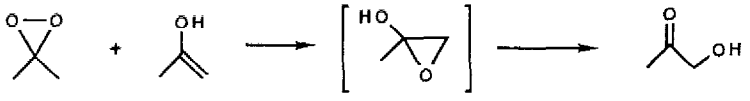
Sawaki has recently shown[11] that esters formed during the photooxidation of diazo compounds may arise via a radical chain mechanism or (in certain cases) a Baeyer-Villiger oxidation by carbonyl oxide intermediates. In the present case, the O_2 trapping experiments can be accommodated by the proposed mechanism shown in Scheme 2 if initial hydrogen-atom abstraction is the favored route. Molecular oxygen should trap (competitively) the benzoyl radical to yield the benzoyl peroxy radical. Subsequent hydrogen-atom abstraction from benzaldehyde by the peroxy radical would yield perbenzoic acid and regenerate the benzoyl radical. The perbenzoic acid would undergo the normal Baeyer-Villiger reaction with the remaining benzaldehyde and yield an addition equivalent of benzoic acid. The results of $^{17}O_2$-labeling experiment for **2a** are consistent with this argument. Sole enrichment of the single-bonded ester oxygen in *p*-anisyl formate as well as ^{17}O-enriched acid would be the result of the Bayer-Villiger oxidation of **2a** by ^{17}O-labeled peracid (generated *in situ*).

In cases, under equal-molar conditions, where aldehyde was recovered, the corresponding equivalents of dioxirane **1** could not be detected. The "unreacted" dioxirane had apparently undergone "thermal" decomposition. Control experiments were carried out to determine the products of this decomposition. Freshly prepared solutions of 0.1 *M* **1** in acetone were stable at low temperature but underwent slow decomposition (18-24 hr) at room temperature. Analysis of the "spent" dioxirane solutions showed acetol (α-hydroxyacetone) to be the major, observable product. No acetone diperoxide (3,3,6,6-tetramethyl-1,2,4,5-tetraoxixane) could be detected[1b] as a decomposition product under the conditions of our experiments. Varying amounts of methyl acetate were also noted in the "spent" solutions; however, methyl acetate was found to be present in the solution before decomposition. Presumably, the methyl acetate co-distilled with the dioxirane during the isolation procedure. No detected increase in the quantity of methyl acetate present was observed. Acetol polymerized slowly under the reaction conditions and readily during isolation procedures. Authentic samples could not be recovered unchanged. Acetol was identified by spectroscopic methods and by conversion to the DNP derivative.

The disappearance of **1** at room temperature showed an inhibition period and was found not to be of the first or second order in agreement with observations reported by Murray.[3] Dioxirane-d_6 solutions in acetone-d_6 were more stable than those of **1** in acetone: addition of base (aq. KOH) to either resulted in the rapid zero order decomposition of dioxirane ($k_H/k_D \sim 4$). In addition, solutions of **1** were found to be sensitive to glass surfaces that had been treated with base. Addition of one equivalent of acetic acid to **1** in acetone had a lesser effect on dioxirane stability. The characteristics of the catalyzed decomposition of **1** suggested

that the enol of acetone may be involved. A possible mechanism to explain the generation of acetol would involve the (rapid) epoxidation of the enol of acetone followed by facile rearrangement (Scheme 3) to the

Scheme 3



observed product. This suggests that solutions of **1** in acetone are enol-free and that the stability of **1** is limited by the rate of enolization of acetone under the reaction conditions. However, this does not rule out the generation of acetol by direct insertion or free-radical processes for non-catalyzed cases. The thermal decomposition of **1** is difficult to detect and prove. Methyl trifluoroacetate has been shown[12] to be the product of the thermal decomposition of methyl(trifluoromethyl)dioxirane. The nature of the thermolysis products from **1** await further experimentation.

In conclusion, the data indicate that oxidation of aldehyde by **1** involves intermolecular, hydrogen-atom abstraction to generate a caged radical pair. Despite an extremely low activation energy for hydrogen-atom abstraction from aldehydes, extrapolation of the results suggests that C-H activation[7] by dioxirane **1** may involve a similar abstraction process. A caged radical pair could explain the unusual stereochemical behavior observed[7] for oxidation of decalins and 1,2-dimethylcyclohexanes. If correct, C-H activation experiments with **1** should be carried out under inert atmosphere, especially if relatively stable radicals can be generated. The stability of **1** in acetone can be limited by the rate of enolization of the solvent.

Acknowledgment is made to the National Science Foundation (CHE-8506665) for partial support of this work.

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(Received in USA 14 July 1989)