Notes

Epoxidation of Alkenes by Dioxirane Intermediates Generated in the Reaction of Potassium Caroate with Ketones

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Received April 28, 1980

Kinetics and ¹⁸O-labeling experiments have provided evidence for the involvement of dioxirane intermediates 2a (Scheme I) in the ketone-catalyzed decomposition of potassium peroxomonosulfate (KHSO₅, hereafter called caroate).¹⁻³

It has been shown that, under the reaction conditions (in water, pH 7.5, 2–10°C), the side reaction involving Bayer-Villiger (BV) oxidation of the ketone (path iii) is negligible with most ketones (acetone, dialkyl ketones, lysis of carboxylate decomposition, the dioxirane intermediate substrates). Evidence for the involvement of dioxirane intermediates 2a, by analogy with the caroate-acetone system as a generalized epoxidation method. These are shown in Table I.

In competition with path i, amounting to ketone catalysis of caroate decomposition, the dioxirane intermediate is capable of oxidizing nucleophilic organic and inorganic substrates (Sₙ, path iii).¹⁻³ As an example, oxidation of phenylpropionic acid, PhC=CHCO₂H, a substrate representative of weakly nucleophilic alkenes, could be achieved by the caroate–ketone system;² this is indicative of the high reactivity of intermediate 2a, as the mentioned alkyne resisted all attempts at oxidation by peroxoacids (as well as by caroate in absence of ketones) under the given conditions. Similarly, trans-cinnaminic acid (3a) failed to react with alkaline hydrogen peroxide, m-chloroperoxybenzoic acid (MCPBA) in CH₂Cl₂ or with caroate alone;² however, as we have already reported, reaction of 3a with caroate-acetone in water affords the trans-epoxide 5b in high yield. As the cis-epoxide 4b could also be obtained in high yield upon reaction of cis-cinnamic acid (4a) with caroate-acetone, the reaction appears to be highly stereospecific.²

We report here further data which illustrate the versatility of the caroate–acetone system as a generalized epoxidation method. These are shown in Table I.

The synthesis of 4,5-epoxy-2-hexenoic acid (5b) in high yield, as the sole reaction product from sorbic acid (5a), shows that epoxidation via dioxirane can be remarkably regioselective. Notice that the sorbic acid 4,5 double bond, which is more nucleophilic, is selectively oxidized. Treatment of 5-hexen-2-one (6a) with caroate and acetone also affords the corresponding epoxide in high yield. It is not surprising, in this case, that caroate in the absence of acetone can also convert the alke in the epoxide in high yield (although substrate conversion is lower). In fact, 6a possesses within the same molecule both an olefinic double bond to be oxidized and the ketone carbonyl group, which clearly can be an efficient substitute for acetone as a dioxirane precursor. Noteworthy is the fact that similar to MCPBA oxidation of unconjugated olefinic ketones, no BV products are generated in this reaction.

For the four alkenes in Table I, the entries illustrate the fact that the caroate–acetone system can be employed to epoxidize olefins which are insoluble in aqueous media by using a benzene-buffered water biphasic system under conditions of phase-transfer catalysis (PTC).¹ In a typical procedure, a solution of caroate in water is added dropwise to a well-stirred biphasic mixture of benzene and buffer (pH ca. 7.5) water at 6°C containing acetone, the alkene, and catalytic amounts of 18-crown-6 as a phase-transfer catalyst (see Experimental Section). Reaction time depends, inter alia, upon alkene structure and the amount of the phase-transfer catalyst used.

The cyclohexene entries B'' and B''' show that tetra- butylyl ammonium hydrogen sulfate can be used instead of 18-crown-6 as the phase-transfer catalyst in the epoxidation.

Similar to the results of olefinic epoxidation by peroxoacids⁶ or by O-alkyloxycarbonylic acids,⁷ a somewhat lower alkene conversion and epoxide yield is achieved with 1-dodecene (9a, a terminal carbon–carbon double bond olefin) when compared with the excellent yields observed in cycloalkene PTC epoxidations.

Finally, the results in Table I show that epoxidation of trans-cinnaminic acid (3a) by caroate–acetone can also be accomplished under PTC conditions.

It is likely that, along with other recent methods,⁶⁻⁹ the herein reported technique of olefin epoxidation by dioxiranes constitutes a new entry into epoxide synthesis. In fact, no systematic efforts were made to optimize epoxide yields by varying systematically reaction conditions, solvents, and reactant-to-catalyst ratios. Yet, the fact that a variety of olefins, water-soluble or insoluble, isolated or carrying diversified functionalities (i.e., α,β-unsaturated carboxylate, conjugated diene carboxylate, and olefinic ketone carbonyl), could all be converted into their corresponding epoxides demonstrates the versatility of this method. Often, the facile opening of the epoxide ring is among the major problems encountered in the synthesis of epoxides which are sensitive to temperature and/or to acid and base.⁹,¹⁰ The method reported here appears to be especially valuable in dealing with such problems for it can provide efficient epoxidation under very mild conditions, i.e., low temperature (2–10°C) and near neutrality (pH 7–8). The synthesis of 4b illustrates this. This oxirane

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⁴ Gokel, G. W.; Durst, H. D. Synthesis 1976, 168; see the references therein.
Table I. Catalysis by Acetone and by Phase-Transfer Agents in the Epoxidation of Alkenes by Caroate

<table>
<thead>
<tr>
<th>alkene</th>
<th>methoda</th>
<th>reacn time, h</th>
<th>alkene conv, %</th>
<th>product</th>
<th>% yieldb</th>
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<td>Ph CO2H</td>
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<td>99.0</td>
<td>Ph CO2H</td>
<td>95.0</td>
</tr>
<tr>
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<td>&lt;0.1</td>
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<td>98.0</td>
<td>Ph CO2H</td>
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<tr>
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<td>CO2H</td>
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<td>72.0</td>
</tr>
</tbody>
</table>

a A, potassium caroate and acetone in water (pH 7.0-7.5, at 2-8 °C); A', same as A but no acetone present; B, caroate and acetone in ca. 1:1 benzene-water (pH 7.5, phosphate buffer) with 18-crown-6 as PTC; B', same as B, but no acetone present; B'', same as B, but Bu,N+HSO,- used as PTC instead than 18-crown-6; B''', same as B', but CH,Cl, used instead of benzene in the biphasic system.

b Yields calculated on the basis of isolated epoxide and alkene reacted, unless noted otherwise.

c Yields determined by GLC. d Sample consisted of a mixture of E and Z stereomers.

is sensitive to acid, base, and temperatures above 50 °C,3 and yet it could be synthesized in high yield by the present method.

As an alternative to dioxirane 2a, the reactive intermediate responsible for epoxidation may also be envisaged as having “carbonyl oxide” structure 2b or singlet biradical methylene peroxide structure 2c.11,12 It has been reported that carbonyl oxides produced under nonozonolysis conditions can act as epoxidizing agents.12a In this case, however, epoxide yields are rather low, and the reaction appears to be only partially stereospecific, which contrasts with the high stereospecificity observed in the epoxidation by the caroate-ketone system. Thus, on the grounds of this and other evidence,2 it appears that the dioxirane ring structure is more suitable at this point for the reactive intermediate arising in the reaction of caroate with ketones. Further studies on this and related systems are now in progress.

Experimental Section

General Methods. Boiling points and melting points were not corrected. 1H NMR spectra were run on Varian E360A or A-60A instruments. IR spectra were taken on a Perkin-Elmer 257 or 177 instrument. GLC experiments were performed on a Hewlett-Packard 5750B (TC detector) or 5700A (FID), using either a 15 ft × 1/4 in. 20% Carbowax 20M on Ditaapor S or a 16 ft × 1/8 in. 5% FFAP on Chromosorb G AW-DMCS column. Mass spectra were obtained by using a Hitachi RMU-6D spectrometer. The pH and pH stat experiments were performed by using a Radiometer (TTT1b/SBR2c) or Metrohm (E336A) potentiograph.

Materials. 18-Crown-6 was prepared as described by Gokel et al.,13 tetrabutylammonium hydrogen sulfate (Aldrich) and the solvents were purified by standard methods. The procedure for (Z)-3-phenylpropenoic acid (4a) has been described,2 (E)-3-Phenylpropenoic acid (3a), 2,4-hexadienoic acid (5a), 5-hexen-2-one (6a), cyclohexene (7a), 1-dodecene (9a), etc.
and epoxides 7-oxabicyclo[4.1.0]heptane (7b), 13-oxabicyclo-[10.1.0]tridecan (8b) were commercial products (Aldrich) and were purified by reported methods. 1,2-Epoxydodecane [9b; bp 99-101 °C (4 mm), lit.14 bp 106-109 °C], prepared by method B, gave spectra identical with samples of the same compound prepared by given procedures.14 Both (E)- and (Z)-3-phenoxylinicarboxylic acids 3b and 4b have been described.

4,5-Epoxy-2-hexenoic acid (5b) was obtained by following method A2 and was recrystallization from CCl4/n-hexane: mp 80-82 (61%, 72 (9), 58 (41, 1.7%); IR (Nujol) 2930, 2670, 2500, 1697, 1654, 1292, 965, 825 cm-1; 'H NMR (CDCl3) 6 1.74-2.03 (m, 5 H), 2.33-2.72 (m, 4 H), 2.09 (s, 3 H), 1.65-1.92 (m, 2 H); mass 160.4.


5,6-Epoxy-2-hexanone (6b) was also obtained by following method A, a freshly prepared solution of potassium peroxomonomosulfate (24 mmol) in water15 is added dropwise (during 2-4 h) to a well-stirred biphasic mixture of benzene-hexane-Et20, 4:1), affording 0.79 g (4.34 mmol, 85% yield) of 3b.

The anion X- is adjusted to 7.5, and it is maintained at this value during the reaction mixture is then acidified (at 2 °C) to pH ca. 3 by the competing peroxide autodecomposition.2 The most important steps of this mechanism are shown in Scheme I.

**Scheme I**

(1) (ArX)- → Ar- + X-

(2) (ArX)- + ArX → ArNu + (ArX)-

The fact that such a variety of substrates and nucleophiles is suitable for this reaction, giving in many cases an excellent yield of substitution product, prompted us to explore the possibility of using this reaction to obtain polymers.5 Two different approaches were used: (1) the reaction of an aromatic substrate bearing two leaving groups and a nucleophile having more than one nucleophilic center was studied; (2) the reaction of a substrate having both the leaving group and the nucleophilic center within the same molecule was also studied.

**Results and Discussion**

**Method I. p-Dihalobenzenes (1) were allowed to react with ketone enolate ions 2 under photostimulation6 (eq 4)**

\[ p-XC6H4\text{COR} + CH_3\text{COR} \rightarrow p-\text{RCOCH}_2\text{CH}_2\text{COR} \]

**3b**

(1a, X = Y = Cl) 2a, R = Me

(1b, X = Y = Br) 2b, R = CMe3

(1c, X = Br, Y = I) 2c, R = CMe5

with an excess of potassium tert-butoxide to ionize the disubstitution product formed (eq 5). The anion 4 was expected to act as a nucleophile that could react further with aryl radicals to produce an oligomeric and/or polymeric product.

In the photostimulated reaction of 1a with a large excess of 2a or 2b, the chloride ion was eliminated to the extent of 83 and 95%, respectively, and a 65% yield of 3b was isolated (see Experimental Section). In the photostimulated reaction of 1a with 2a or 2b and potassium tert-butoxide in a ratio 1:1:4, the yield of chloride ion was 25-50% (theoretical 100% considering two chlorine atoms per molecule of 1a). In the dark there is no reaction (Table I).

The yield of chloride ion indicates that the photostimulated reaction does not proceed to completion, since

2. As a 0.04 M standard solution (isodimetric titers) of potassium peroxomonomosulfate obtained by dissolving Oxone (Du Pont Co.) and EDTANa (ca. 4 x 10-4 M), to prevent trace-metal-catalyzed peroxide decomposition in doubly distilled water. Bicarbonate is used in the competing peroxide autodecomposition.