

# Notes

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

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Kinetics and  $^{18}\text{O}$ -labeling experiments have provided evidence for the involvement of dioxirane intermediates **2a** (Scheme I) in the ketone-catalyzed decomposition of potassium peroxomonosulfate ( $\text{KHSO}_5$ , hereafter called caroate).<sup>1-3</sup>

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, acetophenones, etc.), whereas it becomes significant at lower pH values or with ketones having certain structural features (e.g., cyclobutanone, cyclopentanone).<sup>1-3</sup>

In competition with path i, amounting to ketone catalysis of caroate decomposition, the dioxirane intermediate is capable of oxidizing nucleophilic organic and inorganic substrates (S; path ii).<sup>1-3</sup> As an example, oxidation of phenylpropionic acid,  $\text{PhC}\equiv\text{CCO}_2\text{H}$ , a substrate representative of weakly nucleophilic alkynes, could be achieved by the caroate–ketone system;<sup>2,3</sup> this is indicative of the high reactivity of intermediate **2a**, as the mentioned alkyne resisted all attempts at oxidation by peroxyacids (as well as by caroate in absence of ketones) under the given conditions. Similarly, *trans*-cinammic acid (**3a**) failed to react with alkaline hydrogen peroxide, *m*-chloroperoxybenzoic acid (MCPBA) in  $\text{CH}_2\text{Cl}_2$  or with caroate alone;<sup>3</sup> however, as we have already reported, reaction of **3a** with caroate–acetone in water affords the *trans*-epoxide **3b** in high yield. As the *cis*-epoxide **4b** could also be obtained in high yield upon reaction of *cis*-cinammic acid (**4a**) with caroate–acetone, the reaction appears to be highly stereospecific.<sup>2</sup>

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 alkene into 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).<sup>4</sup> In a typical procedure, a solution of caroate in water is added dropwise to a well-stirred biphasic mixture of benzene and buffered (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 tetrabutylammonium 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 peroxyacids<sup>5</sup> or by *O*-alkylperoxyacetic acids,<sup>6</sup> 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*-cinammic acid (**3a**) by caroate–acetone can also be accomplished under PTC conditions.

It is likely that, along with other recent methods,<sup>6-9</sup> the herein reported technique of olefin epoxidation by dioxirane intermediates 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.,  $\alpha,\beta$ -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.<sup>9,10</sup> 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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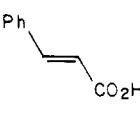
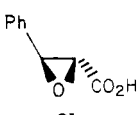
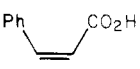
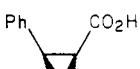
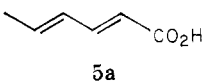
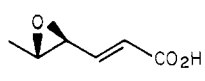
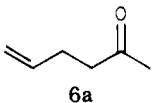
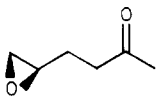
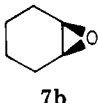
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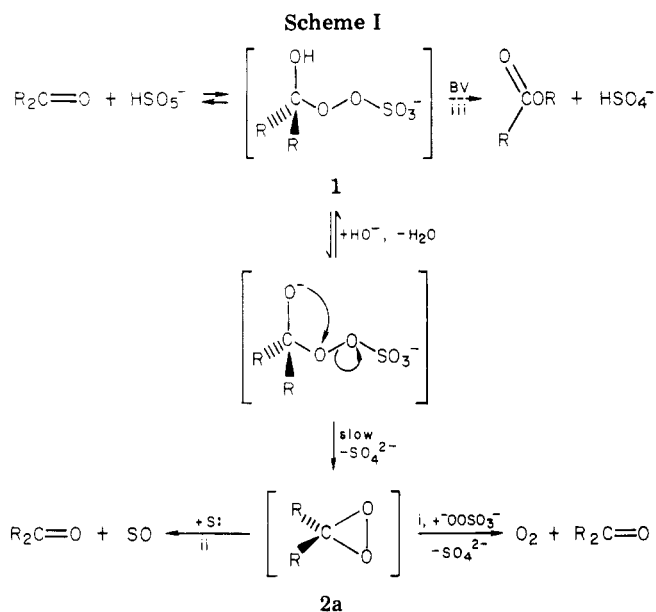
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Table I. Catalysis by Acetone and by Phase-Transfer Agents in the Epoxidation of Alkenes by Caroate

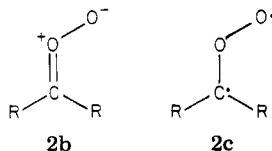
alkene	method <sup>a</sup>	reacn time, h	alkene conv, %	product	% yield <sup>b</sup>
 3a	A	2.3	99.0	 3b	95.0
	A'	5.0	<1.0		<0.1
	B	3.0	98.0		92.0
 4a	A	3.5	90.0	 4b	>90.0
 5a	A	2.0	99.0	 5b	86.0
 6a	A	2.0	99.0	 6b	97.0 <sup>c</sup>
	A'	2.0	52.0		96.0 <sup>c</sup>
cyclohexene (7a)	B	3.0	80.0	 7b	98.0 <sup>c</sup>
	B'	6.0	<2.0		<0.1 <sup>c</sup>
	B''	4.0	70.0		45.0 <sup>c</sup>
	B'''	4.0	97.0		80.0 <sup>c</sup>
cyclododecene <sup>d</sup> (8a)	B	3.0	90.0	1,2-epoxycyclododecene <sup>d</sup> (8b)	85.0
1-dodecene (9a)	B	3.0	60.0	1,2-epoxydodecene (9b)	72.0

<sup>a</sup> 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<sub>4</sub>N<sup>+</sup>HSO<sub>4</sub><sup>-</sup> used as PTC instead than 18-crown-6; B''', same as B'', but CH<sub>2</sub>Cl<sub>2</sub> used instead of benzene in the biphasic system. <sup>b</sup> Yields calculated on the basis of isolated epoxide and alkene reacted, unless noted otherwise. <sup>c</sup> Yields determined by GLC. <sup>d</sup> Sample consisted of a mixture of *E* and *Z* stereoisomers.



is sensitive to acid, base, and temperatures above 50 °C,<sup>3</sup> 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**.<sup>2,11,12</sup> It has been reported



that carbonyl oxides produced under nonozonolysis conditions can act as epoxidizing agents.<sup>12a</sup> 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,<sup>2</sup> 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. <sup>1</sup>H 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 Diatoport 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 p<sup>H</sup> 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.,<sup>13</sup> tetrabutylammonium hydrogen sulfate (Aldrich) and the solvents were purified by standard methods. The procedure for (*Z*)-3-phenylpropenoic acid (**4a**) has been described.<sup>2</sup> (*E*)-3-Phenylpropenoic acid (**3a**), 2,4-hexadienoic acid (**5a**), 5-hexen-2-one (**6a**), cyclohexene (**7a**), cyclododecene (**8a**), 1-dodecene (**9a**),

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and epoxides 7-oxabicyclo[4.1.0]heptane (**7b**), 13-oxabicyclo[10.1.0]tridecane (**8b**) were commercial products (Aldrich) and were purified by reported methods. 1,2-Epoxydodecane [**9b**; bp 99–101 °C (4 mm), lit.<sup>14</sup> bp 106–109 °C (6 mm)], prepared by method B, gave spectra identical with samples of the same compound prepared by given procedures.<sup>8,14</sup> Both (*E*)- and (*Z*)-3-phenyloxiranecarboxylic acids **3b** and **4b** have been described.

**4,5-Epoxy-2-hexenoic acid (5b)** was obtained by following method A<sup>2,3</sup> and was recrystallized from CCl<sub>4</sub>/*n*-hexane: mp 81–83 °C; IR (CS<sub>2</sub>) 2930, 2670, 2500, 1697, 1654, 1292, 965, 825 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 11.07 (br s, 1 H), 6.84 (dd, *J* = 16.0, 6.5 Hz, 1 H), 6.12 (d, *J* = 16.0 Hz, 1 H), 3.22 (dd, *J* = 6.5, 1.5 Hz, 1 H), 2.98 (dq, *J* = 5.0, 1.5 Hz, 1 H), 1.4 (d, *J* = 5.0 Hz, 3 H).

Anal. Calcd for C<sub>6</sub>H<sub>8</sub>O<sub>3</sub>: C, 56.24; H, 6.29. Found: C, 56.20; H, 6.14.

**5,6-Epoxy-2-hexanone (6b)** was also obtained by following method A: bp 52 °C (0.5 mm); IR (CHCl<sub>3</sub>) 2995, 1712, 1400, 1360, 1160, 908, 804, 830, 750 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 2.78–3.02 (m, 1 H), 2.33–2.72 (m, 4 H), 2.09 (s, 3 H), 1.65–1.92 (m, 2 H); mass spectrum (50 eV), *m/e* (relative intensity) 114 (5), 86 (4), 85 (4), 82 (6), 72 (9), 58 (4), 55 (15), 54 (12), 53 (4), 44 (9), 43 (100), 42 (4), 39 (12).

Anal. Calcd for C<sub>6</sub>H<sub>10</sub>O<sub>2</sub>: C, 63.15; H, 8.77. Found: C, 63.28; H, 9.03.

**Epoxidation Procedures.** In the epoxidation of water-soluble olefins (method A), a freshly prepared solution of potassium peroxomonosulfate (24 mmol) in water<sup>15</sup> is added dropwise (during 2–4 h) to a mixture of the alkene (10 mmol) and acetone (0.13 mol) in water at ca. 2 °C. Before the addition is started, the pH is adjusted to 7.5, and it is maintained at this value during the reaction by additions of 0.5 N KOH by use of a pH stat.<sup>2</sup> The reaction mixture is then acidified (at 2 °C) to pH ca. 3 (5% HCl) and extracted with Et<sub>2</sub>O. The ether extracts are dried (MgSO<sub>4</sub>), and the solvent is removed in vacuo, affording the crude epoxide. This is then purified by standard methods.<sup>2,3</sup> In an experiment typical of two-phase epoxidations (method B) a solution of potassium peroxomonosulfate (12 mmol) in water (30 mL)<sup>15</sup> is added dropwise (30 min) to a well-stirred biphasic mixture of benzene (50 mL) and buffered (pH 7.5, 0.05 M phosphate buffer) water (20 mL) kept at 6–8 °C and containing cyclododecene (**8a**; 0.85 g, 5.1 mmol), acetone (4 mL), and 18-crown-6 (0.3 g, 1 mmol) as the phase-transfer catalyst. During the addition the pH is monitored and kept constant by using a pH-stat (0.5 N KOH). The mixture is allowed to stand at 8–10 °C for 3 h with stirring, the benzene layer is then separated, and the aqueous phase is extracted with benzene (10 mL). The combined benzene extracts are dried (MgSO<sub>4</sub>), and after removal of the solvent in vacuo the residue is purified by column chromatography (silica gel, *n*-hexane–Et<sub>2</sub>O, 4:1), affording 0.79 g (4.34 mmol, 85% yield) of epoxide **8b** [bp 100–102 °C (0.2 mm), lit.<sup>16</sup> bp 116–117 °C (4.7 mm)] having spectra identical with those of a purified commercial sample.

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**Registry No.** **3a**, 140-10-3; **3b**, 1566-68-3; **4a**, 102-94-3; **4b**, 73610-79-4; **5a**, 110-44-1; **5b**, 74923-21-0; **6a**, 109-49-9; **6b**, 74877-18-2; **7a**, 110-83-8; **7b**, 286-20-4; (*E*)-**8a**, 1486-75-5; (*Z*)-**8a**, 1129-89-1; *cis*-**8b**, 1502-29-0; *trans*-**8b**, 4683-60-7; **9a**, 112-41-4; **9b**, 2855-19-8.

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## S<sub>RN</sub>1 Mechanism in Bifunctional Systems<sup>1</sup>

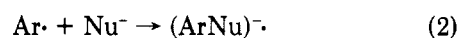
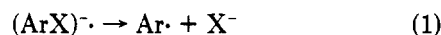
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Since the S<sub>RN</sub>1 mechanism of nucleophilic aromatic substitution of unactivated substrates was discovered,<sup>2</sup> it has been found that this reaction has a wide scope with regard to both the substrates and the nucleophiles that participate.<sup>3,4</sup> The most important steps of this mechanism are shown in Scheme I.<sup>3</sup>

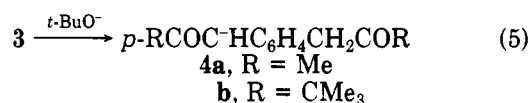
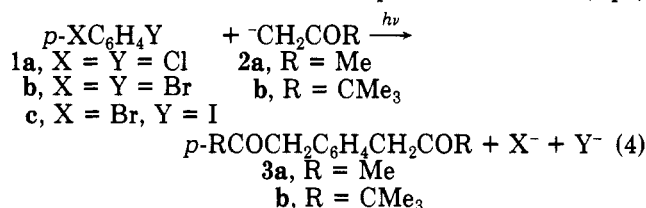
### Scheme I



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.<sup>5</sup> 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 1.** *p*-Dihalobenzenes (**1**) were allowed to react with ketone enolate ions **2** under photostimulation<sup>6</sup> (eq 4)



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 93%, 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

(1) Research supported in part by the Consejo Nacional de Investigaciones Científicas y Técnicas, Argentina.

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