

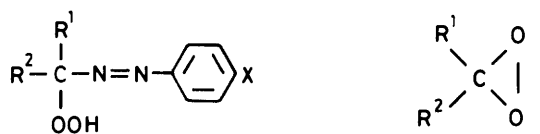
A New Epoxidation Reaction: Base-catalysed Stereospecific Epoxidation with α -Azohydroperoxides

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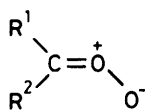
A new stereospecific epoxidation with α -azohydroperoxides (**1**) in basic media is reported. *cis*- and *trans*-Stilbene gave the corresponding epoxides stereospecifically in the reaction with α -azohydroperoxides (**1a—d**) catalysed by pyridine or sodium hydroxide. Similarly, *cis*- β -methylstyrene gave the corresponding *cis*-epoxide. Cyclohexene, trinorborn-2-ene, and tetramethylethylene all gave epoxides in good to high yield in the reaction with (**1a—d**) under the basic conditions. The mechanism of this novel base-catalysed epoxidation is discussed.

Base-catalysed epoxidation by hydroperoxides or peracids has been studied extensively from mechanistic and synthetic points of view.¹⁻³ Recently we have reported a new base-catalysed epoxidation with α -azohydroperoxide (**1a**).⁴ By this reaction, cyclohexene and tetramethylethylene were epoxidised. However, the yield of epoxide was low. In the absence of these olefins, benzoic acid was formed. We accounted for these reactions by assuming a dioxirane^{5,6} or a carbonyl oxide^{7,8} [(**2a**) or (**3a**)] as an intermediate (Scheme 1).

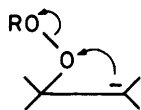


Scheme 1.

- (1) a; $R^1 = Ph, R^2 = H, X = Br$
 b; $R^1 = Ph, R^2 = Me, X = Br$
 c; $R^1 = R^2 = Me, X = Br$
 d, $R^1R^2 = -[CH_2]_5-, X = H$



(3)



(4)

Being interested in base-catalysed epoxidation with hydroperoxides, we investigated further the epoxidation reaction with the α -azohydroperoxides (**1**) in basic media. We found that compounds (**1**) epoxidise olefins stereospecifically in basic media, and a high yield of epoxide is obtained under high-dilution conditions. Part of this work has recently been reported.⁹ This paper describes in full our work on the epoxidation with the azohydroperoxides (**1a—d**).

When a benzene or dioxane solution of an azohydroperoxide (**1**) (10^{-2} — 10^{-4} M) and an olefin (*ca.* 10 equiv.) was stirred at room temperature or heated under reflux in the presence of pyridine or sodium hydroxide [*ca.* 5 equiv. of (**1**)], the epoxide was formed in good to high yields (see Table 1). Table 1 indicates that the epoxidation is stereospecific. Both *cis*-stilbene and *cis*- β -methylstyrene gave the corresponding *cis*-epoxide stereospecifically. Phenyl- and alkyl-substituted olefins gave epoxides (Table 1). On the other hand, electron-deficient olefins such as mesityl oxide and cinnamic acid did not give epoxides.

In the case of azohydroperoxides (**1b—d**), even strong alkalies such as sodium hydroxide are effective as a catalyst in the epoxidation. However, sodium hydroxide is not a good catalyst for (**1a**). This is probably due to the fact that the base-catalysed dehydration of (**1a**), which gives *N*-benzoyl-*N'*-(4-bromophenyl)diazene,¹⁰ competes with the base-catalysed epoxidation.⁴ *N*-Aryl-*N'*-benzoyldiazenes such as *N*-benzoyl-*N'*-(4-bromophenyl)diazene are known to decompose readily to benzoic acid and an aryldiazene by hydrolysis in aqueous basic solution.¹¹ Even in the reaction in pyridine, the dehydration of (**1a**) competes with the epoxidation.⁴ In fact, we found that (**1a**) gave lower yields of epoxide than did (**1b—d**) in pyridine. Examples are shown by the reactions of *trans*-stilbene and *cis*- β -methylstyrene in the presence of pyridine in Table 1.

The data in Table 1 also indicate that the yield of epoxide depends on the concentration of (**1**) in the reactant. The best yield of epoxide was obtained when the reaction was carried out in a 10^{-4} M solution of (**1**). In general, the lower the concentration of (**1**), the higher the yield of epoxide. Examples are shown by the reaction of *cis*-stilbene with (**1b**) catalysed by sodium hydroxide and/or of cyclohexene with (**1a**) catalysed by pyridine (Table 1).

The concentration of the base (pH) also affected the yield of epoxide. In the epoxidation of *trans*-stilbene, for example, a high yield of epoxide was obtained when the pH of a dioxane solution was controlled at *ca.* 9—10. Higher pH values gave poor yields of epoxide (Table 2).

The epoxidation with compounds (**1**) may be of practical value, because the reaction can be carried out in anhydrous organic media with pyridine as a base. This has some advantage when compared with the base-catalysed epoxidation of acid-sensitive compounds by peracids or hydroperoxides in aqueous solution.¹⁻³ The applicability of this reaction is under investigation.

The mechanism of this novel stereospecific epoxidation is of

Table 1. Yield of epoxide

Olefin	Azohydroperoxide (1) (M)	Base	Yield	Epoxide (%) ^a
	(1a) (10 ⁻⁴)	pyridine ^b	48	
	(1b) (10 ⁻⁴)	pyridine ^c	59	
	(1b) (10 ⁻⁴)	NaOH ^b	73	
	(1c) (10 ⁻⁴)	NaOH ^b	76	
	(1d) (10 ⁻⁴)	NaOH ^b	84	
	(1b) (10 ⁻⁴)	NaOH ^b	55	
	(1b) (10 ⁻³)	NaOH ^b	25	
	(1b) (10 ⁻²)	NaOH ^b	8	
	(1c) (10 ⁻⁴)	NaOH ^b	51	
	(1d) (10 ⁻⁴)	NaOH ^b	58	
	(1a) (10 ⁻⁴)	pyridine ^b	59	
	(1b) (10 ⁻⁴)	pyridine ^c	79	
	(1b) (10 ⁻⁴)	NaOH ^b	71	
	(1a) (10 ⁻³)	pyridine ^b	35	
	(1a) (10 ⁻²) ^d	pyridine ^b	24	
	(1b) (10 ⁻⁴)	NaOH ^b	77	
	(1a) (10 ⁻³)	pyridine ^b	23	
	(1b) (10 ⁻⁴)	NaOH ^b	62	
	(1a) (10 ⁻³)	pyridine ^b	51	
	(1a) (10 ⁻²) ^d	pyridine ^b	23	

^a Yield based on the original amount (%) of (1) and determined by g.l.c. ^b Stirred at room temperature. ^c Heated under reflux.

Table 2. pH Dependence of the epoxidation of *trans*-stilbene with (1b)

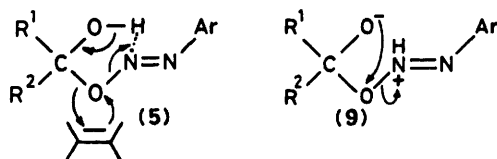
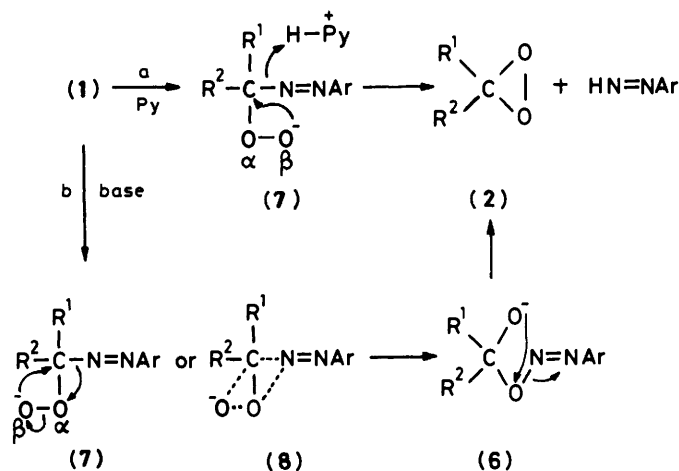
pH	6.8	8.4	9.7	11.2 ^d
Time (h) ^a	24	8	3	1
Yield (%) ^b	0 ^c	27	51	0

^a Disappearance of (1b) at 25 °C. ^b Yield of *trans*-stilbene oxide based on the original amount (%) of (1b) and measured by h.p.l.c. ^c (1b) Was recovered without reaction after this time. ^d (1b) Was decomposed completely under these conditions.

interest. The epoxidation by (1) occurred *only in basic solution*, and does not proceed through direct oxygen transfer from hydroperoxide to olefin as reported previously.⁴ Cyclohexene and tetramethylethylene were not epoxidised by (1a) in benzene at room temperature during 12 h.⁴ In the present study, we also found that none of the epoxidations shown in Table 1 occurred in the absence of base at room temperature during 12 h. Therefore, the mechanism of the epoxidation by (1) in basic media differs substantially from that of the reaction by the α -aza-, α -hydroxy-, and α -azo-hydroperoxides in neutral or weakly acidic media.¹²⁻¹⁴ The stereospecificity of the reaction rules out the step-wise mechanism involving a carbanion of the type (4). An anion such as (4) is proposed as an intermediate of the base-catalysed epoxidation with hydroperoxides, hydrogen peroxide, and peracids.^{1,2}

On the other hand, the mechanism involving dioxirane (2) as a reactive intermediate, as proposed previously,^{4,9,15} accounts well for the stereospecific epoxidation with (1) in basic media. However, it is worth noting that an 'oxenoid' intermediate such as (5), which is derived by protonation of the anion (6), also

accounts for the stereospecific epoxidation. The anion (6) is derived from the peroxy anion (7) by Criegee-type rearrangement^{16,17} of the azo group to the α -oxygen and concomitant attack of the β -oxygen at the aliphatic carbon as indicated by the arrows in (7) or (8) in path b of Scheme 2. Alternatively, by the elimination of the azo group, (6) gives dioxirane (2) which epoxidises the olefin (Scheme 2). Previously we proposed that in the reaction catalysed by pyridine the dioxirane (2) is formed from the peroxy anion (7) by direct nucleophilic attack of the β -oxygen at the aliphatic carbon followed by the liberation of the azo group as indicated by path a in Scheme 2. The analogous



reaction of the liberation of the azo group has recently been reported.¹⁸ However, as cited above, the formation of dioxirane (2) from (7) via (6) or a protonated species (9) is possible. We are investigating details of the reactive species and the mechanism of the base-catalysed reaction with (1) in comparison with the epoxidation by the caroate (potassium hydrogen peroxy-

monosulphate)-acetone system,⁶ in which a dioxirane is proposed as a reactive species.

Experimental

Materials.—Mesityl oxide was oxidised by alkaline hydrogen peroxide to give the corresponding epoxide.¹⁹ *trans*-Epoxy-cinnamic acid was obtained by the oxidation of *trans*-cinnamaldehyde with alkaline hydrogen peroxide.¹⁹ Other authentic epoxides were prepared by the oxidation of the corresponding olefins with *m*-chloroperbenzoic acid.¹⁹ Ether is diethyl ether.

Typical Procedure of G.l.c. Analysis.—A small portion of the reaction mixture obtained below was introduced directly into a gas-liquid chromatograph (Shimadzu GC-6AM) equipped with a 3 m column of silicon SF-96 on Uniport B (10%). Epoxides were identified by comparison of the retention times with those of authentic samples, and the yields of epoxides were determined by using naphthalene or anthracene as an internal standard.

Preparation of α -Azohydroperoxides (1a-d).—Benzaldehyde, acetophenone, and acetone *p*-bromophenylhydrazones were oxygenated in benzene in a manner similar to that described in the literature.²⁰ By these reactions, the corresponding azohydroperoxides (1a) [m.p. 114–115 °C (decomp.)], (1b) [m.p. 46–48 °C (decomp.)], and (1c) [m.p. 42–45 °C (decomp.)] were obtained in 55–100% yield. Cyclohexanone phenylhydrazone was also oxygenated by the similar method to give compound (1d) (oil) in 80% yield. **CAUTION:** The azohydroperoxides (1b-d) are explosive.

Epoxidation of Olefin with α -Azohydroperoxides (1a-d) in the Presence of Pyridine.—To a benzene solution of an azohydroperoxide (1) (2×10^{-2} – 10^{-4} M) was added an olefin [ca. 10 equiv. of (1)] and pyridine [ca. 5 equiv. of (1)], and the mixture was well stirred for several hours at room temperature [for (1a)] or refluxed [for (1b-d)] under nitrogen until the reactant (1) had disappeared (ca. 6–12 h). The solvent was removed under reduced pressure, and the residue was chromatographed on silica gel (t.l.c.). This gave the corresponding epoxide which was identical (m.p., spectral data) with those of the authentic samples.

The yield of epoxide was determined by introducing a small portion of the reaction mixture directly into the g.l.c. instrument, together with an internal standard.

Epoxidation of Olefins with α -Azohydroperoxides (1b-d) in the Presence of Sodium Hydroxide.—To a dioxane solution of an azohydroperoxide (1b-d) (10^{-2} – 10^{-4} M) prepared above was added an olefin [ca. 10 equiv. of (1)] and aqueous sodium hydroxide solution [ca. 5 equiv. of (1)], and the mixture was well stirred at room temperature under nitrogen until all the azohydroperoxide had disappeared (ca. 12 h). The reaction mixture was extracted with diethyl ether, washed, and dried (MgSO₄). Evaporation of the ether gave an oil in each case

which was chromatographed on silica gel (t.l.c.) developed by benzene to give the corresponding epoxide identical with an authentic sample. The yield of epoxide was determined by g.l.c.

pH Dependence of the Base-catalysed Epoxidation of *trans*-Stilbene with Compound (1b).—A dioxane solution of compound (1b) (1.5×10^{-3} M) and *trans*-stilbene [ca. 10 equiv. of (1b)] was stirred at room temperature for several hours [until (1b) had disappeared] in the presence of various concentrations of aqueous sodium hydroxide (see Table 2). The solvent was removed under reduced pressure from the reaction mixture and the residue was then neutralised with aqueous hydrochloric acid. The mixture was extracted with ether and dried (MgSO₄). After the removal of the solvent, the internal standard (azobenzene) was added, and the mixture was diluted with dioxane. The yield of *trans*-stilbene oxide was determined by means of high-pressure liquid chromatography (h.p.l.c.) with a 15 cm column of Nucleosil 5C₁₈ (reverse-phase). The results are shown in Table 2.

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