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STEREOSPECIFIC DEOXYDICHLOROCYCLOPROPANATION OF EPOXIDES BY DICHLOROCARBENE GENERATED IN AN EMULSIFYING SYSTEM†

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Abstract—The reaction of epoxides with dichlorocarbene generated in an emulsifying system was investigated. The products were the corresponding dichlorocyclopropane derivatives. The reaction of *cis*- and *trans*-β-methylstyrene oxides showed the reaction was completely stereospecific. Styrene oxide gave the corresponding dichlorocyclopropane and styrene, where the concentration of the latter was kept in the nearly stationary state during the reaction. Further the competitive reaction of α- and β-methylstyrene oxide showed that introduction of an additional Me group at the α-position accelerated the reaction only 12 times. From these observations the reaction was concluded to involve the two step process, namely, the deoxygenation process and dichlorocyclopropanation process, both of which were stereospecific and practically concerted.

Only very limited work has been done on the reaction of carbenes with epoxides. Wittig and Schlosser described the copper-catalyzed decomposition of diazomethane in styrene oxide yielding styrene but only in poor yield.[1] Nozaki *et al.* reported that the reaction of carbethoxy-, dihalo-, or diphenyl-carbene with styrene oxide gave styrene and the corresponding cyclopropane derivatives, again in poor yield, among a complex mixture of products.[2] The authors have currently been studying the reaction of dichlorocarbene generated in an emulsifying system[3]‡ produced by the addition of triethylbenzylammonium chloride,[4,5] where dichlorocarbene was found to be generated very effectively by suppressing the undesirable hydrolysis in aqueous alkaline solution.§ Thus the emulsifying system generating dichlorocarbene was very successfully applied to the dichlorocarbene insertion into saturated hydrocarbons[4] or the chlorination of alcohols.[5] In this article, the authors wish to report the stereospecific deoxydichlorocyclopropanation of epoxides. The mechanism involving successive deoxygenation and dichlorocyclopropanation, both of which are stereospecific, are presented.

RESULTS AND DISCUSSION

The course of the reaction. The reaction of dichlorocarbene with epoxides gave the corresponding dichlorocyclopropanes in good to fairly good yield. The results are summarized in Table 1. Among the epoxides investigated, only styrene oxide gave an appreciable amount of olefin (styrene, as a deoxygenated product) together with the corresponding dichlorocyclopropane. No product other than olefin or dichlorocyclopropane was isolated from any epoxide investigated. It was observed that an appreciable amount of an epoxide was lost during the reaction probably due to the hydrolysis in aqueous alkaline solution in the presence of the ammonium salt as ascertained by the independent experiments. Thus, on treatment of an epoxide with aqueous alkaline solution even in the absence of chloroform an appreciable amount of the epoxide was still lost. In these circumstances, yield of a dichlorocyclopropane was corrected for the spontaneous hydrolysis of the epoxide and was shown in parentheses in Table 1. The amount of styrene formed from styrene oxide was investigated in different initial concentration of chloroform. The results are summarized in Table 2. On changing the ratio of initial concentration of chloroform to that of styrene oxide, the ratio of the amount of styrene formed to styrene oxide unreacted was found to be nearly constant. This constant ratio did not

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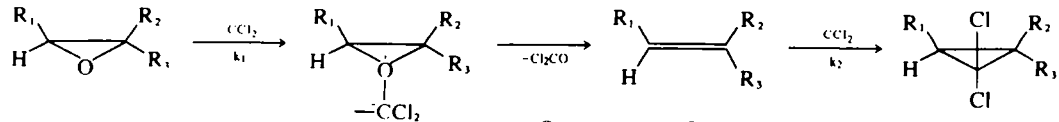
†The major part of this study was presented in Annual Meeting of Japan Chemical Society, Tokyo, Abstract of Papers III, p. 1367 (1972).

‡Original Makosza's procedures[3] are modified by the addition of benzene as an organic phase to make an emulsion.

§Recently the generation of dichlorocarbene with a "phase-transfer catalyst", tricaprylylmethylammonium chloride, in aqueous sodium hydroxide was also reported as an alternative procedure. C. M. Starks, *J. Am. Chem. Soc.* **93**, 195 (1971).



8 **9** **10**

1: $R_1 = Ph$; $R_2 = R_3 = H$, **2**: $R_1 = n\text{-}C_8H_{17}$, $R_2 = R_3 = H$,
3: $R_1 = n\text{-}C_{10}H_{21}$, $R_2 = R_3 = H$, **4**: $R_1 = Ph$, $R_2 = CH_3$, $R_3 = H$,
5: $R_1 = Ph$, $R_2 = H$, $R_3 = CH_3$, **6**: $R_1 = H$, $R_2 = Ph$, $R_3 = CH_3$,
7: $R_1 = R_2 = C_4H_8$, $R_3 = H$,

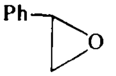
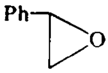
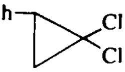
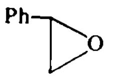
Chart 1.

Table 1. Reaction of epoxide with dichlorocarbene

Epoxide	CHCl$_3$/epoxide	conversion (%)	Yield[a] 9(%)[b]	10(%)
1	10	64	2	32 (73)[c]
2	10	45	—	18 (27)[c]
3	10	14	—	15
5	10	22	—	33
6	10	36	—	20
7	10	61	—	39 (84)[c]

[a] Yield was based on the epoxide consumed, by GLC, calibrated.
[b] Olefins were not detected by GLC except styrene.
[c] Yield in parenthese was based on the epoxide consumed, corrected for the spontaneous hydrolysis.

Table 2. Ratio of products obtained in different initial amount of chloroform

CHCl$_3$$^{(a)}$ /  (a)	PhCH=CH$_2$ / 	 / 
0·25	0·038	0·041
0·50	0·045	0·066
1·0	0·048	0·134
1·5	0·043	0·318
3·0$^{(b)}$	0·045	—

[a] Mole ratio of chloroform and styrene oxide used.
[b] Reaction with the initial addition of equimolar styrene to styrene oxide.

appreciably change in the run where a considerable amount of styrene was added to the system prior to the addition of chloroform. Thus a mixture of styrene (0·02 mol), styrene oxide (0·02 mol) and chloroform (0·06 mol) was treated with aqueous alkaline solution and a surface active reagent at 40° for 4 hr to give styrene and unreacted styrene oxide in a ratio of 0·045 : 1 which was practically the same as the ratio in the absence of styrene initially added. These results indicate that styrene† is the intermediate of the deoxydichlorocyclopropanation and its concentration is practically kept in the stationary state at the early stages of the reaction. Since the stationary ratio of styrene to styrene oxide was found to be nearly constant and small enough, the kinetic steady-state assumption seems to be reasonable. However, for other epoxides employed, intermediarily formed olefins were not found in appreciable amounts among the isolated final products. This may be correlated with the fact that an intermediairly formed olefin is much more reactive to dichlorocarbene than styrene because of the increased π-electron density due to electron-supply from alkyl substituents. Thus a conclusion may be drawn that the deoxydichlorocyclopropanation of epoxides is a two step process, namely, the deoxygenation and the dichlorocyclopropanation process.‡ The deoxygenation process may involve formation of a labile oxygen-ylide§ intermediate **8** via the electrophilic attack of dichlorocarbene on an O atom of an epoxide, followed by the decomposition of the labile ylide to an olefin, which yields dichlorocyclopropanated products by the second attack of dichlorocarbene (Chart 1).

The stereochemistry of the deoxydichlorocyclopropanation

The stereochemistry of the reaction was studied for *cis*-and *trans*-β-methylstyrene oxide (**4** and **5**). The products were found to be *cis*- and *trans* - 1,1 - dichloro - 2 - phenyl - 3 - methylcyclopropane, respectively. This means that the configurations of the starting epoxides were retained during the deoxydichlorocyclopropanation. The observed stereospecificity was more than 95%§ for the *cis*-isomer and more than 96%§ for the *trans*-isomer. Since the addition of dichlorocarbene to an olefin is known to be stereospecific,[6] the deoxygenation process must be also stereospecific as shown in Chart 1.

Two plausible mechanisms may be presented to interpret the stereospecific deoxygenation, the concerted decomposition of an oxygen ylide **8** (path **a** in Chart 2) and the stepwise one (path **b** in Chart 2), where the latter mechanism requires the life-time of **11** to be short enough to retain the stereochemistry.¶ In order to examine these two possibilities, the competitive reaction of α- and *trans*-β-methylstyrene oxide, **5** and **6**, was investigated.

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†Although the appreciable amount of styrene oxide was lost by the hydrolysis, the product ratio still gives k_1/k_2 on assuming a steady state for styrene.

‡The observed steady-state is not necessarily correlated with the two step mechanism of the deoxydichlorocyclopropanation, since an alternative possibility still remains that the two step path is involved only as a side reaction. However, that the run with initial addition of a considerable amount of styrene still gave the same steady state concentration of styrene strongly indicates that the present reaction is expressed by the two-step mechanism.

§The deoxygenation of pyridine-N-oxide by dichlorocarbene and carbethoxycarbene was reported. These reaction were considered to involve oxygen-ylide intermediates. However, any mechanistic study such as the kinetic investigation of the reaction was not carried out. cf. E. E. Schweizer and G. J. O'Neill. *J. Org. Chem.* **28**, 2400 (1963), J. A. Dyakonov, J. V. Madelshtam and O. M. Radul, *Zhur. Org. Khim.* **4**, 723 (1968).

§The stereospecificity was evaluated from the NMR spectra of the isolated cyclopropanes because GLC determination suffered from considerable experimental error in the integration due to the relatively poor separation of the stereoisomers. In the NMR determination, mechanical noise was taken to be the upper limit of the minor product for safety. In these circumstances, 95% and 96% were apparently the lower limits of the stereospecificities. It seems to be reasonable to claim that the reaction is practically stereospecific.

¶It was reported that the optically active styrene oxide reacted with carbethoxymethylenetriphenyphosphorane to give optically active ethyl *trans*-2-phenylcyclopropanecarboxylate, although the stereospecificity and the absolute configuration of products were not determined. D. B. Denney, J. J. Vill and M. J. Boskin, *J. Am. Chem. Soc.* **74**, 3944 (1962).

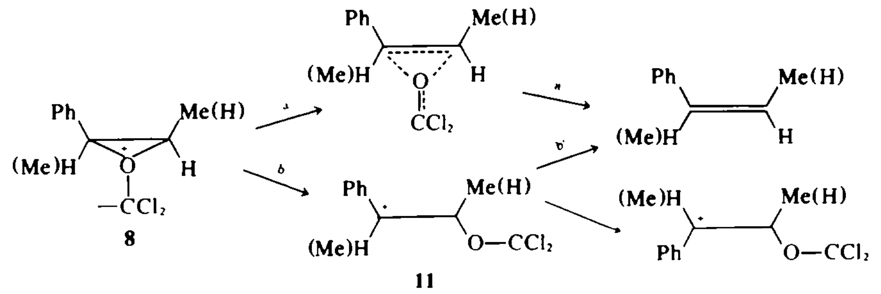

Chart 2.

The rate of the deoxydichlorocyclopropanation of α-methylstyrene oxide was found to be 12 times faster than that of β-methylstyrene oxide. If the deoxygenation process is stepwise, the rate will be markedly affected by the introduction of an alkyl substituent at the α-position because of the expected stabilization of the cation formed at the α-carbon. The rates of solvolyses of mono- and di-methylphenylcarbinyl chloride[7] showed that the generation of the cation at the α-carbon was accelerated by *ca.* 10^3 times by the introduction of an additional Me group at the α-position.† Accordingly, the rate enhancement by a Me substituent observed for the competitive reaction of α- and β-methylstyrene oxides was considered to be too small to be expected from the stepwise deoxygenation (i.e. carbonium ion) mechanism. Thus, the deoxygenation process may be concluded to be concerted and 12 times (considerably large) enhancement of α-methylstyrene oxide compared with β-methylstyrene oxide may indicate that this process still involves a considerable polar character.

The characteristics of the emulsifying system to affect the course of the reaction

A micellar or emulsifying system is composed of a bulk aqueous region, a nonpolor organic region and the boundary surface region, where hydroxide anion is locally concentrated by the Coulombic interaction with the ammonium ion aligned at the boundary surface (Fig. 1). Since the concentration of water seems to be considerably reduced in the surface or inner "core" region, hydroxide anion, if once moves to the surface or inner region, should have increased reactivity because of its decreased magnitude of hydration. Therefore, if chloroform penetrates into this region, the formation of trichloromethyl anion according to eqn (1) will be facilitated. However, the trichloromethyl anion produced also seems to be unstable because of lack of sufficient solvent stabilization. This instability of trichloro methyl anion in the surface region will lead to the fragmentation into dichlorocarbene which is an uncharged species, migrating into the organic layer, and chloride anion which will gain some larger hydration stabilization on migration to the aqueous layer. (eqn 2)

$$CHCl_3 + OH \longrightarrow CCl_3 + H_2O \qquad (1)$$

$$CCl_3 \longrightarrow :CCl_2 + Cl^- . \qquad (2)$$

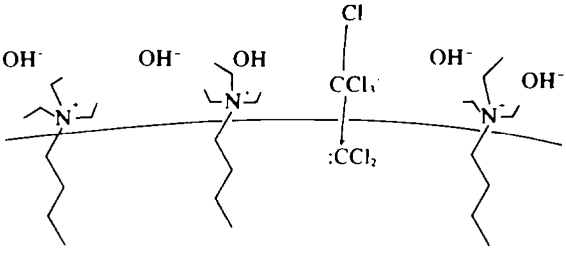

Fig. 1.

Dichlorocarbene in the organic layer seems to be very reactive because of its poor solvation and even the least facile carbene process such as the insertion into C–H bond of a saturated hydrocarbon takes place[4] without any serious difficulty. Another interesting characteristic of the carbene generated in the emulsifying system is that it affords an unfavorable one way (*irreversible*) process such as the complete conversion of an alcohol to the corresponding chloride in 50% sodium hydroxide emulsion.[5] This striking characteristic seems to originate from the "protection" of the product, chlorides, through the incorporation in (or "binding" by) the organic layer by the hydrophobic interaction. Our present success in the deoxydichlorocyclopropanation in very strong alkaline medium apparently due to this protection of the product.[8] The ready decomposition of a labile oxygen-ylide may again be interpreted by the unique effects of the emulsifying system. Since dichlorocarbene can meet with a strongly or moderately hydrophobic epoxide only in a nonpolar organic region, the formation of an oxygen-ylide should take place in this region. However, the oxygen-ylide thus formed seems to gain only poor hydration stabilization in this region, where the oxygen ylide is probably unstable to decompose to uncharged fragments, namely, olefin and phosgene probably in a nearly simultaneous process. That the polar effect observed for α- and β-methylstyrene oxides may be considered somewhat larger than normal simultaneous reactions may be also interpreted by the above mechanism of poor solvation of a transition state.

EXPERIMENTAL

Olefins. β-Methylstyrene was prepared by the dehydration of β-hydroxy-n-propylbenzene with $KHSO_4$ at 200°, the latter was prepared from benzaldehyde and EtMgBr. β-Methylstyrene thus obtained consisted of 88% of *trans*- and 12% of the *cis*-isomer. This mixture of *trans*- and *cis*-β-methylstyrene was irradiated in the presence of acetophenone as sensitizer with a high pressure mercury lamp under N_2 at room temp for 24 hr.[9] After the irradiation, the siomer ratio (*cis* to *trans*) was found to be *ca.* 3:2. The isolation and purification of the *cis*- and the *trans*-isomer were carried out by means of the preparative GLC.

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†Since the solvolysis rate data for the direct comparison of mono-and dimethylphenylcarbinyl chloride were not available in literature, a comparison was made between the solvolysis rate of methylphenylcarbinyl chloride extrapolated to 90% aqueous acetone and that of dimethylphenylcarbinyl chloride observed in 90% aqueous acetone.

Commercially available styrene, α-methylstyrene, 1-decene and 1-dodecene were used. Cyclohexene was prepared by dehydration of cyclohexanol[10] and purified by column distillation.

Epoxides. Commercially available styrene oxide was used after distillation. Other epoxides were prepared by epoxidation of corresponding olefins with peroxybenzoic acid.[11] Styrene oxide, α-methylstyrene oxide,[12] 1-decene oxide,[13] 1-dodecene oxide[13] or cyclohexene oxide[14] used was satisfactorily pure on the basis of GLC and physical properties; 1-decene oxide **2**, b.p. 93°/24 mm (lit.[13] 94°/25 mm), 1-dodecene oxide **3**, b.p. 100°/5 mm (lit.[13] 124–5°/15 mm), α-methylstyrene oxide **6**, b.p. 76°/12 mm (lit.[12] 81–81·5°/14 mm) and cyclohexene oxide **7**, b.p. 130°/760 mm (lit.[14] 130·3–130·5°/760 mm). Each of these compounds showed the same IR and other spectra as those in literature, respectively. Since *cis*- and *trans*-β-methylstyrene oxide isomerized each other in GLC column, purity of each isolated isomer[15] was determined by NMR on the basis of relative intensity of the characteristic absorption of Me protons. *cis*-β-Methylstyrene oxide **4**, boiled at 90°/15 mm (lit.[15] 78–80°/15 mm) and *trans*-β-methylstyrene oxide **5**, boiled at 93°/15 mm (lit.[15] 93–95°/15–16 mm) showed satisfactory spectra.

Dichlorocyclopropanes. The authentic dichlorocyclopropanes were prepared by the reaction of corresponding olefins with dichlorocarbene generated by use of the emulsifying system. Dichlorocyclopropanes obtained as products were 1,1-dichloro-2-phenycyclopropane,[16] 1,1-dichloro-2-n-octylcyclopropane,[17] 1,1-dichloro-2-n-decycyclopropane,[17] 1,1-dichloro-2-methyl-2-phenylcyclopropane,[16] 7,7-dichloronorcarane,[18] and *cis*- and *trans*-1,1-dichloro-2-methyl-3-phenylcyclopropane.[19] *cis*- and *trans*-1,1-Dichloro-2-methyl-3-phenylcyclopropane could not be separated by GLC. Thus from the crude mixture of products of the reaction of *cis*- or *trans*-β-methylstyrene oxide, 1,1-dichloro-2-methyl-3-phenylcyclopropanes were collected by preparative GLC and its isomer composition of *cis* to *trans* was determined by NMR spectrum on the basis of relative intensity of characteristic absorption of Me protons at δ 1·1 for the *cis* isomer and at δ 1·5 for the *trans* isomer.

Reaction of an epoxide with dichlorocarbene

General procedure. The procedure was practically the same for all the epoxides used. Following is the procedure for styrene oxide as a typical example. A mixture of 2·4 g (0·02 mol) styrene oxide, 4 ml benzene, 40 ml 50% NaOH aq and 0·08 g triethylbenzylammonium chloride dissolved in a small amount of water was vigorously stirred at 40° to emulsify and then 16 ml (0·2 mol) of chloroform was added dropwise into the emulsion during the period of 1 hr and the mixture was stirred for further 3 hr. Upon dilution with water, the organic layer was extracted with 30 ml of ether three times. After drying over $NaSO_4$, ether was evaporated. The mixture was analysed by GLC. Products were identified with authentic compounds by comparing their GLC retention times and IR spectra.

The reaction of styrene oxide in different initial amount of chloroform. The reaction of styrene oxide with dichlorocarbene was further studied at the different initial concentration of chloroform, 0·005, 0·01, 0·02, or 0·03–0·02 mol of styrene oxide. The products were analysed by GLC and the amounts of the products, styrene and styrene oxide, were quantitatively determined by using an external calibration standard.

The dichlorocarbene reaction with a mixture of styrene and styrene oxide. A mixture of 2·4 g (0·02 mol) styrene oxide, 2·08 g (0·02 mol) styrene, 8 ml benzene, 80 ml 50% NaOH aq and 0·16 g triethylbenzylammonium chloride was vigorously stirred and 4·8 ml (0·06 mol) chloroform was added dropwise to the mixture at 40° during 1 hr. Separation and determination procedures were the same as described.

The competition reaction of α-methylstyrene oxide with β-methylstyrene oxide. A mixture of 183 mg (1·37 mmol) α-methylstyrene oxide, 183 mg (1·37 mmol) *trans*-β-methylstyrene oxide, 0·6 ml benzene, 6 ml 50% NaOH aq and 15 mg triethylbenzylammonium chloride was treated with 0·24 ml (3 mmol) chloroform as already described. The conversion was determined by GLC to be low enough (considerably below 10%) to discuss the rate ratio. The rate ratio of two epoxides was estimated from the product ratio observed by GLC.

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