Medium Effects on Stereochemistry of Acid-Catalyzed Ethanolysis of *trans*-2,3-Diphenyloxirane

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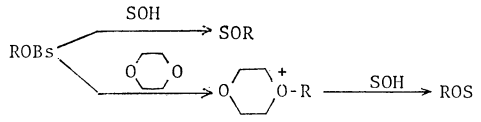
The acid catalyzed ethanolysis of *trans*-2,3-diphenyloxirane was examined in a wide variety of binary ethanolic solvent systems. The reaction proceeded with 26% retention and 74% inversion of configuration in pure ethanol at 50 °C. The dilution of ethanol by hexane or benzene produced almost no change in stereochemistry of the ethanolysis. The addition of acetonitrile, nitromethane, or sulfolane to the ethanolic solution resulted in increased degrees of retention. In binary ethanolic mixtures containing DMSO, DMF, or HMPA, increased ratios of inverted product were obtained. The steric course of the ethanolysis could be controlled from 85% retention–15% inversion (CH_3NO_2:ethanol=20:2 by volume) to 10% retention–90% inversion (HMPA:ethanol=10:12) by the choice of co-solvent. The results are discussed in terms of the solvation-shell concept.

Reaction media have an enormous effect on organic reactions, and many papers have been published on the solvent effects of reaction kinetics. Since the physical properties can be varied continuously by changing the composition of the solvents, binary solvent systems are particularly interesting, and a number of papers have discussed the reaction kinetics in binary solvent mixtures. Arnett and his co-workers have reported that the rates of solvolysis of *t*-butyl chloride in aqueous mixture are determined by changes in the stability of the *ground state* and not of the transition state.[1]

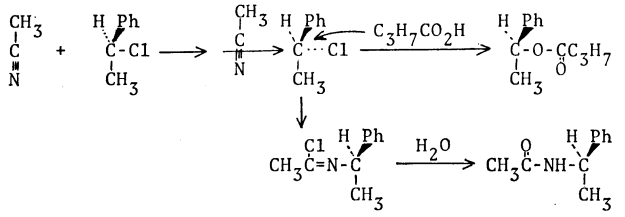
Although the effects of the composition of the binary solvent mixture on the steric course of reaction seem to be interesting, only a few papers have dealt with this problem. The results of the solvolysis of optically active 1-methylheptyl *p*-bromobenzenesulfonate by Weiner and Sneen[2] are the most famous and have been quoted in many texts. The reaction in 75% aqueous dioxane gave inverted 2-octanol in 77% optical purity, whereas the solvolysis in pure water resulted in 100% inversion of configuration. The results were explained by assuming an intermediate, an oxonium ion formed by the S_N2 attack by dioxane.



(1)

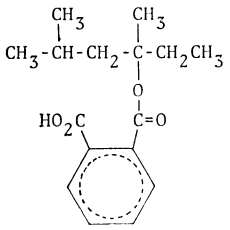
A similar mechanism was proposed by Streitwieser for the solvolysis of optically active 1-butyl-1-*d* *p*-nitrobenzenesulfonate in the mixtures of dibutyl ether and acetic acid.[3]

Okamoto and his co-workers found that the butyrolysis of optically active α-methylbenzyl chloride in pure butanoic acid gave α-methylbenzyl butanoate with 3.5% net inversion. The reaction proceeded faster in the binary solvent system of butanoic acid and acetonitrile than in pure butanoic acid to yield the product with 2.9% net retention. A small amount of *N*-(α-methylbenzyl)acetamide was also isolated with net (3.2%) inversion.[4] The results were explained by the following reaction scheme, which includes a nucleophilic solvation of the ion-pair intermediate from the side opposite to that of the leaving group, *i.e.* a shielding from the back mechanism.



(2)

The largest variation in the steric course of solvolytic reactions with the variation of the composition of binary solvent mixture was found in the acid-promoted methanolysis of 1,3-dimethyl-1-ethylbutyl hydrogen phthalate.[5]



In pure methanol, the steric course of the reaction was 60% net inversion, whereas the result was 100% racemization in a mixture of 20% methanol and 80% nitromethane. The complete discussion and experimental details have not yet been published.

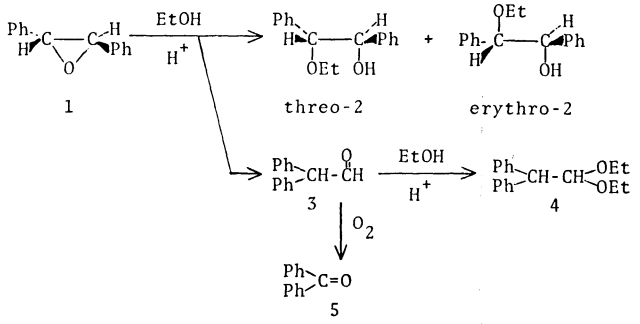
In the steric course of epoxide ring-opening, Italian workers have proposed a shielding from the back mechanism for the trichloroacetolysis of aryl-substituted epoxycyclohexanes.[6] Ito reported that the dielectric constant of the medium is an important factor affecting the steric course of the hydrolysis of 2,3-diphenyloxirane.[7] However, these workers did not explore the effects of the composition of the binary solvent mixture.

Aryloxiranes are interesting compounds for the stereochemical investigations on the medium effects in binary solvent systems. This present paper reports the experimental results of the acid-catalyzed ethanolysis of *trans*-2,3-diphenyloxirane (**1**) in binary ethanolic mixtures containing various kinds of co-solvents (solvents added to ethanol), and discusses the relationship between the steric course of the reaction and the nature of solvation in binary solvent mixtures.

Table 1. Ethanolysis of **1** in pure ethanol at 50 °C

1	$[H^+]$ [a]	Total yield	Product distribution			Ret.[c]
			Rearr.[b]	*threo*-**2**	*erythro*-**2**	
mmol l^{-1}	mmol l^{-1}	%	%	%	%	%
9.1	0.91	92	10	23	67	26
23.2	0.91	93	11	23	66	26
46.4	0.91	99	12	23	65	26
92.7	0.91	93	11	23	66	26
46.4	7.85	89	12	23	65	26
46.4	0.78	92	12	23	65	26

a) H_2SO_4 was used. b) **4**+**5**. c) (*threo*-**2**/**2**)×100.



Scheme 1.

Results

The acid-catalyzed ethanolysis of **1** in pure ethanol gave *threo*- and *erythro*-2-ethoxy-1,2-diphenylethanols (*threo*- and *erythro*-**2**), diphenylacetaldehyde (**3**), and the diethyl acetal of **3** (**4**) as shown in scheme 1. The total yields of the four compounds were more than 90 per cent by GLC analysis and more than 80 per cent after isolation.

The autoxidation catalyzed by potassium carbonate,[8] which was added to neutralize the catalyst acid, converted completely **3** into benzophenone (**5**) (see experimenatl section). Therefore, the yields of **5** were presumed to be those of **3**. To check the possibility of the formation of **5** during the ethanolysis, the reaction mixture was subjected to GLC analysis directly without potassium carbonate treatment. The yield of **5** was less than 0.5 per cent, which would be attributed to the oxidation of **3** under the ethanolysis conditions. As the authors were mainly concerned with the steric course of the ethanolysis of **1**, the detailed processes of the oxidation were not examined.

Table 1 shows the effects of concentrations both of acid and of **1** on the product distribution of the ethanolysis in pure ethanol at 50 °C. The ratio of the two ethanolysis products, *threo*- and *erythro*-**2**, was not affected within experimental error, whereas the reaction rate increased with the increase of acid concentration. This demonstrates that both of the stereoisomers **2** are formed through a common intermediate, *i.e.* the conjugate acid of **1** (**1**-H^+). At high acid-concentrations, 1-ethoxy-2,2-diphenylethylene (**6**) was observed in the latter stage of the reaction and seems to be formed by the elimination of ethanol from **4**.

Table 2. Ethanolysis of **1** in ethanol–CH_3CN at 70 °C

CH_3CN	Yield (%)					Ret.[a]
				threo-	*erythro*-	
vol%	**1**	**4**	**5**	**2**	**2**	%
0	0	15	tr	25	54	31
9	0	19	tr	28	48	37
23	0	21	3	32	41	44
36	0	18	10	35	35	50
46	0	18	12	36	32	53
68	5	10	23	34	18	65
91[b]	33	4	32	21	4	85

a) See foot-note of Table 1. b) Several other products were detected, see text.

Table 2 shows the variation in yield of products with variation of the composition of the ethanol–acetonitrile system at 70 °C. With an increasing percentage of acetonitrile, the reaction rate decreased and the proportion of the retained product (*threo*-**2**) increased, though the yields of the rearranged products, **4** and **5**, also increased. The formation of products other than those listed in Table 2 was negligible except in the case of the solvent system composed of 91% acetonitrile by volume. The products were detected by GLC analysis in the experiment of 91% acetonitrile, and isolation of the products was carried out by column chromatography. The isolated products were as follows: *threo*-**2**, 28%; *erythro*-**2**, 8%; **5**, 21%; **3**, trace; **4**, 13%; **6**, 7%; benzyl phenyl ketone (**7**), 1%; 2-hydroxy-1,2-diphenylethanone (**8**), 4%; diphenylethanedione (**9**), trace; 1,2-diphenylethanol (**10**), 2%; 2,2-diphenylethanol (**11**), 3%. The compound **7** is another rearranged product of **1**, and a trace of **7** was always observed in GLC analyses in all experiments throughout this paper. The last four are the redox-reaction products.

Table 3 shows the results of ethanolysis at 50 °C in the ethanol–acetonitrile system. Similar results to those in Table 2 are observed, but the proportion of the retained product *threo*-**2** at 70 °C was always higher, as compared with the result of the same solvent composition at 50 °C.

Table 4 shows the variation of the product distribution with different times of reaction. As shown in Table 4, **4** seems to be formed by a successive reaction

TABLE 3. ETHANOLYSIS OF **1** IN ETHANOL-CH_3CN AT 50 °C

CH_3CN	Yield (%)					Ret.[a]
vol%	**1**	**4**	**5**	*threo*-**2**	*erythro*-**2**	%
0	0	11	1	22	63	26
9	0	12	2	25	55	31
23	0	12	7	30	48	38
36	7	6	14	32	40	44
46	12	4	14	31	34	48
68	38	2	16	26	17	60
91[b]	73	1	16	14	3	83

a) See foot-note of Table 1. b) Trace amounts of 1,2-diphenylethanol (**10**) and benzyl phenyl ketone (**7**) were observed.

of **3**, and therefore, the mechanism that **4** is a primary reaction product may be ruled out.

Figure 1 shows the effect of the composition of benzene or dioxane systems on the steric course of the ethanolysis at 70 °C. The proportion of retained product increased with an increase in the composition of co-solvents as is the case of acetonitrile, but the effect of benzene or dioxane was smaller than that of acetonitrile. The yields of the rearranged products were found to increase with an increasing proportion of co-solvent in the same manner as acetonitrile.

Figure 2 shows the effects of the composition of various solvent systems at 50 °C. With an increasing percentage of nitromethane, the proportion of the retained product increased as is the case of acetonitrile, while the stereochemical outcome of the ethanolysis was virtually unchanged when hexane was added to the solvent system. Aromatic hydrocarbons and dioxane had slightly retentive effects. In every solvent system, large amounts of the retained product were formed at higher reaction temperatures.

In Table 5 are presented the data of the ethanolysis of **1** in binary solvent systems, ethanol–co-solvent

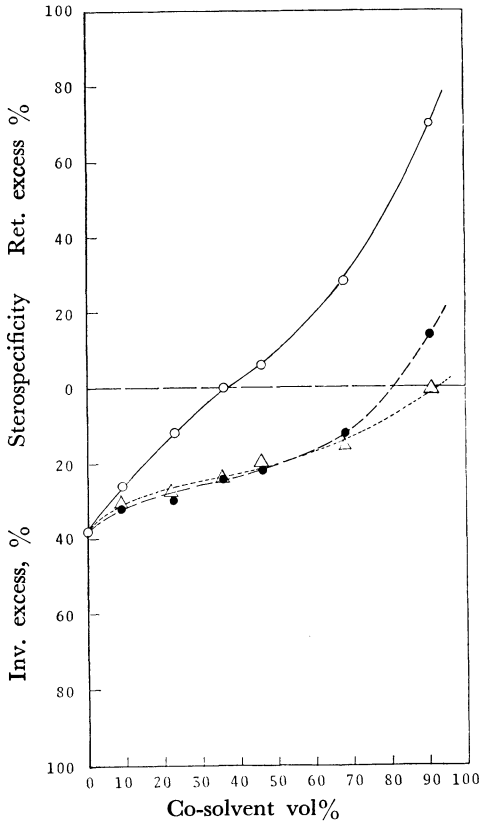


Fig. 1. Co-solvents on stereospecificity of the ethanolysis of **1** in binary solvent systems at 70 °C.
—○—: Acetonitrile, ——●——: dioxane, ---△---: benzene.

(12:10 by volume). Different stereochemical results were observed with change in co-solvent. As the reaction in DMSO, HMPA, and DMF proceeds quite slowly, higher concentrations of acid (10 times) than in the other experiments were used. The nature of these co-solvents was such that **1** gave larger amounts of inverted **2** in these systems than in pure ethanol. In all cases except those of these three co-solvents, the total yield of the four compounds in Scheme 1 was

TABLE 4. ETHANOLYSIS OF **1** AT 50 °C

Solvent[a]	Time	Yield (%)						Ret.
	h	**1**	*threo*-**2**	*erythro*-**2**	**4**	**5**	Others	%
I	0.17	84	4	11	0	2		26
I	0.5	49	10	27	tr	4		27
I	1.0	27	16	44	0.6	7		26
I	1.33	16	19	54	1	7		26
I	1.67	8	20	56	2	7		26
I	3.0	1	21	60	3	6		26
I	3.3	tr	21	60	5	5		26
II	1.0	56	12	36	1	5	b)	24
II	2.0	17	19	53	6	7	b)	27
II	3.0	17	18	54	7	6	b)	25
II	4.0	9	20	56	9	5	b)	26
II	5.0	3	21	60	11	3	b)	26
II	7.0	tr	21	60	13	2	b)	27

a) I, pure ethanol; II, ethanol/hexane=2 : 20 by volume. b) Trace amounts of **7** were observed.

Table 5. Ethanolysis of **1** at 50 °C in ethanol–co-solvent (10 : 12 by volume) mixtures[a]

Co-solvent	Reaction time	Yield (%)[b]					Others[c]	Ret.
	h	**1**	*threo*-**2**	*erythro*-**2**	**4**	**5**		%
Ethanol	8	0	22	63	11	1		26
Hydrocarbons								
Hexane	4	tr	23	64	11	2		26
Cyclohexane	6	0	22	64	11	3		25
Benzene	5	6	26	49	16	tr	**a**	35
Tolucne	6	0	26	54	16	4		33
m-Xylene	4	tr	25	54	19	tr	**a**	32
Mesitylene	6	tr	23	55	12	5	**a**	30
Halides								
CCl_4	1	2	25	68	4	9	**a, b, c, e**	27
$CHCl_2CHCl_2$	6	34	11	21	2	2	**a, b**	33
Ethers								
Bu_2O	6	0	22	63	12	3		25
THF	6	0	17	43	25	11	**a, b**	28
Dioxane	7	48	11	23	7	9		32
DME	6	0	22	45	15	12	**a, b**	33
Diglyme	6	10	18	34	16	13	**a, b**	34
Ketone								
Acetone	6	0	26	40	18	2	**a, b**	40
Nitrogen compounds								
CH_3NO_2	4	0	39	29	32	tr		57
$PhNO_2$	6	39	13	16	1	8	**a, b, c**	44
CH_3CN	8	12	31	34	4	14	**c, e**	48
PhCN[d]	6	—	—	—	—	—	—	41
DMF	72	32	2	10	0	2	**a, b, e**	19
Sulfur compounds								
DMSO	72	0	4	16	10	5	**a, b, c, d, e**	16
Sulfolane[d]	16	—	—	—	—	—	—	44
Phosphorus compound								
HMPA	16	24	3	29	0	7		10

a) Reactions were conducted with **1** (200 mg) in mixtures of ethanol (10 ml) and co-solvent (10 ml), and 2 ml, of 0.01 N sulfuric acid solution in ethanol. When DMSO, DMF, and HMPA were used as co-solvent, 0.1 N sulfuric acid solution was used instead of 0.01 N solution. b) Yields were calcd on the basis of **1** used. c) The other products were as follows: **a**, benzyl phenyl ketone (**7**); **b**, 1-ethoxy-2,2-diphenylethylene (**6**); **c**, 1,2-diphenylethanol (**10**); **d**, 2-hydroxy-1,2-diphenylethanone (**8**), diphenylethanedione (**9**), and/or 2,2-diphenylethanol (**11**); **e**, unidentified products. d) Due to the difficulty of separation of solvent from internal standard on GLC analysis, product yields could not be calculated.

Table 6. Ethanolysis of **1** at 50 °C in ethanol-substituted nitrobenzene mixtures[a]

Nitrobenzene (mmol)	Yield (%)					Ret.
	1	*threo*-**2**	*erythro*-**2**	**4**	**5**	%
Nitrobenzene (0.05)	0	28	44	9	9	39
Nitrobenzene (0.02)	0	27	56	16	1	32
p-Nitrotoluene (0.05)	0	28	47	9	9	37
p-Nitrotoluene (0.02)	0	26	55	16	1	32
m-Nitrotoluene (0.02)	0	26	54	16	1	32
m-Chloronitrobenzene (0.05)	0	27	44	7	9	38
m-Chloronitrobenzene (0.02)	0	26	55	17	1	32
p-Nitroanisole (0.02)	0	27	54	17	1	34

a) Reactions were conducted with **1** (200 mg) in mixtures of ethanol (10 ml) and nitrobenzenes (0.02 mmol or 0.05 mmol), and 2 ml of 0.1 M ethanolic solution of sulfuric acid. The amount of nitrobenzenes are given in parentheses.

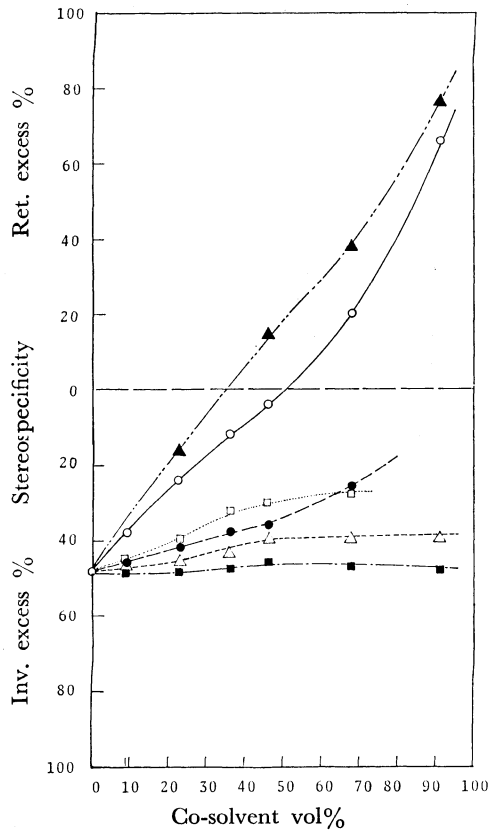


Fig. 2. Co-solvent effects on stereospecificity of the ethanolysis of **1** in binary solvent systems at 50 °C.
—○—: Acetonitrile, ——●——: dioxane, ···□···: benzene, ----▲----: nitromethane, ---△---: mestylene, ——■——: hexane.

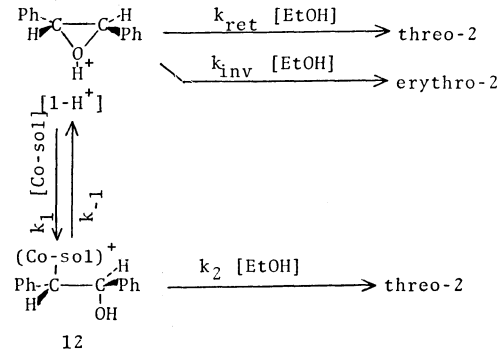
greater than 80 per cent. By-products, **6**–**11** were formed in some solvent systems. but the yield of these by-products was less than 2 per cent. When DMSO was used as the co-solvent, the total yield decreased unexpectedly, but no products other than described above could be isolated.

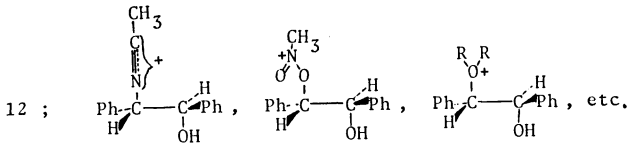
In Table 6 are presented the results of the ethanolysis of **1** in mixtures composed of ethanol and substituted nitrobenzenes. As many of nitrobenzenes are solid and it was difficult to determine the volume ratios, experiments were carried out with fixed mol fractions.

Discussion

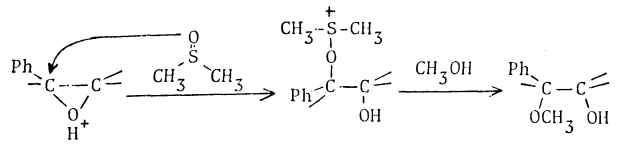
Several kinds of mechanisms have been proporsed to explain the solvent effects on the steric course of solvolysis and these will be examined here in the light of the results reported. From the application of Sneen's mechanism[2] to the reaction, it may be deduced that the co-solvent reacts from the back of the epoxide ring at an ionizing stage of the epoxide C–O bond, as shown in Scheme 2.

Upon closer examination of the experimental results (see Appendix), this scheme meets a difficulty in that the co-solvent should have a stronger nucleophilicity to the conjugate acid of **1** than ethanol. However, the scheme involves the assumption that the co-solvent has no nucleophilicity to co-solvent-participating intermediate (**12**).





Scheme 2.



Scheme 3.

The results reported involve several kinds of data which conflict with the shielding from the back mechanism. For example: 1. The proportion of the retained product decreased in the following orders of co-solvent; benzene>toluene>*m*-xylene>mesitylene; nitrobenzene>*p*-nitrotoluene, which is inverse to the order of nucleophilicity.

2. Swern and his co-workers reported that DMSO reacts with epoxide to yield the alkoxysulfonium salt which is the same type of ion as the assumed intermediate **12** and that this sulfonium ion reacts with alcohol to yield *β*-alkoxy alcohol (Scheme 3).[9] However, the reaction of DMSO with epoxide requires a much higher acid concentration than the ethanolysis experiments reported here. When DMSO was used as co-solvent in our experiment, larger amounts of inverted product were formed than in pure ethanol. These facts make it difficult to assume the alkoxysulfonium ion as an intermediate of the ethanolysis of **1** in DMSO.

3. Acetonitrile, nitromethane, and sulfolane, in which the ethanolysis of **1** yielded large amounts of the retained product, are known as relatively weak bases. Although no data are available to compare directly the nucleophilicity of the solvents toward a carbonium ion, their coordination abilities to metal cations may afford some insight. The coordinating abilities of acetonitrile and nitromethane are much weaker than those of DMSO and DMF. Since the nucleophilic participation of DMSO has been dis proved (see above), it is improbable that acetonitrile or nitromethane, which are poorer nucleophiles than DMSO, participate in the ionizing stage of **1**.

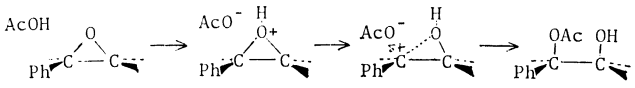
None of the mechanisms proposed for solvolytic

reaction can explain the experimental results reported here.

In the epoxide reactions, the mechanism of the ring-opening leading to the formation of stereoisomeric products has been reviewed by Parker and Isaacs. They discussed the reaction kinetics and stereochemistry and concluded that the reactions took place concurrently in these reactions, one of which gave the retained product and the other the inverted one.[10] This proporsal has been widely accepted, and the results of the reaction of aryl-substituted epoxycyclohexanes reported by Italian workers also supports this concurrent reaction mechanism.[11] The results presented in this paper, that the stereospecificity of the reaction varied widely from 80% inversion excess to 76% retention excess by changing the co-solvent, appear to support Parker and Isaacs' conclusion, in that the results can not be explained by a single mechanism.

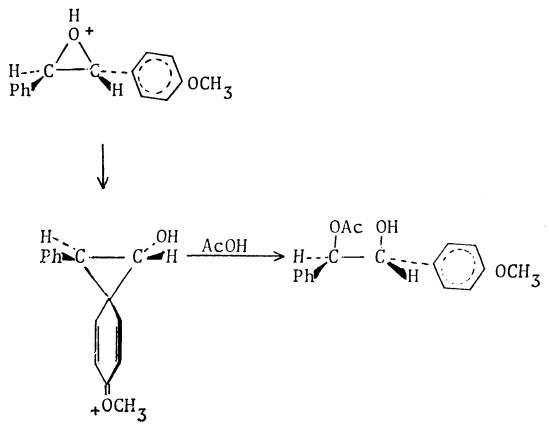
A short comment against the S_N1 mechanism for the epoxide reaction is necessary. By examining the entropies of activation in the acid-catalyzed methanolysis of aryloxiranes, Chapman and his co-workers suggested that the reaction does not proceed *via* an unimolecular mechanism except in the case of 2.2-diphenyloxirane which shows a deviation towards an S_N1 mechanism.[12]

Two mechanisms have been proporsed for the retention reaction, one of the concurrent reactions. Brewster explained the retentive acetolysis of *trans*-2-methyl-2,3-diphenyloxirane in terms of an ion pair in a "cage" of solvent molecules (S_Ni mechanism, Scheme 4).[13]



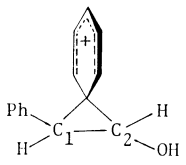
Scheme 4.

Another mechanism is a double inversion or a phenonium-ion mechanism (Scheme 5),[10] and was proporsed as a possible explanation for the results of the acetolysis of 2-(*p*-methoxyphenyl)-3-phenyloxirane.[14] Recently Ito found, however, that the position attacked by acetic acid is not benzyl carbon but *p*-anisyl one of that compound.[15] To explain this by a phenonium-ion mechanism, the participating group should not be a methoxyphenyl but a phenyl group, which is an unlikely process.



Scheme 5.

Although the phenonium-ion mechanism has been employed by many workers, there is no clear evidence to confirm the existence of the phenonium ion substituted by heteroatoms. If the double inversion mechanism were valid here, the phenonium ion (**13**) depicted below should exist as an intermediate and react with ethanol. The existence of this intermediate appears to be unlikely, when the following processes are taken into account. When the bridging phenyl group moves from the center of two carbon atoms (C_1, C_2) towards the C_1 atom, a developing p-orbital on the C_2 carbon atom can conjugate with a lone pair of oxygen atom adjacent to the C_2 carbon atom, and the cation gains additional stabilization energy. At the end of this drift, an oxonium ion or the conjugate acid of the aldehyde is formed which is well established as more stable than the phenonium ion by kinetic evidence.[16] Consequently, the phenonium ion, if it were to be formed, is not an intermediate of the retentive solvolysis but the transition state of the rearrangement to **3**.



(**13**)

As summarized in Table 7, the stereochemical results of the acid-catalyzed solvolysis of **1** are closely related to those of the optically active 2-phenyloxirane. Here, the phenonium ion cannot be an intermediate of the solvolysis of 2-phenyloxirane, since nucleophiles attack the benzyl carbon atom. Therefore, it is unreasonable to consider that the phenonium ion is the intermediate in the solvolysis of **1**, and thus the conclusion drawn is that an S_Ni (ion pair) mechanism opperates in the retentive ethanolysis which is one of the concurrent reactions of **1** (Scheme 6).

As indicated by Parker and Isaacs,[10] the transition state depicted by Brewster is similar to the borderline S_N2 mechanism with the added proviso that the reagent is held close to the epoxide oxygen by electrostatic forces. However, the authors consider that the transition state of retentive ethanolysis of **1** has a stronger

Table 7. Stereochemical results of the acid-catalyzed solvolysis of aryloxiranes

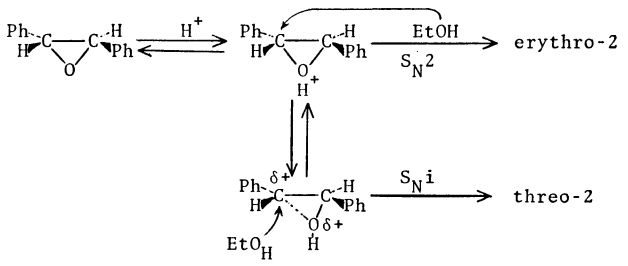
	Alcoholysis	Hydrolysis
2-Phenyloxirane	11% ret–89% inv[a]	50% ret–50% inv[b]
trans-2,3-Diphenyloxirane	26% ret–73% inv[c]	60% ret–40% inv[d]

a) Methanoylsis at 22.8 °C, J. Biggs, N. B. Chapman, and V. Wray, *J. Chem. Soc., B*, **1971**, 71. b) Suspension; C. Dupin and J.-F. Dupin, *Bull. Soc. Chim. Fr.*, **1970**, 249. c) Ethanolysis at 50 °C; this work. d) Extrapolation value from the results on hydrolysis in the mixtures of water and various kinds of co-solvents; unpublished work of this laboratory.

TABLE 8. CO-SOLVENT EFFECTS ON ETHANOLYSIS OF **1**[a] AND PHYSICAL PROPERTIES OF CO-SOLVENTS

Co-solvent	Ret.[b] %	Rearr.[b] %	ε	pK_a of conjugate acid	E_T	
CH_3NO_2	56	32	35.87	−11.7	46.3	group 1
CH_3CN	48	22	37.5	−10.13	46.0	group 1
Sulfolane	44	23	43.3		44.0	group 1
$PhNO_2$	44	24	34.82	−10.39	42.0	group 1
PhCN	41		25.2	−10.45	42.0	group 1
Acetone	40	23	20.7	−6.5	42.2	group 1
Benzene	35	17	2.275		34.5	group 2
Diglyme	34	36				group 2
DME	33	29	7.20	−3.27	38.2	group 2
$CHCl_2CHCl_2$	33	12	8.20			group 2
Toluene	33	20	2.379		33.9	group 2
Dioxane	32	32	2.207	−3.22	36.0	group 2
m-Xylene	32	19	2.374			group 2
Mesitylene	30	17	2.279			group 2
THF	28	38	7.85	−2.08	37.4	group 2
CCl_4	27	12	2.238		32.5	group 2
Hexane	26	12	1.8799		30.9	group 2
Bu_2O	25	15	3.083	−5.40		group 2
Cyclohexane	25	14	2.023			group 2
DMF	20		52.1	(−0.19)[c]	43.8	group 3
DMSO	16		44.68	0	45.0	group 3
HMPA	10	21	30			group 3
Ethanol	26	12	24.55	(−2.2)[d]	51.9	

a) See foot-note a) of Table 5. b) See foot-notes b) and c) of Table 1. c) pK_a of the conjugate acid of *N*,*N*-dimethylacetamide. d) pK_a of the conjugate acid of methanol.



Scheme 6.

tendency toward an S_N1 mechanism than that of the borderline S_N2 reaction giving the inverted product, and this will be discussed in a separate paper.

In Table 8, the stereochemical results in binary solvent systems are given together with the dielectric constants, the pK_a of conjugate acids,[17] and the E_T values[18] of the co-solvents. No direct relationship has been established between the stereochemical results and the physical properties of the co-solvents. However, a detailed examination of Table 8 suggests that the co-solvents can be classified into three groups. The first group (group 1) contains acetonitrile, nitromethane, sulfolane,[19] *etc.*, which have poor basicities and high dielectric constants in which the ethanolysis of **1** yields large amounts of retained product. The second group (group 2) solvents have poor basicities and low dielectric constants, and these co-solvent have no effect or a slightly retentive effect on the ethanolysis of **1**. The third group (group 3) contains aprotic polar solvents such as DMSO, DMF, and HMPA. The difference between the aprotic polar solvents and those of the first group is that the former have a much more basic character, therefore, higher coordinating abilities than those of the first group.

To discuss the function of co-solvents in ethanolysis of **1**, the nature of the solvation has to be known. Solvation shells are most often discussed in terms outlined by Gurney[20] as regions A, B, and C. Region A is one of high order imposed by the influence of the solute on nearby solvent molecules. Region C is a region of unaltered bulk solvent. Region B is a "disordered" compromise region which is influenced comparably both by the forces exerted by the solute which produce region A near the solute and by the solvent-solvent forces which produce region C in the bulk far from the solute.[21]

A modification of Gurney's classification will be made,[22] extended to the solvation of protons in binary solvent mixtures, and used here. Region A is defined as a primary coordination sphere. In region A, the proportion of the solvent with strong basicity, *i.e.* high coordinating ability to a proton, should be larger than in the whole solvent system. For example, in the ethanol–acetonitrile system, the proportion of ethanol in region A should be larger than that in the bulk solution, since ethanol is a stronger base than acetonitrile. In the ethanol–DMSO system, the proportion of DMSO in region A is larger, since DMSO is a

stronger base than ethanol. Region C is a bulk region, in which the composition of solvents is the same as the compostition of the whole solvent system. Region B is defined as a transition region between region A and region C, and influenced by many kinds of forces. Among them, charge-dipole interaction which is a long range intermolecular force appears to be the most important in the present case. It is difficult to estimate the composition of solvents in region B of the binary solvent systems, since the nature of charge-dipole interactions in solution is not yet clear. However, it may be pointed out that the proportion of the solvent of high dielectric constant should be higher in region B than in the bulk solution, since the effects of the dielectric field of the proton can be relaxed by the dielectric polarizability of the solvent. The discussion is clearly oversimplified, but is able to explain the stereochemical results.

It is well established that initial protonation is a fast reversible step in the acid-catalyzed ring-opening reaction of epoxides. Around the proton of the protonated epoxide, solvent molecules build up region A,[23] and the back of the epoxide ring borders on region B.[24,25] Ethanol proportions in the two regions A and B differ by the influence of basicity and dielectric polarizability of co-solvent, and therefore, the effective concentrations of ethanol on both sides of epoxide differ in the *ground state* of ethanolysis. In other words, the effective concentrations[26] of ethanol for S_Ni and S_N2 reactions differ from each other and this difference results in the changes of the steric course of ethanolysis of **1**.

On the basis of the above discussion, the stereochemistry of the ethanolysis can be explained as follows. In binary ethanolic mixtures containing group 1 co-solvents, effective concentration of ethanol to the front of the epoxide is much higher than to the back of the epoxide, since the proportion of co-solvent in region B and that of ethanol in region A are higher than those in the whole solvent system. Consequently, the ethanolysis of **1** in these solvent system yields larger amounts of the retained product than in pure ethanol.[27] In binary ethanolic mixture containing group 3 co-solvents, the strong basicity of the co-solvent results in an increase of co-solvent proportion in region A, and in a decrease of effective concentration of ethanol to the front of the epoxide. Consequently, the ethanolysis of **1** in ethanol-group 3 co-solvent mixtures yields larger amounts of the inverted product. In binary ethanolic mixtures containing group 2 co-solvents, which have low dielectric constants, the probability of the existence of group 2 co-solvents in regions A and B is low, since the two regions are in a dielectric field of positive charge. As a results, the steric course of the ethanolysis of **1** in these solvent mixtures is similar to that in pure ethanol.

The discussion mentioned above may not be limited to the epoxide reaction, and Streitwieser and Doering's results quoted at the beginning of this paper may be explained using this theory.

The medium effects on the steric course of acid-catalyzed solvolitic reactions of **1** and optically active 2-phenyloxirane are now being investigated.

Experimental

Materials. *trans*-2,3-Diphenyloxirane (**1**) was prepared by the *m*-chloroperbenzoic acid oxidation of *trans*-stilbene and recrystallized from hexane and then from benzene, mp 68.5—69.5 °C (lit,[28] 69.0—69.5 °C). Ethanol was dried by Lund and Bjerrum's method.[29] All the co-solvents were dried by the most efficient ways reported in the literature[30] and distilled before use.

erythro-*2-Ethoxy-1,2-diphenylethanol* (erythro-***2***). A mixture of *meso*-1,2-diphenyl-1,2-ethanediol[31] (2.0 g) and triethyloxonium tetrafluoroborate (2.66 g) in dry ether (100 ml) was stirred for 24 h at room temperature, poured into water, and extracted with ether. The ether layer was dried over sodium carbonate and removal of the solvent gave 1.3 g of a white solid. GLC analysis indicated that it contained three products. After separation of the products by column chromatography, *erythro*-**2** (117 mg) was obtained from the middle fraction, mp 52.5—53.5 °C (lit,[32] 45—50 °C). NMR ($CDCl_3$) δ: 1.1[0] (3H, t, J=7 Hz), 2.4[7] (1H, d, J=4 Hz, OH), 3.3[7] (2H, AB part of ABX_3 coupling), 4.4[0] (1H, d, J=5 Hz), 4.8[3] (1H, d d, J=4 and 5 Hz), and 7.1[3] (10H, phenyl). Found: C, 79.47; H, 7.56%. Calcd for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49%.

The other products were the starting material and *meso*-1,2-diethoxy-1,2-diphenylethane.

threo-*2-Ethoxy-1,2-diphenylethanol* (threo-***2***). 2-Ethoxy-1,2-diphenylethanone was reduced with sodium borohydride in the usual way. GLC analysis indicated that the crude product was composed of two components with a ratio of 87:13. The crude product was purified by column chromatography. The major product consisted of *erythro*-**2**, and *threo*-**2** was obtained as the minor one which did not crystallize even after several months. NMR ($CDCl_3$) δ: 1.2[1] (3H, t, J=7 Hz), 1.7 (1H, s, OH), 3.3[9] (2H, q, J=7 Hz), 4.1[8] (1H, d, J=8 Hz), 4.5[8] (1H, d, J=8 Hz), and 7.0[7] (10H, phenyl). Found: C, 79.32; H, 7.52%. Calcd for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49%.

Ethylation of *dl*-1,2-diphenyl-1,2-ethandiol by the oxonium salt gave no reaction.

1,1-Diethoxy-2,2-diphenylethane (***4***). To a solution of **3**[33] (2.0 g) in abs ethanol (70 ml), a drop of concd sulfuric acid was added. The reaction mixture was stirred for 24 h at room temperature. GLC analysis of the reaction mixture indicated 97% conversion to **4**. Distillation of the neutralized reaction mixture gave 1.6 g of **4**: bp 117—119 °C/2.5 mmHg: IR: 1060 and 1120 cm^{-1}; NMR ($CDCl_3$) δ: 1.0[3] (6H, t, J=7 Hz), 3.5 (4H, AB part of ABX_3 coupling $\Delta\nu$=10 Hz, J_{AB}=9.3 Hz, J_{AX}=6.8 Hz, J_{BX}=7.2 Hz), 4.2[3] (1H, d, J=7.8 Hz), 5.0[5] (1H, d, J=7.8 Hz), and 7.3[9] (10H, phenyl).

When anhydrous copper(II) sulfate was used for the acetallization instead of sulfuric acid, initially formed **4** was converted into **6**[34] before acetallization was completed.

Ethanolysis of ***1*** *in Pure Ethanol.* To a 20 ml ethanolic solution of weighed quantities of **1** and dibenzyl ether (internal standard) held in a controlled-temperature block, acidified (H_2SO_4) ethanol (2 ml) was added with vigorous shaking. After a definite period, the reaction mixture (0.5 ml) was pipetted into a sampling tube containing a small amount of potassium carbonate and the tube shaken vigorously. The quenched sample was kept at room temperature for a day and analyzed by GLC.

Ethanolysis of ***1*** *in Binary Solvent Systems.* To a 10 ml ethanolic solution of **1** (200 mg) and dibenzyl ether (30—50 mg, weighed), co-solvent (10 ml) was added and the mixture held in a controlled temperature block. Ethanolic solu-

tion of sulfuric acid (2 ml, *ca* 0.01 N)[35] was added to the mixture and then treated as reported above.

GLC Analysis. The GLC analyses (Hitachi 163 gas chromatograph) were carried out successfully on a 4 m column of 5% PEG-20M on Shimalite W at a column temperature of 205 °C. For example, the retention times of dibenzyl ether, **4**, **5**, **6**, **3**, *threo*-**2**, **7**, *erythro*-**2**, **8**, and three compounds (**9**, **10**, and **11**) were 9.3, 11.4, 12.3, 14.6, 15.2, 18.2, 20.3, 23.8, 25.8, and 31.2 min respectively.

Autoxidation of **3**. To a solution of freshly prepared **3** (10 mg) in ethanol (10 ml), a catalyst was added. The reaction mixture was kept at room temperature for 24 h and subjected to GLC analysis. The conversions of **3** to **5** (catalyst; a small amount of potassium carbonate, a small amount of sodium carbonate, 0.1 ml of 0.1 N sulfuric acid solution in ethanol) were 100, 53, and 0.3%. Only a trace of **5** was found when the ethanolic solution of **3** was allowed to stand for a day without catalyst.

Appendix

From the reaction sequence described in Scheme 1, the following equations may be obtained:

$$\frac{d[\textit{threo}\text{-}\mathbf{2}]}{dt} = k_{ret}[EtOH][\mathbf{1}\text{-}H^+] + \frac{k_1k_2[co\text{-}sol][\mathbf{1}\text{-}H^+][EtOH]}{k_2[EtOH]+k_{-1}},$$

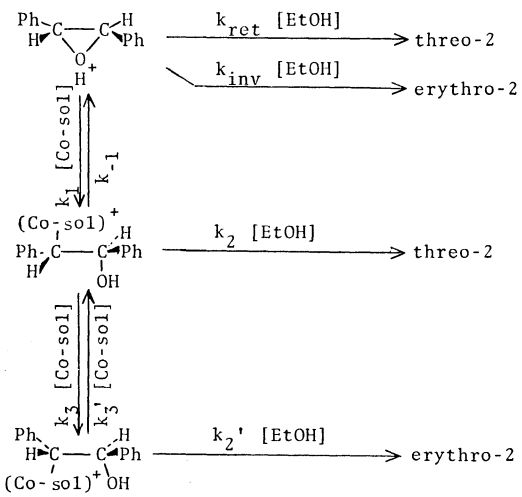
$$\frac{d[\textit{erythro}\text{-}\mathbf{2}]}{dt} = k_{inv}[EtOH][\mathbf{1}\text{-}H^+].$$

Therefore,

$$\frac{[\textit{threo}\text{-}\mathbf{2}]}{[\textit{erythro}\text{-}\mathbf{2}]} = \frac{k_{ret}}{k_{inv}} + \frac{\frac{k_1}{k_{inv}}[co\text{-}sol]}{[EtOH]+\frac{k_{-1}}{k_2}}.$$

If the effective concentrations in reaction kinetics are the same as the molar concentration of the medium, the values 0.48, 2.04, and 0.55 for k_{ret}/k_{inv}, k_1/k_{inv}, and k_{-1}/k_2 respectively can satisfy the experimental results presented in Table 2 except in the case of 91 vol % of acetonitrile concentration. However, the value 2.04 for k_1/k_{inv} indicates that the nucleophilicity of acetonitrile to the conjugate acid of **1** (**1**-H$^+$) is stronger than that of ethanol, whereas the reaction scheme includes an assumption that the co-solvent, as compared with ethanol, has a negligibly small nucleophilicity to the intermediate **12**.

It is difficult to consider that the two orders of the nucleophilicities of ethanol and acetonitrile toward **1**-H$^+$ and **12** have been reversed. The nucleophilicity of co-solvent to **12** is assumed, which leads to the following reaction scheme (Scheme 7).



Scheme 7.

The implications of this reaction-scheme are similar to Streitwieser's. However, a solution of the reaction kinetics using the steady state method leads to the same difficulties as mentioned above since the experimental results are satisfied only when $k_1 > k_{inv}$ and $k_2 > k_3$.

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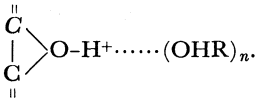
23) Major parts of solvation energies should come from hydrogen bonding from acidic hydrogen of the conjugate acid of epoxide to "bulk ethanol,"



For a detailed discussion of hydrogen bonding from the hydrogen of onium ion to "bulk water," see for example; E. M. Arnett, B. Chawla, L. Bell, M. Taagepera, W. J. Hehre, and R. W. Taft, *J. Am. Chem. Soc.*, **99**, 5729 (1977).

24) A variety of the values for the solvation number of proton have been reported; 1—2,[a] 2.5,[b] 3.9,[c] 5,[d] and 10.[e] The oxonium ion (**1**-H$^+$) in solution can be considered to be formed by substitution of one of the solvent molecules in solvation shell of proton (region A) for the epoxide.

As the first solvation shell of proton (region A) is small, the side opposite to that of the epoxide oxygen of **1** borders on region B.

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25) These structures of solution are easily fading, but have enough life time for epoxide to be attacked in these solution structures, because acidic hydrogen should exist at the epoxide oxygen during the reaction.

26) A similar concept has been discussed in terms of preferential solvation, see Ref 21.

27) If ethanol molecules in region A are completely oriented by the effect of charge of proton, nucleophilicity of the ethanol should be much lower than that of ethanol in region C. However, this problem can be solved by Backrins-Saluja's model for solvation, in which coordination number is always larger than solvation number.[a] In other words, they pointed out the existence of non-solvated coordinated molecules in region A. In the present case, the non-solvated coordinated ethanols in region A have ordinary nucleophilicity to **1** to yield the retained product (*threo*-**2**).

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35) A definite concentration of sulfuric acid solution in ethanol (0.01 N) was prepared initially, but the correction factor decreased gradually on storage. However, the stereochemical results of ethanolysis of **1** in binary solvent systems were not affected by the acid concentration.