Stereochemistry of Elimination Reactions of Halohydrin Derivatives and Related Compounds with Butyllithium[1)]

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The *erythro* and *threo* isomers of 1-bromo-2-methoxy-1,2-diphenylethane (**1**), 1-bromo-2-acetoxy-1,2-diphenylethane (**2**), 1-bromo-2-methylsulfonyloxy-1,2-diphenylethane (**3**), 1-bromo-2-methylthio-1,2-diphenylethane (**4**), stilbene dibromide (**6**), and stilbene dichloride have been prepared. These compounds were allowed to react with butyllithium in various solvents to give *cis*- and *trans*-stilbenes. Depending on the solvent, the stereochemistry of the elimination of **1** changed from a complete *syn*-type (in nonpolar solvents) to a less-selective type. The same tendency was observed in the cases of **2** and **3**. In contrast, *anti*-elimination was favored for **4** and **6**, and a different type of solvent effect was observed. Elimination reactions with lithium metal and pentylmagnesium bromide were also carried out. Possible mechanisms for eliminations are discussed.

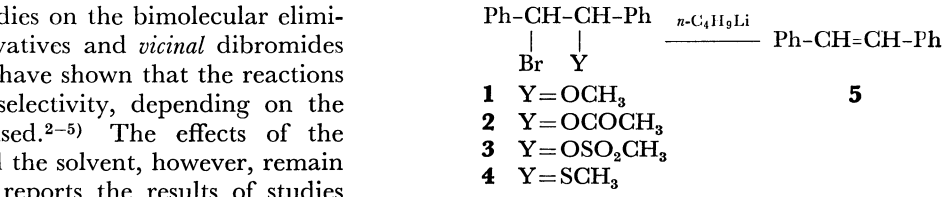
Results of extensive studies on the bimolecular elimination of halohydrin derivatives and *vicinal* dibromides with metal or metal salts have shown that the reactions display a variable stereoselectivity, depending on the nature of the metals used.[2–5)] The effects of the structure of substrates and the solvent, however, remain ambiguous. This paper reports the results of studies on the stereochemistry of the elimination of stilbene halohydrin derivatives and related compounds; in particular, the effects of the leaving group and the solvent were probed.

House and Ro have shown that the treatment of β-halo ethers and esters with zinc in aqueous ethanol or with sodium in tetrahydrofuran gave nonstereospecific elimination products.[2)] They postulated that the organometallics formed by halogen–metal exchanges give olefins by the mechanism of ElcB but not by that of E2, because OR and OCOR are poor leaving-groups. However, since the reactions of metals such as magnesium[6)] and lithium[7)] with alkyl halides to form Grignard and organolithium reagents result in the loss of stereochemical integrity, it is not clear whether the loss of stereospecificity in the reaction of halohydrin derivatives with metal occurs during the halogen–metal exchange or in the subsequent elimination process.

When the halide is treated with an alkyllithium reagent instead of lithium metal, the lithium compound formed is capable of maintaining its configuration, although the degree of retention of configuration is both solvent- and temperature-dependent.[8)] In order to preclude the loss of stereospecificity in the halogen–metal exchange stage, our eliminations were carried out by the use of butyllithium.

Results

The *erythro* and *threo* pairs of 2-substituted 1-bromo-1,2-diphenylethanes were chosen as the substrates because of their accessibility in pure form and the accuracy with which analysis of the products is possible. The *erythro* (**e**) and *threo* (**t**) isomers of 1-bromo-2-methoxy-1,2-diphenylethane (**1**), 1-bromo-2-acetoxy-1,2-diphenylethane (**2**), 1-bromo-2-methylsulfonyloxy-1,2-diphenylethane (**3**), and 1-bromo-2-methylthio-1,2-diphenylethane (**4**) have been prepared. Each compound was allowed to react with butyllithium in various kinds of solvents. The organic products were analyzed by GLPC. *cis*- (**5c**) and *trans*-Stilbenes (**5t**) produced were isolated and identified by means of GLPC, IR, and NMR. The results are summarized in Table 1.



In any attempt to account for stereoselectivity, we must remember that **5t** is much more stable than **5c** under the reaction conditions: the thermodynamical isomer ratio of *trans* to *cis* is 500 at 25 °C.[9)] The exclusive formation of **5c** from **1e** as well as **5t** from **1t** in nonpolar solvents such as diethyl ether and benzene indicates that the stereospecific *syn* elimination occurred in the reaction of **1** with butyllithium in nonpolar solvents. Although the stereospecificities were diminished, the same tendency of *syn* elimination was clearly observed in the cases of **2** and **3**.

The solvent study was limited by the insolubility of the substrates in hydrocarbon solvents. Within the limited range of solvents, however, it was observed that changing the solvent from nonpolar to better solvating ones, such as tetrahydrofuran (THF) or bis(2-methoxyethyl) ether (diglyme), diminished the stereospecificity. The addition of a cation complexing reagent, *N,N,N,N*-tetramethylethylenediamine (TMEDA), also reduced the stereospecificity. The fact that only **5c** was formed, even in the elimination reaction using an excess amount of butyllithium, can eliminate the possibility of isomerization of **5c** to **5t** in nonpolar solvents. In a separated experiment, in which **5c** was treated with an equivalent amount of butyllithium in diglyme under the reaction condition, the recovered **5** was exclusively *cis* isomer. Thus the possibility of isomerization can also be eliminated in a better solvating medium.

When **1e** in diethyl ether was treated with butyllithium at −72 °C and the reaction was quenched

Table 1. Elimination reactions of stilbene halohydrin derivatives with butyllithium

Run	Substrate (mmol)	n-C_4H_9Li (mmol)	Solvent (ml)	Additive (mmol)	React. condition		5		
					Time (min)	Temp (°C)	Yield (%)	*cis* : *trans*	
1	**1e** (1.01)	1.0	Et_2O (50)		30	0	42	100	trace
2	**1e** (1.00)	2.3	Et_2O (50)		30	0	48	100	trace
3	**1e** (1.00)	5.3	Et_2O (50)		30	0	44	100	trace
4	**1e** (1.00)	1.2	Benzene (50)		30	r. t.	22	100	trace
5	**1e** (1.00)	2.0	Benzene (50)		30	r. t.	32	100	trace
6	**1e** (1.05)	2.4	THF (50)		15	0	59	52	48
7	**1e** (1.34)	3.5	Diglyme (50)		10	0	76	22	78
8	**1t** (1.11)	3.5	Et_2O (50)		10	0	53	trace	100
9	**1t** (1.02)	2.4	THF (50)		15	0	48	trace	100
10	**1t** (1.41)	3.5	Diglyme (50)		10	0	93	trace	100
11	**2e** (0.31)	1.48	Hexane (25)		30	0	30	37	63
12	**2e** (0.31)	1.48	Benzene (25)		30	r. t.	28	48	52
13	**2e** (0.31)	1.48	Et_2O (25)		30	0	46	12	88
14	**2e** (0.31)	1.48	THF (25)		30	0	52	12	88
15	**2e** (0.31)	1.48	Diglyme (25)		30	0	84	8	92
16	**2e** (0.31)	1.48	Hexane (25)	TMEDA (1.5)	30	0	13	11	89
17	**2t** (0.31)	1.48	Hexane (25)		30	0	18	8	92
18	**2t** (0.31)	1.48	Benzene (25)		30	r. t.	29	9	91
19	**2t** (0.31)	1.48	Et_2O (25)		30	0	34	4	96
20	**2t** (0·31)	1.48	THF (25)		30	0	5	trace	100
21	**2t** (0.31)	1.48	Diglyme (25)		30	0	23	3	97
22	**3e** (0.28)	2.08	Benzene (25)		30	r. t.	56	57	43
23	**3e** (0.28)	2.08	Et_2O (25)		30	0	49	21	79
24	**3e** (0.28)	2.08	THF (25)		30	0	52	7	93
25	**3e** (0.28)	2.08	Diglyme (25)		30	0	38	7	93
26	**3t** (2.08)	2.08	Benzene (25)		30	r. t.	53	3	97
27	**3t** (0.28)	2.08	Et_2O (25)		30	0	54	4	96
28	**3t** (0.28)	2.08	THF (25)		30	0	22	8	92
29	**3t** (0.28)	2.08	Diglyme (25)		30	0	18	3	97
30	**4e** (0.33) [a]	2.08	Benzene (25)		30	r. t.	37	3	97
31	**4e** (0.33) [a]	2.08	Et_2O (25)		30	0	42	2	98
32	**4e** (0.33) [a]	2.08	THF (25)		30	0	40	trace	100
33	**4e** (0.33) [a]	2.08	Diglyme (25)		30	0	36	2	98
34	**4t** (0.33) [a]	2.08	Benzene (25)		30	r. t.	59	trace	100
35	**4t** (0.33) [a]	2.08	Et_2O (25)		30	0	43	trace	100
36	**4t** (0.33) [a]	1.50	Et_2O (25)		30	0	54	2	98
37	**4t** (0.33) [a]	2.08	THF (25)		30	0	56	6	94
38	**4t** (0.33) [a]	2.08	DME (25)		30	0	49	9	91
39	**4t** (0.33) [a]	2.08	Diglyme (25)		30	0	67	86	14
40	**4t** (0.33) [a]	2.08	Et_2O (25)	TMEDA (2.1)	30	0	10	6	94
41	**4t** (0.32) [a]	1.15	Et_2O (25)	TMEDA (6.5)	30	0	65	20	80
42	**4t** (0.33) [a]	1.50	Et_2O (25)	TMEDA (8.8)	30	0	56	33	67
43	**4t** (0.33) [a]	1.50	Et_2O (25)	CE (1.85) [b] DME (9.2)	30	0	60	19	81
44	**4t** (0.35) [a]	1.15	Et_2O (25)	DME (6.7)	30	0	72	5	95

a) The substrate contained a small amount (less than 5%) of **6**, and the product ratio is uncorrected for the contamination. b) Dicyclohexyl-18-crown-6.

with methanol after 0.5—3 min, small amounts of 1-methoxy-1,2-diphenylethane were detected by GLPC, together with **5c** and unreacted **1e**. This GLPC peak could not be detected any more when the reaction was completed after 30 min.

As can be seen from Table 1, the stereochemical feature of elimination of 1-bromo-2-methylthio derivative (**4**) were quite different from the above-mentioned oxygen analogue (**1**). Recently Trost and Ziman reported that the elimination of 2-bromo-3-ethylthio- and 2-bromo-3-phenylthiobutanes with butyllithium proceeded with a moderate to high degree of *anti* stereoselectivity in THF solution.[10] In our case, the stereospecificity of the elimination was completely lost in nonpolar solvents such as benzene or diethyl ether, while a high *anti* stereoselectivity was observed in a

Table 2. Elimination reactions of stilbene dihalides with butyllithium

Run	Substrate (mmol)	n-C_4H_9Li (mmol)	Solvent (ml)	React. condition		5	
				Time (min)	Temp (°C)	Yield (%)	*cis* : *trans*
45	**6e** (1.21)	1.2	Et_2O (50)	10	0	43[a]	trace 100
46	**6e** (1.20)	2.4	Et_2O (50)	10	0	95	trace 100
47	**6e** (1.05)	3.6	Et_2O (50)	60	−59	35[a]	trace 100
48	**6e** (1.03)	5.5	Diglyme (50)	10	0	99	trace 100
49	**6t** (1.53)	4.4	Et_2O (50)	15	0	100	19 81
50	**6t** (1.54)	4.8	Et_2O (50)	120	−58	100	21 79
51	**6t** (1.53)	5.5	Diglyme (50)	15	0	99	20 80
52	**7e** (1.02)	3.6	Et_2O (80)	10	0	99	trace 100
53	**7t** (1.14)	3.6	Et_2O (50)	10	0	62[a]	3 97

a) Unreacted substrate was recovered.

Table 3. Elimination reactions with lithium metal[a]

Run	Substrate (mmol)	Li (mg-atom)	Reaction time (h)	8	5	
				Yield (%)	Yield (%)	*cis* : *trans*
54	**1e** (2.11)	24	30	9.1	67	13 87
55	**1e** (2.10)	17	50	7.7	79	11 89
56	**1t** (2.17)	17	15	18	18	0 100
57	**1t** (2.10)	26	30	11	6	0 100
58	**1t** (1.74)	16	50	20	trace	

a) The reactions were carried out under reflux in 100 ml of diethyl ether.

highly cation solvating medium such as diglyme. By increasing the cation solvating ability of the solvent, the *anti* elimination was increased. When 5 equivalents of TMEDA or 1 equivalent of crown ether accompanied with 5 equivalents of 1,2-dimethoxyethane (DME) was added, moderate *anti* stereoselectivities were observed even in the diethyl ether medium.

In a similar study by Winkler on phenyllithium-induced debromination of *dl*- and *meso*-2,3-dibromobutanes, an almost exclusive *anti* elimination has been demonstrated.[11] In order to compare with these data, we investigated the stereochemistry of elimination with butyllithium on *vicinal* dibromide as well as dichloride in the present stilbene system. The results are summarized in Table 2.

The debromination of *meso*-stilbene dibromide (**6e**) produced only **5t**, but a mixture of 20% of **5c** and 80% of **5t** was obtained from the *dl*-isomer (**6t**). By the fact that the thermodynamically unstable **5c** was obtained from **6t**, it is apparent that the reaction proceeds by *anti* fashion, but the stereospecificity is considerably lower than in the case of 2,3-dibromobutane. In this case, no solvent effects on the stereochemistry were observed when the solvent was changed from diethyl ether to diglyme.

In the case of *vicinal* dichloride (**7**), the elimination was no longer stereoselective, and **5t** was virtually exclusively obtained from both the *dl* and *meso* isomers.

The present stereochemical results of elimination of bromohydrin derivatives with butyllithium markedly contrast with those using metals such as zinc and sodium, which resulted in nonstereospecific eliminations.[2] There have also been indications that certain metal debrominations may display a variable stereoselectivity, and a surface radical process has been suggested for the debromination reaction of **6** with metals.[4] In order to learn more about the discrepancy of the stereochemistry of elimination with butyllithium and with metal, we undertook the elimination reaction using lithium metal.

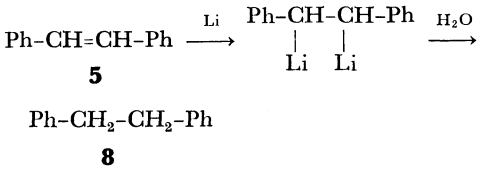
The β-bromo ether **1** was refluxed with lithium metal in diethyl ether. The amounts of **5** and 1,2-diphenylethane (**8**) produced were determined by GLPC analysis and are summarized in Table 3. As the IR spectra of the unreacted **1** recovered from the reaction mixture were superimposable with those of each starting material, the possibility of isomerization during the reaction process could be eliminated.

Since the formation of dilithio compounds from **5** and the other arylated alkenes has been reported,[12] **5t** was allowed to react with lithium metal under the reaction conditions, **8** was obtained after the work-up, as shown in Table 4. These results indicate that **8** was produced by addition of the excess lithium metal to **5** of the elimination product, followed by hydrolysis in the work-up process. Since the relative rate of formation of the dilithio compounds from **5c** and **5t** is not clear, the ratios of **5c** and **5t** in Table 3

Table 4. Reactions of **5** with lithium metal[a]

5t (mmol)	Li (mg-atom)	Reaction time (h)	Yield of **8** (%)
2.04	18	5	37
2.04	16	30	70

a) Reactions were carried out under reflux in 100 ml of diethyl ether.



may not reflect the actual ratios of the elimination process. However, the result that **5c** was obtained only from **1e**, though the yield was not so high, indicates that *syn* elimination has occurred at least partly in the reaction using lithium metal.

Dehydrohalogenation of alkyl halide[13] and debromination of *vicinal* dibromide[4] with Grignard reagents have been investigated in only a few instances. Furthermore, β- and γ-haloalkyl phenyl ethers gave olefin and cyclopropane respectively by the reaction with Grignard reagents in the presence of cobaltous bromide.[14] On the other hand, halogen–metal interchange reactions with Grignard reagents have been established.[15] Zakharkin and his coworkers have made extensive studies of the exchange of Grignard reagents with ordinary alkyl and aryl halides.[16] Highly solvating ethers such as THF and DME favor the exchange. The rate of exchange is dependent on the polarizability of the halogens in the alkyl halides. On the basis of these studies, they have concluded that the mechanism of halogen–metal interchange reaction is the same for both organomagnesium and organolithium compounds. We thus undertook an investigation of the stereochemistry of elimination promoted by pentylmagnesium bromide. The results are given in Table 5.

TABLE 5. ELIMINATION REACTIONS OF **1** WITH PENTYLMAGNESIUM BROMIDE[a]

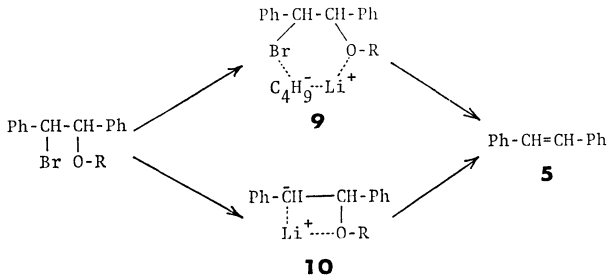
Substrate (mmol)	n-$C_5H_{11}MgBr$ (mmol)	Reaciton time (min)	**5** Yield (%)	*cis* : *trans*	
1e (1.05)	2.0	90	27	0	100
1e (1.01)	2.0	180	49	0	100
1e (1.05)	2.0	360	34	0	100
1t (1.04)	2.0	180	31	0	100
1t (1.04)	2.7	360	33	0	100

a) Reactions were carried out in 50 ml of diethyl ether at 0 °C.

As can be seen from Table 5, **5t** was an exclusive product from both **1e** and **1t**. As the IR spectra of substrates recovered from the reaction mixtures were completely identical with that of the respective starting materials, isomerization of the substrates during the reaction process can be eliminated. The isomerization of **5** also could not be detected under the experimental conditions. The present results indicate the elimination reaction of β-halo ethers promoted by a Grignard reagent to be nonstereospecific.

Discussion

Although a number of mechanistic implications have been reported for the base-catalyzed bimolecular elimination reactions, two possible routes may be considered for the butyllithium-induced *syn* elimination of halohydrin derivatives. One is the process *via* a cyclic transition state such as **9**, and the other is a mechanism which involves a carbanion or the equivalent organolithium reagent (**10**). In both cases, the factor which forces the production of **5c** from the *erythro* isomers of substrates, even against the large thermodynamical instability of the product, is expected to be the coordination between lithium and oxygen atoms. This is proved by the fact that the stereospecificity of *syn* elimination decreased by increasing the cation complexing ability of solvents. The cation complexing ability of the medium increases in the order: hexane < benzene < diethyl ether < THF < DME < diglyme,[17] and is also enhanced by the addition of cation-coordinating reagents such as TMEDA and crown ethers.[18,19]



Scheme 1.

The cyclic transition state (**9**) is similar to that postulated by Letsinger to explain the more rapid *syn* elimination of the elements of methanol when *cis*- and *trans*-1-methoxy-2-phenylcyclohexanes are heated under reflux with butyllithium in a mixture of pentane and diethyl ether.[20] The coordination between lithium and oxygen should be stronger in a nonpolar solvent such as hexane, benzene, or diethyl ether, and weaker in the coordinating solvents. Thus the reduction of stereospecificity in THF or diglyme solvent would seem to occur as a matter of course. However, the fact that considerable lower stereospecificity was observed in the reactions of **2** and **3** in nonpolar solvents in comparison with the reaction of **1** is not conceivable from a concerted mechanism *via* such a cyclic transition state, because it was recently reported by Staley and Beauchamp that the binding energy of an ester to a lithium cation is much stronger than that of an ether.[21]

The alternative mechanism involving a carbanion intermediate (**10**) appears to be more plausible, because of the poor leaving group ability of OR and OCOR. The formation of the carbanion intermediate is also evidenced by the fact that 1-methoxy-1,2-diphenylethane was detected when the reaction of **1** at −72 °C was quenched by methanol. House and Ro postulated a similar intermediate for the nonstereospecific elimination of β-halo ethers and esters with zinc and sodium.[2]

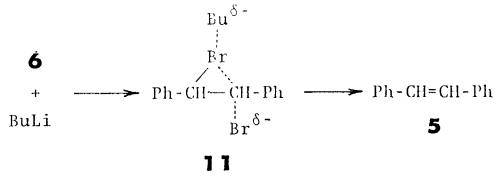
It has been demonstrated that metal–halogen exchange with butyllithium occurs with a high degree of retention of configuration.[8] While spectroscopic studies indicate a polar covalent character for the

carbon–lithium bonds in alkyllithiums, it has also been revealed that alkyllithiums exist in solution in equilibrium with different types of ion pairs: tight, solvent separated, and free ion-pairs, and that such equilibria are affected not only by the structure of the carbanion but also by the solvent polarity, temperature, and the presence of gegenion-coordinating additives.[18] Thus the *erythro*- and *threo*-carbanions (**10**) are expected to be produced from the corresponding isomers of **1**, **2**, and **3**. These carbanions will form tight ion-pairs with lithium cation in nonpolar solvents. A lithium cation, on the other side, may coordinate with the substituent oxygen. The interaction between the metal cation in a tight ion-pair and the substituent oxygen makes it a better leaving group, and appears to force *syn* elimination.

As the coordinating-ability of an OAc group to a lithium cation is stronger than that of a methoxyl group, and a stronger ability is also expected for the OSO_2CH_3 group, higher *syn* selectivities are expected for **2** and **3** than for **1**. The results summarized in Table 1 are, however, inconsistent with this expectation. These results seems to reflect the ease with which the leaving group Y are eliminated. Although there is no exact data to indicate the departing tendencies of various groups, it would be expected by analogy with the behavior of various groups in nucleophilic displacement reactions to decrease in the following order: $OSO_2CH_3 > OAc \gg OR$.[22] The weakening of the bond to the leaving group makes the carbanionic intermediate **10** unstable, so the elimination mechanism is expected to have an E2 character. The *syn* selectivities of the eliminations of **2** and **3** would thus be lower than that of **1**.

In contrast with the bromohydrin derivatives, the *vic*-dibromide (**6**) indicated *anti*-fashion stereoselectivity ; in this reaction no solvent effect was observed in the stereochemistry of elimination. Stereospecific *anti*-debromination has been reported by Winkler in the reaction of 2,3-dibromobutane with phenyllithium.[11] In the present case, due to a very weak binding energy of bromine to a lithium cation, it is expected to be much weaker than that between a phenyl group of the substrate and a lithium cation,[21] and also due to the easily-departing tendency of bromine, an intermediate such as **10** is not conceivable for the debromination of *vic*-dibromide. The fact that changing the solvent from diethyl ether to diglyme has no effect on the stereochemistry of elimination suggests that a lithium cation should not play an important role on the intermediate or the transition state for butyllithium-catalyzed debromination, and that the reaction proceeds through a concerted process.

Although a number of authors have likened dehalogenation to a base-promoted E2 reaction on the basis of stereochemistry, a more detailed approach have been recently outlined by Miller and his coworkers.[23] We believe that an analogous mechanism can be applied to the present butyllithium-induced debromination, as indicated in Scheme 2. The present results indicated lower stereospecificity than Winkler's results, but this is ignorable if the large differences of the configurational stability between the transition states



Scheme 2.

derived from **6e** and **6t** as well as the products are taken into consideration.

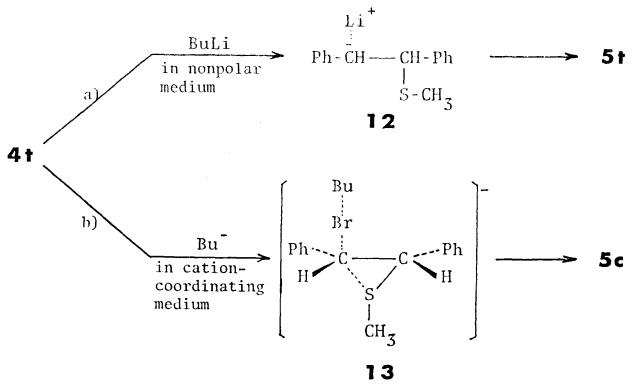
The nonstereospecific results obtained in the butyllithium-induced dechlorination of **7** do not conflict with the above mechanism, because it is well-known that neighboring group participation by chlorine is much weaker than that of bromine; thus the formation of a cyclic transition state such as **11** is difficult for the *vic*-dichloride.

The results of the elimination of **4** contrast markedly with those of the oxygen analogue (**1**), as well as those of the dihalides. In diethyl ether and benzene solvents, the elimination is nonstereospecific, *e.g.*, both *threo* and *erythro* isomers gave thermodynamically stable **5t** exclusively. In diglyme, where the oxygen analogue indicates loss of stereospecificity, however, the elimination converts **4e** into **5t**, and **4t** into 86% of **5c** and 14% of **5t**. The *anti* selectivity is increased by increasing the cation complexing ability of the solvents: THF < DME < diglyme. The addition of cation complexing reagents such as TMEDA and crown ether facilitated the *anti*-elimination. Recently, Panek reported that the rate of geometric isomerization of 1-lithio-1-phenyl-1-butene in hexane solution was enhanced by the addition of cation complexing reagents; the following order was observed: TMEDA > DME > THF > diethyl ether.[19] Furthermore, Walborsky reported that the addition of 1 equiv. dicyclohexyl-18-crown-6 with 5 equiv. of DME was very effective for complexing the lithium cation and making a free carbanion.[24]

A methylthio group may be considered as one of the groups with a lower departing tendency, similar to the methoxyl group. The butyllithium-induced elimination of **4** is thus considered to proceed *via* a carbanion intermediate.

The solvent study indicates that a nonstereospecific elimination results from the tight ion-pair intermediate derived from **4**, and the free ion or the solvent separated ion-pair provides an *anti*-elimination. The coordinating bond strength between a lithium cation and a sulfide sulfur is reported to be very weak, weaker than that between lithium cation and phenyl group.[21] Therefore, there is little effect to force the lithium cation and methylthio group into a *s-cis* conformation. The elimination reaction in nonpolar solvents proceeds *via* a carbanion intermediate (**12**) and the stereochemistry is not specific (Scheme 3, path a).

On the other hand, at present, it appears to be difficult to find a good reason why an *anti* fashion elimination resulted from the free ion of **12**. Although considerable experimental data have been accumulated which indicate that carbanions are stabilized by the adjacent sulfur atom,[25] the participation of sulfur-



Scheme 3.

containing substituents at the β-position with carbanion has rarely been reported. Recently, Kaji and his co-workers reported that the rate of base-catalyzed H–D exchange reactions of substituted cyclopropanes was enhanced by the substitution of a phenylthio group at β-position.[26] They suggested the neighboring sulfur participation in stabilization of the carbanion. Yano and Oae have shown that the rates of the base-catalyzed elimination of a series of γ-(p-substituted phenylthio)propyl bromides are slower than that of the corresponding oxygen analogues and that the ρ value obtained for the sulfur compounds is larger than that for the oxygen compounds.[27] They have suggested the non-bonding participation of a vacant d-orbital of the sulfur atom for the developing double bond to elucidate this phenomena. Furthermore, Howard has proposed a three-membered ring anion involving sulfur, in which the charge of the carbanion is delocalized to the neighboring sulfur atom, as an intermediate of the base-promoted rearrangement of diethyl dithiodiacetate.[28]

In the present case, when a 1-butanide anion pulls bromine off the substrate at the initial stage of the reaction, a vacant 3d-orbital of the sulfur atom assists the developing carbanion at the opposite side from the leaving bromine to form a three-membered ring transition state or an intermediate (**13**). Stereospecific elimination from such an intermediate has been proposed by Trost and Ziman. The desulfurization of *cis*- and *trans*-2-butene episulfides with butyllithium to the corresponding butenes proceeds stereospecifically. They suggested a three-membered ring anion similar to **13** as one of the possible transition state.[10] Thus it is conceivable that the stereospecific *anti* elimination would occur if a neighboring participation of sulfenyl group against the carbanion is taken into account.

When **1** was treated with lithium metal instead of butyllithium, the elimination proceeded with *syn* selectivity, but the selectivity was much lower than the case of organolithium reagent. It has been reported that the reaction of lithium metal with alkyl halides, in which the halogen atom is attached to a tetrahedrally hybridized carbon atom, results in the formation of lithium reagents along with much racemization.[7] Recently a more detailed discussion on the stereochemistry of halogen–lithium exchange reaction with lithium metal has been reported by Walborsky and Aronoff.[7b] Moderate retention of configuration resulted in the reaction of substituted cyclopropyl halide with very finely divided lithium metal, but the optical purity of the produced organolithium compound decreased by increasing the particle size of lithium. It has also been pointed out that the halogen–lithium exchange reaction involves a surface radical process. Thus the loss of stereospecificity in the elimination of **1** with lithium metal is considered to occur during the bromine–lithium exchange process on a lithium metal surface. The nonstereospecific results of House[2] for the use of sodium and zinc metals fit into these considerations.

Halogen–metal exchange reactions involving Grignard reagents have been reported, and it has been found that there is no fundamental difference between exchange reactions in the series of organolithium and magnesium compounds.[16] However, the stereochemistry of the exchange reaction between alkylmagnesium and an alkyl halide is not yet clear. The present result that the Grignard reagent-promoted elimination reaction proceeds nonstereospecifically would imply that the exchange proceeds with racemization. Examinations on these subjects are in progress.

Experimental

IR spectra were obtained using a Hitachi EPI-G2 spectrophotometer. NMR spectra were recorded as $CDCl_3$ solutions on a JEOL PMX-60 spectrophotometer; chemical shifts are reported in parts per million relative to TMS as an internal standard.

Solvents. GR grade diethyl ether was dried over sodium metal and distilled. GR grade THF was distilled from lithium aluminum hydride under nitrogen and stored over 4A molecular sieves. Diglyme was passed through activated alumina, and distilled before use. Bulk solvents were distilled before use.

Reagents. Butyllithium (*ca.* 20% in hexane) was purchased from Merck Co., Inc. and Aldrich Chemical Co. Inc., and titrated before use.[29] Pentylmagnesium bromide in ether was purchased from the Alfa Division of Ventron Corp. and titrated before use.[30] TMEDA was kept over solid sodium hydroxide and used with no further purification. DME was passed through activated alumina before use. Crown ether was purchased from Nippon Soda Co., and was used without further purification. Commercially available GR grade *trans*-stilbene was used without further purification. *cis*-Stilbene, bp 108.5—112.0 °C/2 mmHg, was prepared by the literature procedure.[31]

Preparations of 1-Bromo-2-methoxy-1,2-diphenylethanes (1). Following the procedure developed by House,[2] a solution of 5.4 g (0.03 mol) of **5t**, 10.8 g (0.06 mol) of *N*-bromosuccinimide, 3 ml of acetic acid, and 30 ml of acetone in 300 ml of methanol was allowed to stand for 5 h and then concentrated, diluted with water, and extracted with ether. The ether extract was washed first with water and then with aqueous sodium hydrogencarbonate solution and then dried over sodium sulfate. After removal of ether, petroleum ether was added to the residual oil. The crude bromo ether deposited was recrystallized twice from hexane, giving pure **1e**, mp 120—121 °C (lit,[2] mp 117—118 °C), yield 6.2 g (71%); NMR δ=3.20 (s, 3, OCH_3), 4.63 (d, 1, CHBr), 5.06 (d, 1, J=7 Hz, CHOR), 7.28 (s, 10, C_6H_5). Found: C, 62.12; H, 5.20; Br, 27.43%. Calcd for $C_{15}H_{15}OBr$:

C, 61.86; H, 5.19; Br, 27.45%.

In a similar manner, 5.4 g (0.03 mol) of **5c** afforded 3.7 g (42%) of **1t**, mp 85.5—86.5 °C (lit,[2] mp 86—87.5 °C), NMR δ=3.33 (s, 3, OCH_3), 4.50 (d, 1, CHBr), 5.00 (d, 1, J=8 Hz, CHOR), 7.14 (s, 10, C_6H_5). Found: C, 62.10; H, 5.11; Br, 27.52%. IR of the *threo*-isomer (**1t**) was similar to that of the *erythro*-isomer (**1e**) except for a band at 1215 cm^{-1}, where **1t** exhibited an absorption.

Preparations of 2-Bromo-1,2-diphenylethanols. *erythro*- and *threo*-2-Bromo-1,2-diphenylethanols were prepared by the method of House[32] from **5t** and *cis*-stilbene oxide respectively. The *erythro*-isomer, mp 83.5—85.0 °C (lit,[32] mp 83.5—85.0 °C), and the *threo*-isomer, mp 51.0—52.0 °C (lit,[32] mp 51—52 °C) were used for the following preparations.

*Preparations of 1-Bromo-2-acetoxy-1,2-diphenylethanes (**2**).* To 6.8 g (45 mmol) of *erythro*-2-bromo-1,2-diphenylethanol was added 6.0 ml (64 mmol) of freshly distilled acetic anhydride over a period of 10 min at room temperature. The mixture was stirred at 70 °C for 2 h. 200 ml of water was added to the cooled mixture, which was then extracted with 100 ml of ether three times. The ether extract was washed with water and dried over magnesium sulfate. After removal of ether, the residual product was recrystallized from hexane–petroleum ether, giving **2e**, mp 100.0—100.7 °C (lit,[33] mp 102 °C), yield 6.8 g (87%); NMR δ=1.89 (s, 3, $OCOCH_3$), 5.15 (d, 1, CHBr), 6.50 (d, 1, J=7.5 Hz, CHOAc), 7.23 (s, 10, C_6H_5). Found: C, 60.38; H, 4.61%. Calcd for $C_{16}H_{15}O_2Br$: C, 60.20; H, 4.74%.

In a similar manner, 3.95 g (14.2 mmol) of the *threo*-bromohydrin was treated with 4.0 ml (42.6 mmol) of acetic anhydride to give **2t**, mp 79.5—81.0 °C, yield 3.44 g (70.7%); NMR δ=2.14 (s, 3, $OCOCH_3$), 5.15 (d, 1, CHBr), 6.20 (d, 1, J=4.6 Hz, CHOAc), 7.10 and 7.15 (ds, 10, C_6H_5). Found: C, 60.02; H, 4.62%.

*Preparations of 1-Bromo-2-methylsulfonyloxy-1,2-diphenylethanes (**3**).* To a stirred solution of *erythro*-2-bromo-1,2-diphenylethanol (2.5 g, 9.0 mmol) in 25 ml of pyridine, 1.14 g (10 mmol) of methanesulfonyl chloride was added dropwise at −5 °C. After the mixture had been stirred at 0 °C for 24 h, 5 ml of water was added; then it was extracted with 50 ml each of chloroform three times. The extracts were combined and washed first with dil. sulfuric acid and then with aqueous sodium hydrogencarbonate solution, and dried over sodium sulfate. After removal of chloroform, the residual product was recrystallized from chloroform–petroleum ether. An additional crystallization afforded the pure **3e**, mp 113.5—114.0 °C, yield 1.6 g (50%). NMR δ=2.48 (s, 3, CH_3), 5.15 (d, 1, CHBr), 5.93 (d, 1, J=4.0 Hz, $CHOSO_2$), 7.37 (s, 10, C_6H_5). Found: C, 50.56; H, 4.30; S, 9.11%. Calcd for $C_{15}H_{15}O_3BrS$: C, 50.71; H, 4.26; S, 9.03%.

In a similar manner, 2.5 g of *threo*-2-bromo-1,2-diphenylethanol gave 2.0 g (62.5%) of **3t**, mp 107.0—108.0 °C, NMR δ=2.82 (s, 3, CH_3), 5.17 (d, 1, CHBr), 5.83 (d, 1, J=4.3 Hz, $CHOSO_2$), 7.13 (s, 10, C_6H_5). Found: C, 50.42; H, 4.18; S, 8.62%.

*Preparations of 1-Bromo-2-methylthio-1,2-diphenylethanes (**4**).* The method of Helmkamp[34] was applied to **5**. A solution of 5.0 g (53 mmol) of dimethyl disulfide in 120 ml of dry dichloromethane was placed in a 200 ml four-necked flask protected from moisture. The flask was kept in a cold bath at −20 to −25 °C and was protected from light during the subsequent reaction. A solution of 8.0 g (50 mmol) of bromine in 60 ml of dichloromethane was added dropwise over a period of 2 h with stirring. The mixture was allowed to warm to −15 °C during a 1 h period, then 18.1 g (100 mmol) of **5t** in 140 ml of dichloromethane was added dropwise over a period of 1 h. The mixture was allowed to stand at 0 °C for 24 h. The solvent was stripped off under a reduced pressure; the residual product was recrystallized twice from ligroin to give **4e**, mp 126—127 °C (dec), yield 15.3 g (50%), NMR δ=1.60 (s, 3, SCH_3), 4.20 (d, 1, CHS), 5.10 (d, 1, J=10 Hz, CHBr), 7.28 (s, 10, C_6H_5). Found: C, 58.88; H, 5.15; Br, 27.01; S, 10.30%. Calcd for $C_{15}H_{15}BrS$: C, 58.63; H, 4.92; Br, 26.01; S, 10.44%. Found: *m/e* 306.0085, 308.0095. Calcd for $C_{15}H_{15}BrS$: M, 306.0078; M+2, 308.0059. MS indicated that the sample contained less than 5% of **6**.

In a similar manner, 9.1 g (50.5 mmol) of **5c** gave 9.6 g (61.9%) of **4t**, mp 63 °C, NMR δ=1.91 (s, 3, SCH_3), 4.40 (d, 1, CHS), 5.28 (d, 1, J=9 Hz, CHBr), 7.13 (s, 10, C_6H_5). Found: C, 58.42; H, 4.84; Br, 26.25; S, 10.42%. Found: *m/e* 303.9932, 305.9981, 308.0025. Calcd for $C_{15}H_{15}BrS$: M−2H, 303.9922; M, 306.0078; M+2, 308.0059. MS indicated that the sample contained less than 2% of **6**.

*Preparations of Stilbene Dibromides (**6**).* The *meso*- (**6e**) and *dl*-isomers (**6t**) were prepared according to the procedures developed earlier by the addition of bromine to **5t** in diethyl ether[35] and to **5c** in carbon tetrachloride[36] respectively. The *meso*-isomer (**6e**): mp 237 °C (dec) (lit,[36] mp 237—239 °C (dec)), (Found: C, 49.41; H, 3.32%). The *dl*-isomer (**6t**): mp 110.5—111.5 °C (lit,[36] mp 110— 111 °C), NMR δ=5.44 (s, 2, CHBr), 7.13 (s, 10, C_6H_5), (Found: C, 49.01; H, 3.26%).

*Preparations of Stilbene Dichlorides (**7**).* *meso*- (**7e**) and *dl*-Stilbene dichlorides (**7t**) were prepared according to the procedure developed by Buckles[37] by treating **5t** and **5c** respectively with tetrabutylammonium iodotetrachloride. The *meso*-isomer (**7e**) : mp 190.0—190.5 °C (lit,[37] mp 191—192 °C), NMR δ=5.19 (s, 2, CHCl), 7.36 (s, 10, C_6H_5), (Found: C, 66.79; H, 4.92%). The *dl*-isomer (**7t**): mp 90.0—90.5 °C (lit,[37] mp 91—92 °C), NMR δ=5.20 (s, 2, CHCl), 7.13 (s, 10, C_6H_5), (Found: C, 66.90; H, 4.94%).

A Typical Procedure for the Elimination Reaction with Butyllithium. Reactions were done in a four-necked flask fitted with a reflux condenser, a thermometer, a gas inlet tube, a rubber septum, and a magnetic stirrer. The flask was protected from moisture. All experiments were carried out under nitrogen, passed through a Fieser's solution[38] to remove traces of oxygen, or under argon. *erythro*-1-Bromo-2-methoxy-1,2-diphenylethane (**1e**, 293 mg, 1.01 mmol) in 50 ml of diethyl ether was placed in the flask and cooled in a Dry-Ice bath. The system was flushed with argon gas for 2 h. The solution of butyllithium in hexane (3.0 ml, 1.0 mmol) was added *via* a syringe and the mixture was stirred for 30 min at 0 °C. By the addition of butyllithium, the mixture was turned pale red, but this color disappeared if the solution was flushed with air. The mixture was poured into ice-water, extracted with ether, and dried over sodium sulfate. When excess butyllithium was used, a small amount of methanol was added *via* a syringe to decompose it before treating with water. To the concentrated product, 100 mg of diphenyl ether was added as an internal standard. The mixture was analyzed by GLPC using a silicone OV-17 3% on Chromosorb-W 2 m column at column temperature 160 °C.

In a separate experiment, the reaction product was chromatographed with silica gel (Wako-gel C-200) column using hexane as an elutant, giving **5c**, bp 96—102 °C/3 mm, (Found: C, 93.08; H, 6.91%). It was identified by the comparisons of its GLPC, IR, and NMR data with those of an authentic sample.

A Typical Procedure for the Elimination Reaction with Pentylmagnesium Bromide. The equipment used in these reactions is the same as that used in the butyllithium reactions.

A solution of 295 mg (1.01 mmol) of **1e** in 50 ml of diethyl ether was placed in the flask and cooled in a Dry-Ice bath. The system was flushed with nitrogen. A solution of pentylmagnesium bromide in ether (5.0 ml, 2.0 mmol) was added *via* a syringe and the solution was stirred for 180 min at 0 °C. The reaction mixture was poured into ice-water, extracted with ether, and dried over sodium sulfate. After removal of ether, 107 mg of diphenyl ether was added as an internal standard. The products were analyzed by GLPC; decane, **5t**, and the unreacted substrate were identified. The yield of **5t** was 49%.

Separation of the products was carried out by column chromatography using neutral alumina (W-200) and petroleum ether. The obtained **5t** was contaminated with **1e**, as identified by comparing its NMR spectrum with that of a mixture of **5t** and **1e**. The recovered **1e** has a mp of 110—114 °C; its IR spectrum was superimposable with that of an authentic sample. When **1t** was used as a substrate, the recovered **1t** had a mp of 69—73 °C and its IR spectrum was superimposable with that of an authentic sample. Thus the isomerization of substrates during the reaction process could be eliminated.

In a separate experiment, 219 mg (1.22 mmol) of **5c** was stirred with pentylmagnesium bromide (5.0 ml, 2.0 mmol) for 3 h under the reaction conditions. No **5t** but **5c** alone was detected in the reaction product by means of GLPC.

A Typical Procedure for the Elimination Reaction with Lithium Metal. To a solution of 613 mg (2.11 mmol) of **1e** in 100 ml of diethyl ether was added 164 mg (24 mg-atom) of lithium metal (a lithium wire 3 mm in diameter cut into 1—2 mm lengths). The stirred mixture was refluxed for 30 h under a nitrogen atmosphere. Excess lithium metal was filtered off, and the filtrate was poured into a cold aqueous ammonium chloride solution and extracted with ether. The ether extract was dried over sodium sulfate and concentrated. After adding 108 mg of diphenyl ether as an internal standard, the product was analyzed by GLPC, giving the following yields: **8**, 9.1; **5c**, 8.7; **5t**, 58.3%; a trace of a peak expected to be diphenylacetylene. The product was chromatographed by the use of alumina (W-200) and petroleum ether, giving three fractions: the 1st fraction was **8**, which was identified by means of GLPC, NMR, and IR; the 2nd fraction, mp 124—125 °C, was **5t**, which was identified by means of GLPC and IR; the 3rd fraction was a mixture of **5c** and a trace amount of diphenylacetylene, identified by the retention times of GLPC.

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