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STEREOCHEMISTRY OF ELIMINATION REACTIONS OF HALOHYDRIN DERIVATIVE AND vic-DIBROMIDE BY BUTYLLITHIUM

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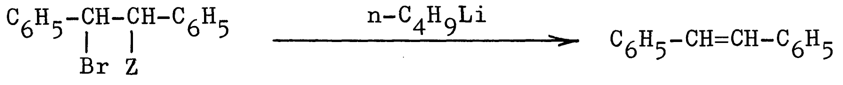
Elimination of 1-bromo-2-methoxy-1,2-diphenylethane with n-butyllithium yielded stilbene in completely stereospecific cis manner in non-polar solvents. A solvent-dependence of the stereochemistry of the elimination reaction was observed.

Although the bimolecular elimination reactions of halohydrin derivatives and vicinal dihalides with metal such as magnesium, zinc, lithium and sodium have been well known, insufficient stereochemical requirements have been obtained so far. Recently the stereochemical consequences of elimination reactions effected by metals have been thoroughly studied with vicinal dibromides.[1,2] In these studies, exclusive trans elimination has been observed in some cases, but the stereochemical result is dependent on the nature of the metal and the solvent.

House and Ro[1] reported that the erythro- and threo-isomers of 1-bromo-2-methoxy-1,2-diphenylethane and another 1-bromo-2-methoxy compounds were allowed to react with zinc and sodium in aqueous ethanol, and that the elimination reactions were not stereospecific. On the other hand, Walborsky[3] obtained the evidence to show the extensive loss of stereospecificity during the process of halogen metal exchange in Grignard reagents formation. In order to preclude the loss of stereospecificity in the halogen metal exchange stage, the investigation of the elimination reaction of halohydrin derivative was undertaken using n-butyllithium.

The erythro- and threo-isomers of 1-bromo-2-methoxy-1,2-diphenylethane (I)[1]



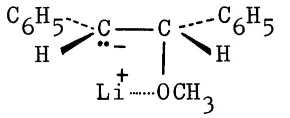
$$C_6H_5\text{-}\underset{Br}{CH}\text{-}\underset{Z}{CH}\text{-}C_6H_5 \xrightarrow{n\text{-}C_4H_9Li} C_6H_5\text{-}CH{=}CH\text{-}C_6H_5$$

I: Z = OCH_3 II: Z = Br III

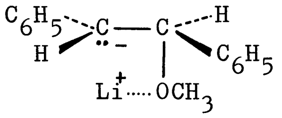
and 1,2-dibromo-1,2-diphenylethane (II) were treated with n-butyllithium in various solvents at various temperatures under nitrogen atmosphere. After the reaction mixture was quenched with ice-water, the organic products were analyzed by vpc. cis- and trans-Stilbenes were isolated and identified by vpc, ir, and nmr. The results are shown in the Table.

Run	Substrates	(m-mole)	n-BuLi (m-mole)	Solvents (50 ml)	React. Conditions		Olefin		
					Time	Temp.(°C)	Yield(%)	cis :	trans
1	erythro-I	(1.01)	1.0	Et_2O	30 min	0	42.0	100	trace
2	"	(1.00)	2.7	"	"	"	45.2	100	trace
3	"	(1.00)	5.3	"	"	"	43.6	100	trace
4	"	(1.00)	2.0	C_6H_6	"	r.t.	31.6	100	trace
5	"	(1.34)	3.5	Diglyme	10	0	76.4	22	78
6	"	(1.14)	5.8	"	"	"	56.4	28	72
7	threo-I	(1.11)	3.5	Et_2O	"	"	52.8	trace	100
8	"	(1.41)	3.5	Diglyme	"	"	92.9	trace	100
9	erythro-II	(1.21)	1.2	Et_2O	"	"	43.0	trace	100
10	"	(1.20)	2.4	"	"	"	95.0	trace	100
11	"	(1.05)	3.6	"	60	-59	34.8	trace	100
12	"	(1.03)	5.5	Diglyme	10	0	99.0	trace	100
13	threo-II	(1.53)	4.4	Et_2O	15	"	100	19	81
14	"	(1.54)	3.1	"	120	-59	100	21	79
15	"	(1.53)	5.5	Diglyme	15	0	98.5	20	80

These results are in marked contrast to those of the reactions involving zinc and sodium metals in aqueous ethanol. Stereospecific cis elimination occurred in the reactions of I in ether and benzene. Carbanions IV are most plausible as an intermediate of this reaction, since they have α-phenyl substituent, which stabilizes the carbanion, and also have a poor leaving group $-OCH_3$ on the β-carbon. Initial metal halogen exchange, which proceeds with retention



(erythro-cisoid-IV)4)



(threo-cisoid-IV)

of configuration,5) produces the erythro- and threo-carbanions (IV) from the corresponding bromides. The formation of the carbanion intermediate is also convinced by the fact that the carbanion, which seems to be less stable than IV, derived from 2-bromo-3-ethylthiobutane could be trapped by methanol.6) These carbanions are expected to form tight ion-pair with Li^+ in non-polar solvents such as ether and benzene. Lithium cation, on the other side, may be coordinated with methoxyl oxygen. The interaction between metal cation in the tight ion-pair and methoxyl oxygen appears to be prone to the stereospecific cis elimination. In diglyme, erythro-I gave a mixture of cis- and trans-olefins in a ratio of 22 to 78. When threo-I was used trans-stilbene was formed exclusively. The carbanion seems to be present as a solvent-separated ion-pair or free anion in diglyme, which is non-polar but highly solvating the metal cation. Since two bulky phenyl groups are eclipsed in erythro-cisoid-carbanion IV, the inversion of the carbanion and bond rotation competes with elimination. On the other hand, since the threo-carbanion takes more stable conformation in cisoid even when it is solvent-separated ion-pair, threo-I gives cis eliminated product in diglyme. The results of runs 5, 6 and 8 are consistent with the apriori theoretical considerations.

Contrary to the methoxyl compounds, debromination from vic-dibromides (II) were not stereospecific. The debromination of erythro-II gave exclusively trans-stilbene, but a mixture of 20% cis-stilbene (the trans elimination product) and 80% trans-isomer (formally, at least, cis elimination) was obtained from threo-II. By the fact that almost exclusive trans elimination has been demonstrated in analogous debrominations of dl- and meso-2,3-dibromobutane with phenyllithium and iodide ion,7) the trans elimination appears to be substantially preferable in the case of dibromide. In the anti-periplanar transition state conceivable for E2 mode trans elimination from threo-II, a large steric compression may operate between two phenyl groups which are oriented gauche to each other, which might be responsible for the observed low stereospecificity. Although there is little convincing evidence for mechanistic arguments of the debromination, it seems likely that the better leaving group bromine shifts the mechanism toward the E2 side from E1cB.[8)]

Further investigation of these elimination reactions is currently in progress.

References and Notes

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4) "Cisoid" refers, in this paper, to the relative position of the carbanion or ion-pair against the leaving groups.

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