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STEREOCHEMISTRY AND REGIOSELECTIVITY OF HALOGEN EXCHANGE REACTIONS OF *vic*-DIHALOALKANES OVER METAL HALIDES

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Stereospecific substitution reaction of halogens with retention of configuration was found in the reaction of 2,3-dibromobutanes over metal halides at 100-200°C, although rapid racemization of optically active 2,3-dibromobutane took place. A reaction mechanism which involves a bridged bromonium-ion intermediate was proposed to explain these results and the regioselectivity of the substitution of 1,2-dibromopropane.

We have recently reported the stereochemistry of elimination reactions of alkyl halides over several solid acids and bases.$^{1,2)}$ It was pointed out that acid-base interactions between substrate and catalyst play important roles in determining the steric course and stereoselectivity. In this communication, we wish to report the stereochemistry of substitution reaction which takes place on solid surface. The reaction studied was the halogen exchange between *vic*-dihaloalkanes and metal halides, as well as the accompanying elimination reactions. Observed stereospecificity and the rapid recemization of 2,3-dibromobutane indicated a bromine-bridged (cyclic bromonium ion) intermediate.

Haloalkyl cations and halonium ions are important reaction intermediates in several reactions such as halogenation.$^{3)}$ The existence as cyclic and acyclic structure in "magic acid" has been substantiated.$^{4)}$ Quantum chemical studies have also been attempted to clarify their properties.$^{5)}$

meso- and dl-2,3-Dihalobutanes were prepared as described before.$^{1,2)}$ 1,2-Dibromopropane was a GR grade reagent (Tokyo Kasei). Optically active 2,3-dibromobutane (6.8°/dm(neat)) was prepared by partial resolution of dl-2,3-dibromobutane by use of brucine$^{6)}$ and used after gas chromatographic purification. Metal halides, commercially obtained, were used after drying at 110°C overnight and grinding to powder, or after impregnating on silica gel (ca. 0.5 mg-metal ion/g). They were heated prior to reaction at 300°C (200°C for $CuCl_2$) for 1 hr in a stream of helium. The same pulse technique as before was utilized.$^{1,2)}$ Products were analyzed by gas chromatography, except for chlorobromopropanes which were measured by nmr. Optical rotation was measured by a polarimeter (Perkin-Elmer).

Reactions of 2,3-dibromobutane. Major reaction of 2,3-dibromobutane over divalent metal chlorides such as $CaCl_2$ and $CuCl_2$ was the exchange of halogen between alkyl and metal halides (Table 1), while elimination reaction predominated in the case of 2-bromobutane. The substitution of halogen at carbons proceeded in a stereospecific way with retention of original configuration; a halogen atom enters from the same side of a reactant molecule as that of the removal of a bromine atom. For example, the reaction of meso- and dl-2,3-dibromobutane produced respectively erythro- and threo-2-chloro-3-bromobutane as mono-substituted products and meso- and dl-2,3-dichlorobutane as di-substituted products (Table 1). Particularly in the case of $CuCl_2$, the reaction occurred rapidly and 100% stereospecifically, showing little deactivation during repeated pulses. Moreover, about a half of chlorine atoms of bulk $CuCl_2$ was able to take part in the reaction, so that this process may be used as a convenient method for stereospecific synthesis of halogen compounds in place of usual reagents like N-halosuccinimide.7) 2-Fluoro-3-bromobutane was also obtained with retention of configuration by the reaction over BaF_2.

Among the accompanying reactions over divalent metal chlorides, debromination proceeded by *anti* elimination, while dehydrobromination from the carbons at 2 and 3 positions was not stereospecific. Dehydrobromination from the 1,2-position, which finally produced butadiene, also took place. These reactions including their selectivity are in marked contrast to those observed with $CsCl-SiO_2$ (Table 1) and $KOH-SiO_2$, as summarized in Fig. 1. Dehydrobromination from 2,3 position by *anti* predominated over the latters.

The retention of configuration during the substitution may be well understood if one considers an intermediate like a bridged bromonium ion (Fig. 2, I and II), which is formed by the elimination of a bromide ion. The interaction of β-bromine with C^+

Table 1. Reactions of 2,3-Dibromobutane over Metal Chlorides at 150°C

Catalyst (weight)	Dibromobutane (pulse no.)	Butene trans	Butene cis	Butadiene	2-Bromo-2-butene trans	2-Bromo-2-butene cis	2,3-Dichlorobutane meso	2,3-Dichlorobutane dl	2-Chloro-3-bromobutane erythro	2-Chloro-3-bromobutane threo	2,3-Dibromobutane meso	2,3-Dibromobutane dl
$CaCl_2-SiO_2$ (35mg)	meso(1)	2.0	0	1.9	1.1	0.4	0.7	0.2	29.8	(4.4)	54.3	(5.2)
	dl (2)	0	1.1	1.1	0.8	0.4	tr		tr	19.0	tr	77.6
$NiCl_2-SiO_2$ (20mg)	meso(1)	2.3	0	2.0	1.3	1.2	tr		15.3	(2.2)	70.0	(5.6)
$CuCl_2$ (107mg)	dl (1)	tr		tr	tr		0	3.2	0	74.0	0	22.8
$CsCl-SiO_2$ (104mg)	meso(1)	0	0	0	1.5	21.2	0	0	2.2	2.2	72.9	tr

Values in parentheses are less accurate.

Table 2. Racemization of Optically Active 2,3-Dibromobutane

Catalyst	Surface area(m^2/g)	Weight (mg)	Reaction temp.(°C)	Substitution (%)	Racemization (%)
none	--	--	150	0	0
$CaCl_2-SiO_2$	428	151	150	16	100
		41	80	0	83
SiO_2	475	51	80	0	37
$CsCl-SiO_2$	342	49	80	0	9

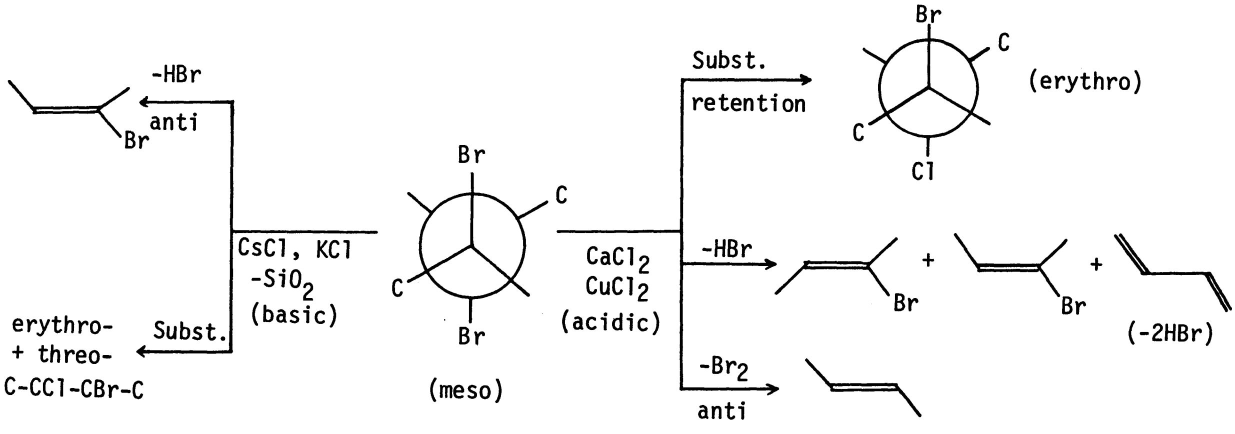


Fig. 1. Reactions of meso-2,3-dibromobutane over metal chlorides.

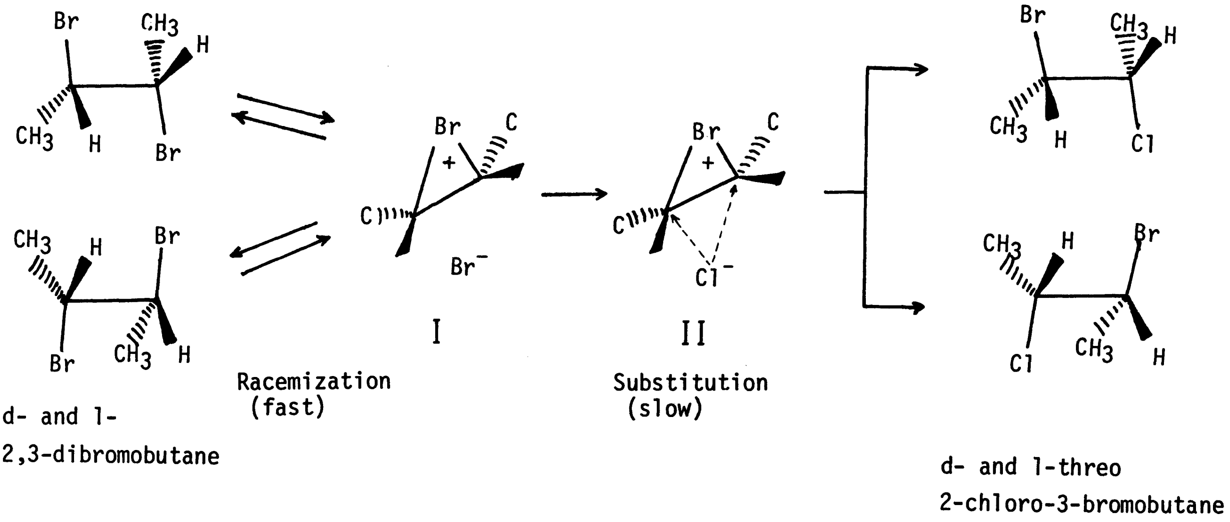


Fig. 2. Reaction scheme for substitution and racemization of dl-2,3-bromobutane.

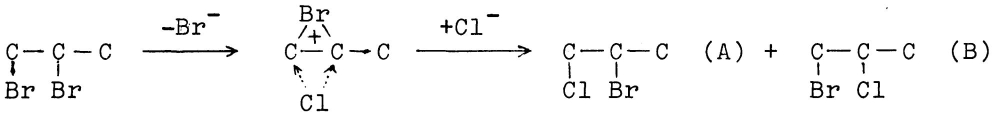
center restricts the rotation about C-C bond and the direction of the entering of a chloride ion. The stereochemistry may alternatively be explained by a concerted mechanism, in which bromine leaves and chlorine enters simultaneously on the same side of a reactant molecule, e.g., from the side facing catalyst surface. However, steric hindrance among chlorine, bromine and methyl group makes the concerted mechanism less probable. Further, the bromine-bridged intermediate explains the stereochemistry of accompanying debromination, since removal of bromine from this intermediate gives directly the butene isomer of *anti* elimination (Fig. 2).

Substitution of halogen also occurred between 2,3-dichlorobutane and $CaBr_2$-SiO_2. In this case, di-substituted products exceeded mono-substituted ones, suggesting that the second substitution *via* a bromonium ion was more rapid than the first one *via* a chloronium ion.

Racemization of 2,3-dibromobutane. As typical results in Table 2 show, racemization of 2,3-dibromobutane (between d- and l-form) took place even under mild conditions where neither substitution nor elimination was observed. The rate of thermal racemization was very small and comparable with that reported for 2,3-dibromopentane.[8] Faster racemization over $CaCl_2$-SiO_2 than CsCl-SiO_2 suggests that this reaction was catalyzed by acid and that breaking or loosening of C-Br bond as C^+--Br^- takes place initially.

The rapid racemization and the retention of configuration during substitution are reasonably interpreted by the reaction scheme shown in Fig. 2, which involves a bridged bromonium ion as a common intermediate. Racemization, that is attained by the exchange of the positions of two bromine atoms, proceeds rapidly *via* I. Substituted products which are racemic (d and l) but retain the starting configuration (erythro or threo) are obtained *via* I ⟶ II.

Reactions of 1,2-dibromopropane. There are two possible mono-substituted products from 1,2-dibromopropane, i.e., 1-chloro-2-bromopropane (A) and 2-chloro-1-bromopropane (B). The latter (B) must be dominant by an open carbocation intermediate, owing to higher stability of secondary alkyl cation than that of primary cation. However, both products were observed in comparable amounts as analyzed by nmr. The ratio of A to B was 0.5 - 0.8 over $CaCl_2$ and $CuCl_2$ at 120-170°C. This fact is also understood by assuming a bridged bromonium ion.



The stereospecific substitution and racemization of 2,3-dibromobutane as well as the regioselectivity of substitution of 1,2-dibromopropane demonstrate the existence and significant roles of a halogen-bridged intermediate in the reactions over solid catalyst. Recent *ab initio* calculation indicates that β-chloroalkyl cation is converted to a bridged chloronium ion without energy barrier.[5]

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