Stereochemical Studies of the Electrolytic Reactions of Organic Compounds. II. Electrolytic Reduction of Optically Active 6-Chloro-2,6-dimethyloctane to the Corresponding Alkane

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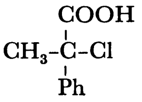
In order to clarify the mechanism of electroreduction of aliphatic halides, optically active 6-chloro-2,6-dimethyloctane(I), in which an (*R*)-(−)-enantiomer was present in excess, was electrolyzed at a mercury cathode in various organic solvents. An (*R*)-(−)-enantiomer was also present in excess in the 2,6-dimethyloctane(II) which was obtained. This result indicates that the reduction of I to II proceeds with an excess of the inversion of the absolute configuration of the starting halide. In this paper, the stereochemistry of a radical intermediate formed at an initial stage in the course of reduction is discussed.

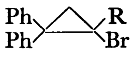
A number of studies of the mechanism of electroreduction of organic halogen compounds have been performed from electrochemical and organic chemical aspects.[1] In recent years there has been a great deal of interest shown in the sterochemistry of the electroreduction of aliphatic halides.[2] Most of studies in this field have dealt with the geometrical isomerism of reactant, intermediate, and/or product, while studies dealing with optical isomerism have been very rare.

Czochralska[3] electrolyzed optically active 2-phenyl-2-chloropropionic acid(III) at a mercury cathode in 90% ethanol containing tertaethylammonium chloride as a supporting electrolyte and obtained optically active 2-phenylpropionic acid, in which the absolute configuration had been inverted, in a high optical yield. At almost the same time, Annino *et al.*[4] also found that the electrolytic reduction of optically active cyclopropyl bromides (IVa—IVd) at a mercury cathode in 95% ethanol are stereochemically controlled by the substituent at the asymmetric carbon. While the reductions of IVa and IVb proceed with the inversion of configuration, the reductions of IVc and IVd proceed with its retention. These facts are very interesting, though the halides used are not typical tertiary alkyl halides.



$$CH_3\text{-}\overset{COOH}{\underset{Ph}{C}}\text{-}Cl$$

III



IVa: R=COOH
IVb: R=$COOCH_3$
IVc: R=COO^-
IVd: R=CH_3

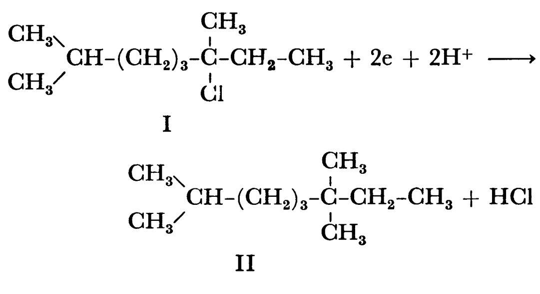
For the first investigation of the substiuent effect, a tertiary halide having as simple as possible substituents should be used. 3-Halo-3-methylhexane is such an alkyl halide, but its optical resolution is very difficult. In this work, (*R*)-(−)-6-chloro-2,6-dimethyloctane(I) derived from natural *l*-linalool was used as the second best sample, because no optical resolution was necessary and the absolute configurations of I and the corresponding alkane were known.

Results and Discussion

Electrolytic results are summarized in Table 1. The electrolytic products consisted of optical isomers of an alkane and a small amount of an optically inactive alkene. The alkane was confirmed to be 2,6-dimethyloctane, in which an (*R*)-(−)-enantiomer is in excess, by its physical properties. On the other hand, although the molecular structure of the alkene($m/e=140$) could not be confimed, its retention volume in gas chromatography was equal to that of the dehydration product of tetrahydrolinalool in hot anhydrous formic acid.

The optical rotation of I used in this work was $[\alpha]^{23}_D-0.34°$. The accurate optical purity could not be estimated because optically pure I has never been prepared. The above value of optical rotation is obtained in the region between 54[5] and 12%[6] of optical purity. On the other hand, the optical rotation of optically pure II is known to be $[\alpha]^{20}_D$ 7.32°.[6] Therefore, the optical yield of II could be shown only by giving its upper and lower limits.

As shown in Table 1, I with $[\alpha]^{23}_D$ −0.34° gave II with minus values of optical rotation, which range from −0.01 to −0.34°, under a variety of electrolytic conditions such as cathode material, solvent, and proton donor. Since I[7] and II[6] with minus values are in (*R*)-configuration, it is concluded that the reduction proceeds with an excess of the inversion of the absolute configuration of I. In the case of a lead cathode, the racemization may be regarded as exclusive.



$$\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>CH\text{-}(CH_2)_3\text{-}\overset{CH_3}{\underset{Cl}{C}}\text{-}CH_2\text{-}CH_3 + 2e + 2H^+ \longrightarrow$$

I

$$\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>CH\text{-}(CH_2)_3\text{-}\overset{CH_3}{\underset{CH_3}{C}}\text{-}CH_2\text{-}CH_3 + HCl$$

II

An essential conclusion drawn from the results of Czochralska[3] was that the electrolytic reduction of alkyl halides proceeds in an S_N2 type mechanism initiated by the attack of an electron to a halogen atom. However, the results of Annino *et al.*[4] cannot be explained by such a mechanism. Since the attack on a halogen is also confirmed through the fact that bridgehead bicyclic halides are reducible at a mercury cathode,[8] there would be no doubt about this point at least in the case of a mercury cathode.

Elving and Pullman[9] generalized the reduction

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TABLE 1. ELECTROLYTIC RESULTS OF 6-CHLORO-2,6-DIMETHYLOCTANE WITH $[\alpha]_D^{23}$ −0.34°

Solvent	Proton donor	Cathode material	Current density A/dm^2	Cathode potential V *vs.* Ag/AgCl	Quantity of electricity passed ×10^6, C/mol	2,6-Dimethyloctane		Optical yield[a,b) %
						Chemical yield, %	$[\alpha]_D^{23}$ deg	
MeO	—	Hg	2.6	−2.20—−2.30	4.4	74	−0.08±0.01	8— 2
EtOH	—	Hg	1.6	−2.15—−2.30	2.9	90	−0.04±0.01	4— 1
EtOH	—	Pb	1.2	−1.85—−2.00	1.7	54	−0.01±0.01	1— 0
EtOH	AcOH	Hg	2.0	−1.55—−2.00	2.7	87	−0.12±0.01	12— 3
EtOH	Et_3NHBr	Hg	0.8	−1.65—−1.95	2.3	47	−0.12±0.02	12— 3
MeCN	—	Hg	2.0	−2.40—−2.45	2.7	96	−0.34±0.01	36— 9
MeCN	—	Hg	0.9	−2.25—−2.35	1.9	84	−0.31±0.04	35— 8
DMF	—	Hg	2.0	−2.20—−2.30	1.9	76	−0.05±0.01	4— 1

a) [(optical purity of product)/(optical purity of reactant)]×100%. b) Upper limit—lower limit.

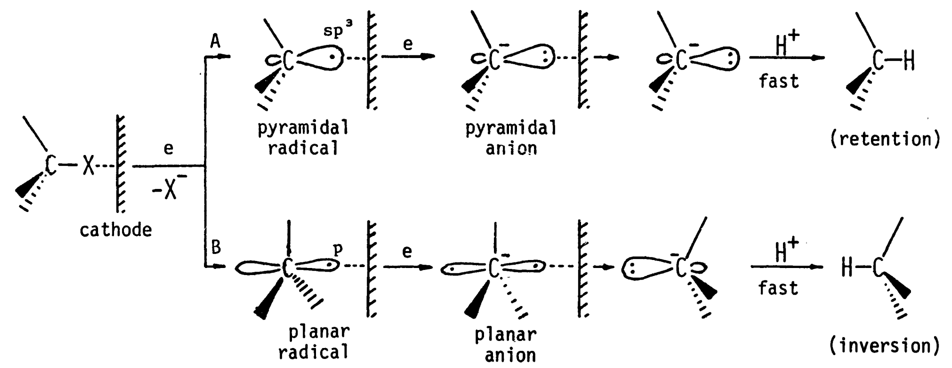

Fig. 1. Schematic mechanisms for the configurational retention and inversion in the electroreduction of alkyl halide to the corresponding alkane.

mechanism of alkyl halides as follows:

$$R\text{-}X \xrightarrow[-X^-]{e} [R\cdot] \xrightarrow{e} [R^-] \xrightarrow{H^+} R\text{-}H$$

where [R·] and [R$^-$] represent electrode complexes or adsorbed species on an electrode surface.

The present paper will employ the steric form of a radical derived from a tertiary alkyl halide in order to rationalize the apparently complicated results of the electroreductions of optically active halides such as I, III, and IVa—IVd.

It is well known that the steric form of a carbon radical can vary from being almost completely planar to being pyramidal with the kind of substituent, although the former is energetically more unstable than the latter.10) While a small alkyl radical, such as the methyl radical, is undoubtedly almost planar,11) there has been no reliable information about the planarity of a large tertiary alkyl radical such as methylethyl-1-(4-methyl)hexylmethyl radical from I. On the other hand, small cyclic alkyl radicals, especially cyclopropyl radicals, are undoubtedly pyramidal.12) The planarity of a radical would be favored by substituents having a π-electron system, such as phenyl or carbonyl groups, because of the favorable interaction between the two electron orbitals paralleled to each other: the p orbital of an unpaired electron of the planar radical and the π electron orbital of the substituent.

According to the above viewpoint, the radicals from III, IVa, and IVb would be planar, while the radical from IVd would be pyramidal. The radical from IVc would be planar in a free environment, but it would be pyramidal in the adsorbed state on a cathode surface because of the electrostatic repulsion of a carboxylate anion from a negatively polarized cathode surface. Although the steric form of the radical from I is ambiguous, it may be acceptable that such a radical could be at least a very shallow pyramid, even if not a plane, considering the fact that an optically active staring compound gave a completely racemized product in a homogeneous reaction involving methylethyl-1-(2-methyl)propylmethyl radical, which resembles the radical from I, as an intermediate.13) The configurational stability of the radical would be increased by the adsorption on an electrode or by the formation of an electrode complex. Generally, a carbanion is configurationally more stable than the corresponding radical. The stability of a carbanion would be increased by a counter cation in the immediate vicinity, while it would be decreased by solvation, especially of the solvent insertion type, to the cation.

As shown in Fig. 1, a pyramidal radical would result in a carbanion which retained its configuration by the introduction of the second electron to the sp^3 orbital of an unpaired electron. On the other hand, the introduction of the second electron to the p orbital of a planar radical would intermediately give a very unstable planar carbanion, which would be immediately converted into an ordinary carbanion having the inverted pyramidal from. This inversion is thought to be due to a steep potential gradient in the immediate vicinty of the cathode. Figure 1 illustrates extreme cases where either retention or inversion occurs exclusively.

In conclusion, it can be actually supposed that the path "B" is slightly predominant in the reduction of I, since the radical intermediate is not a complete plane but a shallow pyramid. Steric hindrance between the three alkyl groups and a cathode is alleviated in a pyramidal radical. Also, the path "B" is more predominant in the cases of III, IVa, and IVb, since their radicals are almost planar even on a cathode. One reason for being planar may be that the p-π interaction described previously is so strong that the contribution of the steric hindrance is more than canceled. In the cases of IVc and IVd, the path "A" is predominant, since nothing causes the corresponding cyclopropyl radicals to be planar.

While the steric configuration of the alkane formed would be mainly controlled by the steric form of an intermediate radical on a cathode, the optical yield would be controlled not only by the configurational stabilities of the radical and the carbanion intermediates but also by the protonation rate of the latter. The fact that proton donors such as acetic acid and triethylamine hydrobromide added in ethanolic catholyte increased the optical yield may partially support the above discussion.

The solvent effect on the optical yield of II can be explained as due to the difference of the proton-donating force to the carbanion intermediate, except for the case of DMF. The reduction in DMF afforded II with an optical rotation equal to one in the case of methanol, though DMF is not only weaker in proton-donating force but also stronger in solvating force to a counter cation of the carbanion intermediate than methanol. There has been no clear explanation of the solvent effect.

Experimenatl

(R)-*(−)-6-Chloro-2,6-dimethyloctane(I).* I was prepared from a commercial natural *l*-linalool with $[\alpha]_D^{23}$ −14.0° (lit,[6] $[\alpha]_D^{20}$ −14.47°), by the literature method.[6] Bp 83—84 °C/15 Torr (lit,[6] 90.2—91.3 °C/21 Torr), n_D^{25} 1.4342 (lit,[6] 1.4346), and $[\alpha]_D^{23}$ −0.34° (lit,[6] $[\alpha]_D^{25}$ −0.42°).

Electrolytic Procedure. An H-type cell divided by a sintered glass diaphragm was used. The cathode was a mercury pool (diameter, 4 cm) or a lead plate (4×3 cm). The catholyte and the anolyte were 50 ml of dried organic solvent(methanol, ethanol, DMF, or acetonitrile) containing 9.95 g of tetraethylammonium chloride as a supporting electrolyte. After nitrogen gas was introduced to the catholyte for one hour in order to remove the oxygen in the solvent, 2.65 g (0.015 mol) of I, and also 0.01 mol of a proton donor (acetic acid or triethylamine hydrobromide) if necessary, were added to the catholyte. A constant current was supplied, which was turned off when the cell voltage rose to above 20 V or when vigorous hydrogen evolution was observed. The temperature of the catholyte was maintained below 20 °C during the electrolysis.

Analysis and Isolation of 2,6-Dimethyloctane. After the electrolysis a large volume of water was added to the catholyte. The separating oil was extracted with ether and the ether extract was dried with anhydrous sodium sulfate. The ethereal solution was analyzed by gas chromatography (apeazone grease L, 100 °C). In the gas-chromatogram, three peaks (corresponding to II, alkene, and unreacted I) appeared.

After the gas chromatographic analysis, the ethereal solution was shaken with concentrated sulfuric acid in order to remove the alkene. The ethereal solution was concentrated by evaporation and the residual oil was distilled under reduced pressure. Gas-chromatographically pure II was obtained as the main fraction: bp 60—62 °C/30 Torr (lit,[6] 99—100 °C/121 Torr); n_D^{25} 1.4091 (lit,[6] 1.4087); mass spectrum (*m/e*) 142(M^+); IR spectrum(cm^{-1}) 2880, 1460, and 1375 as principal absorption bands. No absorption band appeared at 1653 or 888 cm^{-1} related to a double bond in terminal position.[6]

The optical rotation was measured in ethanol by Perkin-Elmer Micro-Polarimeter Model 141.

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