The Stereochemistry of Electroreductions. II. Geminal Dihalocyclopropanes

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Received August 19, 1968

Abstract: Stereochemical correlations between electrochemical (mercury electrode) and zinc or lithium amalgam reductions have been found to hold for geminal dihalocyclopropanes. The reductions of the isomers of 7-bromo-7-chloro[4.1.0]bicycloheptane result in exclusive removal of the bromine with predominant retention of configuration. Results are discussed within a common mechanism for electrochemical and metallic reductions. It is suggested that reductions of geminal dibromo- or dichlorocyclopropanes may occur at either halogen atom rather than just on the *exo* halogen.

We showed in a recent study of the stereochemistry of the electroreduction of optically active bromocyclopropanes that electrochemical stereospecificity can vary from 56% inversion to 38% retention of configuration.[2] The type of stereospecificity found for electroreductions was paralleled roughly for zinc reductions. Mann, Webb, and Walborsky reported similar studies after our paper had been submitted for publication.[3]

Geminal dihalocyclopropanes offer a fruitful series of compounds for stereochemical and mechanistic studies because of the known chemical characteristics of the possible radical, carbanion, and carbonium ion intermediates. The availability of the starting materials and the relatively easy stereochemical analysis of products are also factors in choosing such systems for study. All of the above factors have led to a number of publications on various types of reductions. These include the use of tri-*n*-butyltin hydride,[4] methylsulfinylcarbanion,[5] methylmagnesium bromide,[6] sodium or lithium with alcohols,[7] and chromium(II) sulfate.[8]

Fry and Moore's work[9] on the electrochemical reductions of dichloro- and dibromocyclopropanes is of special significance to this study as we have investigated several of the same systems under only slightly different conditions. In addition, however, we report here the stereochemical results of zinc reductions of several geminal dihalocyclopropanes and both electrochemical and zinc reductions of the isomers of 7-bromo-7-chlorobicyclo[4.1.0]heptane (I). The latter system is of particular mechanistic significance because the general reductions of geminal dichlorides or dibromides give useful information on the over-all stereospecificity but do not show which halogen is removed (*e.g.*, *exo*-halogen reduction with inversion gives the same result as *endo*-halogen reduction with retention). In fact, partial stereospecificity found for such systems might be caused by two competitive stereospecific processes (one on each halogen) occurring in unequal amounts.

Experimental Section

General. Polarographic analyses and controlled potential electrolyses were carried out as described in an earlier paper.[2] Table I lists pertinent polarographic data. Electrolyses were carried out both at potentials near the bottom of the polarographic wave and near the top of the wave with no apparent change in product ratios.

Materials. The dihalocyclopropanes were prepared by known literature methods[10] except for 3,3-dichlorodibenzotricyclo-[3.2.2.0^{2,4}]nonadiene which was furnished to us by Dr. Robert Sequeria. Lithium amalgam was prepared electrolytically in the normal three-compartment cell (1 *M* LiCl–EtOH was electrolyzed for 7 hr at -2.50 V *vs.* Pt and 100–150 mA in the presence of 1150 g of mercury).

Product Analysis. Products were analyzed by nmr spectroscopy by the method of Seyforth, *et al.*,[4] and by gas chromatography.

Both nmr and gas chromatography showed that only the bromine atom is removed in reductions of both isomers of I.

In the case of the two isomers of 3-chlorodibenzotricyclo[3.2.2.0]-nonadiene, only the *exo* isomer (hydrogens *trans* to each other) has been isolated and the triplet at δ 2.01 ppm (*vs.* TMS), $J = 2$ cps assigned. The electrolytic reduction product which crystallized from the aqueous ethanol solution also contained a triplet at δ 3.46 ppm, $J = 7.5$ cps, which was assigned to the *endo* isomer (*cis* hydrogens). The product ratio was then calculated from the ratio of the integrated intensities of these triplets.

Except where noted all compounds could be analyzed on 5 ft × 0.25 in. o.d. 20 w/w% SF-96 on 60–80 Chromosorb P at 135° and a flow rate of 65 cc/min.

Purification of *exo*-7-Bromo-*endo*-7-chlorobicyclo[4.1.0]heptane (I) by Preferential Solvolysis of *endo*-Bromo-*exo*-chloro Derivative. Solvolyses conditions were studied in some detail. The best results were obtained by refluxing 6 g of I with 5.18 g of sodium acetate in 600 ml of glacial acetic acid for 205 hr. At the end of this time the solution was neutralized with sodium carbonate and extracted four times with methylene chloride. The combined extracts were dried with anhydrous magnesium sulfate and concentrated by evaporation. A slow fractional distillation *in vacuo* yielded 1.7 g of *exo*-7-bromo-*endo*-chlorobicyclo[4.1.0]heptane (yield 35% of theoretical) collected at 68–70° (3.3–3.7 mm Hg). This material analyzed as 92% pure by gas chromatography. Of the detectable impurities approximately 4% was 7,7-dichlorobicyclo[4.1.0]heptane (the major impurity of the starting product).

Although a number of columns were investigated none of them gave complete separation of the isomers of I. A resolution (defined as the peak separation divided by the mean of the peak widths) of 0.75 was obtained with a 20 ft × 0.25 in. o.d. column of 5 w/w% Ucon-50HB-280X on 80–100 Chromosorb P at 115° and a flow

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[2] R. Annino, R. E. Erickson, J. Michalovic, and B. McKay, *J. Am. Chem. Soc.*, **88**, 4424 (1966); correction: Table I, $E^1/_3$ should read $E^1/_2$.

[3] C. K. Mann, J. L. Webb, and H. M. Walborsky, *Tetrahedron Letters*, 2249 (1966).

[4] D. Seyferth, H. Yamazoki, and D. L. Alleston, *J. Org. Chem.*, **28**, 703 (1963); T. Ando, F. Namigata, H. Yamanaka, and W. Funasaka, *J. Am. Chem. Soc.*, **89**, 5719 (1967).

[5] C. L. Osborn, T. C. Shields, B. A. Shoulders, C. G. Cardenas, and P. D. Gardner, *Chem. Ind.* (London), 766 (1965).

[6] D. Seyferth and B. Prokai, *J. Org. Chem.*, **31**, 1702 (1966).

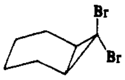
[7] M. Schlosser and G. Heinz, *Angew. Chem.*, **79**, 617 (1967).

[8] H. Nozaki, T. Aratani, and R. Noyori, *Tetrahedron*, **23**, 3645 (1967).

[9] A. J. Fry and R. H. Moore, *J. Org. Chem.*, **33**, 1283 (1968).

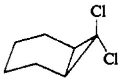
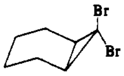
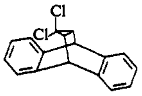
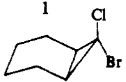
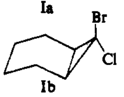
[10] W. von E. Doering and A. K. Hoffmann, *J. Am. Chem. Soc.*, **76**, 6162 (1954).

Table I. Polarographic Data[a]

Compound	Electrolyte[b]	$E_{1/2}$[c]	m,[d] mg/sec	C, mmol/l.	I[d]	αn[e]
I (mixture of Ia and Ib)	0.1 M TEABr	−1.39	1.04	0.45	4.60	0.37
I after 420 hr of acetolysis (*ca.* 90% Ia)	0.1 M TEABr	−1.35	1.04	0.48	4.10	
	0.1 M TEABr	−1.26	1.04	0.45	3.92	0.33[f]

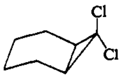
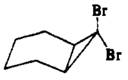
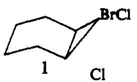
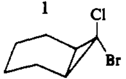
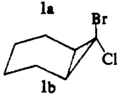
[a] Temperature at 23.8°. [b] In 95% ethanol. [c] *vs.* saturated calomel electrode. [d] Measured at −1.60 V. [e] Slope of plot of log $[i/(i_\alpha - i)]$ *vs.* $E_{DME} = 0.0542/\alpha n$. [f] Although the plot of log $[i/(i_\alpha - i)]$ *vs.* E_{DME} for compound I was linear over the range $0.1i_\alpha$ to $0.9i_\alpha$, this was not the case with 7,7-dibromobicyclo[4.1.0]heptane. The average value of $\alpha n = 0.33$ is reported only to partially characterize the two reduction waves and to illustrate their high degree of irreversibility.

Table II. Stereochemistry in Controlled Potential Electrolyses

Compound	Solvent	Electrolyte	*endo/exo* product ratio	Reference
	CH_3CH_2OH	TEAB	6:1	This work
	DMF	TEAB	3.1:1	This work
	CH_3OH	LiCl	19:1	9
	DMF	LiCl	4.3:1	9
	CH_3CH_2OH	TEAB or LiCl	1.9–2.0:1	This work
	DMF	LiCl	1.1–1.3:1	This work
	CH_3OH	LiCl	1.9:1	9
	DMF	LiCl	1.6:1	9
	CH_3CH_2OH	TEAB	1:3.2	This work
 I	CH_3CH_2OH	LiCl	0.97:1	This work
 Ia	CH_3CH_2OH	TEAB	3.5–3.6:1	This work
	CH_3CH_2OH	LiCl	2.6:1	This work
 Ib	CH_3CH_2OH	LiCl	1:2.6[a]	This work

[a] Calculated from the stereochemical results on the 50:50 mixture and Ia.

Table III. Stereochemistry for Metallic Reductions

Compound	Metal	Solvent	*endo/exo* product ratio
	Zn	HOAc	NR
	Zn	CH_3CH_2OH	5.6:1[a]
	Li(Hg)	CH_3CH_2OH	3.7:1[b]
	Zn	HOAc	5.7:1
	Zn	CH_3CH_2OH-HOAc (10%)	4.6:1
	Zn [d]	CH_3CH_2OH-10% KOH	3.2–3.6:1
	Li(Hg)	CH_3CH_2OH	3.7:1
 I	Zn	HOAc	1.33:1
	Zn	CH_3CH_2OH-HOAc	1.26:1
 Ia	Zn	CH_3CH_2OH-HOAc	18.7:1
 Ib	Zn	CH_3CH_2OH-HOAc	1:4.9[c]

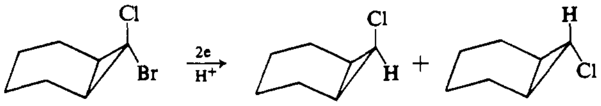
[a] Only 43% of the starting material had reacted after 167 hr. [b] Only 20% of the starting material had reacted after 24 hr. [c] Calculated from stereochemical results on the 50:50 mixture and Ia.

rate of 125 cc/min. This column was used for the analysis of the isomer ratio. The single peak areas were reconstructed by assuming that the resultant curves occurred through the addition of symmetrical ones. It is therefore quite probable that this analysis is accurate to only 4–6% relative. In one instance the chromatograms (previously analyzed as representing a 50:50 mixture) were analyzed with a Du Pont 310 curve resolve. The results (52% *endo*-7-bromo-*exo*-chlorobicyclo[4.1.0]heptane, 48%) were in acceptable agreement with those obtained by the above procedure.

Discussion

Table II shows our stereochemical results for the electroreduction of several dihalocyclopropanes while Table III lists the corresponding values for the zinc reductions.

Coulometric and product analysis established that all reductions proceeded with the uptake of two electrons to produce the monohalobicycloheptane as illustrated below for Ia.



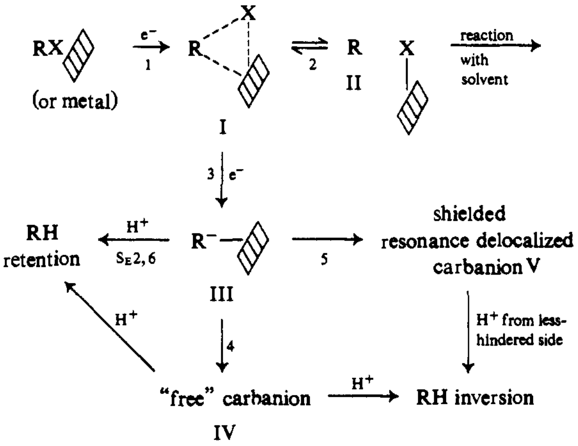
Our major experimental difficulties (outlined in detail in the Experimental Section) were in the preparation of the pure isomers of I. Vapor phase chromatography showed the two isomers to be present in roughly equivalent amounts but no column (of 28 tried) gave sufficient resolution for preparative separation. Finally, following the work of Cristol, Sequeria, and DePuy, who showed that the rate of acetolysis of *endo*-chloro derivative was at least 570 times greater than that of *exo*-chloro derivative,[11] we succeeded in selectively destroying one isomer and preparing relatively pure (90–96%) *exo*-7-bromo-*endo*-7-chlorobicyclo[4.1.0]heptane (Ia). The data for the other isomer (Ib) listed in Tables II and III were calculated by difference using the product ratios obtained by electrolyzing the 50:50 mixture and the relatively pure Ia. The product distribution data for II are therefore much less accurate than the other results listed in Tables II and III.

We wish to emphasize three major points about the significance of the data in Tables II and III.

First, the general correlation of stereospecificity of electrochemical reductions with metal reductions found in our earlier paper and noted by Walborsky is evident for these systems. The results for Ia and Ib show clearly that stereochemical preference is for retention of configuration in these systems.

Second, the relative change in the extent of stereospecificity of product formation increases in the sequence chlorine > bromine. This has been shown not only for our compounds and the closely related work of Fry and Moore[9] but by Walborsky and Young's findings on the retention of configuration during Grignard formation of cyclopropyl halides (found relative retention sequence Cl > Br > I).[12] The long-standing mechanistic question[13] of whether organic halides undergo electrochemical reduction by SN1 or SN2 reactions seems to be clearly resolved by the stereochemical results which indicate that neither analogy is a good one. We have suggested initial attack on halogen while Lambert,[14] in an interesting paper involving correlations of half-wave potentials of organic halides with σ^*, suggests initial attack perpendicular to the carbon–halogen bond. Similarly, in a recent paper Sease, *et al.*,[15] also suggest a negatively charged potential-determining transition state. The general features of stereochemistry, half-wave potential correlations, and variation of stereospecificity with the halogen atom presented in this work fits in well with a mechanism analogous to Walborsky's mechanism of Grignard formation[12] and is consistent with our earlier explanation for the reduction of halocyclopropyl systems.[2] At that time it was proposed that: (1) the initial attack by the electrode occurs on the same side of the molecule as the halogen atom to give an electrode complex with the same configuration as the reactant, and (2) that the over-all stereochemistry is determined by a stereoselective reaction of the free electrode shielded carbanion with solvent or proton. A general reaction scheme is shown in Scheme I.

Scheme I



Formation of III and its subsequent breakdown are the important steps in the mechanism. III can be an organometallic compound or, for electrochemical reductions, can represent either an electrode complex or an actual organomercury derivative as shown by Mann, *et al.*,[3] for some cyclopropyl halides.

The three major pathways available to III have important stereochemical consequences. Reaction 6 can be pictured as a typical SE2 substitution of a proton for a metal on an organometallic bond or for the electrode on the electrode complex III. It is expected to assume maximum importance only for long-lived complexes and true organometallic compounds. In contrast, steps 4 and 5 depict the fate of a carbanion and have their origin in the breakdown of III and the movement of the resulting carbanion away from the electrode. If the carbanion is stable enough to hold its configuration during the time needed to move away from the electrode (as many cyclopropane carbanions would be expected to be) and acquire a proton on the side of the molecule which had originally been next to the electrode, complete retention of configuration is found for RH. If the carbanion is not quite so

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(11) S. J. Cristol, R. M. Sequeria, and C. H. DePuy, *J. Am. Chem. Soc.*, **87**, 4007 (1965).

(12) H. M. Walborsky and A. E. Young, *ibid.*, **86**, 3288 (1964).

(13) See bibliography in ref 2.

(14) F. L. Lambert, *J. Org. Chem.*, **31**, 4184 (1966).

(15) J. W. Sease, F. G. Burton, and S. L. Nickol, *J. Am. Chem. Soc.*, **90**, 2595 (1968).

stable and occasionally inverts before acquiring a proton, one observes predominant but not exclusive retention. Thus either or both of these pathways lead to product with retained configuration as found previously for 1-bromo-1-methyl-2,2-diphenylcyclopropane (found 21% retention),[2] sodium 1-bromo-2,2-diphenylcyclopropanecarboxylate (found 31–38% retention)[2] and for the compounds investigated in this study.

On the other hand, the "resonance delocalized" carbanion can flatten out rapidly and to the extent that a proton is acquired while the electrode shields one side of the flat carbanion (or interacts with it to form a loose complex), inversion predominates over retention. This behavior has been observed for 1-bromo-2,2-diphenylcyclopropane carboxylic acid (found 26–35% inversion),[2] methyl 1-bromo-2,2-diphenylcyclopropanecarboxylate (found 30–56% inversion),[2] and 2-chloro-2-phenylpropionic acid (77–92% inversion).[16]

The formation of a free radical by reaction 2, as suggested by Walborsky and Young for loss of stereospecificity in Grignard formation[12] could also be significant for some systems.

The third point of general interest about the data is in connection with the comparison of our data with that of Fry and Moore.[9] The general assumption of most of the workers who have reduced geminal dihalides similar to ours is that the *exo*-halogen atom is attacked and that the stereochemistry of the product of the reaction is dependent mainly on the type of intermediate (radical or anion) and the solvent. Indeed the extremely high stereospecificities found in some cases (*e.g.*, 99% *exo*-7-bromobicyclo[4.1.0]-heptane found by Osborn, Shields, Shoulders, Cardenas, and Gardner[5] in the methylsulfinylcarbanion reduction of its dibromo precursor) argue strongly for such assumptions. However, as can be noted in Table I, both *exo*- and *endo*-bromo derivatives (I, the mixture, and Ia) are easily reduced electrolytically with only a relatively small change in half-wave potential (probably much less than 0.1 V).[17] Thus, product ratios are not expected to be critically affected by reducing at different potentials and we have no proof that attack does not occur at either halogen atom in dibromo or dichloro derivatives.[18]

Many of the data on reductions of dichloro or dibromo derivatives and the variance of the stereospecificity of Ia and Ib can be explained by considering intermediate IV.

VI VII

For an optically active system such as that studied in our earlier work, a "free" equilibrated carbanion would imply a path of racemization. For the systems studied in this paper however, equilibration of a typical carbanion as shown below will not lead to equivalent amounts of product since the two isomers do not have the same thermodynamic stability. The exact size of the electron pair relative to chlorine is undeterminable and in fact should vary with the solvent.

If attack by the electrode or a metal can be on either halogen of geminal dihalocyclopropane then the stereochemical results indicate the extent of both reaction 4 and the degree of equilibration shown above. Both solvent effects and atom effects (dichloro compounds giving more retention than dibromo compounds) can be explained by this model.

In conclusion, Ia and Ib are excellent compounds for the study of the stereochemistry of organic halide reductions. This study has not only shown that several metallic and electrochemical reductions yield similar stereochemical results with real stereospecificities but has indicated that geminal dibromo or dichloro cyclopropanes may be attacked at either halogen atom.[19]

Acknowledgment. The financial support of PRF Grant 1049-B and NSF Grant GP-4179 is gratefully acknowledged.

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(16) B. Czochraloka, *Chem. Phys. Letters*, **1**, 239 (1967); *Chem. Abstr.*, **67**, 116438*m* (1967), has recently shown this compound to be reduced electrolytically with 77–92% inversion of configuration. Since it had previously been determined (E. Ott and K. Kramer, *Ber.*, **68**, 1655 (1935)) that 2-chloro-2-phenylpropionic acid is reduced with inversion of configuration, the general analogy in stereochemical results between zinc reductions and electrochemical reductions is strengthened.

(17) Since differences in $E^1/_2$ may be due to changes in α and/or k° (the heterogeneous rate constant) it is difficult to assign any real significance to the small difference in half-wave potentials noted for Ia and the mixture Ia + Ib = I.

(18) A referee has suggested that since the half-wave potentials for Ia and Ib (experimentally 0.04 V difference for Ia–Ib mixture *vs.* Ia) are not accurately known, the hypothesis that attack can occur at either halogen in dibromo or dichloro derivatives is unjustified. We suggest here and in the following paragraphs that the opposite hypothesis (preferential attack on *exo* halogen) has, in fact, less experimental justification and that stereochemical results can be rationalized on the basis of attack on either halogen.

(19) We believe that reductions which proceed through free-radical mechanisms, such as those with tri-*n*-butyltin hydride,[4] may also involve attack at either halogen atom. Seyferth, *et al.*,[4] have found the same general product ratios from dibromo or dichloro geminal cyclopropanes with this reagent as we and others have electrochemically. It would be of interest to reduce Ia and Ib with such a reagent. Ando, *et al.*,[4] have recently shown in fact that the tri-*n*-butyltin hydride reduction of fluorochloro or fluorobromo geminal dihalocyclopropanes is completely stereospecific with retention of configuration.