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ELECTROCHEMICAL ASYMMETRIC REDUCTION OF PROCHIRAL CARBONYL COMPOUNDS, OXIMES, AND A *gem*-DIHALIDE ON A POLY-L-VALINE-COATED GRAPHITE ELECTRODE(1)

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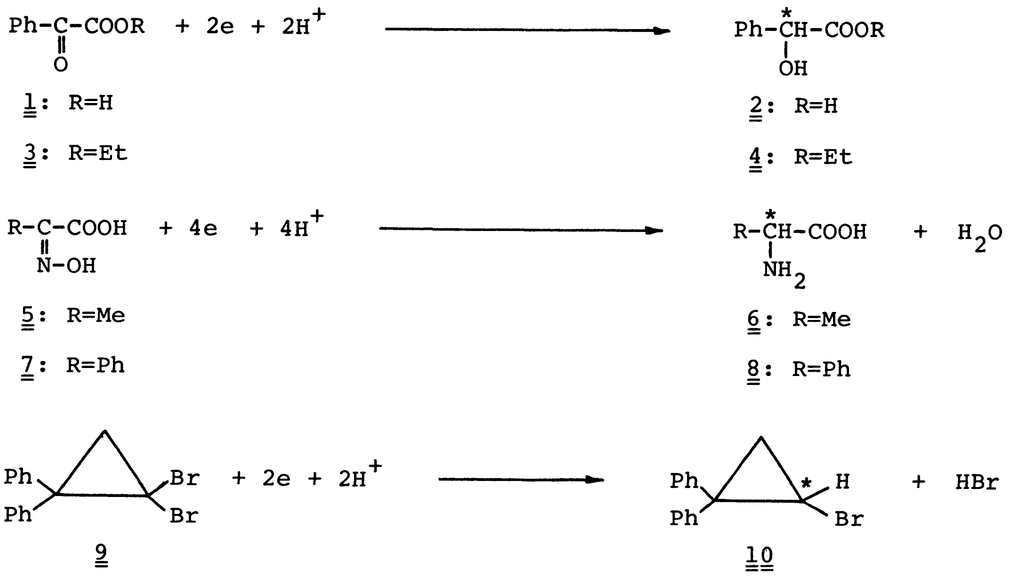
The electrochemical asymmetric reduction of prochiral carbonyl compounds, oximes, and a *gem*-dihalide was examined by using a poly-L-valine-coated graphite electrode. The highest asymmetric yield (16.6%) was obtained in the reduction of 1,1-dibromo-2,2-diphenylcyclopropane to the corresponding monobromocyclopropane.

As summarized by Tilborg and Smit,2) four methods, except for intramolecular asymmetric induction, for electrochemical asymmetric reduction have been reported: The use of (a) chiral solvents, (b) chiral supporting electrolytes, (c) chiral electrode surface active materials (alkaloids), and (d) chiral chemically-modified electrodes. Although the methods (a) and (b) gave 6%3) and 20%4) of asymmetric yields, respectively, in each best case in the reduction of acetophenone, these methods inherently need large amounts of optically-active materials as asymmetry-inducing reagents. In contrast, the other two methods need extremely smaller amounts of the inducing reagents. Moreover, the method (c) gave high asymmetric yields as 47.5%5) and 44.3%6, 7) in the reduction of 2-acetylpyridine (in the presence of 0.5 $\mathrm{mmol\cdot dm^{-3}}$ strychinine) and 1,1-dibromo-2,2-diphenylcyclopropane (**9**) (in the presence of 3.4 $\mathrm{mmol\cdot dm^{-3}}$ emetine), respectively. However, the use of generally expensive and toxic alkaloids may be a disadvantageous point in this method. Chemically-modified electrodes seem to have a very wide application field, as pointed out by Osa *et al*.8) Miller and his co-workers9) reported that a graphite electrode modified chemically with L-phenylalanine gave 9.7% of asymmetric yield in the reduction of ethyl phenylglyoxalate (**3**). This chemically-modified electrode could be also used for the asymmetric oxidation of p-tolyl methyl sulfide to the corresponding chiral sulfoxide to give 2.5% of asymmetric yield.10) Electrochemical asymmetric induction using electrodes modified chemically with chiral compounds should be an excellent method, since very small amounts of inducing reagents can act efficiently. However, there may be a disadvantage in this method due to low coverage of chiral species on electrode surface.

Recently, Osa and his co-workers8) have reported a new method for the electrochemical asymmetric reduction: They obtained 2-6% of asymmetric yields in the reduction of 2-hexanone to 2-hexanol using Raneny-nickel powder electrodes modified with optically-active tartaric acids. Although the asymmetric yields were low, this new method may greatly contribute to further development in the field of electrochemical asymmetric synthesis. More recently, we have found another new method effective for both the asymmetric reduction of olefins and the oxidation of a sulfide. It was the use of chiral poly-amino acid-coated electrodes: The highest asymmetric yield of 43% was obtained using a poly-L-valine-coated graphite electrode in the reduction of 4-methylcoumarin,11) while the highest asymmetric yield (54%) in the oxidation was found in the electrolysis of phenyl cyclohexyl sulfide on a platinum electrode coated with poly-L-valine.12)



In this work, the electrochemical asymmetric reduction on the poly-L-valine-coated graphite electrode was extended to that of some prochiral compounds other than olefins: Carbonyl compounds (1, 3), oximes (5, 7), and a *gem*-dibromo compound (9) were examined. As shown in Table 1, phenylglyoxylic acid (1) and its ethyl ester (3) were reduced to give the corresponding alcoholic compounds (2, 4), but asymmetric yields were not as high as 0-6.7%. In this reduction, it is interesting that the absolute configuration of the excess enantiomer of 2 was opposite to that of 4. The highest asymmetric yield obtained in the reduction of pyruvic acid oxime (5) to alanine (6) was almost equal to that of 4, while phenylglyoxylic acid oxime (7) was reduced in lower asymmetric yields in a whole pH range examined. In contrast to the above starting compounds (1, 3, 5, and 7), 1,1-dibromo-2,2-diphenylcyclopropane (9) was reduced to 1-bromo-2,2-diphenylcyclopropane (10) at pH 4.7[13] to give 16.6% of asymmetric yield as the highest value.

Although 9 gave a fairly good asymmetric yield, results obtained in this work may be not wholly satisfactory, when compared with those in the reduction of olefins.[11] As pointed out in a previous work,[14] passage of large amounts of charge causes a decrease in asymmetric yield: The poly-L-valine-coated electrode has not so long a lifetime under electrolytic conditions. In this work, larger amounts of charge were passed for conveniences of product isolation. This may be one of the causes for lower asymmetric yields. Some attempts to improve the lifetime are in progress. It is important that this new method seems to be useful for the electrochemical asymmetric reduction of a variety of prochiral compounds in addition to olefins.

The starting compounds, 1,[15] 5,[16] 7,[16] and 9[17] were prepared by methods of literatures. The compound, 3 was also prepared by the esterification of 1. The poly-L-valine-coated graphite electrode was prepared by a dipping-method[11] in 0.5% poly-L-valine solution/trifluoroacetic acid. Electrolyses were carried out at 0-5°C by a method similar to that in the previous works.[11, 14] The products, 2,[18] 4, and 10[19] were isolated by extraction with ether from electrolytic solutions and purified by recrystallization or column chromatography, while 6 and 8 were isolated as their N-2,4-dinitrophenyl derivatives:[20] All the products were identified with the independently synthesized samples by comparison of mp, bp, and/or spectra. The asymmetric yields were calculated with reference to optical rotating powers reported for the optically-pure enantiomers: $[\alpha]_D^{22}=150°$[9] for 2, $[\alpha]_D^{20}=128°$[9] for 4, $[\alpha]_D^{20}=13.4°$[21] and $[\alpha]_D^{20}=177.1°$[21] for N-2,4-dinitrophenyl-6 and 8,

Table 1. Electrochemical Asymmetric Reduction of Prochiral Compounds on Poly-L-valine-coated Graphite Electrode

Prochiral compound	pH	Cathode potential[a] /V *vs*. SCE	Current density[b] /A·dm^{-2}	Charge passed[c] /96500 C	Chemical yield /%	Asymmetric yield /%	Configuration[d]
1	0.1	-	1.2	2.0	44	0	-
1	4.7	-	1.2	2.0	31	0.2	(*R*)
1	6.0	-	1.2	2.0	39	0.7	(*R*)
3	0.1	-	2.0	4.0	0	0	-
3	4.7	-	2.0	5.0	29	1.1	(*S*)
3	6.7	-	2.0	4.0	45	0.2	(*S*)
3[e]	6.7	-	2.0	4.0	48	6.7	(*S*)
5	0.1	-	1.2	2.0	18[f]	1.5	(*S*)
5	4.7	-	1.2	2.0	10[g]	3.8	(*S*)
5	6.0	-	1.2	2.0	13[h]	6.2	(*S*)
7	0.1	-	1.2	2.0	21[i]	0.8	(*S*)
7	4.7	-	1.2	2.0	18[f]	2.1	(*S*)
7	6.0	-	1.2	2.0	17[j]	0.4	(*S*)
9	4.7	-1.2	-	4.0	45	5.4	(*R*)
9	4.7	-1.3	-	4.0	48	16.6	(*R*)
9	4.7	-1.4	-	4.0	36	7.8	(*R*)

a) Controlled-potential electrolysis.
b) Constant-current electrolysis.
c) Charge passed divided by amount of substance of the starting compound.
d) Excess enantiomer.
e) Poly-L-tryptophane-coated graphite electrode was used.
f) Current efficiency: 36%.
g) Current efficiency: 20%.
h) Current efficiency: 26%.
i) Current efficiency: 42%.
j) Current efficiency: 34%.

respectively, and $[\alpha]_D^{25}$=203°[6] for **10**.

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