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Electro-organic Reactions on Organic Electrodes. Part 2.[1)] Electrochemical Asymmetric Reduction of Citraconic and Mesaconic Acids on Optically-active Poly(amino acid)-coated Electrodes[2)]

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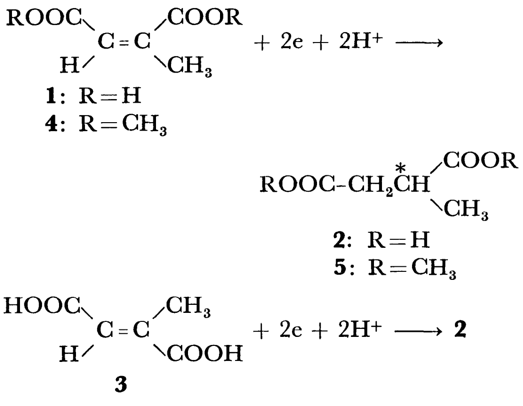
Influence of a number of electrolytic conditions on the asymmetric yield of methylsuccinic acid (**2**) formed in the electrochemical reduction of citraconic acid (**1**) on poly(amino acid)-coated electrodes was examined. The asymmetric yield was greatly affected by the conditions, while the absolute configuration of an excess enantiomer((*S*)-(−)-**2**) remained unchanged even when a polymer with the reversed configuration of the monomer unit was used. The configuration of the excess enantiomer was also unchanged in the asymmetric reduction of mesaconic acid which is the geometrical isomer of **1**.

Some methods for electrochemical asymmetric reduction of prochiral compounds had been reported, as summarized by Tilborg and Smit.[3)] Among the methods, only the use of optically-active alkaloids as an asymmetry-inductor had resulted in high asymmetric yields over 40%.[4,5)] Recently, Osa *et al.*[6)] have reported a new method for the electrochemical asymmetric reduction: They obtained (*S*)-(+)-2-hexanol in 2—6% asymmetric yields from 2-hexanone using Raney-nickel powder electrodes modified with (*S*,*S*)-(−)-tartaric acid. More recently, we have found another new method[1)]: 43 and 25% asymmetric yields were obtained in the reduction of 2-methylcoumarin and citraconic acid (**1**), respectively, on a poly(L-valine)-coated graphite cathode.

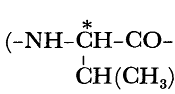
Although a number of studies on polymer-coated electrodes have been recently reported, few papers[7—9)] dealing with their electrosynthetic utilization have been published.

In this work, as a part of studies on electrosyntheses of organic compounds using electrodes modified with organic materials, influences of a number of electrolytic conditions on the asymmetric reduction of **1**, its dimethyl ester (**4**), and mesaconic acid (**3**) on optically-active poly(amino acid)-coated electrodes were examined in detail.



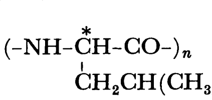
Results and Discussion

*Reduction of Citraconic Acid (**1**) on Graphite Coated with Various Poly(amino acid)s.* Poly(amino acid)s (**6**—**11**) prepared from the corresponding optically-pure amino acids were coated on graphite base electrodes by a dipping method in their solutions. Molecular weights of the poly-amino acids except for poly(L-valine) (**6**) (*ca.* 2000[1)]) were unknown.



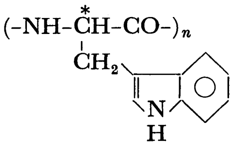
$(\text{-NH-}\overset{*}{\text{C}}\text{H-CO-})_n$ with $\text{CH(CH}_3)_2$

Poly(L-valine) (**6**)
and
Poly(D-valine) (**8**)

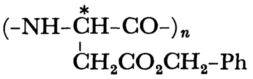


$(\text{-NH-}\overset{*}{\text{C}}\text{H-CO-})_n$ with $\text{CH}_2\text{CH(CH}_3)_2$

Poly(L-leucine) (**7**)

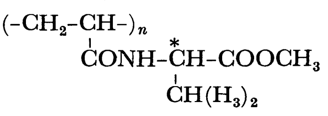


Poly(L-tryptophan) (**9**)



$(\text{-NH-}\overset{*}{\text{C}}\text{H-CO-})_n$ with $\text{CH}_2\text{CO}_2\text{CH}_2\text{-Ph}$

Poly(γ-benzyl L-glutamate) (**10**)



$(\text{-CH}_2\text{-CH-})_n$ with $\text{CONH-}\overset{*}{\text{C}}\text{H-COOCH}_3$, $\text{CH(H}_3)_2$

Poly(*N*-acryloyl-L-valine methyl ester) (**11**)

As shown in Fig. 1, the asymmetric yield of methylsuccinic acid (**2**) has a clear relationship to optical rotating powers of the poly(amino acid)s (**6**—**11**), and poly(L-valine) gave the highest asymmetric yield of 25%. The relationship of the secondary structure(α- and β-forms) of the poly(amino acid)s to the asymmetric yield does not seem to be clear.

Generally, if an asymmetry-inducing reagent with an absolute configuration results in the excess formation of an enantiomer of a compound in an asymmetry-induction reaction, the reagent with the inverted configuration should give another enantiomer inverted configurationaly in the same asymmetric yield under the same conditions. In this viewpoint of the asymmetry induction, it is interesting that both poly(L-valine) (**6**) and poly(D-valine) (**8**), which have the reverse optical rotations and consist of the valine units with the inverted configurations, resulted in the excess formation of the *S*-enantiomer of **2** in different asymmetric yields. This fact suggests that the asymmetry of **2** is induced by the chirality of not only the valine monomer units but also the whole structures of the poly-valines. More generally this should be regarded as one of polymer effects.[10)] Electrochemical asymmetric reduction using optically-active polymer-coated

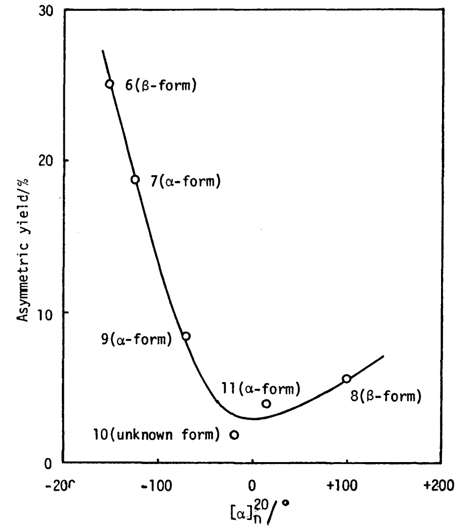


Fig. 1. Relation between optical rotation of poly(amino acid)s (**6**—**11**) and asymmetric yield of methylsuccinic acid (**2**) formed on poly(mino acid)-coated graphite electrodes.
Electrolytic conditions: pH, 6.0; cathodic potential, -1.0 V *vs.* SCE; charge passed, 96500×0.2 C mol^{-1}; temperature, 0—5 °C; concentration of **1**, 0.145 M. Coating solution: 0.5%(w/v). Current efficiency for **2**: 10—80%. Configuration of excess enantiomer of **2**: *S*.

TABLE 1. INFLUENCE OF BASE ELECTRODE MATERIALS COATED[a] WITH POLY(L-VALINE) (**6**) ON ASYMMETRIC YIELD OF METHYLSUCCINIC ACID (**2**)[b] FORMED IN REDUCTION[c] OF CITRACONIC ACID (**1**)

Base electrode material	Asymmetric yield/%
Graphite	8.1
Lead	6.0
Zinc	1.2

a) Coated in 0.5% (w/v) poly(L-valine) trifluoroacetic acid solution. b) Yield and current efficiency: 18—32%. Configuration of excess enantiomer: *S*. c) Electrolytic conditions: pH, 4.7; current density, 1.2 A dm^{-2}; charge passed, 96500×2.0 C mol^{-1}; concentration of **1**, 0.145 M (mol dm^{-3}); temperature, 20 °C.

electrodes may be also characterized by this polymer effect.

*Reduction of Citraconic Acid (**1**) on Some Base Electrodes Coated with Poly(L-valine).* As shown in Table 1, graphite was better as a base electrode material than metals such as lead and zinc.

A poly(L-valine) (**6**) film may be fixed on a graphite surface by hydrogen bonding of the amido groups of **6** with oxygen functions such as COOH, CO and OH, while such a hydrogen bonding can not be formed on the metal surface. Even if the hydrogen bonding with surface oxides of the metals might be formed, it should be exhausively disappeared by reduction of the oxides during electrolysis. The adsorptivity of **6** on the base electrodes seems to be one of important factors in the asymmetric reduction.

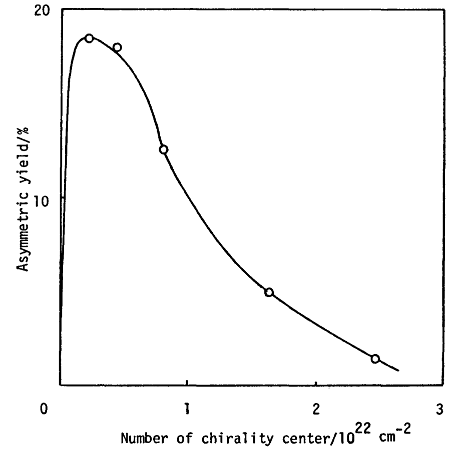


Fig. 2. Influence of number of chirality centers on poly(L-valine)-coated graphite electrode on symmetric yield of methylsuccinic acid (**2**).
Electrolytic conditions: pH, 6.0; current density, 1.2 A dm^{-2}; temperature, 0—5 °C; concentration of **1**, 0.145 M; charge passed, 96500×2.0 C mol^{-1}.
Current efficiency and yield: 10—23%. Configuration of excess enantiomer of **2**: *S*.

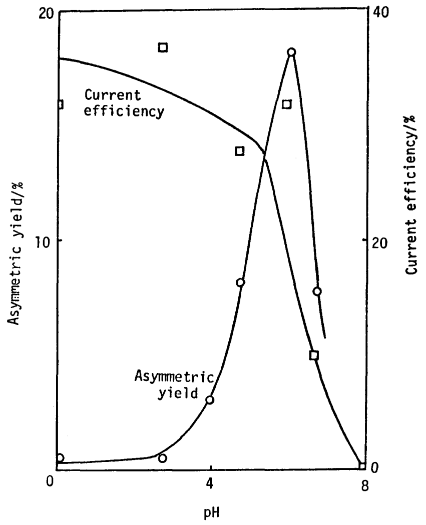


Fig. 3. Influence of pH on asymmetric yield of methylsuccinic acid (**2**) formed in reduction of citraconic acid (**1**) on poly(L-valine)-coated graphite electrode (number of chirality centers, 0.25×10^{22} cm^{-2}).
Electrolytic conditions: current density, 1.2 A dm^{-2}; temperature, 0—5 °C; concentration of **1**, 0.145 M; charge passed, 96500×2.0 C mol^{-2}.
Configuration of excess enantiomer of **2**: *S*.

*Reduction of Citraconic Acid (**1**) on Poly(L-valine) (**6**)-coated Graphite Electrode.* *Influence of Coating Thickness*: Because the thickness of coating films could not be directly measured, the relation between the number of chirality centers on the electrode and the asymmetric yield was examined. As shown in Fig. 2, the highest asymmetric yield was obtained using an electrode with 0.25×10^{22} cm^{-2} of the number of chirality centers. If the density of **6** is in the range of 0.8—1.4 similarly to ordinary organic polymers,[11] the thickness of the film is estimated as $(2.8—1.6) \times 10^{-4}$ cm.

Increase of the thickness resulted in remarkable de-

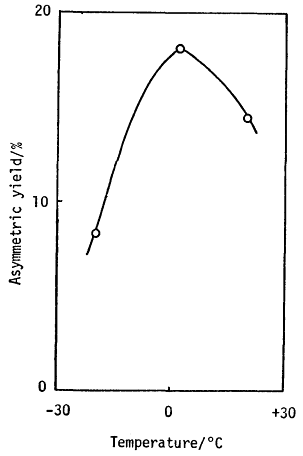


Fig. 4. Influence of temperature on asymmetric yield of methylsuccinic acid (**2**) formed in reduction of citraconic acid (**1**) on poly(L-valine)-coated graphite electrode (number of chirality centers, 0.25×10^{22} cm^{-2}).
Electrolytic conditions: pH, 6.0; current density, 1.2 A dm^{-2}; concentration of **1**, 0.145 M; charge passed, 96500×2.0 C mol^{-1}.
Current efficiency and yield: 10—26%. Configuration of excess enantiomer of **2**: *S*.

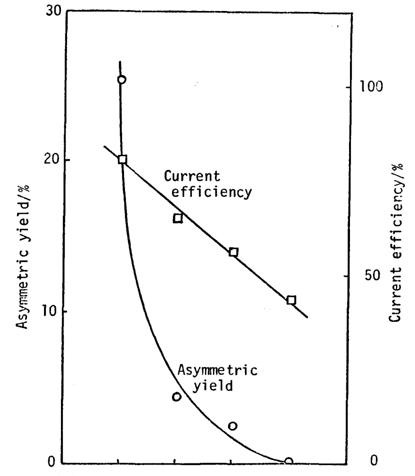


Fig. 5. Influence of cathode potential on asymmetric reduction of citraconic acid (**1**) to methylsuccinic acid(**2**) on poly(L-valine)-coated graphite electrode (number of chirality centers, 0.25×10^{22} cm^{-2}).
Electrolytic conditions: pH, 6.0; temperature, 0—5 °C; concentration of **1**, 0.145 M; charge passed, 96500×0.2 C mol^{-1}.
Configuration of excess enantiomer of **2**: *S*.

crease of the asymmetric yield. This may be suggest that a key step for the asymmetry induction does not occur inside the film. The induction may occur in an interface between the film and the graphite.

Influence of pH: As shown in Fig. 3, the highest asymmetric yield was obtained at pH 6.0, while the cuurent efficiency decreased at pHs higher than 6.0 and **2** was not formed in alkaline solutions. Although such a pH dependence is interesting from an aspect of the asymmetry induction mechanism of this reaction, it is difficult to rationalize clearly the dependence. The asymmetry induction mechanism will be discussed from another aspect in a little more details in the final item of the text.

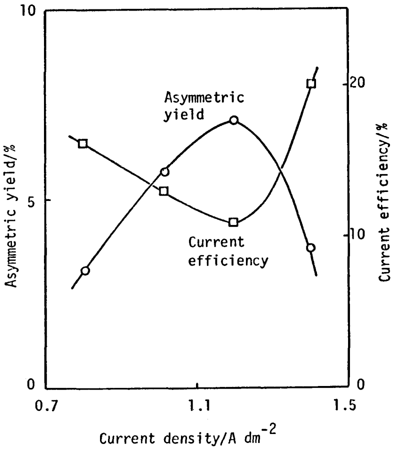


Fig. 6. Influence of current density on reduction of citraconic acid (**1**) to methylsuccinic acid (**2**) on poly(L-valine)-coated graphite electrode (number of chirality centers, 0.25×10^{22} cm^{-2}).
Electrolytic conditions: pH, 4.7; temperature, 20 °C; concentration of **1**, 0.145 M; charge passed, 96500×2.0 C mol^{-1}.
Configuration of excess enantiomer of **2**: *S*.

Influence of Temperature: As shown in Fig. 4, the highest asmmetric yield was obtained at *ca.* 0 °C. In most cases of asymmetric reactions, lower temperature is more favorable. A lower asmmetric yield at −20 °C in this work may be due to an undesirable change in film properties of **6** at such a low temperature, which may be close to its glass transition temperature.

Influence of Cathode Potential: Figure 5 indicates that lower potentials resulted in higher asymmetric yields and current efficiencies. This fact may suggest that hydrogen evolution on the graphite surface decreased the adsorptivity of the **6** film, because hydrogen bubbles might not smoothly go through the film, and consequently the asymmetry-inducing power of the coated electrode was decreased.

Influence of Current Density: The highest asymmetric yield and the lowest current efficiency were obtained at 1.2 A dm^{-2} of current density, as shown in Fig. 6.

Influence of Charge Passed: Influence of charge passed on the asymmetric yield and current efficiency was examined in controlled-potential electrolyses at −1.0 V *vs.* SCE. As shown in Fig. 7, passing of larger amounts of charge, in another word longer time of the electrolyses, resulted in decrease of both the asymmetric yield and current efficiency. The decrease of the former may be caused by the decrease of the asymmetry-inducing power of the **6** film due to contamination of the film-graphite interface during the electrolysis.

Reuse of Electrode: An electrode was repeatedly reused at 1.2 A dm^{-2} of current density passing 96500×2.0 C mol^{-1} of charge for each electrolysis. As shown in Fig. 8, the asymmetry inducing power of **6** was lost at the fifth electrolysis, the film of **6** remained

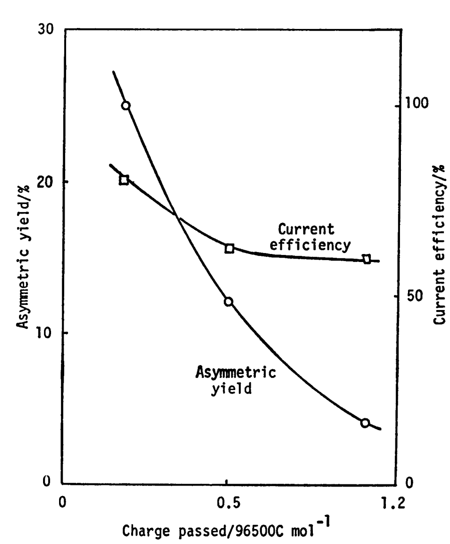


Fig. 7. Influence of charge passed on asymmetric reduction of citraconic acid (**1**) to methylsuccinic acid (**2**) on poly(L-valine)-coated graphite electrode (number of chirality centers, 0.25×10^{22} cm^{-2}).

Electrolytic conditions: pH, 6.0; cathodic potential, −1.0 V *vs.* SCE; temperature 0—5 °C; concentration of **1**, 0.145 M.

Configuration of excess enantiomer of **2**: *S*.

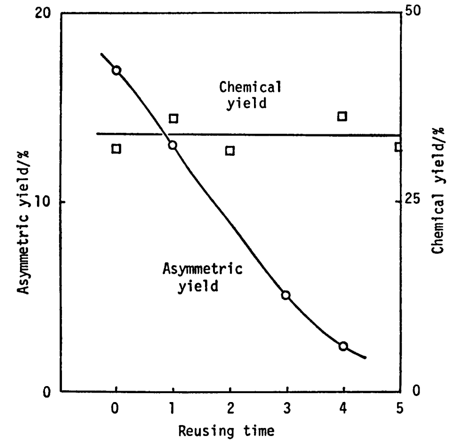


Fig. 8. Asymmetric reduction of citraconic acid (**1**) to methylsuccinic acid (**2**) on reused poly(L-valine)-coated graphite electrode (number of chirality centers, 0.5×10^{22} cm^{-2}).

Electrolytic conditions: pH, 6.0; current density, 1.2 A dm^{-2}; temperature, 0—5 °C; charge passed for each electrolysis, 96500×2.0 C mol^{-1}; concentration of **1**, 0.145 M.

Configuration of excess enantiomer of **2**: *S*,

on the electrode surface. The chemical yield did not change.

Optimization of Asymmetric Reduction of Citraconic Acid (1). The asymmetric reduction of **1** on the poly (L-valine)-coated graphite electrode is optimized under the conditions given in Table 2. From a synthetic aspect, it is undesirable that small amounts of charge passed and/or short electrolysis time are needed to obtain high asymmetric yields. To dissolve this problem, a high current concentration electrolysis using a high surface electrode may be recommended.

TABLE 2. OPTIMIZATION OF ELECTROCHEMICAL ASYMMETRIC REDUCTION OF CITRACONIC ACID (**1**) TO METHYLSUCCINIC ACID (**2**) ON POLY(AMINO ACID)-COATED ELECTRODE

Condition	Optimum
Optically-active poly-amino acid	poly(L-valine)
Base eleactrode material	Graphite
Number of chirality centers on electrode	$0.25\text{X}10^{22}$ cm^{-2}
pH	6.0
Cathode potential	−1.00 *vs.* SCE (Low as possibe)
Current density	1.2 A dm^{-2}
Temperature	0—5 °C
Charge passed	Small as possible
Reusing time of electrode	First use
Electrolysis time	Short as possible

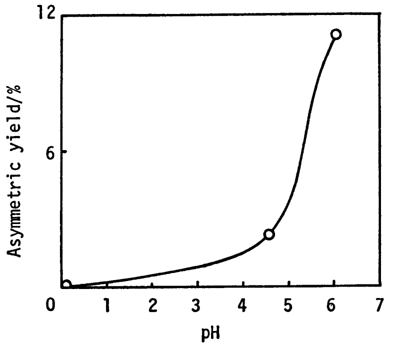


Fig. 9. Asymmetric reduction of mesaconic acid (**3**) to methylsuccinic acid (**2**) on poly(L-valine)-coated graphite electrode (number of chirality centers, 0.25 $\times10^{22}$ cm^{-2}).

Electrolytic conditions: current density, 1.2 A dm^{-2}; temperature, 0—5 °C; charge passed, 96500×2.2 C mol^{-1}; concentration of **1**, 0.145 M.

Current efficiency and yield: 33—45%. Configuration of excess enantiomer of **2**: *S*.

Asymmetric Reduction of Dimethyl Citraconate (4) to Dimethyl Methylsuccinate (5). As shown in Table 3, the asymmetric yield of **5** was extremely low compared with those of **2** formed under the same conditions. This fact suggests that hydrogen bonding of carboxyl groups of **1** contributes to the asymmetry induction.

Asymmetric Reduction of Mesaconic Acid (3) to Methylsuccinic Acid (2). As shown in Fig. 9, **3** gave **2** in lower asymmetric yields than **1**, while both **3** and **1** gave the enantiomer with the *S*-configuration in excess. These results seem to be important tor the discussion of the asymmetry induction mechanism.

Asymmetry Induction Mechanism. The poly(amino acid) film coated on base electrode surface is not electroconductive and does not include any electron-carrier, and also is so thick that any electron can not go through the film. Protons and substrate molecules may go through the film, because electrolyses proceeded smoothly without any remarkable cell-voltage increase. Therefore, electron-transfer to the substrate seems to occur in the interface of the film and the base electrode.

Although the mechanism of electrochemical asym-

TABLE 3. ELECTROCHEMICAL ASYMMETRIC REDUCTION[a] OF DIMETHYL CITRACONATE (**4**) TO DIMETHYL METHYLSUCCINATE (**5**) ON POLY(L-VALINE)-COATED GRAPHITE ELECTRODE (NUMBER OF CHIRALITY CENTERS, 0.5×10^{22} cm^{-2})

Cathode potential *vs.* SCE / V	Current density / A dm^{-2}	Charge passed / 96500 C mol^{-1}	**5**		
			Chemical yield/%	Asymmetric yield/%	Configuration of excess enantiomer
−1.25	—[b]	2.0	33	0.0	—
−1.15	—[b]	2.0	65	2.3	*S*
—[c]	1.2	4.0	14	0.0	—
—[c]	1.0	4.0	21	0.0	—

a) Electrolytic conditions: pH, 4.7; temperature, 0—5 °C; concentration of **4**, 0.145 M. b) Controlled potential electrolysis. c) Constant current electrolysis.

metry induction was discussed on the basis of steric interaction between prochiral substrate and chiral supporting salt molecules by Horner and Skaletz,[12] any essential conclusion has not been reported. Generally, it may be possible to suppose two types of the asymmetry induction mechanisms, as indicated below: (a) Asymmetric electron-transfer and (b) asymmetric protonation. As described above, **4** was not asymmetrically reduced. This fact may be as due to no interaction between S and I* (in the (a)-mechanism) by hydrogen bonding and thus support the (a)-mechanism. In addition, it may also support the (a)-mechanism that **1** and **3** gave **2** with the same configuration in different asymmetric yields: In the (b)-mechanism, **1** and **3** should give **2** in the same asymmetric yield, because an intermediate $H\bar{S}$ formed via no enantio-differentiating step from either of **1** and **3** should be racemic. On the other hand, the (a)-mechanism is not in conflict with the above experimental results: Since *cis*- and *trans*-carboxylic groups interact with I*(**6**), **1** and **3** in somewhat different ways give the different asymmetric yields. Although it is difficult to give a concrete conclusion for the asymmetry induction mechanism, the (a)-mechanism is tentatively proposed for the asymmetry induction mechanism.

$$\text{(a)}\quad S + I^* \rightleftharpoons SI^* \overset{2e+H^+}{\rightleftharpoons} H\bar{S}^* + I^* \xrightarrow{H^+} HS^*H + I^*$$

$$H^+ + I^*$$

$$\upharpoonleft\downharpoonright$$

$$\text{(b)}\quad S \overset{2e+H^+}{\rightleftharpoons} H\bar{S} \xrightarrow{H^+I^*} HS^*HI^* \longrightarrow HS^*H + I^*$$

S: Prochiral substrate.
I: Chiral asymmetry-inducing reagent.
HSH: Product.
*: Chiral species.

Experimental

Materials. Citraconic acid (**1**) and mesaconic acid (**3**) were supplied from Tokyo Kasei Chemical Co., while dimethyl citraconate (**4**) was prepared by the esterification of **3** with diazomethane in ether and purified by silica-gel column chromatography (bp, 98 °C/15 Torr (lit,[13] 92.8 °C/10 Torr, 1 Torr≈133.322 Pa)).

Poly(L-valine) (**6**), poly(L-leucine) (**7**), poly(D-valine) (**8**), and poly(L-tryptophan) (**9**) were prepared from the corresponding optically pure amino acids by the NCA method.[1] Poly(γ-benzyl-L-glutamate) (**10**) was supplied from Dr. K. Komoto of Tokyo Institute of Technology and poly(*N*-acryloyl-L-valine methyl ester) (**11**) was prepared by a following method. To 10 ml of an aqueous solution containing 3.1 g (0.03 mol) of triethylamine and 5.0 g (0.03 mol) of L-valine methyl ester were dropwise added 3.0 g (0.033 mol) of acryloyl chloride and 11 ml (0.033 mol) of 3 mol dm^{-3} NaOH for 5 h under ice-cooling. After the the reaction mixture was acidified (pH 2—3) with 5 mol dm^{-3} HCl, it was extracted with ethyl acetate. By distillation of the extract in the presence of a small amount of hydroquinone, 3.4 g (62%) of *N*-acryloyl-L-valine methyl ester was obtained: bp, 128 °C/10 Torr (lit,[14] 102 °C/3 Torr); MS, *m/e* 185 (M^+); IR (film), 3300, 1760, 1660, and 1630 cm^{-1}. The ester (2.0 g, 0.011 mol) obtained thus was polymerized in 12 ml of dry methanol in the presence of 0.02 g of 2,2′-azobisisobutyronitrile at 50 °C for 2 h. The reaction mixture was poured into 100 ml of water and 0.72 g (36%) of **11** was obtained as precipitates: IR (KBr), 3350, 1750, and 1670 cm^{-1}. Found: C, 58.31; H, 8.27; N, 7.35%. Calcd for $(C_9H_{15}NO_3)_n$: C, 58.36; H, 8.16; 7.56%. The optical rotating powers of all the poly(amino acd)s (**6**—**11**) are given in Fig. 1. The secondary structures confirmed by IR spectra are also given in Fig. 1. The molecular weight (*ca.* 2000) of **6** only could be known.[1] As polymer properties (molecular weight distribution and secondary structure) of poly(amino acid)s are generally affected by their preparative methods and procedures, the same lot products were used for each set of experiments in this work.

Poly(amino acid)-coated Electrodes. The coated electrodes were prepared by the dipping method described in the previous work.[1] Amounts of **6** coated were estimated from its recovery which was made by washing repeatedly the electrode with trifluoroacetic acid or by shaving off the film of **6**: **6** recovered thus was weighed or its nitrogen content was was analyzed.

Electrolysis and Product Analysis. Electrolytic solutions were aqueous ethanol (50—80%) buffered: 1 M (1 M=1 mol dm^{-3}) H_2SO_4 (pH *ca.* 0); 0.5 M $ClCH_2COOH$-0.5 M $ClCH_2COONa$ (pH 2.8); 4 M CH_3COOH-4 M CH_3COONa (pH 4.0); 0.5 M CH_3COOH-0.5 M CH_3COONa (pH 4.7); 0.17 M KH_2PO_4-0.03 M Na_2HPO_4 (pH 6.0); 0.5 M CH_3COONH_4 (pH 6.7, unbuffered); 0.5 M $NaClO_4$ (pH 7.0, unbuffered; 0.05 M $NaHCO_3$-0.1 M Na_2CO_3 (pH *ca.* 10); 0.5 M NaOH (pH *ca.* 14). Procedures for the electrolysis and product analysis were similar to those in the previous work.[1] The asymmetric yields were calculated with reference to optical rotating powers reported for the optically-pure enantiomers: $[\alpha]^{20}_{D}$ +17.9° (*c* 4.4 in ethanol)[15] for *R*-**2** and $[\alpha]^{25}_{D}$ +6.1° (neat)[15] for *R*-**5**.

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