Enantioselective Photoreduction of Tris(acetylacetonato)cobalt(III) by 1,4-Dihydropyridine Derivatives in the Presence of Molecular Aggregates

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Enantioselective photoreduction of Δ- and Λ-tris(acetylacetonato)cobalt(III) ([Co(acac)$_3$]) by achiral or chiral 1,4-dihydronicotinamide derivatives has been performed in the presence of molecular aggregates. Although appreciable enantioselectivity is not observed for the photoreduction of [Co(acac)$_3$] by chiral 1,4-dihydronicotinamides in micellar systems, achiral 1-benzyl-1,4-dihydronicotinamide (BNAH) reduces Δ-[Co(acac)$_3$] in preference to the Λ-form in the presence of bovine serum albumin (BSA). The 1,4-dihydronicotinamide derivative covalently bound to BSA also reduces [Co(acac)$_3$] enantioselectively. Activation parameters for the highly enantioselective reaction between photoexcited BNAH and [Co(acac)$_3$] in the presence of BSA have been estimated and are discussed.

Asymmetric reductions of carbonyl compounds by 1,4-dihydropyridine derivatives have received considerable attention in relation to the biomimetic reaction of a coenzyme, reduced nicotinamide adenine dinucleotide [NAD(P)H],[1] and asymmetric reactions with 1,4-dihydropyridines have hitherto been achieved thermally by the fixed contact interaction between chiral 1,4-dihydropyridines and prochiral (or enantiomeric) substrates with the aid of divalent metal ions such as Mg^{2+} and Zn^{2+}.[1-24] Although a high degree of enantioselection was observed in these reactions, the substrates used for the thermal asymmetric reduction with 1,4-dihydropyridines have been limited to relatively strong oxidants such as keto acids because of the weak reducing ability of 1,4-dihydropyridines. Since the electron donating ability of 1,4-dihydropyridines is remarkably enhanced by photoexcitation [for example, the oxidation potential of the photoexcited state is more negative (*ca.* 3.0 V) than that of the ground state in the case of 1-benzyl-1,4-dihydronicotinamide (BNAH)],[25] enantioselective photoreduction by 1,4-dihydropyridine derivatives might be significant. However, there is no report concerning enantioselective reactions with photoactivated 1,4-dihydropyridine derivatives, probably because it is difficult to ensure an efficient interaction between short-lived photoexcited 1,4-dihydropyridines (lifetime 0.93 ns in methanol in the case of singlet state BNAH)[26] and enantiomeric (or prochiral) substrates.

In this regard, molecular aggregates such as micelles might be expected to enhance the interaction between photoexcited hydrophobic 1,4-dihydropyridines and hydrophobic substrates by concentration of the reactants and increasing the lifetime of the photoactivated reactants when incorporated into molecular aggregates.

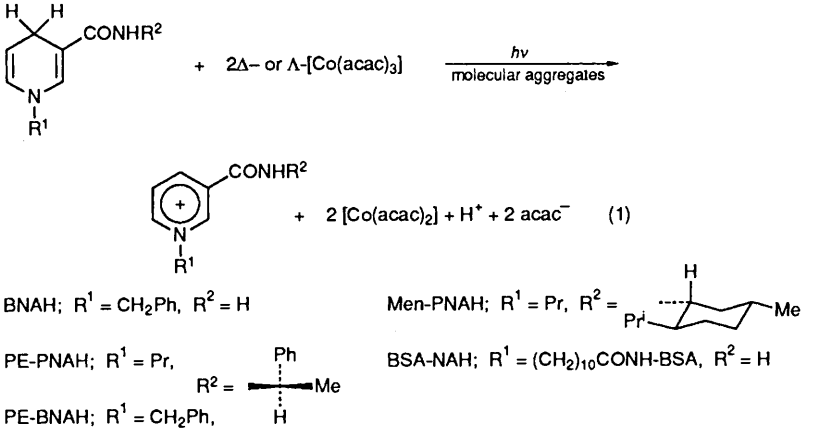
This paper describes the enantioselective photoinduced electron-transfer reactions of achiral and chiral 1,4-dihydropyridines with enantiomeric tris(acetylacetonto)cobalt(III) (Δ- or Λ-[Co(acac)$_3$]) in the presence of molecular aggregates.

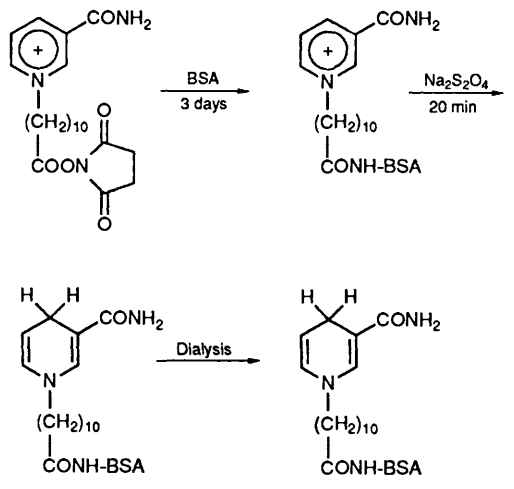
The molecular aggregates employed are anionic sodium dodecyl sulphate (SDS) and cationic dodecyltrimethylammonium chloride (DTAC), and bovine serum albumin (BSA). Surfactants such as SDS and DTAC can concentrate the reactants by hydrophobic interaction within micelles, while a carrier protein BSA can not only concentrate the reactants, but also provide chiral reaction fields in the absence of chiral reactants.

Experimental

Materials and Equipment.—1-Benzyl-1,4-dihydronicotinamide (BNAH),[27] 1-propyl-3-[*N*-(*R*)-(+)-phenylethylcarbamoyl]-1,4-dihydropyridine (PE–PNAH),[4] 1-benzyl-3-[*N*-(*R*)-(+)-phenylethylcarbamoyl]-1,4-dihydropyridine (PE–BNAH),[4] and 1-propyl-3-[*N*-(1*R*,2*S*,5*R*)-(−)-menthylcarbamoyl]-1,4-dihydropyridine (Men–PNAH)[4] were prepared according to literature procedures. The 1,4-dihydronicotinamide covalently bound to BSA (BSA–NAH) *via* an NH_2 group in BSA was synthesized in a manner similar to the literature method as shown in Scheme 1.[20]

Commercially available tris(acetylacetonato)cobalt(III) ([Co(acac)$_3$]) was purified by recrystallization from benzene–





Scheme 1

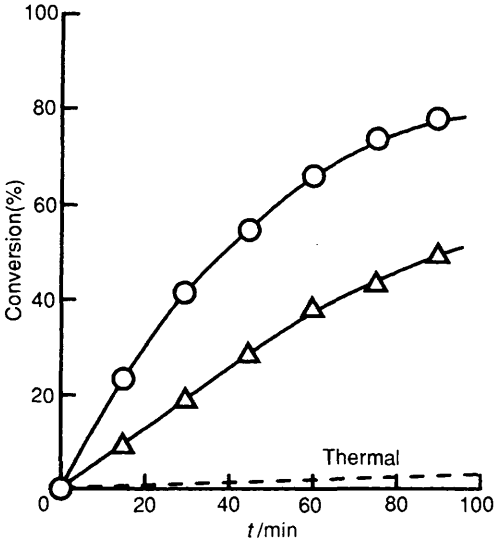


Fig. 1 Time-conversion plots for photoreaction of $[Co(acac)_3]$ by PE–PNAH in the presence of 3.2×10^{-3} mol dm^{-3} SDS (○) and 6.0×10^{-2} mol dm^{-3} DTAC (△) in 10% (v/v) methanol–borate buffer (pH 9.0) at 30 °C

light petroleum (30–60 °C). Δ- and Λ-$[Co(acac)_3]$ were separated by using dibenzoyl-(L and D)-tartaric acids, respectively, according to the literature method.[28] The optical purities of Δ- and Λ-$[Co(acac)_3]$ were confirmed from their CD spectra. The surfactants, sodium dodecyl sulphate (SDS) and dodecyltrimethylammonium chloride (DTAC), were commercially available and used without further purification. The solvents water, methanol and ethanol were distilled and deoxygenated by bubbling N_2 before use.

Absorption spectra were recorded on a JASCO UVIDEC-430A spectrophotometer. Fluorescence spectra were measured by using a JASCO FP-550A fluorescence spectrophotometer at 30 ± 0.1 °C. CD spectra were recorded on a JASCO J-500 spectrophotometer.

Reaction Procedure.—Reaction mixtures containing 1,4-dihydronicotinamides (1.0×10^{-3} mol dm^{-3}), Δ- or Λ-$[Co(acac)_3]$ (1.0×10^{-3} mol dm^{-3}), and BSA ($0–1.5 \times 10^{-3}$ mol dm^{-3}) in 4% (v/v) ethanol–0.05 mol dm^{-3} $Na_2B_4O_7$–HCl buffer solution (pH 9.3) were irradiated by a 400 W mercury lamp in the wavelength range 340–410 nm at 30 ± 0.2 °C. The reaction in the presence of micelles ($0–5.0 \times 10^{-2}$ mol dm^{-3}) in 10% (v/v) methanol–0.02 mol dm^{-3} H_3BO_3–NaOH buffer solution (pH 9.0) was carried out in a manner similar to that used for the BSA system. The amount of $[Co(acac)_3]$ consumed was determined

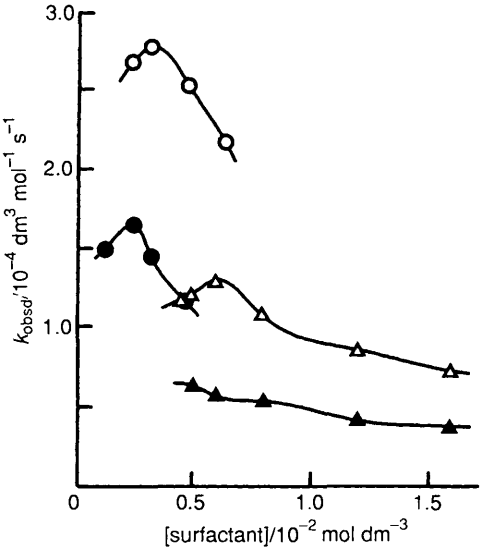


Fig. 2 Micellar effects on pseudo-first-order rate constants obtained for the photoreduction of $[Co(acac)_3]$ by PE–PNAH with SDS (○), by PE–PNAH with DTAC (△), by PE–BNAH with SDS (●), and by PE–BNAH with DTAC (▲)

spectrophotometrically at 595 nm. The optical purity of the remaining $[Co(acac)_3]$ was determined by CD spectra at 574 nm ($\Delta\varepsilon = 8.11$) and 647 nm ($\Delta\varepsilon = 2.99$).[28]

Methods for the determination of the quantum yields of the reaction and the lifetimes (τ) of photoexcited BNAH and BSA–NAH were the same as those described previously.[29–34]

Results and Discussion

Enantioselective Photoreduction of $[Co(acac)_3]$ *by* 1,4-*Dihydronicotinamides in the Presence of Molecular Aggregates.*—Although the reduction of $[Co(acac)_3]$ by PE–PNAH (λ_{max} = 356 nm) in the presence of surfactant micelles proceeded very slowly in the dark, the reaction rates were accelerated remarkably by photoirradiation (λ = 340–410 nm) as shown in Fig. 1. On the other hand, the photoreaction in the absence of micelles did not proceed due to the precipitation of the reactants under the reaction conditions.

All the present photoreactions in the presence of micelles obeyed pseudo-first-order kinetics. Fig. 2 indicates the effect of concentration of SDS and DTAC micelles on the observed rate constants (k_{obsd}) for the photoreduction of $[Co(acac)_3]$ by PE–PNAH and PE–BNAH. The surfactant micelles accelerated the reaction rates by concentrating the reactants through the hydrophobic force, and by increasing the lifetime of photoexcited 1,4-dihydropyridines.[33,34] The observed micellar effects shown in Fig. 2 reflect two competing micellar effects. Firstly, the proportion of reactants in the micellar phase increases with increasing micellar concentration, but high micellar concentration also causes dilution of the reactants within the micellar phase, so as to reduce the k_{obsd} values.

The anionic SDS micelles were more effective than the cationic DTAC micelles at accelerating the photoreaction. As discussed in the previous paper,[33] the negative charge of the SDS micelles promotes the charge separation of the encounter complex between 1,4-dihydronicotinamide and the substrate by stabilizing the positive charge produced on the dihydropyridine ring and by separating an $acac^-$ anion from the reduced $[Co(acac)_3]$. The rate constants for the reaction with PE–BNAH were smaller than those for PE–PNAH due to the unstable nature of PE–BNAH.

The enantiomer rate ratios ($R = k^{\Delta}_{obsd}/k^{\Lambda}_{obsd}$) were calculated from the CD spectrum change of $[Co(acac)_3]$ during

Table 1 Pseudo-first-order rate constants (k_{obsd}) and enantiomer rate ratios ($R = k^{\Delta}_{obsd}/k^{\Lambda}_{obsd}$) obtained for photoreduction of [Co(acac)$_3$] by chiral 1,4-dihydropyridine derivatives (PyH_2) with micelles in 10% (v/v) methanol–H_3BO_3–NaOH buffer (pH 9.0) solution at 30 °C[a]

PyH_2	Surfactant	[surfactant]/ 10^{-2} mol dm^{-3}	k_{obsd}/ 10^{-4} s^{-1}	R
PE–PNAH	SDS	3.2	2.9	1.00
	DTAC	4.5	1.2	1.00
PE–BNAH	SDS	3.2	1.3	1.00
Men–PNAH[b]	SDS	2.4	0.37	1.01

[a] $[PyH_2] = 2.0 \times 10^{-3}$ mol dm^{-3} and [Co(acac)$_3$] = 1.0×10^{-3} mol dm^{-3}. [b] [Men–PNAH] = 5.0×10^{-4} mol dm^{-3} and [Co(acac)$_3$] = 1.0×10^{-3} mol dm^{-3} in 4% (v/v) methanol–H_3BO_3–NaOH buffer (pH 9.0).

Table 2 Observed pseudo-first-order rate constants for photoreduction of Δ- and Λ-[Co(acac)$_3$] by BNAH with BSA[a]

[BSA]/ 10^{-3} mol dm^{-3}	k^{Δ}_{obsd}/ 10^{-5} s^{-1}	k^{Λ}_{obsd}/ 10^{-5} s^{-1}	R
0	6.87	—	—
0.5	2.40	2.11	1.14
1.0	2.13	1.75	1.22
1.5	1.94	1.64	1.18

[a] In 4% (v/v) ethanol–$Na_2B_4O_7$ buffer (pH 9.3) at 30 °C under N_2.

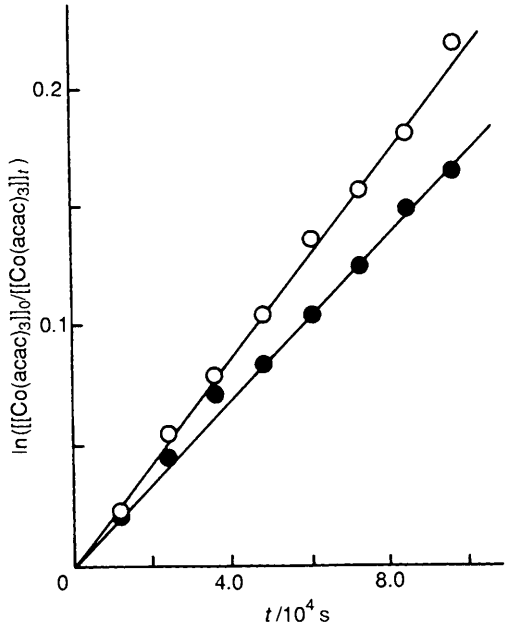


Fig. 3 Plots of $\ln([[Co(acac)_3]]_0/[[Co(acac)_3]]_t)$ *vs.* t for photoreduction of (○) Δ- and (●) Λ-[Co(acac)$_3$] (1.0×10^{-3} mol dm^{-3}) by BNAH (1.0×10^{-3} mol dm^{-3}) with BSA (1.0×10^{-3}) in 4% (v/v) ethanol–$Na_2B_4O_7$ buffer (pH 9.3) at 30 °C under N_2

the photoreaction. The R values obtained for the photoreduction of racemic [Co(acac)$_3$] by the chiral 1,4-dihydropyridine derivatives (PyH_2) with micelles are summarized in Table 1. No appreciable enantioselectivity was observed for the photoreduction with PE–PNAH and PE–BNAH, which possess a chiral *N*-(*R*)-(+)-phenylethyl group, in the presence of SDS or DTAC. Although Men–PNAH reduced [Co(acac)$_3$] enantioselectively, the effect of the chiral (1*R*,2*S*,5*R*)-(−)-menthyl portion on the stereoselection of the enantiomeric [Co(acac)$_3$] was very small. These facts suggest that the photoreduction of [Co(acac)$_3$] by the above chiral 1,4-dihydropyridines in the micellar system proceeds without any

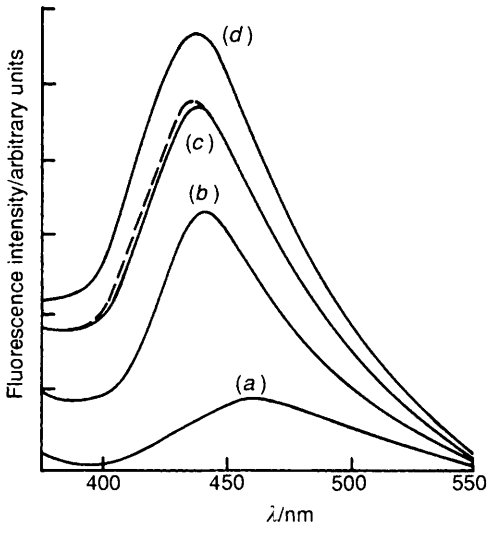


Fig. 4 Fluorescence spectra of BNAH with or without BSA [(*a*) 0, (*b*) 5.0×10^{-5}, (*c*) 1.5×10^{-4}, and (*d*) 1.0×10^{-3} mol dm^{-3}] in 4% (v/v) ethanol–$Na_2B_4O_7$ buffer (pH 9.3) at 30 °C. Broken line is the fluorescence spectrum of BSA–NAH under the same conditions.

effective contact interaction between the photoexcited chiral species and the substrates. In other words, the photoexcited 1,4-dihydropyridines of PE–PNAH, PE–BNAH and Men–PNAH can transfer electrons to the substrates over a relatively long range. Therefore, a more rigid interaction between the reactants is required to achieve the enantioselective photoreduction of [Co(acac)$_3$] by 1,4-dihydropyridines.

In this regard, a carrier protein such as bovine serum albumin (BSA) might be effective, so long as it incorporates both reactants, because it can not only interact strongly with reactants through the considerable hydrophobicity of the protein framework, but also induce an enantioselective interaction between the reactants through its chiral fields.[20]

When achiral BNAH (1.0×10^{-3} mol dm^{-3}) and Δ- or Λ-[Co(acac)$_3$] (1.0×10^{-3} mol dm^{-3}) were allowed to react under photoirradiation (λ = 340–410 nm) in the presence of BSA (1.0×10^{-3} mol dm^{-3}) in 4% (v/v) ethanol–$Na_2B_4O_7$ buffer solutions (pH 9.3) at 30 °C, the amount of [Co(acac)$_3$] consumed satisfied pseudo-first-order kinetics as shown in Fig. 3. The consumption rate of Δ-[Co(acac)$_3$] by BNAH was faster than that of Λ-[Co(acac)$_3$]. Since BNAH is achiral, the enantioselectivity of the present reaction results from the chiral field in BSA.

The pseudo-first-order rate constants (k^{Δ}_{obsd} and k^{Λ}_{obsd}) obtained for the reduction of Δ- and Λ-[Co(acac)$_3$], respectively, at various BSA concentrations are listed in Table 2. The k^{Δ}_{obsd} and k^{Λ}_{obsd} values decreased with increasing BSA concentrations. On the other hand, the enantiomer rate ratio ($k^{\Delta}_{obsd}/k^{\Lambda}_{obsd}$ = 1.0) was enhanced by the presence of BSA, and reached a constant value ($k^{\Delta}_{obsd}/k^{\Lambda}_{obsd}$ = 1.2) with [BSA] > 1.0×10^{-3} mol dm^{-3}.

These concentration effects of BSA might be caused by the incorporation of both the reactants (BNAH and [Co(acac)$_3$]) by the carrier protein BSA, which is reflected in the following phenomena; (*a*) the fluorescence intensity of BNAH, which is sensitive to the medium,[33] increased with increasing BSA concentration, (*b*) the emission maximum (λ_{max} = 460 nm) of BNAH in the absence of BSA shifted toward the shorter wavelength region (λ_{max} = 440 nm) in the presence of BSA (Fig. 4), and (*c*) the absorption maximum of [Co(acac)$_3$] was shifted by BSA from 595 nm (in the aqueous solution) to 585 nm.

With regard to the incorporation of BNAH by BSA, the binding constant of BNAH to BSA can be estimated from the effect

Table 3 Observed pseudo-first-order rate constants for photoreduction of Δ- and Λ-[Co(acac)$_3$] by the BNAH–BSA mixed system or by BSA–NAH in 4% (v/v) ethanol–$Na_2B_4O_7$ buffer (pH 9.3) at 30 °C under N_2[a]

1,4-Dihydronicotinamide	k^{Δ}_{obsd}/ 10^{-5} s^{-1}	k^{Λ}_{obsd}/ 10^{-5} s^{-1}	R
BSA–NAH	0.345	0.291	1.15
BNAH–BSA mixed system	2.13	1.75	1.22

[a] [BNAH] = [BSA–NAH] = 1.0×10^{-3} mol dm^{-3}, [Co(acac)$_3$] = 1.0×10^{-3} mol dm^{-3}, and [BSA] = 1.0×10^{-3} mol dm^{-3}.

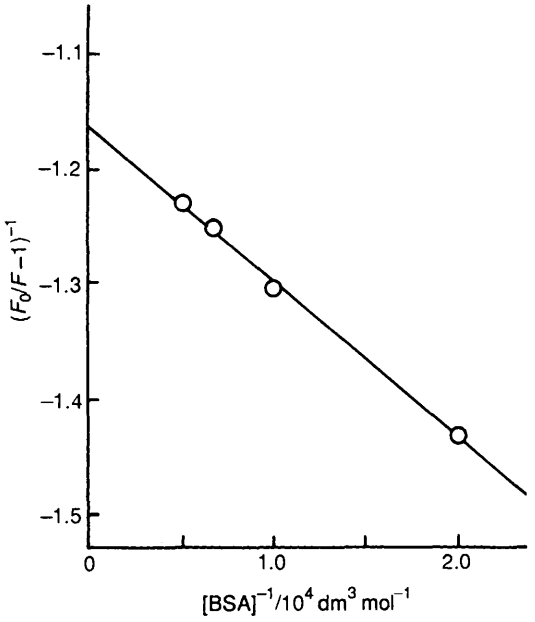


Fig. 5 Plots of $(F_0/F - 1)^{-1}$ *vs.* $[BSA]^{-1}$ in 4% (v/v) ethanol–$Na_2B_4O_7$ buffer (pH 9.3) at 30 °C

of BSA concentration on the fluorescence intensity. The binding constant (K) of BNAH to BSA is related to the fluorescence intensity by eqn. (2),[32] where F_0 and F are the respective

$$\frac{1}{F_0/F - 1} = \frac{1}{1 - \varphi_{BSA}/\varphi_w}\left(\frac{1}{K}\frac{1}{[BSA]} + \frac{\varphi_{BSA}}{\varphi_w}\right) \quad (2)$$

fluorescence intensities of BNAH with BSA and without BSA, and φ_w (or φ_{BSA}) = quantum yield of the fluorescence in the aqueous phase (or in BSA).

As shown in Fig. 5, the plots of $(F_0/F - 1)^{-1}$ *vs.* $[BSA]^{-1}$ gave a linear relationship according to eqn. (2). The K value was estimated to be 1.19×10^4 dm^3 mol^{-1} from the slope and intercept of the line.

On the other hand, the binding constant of [Co(acac)$_3$] to BSA could not be determined because [Co(acac)$_3$] does not emit any fluorescence. However, the incorporation of [Co(acac)$_3$] by BSA was indicated by the shift of its absorption maximum from 595 nm in the aqueous solution to 585 nm in the presence of BSA, as mentioned before. Since no appreciable spectral change of [Co(acac)$_3$] was observed in the micellar system, the interaction of [Co(acac)$_3$] with BSA is stronger than that with the micelles.

The concentration fraction, f of BNAH incorporated into BSA was calculated by eqn. (3) where $[BNAH]_{tot}$ is the total

$$f = \frac{[BNAH]_{BSA}}{[BNAH]_{tot}} = \frac{K[BSA]}{1 + K[BSA]} \quad (3)$$

concentration of BNAH in the solution and $[BNAH]_{BSA}$ is the stoichiometric (bulk) concentration of BNAH in BSA.

As can be seen from eqn. (3), the f values increase with increasing BSA concentration and came close to unity at high BSA concentration. Since the enantioselectivity in the present reaction was induced by the chiral peptide framework in BSA, such a change of the BNAH distribution from the aqueous phase to the BSA field resulted in the increase of the $k^{\Delta}_{obsd}/k^{\Lambda}_{obsd}$ values at high BSA concentration.

The incorporation of BNAH by BSA also affected the reaction rate constant. The enhancement of fluorescence intensity of BNAH by BSA indicates the apolar reaction environment in BSA.[33] Such an apolar environment suppresses the production of ionic and hydrophilic species such as $BNAH^{\bullet+}$, BNA^+, [Co(acac)$_2$], and $acac^-$,[33,34] so that the photoreduction of [Co(acac)$_3$] by BNAH was retarded in the BSA inner phase. The restricted mobility of the reactants in the BSA inner phase also suppresses the photoreaction by enhancing the extent of the back electron transfer. (This cage effect will be discussed in the later parts of this text.) Although BNAH and [Co(acac)$_3$] are concentrated in BSA by hydrophobic interaction, similar to the case of the micellar reaction, the retardation of the photoreaction in the BSA inner phase outweighs the above-mentioned acceleration effects as is reflected by the steady decrease of the k_{obsd} values with increasing BSA concentration.

Such a concentration effect of BSA is also attributable to the different incorporation of the reactants by BSA, *i.e.*, the difference in the binding constants of the reactants results in a change of their molar ratio in BSA with BSA concentration. Therefore, the concentration increase of BSA reduces the chance of a given BSA molecule interacting simultaneously with a molecule of each reactant. Thus, the reaction rate was found to decrease on increasing the concentration of BSA.

In this regard, the employment of 1,4-dihydronicotinamide attached to BSA *via* a covalent bond for the present photoreaction may result in the enhancement of the stereoselective reactivity of the above reductant, because such a modification has the potential to achieve the fixed interaction between the reactants without any dilution effects. Thus, the hybrid-type 1,4-dihydronicotinamide covalently bound to BSA by a C_{11}-alkyl chain, BSA–NAH, was synthesized.

The fluorescence intensity of BSA–NAH was enhanced as compared with that of BNAH in the absence of BSA (Fig. 4). The emission maximum (λ_{max} = 440 nm) of BSA–NAH was about 20 nm shorter than that of BNAH itself. As these results are similar to the difference in the emission maxima between BNAH and the BNAH–BSA mixed system, the 1,4-dihydronicotinamide moiety of BSA–NAH is likely to be located inside the BSA.

The rate constants observed for the photoreduction of Δ- and Λ-[Co(acac)$_3$] by BSA–NAH are listed in Table 3 in addition to that obtained for the BNAH–BSA mixed system under the same reaction conditions. The reaction rate constants (k_{obsd}) and the enantioselectivity ($k^{\Delta}_{obsd}/k^{\Lambda}_{obsd}$) for BSA–NAH were smaller than those for the mixed system. The facts suggests that the covalent bonding of 1,4-dihydronicotinamide to BSA disturbs the reaction of 1,4-dihydronicotinamide with [Co(acac)$_3$], probably because of the restricted mobility of the 1,4-dihydronicotinamide moiety. Such a decrease in the mobility of BNAH might also inhibit the favourable orientation of 1,4-dihydronicotinamide moiety and [Co(acac)$_3$], so as to lower the enantioselectivity.

Kinetic Analysis of Enantioselective Photoreaction of BNAH with Δ- and Λ-[Co(acac)$_3$] in the Presence of BSA.—Some significant factors determining the enantioselectivity of the present reaction were elucidated by the following mechanistic analysis.

The simple mechanism for the photoreduction of [Co(acac)$_3$]

Table 4 Second-order rate constants for electron transfer from BNAH* to Δ- or Λ-[Co(acac)$_3$] in the presence of BSA at 30 °C

[Co(acac)$_3$]	τ/ns	k_{el}/ 10^9 dm^3 mol^{-1} s^{-1}	$k_{el}^{\Delta}/k_{el}^{\Lambda}$
Δ-form	2.08	2.52	1.22
Λ-form		2.07	

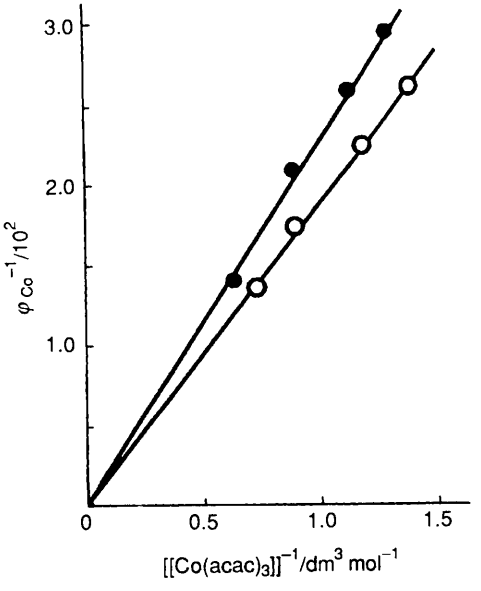


Fig. 6 Plots of φ_{Co} *vs.* [Δ- or Λ-[Co(acac)$_3$]]$^{-1}$ for photoreaction of Δ- (○) or Λ-[Co(acac)$_3$] (●) by BNAH in the presence of BSA

by BNAH can be expressed by eqns. (4a–f).[33] According to eqns. (4a–f), the quantum yields (φ_{Co}) estimated on the basis of

$$\text{BNAH} \xrightarrow{h\nu} \text{BNAH*} \quad (4a)$$

$$\text{BNAH*} \xrightarrow{k_{ic}} \text{BNAH} \quad (4b)$$

$$\text{BNAH*} \xrightarrow{k_f} \text{BNAH} + h\nu \quad (4c)$$

$$\text{BNAH*} + [\text{Co(acac)}_3] \xrightarrow{k_{el}} \text{BNAH}^{\bullet+} + [\text{Co(acac)}_2] + \text{acac}^- \quad (4d)$$

$$\text{BNAH}^{\bullet+} \xrightarrow{k_{H^+}} \text{BNA}^{\bullet} + \text{H}^+ \quad (4e)$$

$$\text{BNA}^{\bullet} + [\text{Co(acac)}_3] \xrightarrow{k_{el}} \text{DNA}^+ + [\text{Co(acac)}_2] + \text{acac}^- \quad (4f)$$

the amount of [Co(acac)$_3$] consumed were related to the [Co(acac)$_3$] concentration by eqn. (5) where τ = the lifetime

$$\frac{1}{\varphi_{Co}} = \frac{1}{k_{el}\tau \cdot [[Co(acac)_2]]} + 1 \quad (5)$$

of photoexcited BNAH (BNAH*) in the absence of [Co(acac)$_3$]. As shown in Fig. 6, the plots of φ_{Co}^{-1} *vs.* [[Co(acac)$_3$]]$^{-1}$ gave straight lines for the photoreduction of Δ- and Λ-[Co(acac)$_3$] by BNAH in the presence of BSA. From the slopes of the lines, the $k_{el}\tau$ values were estimated to be 5.2 and 4.3 dm^3 mol^{-1} for the Δ- and Λ-forms of [Co(acac)$_3$], respectively.

In order to estimate the k_{el} values, the lifetime of BNAH* was determined by fluorescence intensity measurement.[29–33] The k_{el} values calculated from the $k_{el}\tau$ and τ values are listed in Table 4. The ratio of the enantiomer rate constants ($k_{el}^{\Delta}/k_{el}^{\Lambda}$) for the elementary reaction (4d) was coincident with that of the observed rate constants. Therefore, the enantioselectivity of the present reaction results from the selection of enantiomeric substrates during the electron-transfer reaction between BNAH* and [Co(acac)$_3$] [eqn. (4d)].

Table 5 Activation parameters ($\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$ and $\Delta G^{\ddagger}$)[a] estimated for elementary reaction (4d) in 4% (v/v) ethanol–0.05 mol dm^{-3} $Na_2B_4O_7$–HCl buffer solution (pH 9.3)

[BSA]/ 10^{-3} mol dm^{-3}	[Co(acac)$_3$]	$\Delta H^{\ddagger}$/ kJ mol^{-1}	$\Delta S^{\ddagger}$/ J mol^{-1} K^{-1}	$\Delta G^{\ddagger}$/ kJ mol^{-1}
1.0	Δ-form	43.6	81.8	18.8
1.0	Λ-form	47.4	92.9	19.2
0	racemate	56.2	131.2	16.4

[a] Calculated at 303 K.

Thermodynamic Parameters.—The k_{el} values obtained for the present reaction were also affected by the reaction temperature. The activation parameters ($\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$ and $\Delta G^{\ddagger}$) estimated from the linear Arrhenius plots for the electron-transfer reaction between BNAH* and [Co(acac)$_3$] are summarized in Table 5. Although the $\Delta H^{\ddagger}$ value obtained in the presence of BSA was smaller than that in the absence of BSA, the addition of BSA caused the increase of $\Delta G^{\ddagger}$ values, owing to the small $\Delta S^{\ddagger}$ values, so as to retard the reaction rates.

The elementary processes of the electron-transfer reaction of BNAH* with [Co(acac)$_3$] are expressed by eqns. (6a–d). The

$$\text{BNAH*} + [\text{Co(acac)}_3] \longrightarrow [\text{BNAH* Co(acac)}_3] \quad (6a)$$

$$[\text{BNAH* Co(acac)}_3] \longrightarrow [\text{BNAH}^+ \text{Co(acac)}_3^-] \quad (6b)$$

$$[\text{BNAH}^+ \text{Co(acac)}_3^-] \longrightarrow [\text{BNAH}^+ \text{Co(acac)}_2 \cdots \text{acac}^-] \longrightarrow \text{BNAH}^{\bullet+} + [\text{Co(acac)}_2] + \text{acac}^- \quad (6c)$$

$$[\text{BNAH}^+ \text{Co(acac)}_3^-] \longrightarrow [\text{BNAH Co(acac)}_3] \longrightarrow \text{BNAH} + [\text{Co(acac)}_3] \quad (6d)$$

formation of the encounter complex ([BNAH* Co(acac)$_3$]) is a diffusion-controlled process [eqn. (6a)], and the subsequent electron transfer in the encounter complex [eqn. (6b)] might occur immediately because of the strong electron-donating ability of BNAH* ($E_{ox} > -2$ V *vs.* SCE).[25] Although the successor complex ([BNAH$^+$ Co(acac)$_3^-$]) dissociates to BNAH$^{\bullet+}$, [Co(acac)$_2$] and acac$^-$ through some conformational changes expressed by [BNAH$^+$ Co(acac)$_2$ ··· acac$^-$] [eqn. (6c)], the back electron transfer [eqn. (6d)] can occur easily due to the weak reducing ability of BNAH (E_{ox} = 0.76 V *vs.* SCE).[35] Therefore, the efficiency of the dissociation of acac$^-$ from [Co(acac)$_3$] might determine the reaction rates. In this regard, the restricted protein 'cage' in BSA might retard the reaction rates by suppressing such a charge separation process (*viz.* small $\Delta S^{\ddagger}$ values).

In respect to the enantioselectivity, the smaller $\Delta H^{\ddagger}$ value for Δ-[Co(acac)$_3$] than for the Λ-form resulted in faster electron transfer from BNAH* to Δ-[Co(acac)$_3$]. In other words, Δ-[Co(acac)$_3$] and BNAH* (or BNAH) can form an activation complex to stabilize the transition state by tight interaction within BSA.

Thus, the enantioselective electron transfer reactions of 1,4-

dihydronicotinamide were realized by increasing interaction of the reactants with the aid of molecular aggregates.

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