Synchronous enantiomeric enrichment of both reactant and product by absolute asymmetric synthesis using circularly polarized light. Part 3.[1] Numerical simulation and experimental verification of the reversible asymmetric photoisomerization between methyl norbornadiene-2-carboxylate and methyl quadricyclane-1-carboxylate

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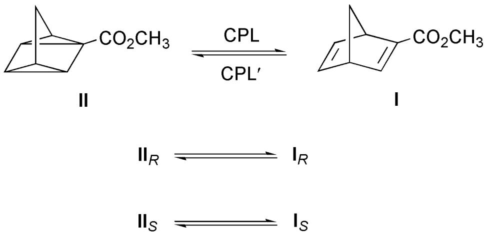
Received (in Cambridge, UK) 22nd January 2001, Accepted 21st June 2001
First published as an Advance Article on the web 14th August 2001

In the first paper of this series, we proposed a new absolute asymmetric synthesis (NAAS) with circularly polarized light (CPL), which can be classified into two subcategories: (a) reversible NAAS (CPL excites both the reactant and product), (b) irreversible NAAS (the reactant only is excited by CPL). In the present paper we deal with reversible NAAS. The numerical simulations, which are based upon the results of the preceding paper of this series, are performed. Using the reversible photoisomerization between methyl norbornadiene-2-carboxylate (**I**) and methyl quadricyclane-1-carboxylate (**II**), it was experimentally verified that the enantiomeric excesses (ee's) of both the reactant and product were critically dependant not only on the anisotropy factors ($g = \Delta\varepsilon/\varepsilon$) of both components, but also on the relative quantum yields of the forward and reverse reactions. In the case of reversible NAAS, the ee of the reactant and the product will concurrently increase according to the conversion, and attain appreciable values at the photostationary state if we appropriately select the system and the CPL-irradiation wavelength in such a way that if the g factors of the product and the reactant are large enough, the sign of the g factor of the product is opposite to that of the reactant, and the photochemical equilibrium constant K is less than unity.

Absolute asymmetric synthesis (AAS) using circularly polarized light (CPL) as a physical chiral source, enabling enantiomeric enrichment without using any chemical chiral source, is an intriguing and unique methodology among asymmetric synthetic procedures, and has recently been discussed in relation to the origin of the homochirality in the biosphere.[2–5] In AAS, asymmetric induction is brought about through the preferential excitation of one of the enantiomers of a racemic mixture upon CPL irradiation. The variety of AAS reactions hitherto reported have been classified into three categories according to the manner of enantiodifferentiation, *i.e.* (a) asymmetric photodestruction, (b) photochemical deracemization, and (c) photochemical asymmetric fixation.[6–8]

In the first paper of this series, we proposed a new category of absolute asymmetric synthesis (NAAS) shown in Scheme 4 of the preceding paper,[1] where both reactant and product are chiral and enantiomeric enrichment occurs in both components. NAAS is classified into two subcategories according to the nature of the photochemical reversibility between the reactant and the product: in class (a), there is a photochemical equilibrium between the reactant and the product because the reaction mixture is irradiated with CPL which excites both the reactant and the product; in class (b), the reaction is irreversible because only the reactant is excited by CPL but the product is not excited because the product does not absorb incident light at the excitation wavelength. For the irreversible NAAS system (class (b)), in the first paper of this series, we derived the theoretical equations for formulating the developing patterns of the enantiomeric excesses (ee's) of both reactants and product as a function of the conversion upon CPL irradiation. These formulae were experimentally verified by the one-way photoisomerization of methyl norbornadiene-2-carboxylate (**I**) to methyl quadricyclane-1-carboxylate (**II**) (Scheme 1) induced by CPL irradiation at 290 nm which is absorbed only by **I**.



Scheme 1 Photoisomerization between **I** and **II**.

In the present study, we deal with the more complicated reversible NAAS system, *i.e.* class (a), where both the reactant and the product absorb CPL and the photoequilibrium is established upon prolonged irradiation. We have simulated numerically the development of the ee's of both reactant and product upon CPL irradiation in the reversible NAAS system. We have examined the validity of the results of these simulations by performing the reversible photoisomerization between **I** and **II** upon excitation by monochromatic CPL generated by an Onuki-type polarizing undulator installed in a synchrotron radiation source. In the first paper of this series we used a xenon arc lamp as the light source for CPL generation. However, this

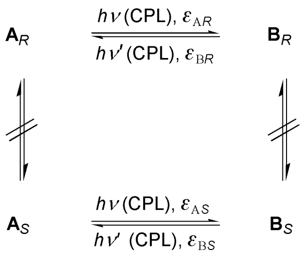
DOI: 10.1039/b100753j

source could not be used at wavelengths less than 280 nm because of low intensity. With the aid of the synchrotron undulator we were able to study the CPL irradiation in the far UV region. The results of the CPL irradiation of the **I–II** system verifies the theoretical conclusions that the ee's of both the reactant and the product and the conversion critically depend upon both the anisotropy (*g*) factors of the reactant and the product but also on the relative rates of the forward and reverse reactions. We will further demonstrate that the method of simulation that is derived in this study is not restricted to NAAS but can be universally applied to AAS.

Results and discussion

Numerical simulations

General scheme for the reaction. We consider a photochemical system in which the enantiomers of the reactant (**A**) are isomerized by irradiation with CPL to the enantiomers of the product (**B**) without racemization (Scheme 2).



Scheme 2 A general scheme for the reversible photoisomerization between reactant (**A**) and product (**B**).

For the reversible photoisomerization the rate equations are expressed as shown in eqns. (1)–(5), where $c_{\mathrm{A}R}$, $c_{\mathrm{A}S}$, $c_{\mathrm{B}R}$, and $c_{\mathrm{B}S}$

$$\frac{\mathrm{d}c_{\mathrm{A}R}}{\mathrm{d}t} = -I_{\mathrm{ex}}\frac{S}{V}(1-10^{-A})\frac{l}{A}\varepsilon_{\mathrm{A}R}c_{\mathrm{A}R}\Phi_{\mathrm{A}} + I_{\mathrm{ex}}\frac{S}{V}(1-10^{-A})\frac{l}{A}\varepsilon_{\mathrm{B}R}c_{\mathrm{B}R}\Phi_{\mathrm{B}} \tag{1}$$

$$\frac{\mathrm{d}c_{\mathrm{A}S}}{\mathrm{d}t} = -I_{\mathrm{ex}}\frac{S}{V}(1-10^{-A})\frac{l}{A}\varepsilon_{\mathrm{A}S}c_{\mathrm{A}S}\Phi_{\mathrm{A}} + I_{\mathrm{ex}}\frac{S}{V}(1-10^{-A})\frac{l}{A}\varepsilon_{\mathrm{B}S}c_{\mathrm{B}S}\Phi_{\mathrm{B}} \tag{2}$$

$$\frac{\mathrm{d}c_{\mathrm{B}R}}{\mathrm{d}t} = -\frac{\mathrm{d}c_{\mathrm{A}R}}{\mathrm{d}t} \tag{3}$$

$$\frac{\mathrm{d}c_{\mathrm{B}S}}{\mathrm{d}t} = -\frac{\mathrm{d}c_{\mathrm{B}R}}{\mathrm{d}t} \tag{4}$$

$$A = l(\varepsilon_{\mathrm{A}R}c_{\mathrm{A}R} + \varepsilon_{\mathrm{A}S}c_{\mathrm{A}S} + \varepsilon_{\mathrm{B}R}c_{\mathrm{B}R} + \varepsilon_{\mathrm{B}S}c_{\mathrm{B}S}) \tag{5}$$

are the concentrations of the enantiomers of the reactant ($\mathbf{A}_R$ and $\mathbf{A}_S$) and the product ($\mathbf{B}_R$ and $\mathbf{B}_S$), I_{ex} is the incident photonic flux expressed as einstein cm^{-2} s^{-1}, S is the area of the cross section of the incident light, V is the volume of the solution, A is the absorbance of the reaction mixture in the reaction cuvette, $\varepsilon_{\mathrm{A}R}$, $\varepsilon_{\mathrm{A}S}$, $\varepsilon_{\mathrm{B}R}$, and $\varepsilon_{\mathrm{B}S}$ are molar extinction coefficients, l is the path length of the reaction cuvette, Φ_{A} and Φ_{B} are the quantum yields of the forward (**A** to **B**) and back (**B** to **A**) reactions.

In the reversible reaction there should be a photostationary state (PSS). We can estimate the concentrations of the reactant and the product at the PSS by using eqns. (1) and (2). At the PSS eqn. (6) holds from which eqns. (7) and (8) can be derived.

$$\frac{\mathrm{d}c_{\mathrm{A}R}}{\mathrm{d}t} = \frac{\mathrm{d}c_{\mathrm{A}S}}{\mathrm{d}t} = 0 \tag{6}$$

$$\varepsilon_{\mathrm{A}R}c_{\mathrm{A}R}^{\mathrm{PSS}}\,\Phi_{\mathrm{A}} = \varepsilon_{\mathrm{B}R}c_{\mathrm{BR}}^{\mathrm{PSS}}\Phi_{\mathrm{B}} \tag{7}$$

$$\varepsilon_{\mathrm{A}S}c_{\mathrm{A}S}^{\mathrm{PSS}}\,\Phi_{\mathrm{A}} = \varepsilon_{\mathrm{B}S}c_{\mathrm{B}S}^{\mathrm{PSS}}\Phi_{\mathrm{B}} \tag{8}$$

By using these equations and the mass balance for the photoisomerization (see Appendix for details) we obtain eqn. (9), where eqns. (10)–(14) hold.

$$\text{conversion at PSS} = \frac{1}{2}\left\{\frac{1}{1+(PK)^{-1}} + \frac{1}{1+(MK)^{-1}}\right\} \tag{9}$$

$$P = \frac{2+g_{\mathrm{B}}}{2+g_{\mathrm{A}}} \tag{10}$$

$$M = \frac{2-g_{\mathrm{B}}}{2-g_{\mathrm{A}}} \tag{11}$$

$$K = \frac{\varepsilon_{\mathrm{B}}\Phi_{\mathrm{B}}}{\varepsilon_{\mathrm{A}}\Phi_{\mathrm{A}}} \tag{12}$$

$$g_{\mathrm{A}} = 2\frac{\varepsilon_{\mathrm{A}R} - \varepsilon_{\mathrm{A}S}}{\varepsilon_{\mathrm{A}R} + \varepsilon_{\mathrm{A}S}} \tag{13}$$

$$g_{\mathrm{B}} = 2\frac{\varepsilon_{\mathrm{B}R} - \varepsilon_{\mathrm{B}S}}{\varepsilon_{\mathrm{B}R} + \varepsilon_{\mathrm{B}S}} \tag{14}$$

Method of simulation. For obtaining the numerical solution of the differential equations a fourth-order Runge–Kutta method[9] was employed. If we use the reduced reaction time, $t^* = tI_{\mathrm{ex}}\{(\varepsilon_{\mathrm{A}R} + \varepsilon_{\mathrm{A}S})/2\}(Sl/V)\Phi_{\mathrm{A}}(\ln 10)$, as a measure of the reaction time, eqns. (1) through (4) are transformed into eqns. (13)–(16) where $\varepsilon_{\mathrm{A}} = (\varepsilon_{\mathrm{A}R} + \varepsilon_{\mathrm{A}S})/2$, $\varepsilon_{\mathrm{B}} = (\varepsilon_{\mathrm{B}R} + \varepsilon_{\mathrm{B}S})/2$, and eqn. (5) holds.

$$\frac{\mathrm{d}c_{\mathrm{A}R}}{\mathrm{d}t^*} = -\frac{(1-10^{-\mathrm{A}})}{A\ln 10}\left(\frac{\varepsilon_{\mathrm{A}R}}{\varepsilon_{\mathrm{A}}}c_{\mathrm{A}S} - K\frac{\varepsilon_{\mathrm{B}R}}{\varepsilon_{\mathrm{B}}}c_{\mathrm{B}R}\right) \tag{13}$$

$$\frac{\mathrm{d}c_{\mathrm{A}S}}{\mathrm{d}t^*} = -\frac{(1-10^{-\mathrm{A}})}{A\ln 10}\left(\frac{\varepsilon_{\mathrm{A}S}}{\varepsilon_{\mathrm{A}}}c_{\mathrm{A}S} - K\frac{\varepsilon_{\mathrm{B}S}}{\varepsilon_{\mathrm{B}}}c_{\mathrm{B}S}\right) \tag{14}$$

$$\frac{\mathrm{d}c_{\mathrm{B}R}}{\mathrm{d}t^*} = -\frac{\mathrm{d}c_{\mathrm{A}R}}{\mathrm{d}t^*} \tag{15}$$

$$\frac{\mathrm{d}c_{\mathrm{B}S}}{\mathrm{d}t^*} = -\frac{\mathrm{d}c_{\mathrm{A}S}}{\mathrm{d}t^*} \tag{16}$$

$$A = l(\varepsilon_{\mathrm{A}R}c_{\mathrm{A}R} + \varepsilon_{\mathrm{A}S}c_{\mathrm{A}S} + \varepsilon_{\mathrm{B}R}c_{\mathrm{B}R} + \varepsilon_{\mathrm{B}S}c_{\mathrm{B}S}) \tag{5}$$

For the numerical integration we need the values of six parameters ($\varepsilon_{\mathrm{A}R}$, $\varepsilon_{\mathrm{A}S}$, $\varepsilon_{\mathrm{B}R}$, $\varepsilon_{\mathrm{B}S}$, K, and l) and the initial values of the concentrations ($c_{\mathrm{A}R0}$, $c_{\mathrm{A}S0}$, $c_{\mathrm{B}R0}$, and $c_{\mathrm{B}S0}$). If we know the values of ε_A, g_A, ε_B, g_B, c_0, and A_0, we can calculate the values we need by using eqns. (17)–(23).

$$\varepsilon_{\mathrm{A}R} = (2 + g_\mathrm{A})\varepsilon_\mathrm{A}/2 \tag{17}$$

$$\varepsilon_{\mathrm{A}S} = (2 - g_\mathrm{A})\varepsilon_\mathrm{A}/2 \tag{18}$$

$$\varepsilon_{\mathrm{B}R} = (2 + g_\mathrm{B})\varepsilon_\mathrm{B}/2 \tag{19}$$

$$\varepsilon_{\mathrm{B}S} = (2 - g_\mathrm{B})\varepsilon_\mathrm{B}/2 \tag{20}$$

$$c_{\mathrm{A}R0} = c_{\mathrm{A}S0} = c_0/2 \tag{21}$$

$$c_{\mathrm{B}R0} = c_{\mathrm{B}S0} = 0 \tag{22}$$

$$l = A_0/\varepsilon_\mathrm{A}c_0 \tag{23}$$

The direct estimation of the value of K is relatively difficult, because the evaluation of Φ's is difficult. However, we can estimate the value of K indirectly by using eqn. (9). Eqn. (9) shows that the parameter K is a function of P, M, and the conversion at the PSS. Therefore, by using the values of g_A, g_B and the conversion at the PSS, we can estimate the value of K. Once the values of the concentrations are obtained, we can calculate the values of the ee of the reactant (**A**) and the product (**B**) by using eqns. (24) and (25).

$$\text{ee of the reactant } (\mathbf{A}) = \frac{c_{\mathrm{A}R} - c_{\mathrm{A}S}}{c_{\mathrm{A}R} + c_{\mathrm{A}S}} \tag{24}$$

$$\text{ee of the product } (\mathbf{B}) = \frac{c_{\mathrm{B}R} - c_{\mathrm{B}S}}{c_{\mathrm{B}R} + c_{\mathrm{B}S}} \tag{25}$$

Effect of the sign and the absolute value of *g* factors on ee. Fig. 1 is the result of the simulations for examining how the sign of the g factor of the reactant and the product affects the ee of the reactant and the products. The simulation was done for hypothetical cases: case 1 ($g_\mathrm{A} \times g_\mathrm{B} > 0$: $g_\mathrm{A} = 1$ and $g_\mathrm{B} = 1$ or $g_\mathrm{A} = -1$ and $g_\mathrm{B} = -1$; $K = 0.072$), and case 2 ($g_\mathrm{A} \times g_\mathrm{B} < 0$: $g_\mathrm{A} = 1$ and $g_\mathrm{B} = -1$ or $g_\mathrm{A} = -1$ and $g_\mathrm{B} = 1$; $K = 0.072$).

As shown in Fig. 1a, in case 1, the ee of the reactant (**A**) increases at the beginning of the reaction, and decreases with the progress of the reaction. It reaches zero at the PSS. In case 2, the ee of the reactant (**A**) increases monotonically and reaches its maximum at the PSS.

As shown in Fig. 1b, in case 1, the ee of the product (**B**) gradually decreases from the beginning of the reaction and reaches zero at the PSS. In case 2 the ee of the product (**B**) increases with the progress of the reaction and reaches a maximum at the PSS.

In case 2, both the ee of the reactant (**A**) and the ee of the product (**B**) increase with the progress of the reaction. In general, both the ee of the reactant and the ee of the product increase if the signs of the g factors of the reactant and product are opposite to each other. The synchronous enantiomeric enrichment of the reactant and product on prolonged irradiation is the result of the preferential excitation of the minor product isomer of the back reaction. The preferential excitation of the minor product isomer on the back reaction enhances the enrichment of the major product isomer.

If the signs of the g factors of the reactant and product are the same, the back reaction reduces the accumulation of the major product isomer by the preferential excitation of the same isomer. This leads to unsuccessful enantiomeric enrichment of both the reactant and the product at the PSS.

These behaviors of the ee of product (**B**) are quite different from the results reported in the preceding paper dealing with the one-way photoisomerization of the reactant (**I**) to product (**II**) by CPL irradiation.[1] In one-way photoisomerization, the relationship between the ee of the reactant, the product and the conversion is naturally dependent upon only the g factor of the starting material. The g factor of the product does not affect the ee of the reactant and the product because the product is not excited by the CPL irradiation. The ee of the product decreases with the progress of the reaction, with the ee of the product being $g/2$ at the initial stage of the reaction and approaching zero at the final stage.

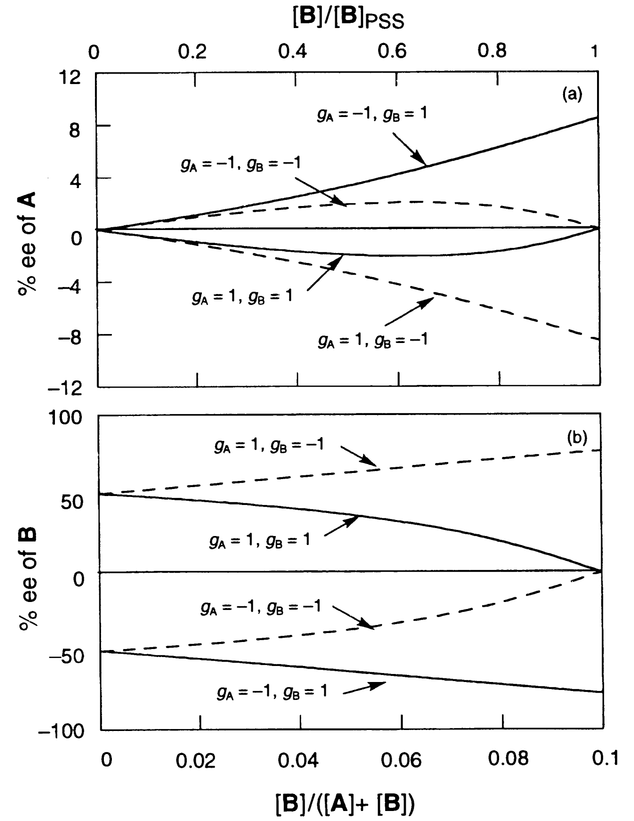


Fig. 1 Effect of the sign of g factors of reactant (**A**) and of product (**B**) on the enantiomeric enrichment induced by CPL irradiation of the reversible photoisomerization system. Numerical simulations were carried out for four different combinations of the signs of g factors. $K = 0.1$. (a) The evolution of the enantiomeric excess of reactant **A** with the progress of the reaction. (b) The enantiomeric excess of the product **B**.

At the initial stage of the reversible photoisomerization the behavior of the ee of the reactant and the product is similar to the one-way photoisomerization by CPL irradiation. The ee of the reactant should be zero and the ee of the product should be $g/2$ at the beginning of the reaction, however, with the progress of the photoisomerization, the product begins to be excited by the CPL irradiation. Thus, the effect of g factor of the product begins to contribute to the ee of the reactant.

If the sign of the g factor of the reactant is the same as that of the product, the enantiomeric enrichment of the reactant is depressed with the progress of the reaction, however, if the sign of the g factor of the product is opposite to that of the reactant, the enantiomeric enrichment of the reactant is amplified with the progress of the reaction. Thus, in AAS, the combination pattern of the signs of the g factors of the reactant and product at the CPL-irradiation wavelength will give a remarkable effect on the relationship between the ee's of the reactant and product and the conversion.

Effect of the value of *K* on ee. Fig. 2 was obtained from simulations for the case $g_\mathrm{A} \times g_\mathrm{B} < 0$: $g_\mathrm{A} = 1.0$ and $g_\mathrm{B} = -1.0$ or $g_\mathrm{A} = -1.0$ and $g_\mathrm{B} = 1.0$. The simulations show how the value of K affects on the relationship between the ee of the reactant,

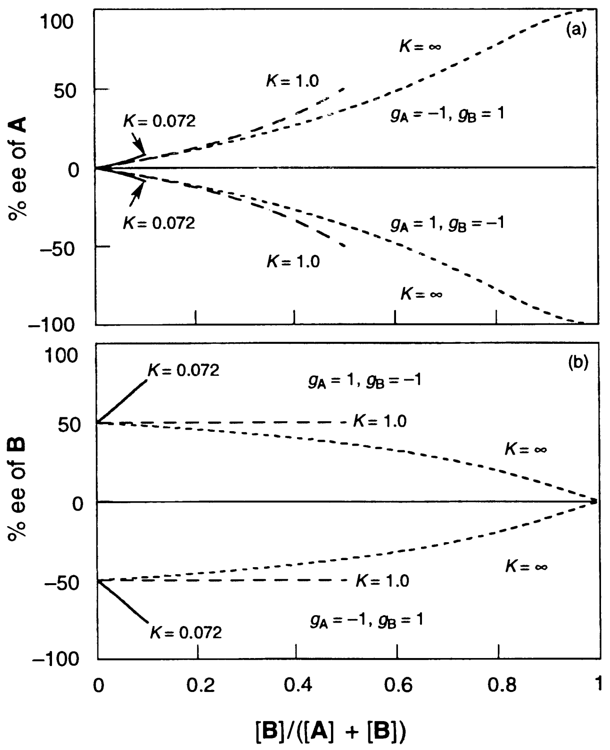


Fig. 2 Effect of the value of *K* on the enantiomeric enrichment induced by CPL irradiation of the reversible photoisomerization system. Numerical simulations were carried out for three different values of *K* (0.072, 1.0 and ∞), assuming two different combinations of the values of *g* factors, $g_A = -1$ and $g_B = 1$ or $g_A = 1$ and $g_B = -1$. (a) The evolution of the enantiomeric excess of reactant **A** with the progress of the reaction. (b) The enantiomeric excess of the product **B**.

product and the conversion for the case, where the sign of the *g* factor of the product is opposite to that of the reactant. Fig. 2a shows that if *K* is less than 1, the ee of the reactant (**A**) increases with the progress of the reaction, and that if *K* is greater than 1, the ee of the reactant decreases with the progress of the reaction. In an extreme case, if *K* is ∞, which means that the reaction proceeds in one way (class (b) in the NAAS), the ee of the reactant becomes 100% at the end of the reaction. However, Fig. 2b shows that the larger the *K* becomes, the more gently the ee of the product (**B**) decreases, thus if *K* is ∞, the ee of the product becomes 0 at the end of the reaction.

Thus, *K* also gives a remarkable effect on the relationship between the ee of the reactant, product and the conversion, especially on the relationship for the reactant. The ratio of the rates of the forward and back reactions determines the extent of the enhancement of the enantiomeric enrichment of the product by the back reaction.

Effect of the absorbance of the solution on the relationship between the ee and the conversion. In the preceding paper we have reported that, in the one-way photoisomerization, the absorbance of the solution does not affect the relationship between the ee's of the reactant and product and the conversion.[1] Here, for the reversible photoisomerization, the effect of the absorbance of the solution on the relationship was examined by numerical simulation. In this simulation, in order to get the same conversion at the PSS, we kept the value of *K* constant. When we change the value of the initial absorbance of the solution (*i.e.* the value of ε_A), the value of ε_B or Φ_B was tuned in order to keep the value of *K* constant. However, for the same values of *g* factors and *K*, the obtained curves indicating the relationship between the ee's of the reactant, product and the conversion were exactly the same. We could not find any effect of the absorbance on the relationship between the ee's of the reactant and product and the conversion.

Table 1 Sign of *g* factors of reactant and product at the wavelength of CPL irradiation

Case	Irradiation wavelength	Reactant		Product	
		l-CPL	*r*-CPL	*l*-CPL	*r*-CPL
1	245 nm	$g_{II} > 0$	$g_{II} < 0$	$g_I = 0$	$g_I = 0$
2	255 nm	$g_{II} > 0$	$g_{II} < 0$	$g_I < 0$	$g_I > 0$
3	245 nm	$g_I = 0$	$g_I = 0$	$g_{II} > 0$	$g_{II} < 0$

Simulation using the parameters for the I–II system

In the above simulations, the values of the parameters were arbitrarily given. Next, the relationship between the ee of the reactant and product and the conversion was simulated for the real system based on the actual chiroptical properties of **I** and **II**. The wavelength of CPL irradiation (λ_{CPL}) was selected by taking account of the chiroptical properties of **I** and **II** shown in Fig. 2 of the preceding paper.[1] The definition of the anisotropy factor *g* is also the same as described in the preceding paper.[1]

By considering the results derived from the above discussions, we selected three wavelengths as shown in Table 1. Case (1), $\lambda_{CPL} = 245$ nm (**A** (reactant) = **II**, **B** (product) = **I**; $g_{II} = -0.0074$ and $g_I = 0$ for *r*-CPL, or $g_{II} = 0.0074$ and $g_I = 0$ for *l*-CPL, conversion at PSS = 0.4, $K = 0.667$); Case (2), $\lambda_{CPL} = 255$ nm (**A** = **II**, **B** = **I**; $g_{II} = -0.0074$ and $g_I = 0.005$ for *r*-CPL, or $g_{II} = 0.0074$ and $g_I = -0.005$ for *l*-CPL, conversion at PSS = 0.23, $K = 0.299$); Case (3), $\lambda_{CPL} = 245$ nm (**A** = **I**, **B** = **II**; $g_I = 0$ and $g_{II} = -0.0074$ for *r*-CPL, or $g_I = 0$ and $g_{II} = 0.0074$ for *l*-CPL, conversion at PSS = 0.6, $K = 1.50$).

In case (1), **II** is irradiated with CPL at 245 nm. Although **II** is excited enantioselectively by CPL, no selection works on the excitation of **I**, because g_I is zero at 245 nm. The function of the CPL for **I** is the same as the linearly polarized or non-polarized light, that is CPL isomerizes **I** to **II** non-enantioselectively.

When **II** is irradiated with CPL at 255 nm (case (2)), the CPL not only acts as a chiral source for **II**, but it also acts as a chiral source for **I**. The sign of the *g* factor of **II** is the opposite to that of **I** at this wavelength.

In case (3), we start the reaction by taking **I** as the reactant. In this case **I** is excited non-enantioselectively by CPL, but **II** is excited enantioselectively by CPL. The enantiomeric enrichment is promoted only by the back reaction through the preferential excitation of one of the product isomers.

Evaluation of the simulations by comparing with experimental results

Chiroptical properties and stereochemical outcome of the photoisomerization of the I–II system. The chiroptical properties of **II** and **I** in acetonitrile have been reported.[1]

II irradiation at 245 nm (case (1)). In the first paper of this series we reported that (−)-**I** isomerizes to (+)-**II** when **I** is irradiated at 290 nm, and that **I** quantitatively isomerizes to **II** without any side reactions.[1] Also for the irradiation at 245 nm the absence of any side reactions was verified. The reaction mixture was analyzed using GC with biphenyl as an internal standard. Other signals except for **I** and **II** were not observed on the GC charts and the total amount of **I** and **II** was retained. In the UV absorption spectra of the reaction mixture during the reaction two isosbestic points were observed at 208 nm and 212 nm. These results showed that **II** photochemically isomerized to **I** without any side reactions.

Therefore, the conversions of **II** to **I** were determined with the intensities of the UV absorption at 280 nm reflecting the concentration of product **I**. Fig. 3 shows the relationship between the conversion and the dose when the solutions of **II** are irradiated with CPL and LPL at 245 nm.

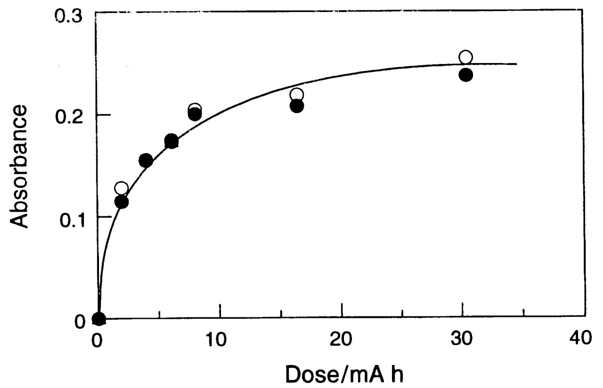


Fig. 3 Relationship between the absorbance at 280 nm and the dose for the solution of **II** ($[\mathbf{II}]_0$ = 0.87 mM) irradiated with CPL and LPL at 245 nm: (○); *l*-CPL, *r*-(●); CPL, (▲); LPL.

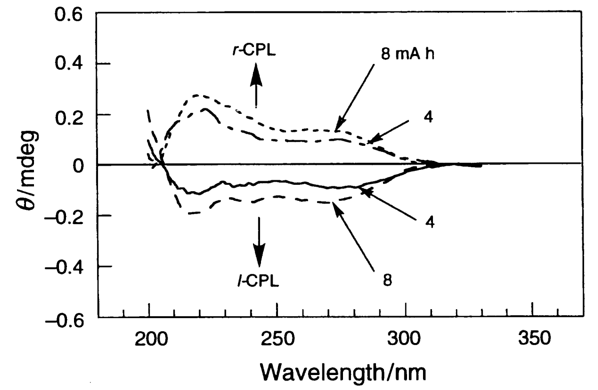


Fig. 4 Typical changes in CD spectrum when the solution of **II** in acetonitrile was irradiated at 245 nm with *l*- and *r*-CPL. The CD spectra were measured after dilution of the reaction mixture to $\frac{1}{3}$ ($[\mathbf{II}]_0 = 0.87$ mM).

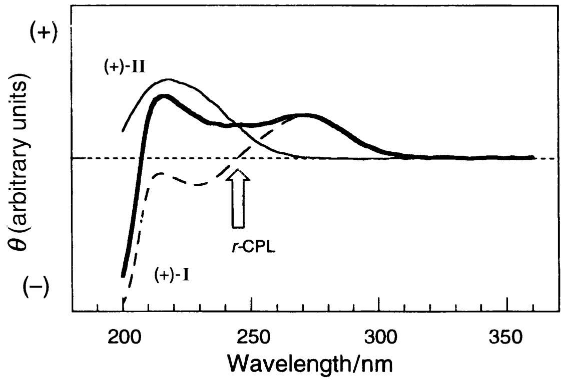


Fig. 5 Spectral simulation of the CD spectrum of the solution of **II** after irradiation at 245 nm with *r*-CPL.

The changes in a typical CD spectrum for the solutions of **II** irradiated with *l*- and *r*-CPL at 245 nm are shown in Fig. 4. Upon CPL irradiation, two peaks emerged at 215 nm and 270 nm and the intensities became greater with the progress of the reaction.

Fig. 5 is the result of the spectral simulation of the change in the CD spectrum of **II** upon irradiation with *r*-CPL at 245 nm. When the solution of **II** was irradiated with *r*-CPL at 245 nm, (−)-**II** was preferentially excited and consumed to leave (+)-**II**. The excited (−)-**II** isomerizes to (+)-**I**.[1] Because the photoisomerization is a unimolecular reaction, the consumption of one mole of (−)-**II** should be accompanied by the production of one mole of (+)-**I**. Therefore, the changes in the CD spectra when the solution of **II** is irradiated with *r*-CPL at 245 nm should be the evolution of the CD spectra composed of (+)-**II** and (+)-**I** in a 1 : 1 ratio, which is depicted as the bold-solid line in Fig. 5. In the same manner, when the solution of **II** is irradiated with *l*-CPL at 245 nm, the changes in the CD spectra should be those of the evolution of the CD spectra composed of (−)-**II** and (−)-**I** in 1 : 1 ratio. Indeed, the changes in the CD spectra observed on CPL irradiation (Fig. 4) were nearly identical to the simulated spectra.

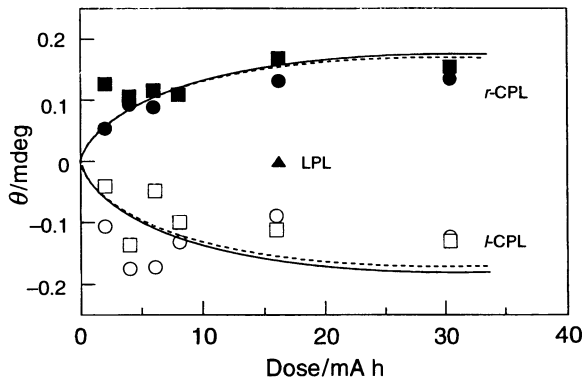


Fig. 6 Relationship between the ellipticity of the solution of **II** irradiated with CPL and the dose: (○), irradiation with *l*-CPL, ellipticity at 280 nm; (□), *l*-CPL, ellipticity at 245 nm; (●), *r*-CPL, ellipticity at 280 nm and (■), *r*-CPL, ellipticity at 245 nm; (▲), LPL ellipticity at 280 nm. The curve drawn by interpolation: —, 280 nm; ---, 245 nm.

By using the changes in CD spectra, we can evaluate the degree of the enantiomeric enrichment of **I** and **II**. The enantiomeric enrichment of **I** was determined from the ellipticity at 280 nm, because **II** does not show any CD signal at 280 nm. The enantiomeric enrichment of **II** was determined from the ellipticity at 245 nm because the magnitude of the $\Delta\varepsilon$ of (+)- and (−)-**I** was incidentally zero at 245 nm.

Fig. 6 shows the relationship between the ellipticity and the dose. Upon CPL irradiation the ellipticity at 245 and 280 nm first increased and then became constant with time. As shown in Fig. 5, the intensities of the UV absorption at 280 nm also became constant after a large dose of CPL irradiation at 245 nm. This means that the system reached a photostationary state after a large dose of irradiation.

The relationships between the ee and the conversion (the progress of the photoisomerization of **II** to **I**) are shown in Fig. 7. The values of the ee and the conversion were obtained from the results derived from the CD and UV measurements.[1]

Fig. 7 shows the experimental and simulation results. The ee of **II** increases with the increasing conversion, and correspondingly the ee of **I** decreases with increasing conversion. The results of the simulations showed good agreement with the experimental results. In this case the dependence of the ee's on the conversion is very much like those observed for the one-way photoisomerization.[1]

II irradiation at 255 nm (case (2)). The UV spectral changes of the solution of **II** irradiated with CPL at 255 nm were very similar to those shown in Fig. 3. Upon irradiation with CPL at 255 nm, the absorption at 280 nm became more intense. Two isosbestic points in the UV spectra were also observed at 208 nm and 212 nm. GC analysis showed no byproducts. The results showed that the photoreaction proceeded without any side reactions. These observations were quite similar to those in case (1). The conversions of **II** to **I** were determined with the UV absorbance at 280 nm in a similar manner to case (1).

The changes in the CD spectra were also very similar to those in case (1), shown in Fig. 5. Therefore, the enantiomeric enrichment of **I** was determined from the ellipticity at 280 nm and the enantiomeric enrichment of **II** was determined from the ellipticity at 245 nm.

Fig. 8 shows the experimental results and the results of the simulation. The ee of **II** increases with the progress of the

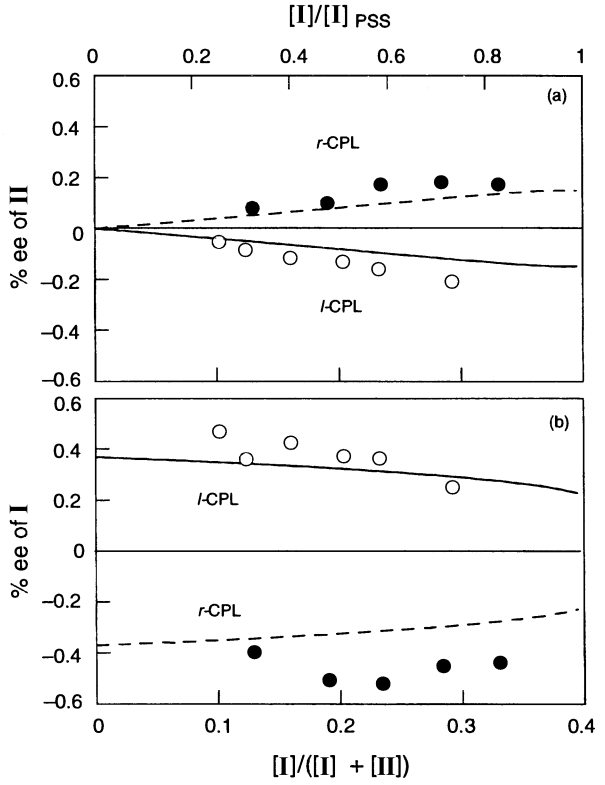


Fig. 7 Numerical simulation and experimental data for the evolution of the enantiomeric excess of the reactant **II** and the product **I** with the progress of the reaction upon the irradiation of the solution of **II** with *r*-CPL and *l*-CPL at 245 nm. Numerical simulations were carried out by using the following values of the parameters: $g_{II} = -0.0074$ and $g_I = 0$ for *r*-CPL irradiation; and $g_{II} = 0.0074$ and $g_I = 0$ for *l*-CPL irradiation: $K = 0.667$. (a) % ee of the reactant (**II**), (b) % ee of product (**I**). Experimental data: (○), *l*-CPL; (●), *r*-CPL. Simulation curve: —, *l*-CPL; ---, *r*-CPL.

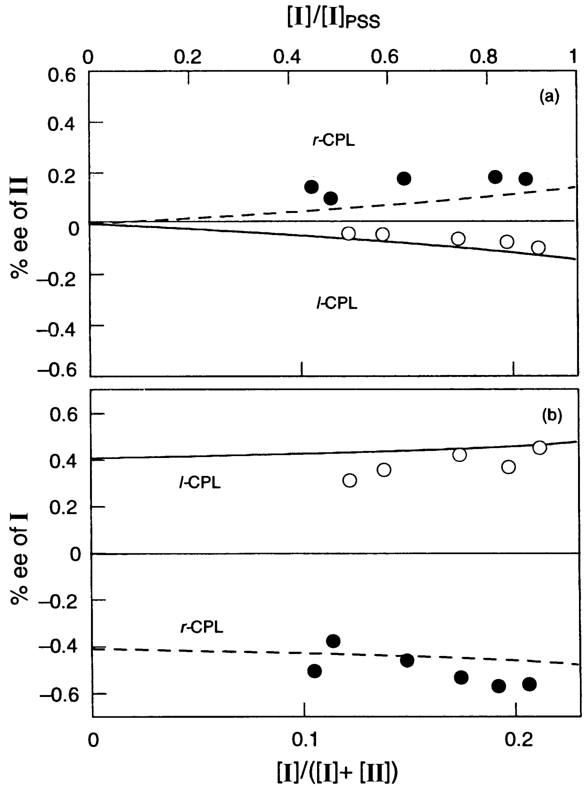


Fig. 8 Numerical simulation and experimental data for the evolution of the enantiomeric excess of the reactant **II** and the product **I** with the progress of the reaction upon the irradiation of the solution of **II** with *r*-CPL and *l*-CPL at 255 nm. Numerical simulations were carried out by using the following values of the parameters: $g_{II} = -0.0074$ and $g_I = 0.005$ for *r*-CPL irradiation; and $g_{II} = 0.0074$ and $g_I = -0.005$ for *l*-CPL irradiation: $K = 0.299$. (a) % ee of the reactant (**II**), (b) % ee of product (**I**). Experimental data: (○), *l*-CPL; (●), *r*-CPL. Simulation curve: —, *l*-CPL; ---, *r*-CPL.

reaction. The ee of **I** also increases with the progress of the reaction in contrast to the behavior of the ee of **I** in the case (1) experiment. The synchronous enantiomeric enrichment of the reactant and product on prolonged irradiation is the result of the preferential excitation of the minor product isomer in the back reaction. For the irradiation with *r*-CPL, for example, the forward reaction produces (+)-**I** preferentially, and the back reaction consumes (−)-**I** preferentially. Therefore the accumulation of (+)-**I** is enhanced by the back reaction at the prolonged irradiation. The experimental results and the results of the simulation showed a good agreement with each other.

I irradiation at 245 nm (case (3)). As case (3) we have selected the photoisomerization of **I** to **II** by CPL at 245 nm ($g_I = 0$ and $g_{II} = \pm 0.0074$, $K = 1.50$). Under these conditions the enantiomeric enrichment is promoted only by the back reaction through the preferential excitation of the product.

The UV spectral changes of the solution of **I** irradiated with CPL at 245 nm were very similar to those shown in the first paper of this series.[1] Upon irradiation with CPL at 245 nm, the absorption at 280 nm became smaller, and two isosbestic points in the UV spectra were observed at 208 nm and 212 nm, which indicate that the photoreaction proceeded without any side reactions.

The changes in the CD spectra were analogous to cases (1) and (2). Therefore we used the same method for determining the enantiomeric excess of the reactant and product.

Fig. 9 is the result of the simulation and the experimental examination of the case. The ee of **I** and **II** concurrently increases with the conversion. The results of the simulations reproduce the trends in the changes in the ee's with the progress of the reaction. However, there is still disagreement between the results of the simulations and the experimental results. The reason for the discrepancy is not clear, but it might be caused by the wide (full width at half maximum is about 25 nm) and asymmetrically shaped spectrum of the CPL generated by the Onuki-type polarizing undulator installed in the electron storage ring NIJI-II.[10,11] In the spectral profile of the CPL the contribution of the light at the longer wavelength is larger than that at the shorter wavelength. The chiroptical properties of **I** and **II** may enhance this effect. The *g* factor is zero at 245 nm, but, at both sides of this wavelength, the *g* factor is not zero. The magnitude of the *g* factor is larger at the longer wavelength half of the band than at the shorter wavelength half. If the bandwidth of the CPL source is large, the *g* value at the longer wavelength half of the spectrum contributes much more to the reaction. In order to check this possibility, we tried simulations using the estimated average of the values of the *g* factor over the spectrum of CPL ($g_I = \pm 0.002$, $g_{II} = \pm 0.0074$). The results of the simulations showed a good agreement with the experimental results.

Conclusions

We have proposed in this work a reversible new absolute asymmetric synthesis (NAAS) which has been examined using a photochemical system producing chiral product. The systems are photochemically reversible between the reactant and the product, with enantiomers that do not interconvert with each other photochemically or thermally at ambient temperature. NAAS may be classified into two subcategories according to the photochemical reversibility between the reactant and the product: in class (a), there is a photochemical equilibrium

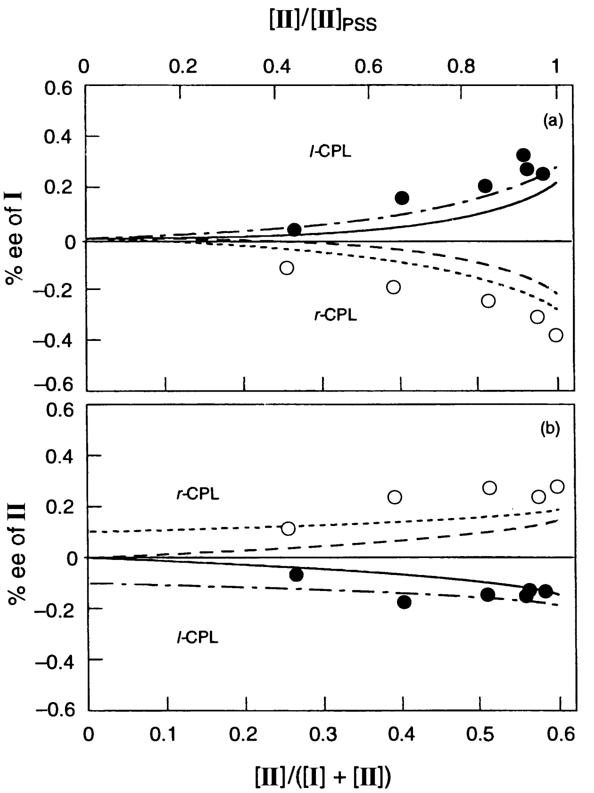


Fig. 9 Numerical simulation and experimental data for the evolution of the enantiomeric excess of the reactant **I** and the product **II** with the progress of the reaction upon irradiation of the solution of **I** with *r*-CPL and *l*-CPL at 245 nm. Numerical simulations were carried out by using the following values of the parameters: $g_\mathrm{I} = 0$ and $g_\mathrm{II} = -0.0074$ for *r*-CPL irradiation; and $g_\mathrm{I} = 0$ and $g_\mathrm{II} = 0.0074$ for *l*-CPL irradiation: $g_\mathrm{I} = -0.002$ and $g_\mathrm{II} = -0.0074$ for *r*-CPL irradiation; and $g_\mathrm{I} = 0.002$ and $g_\mathrm{II} = 0.0074$ for *l*-CPL irradiation $K = 1.50$. (a) % ee of the reactant (**II**), (b) % ee of product (**I**). Experimental data: (○), *l*-CPL; (●), *r*-CPL. Simulation curve: —, $g_\mathrm{I} = 0$ and $g_\mathrm{II} = -0.0074$, *r*-CPL; ---, $g_\mathrm{I} = 0$ and $g_\mathrm{II} = 0.0074$, *l*-CPL: – - –, $g_\mathrm{I} = -0.002$ and $g_\mathrm{II} = -0.0074$, *r*-CPL; – – – –, $g_\mathrm{I} = 0.002$ and $g_\mathrm{II} = 0.0074$, *l*-CPL.

between the reactant and the product because the reaction mixture is irradiated with CPL which excites both the reactant and the product; in class (b), the reaction is irreversible because the reactant is excited by CPL but the product is not excited because the product does not absorb incident light at the excitation wavelength.

In this report, for class (a), the numerical simulations based on the rate expressions for the reaction were used to obtain the relationship between the ee of the product and the conversion by CPL irradiation. The validity of the results of the simulations were checked by performing reversible photoisomerization between **I** and **II** upon excitation by the monochromatic CPL generated by an Onuki-type polarizing undulator installed in a synchrotron radiation source. The simulations showed good agreement with the experimental results. These results experimentally verify that the relationship between the ee of the reactant and product and the conversion remarkably depends upon the *g* factors of the reactant and the product and the ratio of the rates of forward and back reactions.

The above consideration will be very helpful in predicting the enantiomeric enrichment upon CPL irradiation only from the chiroptical properties of the reactant and the product, even if a system other than the **I–II** system is used.

Furthermore, the results obtained from the theoretical and experimental verification suggest that, if the *g* factors of the product and reactant are large enough, the sign of the *g* factor of the product is opposite to that of the reactant at the irradiation, and *K* is less than unity, the ee of the reactant and the product will concurrently increase according to the conversion and attain some appreciable values at the photostationary state. This shows that Kagan's speculation, which suggests that the enantiomeric purity of the products decreases throughout the course of the photolysis, is incorrect in class (b) NAAS reactions.[12] Our conclusion reveals that the concurrent enantiomeric enrichment of both the reactant and the product will occur with the progress of the photoreaction using CPL irradiation. To further extend the understanding of this approach, an examination of the molecular structure and how this may influence the ee of the reactant and product is currently being undertaken.

Experimental

General

UV spectra were measured with a JASCO V-560 spectrometer. CD spectra were measured with a JASCO J-725 CD spectrometer. Gas chromatographic analysis was performed on a Shimadzu GC14-A instrument.

Materials

Methyl norbornadiene-2-carboxylate (methyl bicyclo[2.2.1]-hepta-2,5-diene-2-carboxylate, **I**) was synthesized according to methods reported in Part 1.[1] Methyl quadricyclane-1-carboxylate (methyl tetracyclo[3.2.0.0^{2,7}.0^{4,6}]heptane-1-carboxylate, **II**) was also synthesized according to methods reported in Part 1.[1] Acetonitrile (Merck, UV spectroscopic grade) was used as received.

Photolysis

Acetonitrile solutions of **II** (0.72–0.87 mM) and **I** (0.73 mM) were sealed in a rectangular quartz cell (1 × 1 cm) under an argon atmosphere, and were irradiated by *l*- and *r*-CPL generated by an Onuki-type polarizing undulator installed in the electron storage ring NIJI-II operated at the Optical Radiation Laboratory of the Electrotechnical Laboratory at Tsukuba, producing highly pure, intense, monochromatic CPL at any wavelengths down to the vacuum UV region, and therefore is the most suitable CPL source for the NAAS studies.[10,11,13,14]

Photolyses were carried out for several irradiation periods for each series of samples of **I** and **II**. The photolyzed solutions were subjected to UV and CD spectral analysis as well as gas chromatographic analysis over a CBP-1 column (Shimadzu). The CD spectra were measured using a cylindrical Suprasil cell (1.3 cm i.d., 1 cm path).

Appendix

The derivation of eqn. (9) to form eqns. (7) and (8) is as follows.

By using the eqns. (7), (8), and (17) to (20), we obtain eqns. (26) and (27).

$$\frac{c_{\mathrm{A}R}^{\mathrm{PSS}}}{c_{\mathrm{B}R}^{\mathrm{PSS}}} = \frac{\varepsilon_{\mathrm{A}R}}{\varepsilon_{\mathrm{B}R}} \frac{\Phi_\mathrm{A}}{\Phi_\mathrm{B}} = \frac{2 + g_\mathrm{A}}{2 + g_\mathrm{B}} \frac{\varepsilon_\mathrm{A}\Phi_\mathrm{A}}{\varepsilon_\mathrm{B}\Phi_\mathrm{B}} \tag{26}$$

$$\frac{c_{\mathrm{A}S}^{\mathrm{PSS}}}{c_{\mathrm{B}S}^{\mathrm{PSS}}} = \frac{\varepsilon_{\mathrm{A}S}}{\varepsilon_{\mathrm{B}S}} \frac{\Phi_\mathrm{A}}{\Phi_\mathrm{B}} = \frac{2 - g_\mathrm{A}}{2 - g_\mathrm{B}} \frac{\varepsilon_\mathrm{A}\Phi_\mathrm{A}}{\varepsilon_\mathrm{B}\Phi_\mathrm{B}} \tag{27}$$

The mass balance for the isomerization gives us the relationship shown in eqns. (28) and (29). By using these equations we derive eqns. (30) and (31).

$$c_{\mathrm{A}R}^{\mathrm{PSS}} = c_{\mathrm{A}R0} - c_{\mathrm{B}R}^{\mathrm{PSS}} \tag{28}$$

$$c_{\mathrm{A}S}^{\mathrm{PSS}} = c_{\mathrm{A}S0} - c_{\mathrm{B}S}^{\mathrm{PSS}} \tag{29}$$

$$\frac{c_{\mathrm{A}R0}}{c_{\mathrm{B}R}^{\mathrm{PSS}}} = 1 + \frac{2 + g_{\mathrm{A}}}{2 + g_{\mathrm{B}}} \frac{\varepsilon_{\mathrm{A}} \Phi_{\mathrm{A}}}{\varepsilon_{\mathrm{B}} \Phi_{\mathrm{B}}} \tag{30}$$

$$\frac{c_{\mathrm{A}S0}}{c_{\mathrm{B}S}^{\mathrm{PSS}}} = 1 + \frac{2 - g_{\mathrm{A}}}{2 - g_{\mathrm{B}}} \frac{\varepsilon_{\mathrm{A}} \Phi_{\mathrm{A}}}{\varepsilon_{\mathrm{B}} \Phi_{\mathrm{B}}} \tag{31}$$

By definition the conversion at PSS is expressed as eqn. (32), where eqns. (10)–(12) hold.

$$\begin{aligned} x^{\mathrm{PSS}} &= \frac{c_{\mathrm{B}S}^{\mathrm{PSS}} + c_{\mathrm{B}S}^{\mathrm{PSS}}}{c_{\mathrm{A}R0} + c_{\mathrm{A}S0}} = \frac{1}{2} \left(\frac{c_{\mathrm{B}R}^{\mathrm{PSS}}}{c_{\mathrm{A}R0}} + \frac{c_{\mathrm{B}S}^{\mathrm{PSS}}}{c_{\mathrm{A}S0}} \right) \\ &= \frac{1}{2} \left\{ \frac{1}{1 + (PK)^{-1}} + \frac{1}{1 + (MK)^{-1}} \right\} \end{aligned} \tag{32}$$

$$P = \frac{2 + g_{\mathrm{B}}}{2 + g_{\mathrm{A}}} \tag{10}$$

$$M = \frac{2 - g_{\mathrm{B}}}{2 - g_{\mathrm{A}}} \tag{11}$$

$$K = \frac{\varepsilon_{\mathrm{B}} \Phi_{\mathrm{B}}}{\varepsilon_{\mathrm{A}} \Phi_{\mathrm{A}}} \tag{12}$$

Acknowledgements

We thank Mr Hiroshi Hayakawa for adjusting the JASCO J-725 CD spectrometer, and Dr Simon Everitt (Inoue Photochirogenesis Project) for discussions and insights, as well as corrections and improvements arising from preliminary reading of this manuscript.

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