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Asymmetric transformation of chiral auxiliary-substituted *N*-acyl-α-dehydro(1-naphthyl)alanines into 3,4-dihydrobenzo[*f*]quinolinone derivatives via photoinduced electron transfer

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Abstract—Electron transfer-initiated photocyclizations of the title compounds [(*Z*)-**1**] with an (*S*)-alanine methyl ester auxiliary in methanol containing a tertiary amine were found to give (*S*,*S*)- and (*R*,*S*)-3,4-dihydrobenzo[*f*]quinolinones (**2**) as major products. The magnitude of diastereomeric excess (de) for (*S*,*S*)-**2** was varied from 0 to 55%, depending on the properties of the amine and solvent employed. The mechanism of asymmetric induction in the photocyclization process eventually affording **2** was discussed based on solvent, tertiary amine and temperature effects on the de value.

1. Introduction

Organic photochemistry has continued to contribute to the development of efficient and selective transformations for the preparation of complicated molecules which could not have been synthesized by conventional methods.[1] There are many cases where the products derived from photocyclization and photoaddition reactions of organic compounds are formed via prochiral intermediates. Thus far, much attention has been given to developing novel asymmetric reactions utilizing these photoreactions in liquid and solid phases.[2–4] Many asymmetric photoreactions giving chiral products in high enantio- and diastereoselectivities have been reported in recent years.[4] However, there are only a few asymmetric photoreactions of synthetic utility, especially in liquid phase. In the course of our systematic study regarding photoinduced electron transfer (ET) reactions of α-dehydroamino acid derivatives, we found that ET-initiated photocyclizations of *N*-acyl-α-dehydro(1-naphthyl)alanines in methanol containing triethylamine (TEA) give racemic 3,4-dihydrobenzo[*f*]quinolinones.[5] The fact that many heterocyclic compounds having the dihydroquinolinone ring exhibit pharmacological and physiological activities allows us to expect such an activity also for chiral dihydrobenzoquinolinones.[6] Thus, the incorporation of a chiral auxiliary into the starting α-dehydro(1-naphthyl)-alanine derivative makes it possible to develop novel asymmetric photoreactions enabling the construction of chiral dihydrobenzoquinolinone ring in liquid phase and then to shed some light on the mechanism of ET-initiated photocyclizations found by us. For these ends we synthesized (*Z*)-*N*-acyl-α-dehydro(1-naphthyl)alanines [(*Z*)-**1a–c**] having an (*S*)- or (*R*)-alanine methyl ester auxiliary and investigated the effects of chiral auxiliary, tertiary amine, solvent and temperature on the magnitude of diastereomeric excess (de).

2. Results and discussion

The starting (*Z*)-**1a–c** were prepared in good yields by the ring-opening reactions of (*Z*)-1-naphthyl-substituted oxazolones with (*S*)-alanine (**1a**,**b**) or (*R*)-alanine (**1c**) methyl ester.[7] After a nitrogen-purged methanol solution of (*Z*)-**1a** (3.75×10^{-3} mol dm^{-3}) containing TEA (0.10 mol dm^{-3}) was irradiated with Pyrex-filtered light (>280 nm) from a 400 W high-pressure Hg lamp for 70 min at room temperature, the product mixture obtained was subjected to column chromatography over silica gel, which allowed us to isolate the starting (*Z*)-**1a** (yield, 8.1%), (*E*)-**1a** (4.0%), a mixture of (*S*,*S*)-**2a** and (*R*,*S*)-**2a** (32.9%), and benzo[*f*]isoquinoline derivative (**3a**) (21.8%) (Scheme 1). The structures of isolated products were determined based on their spectroscopic and physical properties and were confirmed by the $^{1}H-^{1}H$ and $^{13}C-^{1}H$ COSY spectra of these products. The same product distribution was obtained

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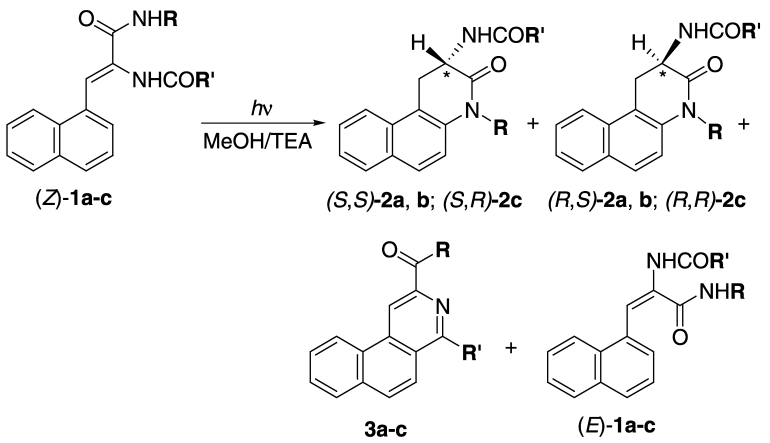


1a (**R**= (*S*)-*CH(Me)CO_2Me, **R'**= Me), **1b** (**R**= (*S*)-*CH(Me)CO_2Me, **R'**= Ph), **1c** (**R**= (*R*)-*CH(Me)CO_2Me, **R'**= Me)

Scheme 1.

also by the 150 min irradiation of (*Z*)-**1b** (3.75×10^{-3} mol dm^{-3}), and (*Z*)-**1b** (yield, 4.5%), (*E*)-**1b** (4.0%) and diastereomeric mixtures of **2b** (34.4%) were isolated by usual workup of the **1b**-derived reaction mixture. The very low ^{1}H NMR yield of **3b** (1.5%) made its isolation virtually impossible. The diastereomeric mixture of (*S*,*S*)-**2a**,**b** and (*R*,*S*)-**2a**,**b** could be separated by repeated preparative TLC (silica gel). From a ^{1}H NMR spectral analysis of each diastereomer of **2a**,**b** we see that the methine proton signals in the chiral auxiliary of each diastereomer are detected at different positions (5.26 and 5.04 ppm for **2a**; 5.35 and 5.16 ppm for **2b**). An X-ray structural analysis of single crystal derived from the diastereomer of **2b** (showing its methine proton signal at 5.16 ppm) revealed that the asymmetric carbon in the dihydroquinolinone ring has the (*R*)-configuration (Fig. 1). Furthermore, a comparison of circular dichroism (CD) spectra of the (*R*,*S*)-**2b** and (*S*,*S*)-**2b** confirmed that the dihydroquinolinone ring having (*R*)- and (*S*)-configurations gives CD bands of positive and negative signs at 250 nm, respectively (Fig. 2). Thus, the absolute configuration of the asymmetric carbon in the ring can be definitely determined by ^{1}H NMR and CD spectral analyses of a given diastereomer and, additionally, the area ratio of the methine proton signals (detected at 5.26 [(*S*,*S*)-**2a**], 5.35 [(*S*,*S*)-**2b**], 5.04 [(*R*,*S*)-**2a**], and 5.16 ppm [(*R*,*S*)-**2b**]) allows us to estimate the magnitude of de.

In Table 1 are summarized conversion of (*Z*)-**1**, selectivity for **2**, and % de obtained after the 5 h irradiation in methanol at room temperature. Although steric bulkiness of the chiral auxiliary R lowers the selectivity for **2** as compared to R=Me (88→49%),[5] the presence of the (*S*)-alanine auxiliary resulted in a preferential formation of (*S*,*S*)-**2a** (de=9%). The observation that the irradiation of (*Z*)-**1c** possessing the (*R*)-alanyl group under the same conditions

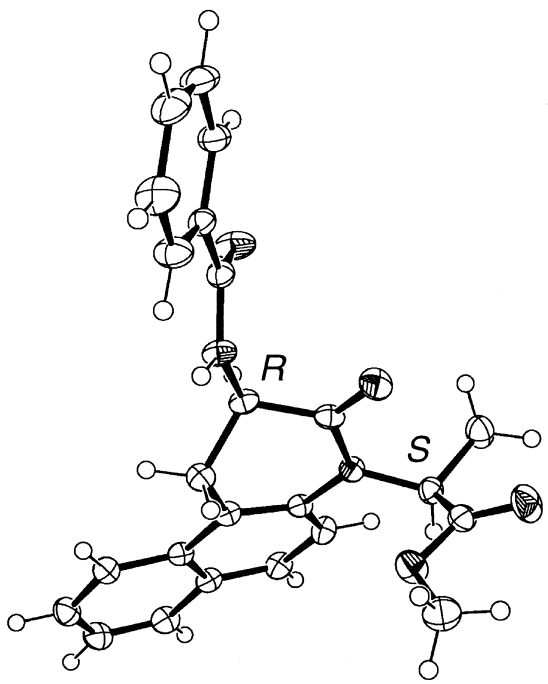


Figure 1. ORTEP drawing of (*R*,*S*)-**2b**.

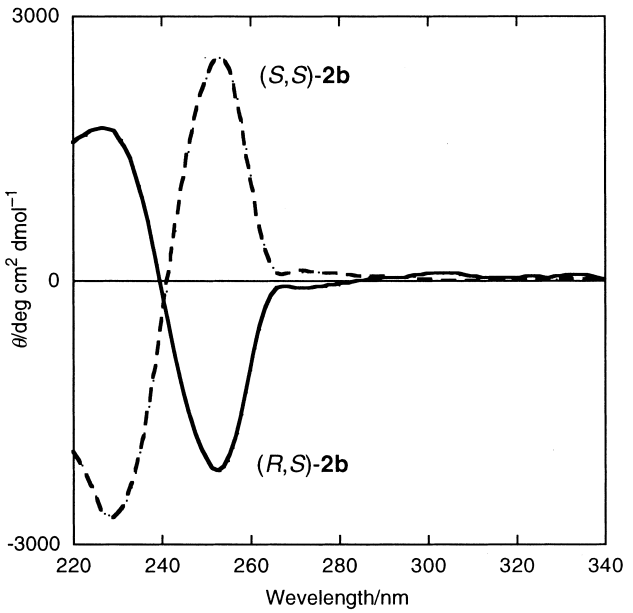


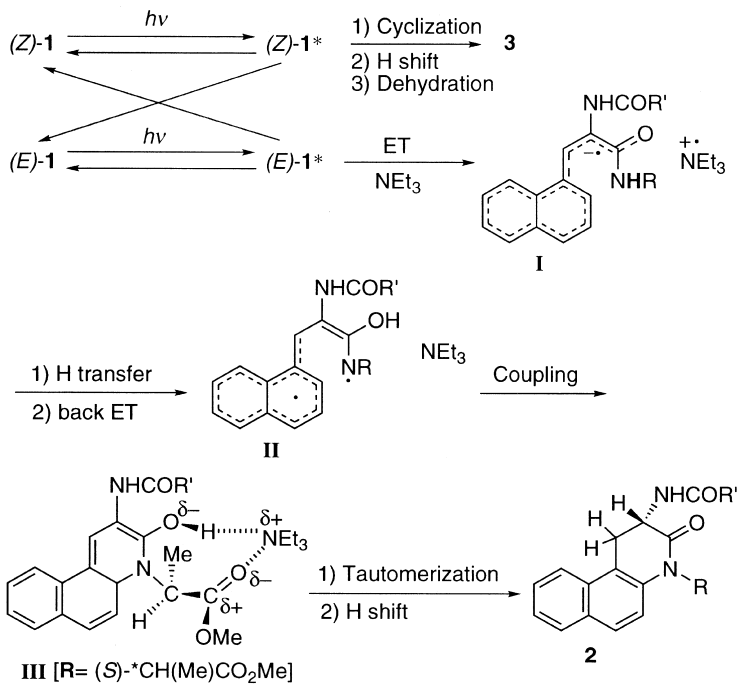
Figure 2. Circular dichroism spectra of (*S*,*S*)-**2b** and (*R*,*S*)-**2b** (4.0×10^{-5} mol dm^{-3}) in MeOH at room temperature.

Table 1. Chiral auxiliary, tertiary amine, temperature and solvent effects on the conversion of (*Z*)-**1**, selectivity or **2**, and diasterermeric excess for (*S*,*S*)-**2** or (*R*,*R*)-**2** obtained by the 5 h irradiation of (*Z*)-**1** (3.75×10^{-3} mol dm^{-3})

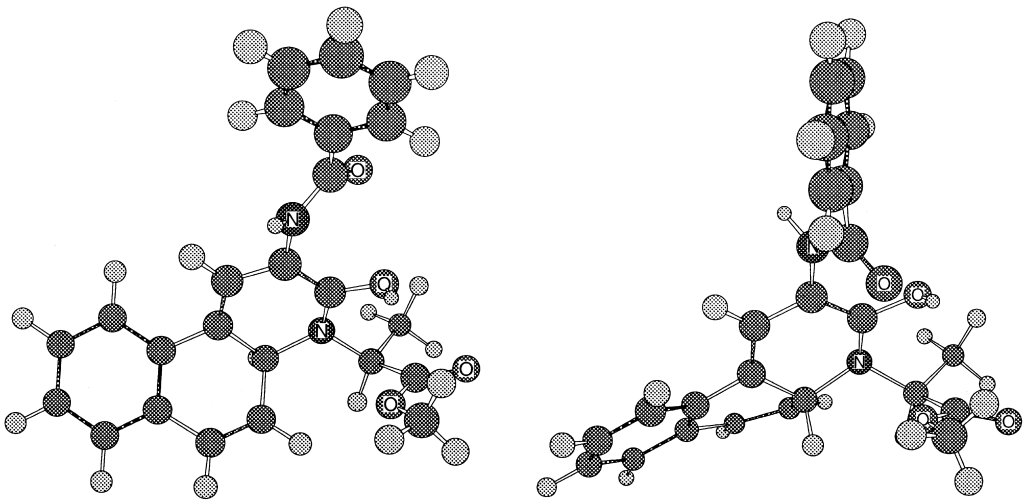
(*Z*)-**1**	Tertiary amine	Solvent	Temperature (°C)	Conversion (%)[a]	Selectivity (%)[b]	(*S*,*S*)-**2** (%)[c]	(*R*,*S*)-**2** (%)[c]	de (%)
1a	TEA	MeOH	25	79	49	54.5	45.5	9
1b	TEA	MeOH	25	46	45	56.5	43.5	13
1c	TEA	MeOH	25	79	39	54.5[d]	45.5[e]	9
1a	TMA[f]	MeOH	25	72	48	59.0	41.0	18
1a	MP[g]	MeOH	25	74	52	65.5	34.5	31
1a	PEP[h]	MeOH	25	65	55	50.0	50.0	0
1b	MP	MeOH	25	70	20	67.5	32.5	35
1a	TEA	MeOH	−30	63	64	57.0	43.0	14
1a	TEA	MeOH	−78	65	90	55.5	44.5	11
1a	TEA	MeOH–MeCN (1:1 v/v)	25	82	30	63.0	37.0	26
1a	TEA	MeOH–MeCN (1:9 v/v)	25	63	9	77.5	22.5	55
1a	MP	MeOH–MeCN (1:9 v/v)	25	67	13	72.0	28.0	44

[a] Conversion was estimated by subtracting the sum of composition of (*Z*)-**1** and (*E*)-**1** from 100.
[b] Selectivity for **2** was evaluated by dividing the composition of **2** by the sum of the composition of each photoproduct, where the composition of (*E*)-**1** was excluded from the calculation of this selectivity.
[c] Composition in a mixture of both diastereomers.
[d] (*R*,*R*)-**2c**.
[e] (*S*,*R*)-**2c**.
[f] Timethylamine.
[g] l-Methylpiperidine.
[h] *N*-Isopropyl-*N*-ethylisopropylamine.

gives preferentially (*R*,*R*)-**2c** in the same de demonstrates the occurrence of asymmetric induction in the cyclization process eventually yielding **2**. It was suggested in the previous study that the asymmetric carbon at the 3-position in the dihydrobenzoquinolinone ring is generated by tautomerization of the enol intermediate **III** (formed via the biradical intermediate **II**), as shown in Scheme 2.[5] Evidence in support of this suggestion comes from the fact that deuterium attached to the alanine auxiliary-substituted amide nitrogen is transferred to the 3-position in the quinolinone ring on irradiation in MeOD as well as in acetonitrile.[5] Furthermore, a ^{1}H NMR spectral analysis of a CD_3OD solution of (*S*,*S*)- or (*R*,*S*)-**2** containing TEA (0.10 mol dm^{-3}), which was permitted to stand for 12 h at room temperature, showed no occurrence of the racemization of each diastereomer. This result confirms that the asymmetric protonation takes place on forming the dihydroquinolinone ring. An inspection of the ORTEP drawing for (*R*,*S*)-**2b** indicates the methoxycarbonyl group in the (*S*)-alanyl moiety to be directed preferentially to one of the two diastereofaces and, hence, allows us to expect that there are differences in the extent of hydrogen-bonding and electronic interactions of TEA with **III** between two diastereofaces. Taking into account that the cyclization of **II** forms two stereoisomers **IIIA** and **IIIB** (Fig. 3), conformations of (*S*)-alanine auxiliary in these two stereoisomers are optimized through MM2 and PM5 calculations. Figure 3 shows that the conformation of each (*S*)-alanine auxiliary is



Scheme 2.



IIIA **IIIB**

Figure 3. Energy-minimized conformation of **IIIA** and **IIIB**.

very similar to that for (*R*,*S*)-**2b** in the solid state, strongly suggesting that the enol intermediate **III** adopts a similar conformation in solution. Accordingly, we are able to provide a good explanation for factors that control the observed asymmetric induction by invoking more favorable hydrogen-bonding and electronic interactions (shown in Scheme 2) in one diastereoface than in the other. The nitrogen atom in a TEA molecule is positively charged by forming a hydrogen bond to the hydroxy hydrogen of the enol intermediate **III** and its nitrogen is stabilized through an electrostatic interaction with the methoxy and/or carbonyl oxygen in the alanine auxiliary. As evident from Figure 3, the hydroxy proton adds to the olefinic carbon preferentially from one diastereoface to give (*S*,*S*)-diastereomer in excess. Asymmetric transformation of (*Z*)-**1b** into (*S*,*S*)-**2b** was achieved in a similar de (Table 1).

Since TEA as an electron donor is considered to exist in the very vicinity of a given substrate during the photocyclization process, Scheme 2 allows us to predict that the magnitude of de for (*S*,*S*)-**2a** strongly depends on the steric bulkiness about the tertiary amino nitrogen, namely, a decrease in this bulkiness results in an enhanced de by strengthening hydrogen-bonding and electrostatic interactions described above and an increase in the bulkiness gives the reverse result. The finding that the de value is increased in the following order: PEP$\ll$TEA$<$TMA$<$MP is consistent with our prediction (Table 1) and, hence, substantiates the mechanism for the observed asymmetric induction. If we consider that reaction temperature exerts a great effect on the extent of hydrogen-bonding interaction, an examination of temperature effects on the de value may shed some light on the mechanism of the asymmetric photocyclization of (*Z*)-**1**. Although this value was not much influenced by temperature, pronounced temperature effects on the selectivity for **2** was observed (49$\rightarrow$90%). It is very likely that an increase in the polarity and hydrogen-bonding solvation ability of methanol contributes to an increase in the selectivity. Because a decrease in temperature may enhance the ability of TEA to form hydrogen bonds with the enol intermediate **III** and methanol to almost the same extent, it is reasonable to conclude that hydrogen-bonding interaction between TEA and methanol lowers the magnitude of de for (*S*,*S*)-**2**. If we accept these considerations, the use of acetonitrile as a co-solvent is predicted to strengthen hydrogen-bonding and electrostatic interactions between the tertiary amino nitrogen and the enol **III** and, hence, to result in a net increase in de for (*S*,*S*)-**2**. In Table 1 are collected the results obtained for the (*Z*)-**1a**-TEA and (*Z*)-**1a**-MP systems. As predicted, the de value increases with an increase in concentration of the aprotic polar solvent, providing additional proof of the mechanism for asymmetric induction in our systems.

3. Conclusions

It was found that the irradiation of α-dehydronaphthylalanines having (*S*)-alanine auxiliary in methanol containing a tertiary amine preferentially gives (*S*,*S*)-dihydrobenzoquinolinones. The use of a mixture of acetonitrile and methanol as a solvent increased de for these quinolinones up to 55%. Analyses of tertiary amine and solvent effects on the magnitude of de strongly suggested that hydrogen-bonding and electrostatic interactions between a given tertiary amine and the enol intermediate play an important role in bringing about the asymmetric photocyclization of (*S*)-alanine methyl ester-substituted α-dehydro(1-naphthyl)alanine derivatives.

4. Experimental

4.1. General

^{1}H and ^{13}C NMR and IR spectra were taken with a JEOL JNM-A500 spectrometer and a Hitachi 270-30 infrared spectrometer, respectively. Chemical shifts were determined using tetramethylsilane as an internal standard. UV absorption spectra were recorded on a Shimadzu UV-2200 spectrophotometer. A cell with a 10 mm pathlength was used. Circular dichroism spectra were recorded on a Nihonbunko J-600 spectropolarimeter. The optical rotations were measured on a Nihonbunko DIP-370 polarimeter.

Elemental analyses were performed on a Perkin–Elmer PE2400 series II CHNS/O analyzer. MeOH and MeCN were purified according to the standard procedures and freshly distilled prior to use. TEA was fractionally distilled from sodium hydroxide. All other reagents used were obtained from commercial sources and were of the highest grade available. MM2 and PM5 calculations were accomplished by using CAChe 5.0 for Windows available from Fujitsu Ltd, 2002.

4.2. General procedure for the synthesis of (*Z*)-2-methyl-4-(1-naphthylmethylene)-5(4*H*)-oxazolone and (*Z*)-4-(1-naphthylmethylene)-2-phenyl-5(4*H*)-oxazolone

N-Acetylglycine or *N*-benzoylglycine (0.087 mol), 1-naphthaldehyde (16.1 g, 0.103 mol), and sodium aceate (5.3 g, 0.067 mol) were added to acetic anhydride (100 mL) and the resulting mixture was heated at 75–85 °C for 6 h (*N*-acetylglycine) or 1 h (*N*-benzoylglycine) with stirring. The mixture was cooled with ice and the solid separated out was collected by filtration with suction and washed with water, small amounts of cold EtOH and then with dry hexane. After the crude product had been air-dryed at room temperature, it was recrystallized from hexane–$CHCl_3$ to give yellow crystals (40–50%).

4.2.1. (*Z*)-2-Methyl-4-(1-naphthylmethylene)-5(4*H*)-oxazolone. Mp 159.0–160.0 °C. IR (KBr): 1760, 1650, 1260 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 2.43 (3H, s), 7.54 (1H, dd, *J*=7.3, 7.9 Hz), 7.58 (1H, dd, *J*=7.3, 8.6 Hz), 7.61 (1H, dd, *J*=7.3, 8.6 Hz), 7.88 (1H, d, *J*=7.9 Hz), 7.93 (1H, d, *J*=8.6 Hz), 8.02 (1H, s), 8.24 (1H, d, *J*=8.6 Hz), 8.75 (1H, d, *J*=7.3 Hz).

4.2.2. (*Z*)-2-Phenyl-4-(1-naphthylmethylene)-5(4*H*)-oxazolone. Mp 166.0–167.0 °C. IR (KBr): 1797, 1647, 1167 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.54 (2H, dd, *J*=7.3, 7.6 Hz), 7.55 (1H, dd, *J*=8.6, 8.6 Hz), 7.62 (1H, dd, *J*=7.3, 7.3 Hz), 7.63 (1H, dd, *J*=8.6, 8.6 Hz), 7.64 (1H, dd, *J*=6.7, 8.6 Hz), 7.90 (1H, d, *J*=8.6 Hz), 7.97 (1H, d, *J*=8.6 Hz), 8.13 (1H, s), 8.21 (2H, d, *J*=7.6 Hz), 8.31 (1H, d, *J*=8.6 Hz), 9.03 (1H, d, *J*=6.7 Hz).

4.3. General procedure for the synthesis of (*Z*)-2-acetylamino-*N*-[(*S*)-1-(methoxycarbonyl)ethyl]-3-(1-naphthyl)-2-propenamide [(*Z*)-1a], (*Z*)-2-benzoylamino-*N*-[(*S*)-1-(methoxycarbonyl)ethyl]-3-(1-naphthyl)-2-propenamide [(*Z*)-1b] and (*Z*)-2-acetylamino-*N*-[(*R*)-1-(methoxycarbonyl)ethyl]-3-(1-naphthyl)-2-propenamide [(*Z*)-1c]

(*Z*)-2-Methyl-4-(1-naphthylmethylene)-5(4*H*)-oxazolone (for **1a**,**c**, 0.010 mol) or (*Z*)-4-(1-naphthylmethylene)-2-phenyl-5(4*H*)-oxazolone (for **1b**, 0.010 mol) was added to dry $CHCl_3$ (30 mL) containing triethylamine (0.012 mol) and (*S*)-alanine methyl ester hydrochloride (for **1a**,**b**, 0.010 mol) or (*R*)-alanine methyl ester hydrochloride (for **1c**, 0.010 mol) and the resulting solution was refluxed for 1–2 h. The reaction mixture was washed with water (50 mL) and then $CHCl_3$ layer was dried over $MgSO_4$. After removal of the solvent under reduced pressure, the solid obtained was recrystallized twice from EtOAc affording colorless crystals (40–60%).

4.3.1. (*Z*)-2-Acetylamino-*N*-[(*S*)-1-(methoxycarbonyl)-ethyl]-3-(1-naphthyl)-2-propenamide [(*Z*)-1a]. Mp 149.0–150.0 °C. IR (KBr): 3220, 3052, 2986, 2950, 1746, 1650, 1632 cm^{-1}. $[\alpha]_D^{25}$=+47.3 (*c*=0.5, MeOH). ^1H NMR (500 MHz, DMSO-d_6): δ 1.37 (3H, d, *J*=6.7 Hz), 1.83 (3H, s), 3.66 (3H, s), 4.44 (1H, dq, *J*=6.7, 6.7 Hz), 7.51–7.60 (5H, m), 7.90 (1H, d, *J*=7.9 Hz), 7.94–7.96 (2H, m), 8.47 (1H, d, *J*=6.7 Hz), 9.25 (1H, s). ^{13}C NMR (125 MHz, DMSO-d_6): δ 16.9, 22.7, 48.2, 51.9, 124.2, 124.6, 125.5, 126.1, 126.3, 126.4, 128.5 (2C), 131.0, 131.3, 132.0, 133.2, 164.9, 169.4, 173.1. Anal. calcd (found) for $C_{19}H_{20}N_2O_4$: C, 67.05 (67.10); H, 5.92 (6.04); N, 8.23% (8.12%).

4.3.2. (*Z*)-2-Benzoylamino-*N*-[(*S*)-1-(methoxycarbonyl)-ethyl]-3-(1-naphthyl)-2-propenamide [(*Z*)-1b]. Mp 168.5–169.0 °C. IR (KBr): 3256, 3040, 1752, 1632, 1620 cm^{-1}. $[\alpha]_D^{25}$=+55.7 (*c*=0.5, MeOH). ^1H NMR (500 MHz, DMSO-d_6): δ 1.39 (3H, d, *J*=7.3 Hz), 3.68 (3H, s), 4.48 (1H, dq, *J*=7.3, 7.3 Hz), 7.43 (2H, dd, *J*=7.3, 7.3 Hz), 7.45 (1H, dd, *J*=7.3, 7.9 Hz), 7.52 (1H, dd, *J*=7.3, 7.3 Hz), 7.55 (1H, dd, *J*=6.7, 7.9 Hz), 7.59 (1H, dd, *J*=6.7, 8.6 Hz), 7.66 (1H, d, *J*=7.3 Hz), 7.77 (1H, s), 7.83 (2H, d, *J*=7.3 Hz), 7.87 (1H, d, *J*=7.9 Hz), 7.94 (1H, d, *J*=7.9 Hz), 8.04 (1H, d, *J*=8.6 Hz), 8.62 (1H, d, *J*=7.3 Hz), 9.74 (1H, s). ^{13}C NMR (125 MHz, DMSO-d_6): δ 16.9, 48.2, 51.9, 124.2, 125.4, 126.0, 126.1, 126.4, 126.5, 127.8 (2C), 128.1 (2C), 128.4, 128.5, 131.0, 131.3, 131.5, 131.8, 133.2, 133.8, 164.8, 166.1, 173.0. Anal. calcd (found) for $C_{24}H_{22}N_2O_4$: C, 71.63 (71.47); H, 5.51 (5.30); N, 6.96% (6.80%).

4.3.3. (*Z*)-2-Acetylamino-*N*-[(*R*)-1-(methoxycarbonyl)-ethyl]-3-(1-naphthyl)-2-propenamide [(*Z*)-1c]. Mp 149.0–150.0 °C. IR (KBr): 3220, 3052, 2986, 2950, 1746, 1650, 1632 cm^{-1}. $[\alpha]_D^{25}$=−42.4 (*c*=0.5, MeOH). ^1H NMR (500 MHz, DMSO-d_6): δ 1.37 (3H, d, *J*=6.7 Hz), 1.83 (3H, s), 3.66 (3H, s), 4.44 (1H, dq, *J*=6.7, 6.7 Hz), 7.51–7.60 (5H, m), 7.90 (1H, d, *J*=7.9 Hz), 7.94–7.96 (2H, m), 8.47 (1H, d, *J*=6.7 Hz), 9.25 (1H, s). ^{13}C NMR (125 MHz, DMSO-d_6): δ 16.9, 22.7, 48.2, 51.9, 124.2, 124.6, 125.5, 126.1, 126.3, 126.4, 128.5 (2C), 131.0, 131.3, 132.0, 133.2, 164.9, 169.4, 173.1. Anal. calcd (found) for $C_{19}H_{20}N_2O_4$: C, 67.05 (66.62); H, 5.92 (5.97); N, 8.23% (7.85%).

4.4. General procedure for the irradiation of (*Z*)-1a–c

For the purpose of analyzing the effects of chiral auxiliary, tertiary amine, and solvent on the magnitude of de, a MeOH or MeOH–MeCN solution (10 mL) of (*Z*)-**1** (3.75×10^{-3} mol dm^{-3}) containing tertiary amine (0.10 mol dm^{-3}) was irradiated under nitrogen at room temperature with Pyrex-filtered light from a 450 W high-pressure Hg lamp for 5.0 h (MeOH solution) or 10 h (MeOH–MeCN solution). After removal of the solvent under reduced pressure, the mixture obtained was dissolved in $CHCl_3$ and washed twice with 0.1 mol dm^{-3} HCl (20 mL). $CHCl_3$ layer was concentrated to dryness in vacuo. The resulting residue was dissolved in DMSO-d_6 and subjected to ^1H NMR spectral analysis. The composition was estimated from the area ratio of a given ^1H NMR signal for each compound. In order to analyze the temperature effect on the magnitude of de, a MeOH solution (100 mL) of (*Z*)-**1a** (3.75×10^{-3} mol dm^{-3}) in the presence of TEA (0.10^{-3} mol dm^{-3}) was irradiated under nitrogen with

Pyrex-filtered light from a 400 W high-pressure Hg lamp at −30 or −78 °C. After 2.0 h irradiation, an appropriate amount of the solution (10 mL) being irradiated was pipetted off and concentrated to dryness in vacuo. The resulting residue was dissolved in DMSO-d_6 and subjected to ^{1}H NMR spectral analysis. For the ^{2}H (D) tracer experiment a MeOD solution (10 mL) of (*Z*)-**1a** (3.75×10^{-3} mol dm^{-3}) was allowed to stand for 12 h in the presence of TEA (0.10 mol dm^{-3}) and then irradiated for 5.0 h. After the solution had been concentrated to dryness, the resulting residue was dissolved in DMSO-d_6 and subjected to ^{1}H NMR spectral analysis.

On the other hand, a solution (500 mL) of (*Z*)-**1a**,**b** (3.75×10^{-3} mol dm^{-3}) in MeOH containing TEA (0.10 mol dm^{-3}), placed in a Pyrex vessel, was irradiated for a given period of time under nitrogen with Pyrex-filtered light from a 400 W high-pressure Hg lamp at room temperature. After 70 min (**1a**) or 150 min (**1b**) irradiation, an appropriate amount of the solution (5 mL) being irradiated was pipetted off and concentrated to dryness in vacuo giving the residue which was subjected to ^{1}H NMR spectral analysis in DMSO-d_6. The remaining solutions of **1a**,**b** were concentrated to dryness under reduced pressure and the resulting residues were subjected to column chromatography over silica gel (230 mesh, Merck) eluting with EtOAc–hexane. For the purpose of isolating each diastereomer of **2a** and **2b**, preparative TLC plate (silica gel) was also used. Physical and spectroscopic properties of (*E*)-**1a**,**b**, (*S*,*S*)-**2a**,**b**, (*R*,*S*)-**2a**,**b** and **3a** are as follows.

4.4.1. (*E*)-1a. Mp 102.0–103.0 °C. IR (KBr): 3276, 3048, 2952, 1740, 1678, 1626 cm^{-1}. $[\alpha]_D^{25}=-46.4$ (c=0.5, MeOH). ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.05 (3H, d, J=6.7 Hz), 2.03 (3H, s), 3.51 (3H, s), 4.26 (1H, dq, J=6.7, 7.3 Hz), 7.40 (1H, dd, J=7.3, 8.6 Hz), 7.44 (1H, d, J=7.3 Hz), 7.46 (1H, s), 7.52 (1H, dd, J=6.7, 7.9 Hz), 7.55 (1H, dd, J=6.7, 7.3 Hz), 7.80 (1H, d, J=8.6 Hz), 7.91 (1H, d, J=7.9 Hz), 8.00 (1H, d, J=7.3 Hz), 8.30 (1H, d, J=7.3 Hz), 9.74 (1H, s). ^{13}C NMR (125 MHz, DMSO-d_6): δ 16.4, 23.4, 47.4, 51.7, 114.0, 124.4, 125.4, 125.7, 125.9, 126.0, 127.1, 128.2, 131.2, 132.0, 133.0, 133.8, 164.1, 168.5, 172.3. Anal. calcd (found) for $C_{19}H_{20}N_2O_4$: C, 67.05 (67.04); H, 5.92 (6.06); N, 8.23% (8.48%).

4.4.2. (*E*)-1b. Mp 128.5–130.0 °C. IR (KBr): 3274, 3058, 2950, 1743, 1644 cm^{-1}. $[\alpha]_D^{25}=-45.2$ (c=0.5, MeOH). ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.12 (3H, d, J=6.7 Hz), 3.53 (3H, s), 4.31 (1H, dq, J=6.7, 7.3 Hz), 7.36 (1H, s), 7.44 (1H, dd, J=7.3, 7.9 Hz), 7.53–7.56 (2H, m), 7.54 (2H, dd, J=7.3, 7.3 Hz), 7.57 (1H, dd, J=6.7, 7.9 Hz), 7.61 (1H, d, J=7.3, 7.3 Hz), 7.84 (1H, d, J=7.9 Hz), 7.94 (1H, d, J=7.9 Hz), 7.98 (2H, d, J=7.3 Hz), 8.06 (1H, d, J=7.9 Hz), 8.37 (1H, d, J=7.3 Hz), 10.26 (1H, s). ^{13}C NMR (125 MHz, DMSO-d_6): δ 16.5, 47.4, 51.6, 116.9, 124.4, 125.4, 125.7, 126.0, 126.2, 127.3, 127.7 (2C), 128.2, 128.3 (2C), 131.2, 131.5, 131.6, 133.0, 133.8, 133.9, 163.8, 165.0, 172.4. Anal. calcd (found) for $C_{24}H_{22}N_2O_4$: C, 71.63 (71.78); H, 5.51 (5.26); N, 6.96% (6.78%).

4.4.3. (3*S*)-2-Acetylamino-3,4-dihydro-1-[(*S*)-1-(methoxycarbonyl)ethyl]-2(1*H*)-benzo[*f*]quinolinone [(*S*,*S*)-2a]. Mp 86.0–89.0 °C. IR (KBr): 3316, 3064, 2986, 2950, 1746, 1659, 1635 cm^{-1}. $[\alpha]_D^{25}=+35.2$ (c=0.5, MeOH). CD (MeOH) $[\theta]_{250}=-1488$. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.49 (3H, d, J=6.7 Hz), 1.92 (3H, s), 3.01 (1H, dd, J=15.9, 15.3 Hz), 3.60 (1H, dd, J=15.3, 5.5 Hz), 3.60 (3H, s), 4.51 (1H, ddd, J=15.9, 7.9, 5.5 Hz), 5.26 (1H, q, J=6.7 Hz), 7.45 (1H, dd, J=8.3, 7.3 Hz), 7.53 (1H, d, J=9.2 Hz), 7.56 (1H, dd, J=8.6, 7.3 Hz), 7.90 (1H, d, J=9.2 Hz), 7.90 (1H, d, J=8.3 Hz), 8.01 (1H, d, J=8.6 Hz), 8.37 (1H, d, J=7.9 Hz). ^{13}C NMR (125 MHz, DMSO-d_6): δ 15.1, 22.6, 27.1, 48.2, 52.1, 53.6, 116.2, 119.1, 123.3, 124.9, 127.2, 128.2, 128.3, 129.9, 130.7, 136.3, 168.3, 169.4, 171.0. Anal. calcd (found) for $C_{19}H_{20}N_2O_4$: C, 67.05 (66.75); H, 5.92 (5.71); N, 8.23% (8.18%).

4.4.4. (3*S*)-2-Benzoylamino-3,4-dihydro-1-[(*S*)-1-(methoxycarbonyl)ethyl]-2(1*H*)-benzo[*f*]quinolinone [(*S*,*S*)-2b]. Mp 184.0–186.0 °C. IR (KBr): 3404, 2944, 1746, 1680, 1650 cm^{-1}. $[\alpha]_D^{25}=+7.6$ (c=0.5, MeOH). CD (MeOH) $[\theta]_{250}=-2036$. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.54 (3H, d, J=6.7 Hz), 3.29 (1H, dd, J=15.2, 14.6 Hz), 3.62 (3H, s), 3.70 (1H, dd, J=15.2, 6.1 Hz), 4.80 (1H, ddd, J=14.6, 8.6, 6.1 Hz), 5.35 (1H, q, J=6.7 Hz), 7.48 (1H, dd, J=7.9, 7.9 Hz), 7.52 (2H, dd, J=7.3, 7.9 Hz), 7.58 (1H, d, J=9.2 Hz), 7.58–7.60 (2H, m), 7.94 (1H, d, J=9.2 Hz), 7.94 (1H, d, J=7.9 Hz), 7.95 (2H, d, J=7.3 Hz), 8.09 (1H, d, J=8.5 Hz), 8.90 (1H, d, J=8.6 Hz). ^{13}C NMR (125 MHz, DMSO-d_6): δ 15.1, 26.8, 48.6, 52.1, 53.5, 116.1, 119.1, 123.3, 124.8, 127.2, 127.4 (2C), 128.2, 128.3 (3C), 129.9, 130.6, 131.5, 134.0, 136.3, 166.1, 168.3, 171.0. Anal. calcd (found) for $C_{24}H_{22}N_2O_4$: C, 71.63 (71.80); H, 5.51 (5.34); N, 6.96% (6.59%).

4.4.5. (3*R*)-2-Acetylamino-3,4-dihydro-1-[(*S*)-1-(methoxycarbonyl)ethyl]-2(1*H*)-benzo[*f*]quinolinone [(*R*,*S*)-2a]. Mp 111.0–113.0 °C. IR (KBr): 3304, 3052, 2992, 2950, 1743, 1656, 1640 cm^{-1}. $[\alpha]_D^{25}=-60.0$ (c=0.5, MeOH). CD (MeOH) $[\theta]_{250}=+1803$. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.57 (3H, d, J=6.7 Hz), 1.94 (3H, s), 2.96 (1H, dd, J=15.3, 15.3 Hz), 3.62 (3H, s), 3.64 (1H, dd, J=15.3, 6.1 Hz), 4.55 (1H, ddd, J=15.3, 7.9, 6.1 Hz), 5.04 (1H, q, J=6.7 Hz), 7.34 (1H, d, J=8.5 Hz), 7.46 (1H, dd, J=8.5, 6.7 Hz), 7.56 (1H, dd, J=8.5, 6.7 Hz), 7.91 (1H, d, J=8.5 Hz), 7.91 (1H, d, J=8.5 Hz), 8.02 (1H, d, J=8.5 Hz), 8.39 (1H, d, J=7.9 Hz). ^{13}C NMR (125 MHz, DMSO-d_6): δ 14.6, 22.6, 26.2, 48.1, 52.2, 54.0, 116.3, 119.2, 123.3, 124.9, 127.2, 128.3, 128.4, 129.9, 130.6, 136.5, 168.5, 169.5, 170.9. Anal. calcd (found) for $C_{19}H_{20}N_2O_4\cdot H_2O$: C, 63.68 (63.95); H, 6.19 (5.86); N, 7.82% (7.44%).

4.4.6. (3*R*)-2-Benzoylamino-3,4-dihydro-1-[(*S*)-1-(methoxycarbonyl)ethyl]-2(1*H*)-benzo[*f*]quinolinone [(*R*,*S*)-2b]. Mp 110.5–111.0 °C. IR (KBr): 3416, 2948, 1746, 1682, 1664 cm^{-1}. $[\alpha]_D^{25}=-10.0$ (c=0.02, MeOH). CD (MeOH) $[\theta]_{250}=+2306$. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.59 (3H, d, J=6.7 Hz), 3.29 (1H, dd, J=15.9, 14.6 Hz), 3.65 (3H, s), 3.72 (1H, dd, J=15.9, 6.1 Hz), 4.84 (1H, ddd, J=14.6, 8.2, 6.1 Hz), 5.16 (1H, q, J=6.7 Hz), 7.36 (1H, d, J=9.2 Hz), 7.48 (1H, dd, J=7.3, 7.9 Hz), 7.53 (2H, dd, J=6.7, 7.9 Hz), 7.59 (1H, dd, J=7.9, 8.5 Hz), 7.59 (1H, dd, J=7.9, 7.9 Hz), 7.95 (1H, d, J=7.3 Hz), 7.95 (1H, d, J=9.2 Hz), 7.96 (2H, d, J=6.7 Hz), 8.09 (1H, d, J=8.5 Hz), 8.88 (1H, d, J=8.2 Hz). ^{13}C NMR (125 MHz, DMSO-d_6): δ 14.5, 26.5, 48.6, 52.2, 53.6, 116.3, 119.3, 123.3, 124.9, 127.2, 127.5

(2C), 128.28, 128.30 (3C), 129.8, 130.6, 131.5, 134.0, 136.3, 166.4, 168.4, 170.9. Anal. calcd (found) for $C_{24}H_{22}N_2O_4$: C, 71.63 (71.58); H, 5.51 (5.42); N, 6.96% (6.69%).

4.4.7. 2-[(*S*)-1-(Methoxycarbonyl)ethylaminocarbonyl]-4-methylbenzo[*f*]isoquinoline (3a). Mp 117.0–118.0 °C. IR (KBr): 3340, 3040, 2986, 2944, 1743, 1668, 1623 cm^{-1}. $[\alpha]_D^{25}=-38.4$ (c=0.5, MeOH). ^1H NMR (500 MHz, DMSO-d_6): δ 1.54 (3H, d, J=7.3 Hz), 3.04 (3H, s), 3.72 (3H, s), 4.70 (1H, dq, J=7.3, 7.3 Hz), 7.78–7.86 (2H, m), 8.07–8.18 (3H, m), 8.85–8.93 (1H, m), 9.06–9.13 (2H, m). ^{13}C NMR (125 MHz, DMSO-d_6): δ 17.3, 22.5, 47.9, 52.1, 113.4, 122.7, 123.7, 126.4, 127.9, 128.6, 128.7, 129.1, 129.7, 132.8, 134.4, 143.5, 157.2, 164.0, 172.8. Anal. calcd (found) for $C_{19}H_{18}N_2O_3$: C, 70.79 (70.62); H, 5.86 (5.86); N, 8.64% (8.64%).

4.5. X-ray crystallographic analysis of (*R*,*S*)-2b

A colorless crystal (of the molecular formula $C_{24}H_{22}N_2O_4$) having approximate dimensions of 0.23×0.20×0.20 mm^3 was mounted on a glass fiber in a random orientation. Preliminary examination and data collection were performed with Mo K_α radiation (λ=0.71069 Å) on a Rigaku RAXIS-RAPID equipped with an imaging plate. Data collection and cell refinement: MSC/AFC diffractometer control. Data reduction: *teXsan for windows version 1.06*.[8] Structure solution: *SIR92*.[9] Refinement: *SHELXL97*.[10]

4.6. Crystal data for (*R*,*S*)-2b

$C_{24}H_{22}N_2O_4$, f_w=402.45; monoclinic, space group $P2_1$; a=6.0757(7), b=19.3406(2), c=8.5842(1) Å, α=90, β=102.961(4), V=90°, V=983.0(2) $Å^3$; Z=2; D_{calc}=1.360 g cm^{-3}; R=0.0414, $wR(F^2)$=0.1164. Crystallographic data (excluding these structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 220636. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

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