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Photoinduced electron transfer-initiated asymmetric cyclization of *N*-benzoyl-α-dehydronaphthylalanine alkyl esters carrying chiral and bulky auxiliaries

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Abstract—The irradiation of the title compounds [(*Z*)-**1**] having (*S*)-(+)-*sec*-butyl, (−)-mentyl and related chiral auxiliaries in methanol and 1,2-dichloroethane containing 2-(diethylamino)ethanol afforded chiral auxiliary-substituted (4*S*,5*S*)-, (4*R*,5*R*)-, (4*R*,5*S*)- and (4*S*,5*R*)-4,5-dihydrooxazole derivatives (**2**) along with (*E*)-**1**. It was found that the photoinduced electron transfer-initiated cyclization of **1** gives either of the two diastereomers for *cis*-**2** and *trans*-**2** in diastereomeric excess whose value varies from 6% to 81% depending on solvent and chiral auxiliary.

Excited-state chemistry for organic molecules has continued to contribute to the development of novel synthetic methods that enable the construction of pharmaceutically useful hetero atom-containing rings.[1] While sophisticated organic photochemistry has also contributed to the enhancement of enantio- and diastereoselectivities in many asymmetric reactions,[2–5] there have been only a few enantio- and diastereodifferentiating photochemical reactions of synthetic utilities, particularly in liquid phase. Since photoinduced electron transfer (PET) reactions may construct heterocyclic rings with high efficiencies,[6] we attempted to develop a novel diastereodifferentiating photocyclization of *N*-benzoyl-α-dehydronaphthylalaninamides carrying some chiral auxiliaries via ET. Fortunately, we found the highly diastereoselective formation of 3,4-dihydrobenzoquinolinone derivatives.[7] In addition, a detailed analysis of tertiary amine, solvent, chiral auxiliary and temperature effects on the diastereomeric excess (de) demonstrated that diastereoselectivity in this photocyclization strongly depends on the steric and electronic factors of a given chiral auxiliary. In this respect it was quite recently found that the PET reaction of alkyl ester analog for the above α-dehydroamino acid derivatives selectively affords 4,5-dihydrooxazole derivatives even in less polar solvents.[8] Because these products possess two asymmetric carbons in a dihydrooxazole ring, it is possible to expand the PET-initiated cyclization of *N*-acyl-α-dehydronaphthylalanine alkyl esters to a novel type of asymmetric photoinduction by introducing a chiral auxiliary into the ester moiety. For further expansion of our study on the asymmetric photocyclization of *N*-acyl-α-dehydroamino acid derivatives, we synthesized chiral auxiliary-substituted (*Z*)-*N*-benzoyl-α-dehydro(1-naphthyl)alanine alkyl esters [(*Z*)-**1a**–**d**] and investigated substituent (R), solvent, tertiary amine and temperature effects on the extent to which one diastereomer is formed in excess (Chart 1).

The starting (*Z*)-isomers [(*Z*)-**1a**–**d**] were prepared in good yields (52–61%) by the ring-opening reactions of (*Z*)-4-(1-naphthylmethylene)-2-phenyl-5(4*H*)-oxazolone with the corresponding chiral alcohols in the presence of triethylamine (TEA).[9,10] After a nitrogen-saturated methanol solution of (*Z*)-**1a** (4.0×10^{-3} mol dm^{-3},

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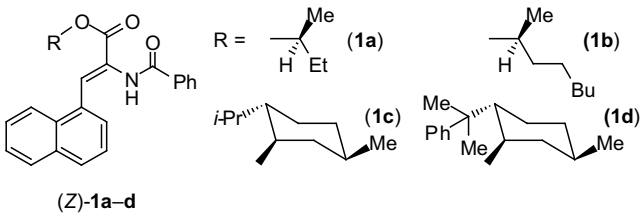
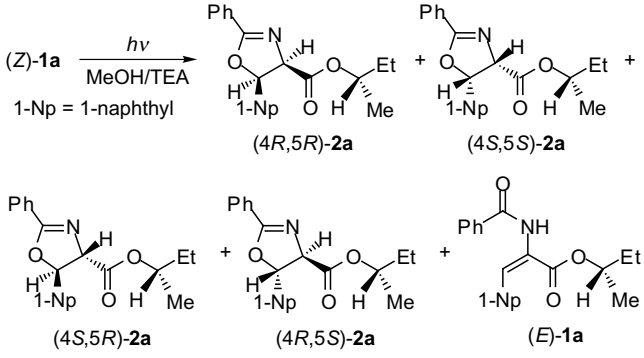


Chart 1.

500 mL) containing TEA (0.10 mol dm^{-3}) was irradiated with Pyrex-filtered light (>280 nm) from a 400 W high-pressure Hg lamp for 5 h at room temperature (conversion, ≈100%), the reaction mixture obtained was subjected to preparative thin layer chromatography over silica gel (eluent: EtOAc–hexane or EtOAc–$CHCl_3$). This chromatography allowed us to isolate *cis*- and *trans*-4-[(*S*)-*sec*-butoxycarbonyl]-5-(1-naphthyl)-2-phenyl-4,5-dihydrooxazoles as their diastereomeric mixtures [*cis*-**2a**: (4*R*,5*R*)-**2a** + (4*S*,5*S*)-**2a**, 78%; *trans*-**2a**: (4*S*,5*R*)-**2a** + (4*R*,5*S*)-**2a**, 8% yield] having the vicinal coupling constants ($J_{4,5}$) of 10.3 Hz and 6.3 Hz in DMSO-d_6, respectively, as shown in Scheme 1.[11] The (*E*)-isomer of **1a** was isolated independently from the reaction mixture, which was irradiated for 0.5 h under the same conditions (conversion, 20%), by similar workup (Scheme 1).[12] In addition, a combination of preparative thin layer, reversed phase and normal phase chromatographic techniques made it possible to separate and isolate four diastereomers derived from *cis*-**2a** and *trans*-**2a**.

In order to determine the absolute configuration of four diastereomers isolated, enantiomeric *cis*-4-(*tert*-butoxycarbonyl)-5-(1-naphthyl)-2-phenyl-4,5-dihydrooxazoles (*cis*-**3**) (isolated in the previous study[8]) was separated into (4*S*,5*S*)-**3** ($[\theta]_{220}$ +1390 deg cm^2 $dmol^{-1}$) and (4*R*,5*R*)-**3** ($[\theta]_{220}$ −1120 deg cm^2 $dmol^{-1}$) by using a chiral HPLC column. Because the sign of circular dichroism (CD) band at 220 nm reflects the absolute configuration of the enantiomers at the 5-position on the dihydrooxazole ring, it is possible to unambiguously determine the configuration at this position for a given diastereomer from the sign of its CD band at 220 nm. A single crystal showing the CD band of positive sign was successfully developed and its structure was ana-



Scheme 1.

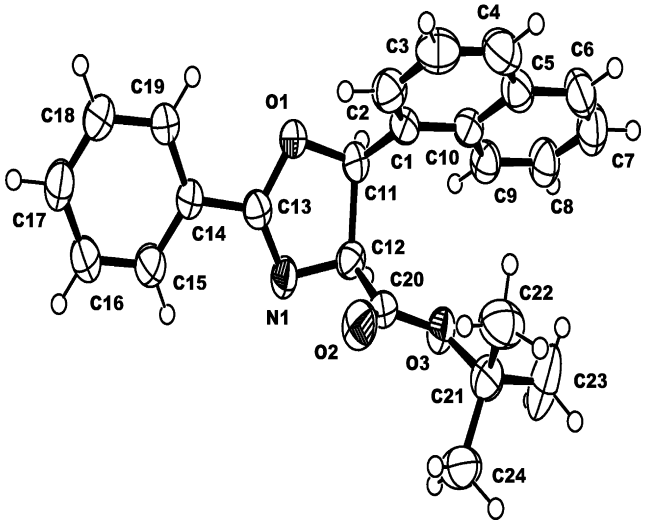


Figure 1. ORTEP drawing of (4*S*,5*S*)-**3**.

lyzed.[13] The ORTEP drawing depicted in Figure 1 led us to conclude that (4*S*,5*S*)-**2a** and (4*R*,5*S*)-**2a** exhibit the CD bands of positive sign and those of negative sign are attributable to (4*R*,5*R*)-**2a** and (4*S*,5*R*)-**2a**.[11] Based on these configurational assignments as well as on the diastereomeric composition ratios for *cis*-**2a** (^{1}H NMR spectral analysis) and *trans*-**2a** (^{1}H NMR spectral and/or HPLC analysis), we were able to demonstrate that the PET-type cyclization of (*Z*)-**1a** affords (4*R*,5*R*)-**2a** (de = 10%) and (4*S*,5*R*)-**2a** (de = 13%) in excess under given conditions. For examining the TEA-catalyzed isomerization of these two diastereomers, their methanol solutions containing the amine (0.10 mol dm^{-3}) were allowed to stand for 3–4 h at room temperature, and only the very little isomerization was observed (<5%, ^{1}H NMR spectral analysis).

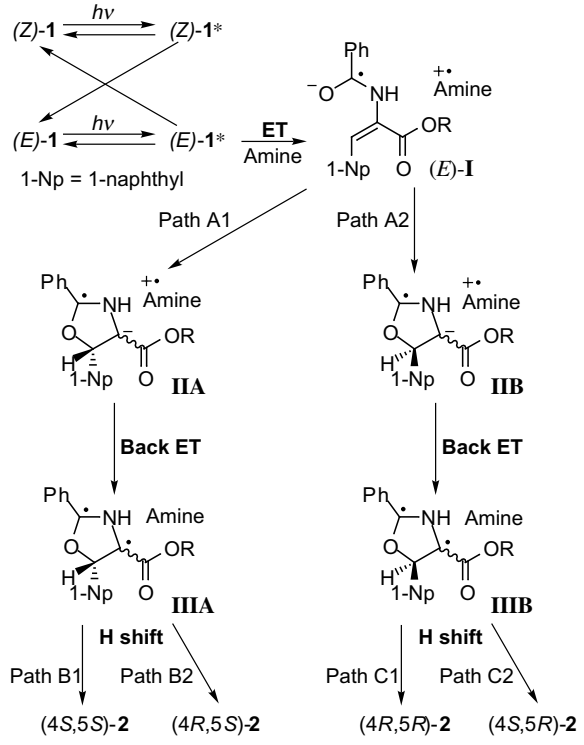
In Table 1 are summarized substituent (chiral auxiliary), solvent and tertiary amine effects on the photoreactivity (conversion) of **1** and the de value of a given diastereomer for *cis*-**2** and *trans*-**2**. As seen from the data of this table, 2-(diethylamino)ethanol (DEAE) used instead of TEA increased both the de values estimated in methanol and 1,2-dichloroethane and, hence, is a better tertiary amine for inducing higher diastereoselectivity, probably, through stronger hydrogen-bonding interaction with a reaction intermediate. Interestingly, the change in solvent from methanol to 1,2-dichloroethane reversed the configuration of major diastereomer for *cis*-**2a** without affecting it for *trans*-**2a**. If we consider the great hydrogen-bonding solvation ability of the former solvent, this interesting finding implies that there is a difference in the asymmetric induction mechanism between these two solvents. Similar results were obtained for the asymmetric photocyclization of **1b** bearing an (*S*)-1-methylheptyl auxiliary. In the previous study it was found that steric bulkiness of the alkyl group bonded to the carboxy oxygen atom in *N*-benzoyl-α-dehydro(1-naphthyl)alanine alkyl esters greatly enhances selectivity for the *cis*-dihydrooxazole isomer.[8] Since the dihydrooxazole-forming photocyclization is a kinetically controlled process, this finding stimulated us to introduce a more bulky auxil-

Table 1. Substituent, solvent and tertiary amine effects on the photoreactivity of **1** and the de for *cis*-**2** and *trans*-**2**, obtained by the 3 h irradiation of (*Z*)-**1** (4.0×10^{-3} mol dm^{-3}) in the presence of TEA or DEAE (0.10 mol dm^{-3}) at room temperature

Compound	Solvent	Amine	Composition and de (%)							
			(*Z*)-**1**	(*E*)-**1**	*cis*-**2**			*trans*-**2**		
					(4*R*,5*R*)-**2**	(4*S*,5*S*)-**2**	de	(4*S*,5*R*)-**2**	(4*R*,5*S*)-**2**	de
(*Z*)-**1a**	MeOH	TEA	9.3	21.8	29.3	24.0	10	8.8	6.8	13
(*Z*)-**1a**	CH_2ClCH_2Cl	TEA	2.5	3.4	26.2	29.1	5	23.1	15.7	19
(*Z*)-**1a**	MeOH	DEAE	10.2	22.8	8.9	6.2	18	30.7	21.2	18
(*Z*)-**1a**	CH_2ClCH_2Cl	DEAE	8.3	18.0	18.3	20.6	6	19.8	15.0	14
(*Z*)-**1b**	MeOH	DEAE	12.2	20.5	30.9	24.4	12	7.0	5.0	17
(*Z*)-**1b**	CH_2ClCH_2Cl	DEAE	7.6	12.5	24.9	29.0	8	14.0	12.0	8
(*Z*)-**1c**	MeOH	DEAE	11.0	30.5	19.3	28.9	20	3.4	6.9	34
(*Z*)-**1c**	CH_2ClCH_2Cl	DEAE	4.5	9.5	33.7	26.0	13	8.5	17.8	35
(*Z*)-**1d**	MeOH	DEAE	20.2	36.1	4.3	20.2	65	2.8	16.4	71
(*Z*)-**1d**	CH_2ClCH_2Cl	DEAE	29.2	29.2	5.0	7.0	17	2.8	26.8	81

iary group into the ester moiety of (*Z*)-**1**. For this group, (−)-mentyl and (−)-8-phenylmentyl auxiliaries were chosen. Careful diastereomeric analysis of the isolated products **2c** and **2d** revealed that the mentyl group influences the asymmetric photocyclization process in a different manner from the *sec*-butyl one: In most cases the configuration of major diastereomer is reversed and de is greatly enhanced particularly for **2d**-derived diastereomers.

Our attention is now directed to the mechanism of PET-initiated asymmetric cyclization for **1**, where the radical ion pairs (*E*)-**I** and **II** and the biradical **III** are involved as key reaction intermediates (see Scheme 2).[8,14] Hydrogen-bonding interactions of these intermediates with methanol or tertiary amine are considered to contribute to the control of de, so that temperature effects on the de value may provide significant information regarding the asymmetric induction mechanism. As shown in Table 2, the de values of (4*R*,5*R*)-**2c** and (4*R*,5*S*)-**2c** in 1,2-dichloroethane are both increased with a lowering of temperature, whereas there is a sudden decrease in de for both (4*S*,5*S*)-**2c** and (4*R*,5*S*)-**2c** estimated in methanol at −78 °C. The former finding is consistent with the participation of a hydrogen-bonding interaction between DEAE and **III**, while the latter finding suggests that hydrogen-bonding and/or electrostatic interaction of methanol molecules with (*E*)-**I** is a major factor controlling de in the protic solvent. The intermediate (*Z*)-**I** should also be formed by ET from DEAE to (*Z*)-**1*** but the cyclization of the (*Z*)-isomer is unable to proceed from this configuration to afford the corresponding intermediate **II**. Thus, (*Z*)-**I** is very likely to undergo exclusive back ET to regenerate (*Z*)-**1** and the amine. In addition to mechanistic information obtained from the previous study, these considerations substantiate Scheme 2 in which asymmetry at the 5- and 4-positions on the dihydrooxazole ring is induced in the stages of the **II**-forming cyclization (π-face selective intramolecular addition) and the hydrogen shift in **III**, respectively.



Scheme 2.

Because configurational interconversion between **IIA** and **IIB** or between **IIIA** and **IIIB** is very unlikely to occur during irradiation, it is possible to estimate the compositions of **IIIA** and **IIIB** (or **IIA** and **IIB**), as well as the rate ratios of paths A–C, based on the composition of each diastereomer for *cis*-**2** and *trans*-**2** collected in Table 1 (Table 3). A comparison between the compositions of **IIIA** and **IIIB** thus estimated shows that asymmetric induction in 1,2-dichloroethane solutions of **1a–c** is achieved at the step of hydrogen shift in **III**, while a difference in the **II**-forming cyclization rate is mainly responsible for this induction in methanol. Since rate ratios for paths B and C depend on chiral auxiliary and temperature in any solvents, hydrogen-bonding and steric interactions of DEAE with **IIIA** and **IIIB** may change the relative rates of paths B1 and C1 and paths B2 and C2 to a different extent, in the hydrogen shift in **III**. In the π-face selective intramolecular addition, both the steric bulkiness of chiral auxiliary and the hydrogen-bonding solvation of the radical ion pair

Table 2. Temperature effects on the photoreactivity of **1c** and the de for *cis*-**2c** and *trans*-**2c**, obtained by the 3 h or 1 h (−78 °C) irradiation of (*Z*)-**1c** (4.0×10^{-3} mol dm^{-3}) in methanol and 1,2-dichloroethane containing DEAE (0.10 mol dm^{-3})

Solvent	Temperature (°C)	Composition and de (%)							
		(*Z*)-**1c**	(*E*)-**1c**	*cis*-**2c**			*trans*-**2c**		
				(4*R*,5*R*)-**2c**	(4*S*,5*S*)-**2c**	de	(4*S*,5*R*)-**2c**	(4*R*,5*S*)-**2c**	de
MeOH	50	11.2	27.8	17.2	33.6	32	3.4	6.8	33
MeOH	rt	11.0	30.5	19.3	28.9	20	3.4	6.9	34
MeOH	−78	13.0	77.3	4.4	4.4	0	0.4	0.5	11
CH_2ClCH_2Cl	50	12.7	22.9	23.5	19.5	9	8.3	13.1	22
CH_2ClCH_2Cl	rt	4.5	9.5	33.7	26.0	13	8.5	17.8	35
CH_2Cl_2[a]	−78	2.0	4.9	42.5	22.8	30	7.3	20.5	47

[a] Because 1,2-dichloroethane is solidified at −78 °C, dichloromethane was used instead.

Table 3. Substituent and solvent effects on the composition of **III** and the rate ratio (R_r) of given two competitive paths, obtained by the 3 h irradiation of (*Z*)-**1** (4.0×10^{-3} mol dm^{-3}) in the presence of DEAE (0.10 mol dm^{-3}) at room temperature

Compound	Solvent	Composition of **III** (%) and R_r				
		IIIA	**IIIB**	R_r (A1/A2)	R_r (B1/B2)	R_r (C1/C2)
(*Z*)-**1a**	MeOH	27.4	39.6	0.7	0.3	0.3
	CH_2ClCH_2Cl	35.6	38.1	0.9	1.4	0.9
(*Z*)-**1b**	MeOH	29.4	37.9	0.8	4.9	4.4
	CH_2ClCH_2Cl	41.0	38.9	1.1	2.4	1.8
(*Z*)-**1c**	MeOH	35.8	22.7	1.6	4.2	5.7
	CH_2ClCH_2Cl	43.8	42.2	1.0	1.5	4.0
(*Z*)-**1d**	MeOH	36.6	7.1	5.2	1.2	1.5
	CH_2ClCH_2Cl	33.8	7.8	4.3	0.3	1.8

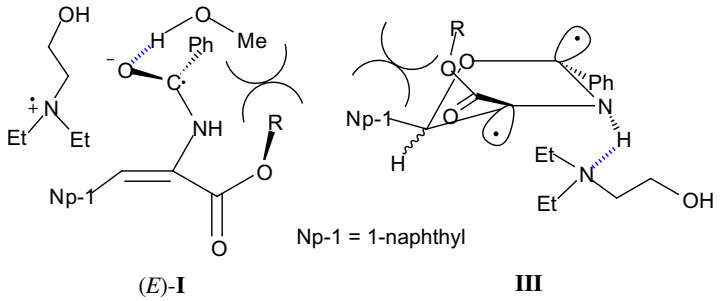


Figure 2. Schematic illustration for steric effects of the chiral auxiliary R on the hydrogen-bonding interactions between (*E*)-**I** and methanol and between **III** and DEAE.

(*E*)-**I** by methanol are considered to cause a difference in rate for paths A1 and A2. Surprisingly, the introduction of a (−)-8-phenylmentyl auxiliary group resulted in a considerable increase in the relative composition of **IIIA** in any solvents examined. This suggests that a steric repulsion between the bulky chiral auxiliary and the naphthyl chromophore in **II** is a dominant factor controlling the relative rate of path A, irrespective of solvent property. It is likely that the bulky phenylmentyl group exists preferentially in the *re* face of the cyclized radical ion pair **II** to be responsible for the observed π-face selective intramolecular addition. On the other hand, the observation of much lower de (than expected) for (4*S*,5*S*)-**2d** must be related to the greatly diminished relative rate of path B1. The phenylmentyl group should serve to slow down the rate of hydrogen shift in the *re* face of the biradical intermediate **IIIA**.

In conclusion, it was demonstrated that steric effects of chiral auxiliary on the hydrogen-bonding solvation of the intermediate (*E*)-**I** in methanol as well as on the hydrogen-bonding interaction between the intermediate **III** and tertiary amine in 1,2-dichloroethane are major factors controlling the novel asymmetric photoinduction observed (Fig. 2). Additionally, the introduction of a highly bulky chiral auxiliary induced a large asymmetry in the stage of the **II**-forming cyclization process, irrespective of the solvation ability of a given solvent.

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10. Data for (*Z*)-**1a**. Mp 113.5–114.5 °C. IR (KBr): 3336, 1654, 1577 cm^{-1}. $[\alpha]_D^{25}$ +20.2 (*c* 0.5, MeOH). ^1H NMR (600 MHz, DMSO-d_6): δ 0.89 (3H, t, $J = 7.6$ Hz), 1.24 (3H, d, $J = 6.2$ Hz), 1.59 (2H, dq, $J = 6.9$, 7.6 Hz), 4.90 (1H, tq, $J = 6.2$, 6.9 Hz), 7.45 (2H, dd, $J = 7.6$, 8.3 Hz), 7.50 (1H, dd, $J = 6.9$, 8.3 Hz), 7.53 (1H, dd, $J = 7.6$, 7.6 Hz), 7.55–7.59 (2H, m), 7.70 (1H, d, $J = 6.9$ Hz), 7.81 (2H, d, $J = 7.6$ Hz), 7.87 (1H, s), 7.92 (1H, d, $J = 8.3$ Hz), 7.95 (1H, d, $J = 8.3$ Hz), 7.99 (1H, d, $J = 8.3$ Hz), 9.95 (1H, s). ^{13}C NMR (150 MHz, DMSO-d_6) δ 9.4, 19.1, 28.2, 72.9, 124.0, 125.4, 126.2, 126.6, 126.7, 127.6 (2C), 128.3 (2C), 128.5, 129.1, 129.2, 129.7, 130.5, 130.9, 131.7, 133.2, 133.5, 166.4, 166.5. Anal. Calcd for $C_{24}H_{23}NO_3$: C, 77.19; H, 6.21; N, 3.75. Found: C, 77.18; H, 6.23; N, 3.46.
11. Data for (4*R*,5*R*)-**2a**. Mp 111.0–111.5 °C. IR (KBr): 1734, 1653 cm^{-1}. $[\alpha]_D^{25}$ −460.7 (*c* 0.5, MeOH). $[\theta]_{220}$ −420 deg cm^2 $dmol^{-1}$ (2.0×10^{-5} mol dm^{-3}, MeOH). ^1H NMR (600 MHz, DMSO-d_6): δ −0.33 (3H, d, $J = 6.3$ Hz), 0.54 (3H, t, $J = 7.5$ Hz), 1.02 (2H, dq, $J = 7.5$, 7.5 Hz), 4.01 (1H, tq, $J = 7.5$, 7.5 Hz), 5.57 (1H, d, $J = 10.3$ Hz), 6.83 (1H, d, $J = 10.3$ Hz), 7.48 (1H, dd, $J = 7.5$, 7.5 Hz), 7.51 (1H, d, $J = 7.5$ Hz), 7.56–7.60 (2H, m), 7.57 (2H, dd, $J = 7.5$, 8.0 Hz), 7.65 (1H, dd, $J = 7.5$, 7.5 Hz), 7.89 (1H, d, $J = 7.5$ Hz), 7.95 (1H, d, $J = 8.0$ Hz), 8.06 (2H, d, $J = 8.0$ Hz), 8.10 (1H, d, $J = 8.6$ Hz). ^{13}C NMR (150 MHz, DMSO-d_6): δ 8.9, 16.7. 27.6, 71.7, 72.1, 80.2, 123.1, 123.8, 125.1, 125.9, 126.2, 126.8, 128.2 (2C), 128.3, 128.4, 128.9 (2C), 130.1, 132.0, 132.2, 133.0, 165.0, 168.3. Anal. Calcd for $C_{24}H_{23}NO_3$: C, 77.19; H, 6.21; N, 3.75. Found: C, 76.96; H, 5.99; N, 3.67.

Data for (4*S*,5*S*)-**2a**. Mp 90.5–91.0 °C. IR (KBr): 1734, 1653 cm^{-1}. $[\alpha]_D^{25}$ +365.5 (*c* 0.5, MeOH). $[\theta]_{220}$ +300 deg cm^2 $dmol^{-1}$ (2.0×10^{-5} mol dm^{-3}, MeOH). ^1H NMR (600 MHz, DMSO-d_6): δ 0.12 (3H, t, $J = 7.5$ Hz), 0.39 (2H, dq, $J = 7.5$, 7.5 Hz), 0.60 (3H, d, $J = 6.3$ Hz), 3.96 (1H, tq, $J = 7.5$, 7.5 Hz), 5.53 (1H, d, $J = 10.3$ Hz), 6.81 (1H, d, $J = 10.3$ Hz), 7.50 (1H, dd, $J = 7.5$, 8.0 Hz), 7.55–7.56 (2H, m), 7.56 (2H, dd, $J = 6.9$, 7.5 Hz), 7.59 (1H, d, $J = 7.5$ Hz), 7.65 (1H, dd, $J = 7.5$, 7.5 Hz), 7.89 (1H, d, $J = 8.0$ Hz), 7.95 (1H, d, $J = 8.0$ Hz), 8.05 (2H, d, $J = 6.9$ Hz), 8.08 (1H, d, $J = 8.6$ Hz). ^{13}C NMR (150 MHz, DMSO-d_6): δ 8.3, 18.1, 26.7, 71.9, 72.6, 80.3, 123.2, 123.6, 125.1, 125.9, 126.3, 126.8, 128.1 (2C), 128.3, 128.4, 128.8 (2C), 129.9, 131.9, 132.2, 133.0,165.1, 168.1. Anal. Calcd for $C_{24}H_{23}NO_3$: C, 77.19; H, 6.21; N, 3.75. Found: C, 76.87; H, 6.12; N, 3.61.

Data for (4*S*,5*R*)-**2a**. Oily liquid. IR (NaCl): 1734, 1639, 1577 cm^{-1}. $[\alpha]_D^{25}$ +73.7 (*c* 0.5, MeOH). $[\theta]_{220}$ −50 deg cm^2 $dmol^{-1}$ (2.0×10^{-5} mol dm^{-3}, MeOH). ^1H NMR (600 MHz, DMSO-d_6): δ 0.88 (3H, t, $J = 7.5$ Hz), 1.24 (3H, d, $J = 6.3$ Hz), 1.62 (2H, dq, $J = 7.5$, 7.5 Hz), 4.76 (1H, d, $J = 6.3$ Hz), 4.95 (1H, tq, $J = 7.5$, 7.5 Hz), 6.65 (1H, d, $J = 6.3$ Hz), 7.52–7.54 (2H, m), 7.58 (2H, dd, $J = 7.5$, 7.5 Hz), 7.59–7.61 (2H, m), 7.65 (1H, dd, $J = 7.5$, 7.5 Hz), 7.92–7.93 (1H, m), 7.97 (1H, d, $J = 8.0$ Hz), 8.04 (1H, d, $J = 7.5$ Hz), 8.05 (2H, d, $J = 7.5$ Hz). ^{13}C NMR (150 MHz, DMSO-d_6): δ 9.4, 19.1, 28.0, 71.9, 73.6, 75.7, 80.8, 122.5, 122.8, 125.5, 126.3, 126.4, 126.7, 128.3 (2C), 129.0 (2C), 129.1, 129.2, 132.4, 133.5, 134.6, 164.6, 170.2. HR EI-MS *m*/*z* calcd for $C_{24}H_{23}NO_3$: 373.1678. Found: 373.1678.

Data for (4*R*,5*S*)-**2a**. Oily liquid. IR (NaCl): 1734, 1653, 1560 cm^{-1}. $[\alpha]_D^{25}$ +108.9 (*c* 0.5, MeOH). $[\theta]_{220}$ +150 deg cm^2 $dmol^{-1}$ (2.0×10^{-5} mol dm^{-3}, MeOH). ^1H NMR (600 MHz, DMSO-d_6): δ 0.87 (3H, t, $J = 7.5$ Hz), 1.28 (3H, d, $J = 6.3$ Hz), 1.59 (2H, dq, $J = 7.5$ Hz), 4.78 (1H, d, $J = 6.3$ Hz), 4.95 (1H, tq, $J = 7.5$, 7.5 Hz), 6.66 (1H, d, $J = 6.3$ Hz), 7.51 (1H, d, $J = 8.0$ Hz), 7.54 (1H, dd, $J = 7.5$, 8.0 Hz), 7.58 (2H, dd, $J = 7.5$, 7.5 Hz), 7.60–7.62 (2H, m), 7.67 (1H, dd, $J = 6.3$, 7.5 Hz), 7.96–7.98 (2H, m), 8.02–8.04 (1H, m), 8.05 (2H, d, $J = 7.5$ Hz). ^{13}C NMR (150 MHz, DMSO-d_6): δ 9.3, 19.1, 28.1, 73.4, 75.7, 78.5, 80.7, 122.6, 122.9, 125.5, 126.3, 126.4, 126.7, 128.3 (2C), 129.0 (2C), 129.1, 129.2, 132.4, 133.5, 134.6, 164.5, 170.2. HR EI-MS *m*/*z* calcd for $C_{24}H_{23}NO_3$: 373.1678. Found:373.1678.
12. Data for (*E*)-**1a**. Mp 118.5–119.0 °C. IR (KBr): 3454, 1654, 1560 cm^{-1}. $[\alpha]_D^{25}$ −1.6 (*c* 0.5, MeOH). ^1H NMR (600 MHz, DMSO-d_6): δ 0.50 (3H, t, $J = 7.6$ Hz), 0.83 (3H, d, $J = 5.2$ Hz), 1.19 (2H, dq, $J = 6.3$, 7.6 Hz), 4.60 (1H, tq, $J = 5.2$, 6.3 Hz), 7.27 (1H, s), 7.33 (1H, d, $J = 6.9$ Hz), 7.47 (1H, dd, $J = 7.5$, 7.5 Hz), 7.56 (2H, dd, $J = 7.5$, 8.0 Hz), 7.54–7.58 (2H, m), 7.63 (1H, dd, $J = 6.9$, 7.5 Hz), 7.88 (1H, d, $J = 7.6$ Hz), 7.99 (2H, d, $J = 8.0$ Hz), 8.00 (1H, dd, $J = 6.9$, 6.9 Hz), 8.02 (1H, d, $J = 8.0$ Hz), 10.6 (1H, s). ^{13}C NMR (150 MHz, DMSO-d_6) δ 8.9, 18.2, 27.6, 72.3, 120.0, 122.2, 124.6, 125.3, 125.9, 126.1, 126.3, 127.7 (2C), 127.9, 128.3, 128.5 (2C), 131.2, 131.9, 132.0, 132.1, 133.0, 164.0, 165.0. Anal. Calcd for $C_{24}H_{23}NO_3$: C, 77.19; H, 6.21; N, 3.75. Found: C, 77.34; H, 6.25; N, 3.61.

13. A 10×150-mm Chiralcel OJ column was used as a Chiral HPLC column for isolating (4*S*,5*S*)-**3** and (4*R*,5*R*)-**3**. Crystal data for (4*S*,5*S*)-**3**: $C_{24}H_{23}NO_3$, fw = 373.45; colourless prism, $0.35 \times 0.15 \times 0.10$ mm, orthorhombic, space group $P2_12_12_1$ (#19); $a = 8.239(3)$ Å, $b = 10.024(4)$ Å, $c = 24.467(9)$ Å, $V = 2020.6(12)$ Å^3; $Z = 4$; $D_{calc} = 1.228$ g cm^{-3}; $R = 0.0634$, $wR_2 = 0.0582$. Crystallographic data of (4*S*,5*S*)-**3** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 636944. 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).
14. Based on *N*-acyl substituent effects on the fluorescence intensity and photoreactivity of *N*-aroyl-α-dehydro(1-naphthyl)alanine *tert*-butyl esters, we previously proposed the radical ion pair intermediate (*E*)-**I**.[8] The progress of π-face selective intramolecular addition within the (*E*)-**1**-derived radical anion (path A) is required for inducing asymmetry at the 5-position on the dihydrooxazole ring. This asymmetric addition results in a preferential formation of either the cyclized radical ion pair **IIA** or the **IIB**. There are two possible routes for back ET in the radical ion pair **II**. One is the transfer of unpaired electron from the 2-position on the oxazole ring to the amine radical cation, which gives a zwitterion intermediate. The other is the transfer of one of the paired electrons from the 4-position on the oxazole ring to the amine radical cation, as shown in Scheme 2. The electron-deficient carbon generated at the 2-position on the ring of the zwitterion is considered to greatly promote the dissociation of the N–H proton. If so, intramolecular proton shift in this intermediate is very unlikely to occur depending on the hydrogen-bonding ability of a given tertiary amine. Tertiary amine and temperature effects on the de for *cis*-**2** and *trans*-**2** in 1,2-dichloroethane favour the existence of the biradical intermediate **III**.
While π-face selective intramolecular addition in (*E*)-**I** induces asymmetry at the 5-position on the oxazole ring of **2**, asymmetric induction at the 4-position on this ring is accomplished by preferential hydrogen shift in either the *re* or the *si* face of **III** (Paths B and C in Scheme 2). The simultaneous C=N bond formation may provide a driving force for this hydrogen shift eventually leading to *cis*-**2** and *trans*-**2**. The finding that hydrogen-boding interaction between **III** and tertiary amine is a major factor controlling de in 1,2-dichloroethane led us to propose hydrogen bond-assisted hydrogen shift in the *re* or the *si* face (Fig. 2).