HETEROCYCLES, Vol. 83, No. 10, 2011, pp. 2255 - 2263. © 2011 The Japan Institute of Heterocyclic Chemistry
Received, 21st May, 23011, Accepted, 19th July, 2011, Published online, 22nd July, 2011
DOI: 10.3987/COM-11-12265

ASYMMETRIC PHOTOCYCLIZATION REACTIONS OF *N*-ACETYL-α-DEHYDRO(1-NAPHTHYL)ALANINAMIDES IN THE PRESENCE OF CHIRAL AMINE

Kei Maekawa, Toshiyuki Tanami, Tetsutaro Igarashi, and Tadamitsu Sakurai *

Department of Material and Life Chemistry, Faculty of Engineering, Kanagawa University, Kanagawa-ku, Yokohama 221-8686, Japan

Abstract – Irradiation of the title compound having an *N*'-methyl group in 2-propanol and dichloromethane containing (*S*)-1-methyl-2-pyrrolidinemethanol at room temperature afforded (*R*)-3,4-dihydrobenzo[*f*]quinolinone derivative in enantiomeric excesses (ee's) of 7 and 30%, respectively. On the other hand, the corresponding (*S*)-enantiomer was obtained in 21–23% ee's on room temperature irradiation in the above solvents containing (*S*)-nicotine which enhanced these ee values up to 34–59% at –78 °C.

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. Taking into account the potential that in many cases photoinduced electron transfer reactions are able to construct heterocyclic rings with high efficiencies,[6] we attempted to develop a new type of diastereodifferentiating cyclization of *N*-acyl-α-dehydronaphthylalaninamides carrying some chiral auxiliaries via photoinduced electron transfer in the polar solvents, methanol and acetonitrile, and found the highly diastereoselective photocyclization that proceeds catalytically through electron transfer from triethylamine to the excited-state naphthylalaninamide derivatives.[7] A detailed analysis of the effects of tertiary amine, solvent, chiral auxiliary, and temperature on the diastereomeric excess (de) demonstrated that hydrogen bonding interactions between diastereomeric enol-type intermediates and a given tertiary amine as well as relative stabilities of these intermediates play essential roles in controlling the magnitude of de. The former finding allowed us to predict the progress of catalytic and

enantioselecive photocyclization of *N*-acyl-α-dehydronaphthylalaninamides in the presence of chiral amine. In recent years much attention is being directed to the photoinduced electron transfer-catalyzed asymmetric cyclization reaction proceeding through an exciplex or an ion radical pair intermediate.[7,8] Enantiomeric excesses (ee's) obtained for highly enantioselective and catalytic sensitization reactions reported so far are in the range of 58–77% in the presence of 15–30 mol% catalysts,[8] and hence an attempt to develop such photoinduced electron transfer-initiated asymmetric sensitization reactions of high ee values is attractive and also of great significance from mechanistic and synthetic points of view. For this attempt we selected (*S*)-proline-based chiral amines, namely, prolinamide (PA), 1-methyl-2-pyrrolidinemethanol (MPM), and nicotine (NT) as electron donor catalysts and investigated the effects of chiral amine, temperature, and substituent on the asymmetric sensitization reaction of *N*-acetyl-α-dehydro(1-naphthyl)alaninamide derivatives (**1a**–**d**) in the less polar solvents, 2-propanol and dichloromethane, which are considered to greatly suppress the dissociation of ion radical pairs formed, hoping to shed much more light on the role of key intermediates proposed previously (Chart 1).

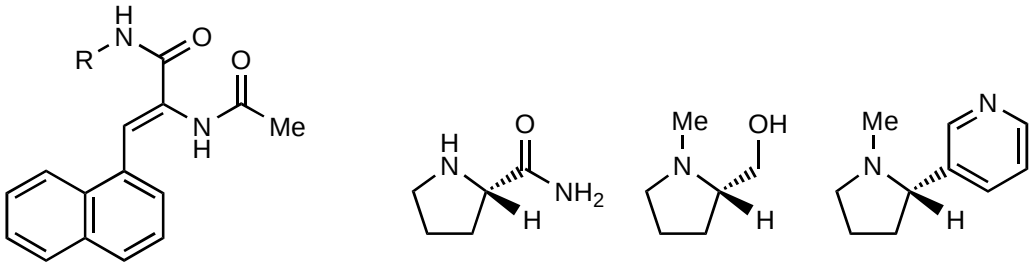
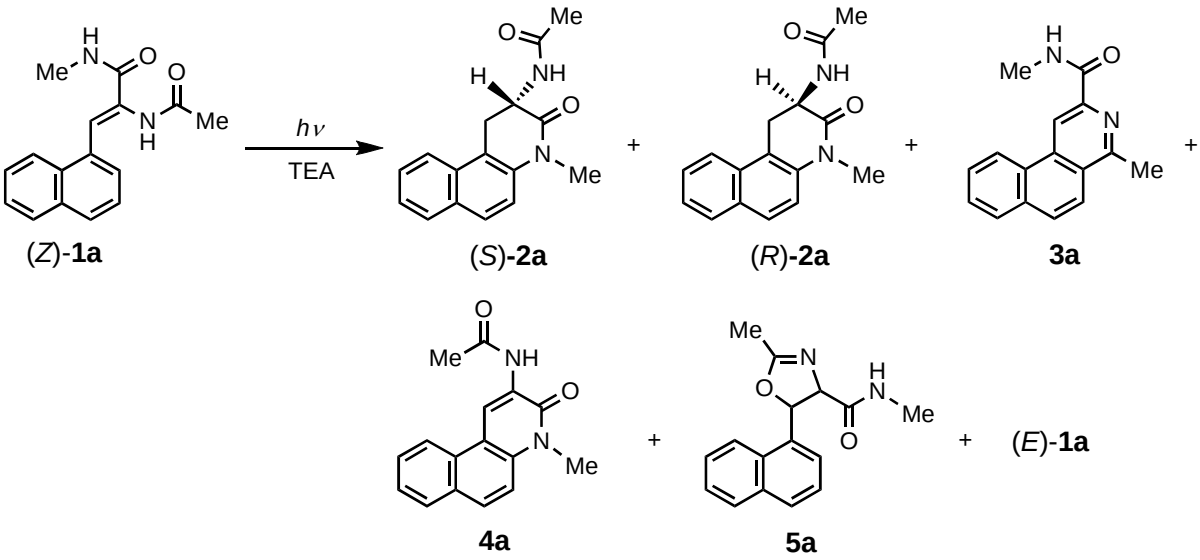


Chart 1

The (*Z*)-isomers of **1a**–**d** were prepared in high yields (72–93%) by the ring-opening reactions of (*Z*)-4-(1-naphthylmethylene)-2-methyl-5(4*H*)-oxazolone with the corresponding primary amines in the presence of triethylamine (TEA).[6c,9] After a nitrogen-saturated 2-propanol solution of (*Z*)-**1a** (3.75×10^{-3} mol dm^{-3}, 200 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 1 h at room temperature (rt; conversion, 70%), the reaction mixture obtained was subjected to preparative thin layer chromatography over silica gel (eluent: EtOAc-hexane or EtOAc-$CHCl_3$). Usual workup allowed us to isolate 3-acetylamino-3,4-dihydro-1-methyl-2(1*H*)-benzo[*f*]quinolinone (**2a**; isolated yield, 22%) as its enantiomeric mixture, 3-(methylaminocarbonyl)-1-methylbenzo[*f*]isoquinoline (**3a**; 14%), and 3-acetylamino-1-methyl-2(1*H*)-benzo[*f*]quinolinone (**4a**; 18%), in addition to (*E*)-**1a** (Scheme 1).[10] Although ^{1}H NMR signals for *cis*-4-(methylaminocarbonyl)-5-(1-naphthyl)-2-methyl-4,5-dihydrooxazole (*cis*-**5a**; NMR yield, <1%) having the vicinal coupling constant ($J_{4,5}$) of 10.7 Hz were detected at 5.03 and 6.51 ppm in DMSO-d_6,

its isolation was not attempted. In the previous studies we have already shown that the moderate fluorescence quenching of the (*Z*)-α-dehydronaphthylalaninamide derivative by TEA as well as the large negative value of free energy change for electron transfer provides evidence in support of an electron transfer mechanism for formation of the corresponding 3,4-dihydro-2(1*H*)-benzo[*f*]quinolinone.[6c,6d] In addition to this evidence, the finding that without TEA the dihydroquinolinone **2a** is not formed at all substantiates the above mechanism. Similar product distribution was observed also in dichloromethane.



Scheme 1

The dihydrobenzoquinolinone rings having (*S*)- and (*R*)-configurations in the product **2** were previously proved to exhibit relatively intense circular dichroism (CD) bands of negative and positive signs at 255 nm, respectively.[7b] Based on this finding, it was possible to determine the absolute configuration of the enantiomer formed in excess and the magnitude of ee for this enantiomer by separating the **2**-derived racemate into (*S*)- (retention time = 13–15 min) and (*R*)-enantiomers (20–31 min) using a chiral HPLC column [mobile phase, *i*-PrOH:hexane = 1:2 (**2a**) or 1:3 (**2b**–**d**) v/v] and then by measuring their CD spectra in methanol. A nitrogen-saturated 2-propanol or dichloromethane solution of (*Z*)-**1** (3.75×10^{-3} mol dm^{-3}, 50 mL) containing a given chiral amine (0.10 mol dm^{-3}) was irradiated under similar conditions at rt or –78 °C. After the reaction mixture irradiated for 1.5 h (rt) or 0.5 h (–78 °C) had been concentrated to dryness in vacuo, the resulting residue was dissolved in chloroform, washed with 0.20 mol dm^{-3} hydrochloric acid and dried for HPLC and ^{1}H NMR spectral analyses. In Table 1 are summarized conversion of (*Z*)-**1**, selectivity of **2**, and ee and configuration for major enantiomer obtained in a given solvent containing PA, MPM or NT at each temperature. While the use of PA induced asymmetry at 3-position on the dihydroquinolinone ring in 4–6% ee in any solvents at rt, a much larger ee (30%) was obtained with the configurational change of major enantiomer upon performing the asymmetric photocyclization in dichloromethane containing (*S*)-MPM. These

alterations in configuration and ee for major enantiomer suggests that the mode in which chiral amine interacts with key intermediates depends on the structure of this amine as well as on the property of solvent. Interestingly, the change in chiral amine from MPM to NT reversed the configuration of major enantiomer with accompanying a remarkable enhancement in ee in 2-propanol at rt. If we take into account that there are two hydrogen-bonding sites in both of these amines, the above finding is consistent with the involvement of different types of hydrogen-bonding interactions in the ee-determining step of the dihydrobenzoquinolinone derivative **2**.

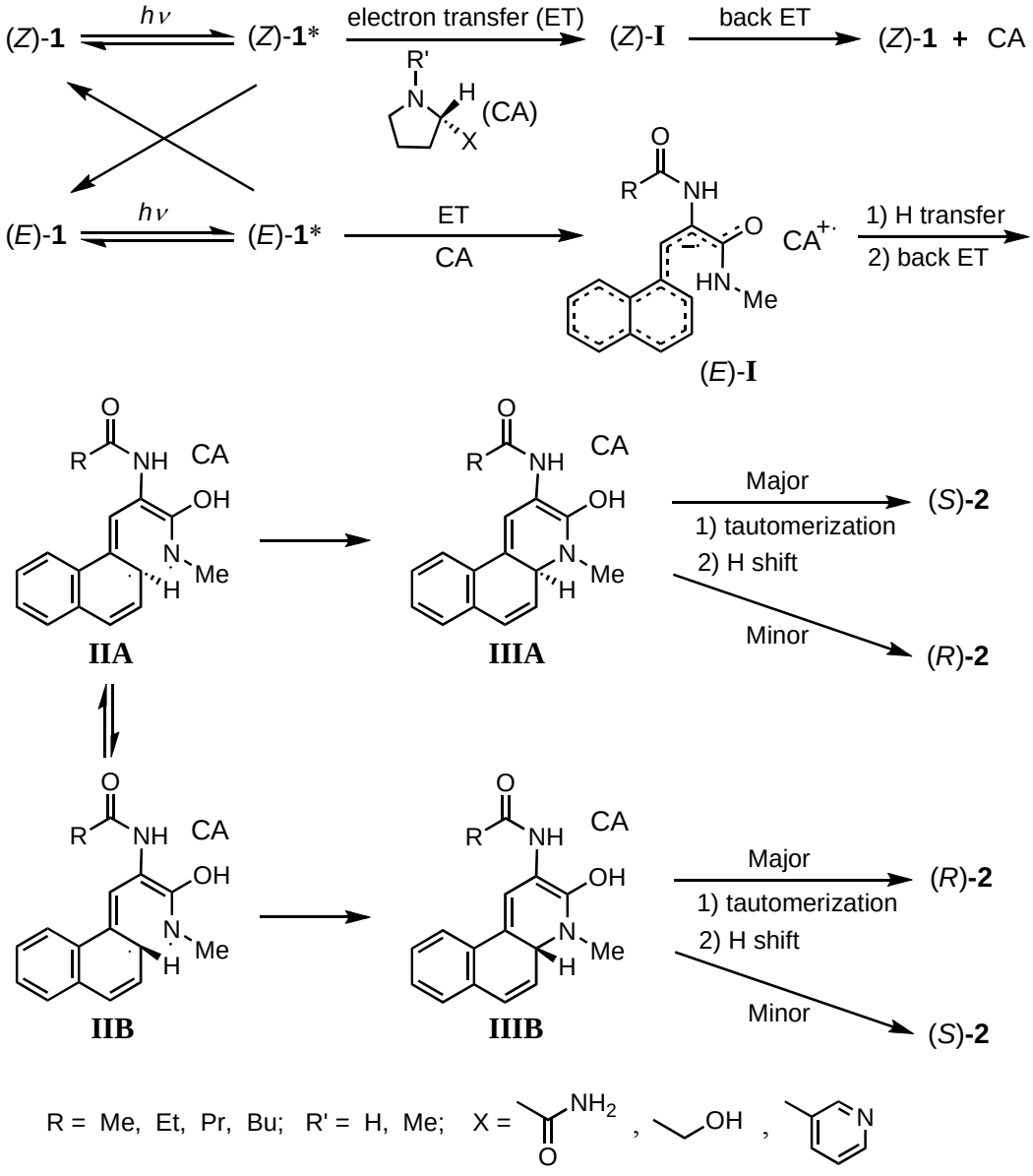
Table 1. Chiral amine, solvent, temperature, and substituent effects on the conversion of **1**, selectivity of **2**, and ee for (*S*)-**2** or (*R*)-**2** obtained by the 1.5 h (rt) or 0.5 h (Ğ78 ¡C) irradiation of (*Z*)-**1**

(*Z*)-**1**	Amine	Solvent	Temperature (¡C)	Conversion (%)[a]	Selectivity (%)[b,c]	ee (%)	Major enantiomer
1a	PA	*i*-PrOH	rt	100	54	6	*S*
1a	PA	CH_2Cl_2	rt	100	16	4	*S*
1a	MPM	*i*-PrOH	rt	94	57	7	*R*
1a	MPM	CH_2Cl_2	rt	96	31	30	*R*
1a	NT	*i*-PrOH	rt	95	41	23	*S*
1a	NT	CH_2Cl_2	rt	100	9	21	*S*
1a	MPM	*i*-PrOH	Ğ78	57	95	9	*R*
1a	MPM	CH_2Cl_2	Ğ78	67	82	34	*R*
1a	NT	*i*-PrOH	Ğ78	52	90	59	*S*
1a	NT	CH_2Cl_2	Ğ78	34	24	34	*S*
1b	NT	*i*-PrOH	Ğ78	50	82	55	*S*
1c	NT	*i*-PrOH	Ğ78	42	80	54	*S*
1d	NT	*i*-PrOH	Ğ78	46	63	46	*S*

[a] Conversion was estimated by subtracting the sum of the composition for (*Z*)-**1** and (*E*)-**1** from 100.
[b] Selectivity for **2** was evaluated by dividing the composition for **2** by the sum of compositions for **2**Ğ**5**.
[c] There were no ^{1}H NMR signals attributable to the compound(s) other than **1**Ğ**5**. Thus, it is possible to estimate the ^{1}H NMR yield of **2** by the selectivity of **2** times the conversion rate of **1**.

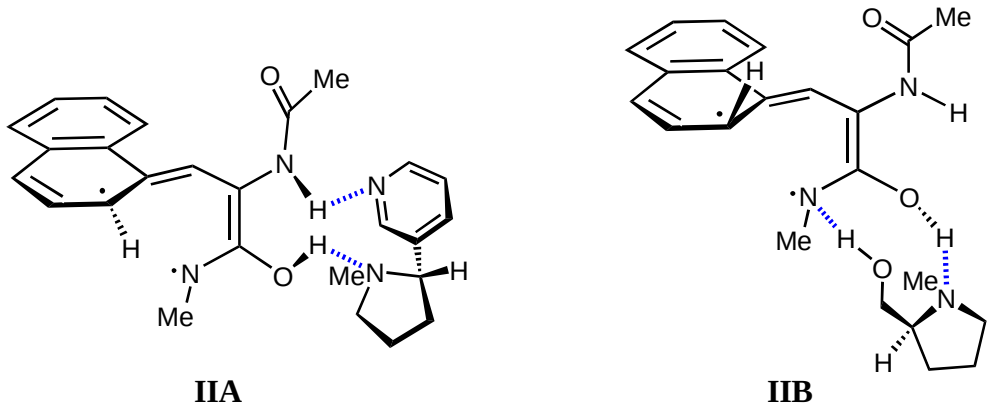
Temperature effects on the magnitude of asymmetric induction (de) in our previous studies showed that temperature exerts a great effect not only on the relative stability of diastereomeric enol-type biradical

intermediates but also on the ability of TEA to form hydrogen bonds to protic solvents as well as to these intermediates. As demonstrated in Table 1, a lowering of temperature in the NT-catalyzed asymmetric photocyclization of (*Z*)-**1a** in any solvents greatly enhanced ee for the corresponding (*S*)-**2a** with a considerable increase in the selectivity of this product, whereas ee for (*R*)-**2a** obtained in excess by the MPM-catalyzed asymmetric reaction was only slightly increased. This observation substantiates the participation of a different mode of hydrogen-bonding interaction between the given chiral amine and the biradical intermediate and also is consistent with the existence of the interaction of this amine with the solvent. Interestingly, an increase in the bulkiness of the substituent R attached to the amide nitrogen in (*Z*)-**1** showed a clear tendency to diminish the magnitude of ee for (*S*)-**2**, suggesting that the amide N–H hydrogen is involved in the hydrogen bonding formed between NT and the intermediate described above.



Scheme 2

Our attention is now directed to the mechanism of photoinduced electron transfer-initiated asymmetric cyclization for (*Z*)-**1**. We proposed in a previous study that the radical ion pair **I**, the enol-type biradical **II**, and the cyclized enol-type intermediate **III** are involved as key reaction intermediates (Scheme 2).[7b] It is well known that the amide N–H hydrogen and carbonyl oxygen act as hydrogen-bond donor and hydrogen-bond acceptor, respectively.[11a] Thus, a given chiral amine is considered to form a hydrogen bond to the amide N–H hydrogen and to exist in the neighborhood of the α-dehydronaphthylalaninamide derivative **1**.[11b] On the other hand, the previous result (that at the early stage of the photocyclization reaction the composition ratio of (*Z*)-**1** and (*E*)-**1** exhibits a negligible dependence on the TEA concentration) is consistent with the hypothesis that the (*Z*)-**1** radical anion is isomerized to its (*E*)-isomer to a negligible extent and, hence, the radical ion pair (*Z*)-**I** undergoes exclusive back electron transfer to regenerate (*Z*)-**1** and chiral amine (Scheme 2).[6d] Additionally, interconversion between **IIIA** and **IIIB** is very unlikely to occur during the asymmetric reaction, so that we were led to propose that the extent to which a given dynamic equilibrium is shifted to either **IIA** or **IIB** is a major factor governing the magnitude of ee for **2**. MM2 and PM5 calculations of the conformation of **III** derived from chiral auxiliary-substituted *N*-acetyl-α-dehydronaphthylalaninamide confirmed that steric repulsion between hydrogen at the 2-position in the hydronaphthalene ring and the auxiliary group determines the relative stabilities of **III** and its precursor **II**, and also controls the magnitude of asymmetric induction in the tautomerization of the former cyclized enol-type intermediate.[7b] In the absence of the chiral auxiliary group the chiral amines PA, MPM, and NT play the role of this group through hydrogen-bonding interactions with the enol hydroxy hydrogen, the acetylamino hydrogen, and the methylamino nitrogen in **II** and **III**. These interactions should assist the tautomerization in either the *re* or the *si* face of the latter intermediate to induce asymmetry at the 3-position in the dihydroquinolinone ring of **2**.



IIA **IIB**

Figure 1. Schematic illustration for hydrogen bonding interactions between the enol-type biradical **II** and the chiral amine NT (**IIA**) or MPM (**IIB**)

The fact that in the presence of NT and MPM (*S*)-**2** and (*R*)-**2** are produced in excess, respectively, reveals that at two different sites the former amine is preferentially hydrogen bonded to **IIA** in the *si* face and the latter to **IIB** in the *re* face, as depicted in Figure 1 (R = Me). These two-site hydrogen-bonding interactions of **IIA** with NT in the *si* face and of **IIB** with MPM in the *re* face are considered to greatly shift a given equilibrium to **IIA** and **IIB** to produce (*S*)-**2** and (*R*)-**2** in excess, respectively. The above considerations allow us to interpret a much less enantioselectivity for the **1a**/PA system in terms of less favorable two-site hydrogen-bonding interactions in this system (Table 1). As already described, there exist interactions of the chiral amines not only with the enol-type intermediates **II** and **III** but also with the solvent, depending on temperature. Thus, the observation of the higher ee value in 2-propanol than in dichloromethane, especially in the presence of NT at –78 °C, suggests that the protic solvent molecules are involved in additional hydrogen-bonding interactions with **IIA** and **IIB** so as to enhance the relative stability of the former enol-type biradical intermediate.

ACKNOWLEDGMENTS

This research was partially supported by a “Scientific Frontier Research Project” from the Ministry of Education, Sports, Culture, Science and Technology, Japan.

REFERENCES AND NOTES

1. a) ‘Synthetic Organic Photochemistry,’ ed. by W. M. Horspool, Plenum, New York, 1984; b) ‘Handbook of Photochemistry and Photobiology,’ Vol. 2, ed. by H. S. Nalwa, American Scientific Publishers, Stevenson Ranch, 2003; c) ‘Synthetic Organic Photochemistry,’ ed. by A. G. Griesbeck and J. Mattay, Marcel Dekker, New York, 2005; d) A. G. Griesbeck, N. Hoffmann, and K. Warzecha, *Acc. Chem. Res*., 2007, **40**, 128.
2. a) S. Kohmoto, Y. Miyaji, M. Tsuruoka, K. Kishikawa, M. Yamamoto, and K. Yamada, *J. Chem. Soc., Perkin Trans. 1*, 2001, 2082; b) P. Formentin, M. J. Sabater, M. N. Chretien, H. Garcia, and J. C. Scaiano, *J. Chem. Soc. Perkin Trans. 2*, 2002, 164; c) S. C. Shim, D. S. Kim, D. J. Yoo, T. Wada, and Y. Inoue, *J. Org. Chem*., 2002, **67**, 5718.
3. a) A. Joy, J. R. Scheffer, and V. Ramamurthy, *Org. Lett*., 2000, **2**, 119; b) J. R. Scheffer, *Can. J. Chem*., 2001, **79**, 349; c) L. S. Kaanumalle, J. Sivaguru, N. Arunkumar, S. Karthikeyan, and V. Ramamurthy, *Chem. Commun*., 2003, 116.
4. a) A. G. Griesbeck, W. Kramer, and J. Lex, *Angew. Chem. Int. Ed*., 2001, **40**, 577; b) S. Jones and J. C. C. Atherton, *Tetrahedron: Asymmetry*, 2001, **12**, 1117; c) T. Bach, H. Bergmann, B. Grosch, and K. Harms, *J. Am. Chem. Soc*., 2002, **124**, 7982; d) K. C. W. Chong, J. Sivaguru, T. Shichi, Y. Yoshimi, V. Ramamurthy, and J. R. Scheffer, *J. Am. Chem. Soc*., 2002, **124**, 2858.
5. a) A. G. Griesbeck and U. J. Meierhenrich, *Angew. Chem. Int. Ed*., 2002, **41**, 3147; b) ‘Chiral

Photochemistry', ed. by Y. Inoue and V. Ramamurthy, Marcel Dekker, New York, 2004; c) C. Müller and T. Bach, *Aust. J. Chem.*, 2008, **61**, 557; d) N. Hoffmann, *Chem. Rev.*, 2008, **108**, 1052.

6. a) F. D. Lewis, G. D. Reddy, D. M. Bassani, S. Schneider, and M. Gahr, *J. Am. Chem. Soc.*, 1994, **116**, 597; b) F. D. Lewis, D. M. Bassani, E. L. Burch, B. E. Cohen, J. A. Engleman, G. D. Reddy, S. Schneider, W. Jaeger, P. Gedeck, and M. Gahr, *J. Am. Chem. Soc.*, 1995, **117**, 660; c) K. Maekawa, T. Igarashi, K. Kubo, and T. Sakurai, *Tetrahedron*, 2001, **57**, 5515; d) K. Maekawa, A. Shinozuka, M. Naito, T. Igarashi, and T. Sakurai, *Tetrahedron*, 2004, **60**, 10293; e) K. Maekawa, T. Sasaki, K. Kubo, T. Igarashi, and T. Sakurai, *Tetrahedron Lett.*, 2004, **45**, 3663.
7. a) K. Maekawa, K. Kubo, T. Igarashi, and T. Sakurai, *Tetrahedron*, 2004, **60**, 1183; b) K. Maekawa, K. Kubo, T. Igarashi, and T. Sakurai, *Tetrahedron*, 2005, **61**, 11211.
8. a) R. Hoffmann and Y. Inoue, *J. Am. Chem. Soc.*, 1999, **121**, 10702; b) S. Asaoka, T. Wada, and Y. Inoue, *J. Am. Chem. Soc.*, 2003, **125**, 3008; c) A. Bauer, F. Westkämper, S. Grimme, and T. Bach, *Nature*, 2005, **436**, 1139.
9. K. Noda, Y. Shimohigashi, and N. Izumiya, 'The Peptides–Analysis, Synthesis, Biology,' Vol. 5 (Part B), ed. by E. Gross and J. Meienhofer, Academic Press, New York, 1983, pp. 305–308.
   Data for (*Z*)-**1a**: mp 190.0–190.5 °C (EtOH-hexane); IR (KBr) ν/cm^{-1} = 3340, 3236, 3180, 1644, 1628; ^{1}H NMR (500 MHz, DMSO-d_6) δ = 1.84 (3H, s), 2.72 (3H, d, J = 4.6 Hz), 7.51–7.58 (5H, m), 7.90 (1H, d, J = 8.3 Hz), 7.94–7.98 (2H, m), 8.04 (1H, q, J = 4.6 Hz), 9.24 (1H, s); ^{13}C NMR (125 MHz, DMSO-d_6) δ = 22.7, 26.2, 124.2, 124.2, 125.5, 126.0, 126.2, 126.3, 128.3, 128.4, 131.1, 131.3, 133.2, 132.5, 165.2, 169.5. Anal. Calcd for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44. Found: C, 71.49; H, 5.73; N, 10.31.
10. Data for (*E*)-**1a**: mp 167.5–168.5 °C (EtOAc-hexane); IR (KBr) ν/cm^{-1} = 3268, 1626, 1615; ^{1}H NMR (500 MHz, DMSO-d_6) δ = 2.02 (3H, s), 2.43 (3H, d, J = 4.9 Hz), 7.36 (1H, d, J = 6.7 Hz), 7.42 (1H, dd, J = 6.7, 7.3 Hz), 7.44 (1H, s), 7.53 (1H, dd, J = 6.7, 7.3 Hz), 7.56 (1H, dd, J = 6.7, 7.3 Hz), 7.78 (1H, q, J = 4.9 Hz), 7.79 (1H, d, J = 7.3 Hz), 7.91 (1H, d, J = 7.3 Hz), 8.00 (1H, d, J = 7.3 Hz), 9.75 (1H, s); ^{13}C NMR (125 MHz, DMSO-d_6) δ = 23.5, 25.7, 112.9, 124.4, 125.2, 125.4, 125.8, 126.0, 127.1, 128.3, 131.2, 132.5, 133.1, 134.7, 165.1, 168.6. Anal. Calcd for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44. Found: C, 71.50; H, 6.01; N, 10.32.
    Data for **2a**: mp 231.5–232.5 °C (EtOH-hexane); IR (KBr) ν/cm^{-1} = 3320, 1672, 1634; $[\alpha]_D^{25}$ = +105.4 [(*S*)-**2a**], –106.0 [(*R*)-**2a**] (*c* 0.5, MeOH); CD (4.0×10^{-5} mol dm^{-3}, MeOH) $[\theta]_{250}$ = –984 [(*S*)-**2a**], +1019 [(*R*)-**2a**]; ^{1}H NMR (500 MHz, DMSO-d_6) δ = 1.95 (3H, s), 3.01 (1H, dd, J = 14.7, 15.7 Hz), 3.41 (3H, s), 3.65 (1H, dd, J = 6.1, 15.7 Hz), 4.57 (1H, ddd, J = 6.1, 7.9, 14.7 Hz), 7.45 (1H, dd, J = 7.0, 7.9 Hz), 7.49 (1H, d, J = 8.9 Hz), 7.56 (1H, dd, J = 7.0, 7.9 Hz), 7.91 (1H, d, J = 7.9 Hz), 7.93 (1H, d, J = 8.9 Hz), 8.01 (1H, d, J = 7.9 Hz), 8.34 (1H, d, J = 7.9 Hz); ^{13}C NMR (125 MHz, DMSO-d_6) δ = 22.6, 26.8, 30.3, 48.0, 116.1, 117.6, 123.0, 124.5, 127.0, 128.0, 128.3, 129.6, 130.5,

137.1, 168.2, 169.3. Anal. Calcd for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44. Found: C, 71.52; H, 5.86; N, 10.41.

Data for **3a**: mp 135.0–136.0 °C (EtOAc-hexane); IR (KBr) ν/cm^{-1} = 3406, 1659; ^{1}H NMR (500 MHz, DMSO-d_6) δ = 2.94 (3H, d, J = 4.9 Hz), 3.03 (3H, s), 7.81–7.85 (2H, m), 8.11 (1H, d, J = 9.2 Hz), 8.12–8.14 (1H, m), 8.16 (1H, d, J = 9.2 Hz), 8.84 (1H, q, J = 4.9 Hz), 8.91–8.93 (1H, m), 9.11 (1H, s); ^{13}C NMR (125 MHz, DMSO-d_6) δ = 22.5, 26.0, 112.8, 122.7, 123.8, 126.1, 127.9, 128.6, 128.7, 129.0, 129.5, 132.8, 134.5, 144.3, 157.0, 164.7. Anal. Calcd for $C_{16}H_{14}N_2O$: C, 76.78; H, 5.64; N, 11.19. Found: C, 76.69; H, 5.71; N, 11.37.

Data for **4a**: mp 208.0–208.5 °C (EtOAc-hexane); IR (KBr) ν/cm^{-1} = 3316, 1680, 1605; ^{1}H NMR (500 MHz, DMSO-d_6) δ = 2.25 (3H, s), 3.88 (3H, s), 7.58 (1H, dd, J = 6.7, 7.3 Hz), 7.73 (1H, dd, J = 6.7, 8.5 Hz), 7.81 (1H, d, J = 9.2 Hz), 8.02 (1H, d, J = 7.3 Hz), 8.07 (1H, d, J = 9.2 Hz), 8.30 (1H, d, J = 8.5 Hz), 9.58 (1H, s), 9.61 (1H, s); ^{13}C NMR (125 MHz, DMSO-d_6) δ = 24.3, 30.7, 113.8, 115.3, 115.4, 121.5, 125.4, 127.8, 128.2, 128.7, 128.9, 129.1, 129.5, 134.0, 156.7, 170.1. Anal. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.47; H, 5.02; N, 10.63.

11. a) A. Fersht, 'Enzyme Structure and Mechanism,' 2nd ed, W. H. Freeman, New York, 1985, pp. 1–46; b) K. Miyoshi, K. Kubo, T. Sakurai, and H. Inoue, *Nippon Kagaku Kaishi*, 1999, 37.