Tetrahedron 65 (2009) 5676–5679

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Catalytic enantioselective conjugate addition of aromatic amines to fumarate derivatives: asymmetric synthesis of aspartic acid derivatives

Seung Hee Kang, Young Ku Kang, Dae Young Kim *

Department of Chemistry, Soonchunhyang University, Asan, Chungnam 336-745, Republic of Korea

ARTICLE INFO

Article history:
Received 20 April 2009
Received in revised form 15 May 2009
Accepted 16 May 2009
Available online 23 May 2009

Keywords:
Chiral palladium catalysts
Conjugate addition
Fumarates
Aspartic acids

ABSTRACT

The catalytic enantioselective conjugate addition of aromatic amines to fumarate derivatives promoted by chiral palladium complexes is described. Treatment of aniline derivatives with fumaryl pyrrolidinone as Michael acceptor under mild reaction conditions afforded the corresponding chiral aspartic acid derivatives with excellent enantiomeric excesses (83–96% ee).

1. Introduction

Aspartic acid derivatives are widely used as pharmaceuticals and fundamental synthetic building blocks for preparation of biologically valuable molecules.[1] The development of stereoselective synthetic methods for the preparation of natural and non-natural α-amino acid derivatives has attracted considerable attention over the past decades.[2] The most popular methods for the catalytic asymmetric synthesis of aspartic acid derivatives are C–C bond formation using chiral templates[3] and include the Mannich reaction[4] of chiral sulfinimines and Michael addition of aromatic amines with chiral Lewis acid.[5]

The catalytic enantioselective aza-Michael reaction[6] of aromatic amines to α,β-unsaturated carbonyl compounds was first investigated by Jørgensen et al.[7] The reaction of aniline with *N*-alkenoyl oxazolidinones proceeds well in the presence of Ni(II)–bisoxazoline complexes as the Lewis acid catalyst. In 2003, Togni reported the addition of aromatic amines to α,β-unsaturated compounds catalyzed by Ni-complexes coordinated by chiral tridendate phosphines.[8] Subsequently, Hii and Sodeoka groups reported the enantioselective addition of aromatic amines to α,β-unsaturated carbonyl compounds such as *N*-alkenoyl oxazolidinones or *N*-alkenoyl carbamates using cationic BINAP–palladium complexes.[9,10] Recently, Collin reported the aza-Michael addition of aromatic amines to furmaryl oxazolidinone catalyzed by chiral samarium iodobinaphtholate.[5]

2. Results and discussion

As part of a research program related to the development of synthetic methods for the enantioselective construction of stereogenic carbon centers,[11] we reported the catalytic enantioselective Michael reaction to α,β-unsaturated ketones[12] and α-hydrazination of active methines[13] promoted by chiral catalysts. We decided to study the asymmetric aza-Michael reaction of aromatic amines to fumarate derivatives affording chiral aspartic acid derivatives. To the best of our knowledge, there are no examples of asymmetric aza-Michael reaction of amines to fumarate derivatives in the presence of chiral palladium complexes.

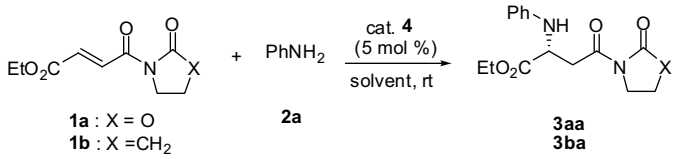
In this article, we wish to report the catalytic enantioselective conjugate addition of aromatic amines to fumarate derivatives in the presence of air- and moisture-stable chiral palladium complexes.[14]

A survey of some reaction parameters was performed, and some representative results are presented in Table 1. Our investigation began with the catalytic enantioselective conjugate addition of aniline (**2a**) to fumaryl oxazolidinone **1a** in toluene at room temperature in the presence of 5 mol % of dicationic palladium complexes **4** (Fig. 1). We surveyed the effect of structure of palladium complexes **4**. High yields with moderate to high enantioselectivities (29–83% ee) were observed for structurally variable palladium catalysts (entries 1–12). Under the standard reaction conditions, catalyst **4a** exhibited better enantioselectivity (81% ee, entry 1). Changing the substituent of the fumaryl functionality effects the rate of the

* Corresponding author. Tel.: +82 41 530 1244; fax: +82 41 530 1247.
E-mail address: dyoung@sch.ac.kr (D.Y. Kim).

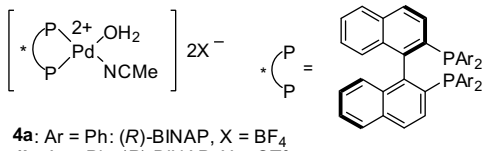
0040-4020/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2009.05.037

Table 1
Optimization of the reaction conditions



Entry	1	Cat. 4	Solvent	Time (h)	Yield[a] (%)	ee[b] (%)
1	**1a**	**4a**	Toluene	74	**3aa**, 90	81
2	**1a**	**4b**	Toluene	80	**3aa**, 94	80
3	**1a**	**4c**	Toluene	82	**3aa**, 91	75
4	**1a**	**4d**	Toluene	82	**3aa**, 90	61
5	**1a**	**4e**	Toluene	3 d	**3aa**, 95	80
6	**1a**	**4f**	Toluene	3 d	**3aa**, 92	78
7	**1a**	**4g**	Toluene	3 d	**3aa**, 96	69
8	**1a**	**4h**	Toluene	3 d	**3aa**, 90	51
9	**1a**	**4i**	Toluene	6 d	**3aa**, 91	53
10	**1a**	**4j**	Toluene	8 d	**3aa**, 97	34
11	**1a**	**4k**	Toluene	6 d	**3aa**, 94	29
12	**1a**	**4l**	Toluene	5 d	**3aa**, 90	33
13	**1b**	**4a**	Toluene	24	**3ba**, 91	87
14	**1b**	**4e**	Toluene	24	**3ba**, 90	85
15	**1b**	**4i**	Toluene	20	**3ba**, 91	85
16	**1b**	**4a**	*p*-Xylene	15	**3ba**, 91	93
17	**1b**	**4a**	Benzene	7	**3ba**, 94	87
18	**1b**	**4a**	Hexane	14	**3ba**, 90	77
19	**1b**	**4a**	THF	50	**3ba**, 71	93
20	**1b**	**4a**	DCM	47	**3ba**, 50	93
21	**1b**	**4a**	MeOH	80	**3ba**, 0	—

[a] Yield of isolated product.
[b] Enantiopurity of **3** was determined by HPLC analysis using Whelk-O1 (for **3aa**) and Chiralpak AD-H (for **3ba**) columns.



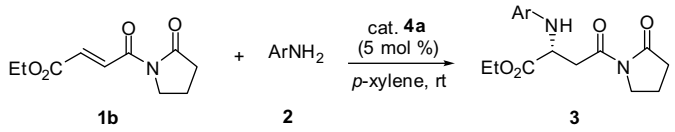
4a: Ar = Ph: (*R*)-BINAP, X = BF_4
4b: Ar = Ph: (*R*)-BINAP, X = OTf
4c: Ar = Ph: (*R*)-BINAP, X = PF_6
4d: Ar = Ph: (*R*)-BINAP, X = SbF_6
4e: Ar = 4-Me-C_6H_4: (*R*)-Tol-BINAP, X = BF_4
4f: Ar = 4-Me-C_6H_4: (*R*)-Tol-BINAP, X = OTf
4g: Ar = 4-Me-C_6H_4: (*R*)-Tol-BINAP, X = PF_6
4h: Ar = 4-Me-C_6H_4: (*R*)-Tol-BINAP, X = SbF_6
4i: Ar = 3,5-Me_2-C_6H_3: (*R*)-Xylyl-BINAP, X = BF_4
4j: Ar = 3,5-Me_2-C_6H_3: (*R*)-Xylyl-BINAP, X = OTf
4k: Ar = 3,5-Me_2-C_6H_3: (*R*)-Xylyl-BINAP, X = PF_6
4l: Ar = 3,5-Me_2-C_6H_3: (*R*)-Xylyl-BINAP, X = SbF_6

Figure 1. Structures of chiral palladium catalysts.

reaction and enantioselectivities (entries 1 and 13). Fumaryl pyrrolidinone **1b**[15] was found to be a superior Michael acceptor in terms of reaction time and enantioselectivity. Next, we examined the reaction in various solvents. Reactions performed in non-polar solvents such as *p*-xylene, THF and dichloromethane generally afforded better results in terms of enantioselectivities (entries 13 and 16–21). No reaction occurred in MeOH. From these observations, we choose the *p*-xylene as solvent of choice in further studies. The absolute configuration of **3aa** was established by comparison of the optical rotation and chiral HPLC analysis with previously reported values.[5]

To examine the generality of the addition of aromatic amines **2** to fumaryl pyrrolidinone **1b** in the presence of chiral palladium catalyst **4a**, we studied the aza-Michael reaction of other aniline derivatives **2b**–**2f**. As it can be seen by the results summarized in Table 2, the corresponding aspartic acid derivatives **3** were obtained in high to excellent yields with enantioselectivities (83–96% ee). We examined

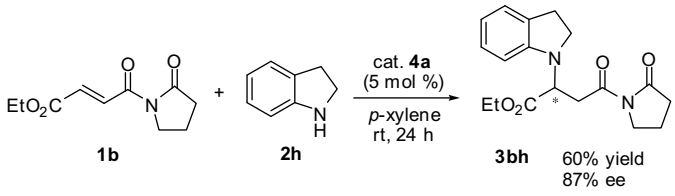
Table 2
Catalytic enantioselective conjugate addition of aromatic amines to fumarates



Entry	2, Ar	Time (h)	Yield[a] (%)	ee[b] (%)
1	**2a**, Ph	15	**3ba**, 91	93 (*R*)[c]
2	**2b**, *p*-EtO_2C–Ph	24	**3bb**, 90	95
3	**2c**, *p*-*n*-BuO_2C–Ph	20	**3bc**, 95	96
4	**2d**, *p*-Cl–Ph	15	**3bd**, 92	91
5	**2e**, *p*-Et–Ph	12	**3be**, 95	89
6	**2f**, *m*-CF_3–Ph	12	**3bf**, 80	83
7	**2g**, *p*-OMe–Ph	12	**3bg**, 81	83

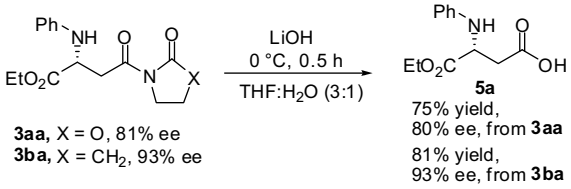
[a] Yield of isolated product.
[b] Enantiopurity of **3** was determined by HPLC analysis using Chiralpak AD-H (for **3ba**, **3bc**, **3bd**, **3be**, **3bf**, and **3bg**) and Chiralcel OD-H (for **3bb**) columns.
[c] Absolute configuration was determined by comparison of the optical rotation and the chiral HPLC data of the corresponding hydrolyzed mono-ethyl ester **5a**.[5].

the conjugate addition of secondary aromatic amines **2h** to fumaryl pyrrolidinone **1b** using chiral palladium catalyst **4a** at room temperature. In the presence of 5 mol % of catalyst **4a**, the aza-Michael reaction proceeded to afford the α-amino acid **3bh** after 24 h with 87% ee (Scheme 1). In contrast, the conjugate addition of secondary amines such as piperidine and pyrrolidine proceeded with excellent yields (>95%) but at much lower enantioselectivties of between 13 and 10% ee after 6 h at room temperature.



Scheme 1.

Finally, the pyrrolidinone-derived products of these reactions were readily converted to the corresponding *N*-phenyl aspartic acid mono-ethyl esters. Product **3** was hydrolyzed by employing LiOH at 0 °C, affording *N*-phenyl aspartic acid mono-ethyl esters **5a** without loss of enantioselectivity (Scheme 2).



Scheme 2.

3. Conclusion

In conclusion, we have developed an efficient catalytic aza-Michael reaction of aromatic amines using air- and moisture-stable chiral palladium complexes. The desired aspartic acid derivatives were obtained in excellent yields (80–95%) with enantioselectivities (83–96% ee). We believe that this synthetic method provides an efficient route for the preparation of chiral aspartic acid derivatives, and the availability of these compounds should facilitate medicinal chemical studies in various fields. Further details and application of this aza-Michael reaction will be presented in due course.

4. Experimental section

4.1. General

All reactions were performed under an atmosphere of nitrogen in oven-dried glassware with magnetic stirring and monitored by analytical thin layer chromatography (TLC) using Merck precoated silica gel plates with F_{254} indicator. Visualization on TLC was achieved by use of UV light (254 nm) and treatment with phosphomolybdic acid stain followed by heating. Dry tetrahydrofuran (THF) was freshly distilled from Ph_2CO–Na. Other solvents were purified by usual methods. Visualization was accomplished by UV light (254 nm), I_2, *p*-anisaldehyde, ninhydrin, and phosphomolybdic acid, solution as an indicator. Purification of reaction products was carried out by flash chromatography using E. Merck silica gel 60 (230–400 mesh). ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AC 200 (200 MHz for ^{1}H, 50 MHz for ^{13}C). Chemical shift values (δ) are reported in parts per million relative to Me_4Si (δ 0.0 ppm). The proton spectra are reported as follows δ (multiplicity, coupling constant *J*, number of protons). Multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br (broad). Mass spectra were measured on Sciex API-2000 and Jeol HX110/110A using electrospray ionization technique. Optical rotations were measured on a JASCO-DIP-1000 digital polarimeter with a sodium lamp. Melting points were determined using an electrothermal apparatus. The enantiomeric excesses (ee's) were determined by HPLC. HPLC analysis was performed on Younglin M930 Series and Younglin M720 Series, measured at 254 nm using the indicated chiral column. Fumaryl derivatives **1**[15,16] and chiral palladium complexes **4**[9,14] were prepared by previous reports.

4.2. General procedure for the aza-Michael reaction of aromatic amines 2 to fumaryl pyrrolidinone 1b

To a stirred solution of fumaryl pyrrolidinone **1b** (317 mg, 1.5 mmol) and catalyst **4a** (48 mg, 0.05 mmol) in *p*-xylene (5 mL) was added the aromatic amine **2** (1.0 mmol) dropwise at room temperature. Reaction mixture was stirred for 12–24 h, concentrated, and purified by flash chromatography (silica gel, ethyl acetate/hexane=1/2) to afford the β-amino *N*-acylpyrrolidinones **3**.

*4.2.1. (R)-Ethyl 4-oxo-4-(2-oxopyrrolidin-1-yl)-2-phenylaminobutanoate (**3ba**)*

$[\alpha]_D^{24}$ −1.9 (*c* 1.0, $CHCl_3$) for 93% ee; ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.19–7.06 (m, 2H), 6.72–6,64 (m, 3H), 4.70–4.41 (m, 2H), 4.18 (q, *J*=7.4 Hz, 2H), 3.75 (t, *J*=7.8 Hz, 2H), 3.66–3.38 (m, 2H), 2.54 (t, *J*=7.8 Hz, 2H), 2.05–1.9 (m, 2H), 1.22 (t, *J*=7.3 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ=175.5, 172.4, 170.9, 146.4, 129.1, 117.6, 113.5, 61.3, 52.8, 45.1, 39.4, 33.2, 16.9, 13.9; ESI-HRMS: *m*/*z* calcd for $C_{16}H_{21}N_2O_4$ $[M+H]^+$: 305.1501; found: 305.1498; HPLC (AD-H, *n*-hexane/2-propanol: 80/20) 1.0 mL/min, 254 nm, t_R=25.4 min (major), t_R=32.0 min (minor).

*4.2.2. Ethyl 4-(4-ethoxy-1,4-dioxo-1-(2-oxopyrrolidin-1-yl)butan-2-ylamino)benzoate (**3bb**)*

Mp: 119.5–121 °C; $[\alpha]_D^{25}$−3.9 (*c* 1.0, $CHCl_3$) for 95% ee; ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.89–7.85 (m, 2H), 6.65–6.60 (m, 2H), 4.99 (d, *J*=8.7 Hz, 1H), 4.59–4.49 (m, 1H), 4.31 (q, *J*=7.0 Hz, 2H), 4.21 (q, *J*=7.0 Hz, 2H), 3.79 (t, *J*=7.0 Hz, 2H), 3.65–3.41 (m, 2H), 2.59 (t, *J*=7.9 Hz, 2H), 2.11–1.96 (m, 2H), 1.35 (t, *J*=6.9 Hz, 3H), 1.25 (t, 3H, *J*=7.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ=175.6, 171.7, 170.8, 166.5, 150.2, 131.3, 119.5, 112.0, 61.5, 60.1, 51.9, 45.1, 39.2, 33.2, 17.0, 14.3, 13.9; ESI-HRMS: *m*/*z* calcd for $C_{19}H_{25}N_2O_6$ $[M+H]^+$: 377.1713; found: 377.1716; HPLC (OD-H, *n*-hexane/2-propanol: 80/20) 1.0 mL/min, 254 nm, t_R=23.7 min (major), t_R=32.6 min (minor).

*4.2.3. Butyl 4-(4-ethoxy-1,4-dioxo-1-(2-oxopyrrolidin-1-yl)butan-2-ylamino)benzoate (**3bc**)*

$[\alpha]_D^{26}$−7.1 (*c* 1.0, $CHCl_3$) for 96% ee; ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.89–7.85 (m, 2H), 6.65–6.61 (m, 2H), 5.0 (d, *J*=8.5 Hz, 1H), 4.59–4.49 (m, 1H), 4.29–4.09 (m, 4H), 3.79 (t, *J*=7.2 Hz, 2H), 3.65–3.37 (m, 2H), 2.59–2.47 (t, *J*=8.1 Hz, 2H), 2.11–1.96 (m, 2H), 1.78–1.65 (m, 2H), 1.55–1.36 (m, 2H), 1.26 (t, *J*=8 Hz, 3H), 0.96 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ=175.4, 171.5, 170.6, 166.3, 150.1, 131.1, 119.2, 111.8, 63.8, 61.3, 51.7, 44.9, 39.0, 33.0, 30.5, 18.9, 16.8, 13.7, 13.4; ESI-HRMS: *m*/*z* calcd for $C_{21}H_{29}N_2O_6$ $[M+H]^+$: 405.2026; found: 405.2025; HPLC (AD-H, *n*-hexane/2-propanol: 80/20) 1.0 mL/min, 254 nm, t_R=52.2 min (major), t_R=79.5 min (minor).

*4.2.4. Ethyl 2-(4-chlorophenylamino)-4-oxo-4-(2-oxopyrrolidin-1-yl)butanoate (**3bd**)*

$[\alpha]_D^{24}$−13.0 (*c* 1.0, $CHCl_3$) for 91% ee; ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.14–7.10 (m, 2H), 6.63–6.58 (m, 2H), 4.51–4.44 (m, 2H), 4.19 (q, *J*=7.0 Hz, 2H), 3.79 (t, *J*=7.2 Hz, 2H), 3.62–3.37 (m, 2H), 2.60 (t, *J*=7.9 Hz, 2H), 2.11–1.96 (m, 2H) 1.24 (t, *J*=7.0 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ=175.2, 171.9, 170.6, 144.8, 128.7, 122.6, 114.4, 61.1, 52.7, 44.9, 39.0, 33.0, 16.67, 13.7; ESI-HRMS: *m*/*z* calcd for $C_{16}H_{20}ClN_2O_4$ $[M+H]^+$: 339.1112; found: 339.1109; HPLC (AD-H, *n*-hexane/2-propanol: 80/20) 1.0 mL/min, 254 nm, t_R=32.9 min (major), t_R=53.8 min (minor).

*4.2.5. Ethyl 2-(4-ethylphenylamino)-4-oxo-4-(2-oxopyrrolidin-1-yl)butanoate (**3be**)*

$[\alpha]_D^{26}$−3.8 (*c* 1.0, $CHCl_3$) for 89% ee; ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.03–6.98 (m, 2H), 6.64–6.60 (m, 2H), 4.46–4.43 (m, 2H), 4.19 (q, *J*=7.1 Hz, 2H), 3.78 (t, *J*=7.2 Hz, 2H), 3.61–3.38 (m, 2H), 2.62–2.47 (m, 4H), 2.09–1.98 (m, 2H), 1.27–1.13 (m, 6H); ^{13}C NMR (50 MHz, $CDCl_3$): δ=175.4, 172.6, 171.1, 144.3, 134.2, 128.4, 114.5, 61.2, 53.3, 45.1, 39.5, 33.2, 28.1, 17.0, 15.7, 13.1; ESI-HRMS: *m*/*z* calcd for $C_{18}H_{25}N_2O_4$ $[M+H]^+$: 333.1814; found: 333.1816; HPLC (AD-H, *n*-hexane/2-propanol: 80/20) 1.0 mL/min, 254 nm, t_R=23.9 min (major), t_R=30.8 min (minor).

*4.2.6. Ethyl 2-(3-trifluoromethylphenylamino)-4-oxo-4-(2-oxopyrrolidin-1-yl)butanoate (**3bf**)*

Mp: 96–97.5 °C; $[\alpha]_D^{24}$ −7.0 (*c* 1.0, $CHCl_3$) for 83% ee; ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.30–7.22 (m, 1H), 6.98–6.79 (m, 3H), 4.74 (d, *J*=8.7 Hz, 1H), 4.54–4.45 (m, 1H), 4.20 (q, *J*=7.2 Hz, 2H), 3.79 (t, *J*=7.2 Hz, 2H), 3.65–3.38 (m, 2H) 2.60 (t, *J*=8.1 Hz, 2H), 2.11–1.96 (m, 2H), 1.24 (t, *J*=7 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ=175.6, 171.9, 170.7, 146.8, 131.2 (q, *J*=31.5 Hz), 129.5, 124.1 (q, *J*=270 Hz), 115.9, 114.4, 119.1, 61.4, 52.4, 45.1, 39.3, 33.1, 16.9, 13.8; ESI-HRMS: *m*/*z* calcd for $C_{17}H_{20}F_3N_2O_4$ $[M+H]^+$: 373.1375; found: 373.1372; HPLC (AD-H, *n*-hexane/2-propanol: 80/20) 1.0 mL/min, 254 nm, t_R=14.7 min (major), t_R=20.5 min (minor).

*4.2.7. Ethyl 2-(4-methoxyphenylamino)-4-oxo-4-(2-oxopyrrolidin-1-yl)butanoate (**3bg**)*

$[\alpha]_D^{24}$−13.4 (*c* 1.1, $CHCl_3$) for 83% ee; ^{1}H NMR (200 MHz, $CDCl_3$): δ=6.71–6.67 (m, 2H), 6.61–6.57 (m, 2H), 4.33–4.31 (m, 1H), 4.17–4.12 (m, 1H), 4.10 (q, *J*=6.8 Hz, 2H), 3.71 (t, *J*=7.1 Hz, 2H), 3.65 (s, 3H), 3.52–3.24 (m, 2H), 2.50 (t, *J*=8.2 Hz, 2H), 1.98–1.90 (m, 2H), 1.15 (t, *J*=6.8 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ=175.5, 172.8, 171.2, 152.8, 140.7, 115.6, 114.7, 61.3, 55.6, 54.4, 45.2, 39.2, 33.4, 17.1, 14.0; ESI-HRMS: *m*/*z* calcd for $C_{17}H_{23}N_2O_5$ $[M+H]^+$: 335.1607; found: 335.1605; HPLC (AD-H, *n*-hexane/*iso*-propanol: 80/20) 1.0 mL/min, 254 nm, t_R=30.5 min (major), t_R=42.4 min (minor).

*4.2.8. Ethyl 3-(indolin-1-yl)-4-oxo-4-(2-oxopyrrolidin-1-yl)butanoate (**3bh**)*

$[\alpha]_D^{24}$ +64.7 (*c* 1.0, $CHCl_3$) for 89% ee; ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.06–6.99 (m, 2H), 6.68–6.52 (m, 2H), 4.87–4.80 (m, 1H), 4.14 (q,

J=7.0 Hz, 2H), 3.83–3.17 (m, 6H), 2.96 (t, J=8.3 Hz, 2H), 2.59 (t, J=8.0 Hz, 2H), 2.10–1.95 (m, 2H), 1.17 (t, J=7.1 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ=175.2, 171.1, 170.4, 148.4, 129.3, 126.8, 124.2, 117.7, 106.9, 60.1, 54.4, 48.9, 45.1, 35.0, 33.2, 28.0, 16.8, 13.9; ESI-HRMS: m/z calcd for $C_{18}H_{23}N_2O_4$ $[M+H]^+$: 331.1658; found: 331.1655; HPLC (AD-H, n-hexane/2-propanol: 80/20) 1.0 mL/min, 254 nm, t_R=9.4 min (major), t_R=11.5 min (minor).

*4.2.9. (R)-4-Ethoxy-4-oxo-3-(phenylamino)butanoic acid (**5a**)*

$[\alpha]_D^{26}$ +8.6 (c 1.0, $CHCl_3$) for 85% ee; ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.44 (br, 2H), 7.22–7.14 (m, 2H), 6.81–6.65 (m, 3H), 4.46–4.40 (m, 1H), 4.19 (q, J=7.0 Hz, 2H), 2.91–2.83 (m, 2H), 1.95 (t, J=7.0 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ=176.2, 172.2, 146.0, 130.9, 119.0, 114.0, 61.7, 53.4, 37.1, 14.0; HPLC (AD-H, n-hexane/2-propanol: 80/20) 1.0 mL/min, 254 nm, t_R=11.7 min (minor), t_R=12.4 min (major).

Acknowledgements

This research was financially supported by the Ministry of Education, Science, Technology (MEST) and Korea Industrial Technology Foundation (KOTEF) through the Human Resource Training Project for Regional Innovation.

References and notes

1. (a) Iijima, K.; Katada, J.; Hayashi, Y. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 413; (b) Petrov, V. I.; Sergeev, V. S.; Onishchenko, N. V.; Piotrovskii, L. B. *Bull. Exp. Biol. Med.* **2001**, 342; (c) Bai, R. L.; Verdier-Pinard, P.; Gangwar, S.; Stessman, C. C.; McClure, K. J.; Sausville, E. A.; Pettit, G. R.; Bates, R. B.; Hamel, E. *Mol. Pharmacol.* **2001**, *59*, 462; (d) Peris, G.; Jakobsche, C. E.; Miller, S. J. *J. Am. Chem. Soc.* **2007**, *129*, 8710; (e) Xiong, X.-B.; Mahmud, A.; Uludag, H.; Lavasanifar, A. *Biomacromolecules* **2007**, *8*, 874.
2. Reviews on synthesis of α-amino acids, see: (a) Duthaler, R. O. *Tetrahedron* **1994**, *50*, 1539; (b) Arend, M. *Angew. Chem., Int. Ed.* **1999**, *38*, 2873; (c) Kotha, S. *Acc. Chem. Res.* **2003**, *36*, 342; (d) Najera, C.; Sansano, J. M. *Chem. Rev.* **2007**, *107*, 4584; Reviews on synthesis of β-amino acids, see: (e) Juaristi, E. *Enantioselective Synthesis of β-Amino Acids*; Wiley-VCH: New York, NY, 1997; (f) Cardillo, G.; Tomasini, C. *Chem. Soc. Rev.* **1996**, *25*, 117; (g) Liu, M.; Sibi, M. P. *Tetrahedron* **2002**, *58*, 7991; (h) Seebach, D.; Beck, A. K.; Capone, S.; Deniau, G.; Groselj, U.; Zass, E. *Synthesis* **2009**, 1.
3. (a) Ender, D.; Schankat, J.; Klatt, M. *Synlett* **1994**, 795; (b) Takatori, K.; Nichihara, M.; Kajiwara, M. *J. Labelled Compd. Radiopharm.* **1999**, *42*, 701; (c) Alvarez-Ibarra, C.; Casky, A.; Maroto, R.; Quiroga, M. L. *J. Org. Chem.* **1995**, *60*, 7934; (d) Burtin, G.; Corringer, P.-J.; Young, D. W. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3451; (e) Rees, D. O.; Bushby, N.; Harding, J. R.; Song, C.; Willis, C. *J. Labelled Compd. Radiopharm.* **2007**, *50*, 399.
4. Jacobsen, M. F.; Skrydstrup, T. *J. Org. Chem.* **2003**, *68*, 7112.
5. (a) Reboule, I.; Gil, R.; Collin, J. *Tetrahedron: Asymmetry* **2005**, *16*, 3881; (b) Reboule, I.; Gil, R.; Collin, J. *Eur. J. Org. Chem.* **2008**, 532.
6. (a) Xu, L.-W.; Xia, C.-G. *Eur. J. Org. Chem.* **2005**, 633; (b) Davies, S. G.; Smith, A. D.; Price, P. D. *Tetrahedron: Asymmetry* **2005**, *16*, 2833; (c) Hong, S.; Marks, T. J. *Acc. Chem. Res.* **2004**, *37*, 673; (d) Sibi, M. P.; Manyem, S. *Tetrahedron* **2000**, *56*, 8033.
7. Zhuang, W.; Hazell, R. G.; Jørgensen, K. A. *Chem. Commun.* **2001**, 1240.
8. Fadini, L.; Togni, A. *Chem. Commun.* **2003**, 30.
9. (a) Li, K.; Hii, K. K. *Chem. Commun.* **2003**, 1132; (b) Li, K.; Cheng, X.; Hii, K. K. *Eur. J. Org. Chem.* **2004**, 959; (c) Phua, P. H.; de Vries, J. G.; Hii, K. K. *Adv. Synth. Catal.* **2005**, *347*, 1775; (d) Phua, P. H.; White, A. J. P.; de Vries, J. G.; Hii, K. K. *Adv. Synth. Catal.* **2006**, *348*, 587; (e) Phua, P. H.; Mathew, S. P.; White, A. J. P.; de Vries, J. G.; Blackmond, D. G.; Hii, K. K. *Chem.—Eur. J.* **2007**, *13*, 4602.
10. Hamashima, Y.; Somei, H.; Shimura, Y.; Tamura, T.; Sodeoka, M. *Org. Lett.* **2004**, *6*, 1861.
11. (a) Kim, D. Y.; Park, E. J. *Org. Lett.* **2002**, *4*, 545; (b) Park, E. J.; Kim, M. H.; Kim, D. Y. *J. Org. Chem.* **2004**, *69*, 6897; (c) Kim, H. R.; Kim, D. Y. *Tetrahedron Lett.* **2005**, *46*, 3115; (d) Kang, Y. K.; Cho, M. J.; Kim, S. M.; Kim, D. Y. *Synlett* **2007**, 1135; (e) Kang, Y. K.; Kim, D. Y. *Bull. Korean Chem. Soc.* **2008**, *29*, 2093; (f) Lee, N. R.; Kim, S. M.; Kim, D. Y. *Bull. Korean Chem. Soc.* **2009**, *30*, 829.
12. (a) Kim, D. Y.; Huh, S. C.; Kim, S. M. *Tetrahedron Lett.* **2001**, *42*, 6299; (b) Kim, D. Y.; Huh, S. C. *Tetrahedron* **2001**, *57*, 8933; (c) Kim, D. Y.; Choi, Y. J.; Park, H. Y.; Joung, C. U.; Koh, K. O.; Mang, J. Y.; Jung, K. Y. *Synth. Commun.* **2003**, *33*, 435.
13. (a) Kang, Y. K.; Kim, D. Y. *Tetrahedron Lett.* **2006**, *47*, 4565; (b) Lee, J. H.; Bang, H. T.; Kim, D. Y. *Synlett* **2008**, 1821; (c) Kim, S. M.; Lee, J. H.; Kim, D. Y. *Synlett* **2008**, 2659; (d) Jung, S. H.; Kim, D. Y. *Tetrahedron Lett.* **2008**, *49*, 5527; (e) Kim, D. Y. *Bull. Korean Chem. Soc.* **2008**, *29*, 2036; (f) Mang, J. Y.; Kim, D. Y. *Bull. Korean Chem. Soc.* **2008**, *29*, 2091; (g) Mang, J. Y.; Kwon, D. G.; Kim, D. Y. *J. Fluorine Chem.* **2009**, *130*, 259; (h) Mang, J. Y.; Kwon, D. G.; Kim, D. Y. *Bull. Korean Chem. Soc.* **2009**, *30*, 249.
14. (a) Li, K.; Horton, P. N.; Hursthouse, M. B.; Hii, K. K. *J. Organomet. Chem.* **2003**, *665*, 250; (b) Kim, S. M.; Kim, H. R.; Kim, D. Y. *Org. Lett.* **2005**, *7*, 2309; For an aquapalladium complex, see: (c) Shimada, T.; Bajracharya, G. B.; Yamamoto, Y. *Eur. J. Org. Chem.* **2005**, 59 and references cited therein; (d) Vicente, J.; Arcas, A. *Coord. Chem. Rev.* **2005**, *249*, 1135.
15. Pyrrolidinone-derived enoates as Michael acceptor, see: (a) Sibi, M. P.; Liu, M. *Org. Lett.* **2000**, *2*, 3393; (b) Guerin, D. J.; Miller, S. J. *J. Am. Chem. Soc.* **2002**, *124*, 2134.
16. (a) Evans, D. A.; Miller, S. J.; Leckta, T.; Vonmatt, P. *J. Am. Chem. Soc.* **1999**, *121*, 7559; (b) Ho, G.-J.; Mathre, D. J. *J. Org. Chem.* **1995**, *60*, 2271.