CHEMISTRY
AN ASIAN JOURNAL

DOI: 10.1002/asia.200600093

Chiral Scandium Catalysts for Enantioselective Michael Reactions of β-Ketoesters

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Abstract: A highly enantioselective Michael reaction of β-ketoesters with α,β-unsaturated ketones promoted by a chiral scandium catalyst has been developed. In the presence of $Sc(OTf)_3$ and (*S*,*S*)-6,6′-bis(1-hydroxy-2,2′-dimethylpropyl)-2,2′-bipyridine, the desired Michael reactions proceeded smoothly in dichloroethane at 40 °C to afford the corresponding adducts in good to high yields with excellent enantioselectivities in most cases. It was found in this reaction that a lower concentration of the reaction mixture was key to attaining high enantioselectivities.

Keywords: addition reactions · asymmetric catalysis · Lewis acids · homogeneous catalysis · scandium

Introduction

Michael reactions of 1,3-dicarbonyl compounds are among the most fundamental and important carbon–carbon bond-forming reactions.[1] Recent interest in this reaction has focused on the development of a catalytic enantioselective version for the synthesis of optically active 1,5-dicarbonyl compounds.[2] Although several chiral catalysts for this reaction, such as chiral bases,[3] chiral crown ethers with metals,[4] and chiral transition-metal complexes,[5,6] including bimetallic systems,[7] have been reported, chemical yields, stereoselectivities, catalyst loading, and so on are not yet satisfactory in some cases. Furthermore, the lack of substrate generality is a serious issue in catalytic asymmetric Michael reactions in many cases, and the development of more-efficient and powerful catalysts is strongly desired.

Recently our group has been interested in the use of scandium Lewis acids in organic synthesis.[8] Scandium is expected to have the strongest Lewis acidity among rare-earth metals, is compatible with water and Lewis bases, and is regarded as one of the standard and, more importantly, environmentally benign Lewis acids. After the first report on a chiral scandium catalyst,[9] several enantioselective reactions with such catalysts were developed in organic solvents or even in aqueous media.[10] In the course of our investigations to develop efficient asymmetric catalysis, we found an effective scandium catalyst for Michael reactions. Herein we describe a chiral scandium catalyst for highly enantioselective Michael reactions of β-ketoesters with α,β-unsaturated ketones.

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Results and Discussion

Nakajima et al. reported a combination of $Sc(OTf)_3$ and a chiral biquinoline *N*,*N*′-dioxide as a chiral scandium catalyst for Michael reactions.[11] Although the unique chirality of the dioxide is utilized elegantly in combination with the scandium Lewis acid, the enantioselectivity and substrate scope were not satisfactory.

We recently found that the combination of $Sc(OTf)_3$ with a chiral bipyridine ligand was effective for the enantioselective hydroxymethylation of silicon enolates with an aqueous solution of formaldehyde.[12] Encouraged by the results, we decided to apply this chiral catalyst to Michael reactions of 1,3-dicarbonyl compounds. As $Sc(OTf)_3$ and chiral bipyridine **1**[13] are not completely soluble in dichloromethane, we first combined $Sc(OTf)_3$ (5 mol %) and **1** (7.5 mol %) in CH_3CN at 30 °C for 30 min (the system was completely soluble), and the solvent was removed under reduced pressure. β-Ketoester **2a** was then allowed to react with methyl vinyl ketone (MVK) in dichloromethane at 10 °C to afford the corresponding Michael adduct in 22 % yield with 53 % *ee* (Table 1, entry 1). Interestingly, the chemical yield and the enantioselectivity improved when the reactions were con-

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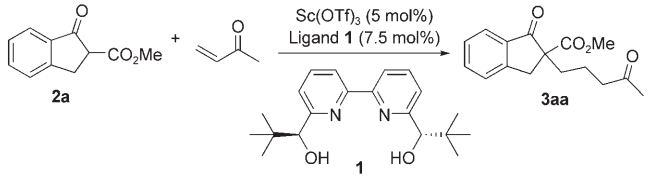
ducted at higher temperatures (Table 1, entries 2 and 3). As for solvents, dichloroethane gave slightly better enantiomeric excesses, whereas toluene and a mixed solvent of CH_3CN

Table 1. Optimization of reaction conditions.[a]



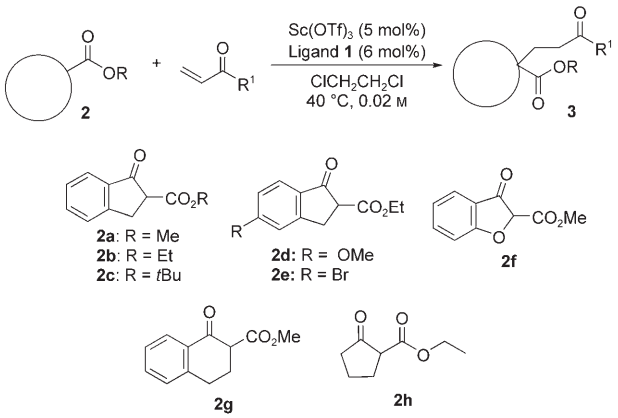
Entry	Conditions	Yield[b] [%]	ee[c] [%]
1	CH_2Cl_2, 10 °C, 0.08 M, 72 h	22	53
2	CH_2Cl_2, 20 °C, 0.08 M, 72 h	61	80
3	CH_2Cl_2, 30 °C, 0.08 M, 72 h	98	81
4	$ClCH_2CH_2Cl$, 30 °C, 0.08 M, 72 h	94	84
5	toluene, 10 °C, 0.08 M, 40 h	quant.	5
6	CH_3CN/CH_2Cl_2 (3/5.2), 30 °C, 0.08 M, 72 h	76	8
7	$ClCH_2CH_2Cl$, 30 °C, 0.04 M, 72 h	96	89
8	$ClCH_2CH_2Cl$, 60 °C, 0.04 M, 24 h	92	91
9	$ClCH_2CH_2Cl$, 30 °C, 0.02 M, 69 h	97	94
10	$ClCH_2CH_2Cl$, 30 °C, 0.02 M, 50 h	94	92

[a] The catalyst was prepared from $Sc(OTf)_3$ and **1** in CH_3CN at 30 °C for 0.5 h and the solvent was removed under reduced pressure, except for entry 10. In entry 10, the catalyst was prepared from $Sc(OTf)_3$ (5 mol %) and **1** (6 mol %) in dichloroethane at 60 °C for 1 h, to which the substrates were added without removal of the solvent. [b] Yield of isolated product after silica-gel chromatography. [c] The *ee* values were determined by chiral HPLC analysis.

and dichloromethane showed poor selectivities. Remarkably, concentration of the reaction mixture was found to influence the enantioselectivity significantly, and we were delighted to find that the desired adduct was obtained in 96 % yield with 89 % *ee* at lower concentrations (0.04 M) (Table 1, entry 7). The yield and the enantioselectivity improved further at lower concentration (Table 1, entry 9). Finally, more-practical conditions, use of dichloroethane for both the preparation of the catalyst and the reaction, and lower loading of chiral bipyridine **1** (6 mol %) gave the same level of yield and enantioselectivity.

Several substrates were subjected to the practical, optimized reaction conditions, and the results are summarized in Table 2. Methyl ester **2a**, ethyl ester **2b**, as well as *tert*-butyl ester **2c** led to products with excellent enantioselectivities (Table 2, entries 1–5). In previous reports by other groups, *tert*-butyl esters gave higher selectivities, but methyl esters showed poor stereoselectivities.[5c,11] Notably, high enantioselectivities were attained, regardless of the ester parts of the β-ketoesters in the present reaction system. Other indanone derivatives **2d** and **2e** also reacted with MVK or ethyl vinyl ketone (EVK) well to afford the corresponding Michael adducts in high yields with excellent enantiomeric excesses (Table 2, entries 6–9). The synthetically useful 1,3-dicarbonyl compound **2f** also gave the desired adduct **3fa** with excellent enantioselectivity (Table 2, entry 10). The reaction of tetralone **2g** with EVK gave **2gb**

Table 2. Chiral Sc-catalyzed enantioselective Michael reactions.[a]



Entry	**2**	R^1	*t* [h]	Product	Yield[b] [%]	*ee*[c] [%]
1	**2a**	Me	50	**3aa**	94	92
2	**2a**	Et	48	**3ab**	98	93
3	**2b**	Me	60	**3ba**	81	90
4	**2b**	Et	38	**3bb**	95	93
5	**2c**	Me	120	**3ca**	61	91
6	**2d**	Me	13	**3da**	88	95
7	**2d**	Et	20	**3db**	81	95
8	**2e**	Me	28	**3ea**	85	85
9	**2e**	Et	20	**3eb**	84	84
10	**2f**	Me	24	**3fa**	72	94
11[d]	**2g**	Et	110	**3gb**	54	92
12	**2h**	Me	36	**3ha**	69	61
13[e]	**2a**	Et	110	**3ab**	93	93

[a] The catalyst was prepared from $Sc(OTf)_3$ (5 mol %) and **1** (6 mol %) in dichloroethane at 60 °C for 1 h; the substrates were added without removal of the solvent. [b] Yield of isolated product after silica-gel chromatography. [c] The *ee* values were determined by chiral HPLC analysis. [d] The reaction was carried out at 60 °C with $Sc(OTf)_3$ (5 mol %) and **1** (7.5 mol %). [e] $Sc(OTf)_3$ (1 mol %) and **1** (1.2 mol %) were employed.

with high enantioselectivity, albeit in moderate yield (Table 2, entry 11). Simple β-ketoester **2h** reacted with MVK to afford the corresponding Michael adduct in 69 % yield with 61 % *ee*. Furthermore, the reaction proceeded smoothly, even when the loading of the chiral catalyst was 1 mol % (Table 2, entry 13). Whereas most catalytic asymmetric Michael reactions lack substrate generality, it is noteworthy that the present reaction has a wide substrate scope, especially when compared with reactions with other chiral scandium catalysts.[11]

The assumed catalytic cycle is shown in Scheme 1. The β-ketoester reacts with the chiral scandium catalyst to form a chiral scandium enolate and trifluoromethane sulfonic acid (TfOH). The scandium enolate attacks the α,β-unsaturated ketone activated by TfOH to form the corresponding Michael adduct, initially an enolate form, which is quenched by TfOH to give a 1,5-dicarbonyl compound, with concomitant regeneration of the chiral scandium catalyst.

Efficient chiral induction occurs in the reaction of the scandium enolate with the α,β-unsaturated ketone. The proposed transition-state model at this stage is shown in Figure 1. On the basis of the X-ray crystal-structure analysis of the **1**–$ScBr_3$ complex,[12] we assume a pentagonal bipyra-

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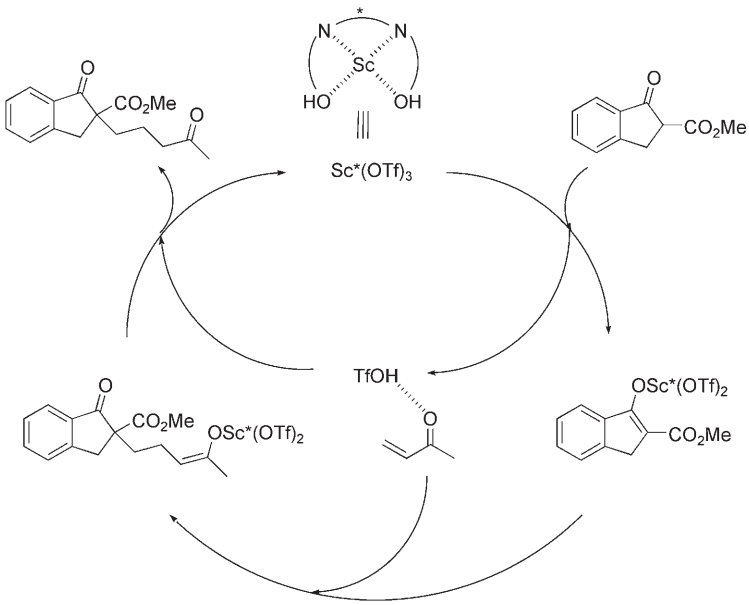

Scheme 1. Assumed catalytic cycle of the reaction.

midal structure in which the hydroxy groups of **1** coordinate to Sc^{3+} in a tetradentate manner. In this model, the *Si* face of the scandium enolate is shielded by the *tert*-butyl group of **1**, and the enolate attacks an α,β-unsaturated ketone at

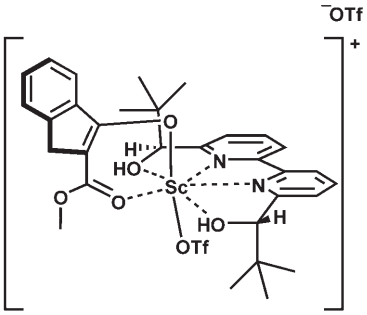

Figure 1. Assumed transition state in the addition of the scandium enolate to the α,β-unsaturated ketone.

the *Re* face in a highly enantioselective manner. This model explains the absolute configuration of the Michael adducts obtained in this reaction.

Conclusions

In summary, we have developed a chiral scandium catalyst that promotes the highly enantioselective Michael reaction of β-ketoesters with α,β-unsaturated ketones. In the presence of $Sc(OTf)_3$ and chiral bipyridine **1**, the desired reactions proceeded smoothly in dichloroethane at 40°C to afford the corresponding Michel adducts in good to high yields with excellent enantioselectivities in most cases. It is noteworthy that a low concentration of the reaction mixture is key to obtaining high enantioselectivities. Whereas the substrate scope has not yet been fully investigated, indanone, tetralone, and cyclopentanone derivatives are good Michael donors in the present system. Further investigations to utilize the present asymmetric reaction for the synthesis of biologically important compounds are now in progress.

Experimental Section

General

IR spectra were recorded on a Jasco FT/IR-610 infrared spectrometer. ^1H and ^{13}C NMR spectra were recorded on a JEOL JNM-LA400 spectrometer in $CDCl_3$. Tetramethylsilane (TMS) served as internal standard ($\delta = 0$ ppm) for ^1H NMR spectra, and $CDCl_3$ was used as the internal standard ($\delta = 77.0$ ppm) for ^{13}C NMR spectra. Column chromatography was conducted on Silica gel 60 (Merck) and preparative thin-layer chromatography (PTLC) was carried out on Wakogel B-5F. Dichloromethane and dichloroethane were distilled from P_2O_5 and then from CaH_2 and stored over 4-Å molecular sieves. All other solvents and chemical compounds were purified by standard procedures. β-Ketoesters **2a–h** were prepared by reported methods.[11b,13] Methyl vinyl ketone (MVK) and ethyl vinyl ketone (EVK) were purchased from Tokyo Kasei Kogyo Co., LTD, and were used after distillation.

Syntheses

Typical procedure (**3aa**): Scandium triflate (9.5 mg, 0.019 mmol) and **1** (7.7 mg, 0.023 mmol) in dichloroethane (3.0 mL) were stirred for 1 h at 60°C under an argon atmosphere, and the solution was cooled to 40°C. Dichloroethane (12.0 mL) was added to the solution, and the mixture was stirred for 20 min at the same temperature. β-Ketoester **2a** (73.3 mg, 0.386 mmol) in dichloroethane (2.0 mL) was added to the mixture, followed by methyl vinyl ketone (64 μL, 0.769 mmol) in dichloroethane (1.0 mL). After 50 h, the reaction was quenched with water. The resultant mixture was extracted with dichloromethane (3 times), washed with HCl (aq. 1 N) and brine. The organic layer was then dried over anhydrous Na_2SO_4. The solvents were evaporated, and the residue was purified by preparative TLC (silica gel, hexane/ethyl acetate 2:1) to give the Michael adduct **3aa** (94.0 mg, 0.361 mmol) in 94% yield. The enantiomeric excess of the product was determined by chiral HPLC analysis (92% *ee* (*R*)). The absolute configuration was determined by comparison of the optical rotation with that of the literature value.

3ab: $[\alpha]_D^{21} = +65.4$ ($c = 1.04$, $CHCl_3$) (93% *ee*); IR (neat): $\tilde{\nu} = 1745$, 1711 cm^{-1};^1H NMR ($CDCl_3$): $\delta = 1.03$ (t, $J = 7.3$ Hz, 3H), 2.22 (ddd, $J = 14.0$, 10.0, 6.0 Hz, 1H), 2.28 (ddd, $J = 14.0$, 10.0, 6.0 Hz, 1H), 2.41 (q, $J = 7.6$ Hz, 2H), 2.48 (ddd, $J = 19.2$, 9.6, 5.6 Hz, 1H), 2.59 (ddd, $J = 19.2$, 9.6, 5.6 Hz, 1H), 3.05 (d, $J = 17.4$ Hz, 1H), 3.68 (d, $J = 17.4$ Hz, 1H), 3.70 (s, 3H), 7.41 (t, $J = 7.3$ Hz, 1H), 7.48 (d, $J = 7.4$ Hz, 1H), 7.64 (t, $J = 6.8$ Hz, 1H), 7.78 ppm (d, $J = 7.8$ Hz, 1H); ^{13}C NMR ($CDCl_3$): $\delta = 7.8$, 28.7, 35.9, 37.5, 37.8, 52.8, 59.3, 124.9, 126.4, 128.0, 135.1, 135.5, 152.6, 171.2, 202.3, 210.2 ppm; elemental analysis: calcd for $C_{16}H_{18}O_4$: C 70.06, H 6.61; found: C 69.81, H 6.64; HPLC (Daicel Chiralpak OJ, hexane/*i*PrOH 9:1, flow rate = 0.5 mL min^{-1}): $t_R = 35.1$ min (minor), $t_R = 40.8$ min (major).

3ba: $[\alpha]_D^{21} = +55.3$ ($c = 0.99$, $CHCl_3$) (94% *ee*); ^1H NMR ($CDCl_3$): IR (neat): $\tilde{\nu} = 1743$, 1712 cm^{-1}; $\delta = 1.21$ (t, $J = 6.9$ Hz, 3H), 2.13 (s, 3H), 2.22–2.25 (m, 2H), 2.48–2.56 (m, 1H), 2.59–2.68 (m, 1H), 3.03 (d, $J = 17.2$ Hz, 1H), 3.67 (d, $J = 17.2$ Hz, 1H), 4.16 (q, $J = 8.2$ Hz, 2H), 7.41 (t, $J = 6.9$ Hz, 1H), 7.48 (d, $J = 7.8$ Hz, 1H), 7.64 (t, $J = 7.8$ Hz, 1H), 7.77 ppm (d, $J = 7.4$ Hz, 1H); ^{13}C NMR ($CDCl_3$): $\delta = 14.0$, 28.5, 29.9, 37.9, 38.8, 59.2, 61.7, 124.8, 126.4, 127.9, 135.1, 135.5, 152.5, 171.1, 202.4, 207.6 ppm; elemental analysis: calcd for $C_{16}H_{18}O_4$: C 70.06, H 6.61; found: C 69.79, H 6.68; HPLC (Daicel Chiralpak OJ, hexane/*i*PrOH 4:1, flow rate = 1.0 mL min^{-1}): $t_R = 12.1$ min (minor), $t_R = 17.7$ min (major).

3bb: $[\alpha]_D^{21} = +52.0$ ($c = 0.91$, $CHCl_3$) (93% *ee*); IR (neat): $\tilde{\nu} = 1739$, 1712 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 1.03$ (t, $J = 7.4$ Hz, 3H), 2.13 (t, $J = 7.3$ Hz, 3H), 2.17–2.30 (m, 2H), 2.40 (q, $J = 7.3$ Hz, 2H), 2.42–2.52 (m,

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1H), 2.53–2.63 (m, 1H), 3.03 (d, J=17.6 Hz, 1H), 3.66 (d, J=17.6 Hz, 1H), 4.16 (q, J=7.4 Hz, 2H), 7.41–7.43 (m, 1H), 7.45–7.48 (d, J=7.6 Hz, 1H), 7.61–7.65 (m, 1H), 7.76–7.78 ppm (d, J=7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ=7.6, 14.0, 28.7, 35.9, 37.5, 37.8, 59.3, 61.6, 124.8, 126.4, 127.9, 135.1, 135.4, 152.6, 171.1, 202.3, 210.2 ppm; elemental analysis: calcd for $C_{17}H_{20}O_4$: C 70.81, H 6.99; found: C 70.54, H 7.19; HPLC (Daicel Chiralpak OJ, hexane/*i*PrOH 4:1, flow rate=1.0 mL min^{-1}): t_R=11.0 min (minor), t_R=12.4 min (major).

3da: $[\alpha]_D^{20}$=+72.4 (c=0.66, $CHCl_3$) (95% *ee*); IR (neat): $\tilde{\nu}$=1697, 1608 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ=1.21 (t, J=6.9 Hz, 3H), 2.12 (s, 3H), 2.20 (ddd, J=14.4, 10.0, 6.0 Hz, 1H), 2.26 (ddd, J=14.4, 10.0, 6.0 Hz, 1H), 2.49 (ddd, J=17.6, 10.0, 6.0 Hz, 1H), 2.60 (ddd, J=17.6, 10.0, 6.0 Hz, 1H), 2.98 (ddd, J=17.4 Hz, 1H), 3.62 (d, J=17.4 Hz, 1H), 3.90 (s, 3H), 4.16 (q, J=7.9 Hz, 2H), 6.90–6.95 (m, 2H), 7.69 ppm (d, J=8.2 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ=13.9, 28.4, 29.7, 37.5, 38.7, 55.6, 59.3, 61.4, 109.3, 115.9, 126.3, 128.1, 155.6, 165.8, 171.1, 200.2, 207.4 ppm; elemental analysis: calcd for $C_{17}H_{20}O_5$: C 67.09, H 6.62; found: C 66.81, H 6.55; HPLC (Daicel Chiralpak OJ, hexane/*i*PrOH 4:1, flow rate=1.0 mL min^{-1}): t_R=12.6 min (minor), t_R=19.3 min (major).

3db: $[\alpha]_D^{22}$=+80.6 (c=0.20, $CHCl_3$) (95% *ee*); IR (neat): $\tilde{\nu}$=1734, 1708 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ=1.03 (t, J=7.4 Hz, 3H), 1.21 (t, J=7.4 Hz, 3H), 2.17–2.30 (m, 2H), 2.42 (q, J=7.4 Hz, 2H), 2.44–2.60 (m, 2H), 2.97 (d, J=17.4 Hz, 1H), 3.61 (d, J=17.4 Hz, 1H), 3.90 (s, 3H), 4.16 (q, 7.4 Hz, 2H), 6.80–6.95 (m, 2H), 7.69–7.71 ppm (m, 1H); ^{13}C NMR ($CDCl_3$): δ=7.8, 14.0, 28.7, 35.9, 37.5, 37.6, 55.7, 59.6, 61.6, 109.4, 116.0, 126.5, 128.3, 155.7, 165.9, 171.2, 200.3, 210.4 ppm; HRMS: calcd for $C_{18}H_{23}O_5$: 319.1545 [M^+]; found: 319.1542; HPLC (Daicel Chiralpak AD, hexane/*i*PrOH 9:1, flow rate=1.0 mL min^{-1}): t_R=21.1 min (minor), t_R=30.8 min (major).

3ea: $[\alpha]_D^{22}$=+61.5 (c=1.15, $CHCl_3$) (85% *ee*); IR (neat): $\tilde{\nu}$=1730, 1712 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ=1.21 (t, J=6.9 Hz, 3H), 2.13 (s, 3H), 2.21–2.25 (m, 2H), 2.52 (ddd, J=15.6, 8.7, 5.5 Hz, 1H), 2.60 (ddd, J=15.6, 8.7, 5.5 Hz, 1H), 3.01 (d, 17.5 Hz, 1H), 3.64 (d, J=17.5 Hz, 1H), 4.16 (q, J=6.9 Hz, 2H), 7.56–7.62 (m, 1H), 7.63–7.66 ppm (m, 2H); ^{13}C NMR ($CDCl_3$): δ=14.0, 28.4, 29.9, 37.5, 38.7, 59.3, 61.8, 126.0, 129.7, 130.9, 131.6, 134.0, 154.0, 170.6, 201.1, 207.3 ppm; elemental analysis: calcd for $C_{16}H_{17}BrO_4$: C 54.41, H 4.85; found: C 54.16, H 4.73; HPLC (Daicel Chiralpak AD-H, hexane/*i*PrOH 4:1, flow rate=1.0 mL min^{-1}) t_R=9.9 min (minor), t_R=13.8 min (major).

3eb: $[\alpha]_D^{23}$=+49.2 (c=0.48, $CHCl_3$) (84% *ee*); IR (neat): $\tilde{\nu}$=1730, 1714 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ=1.03 (t, J=7.4 Hz, 3H), 1.21 (t, J=7.2 Hz, 3H), 2.23–2.27 (m, 2H), 2.40 (q, J=7.4 Hz, 2H), 2.38–2.50 (m, 1H), 2.54–2.62 (m, 1H), 3.01 (d, J=17.4 Hz, 1H), 3.64 (d, J=17.4 Hz, 1H), 4.16 (q, J=7.2 Hz, 2H), 7.54–7.56 (m, 1H), 7.61–7.66 ppm (m, 2H); ^{13}C NMR ($CDCl_3$): δ=7.8, 14.0, 28.5, 35.9, 37.4, 59.5, 61.8, 77.2, 126.0, 129.7, 130.9, 131.6, 134.0, 154.1, 170.6, 201.1, 210.0 ppm ; elemental analysis: calcd for $C_{17}H_{19}BrO_4$: C 55.60, H 5.21; found: C 55.43, H 5.29; HPLC (Daicel Chiralpak AD, hexane/*i*PrOH 9:1, flow rate=1.0 mL min^{-1}): t_R=13.8 min (minor), t_R=17.9 min (major).

3fa: $[\alpha]_D^{26}$=+88.9 (c=0.53, $CHCl_3$) (94% *ee*); IR (neat): $\tilde{\nu}$=1752, 1717 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ=2.13 (s, 3H), 2.23–2.40 (m, 1H), 2.52–2.65 (m, 3H), 3.57 (s, 3H), 7.16–7.27 (m, 2H), 7.67–7.69 ppm (m, 2H); ^{13}C NMR ($CDCl_3$): δ=27.8, 29.8, 37.1, 53.4, 90.2, 113.5, 119.4, 122.9, 125.1, 138.7, 166.1, 172.1, 195.6, 206.2 ppm; HRMS: calcd for $C_{14}H_{15}O_5$: 263.0919 [M^+]; found: 263.0924; HPLC (Daicel Chiralpak OD, hexane/*i*PrOH=9:1, flow rate=1.0 mL min^{-1}): t_R=40.0 min (minor), t_R=45.9 min (major).

3gb: $[\alpha]_D^{24}$=−37.9 (c=0.43, $CHCl_3$) (87% *ee*); IR (neat): $\tilde{\nu}$=1732, 1714 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ=1.05 (t, J=7.4 Hz, 3H), 2.10–2.19 (m, 2H), 2.25–2.30 (m, 1H), 2.43 (q, J=7.4 Hz, 2H), 2.60–2.72 (m, 2H), 2.54–2.72 (m, 1H), 2.97–3.03 (m, 2H), 3.68 (s, 3H), 7.21 (d, J=7.8 Hz, 1H), 7.23–7.33 (m, 1H), 7.46–7.52 (m, 1H), 8.03 ppm (d, J=7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ=7.8, 25.8, 27.7, 31.5, 35.8, 37.6, 52.4, 56.7, 126.8, 127.9, 128.7, 131.8, 133.6, 142.8, 172.3, 195.3, 210.3 ppm; elemental analysis: calcd for $C_{17}H_{20}O_4$: C 70.81, H 6.99; found: C 70.51, H 7.11; HPLC (Daicel Chiralpak AD, hexane/*i*PrOH 9:1, flow rate=1.0 mL min^{-1}): t_R=11.6 min (minor), t_R=13.5 min (major).

3aa,[11b] **3ca**,[5c] and **3ha**[11b] are known compounds.

Acknowledgements

This work was partially supported by a Grant-in-Aid for Scientific Research from the Japan Society for the Promotion of Science (JSPS).

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Received: March 24, 2006
Published online: July 3, 2006

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