# Diastereoselective reactions of 1,1′-binaphthyl ester enolates with carbonyl electrophiles

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**Diastereoselectivity in the aldol and the conjugate additions of 2′-hydroxy-1,1′-binaphthyl ester enolates with a variety of carbonyl electrophiles has been examined. The ester enolate generated by BuLi reacts with several aldehydes to give the *threo* products preferentially with high diastereoselectivity and in good yield. Satisfactory diastereoselectivity has also been observed in the minor *erythro* derivatives. A mechanistic interpretation of the results is made on the basis of the absolute stereochemistry of the products.**

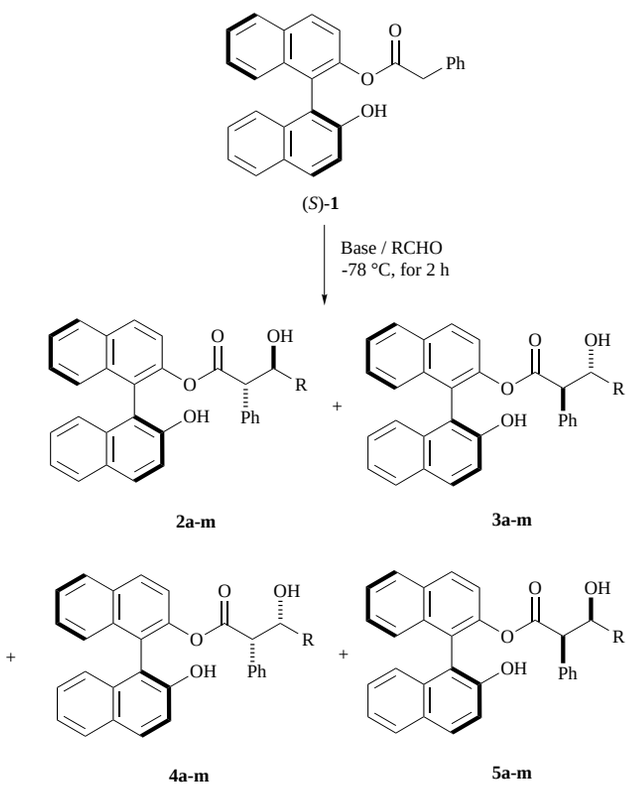


## Introduction

Carbon–carbon bond-forming reactions, such as aldol and Michael reactions, play an important role in synthetic organic chemistry, and their directed versions have been widely used for the selective construction of the carbon skeleton of a variety of useful compounds.[1] Earlier, we reported the highly diastereoselective alkylation of the ester anion of 2′-hydroxy-1,1′-binaphthalene as the result of complex-induced proximity effects (CIPE) in enolate formation,[2] and demonstrated that the 2′-hydroxy-1,1′-binaphthalene acts as an effective stereochemical controller in stoichiometric reactions.[3] These approaches were successfully applied to the asymmetric synthesis of clinically important drugs[4] as well as non-racemic uncommon α-amino acid derivatives.[5] As an extension to the alkylation of binaphthyl ester enolates, we have examined the diastereoselective aldol and Michael-type reactions of binaphthyl ester enolates with a variety of carbonyl electrophiles. Despite the numerous methods available for asymmetric aldol reactions, including enolates of ketones, amides and imides, very few approaches involving enolates of carboxylic esters have been reported.[6]

## Results and discussion

The aldol reaction of the anion of optically active (*S*)-2′-hydroxy-1,1′-binaphthyl phenylacetate (*S*)-**1**[2] with benzaldehyde was first examined under a variety of reaction conditions, the chemical yield and the *syn*/*anti* ratio of the products being studied. Of the bases evaluated, BuLi gave the best result with respect to both chemical yield and diastereoselectivity in THF† at −78 °C a mixture of **2**–**5a** (Table 1) being obtained. With BuLi as a base, increased chemical yields were observed with the solvent systems THF–toluene, THF–DME† and THF–ether.† The addition of HMPA,† which has a strong ligating ability, interfered with the reaction. Diastereoselectivity was determined by HPLC and/or $^1$H NMR analysis. Despite a few exceptions, it has been well documented for aldol reactions that a small vicinal coupling constant of 3–6 Hz is attributable to an *erythro* (*syn*) relationship, while a larger one of 7–9 Hz is attributable to a *threo* (*anti*) relationship.[7] Consequently, the *syn*/*anti* stereochemistry of the adducts was deduced by comparing the vicinal coupling constants of the adducts by $^1$H NMR spectrometry (see Table 6 in Experimental section); this assignment was later supported by chemical transformation and an X-ray analysis (*vide infra*). Of the *anti* products **2a** and **3a**, the α-proton of the major diastereoisomer **2a** appeared at higher field, while the β-proton and both hydroxy protons shifted to lower field (Table 7 in Experimental section). These observations also suggested that the stereostructure of the major products was as shown in **2** and **3**.



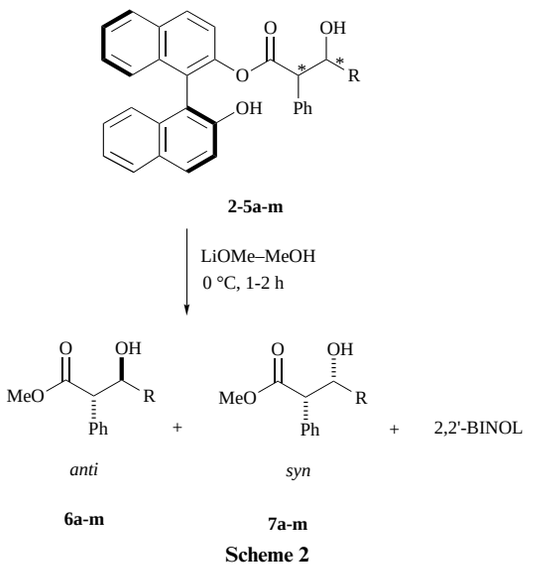

**Scheme 1** R = **a** = Phenyl; **b** = 1-naphthyl; **c** = 2-naphthyl; **d** = styryl; **e** = 4-methoxyphenyl; **f** = ethyl; **g** = isopropyl; **h** = 2-furyl; **i** = 3-furyl; **j** = 5-methyl-2-furyl; **k** = 2-thienyl; **l** = 3-pyridyl; **m** = 4-pyridyl

The aldol reactions of the anion of **1** with several aromatic and aliphatic aldehydes other than benzaldehyde were carried out (Scheme 1), and these results are given in Table 2. In general, satisfactory chemical yields of more than 90% were obtained with aromatic aldehydes, but not with aliphatic aldehydes. Again, the *syn*/*anti* ratio increased slightly when toluene was added to THF. The stereoselectivity depended on the structure of the aldehydes used. Thus, a relatively high *syn*/*anti* ratio was observed for 2-naphthaldehyde, *trans*-cinnamaldehyde and *p*-anisaldehyde (entries 3 to 5), and a lower selectivity was obtained with the less bulky propionaldehyde (entry 6 *vs.* 7). The selectivity of the adducts of 3-furaldehyde and thiophenecarbaldehyde was superior to those of 2-furaldehyde and 5-methyl-2-furaldehyde (entries 8 to 11), and the adducts from

† THF = tetrahydrofuran, DME = dimethyl ether, ether = diethyl ether, HMPA = hexamethylphosphoramide, LDA = lithium diisopropylamide.

pyridinecarbaldehydes showed low selectivity (entries 12 and 13). *threo* Products were generally obtained with good diastereoselectivity in preference to *erythro* adducts. The diastereoselectivity of the minor *erythro* adducts **4** and **5** could not be determined at that time, but was evaluated later by the chemical transformations described below.

To confirm the absolute stereochemistry of the aldol products **2**–**5a**–**m**, we next tried to remove the chiral auxiliary to give the β-hydroxy carboxylates **6**,**7a**–**m**. Under hydrolytic conditions using NaOH or LiOH in aqueous MeOH, the retro-aldol reaction took place to give recovery of binaphthol and the corresponding aldehyde. On the other hand, under the conditions used for the ester exchange, LiOMe–MeOH, the aldol products **2**–**5a**–**m** were converted into a separable *syn*/*anti* diastereoisomeric mixture of the methyl esters **6a**–**m** and **7a**–**m** in satisfactory yield, together with binaphthol without any loss of optical purity (Scheme 2).




**Scheme 2**

The *anti* stereochemistry of the major diastereoisomers **6** from **2** was confirmed by comparison with the physical data in the literature,[8] and the absolute stereostructure of **6a** was proven to be 2*S*,3*R* by comparison with the sign of the reported specific rotation.[9] Authentic samples of the racemic mixture of the *syn* and *anti* diastereoisomers **6** and **7** were prepared independ-

**Table 1** Reaction conditions for the aldol reaction of **1** with benzaldehyde

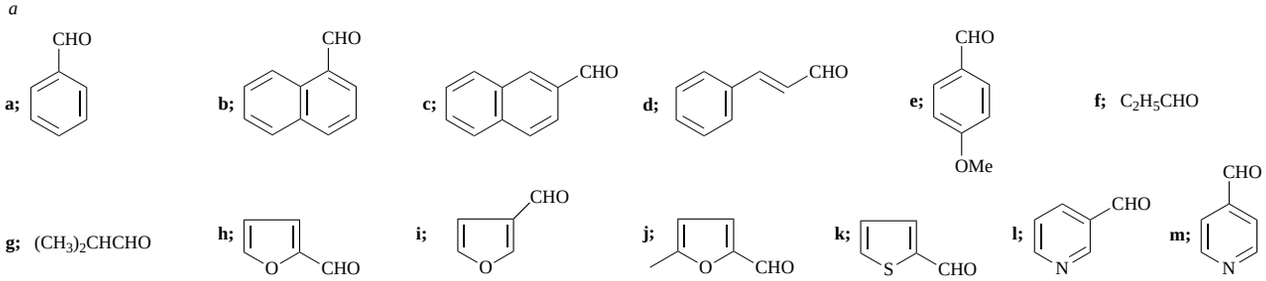
| Base | Solvent | Yield[a] (%) | *anti*:*syn*[b,c] |
|---|---|---|---|
| BuLi | THF | 97 | 93:7[d] |
| BuLi | THF–toluene (3:1) | 93 | 94:6 |
| BuLi | THF–DME (2:1) | 97 | 92:8 |
| BuLi | THF–ether (2:1) | 88 | 96:4 |
| BuLi | THF–HMPA (3%) | 28 | 87:13 |
| LDA | THF | 70 | 88:12 |
| LTMP | THF | 32 | 85:15 |
| KDA | THF | 47 | 90:10 |
| LHMDS | THF | 62 | 90:10 |
| BuLi–$MgBr_2$ | THF | 39[e] | 53:47 |
| NaH | THF | —[f] | — |

[a] Isolated yield. [b] **2a** + **3a**:**4a** + **5a**. [c] Determined by HPLC using a Puresil $C_{18}$ column. [d] A crystalline compound of 100:1 ratio was obtained after one recrystallization. [e] A 33% yield of 2,2′-BINOL was recovered. [f] **1** and 2,2′-BINOL were recovered.

**Table 2** The aldol reaction of **1** with RCHO

| Entry | RCHO[a] | Solvent | Prod. | Yield[b] (%) | *anti*:*syn*[c,d] | % de (*anti*)[e] | HPLC cond. (MeOH–$H_2O$) |
|---|---|---|---|---|---|---|---|
| 1 | **a** | THF | **2–5 a** | 97 | 97:3 | 76 | 75:25 |
| 2 | **b** | THF | **2–5 b** | 95 | 60:40 | 70 | 70:30 |
| 3 | **c** | THF | **2–5 c** | 98 | 94:6 | 68 | 75:25 |
| | | THF–toluene = 2:1 | | 61 | 99:1 | 60 | |
| | | THF–ether = 3:1 | | 80 | 89:11 | 48 | |
| 4 | **d** | THF | **2–5 d** | 91 | 87:13 | 82 | 72:28 |
| | | THF–toluene = 3:1 | | 59 | 88:12 | 80 | |
| | | THF–ether = 3:1 | | 91 | 87:13 | 68 | |
| 5 | **e** | THF | **2–5 e** | 94 | 94:6 | 64 | 75:25 |
| | | THF–toluene = 3:1 | | 85 | 100:0 | 70 | |
| | | THF–ether = 3:1 | | 78 | 99:1 | 55 | |
| 6 | **f** | THF | **2–5 f** | 71[f] | 62:38 | —[g] | 75:25 |
| 7 | **g** | THF | **2–5 g** | 58 | 98:2 | 70 | 75:25 |
| 8 | **h** | THF | **2–5 h** | 99 | 37:63 | 30 | 70:30 |
| | | THF–toluene = 3:1 | | 89 | 46:54 | 30 | |
| 9 | **i** | THF | **2–5 i** | 95 | 86:14 | 72 | 70:30 |
| 10 | **j** | THF | **2–5 j** | 99 | 79:21 | 34 | 72:28 |
| | | THF–toluene = 3:1 | | 84 | 69:31 | 33 | |
| 11 | **k** | THF | **2–5 k** | 97 | 89:11 | 60 | 70:30 |
| | | THF–toluene = 3:1 | | 92 | 95:5 | 62 | |
| 12 | **l** | THF | **2–5 l** | 91[h] | 54:46[i] | 48 (74)[j] | — |
| 13 | **m** | THF | **2–5 m** | 90[h] | 30:70[i] | 27 (60)[j] | — |

*a*




[b] Combined isolated yield. [c] **2** + **3**:**4** + **5**. [d] Determined by HPLC analysis using a Puresil $C_{18}$ column. [e] The % de of the minor *syn* products was not determined. [f] Reacted for 7 h. [g] Not determined. [h] Reacted for 5 min. [i] Determined by $^1H$ NMR (400 MHz). [j] The % de of *syn* products.

**Table 3** Transesterification of **2**–**5a**–**m** with lithium methoxide

| | Starting from **2**–**5** | | | | | |
|---|---|---|---|---|---|---|
| Entry | Compd. | *anti*:*syn* | Yield (%)[a] | Major prod. (% ee) | Minor prod. (% ee) | Cond. for HPLC analysis (chiral column,[b] eluent[c]) |
| 1 | **a** | 93:7 | 75 | *anti* (77) | *syn* (65) | *anti* (OD, 10), *syn* (AD, 8) |
| 2 | **b** | 60:40 | 71 | *anti* (70) | *syn* (90) | *anti* (AD, 15), *syn* (OJ, 30) |
| 3 | **c** | 94:6 | 67 | *anti* (67) | — | *anti* (AS, 10), *syn* (AD, 15) |
| 4 | **d** | 87:13 | 72 | *anti* (79) | *syn* (64) | *anti* (AD, 15), *syn* (AS, 8) |
| 5 | **e** | 94:6 | 68 | *anti* (65) | — | *anti* (AS, 12), *syn* (AS, 15) |
| 6 | **f** | 62:38 | 82 | *anti* (69) | *syn* (88) | *anti* (AD, 1)[d], *syn* (AD, 2)[d] |
| 7 | **g** | 98:2 | 79 | *anti* (67) | — | *anti* (AD, 3)[d], *syn* (AD, 3)[d] |
| 8 | **h** | 37:63 | 60 | *syn* (94) | *anti* (22) | *anti* (OJ, 10)[d], *syn* (AD, 15)[d] |
| 9 | **i** | 86:14 | 85 | *anti* (70) | *syn* (83) | *anti* (OJ, 10)[d], *syn* (AD, 5)[d] |
| 10 | **j** | 69:31 | 72 | *anti* (32) | *syn* (94) | *anti* (OJ, 10)[d], *syn* (AD, 20)[d] |
| 11 | **k** | 89:11 | 74 | *anti* (60) | *syn* (85) | *anti* (OJ, 15)[d], *syn* (OJ, 20)[d] |
| 12 | **l** | 54:46 | 75 | *anti* (47) | *syn* (73) | *anti* (OJ, 12)[e] *syn* (OJ, 15)[e] |
| 13 | **m** | 30:70 | 83 | *syn* (60) | *anti* (26) | *anti* (OJ, 15)[e] *syn* (OJ, 15)[e] |

[a] Combined isolated yield. [b] Daicel Chem. Ind. LTD. [c] % of Pr$^i$OH in hexane. [d] Detected at 235 nm. [e] Diethylamine (0.01%) was added.

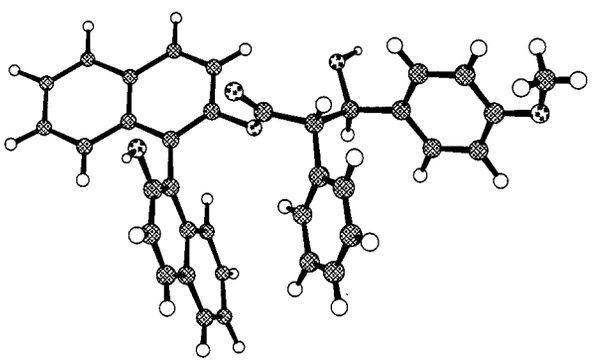
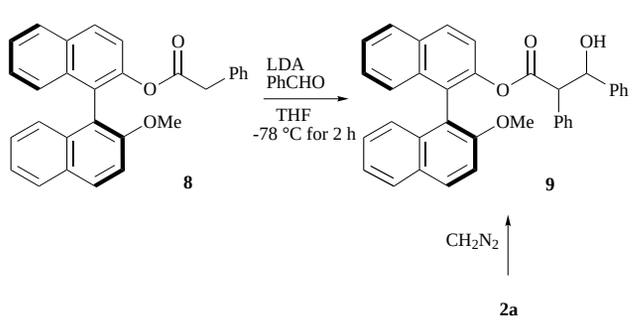


**Fig. 1** Crystal structure of (*S*,*S*,*R*)-**2e**

ently by reaction of the enolate of methyl phenylacetate and the corresponding aldehyde, and the enantiomeric excess (ee) of each diastereoisomer was determined by HPLC analysis on a chiral stationary phase. These HPLC analyses also indicated that no significant racemization occurred during the ester exchange reaction. These results are summarized in Table 3. In addition, the absolute structure of one of the major *anti*-diastereoisomers **2e** was unambiguously determined by X-ray analysis (Fig. 1).

When 2′-methoxy-1,1′-binaphthalen-2-yl phenylacetate **8**[2] was used as a substrate for the aldol reaction with benzaldehyde under the same reaction conditions as above, no aldol adducts formation was detectable, probably because of lack of effective CIPE[2] in the enolate formation. However, the reaction using LDA as a base provided the aldol adducts in a much lower yield (9%) with an *anti*/*syn* ratio of 89:11 (Scheme 3). The diastereo-




**Scheme 3**

selectivity of the major *anti* adduct **9** was deduced by comparison of the HPLC analysis with that of an authentic sample **9** obtained by treatment of **2a** with $CH_2N_2$, which gave only 12% de of **9**. These experiments clearly suggest that the free hydroxy group at the 2′ position plays a crucial role in both the reactivity and the induction of diastereoselectivity.[2]

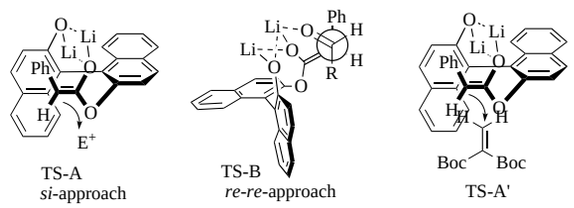



**Fig. 2** Mechanistic explanation for observed stereochemistry in the aldol and related reactions

Earlier we reported the asymmetric alkylation of the ester enolate of (*S*)-**1** with alkyl halides in which the *E*-enolate forms preferentially by the action of BuLi or LDA in THF and the approach of the electrophiles is directed from the less-hindered *si*-face of the enolate (TS-A in Fig. 2) to give the *S*,*S*-product selectively. According to this hypothesis, the rigidly fixed lithium enolate influences the direction of the approach of the electrophile such that the combination of the *si*-face of the *E*-enolate of (*S*)-**1** and the *si*-face of the aldehyde carbonyl would lead to the *anti* product of *S*,*R*,*S*-conformation (*S*,*R*,*R* for **2f** and **g**). However, the observed stereochemistry of the major *anti* product, *S*,*S*,*R*, is inconsistent with the proposed TS-A. Furthermore, even the six-membered transition state, which is generally accepted for the aldol reaction, can not account for the observed stereochemistry. Consequently, we proposed an acyclic TS of chelated lithium enolate involving the aldehyde carbonyl and a 2′-hydroxy group (TS-B in Fig. 2). The *re-re* approach in TS-B may explain the stereochemical course of the present aldol reaction. The π-face of the aldehyde to be attacked, *i.e.* the *syn* or *anti* stereochemistry of the products, depends on the identity of the group R. Generally, an approach to the *re*-face of the aldehyde might be favourable due to gauche interaction between R and the phenyl ring of the enolate, if R lacks heteroatoms with lone-pair electrons. The reverse may also occur to give the *syn* product, when R bearing heteroatoms occupies a position gauche to the phenyl group to avoid repulsive interaction between ester oxygens or the naphthalene ring.

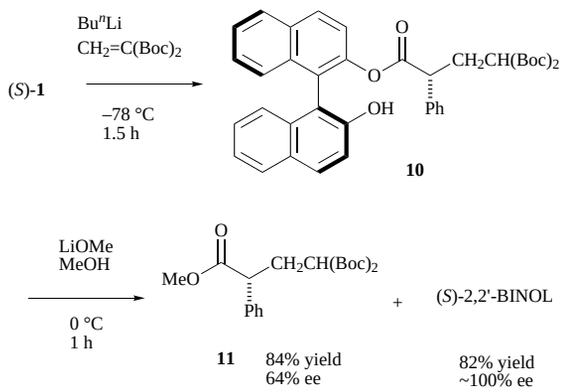
The selectivity in the reaction of the ester enolate of 1,1′-binaphthyl-2,2′-diol (BINOL) with electrophiles other than aldehydes or alkyl halides was examined next. The ester enolate failed to react with alkyl or aryl ketones such as benzophenone and cyclohexanone in satisfactory yield under the same reaction conditions as those used for the aldol reaction mentioned above, probably because of steric constraints. No significant reactivity of the enolate was observed in the Michael reaction with methyl acrylate, methyl vinyl ketone and acrylonitrile, and no noticeable diastereoselectivity was observed with cyclopent-2-enone as a Michael acceptor. On the other hand, the lithium

**Table 4** The Michael reaction of **1** with methylenemalonate

| Solvent | Yield (%)[a] | de (%)[b] |
|---|---|---|
| THF | 63 | 63 |
| Ether | 51 | 38 |
| Toluene | 6 | — |
| DME | 57 | 41 |
| THF–ether (2 : 1) | 81 | 66[c] |
| THF–toluene (2 : 1) | 96 | 56[c] |
| THF–DME (2 : 1) | 82 | 65[c] |

[a] Isolated yield. [b] Determined by HPLC using a silica gel column. [c] Determined by $^1$H NMR (400 MHz) for the C-2′ hydroxy signal.

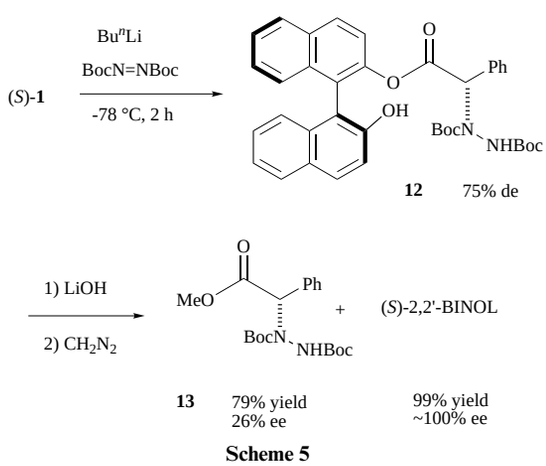
enolate of (*S*)-**1** underwent conjugate addition with an activated Michael acceptor, di-*tert*-butyl methylenemalonate, in good yield (85%) and with moderate diastereoselectivity (65% de) (Scheme 4). The reactions were carried out under different




**Scheme 4**

reaction conditions and the diastereoisomer ratio was determined by $^1$H NMR (at 400 MHz) analysis. These results are listed in Table 4. Among the solvents examined, a combination of THF with ether, toluene or DME gave better chemical yield and selectivity. The Michael adduct **10** was converted into the methyl ester **11** in a manner similar to the transformation of the aldol product by LiOMe in 84% yield. HPLC analysis on a reverse chiral stationary phase showed that the methyl ester of 64% ee was obtained starting from **10** of 65% de. While the absolute stereostructure of **11** has yet to be determined, it is believed to be *S* from mechanistic considerations having been formed *via* a transition state of type TS-A′ (Fig. 2).

Electrophilic amination is an efficient synthetic strategy for the construction of α-amino acid derivatives, including those that are non-proteinogenic. DBAD (di-*tert*-butyl azodicarboxylate) is an electrophilic amine source. As an extension of the Michael-type reaction of the binaphthyl ester enolate, the conjugate addition of the anion to DBAD was investigated (Scheme 5). The reactions proceeded quite smoothly to give **12**




**Scheme 5**

**Table 5** Conjugate addition of the anion of (*S*)-**1** with DBAD

| Solvent | Yield (%)[a] | de (%)[b] | Config. at C-2[c] |
|---|---|---|---|
| THF | 97 | 75 | *S* |
| THF–ether (2 : 1) | 99 | 68 | *S* |
| THF–toluene (2 : 1) | 99 | 61 | *S* |

[a] Isolated yield. [b] Determined by HPLC analysis using a Puresil $C_{18}$ column. [c] Determined by the $[\alpha]_D$ of the methyl ester **13**.

in an excellent yield of up to 99%, and the results are summarized in Table 5. Thus, a diastereoselectivity of 61–75% was observed by reversed-phase HPLC analysis of the products. The *S* configuration at the position α to the carbonyl was confirmed by chemical transformation to the known methyl ester **13**. Unlike the situation with the aldol or Michael products, removal of the chiral auxiliary group proved to be troublesome, and led to significant racemization. Thus, hydrolysis of **12** of 75% de by LiOH–MeOH–$H_2O$ followed by methylation with $CH_2N_2$ gave the methyl ester **13** (79%). However, the ee fell to 26%. Furthermore, the ester exchange with LiOMe–MeOH could not prevent racemization (from 64% de to 6% ee). Conversion of the methyl ester **13** to phenylglycine has already been reported by Evans and his co-workers.[10] The *si*-approach in a transition state analogous to TS-A leads to an absolute stereostructure of *S*,*S* for the product **12**, and this was confirmed by comparing the sign of the specific rotation of the methyl ester **13** with that which has been previously reported.[10]

In conclusion, we have investigated diastereoselectivity in the reaction of a chiral ester enolate with achiral carbonyl electrophiles. The ester enolate of BINOL generated by BuLi reacted with several aldehydes to give the *threo* products preferentially with high diastereoselectivity in good yield. Satisfactory diastereoselectivity was also found in the minor *erythro* derivatives. With axially chiral binaphthol as an auxiliary in the stoichiometric transformation, the present study demonstrates that non-racemic β-hydroxy carboxylic acid derivatives can be prepared with some degree of stereochemical prediction. Since β-hydroxy carboxylic acids often occur as a structural unit in biologically important compounds such as natural products, this method may be used to prepare these compounds. Use of this auxiliary was also extended to Michael-type reactions. Regarding the mechanisms of these reactions, the remaining hydroxy group at the 2′ position of the auxiliary may play an important role in bringing about the high degree of diastereoselectivity. Related reactions with other types of electrophiles as well as elucidation of the precise mechanism are in progress.

## Experimental

### General

Unless otherwise specified, all $^1$H NMR spectra were taken at 200 or 400 MHz in $CDCl_3$ with chemical shifts being reported at $\delta$ ppm from tetramethylsilane as an internal standard; coupling constants are expressed in Hz. IR spectra were measured in $CHCl_3$. THF, Ether, DME and toluene were distilled from sodium benzophenone ketyl, and $CH_2Cl_2$ was from calcium hydride and MeOH was from magnesium. Unless otherwise noted, all reactions were run under an argon or a nitrogen atmosphere. All extracted organic solutions were dried over anhydrous $MgSO_4$. Flash column chromatography was carried out with silica gel 60 spherical (150–325 mesh) and silica gel 60 F254 plates (Merck) were used for preparative TLC (pTLC). Diastereoisomeric excesses (de) were determined by HPLC on a Puresil $C_{18}$ column (Waters Co.) with MeOH–$H_2O$ or $^1$H NMR (400 MHz). The enantiomeric excess (ee) of methyl propanoate derivatives was determined by HPLC on Chiralpak AS, AD, OD, or OJ column (Daicel Co.) with hexane–Pr$^i$OH, or on Ceramospher (chiral) Ru-1 column (Shiseido Co.) with MeOH. The analysis of the recovered (*S*)-(−)-binaphthol was carried

out in a Chiralpak AS column with hexane–Pr$^i$OH (80 : 20). $[\alpha]_D$ Values recorded in units of $10^{-1}$ deg cm$^2$ g$^{-1}$.

**General procedure for the aldol reaction of the anion of 1**

The preparation of **2a** is typical. To a solution of (*S*)-**1**[2] (200 mg, 0.50 mmol) in THF (8 cm$^3$) was added butyllithium (1.62 M in hexane; 642 μl, 1.04 mmol, 2.1 equiv.) at −78 °C. After being stirred for 5 min, the above enolate solution was treated with benzaldehyde (52.8 μl, 0.52 mmol, 1.05 equiv.), added dropwise, and the resulting mixture was stirred at −78 °C for 2 h. The reaction mixture was then poured into cold 10% aqueous $NH_4Cl$, and extracted with AcOEt. The extracts were washed with water, dried and evaporated under reduced pressure. The residual products of **2**–**5a** were analyzed by HPLC (for conditions, see Table 3) and purified by pTLC (hexane–$CH_2Cl_2$–AcOEt = 4 : 1 : 1, 2 times) to give **2**–**5a** (246 mg, 97%) as amorphous solids.

**2′-Hydroxy-1,1′-binaphthalen-2-yl 3-hydroxy-2,3-diphenylpropanoate 2a and 3–5a.** Compound **2a**: mp 169–170 °C; plates (from hexane and ether); $[\alpha]_D^{20}$ −86.0 (*c* 1.1, in $CHCl_3$) (Found: C, 82.28; H, 5.00. Calc. for $C_{35}H_{26}O_4$: C, 82.34; H, 5.13%); $\nu_{max}$/cm$^{-1}$ 3550, 3080–2920, 1740 and 1170–1140; $\delta_H$(400 MHz) 2.55 (1H, d, *J* 4.0), 3.70 (1 H, d, *J* 9.7), 4.95 (1H, dd, *J* 9.7 and 3.9), 5.23 (1H, s), and 6.64–8.05 (22H, m).

Compounds **3**–**5a** IR spectra the same as above for **2a**; $\delta_H$(200 MHz) 2.12 (br d; **4**,**5a**), 2.49 (br d; **3a**), 3.72 (d, *J* 7.3; **4**,**5a**), 3.74 (d, *J* 9.7; **3a**), 4.83 (overlapped; **4a**), 4.84 (overlapped; **3a**), 5.01 (1H, s; **4**,**5a**), 5.21 (1H, s; **3a**) and 6.64–8.05 (22H, m; **3**–**5a**).

**2′-Hydroxy-1,1′-binaphthalen-2-yl 3-hydroxy-3-(1-naphthyl)-2-phenylpropanoate 2–5b.** 95% Yield; amorphous solid; $\nu_{max}$/cm$^{-1}$ 3530, 3070–2840, 1735 and 1150–1070; *m*/*z* 560 (M$^+$); $\delta_H$(400 MHz) 2.64 (br s; **4**,**5b**), 2.74 (br s; **3b**), 2.82 (1H, br s; **2b**), 3.92 (d, *J* 4.4; **4**,**5b**), 4.16 (1H, d, *J* 9.5; **2b**), 4.23 (d, *J* 8.8; **3b**), 5.28 (1H, s; **2b**), 5.40 (d, *J* 4.0; **4**,**5b**), 5.55 (d, *J* 9.2; **3b**), 5.59 (1H, d, *J* 9.5; **2b**), and 6.61–8.06 (24H, m; **2**–**5b**); *m*/*z* (EI) 560 (M$^+$) (Found: M$^+$, 560.2021. $C_{39}H_{28}O_4$ requires 560.1988).

**2′-Hydroxy-1,1′-binaphthalen-2-yl 3-hydroxy-3-(2-naphthyl)-2-phenylpropanoate 2–5c.** 98% Yield; amorphous solid; $\nu_{max}$/cm$^{-1}$ 3535, 3080–2840, 1743 and 1150; $\delta_H$(400 MHz) 2.20 (d, no resolution; **4**,**5c**), 2.59 (d, *J* 4.0; **3c**), 2.69 (1H, d, *J* 4.0; **2c**), 3.83 (d, *J* 7.0; **4**,**5c**), 3.84 (1H, d, *J* 9.5; **2c**), 3.89 (d, *J* 9.5; **3c**), 4.97 (1H, s; **4**,**5c**), 5.02 (m; **3**–**5c**), 5.13 (1H, dd, *J* 9.5 and 4.0; **2c**), 5.22 (1H, s; **3c**), 5.23 (1H, s; **2c**) and 6.61–8.06 (24H, m; **2**–**5c**); *m*/*z* (EI) 560 (M$^+$) (Found: M$^+$, 560.2008. $C_{39}H_{28}O_4$ requires 560.1988).

**2′-Hydroxy-1,1′-binaphthalen-2-yl (*E*)-3-hydroxy-2,5-diphenylpent-4-enoate 2–5d.** 91% Yield; amorphous solid; $\nu_{max}$/cm$^{-1}$ 3530, 3080–2840, 1740 and 1170–1150; *m*/*z* 536 (M$^+$); $\delta_H$(400 MHz) 1.85 (br s; **4**,**5d**), 2.31 (br s; **3d**), 2.38 (1H, br s; **2d**), 3.58 (1H, d, *J* 9.2; **2d**), 3.62 (d, *J* 7.3; **4**,**5d**), 3.63 (d, *J* 9.2; **3d**), 4.47 (br t; **4**,**5d**), 4.61 (1H, br t, *J* 7.3; **2d**), 4.57 (br t; **3d**), 5.15 (s; **4**,**5d**), 5.21 (s; **3d**), 5.24 (1H, s; **2d**), 5.76 (dd, *J* 16.1 and 5.9; **3d**), 5.79 (1H, dd, *J* 15.8 and 6.2; **2d**), 5.97 (dd, *J* 16.1 and 7.0; **4**,**5d**), 6.34 (1H, d, *J* 15.4; **2d**), 6.49 (d, *J* 16.1; **3d**), 6.77 (d, *J* 7.3; **4**,**5d**) and 6.92–8.05 (22H, m; **2**–**5d**); *m*/*z* (EI) 536 (M$^+$) (Found: M$^+$, 536.2036. $C_{37}H_{28}O_4$ requires 536.1987).

**2′-Hydroxy-1,1′-binaphthalen-2-yl 3-hydroxy-3-(4-methoxyphenyl)-2-phenylpropanoate 2–5e.** 94% Yield; **2e**: mp 159–160 °C; plates (from hexane and ether); $[\alpha]_D^{20}$ −99.9 (*c* 1.02, in $CHCl_3$) (Found: C, 78.63; H, 5.26. Calc. for $C_{36}H_{28}O_5 \cdot 1/2H_2O$: C, 78.67; H, 5.32%); $\nu_{max}$/cm$^{-1}$ 3540, 3080–2840, 1735 and 1170–1150; $\delta_H$(400 MHz) 2.45 (1H, d, *J* 3.7), 3.67 (3H, s), 3.70 (1H, d, *J* 9.9), 4.90 (1H, dd, *J* 9.9 and 3.3), 5.24 (1H, s) and 6.58–8.07 (21H, m); *m*/*z* (EI) 540 (M$^+$) (Found: M$^+$, 540.1956. $C_{36}H_{28}O_5$ requires 540.1937).

Compounds **3**–**5e**: IR the same as **2e**; $\delta_H$(400 MHz) 2.38 (d, *J* 3.8; **3e**), 3.66 (s; **3e**), 3.73 (d, *J* 7.8; **4**,**5e**), 3.74 (d, *J* 9.7; **3e**), 3.81 (s; **4**,**5e**), 4.80 (dd, *J* 9.5 and 3.7; **3e**), 4.81 (d, *J* 7.4; **4**,**5e**), 5.20 (s; **3e**) and 6.58–8.07 (21H, m; **3**–**5e**).

**2′-Hydroxy-1,1′-binaphthalen-2-yl 3-hydroxy-2-phenylpentanoate 2–5f.** 71% Yield; amorphous solid; $\nu_{max}$/cm$^{-1}$ 3534, 3080–2880, 1734 and 1150; $\delta_H$(400 MHz) 0.68 (t, *J* 7.3; **4**,**5f**), 0.72 (3H, t, *J* 7.3; **2f**), 0.93 (m; **4**,**5f**), 1.07 (2H, m; **2f**), 2.12 (br d; **3f**), 2.17 (1H, br d; **2f**), 3.40 (d, *J* 7.3; **4**,**5f**), 3.42 (1H, d, *J* 8.8; **2f**), 3.48 (d, *J* 9.3; **3f**), 3.68 (m; **4**,**5f**), 3.75 (m; **3f**), 3.81 (1H, m; **2f**), 5.17 (s; **3f**), 5.23 (1H, s; **2f**), 6.77–8.05 (17H, m; **2**–**5f**); *m*/*z* (EI) 462 (M$^+$) (Found: M$^+$, 462.1860. $C_{31}H_{26}O_4$ requires 462.1831).

**2′-Hydroxy-1,1′-binaphthalen-2-yl 3-hydroxy-2-phenyl-4-methylpentanoate 2–5g.** 58% Yield; amorphous solid; $\nu_{max}$/cm$^{-1}$ 3535, 3060–2880, 1732 and 1170–1150; $\delta_H$(400 MHz) 0.66 (3H, d, *J* 6.8; **2g**), 0.67 (d, *J* 6.8; **3g**), 0.69 (3H, d, *J* 6.8; **2g**), 0.72 (d, *J* 6.8; **3g**), 1.13 (1H, m; **2g**), 1.96 (br d; **3g**), 2.03 (1H, d, *J* 5.9; **2g**), 3.58 (1H, d, overlapped; **2g**), 3.60 (d, overlapped; **3g**), 3.69 (1H, m; **2g**), 5.14 (s; **3g**), 5.20 (1H, s; **2g**) and 6.79–8.05 (17H, m; **2**–**5g**); *m*/*z* (EI) 476 (M$^+$) (Found: M$^+$, 476.1995. $C_{32}H_{28}O_4$ requires 476.1987).

**2′-Hydroxy-1,1′-binaphthalen-2-yl 3-hydroxy-3-(2-furyl)-2-phenylpropanoate 2–5h.** 99% Yield; amorphous solid; $\nu_{max}$/cm$^{-1}$ 3675, 3540, 3080–2900, 1747 and 1170–1150; $\delta_H$(400 MHz) 1.96 (1H, d, *J* 4.4; **4h**), 2.63 (d, *J* 5.5; **2h**), 4.01 (1H, d, *J* 8.4; **4h**), 4.05 (d, *J* 9.5; **2h**), 4.09 (d, *J* 9.2; **3h**), 4.94 (dd, *J* 9.2 and 5.5; **3h**), 5.01 (dd, *J* 9.3 and 5.7; **2h**), 5.06 (1H, dd, *J* 8.4 and 4.0; **4h**), 5.09 (1H, s; **4h**), 5.18 (s; **3h**), 5.22 (s; **2h**), 5.85–6.31 (2H, m; **2**–**5f**) and 6.67–8.07 (18H, m; **2**–**5h**); *m*/*z* (EI) 500 (M$^+$) (Found: M$^+$, 500.1650. $C_{33}H_{24}O_5$ requires 500.1623).

**2′-Hydroxy-1,1′-binaphthalen-2-yl 3-hydroxy-3-(3-furyl)-2-phenylpropanoate 2–5i.** 95% Yield; amorphous solid; $\nu_{max}$/cm$^{-1}$ 3535, 3080–2900, 1735 and 1150; $\delta_H$(400 MHz) 1.94 (br d; **4**,**5i**), 2.47 (br d; **3i**), 2.53 (br d, 1H; **2i**), 3.68 (1H, d, *J* 9.5; **2i**), 3.69 (d, *J* 7.7; **4**,**5i**), 3.73 (d, *J* 9.5; **3i**), 4.90 (d, *J* 7.7; **4**,**5i**), 4.98 (1H, d, *J* 9.2; **2i**), 5.10 (s; **4**,**5i**), 5.18 (s; **3i**), 5.22 (1H, s; **2i**), 5.94 (br s; **4**,**5i**), 5.95 (1H, br s; **2i**), 6.15 (br s; **3i**) and 6.68–8.07 (19H, m; **2**–**5i**); *m*/*z* (EI) 500 (M$^+$) (Found: M$^+$, 500.1631. $C_{33}H_{24}O_5$ requires 500.1624).

**2′-Hydroxy-1,1′-binaphthalen-2-yl 3-hydroxy-3-(5-methyl-2-furyl)-2-phenylpropanoate 2–5j.** 99% Yield; amorphous solid; $\nu_{max}$/cm$^{-1}$ 3690, 3535, 3080–2840, 1746 and 1170–1150; $\delta_H$(400 MHz) 1.86 (br s; **4**,**5j**), 2.04 (s; **3j**), 2.15 (3H, s; **2j**), 2.27 (s; **4**,**5j**), 2.59 (1H, br s; **2**,**3j**), 4.00 (d, *J* 9.2; **4**,**5j**), 4.05 (1H, d, *J* 9.5; **2j**), 4.08 (d, *J* 9.5; **3j**), 4.88 (d, *J* 9.5; **3j**), 4.95 (1H, d, *J* 9.5; **2j**), 5.02 (d, *J* 9.2; **4**,**5j**), 5.11 (s; **4**,**5j**), 5.20 (s; **3j**), 5.24 (1H, s; **2j**), 5.64–6.02 (2H, m; **2**–**5j**) and 6.67–8.07 (17H, m; **2**–**5j**); *m*/*z* (EI) 514 (M$^+$) (Found: M$^+$, 514.1755. $C_{34}H_{26}O_5$ requires 514.1780).

**2′-Hydroxy-1,1′-binaphthalen-2-yl 3-hydroxy-3-(2-thienyl)-2-phenylpropanoate 2–5k.** 97% Yield; amorphous solid; $\nu_{max}$/cm$^{-1}$ 3540, 3080–2900, 1740 and 1150; $\delta_H$(400 MHz) 2.14 (d, *J* 3.3; **4**,**5k**), 2.74 (d, *J* 4.8; **3k**), 2.77 (1H, d, *J* 4.4; **2k**), 3.80 (1H, d, *J* 9.5; **2k**), 3.82 (d, no resolution; **4**,**5k**), 3.83 (d, *J* 9.5; **3k**), 5.03 (s; **4**,**5k**), 5.18 (s; **3k**), 5.19 (1H, s; **2k**), 5.20 (no resolution; **3**–**5k**), 5.25 (1H, dd, *J* 9.3 and 4.6; **2k**) and 6.43–8.07 (20H, m; **2**–**5k**); *m*/*z* (EI) 516 (M$^+$) (Found: M$^+$, 516.1436. $C_{33}H_{24}O_4S$ requires 516.1396).

**2′-Hydroxy-1,1′-binaphthalen-2-yl 3-hydroxy-3-(3-pyridyl)-2-phenylpropanoate 2–5l.** 91% Yield; amorphous solid; $\nu_{max}$/cm$^{-1}$ 3542, 3080–2970, 1733 and 1150; $\delta_H$(400 MHz) 3.60 (d, *J* 6.3; **4**,**5l**), 3.63 (1H, d, *J* 9.8; **2l**), 3.72 (d, *J* 9.8; **3l**), 4.80 (d, *J* 5.9; **4l**), 4.83 (d, *J* 9.8; **3l**), 4.96 (1H, d, *J* 9.8; **2l**), 5.00 (d, *J* 6.4; **5l**) and 6.55–8.54 (21H, m; **2**–**5l**); *m*/*z* (EI) 511 (M$^+$) (Found: M$^+$, 511.1815. $C_{34}H_{25}NO_4$ requires 511.1783).

**2′-Hydroxy-1,1′-binaphthalen-2-yl 3-hydroxy-3-(4-pyridyl)-2-phenylpropanoate 2–5m.** 90% Yield; amorphous solid; $\nu_{max}$/cm$^{-1}$ 3536, 3080–2920, 1732 and 11.50; $\delta_H$(400 MHz) 3.58 (1H, d, *J* 5.6; **4m**), 3.65 (d, *J* 6.3; **5m**), 3.66 (d, *J* 9.4; **2m**), 3.71 (d, *J* 9.4; **3m**), 4.74 (d, *J* 5.6; **4m**), 4.81 (d, *J* 9.4; **3m**), 4.92 (d, *J* 9.4; **2m**), 4.97 (d, *J* 6.3; **5m**) and 6.55–8.38 (21H, m; **2**–**5m**); *m*/*z* (EI) 511 (M$^+$) (Found: M$^+$, 511.1811. $C_{34}H_{25}NO_4$ requires 511.1783).

### X-Ray analysis of 2e

**Crystal data.** $C_{36}H_{28}O_5$, $M = 540.61$, Monoclinic, Noncent, $a = 17.563(11)$, $b = 9.554(3)$, $c = 18.330(8)$ Å, $\beta = 112.62(4)°$, $V = 2839.1$ Å$^3$ (by least squares refinement for 25 reflections with $15.08 < \theta < 24.20$, $\lambda = 0.7107$ Å, $T = 295$ K) space group $C2$ (no. 5), $Z = 4$, $D_c = 1.265$ g cm$^{-3}$, dimension $0.4 \times 0.3 \times 0.1$ mm, $\mu$(Mo-K$\alpha$) = 0.138 mm$^{-1}$, $F(000) = 1136$. Full crystallographic details, excluding structure factor tables, have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 1*, available *via* the RSC Web pages (http://www.rsc.org/authors). Any request to the CCDC for this material should quote the full literature citation and the reference number 207/168.

### Data collection and processing

Rigaku AFC-5 diffractometer, graphite monochromated Mo-K$\alpha$ radiation; $\omega$–$2\theta$ scan method. 2589 Reflections measured ($4.56 < 2\theta < 50.0$, $h$, $k$, $\pm l$) 2499 unique ($R_{int} = 0.0149$), giving 2298 observed [$F > 3.00\ \sigma(F)$] which were used in all further calculations.

### Structure solution and refinement

The structure was solved by direct methods with the program MULTAN88.[11] The positional parameters and anisotropic thermal factors of the non-H atoms were refined by the full-matrix least-squares method $R = 0.068$, $R_w = 0.086$. Maximum peak in the final $\Delta F$ was 0.27 e Å$^{-3}$. All calculations were carried out using the KPPXRAY[12] package in the Data Processing Center of Kyoto University.

**Table 6** Comparison of the vicinal coupling constants $J_{ab}$ of the aldol adducts in the $^1$H NMR spectra (400 MHz)[a]

| Compd. **2**–**5** | *anti* (**2** or **3**) major (minor) | *syn* (**4** or **5**) major (minor) |
|---|---|---|
| **a** | 9.7 (9.7) | 7.3 (—)[b] |
| **b** | 9.5 (9.2) | 4.0 (—)[b] |
| **c** | 9.5 (9.5) | 7.0 (—)[b] |
| **d** | 9.2 (9.2) | 7.3 (—)[b] |
| **e** | 9.9 (9.7) | 7.8 (—)[b] |
| **f** | 8.8 (9.3) | 7.3 (—)[b] |
| **g** | 9.5 (9.5) | —[b] (—)[b] |
| **h** | 9.5 (9.2) | 8.4 (—)[b] |
| **i** | 9.5 (9.5) | 7.7 (—)[b] |
| **j** | 9.5 (9.5) | 9.2 (—)[b] |
| **k** | 9.5 (9.5) | —[b] (—)[b] |
| **l** | 9.8 (9.8) | 5.9 (6.4) |
| **m** | 9.4 (9.4) | 5.6 (6.3) |

[a] Measured in $CDCl_3$. Chemical shifts in ppm downfield from $Me_4Si$. [b] Could not be determined because of poor resolution or because only trace amounts were obtained.

### General procedure for transesterification of 2–5a–m to methyl esters 6,7a–m

The transformation of **2a** to **6a** and **7a** is typical. A solution of **2a** (139 mg, 0.26 mmol) in MeOH (3 cm$^3$) was treated with LiOMe (1.17 M in MeOH, 0.67 cm$^3$; 0.86 mmol, 3 equiv.) at 0 °C. The mixture was stirred at 0 °C for 1 h after which it was poured into cold 10% aqueous $NH_4Cl$ and extracted with AcOEt. The extract was washed with water, dried and evaporated under reduced pressure. The residual product was purified by pTLC (hexane–acetone = 3:1, 2 times) to give (*S*)-(−)-binaphthol (71 mg, 95%, >99% ee) and **6a** and **7a** (50.4 mg, 75%). The diastereoisomeric mixture was separated by pTLC (hexane–AcOEt = 3:1) and the enantiomeric excess was analyzed by HPLC analysis on a chiral stationary phase with the solvent system of Pr$^i$OH and hexane (see Table 3).

**Methyl 3-hydroxy-2,3-diphenylpropanoate 6a**
70% Yield; amorphous solid; $[\alpha]_D^{18}$ −122.6 (*c* 1.22, in MeOH, 77% ee); $\nu_{max}$/cm$^{-1}$ 3600, 3080–2840, 1725 and 1160; $\delta_H$(200 MHz) 3.16 (d, 1H, d, *J* 4.0), 3.73 (3H, s), 3.88 (1H, d, *J* 9.4), 5.18 (1H, dd, 9.4 and 3.8) and 7.07–7.26 (10H, m); *m*/*z* (EI) 256 (M$^+$) (Found: M$^+$, 256.1102. $C_{16}H_{16}O_3$ requires 256.1099).

**Methyl 3-hydroxy-3-(1-naphthyl)-2-phenylpropanoate 6b.** 55% Yield; amorphous solid; $[\alpha]_D^{18}$ −79.4 (*c* 2.7, in $CHCl_3$, 70% ee); $\nu_{max}$/cm$^{-1}$ 3600, 3080–2840, 1726 and 1160; $\delta_H$(200 MHz) 3.60 (1H, d, *J* 5.2), 3.73 (3H, s), 4.34 (1H, d, *J* 8.3), 5.88 (1H, dd, *J* 8.4 and 5.1), 7.11 (5H, s), 7.26–7.46 (4H, m), 7.69–7.83 (2H, m) and 8.14 (1H, m); *m*/*z* (EI) 306 (M$^+$) (Found: M$^+$, 306.1225. $C_{20}H_{18}O_3$ requires 306.1256).

**Methyl 3-hydroxy-3-(1-naphthyl)-2-phenylpropanoate 7b.** 16% Yield: amorphous solid; $[\alpha]_D^{18}$ −189 (*c* 0.4, in $CHCl_3$, 90% ee); $\nu_{max}$/cm$^{-1}$ 3570, 3080–2840, 1730 and 1220–1160; $\delta_H$(200 MHz) 3.17 (1H, br d, *J* 2.6), 3.60 (3H, s), 4.24 (1H, d, *J* 5.6), 6.16 (1H, dd, *J* 5.5 and 1.9) and 7.08–8.21 (12H, m); *m*/*z* (EI) 306 (M$^+$) (Found: M$^+$, 306.1261. $C_{20}H_{18}O_3$ requires 306.1256).

**Methyl 3-hydroxy-3-(2-naphthyl)-2-phenylpropanoate 6c.** 63% Yield; amorphous solid; $[\alpha]_D^{18}$ −135.6 (*c* 1.01, in $CHCl_3$, 67% ee); $\nu_{max}$/cm$^{-1}$ 3600, 3080–2840, 1730 and 1160; $\delta_H$(200 MHz) 3.35 (1H, br s), 3.72 (3H, s), 3.99 (1H, d, *J* 9.2), 5.34 (1H, dd, *J* 9.2 and 3.4) and 7.08–7.77 (12H, m); *m*/*z* (EI) 306 (M$^+$) (Found: M$^+$, 306.1232. $C_{20}H_{18}O_3$ requires 306.1256).

**Methyl (*E*)-3-hydroxy-2,5-diphenylpent-4-enoate 6d.** 63% Yield; amorphous solid; $[\alpha]_D^{18}$ −146.2 (*c* 1.1, in $CHCl_3$, 79% ee); $\nu_{max}$/cm$^{-1}$ 3600, 3080–2840, 1730 and 1195–1170; $\delta_H$(200 MHz) 3.06 (1H, d, *J* 4.8), 3.72 (3H, s), 3.77 (1H, d, no resolution), 4.86 (1H, m), 6.01 (1H, dd, *J* 15.9 and 5.9), 6.52 (1H, d, *J* 16.0), 7.24 (5H, s) and 7.32 (5H, s); *m*/*z* (EI) 282 (M$^+$) (Found: M$^+$, 282.1229. $C_{18}H_{18}O_3$ requires 282.1256).

**Methyl (*E*)-3-hydroxy-2,5-diphenylpent-4-enoate 7d.** 9% Yield; colourless oil; $[\alpha]_D^{18}$ −57.2 (*c* 0.46, in $CHCl_3$, 64% ee); $\nu_{max}$/cm$^{-1}$ 3580, 3080–2840, 1730 and 1160; $\delta_H$(200 MHz) 2.41 (1H, d, *J*

**Table 7** Comparison of the chemical shifts of the *anti* isomers **2a**–**m** and **3a**–**m** in the $^1$H NMR spectra (400 MHz)[a]

| Compd. **2** and **3** | β-OH | | α-Proton | | β-Proton | | 2′-OH | |
|---|---|---|---|---|---|---|---|---|
| | major | minor | major | minor | major | minor | major | minor |
| **a** | 2.55 | 2.49 | 3.70 | 3.74 | 4.95 | 4.84 | 5.23 | 5.21 |
| **b** | 2.82 | 2.74 | 4.16 | 4.23 | 5.59 | 5.55 | 5.28 | —[b] |
| **c** | 2.69 | 2.59 | 3.84 | 3.89 | 5.13 | 5.02 | 5.23 | 5.22 |
| **d** | 2.38 | 2.31 | 3.58 | 3.63 | 4.61 | 4.57 | 5.24 | 5.21 |
| **e** | 2.45 | 2.38 | 3.70 | 3.74 | 4.90 | 4.80 | 5.24 | 5.20 |
| **f** | 2.17 | 2.12 | 3.42 | 3.48 | 3.81 | 3.75 | 5.23 | 5.17 |
| **g** | 2.03 | 1.96 | 3.58 | 3.60 | 3.69 | —[b] | 5.20 | 5.14 |
| **h** | 2.63 | —[b] | 4.05 | 4.09 | 5.01 | 4.94 | 5.22 | 5.18 |
| **i** | 2.53 | 2.47 | 3.68 | 3.73 | 4.98 | —[b] | 5.22 | 5.18 |
| **j** | 2.15 | 2.04 | 4.05 | 4.08 | 4.95 | 4.88 | 5.24 | 5.20 |
| **k** | 2.77 | 2.74 | 3.80 | 3.83 | 5.25 | —[b] | 5.19 | 5.18 |
| **l** | —[b] | —[b] | 3.63 | 3.72 | 4.96 | 4.83 | —[b] | —[b] |
| **m** | —[b] | —[b] | 3.66 | 3.71 | 4.92 | 4.81 | —[b] | —[b] |

[a] Measured in $CDCl_3$. Chemical shifts in ppm downfield from $Me_4Si$. [b] Not assigned.

2.5), 3.67 (3H, s), 3.78 (1H, d, *J* 7.2), 4.86 (1H, m), 6.19 (1H, dd, *J* 15.9 and 6.8), 6.66 (1H, d, *J* 15.8) and 7.24–7.40 (10H, m); *m*/*z* (EI) 282 ($M^+$) (Found: $M^+$, 282.1219. $C_{18}H_{18}O_3$ requires 282.1256).

**Methyl 3-hydroxy-3-(4-methoxyphenyl)-2-phenylpropanoate 6e.** 64% Yield; colourless oil; $[\alpha]_D^{18}$ −116.7 (*c* 2.5, in $CHCl_3$, 65% ee); $\nu_{max}/cm^{-1}$ 3600, 3080–2840, 1727 and 1170; $\delta_H$(200 MHz) 3.07 (1H, d, *J* 3.8), 3.73 (6H, s), 3.86 (1H, d, *J* 9.5), 5.15 (1H, dd, *J* 9.5 and 3.6), 6.69–6.75 (2H, m) and 7.00–7.26 (7H, m); *m*/*z* (EI) 286 ($M^+$) (Found: $M^+$, 286.1203. $C_{17}H_{18}O_4$ requires 286.1205).

**Methyl 3-hydroxy-2-phenylpentanoate 6f.** 51% Yield; amorphous solid; $[\alpha]_D^{20}$ −61.6 (*c* 0.70, in $CHCl_3$, 69% ee); $\nu_{max}/cm^{-1}$ 3590, 3080–2840, 1721 and 1170; $\delta_H$(200 MHz) 0.92 (3H, t, *J* 7.3), 1.29 (2H, m), 2.79 (1H, br d, *J* 4.8), 3.59 (1H, d, *J* 9.1), 3.69 (3H, s), 4.10 (1H, m) and 7.25–7.36 (5H, m); *m*/*z* (EI) 208 ($M^+$) (Found: $M^+$, 208.1124. $C_{12}H_{16}O_3$ requires 208.1099).

**Methyl 3-hydroxy-2-phenylpentanoate 7f.** 31% Yield; colourless oil; $[\alpha]_D^{20}$ −84.2 (*c* 0.87, in $CHCl_3$, 88% ee); $\nu_{max}/cm^{-1}$ 3586, 3080–2840, 1729 and 1160; $\delta_H$(200 MHz) 1.00 (3H, t, *J* 7.3), 1.42 (2H, m), 2.41 (1H, br d, *J* 2.3), 3.61 (1H, d, *J* 6.3), 3.69 (3H, s), 4.13 (1H, m) and 7.36 (5H, s); *m*/*z* (EI) 208 ($M^+$) (Found: $M^+$, 208.1106. $C_{12}H_{16}O_3$ requires 208.1099).

**Methyl 3-hydroxy-2-phenyl-4-methylpentanoate 6g.** 77% Yield; amorphous solid; $[\alpha]_D^{18}$ −60.6 (*c* 0.79, in $CHCl_3$, 67% ee); $\nu_{max}/cm^{-1}$ 3600, 3080–2880, 1724, 1170 and 750; $\delta_H$(200 MHz) 0.87 (3H, d, *J* 6.8), 0.94 (3H, d, *J* 6.9), 1.45 (1H, m), 2.61 (1H, br d, *J* 3.3), 3.68 (3H, s), 3.74 (1H, d, *J* 9.4), 4.07 (1H, m) and 7.32 (5H, s); *m*/*z* (EI) 222 ($M^+$) (Found: $M^+$, 222.1258. $C_{13}H_{18}O_3$ requires 222.1256).

**Methyl 3-hydroxy-3-(2-furyl)-2-phenylpropanoate 6h.** 22% Yield; amorphous solid; $[\alpha]_D^{19}$ −29.2 (*c* 1.74, in $CHCl_3$, 22% ee); $\nu_{max}/cm^{-1}$ 3600, 3080–2840, 1727 and 1170; $\delta_H$(200 MHz) 3.33 (1H, d, *J* 5.5), 3.72 (3H, s), 4.20 (1H, d, *J* 9.1), 5.21 (1H, dd, *J* 9.1 and 5.5), 6.04 (1H, br d, *J* 2.9), 6.18 (1H, dd, *J* 3.3 and 1.8) and 7.20–7.31 (6H, m); *m*/*z* (EI) 246 ($M^+$) (Found: $M^+$, 246.0885. $C_{14}H_{14}O_4$ requires 246.0892).

**Methyl 3-hydroxy-3-(2-furyl)-2-phenylpropanoate 7h.** 38% Yield; amorphous solid; $[\alpha]_D^{19}$ −115.8 (*c* 1.15, in $CHCl_3$, 94% ee); $\nu_{max}/cm^{-1}$ 3585, 3080–2840, 1732 and 1160; $\delta_H$(200 MHz) 2.51 (1H, br d, *J* 3.7), 3.60 (3H, s), 4.13 (1H, d, *J* 8.2), 5.33 (1H, dd, *J* 8.1 and 2.9), 6.25 (1H, br d, *J* 3.3), 6.31 (1H, br d, *J* 3.3 and 1.8) and 7.26–7.39 (6H, m); *m*/*z* (EI) 246 ($M^+$) (Found: $M^+$, 246.0875. $C_{14}H_{14}O_4$ requires 246.0892).

**Methyl 3-hydroxy-3-(3-furyl)-2-phenylpropanoate 6i.** 73% Yield; amorphous solid; $[\alpha]_D^{18}$ −87.2 (*c* 3.6, in $CHCl_3$, 70% ee); $\nu_{max}/cm^{-1}$ 3600, 3080–2840, 1725 and 1200–1170; $\delta_H$(200 MHz) 3.27 (1H, br s), 3.71 (3H, s), 3.85 (1H, d, *J* 9.2), 5.21 (1H, br d, *J* 8.9), 6.13 (1H, s), 7.09 (1H, s) and 7.18–7.25 (7H, m); *m*/*z* (EI) 246 ($M^+$) (Found: $M^+$, 246.0894. $C_{14}H_{14}O_4$ requires 246.0892).

**Methyl 3-hydroxy-3-(3-furyl)-2-phenylpropanoate 7i.** 12% Yield; amorphous solid; $[\alpha]_D^{18}$ −89.7 (*c* 0.48, in $CHCl_3$, 83% ee); $\nu_{max}/cm^{-1}$ 3580, 3080–2840, 1730 and 1160; $\delta_H$(200 MHz) 2.47 (1H, br s), 3.61 (3H, s), 3.84 (1H, d, *J* 7.9), 5.29 (1H, d, *J* 7.8), 6.34 (1H, br s) and 7.32–7.38 (7H, m); *m*/*z* (EI) 246 ($M^+$) (Found: $M^+$, 246.0893. $C_{14}H_{14}O_4$ requires 246.0892).

**Methyl 3-hydroxy-3-(5-methyl-2-furyl)-2-phenylpropanoate 6j.** 50% Yield; amorphous solid; $[\alpha]_D^{18}$ −50.2 (*c* 2.67, in $CHCl_3$, 32% ee); $\nu_{max}/cm^{-1}$ 3598, 3080–2840, 1728 and 1170; $\delta_H$(200 MHz) 2.23 (3H, s), 3.20 (1H, d, *J* 5.5), 3.73 (3H, s), 4.19 (1H, d, *J* 9.2), 5.14 (1H, dd, *J* 9.1 and 5.4), 5.75 (1H, m), 5.90 (1H, d, *J* 2.9) and 7.23 (5H, s); *m*/*z* (EI) 260 ($M^+$) (Found: $M^+$, 260.1048. $C_{15}H_{16}O_4$ requires 260.1049).

**Methyl 3-hydroxy-3-(5-methyl-2-furyl)-2-phenylpropanoate 7j.** 22% Yield; amorphous solid; $[\alpha]_D^{18}$ −102.5 (*c* 0.65, in $CHCl_3$, 94% ee); $\nu_{max}/cm^{-1}$ 3586, 3080–2840, 1732 and 1160; $\delta_H$(200 MHz) 2.22 (1H, d, *J* 3.7), 2.29 (1H, s), 3.61 (3H, s), 4.11 (1H, d, *J* 8.7), 5.26 (1H, dd, *J* 8.8 and 3.4), 5.89 (1H, m), 6.16 (1H, d, *J* 3.2) and 7.27–7.41 (5H, m); *m*/*z* (EI) 260 ($M^+$) (Found: $M^+$, 260.1011. $C_{15}H_{16}O_4$ requires 260.1049).

**Methyl 3-hydroxy-3-(2-thienyl)-2-phenylpropanoate 6k.** 66% Yield; amorphous solid; $[\alpha]_D^{18}$ −103.0 (*c* 1.16, in $CHCl_3$, 60% ee); $\nu_{max}/cm^{-1}$ 3600, 3080–2900, 1727 and 1160; $\delta_H$(200 MHz) 3.41 (1H, d, *J* 4.6), 3.73 (3H, s), 3.95 (1H, d, *J* 9.2), 5.47 (1H, dd, *J* 9.1 and 4.4), 6.59 (1H, br d, *J* 3.5), 6.78 (1H, dd, *J* 5.1 and 3.5) and 7.15–7.26 (6H, m); *m*/*z* (EI) 262 ($M^+$) (Found: $M^+$, 262.0654. $C_{14}H_{14}O_3S$ requires 262.0664).

**Methyl 3-hydroxy-3-(2-thienyl)-2-phenylpropanoate 7k.** 8% Yield; amorphous solid; $\nu_{max}/cm^{-1}$ 3585, 2840–3080, 1730 and 1160; $\delta_H$(200 MHz) 2.64 (1H, d, *J* 2.9), 3.58 (3H, s), 3.94 (1H, d, *J* 8.1), 5.58 (1H, dd, *J* 8.1 and 2.3), 6.92–7.01 (2H, m) and 7.23–7.44 (6H, m); *m*/*z* (EI) 262 ($M^+$) (Found: $M^+$, 262.0643. $C_{14}H_{14}O_3S$ requires 262.0664).

**Methyl 3-hydroxy-3-(3-pyridyl)-2-phenylpropanoate 6l,7l.** 75% Combined yield; mixture of inseparable diastereoisomers; amorphous solid; $\nu_{max}/cm^{-1}$ 3595, 3080–2920, 1728 and 1165; $\delta_H$(200 MHz) 3.58 (s; **7l**), 3.74 (3H, s; **6l**), 3.84 (1H, d, *J* 9.6; **6l**), 3.85 (d, *J* 6.7; **7l**), 5.23 (1H, d, *J* 9.6; **6l**), 5.35 (1H, d, *J* 7.0; **7l**), 7.03–7.72 (7H, m; **6**,**7l**) and 8.19–8.51 (2H, m; **6**,**7l**); *m*/*z* (EI) 257 ($M^+$) (Found: $M^+$, 257.1045. $C_{15}H_{15}NO_3$ requires 257.1052).

**Methyl 3-hydroxy-3-(4-pyridyl)-2-phenylpropanoate 6m,7m.** 83% Combined yield; mixture of inseparable diastereoisomers; amorphous solid; $\nu_{max}/cm^{-1}$ 3580, 3080–2960, 1728 and 1165; $\delta_H$(200 MHz) 3.62 (3H, s; **7m**), 3,73 (s; **6m**), 3.79 (d, *J* 9.2; **6m**), 3.83 (1H, d, *J* 6.2; **7m**), 5.17 (d, *J* 9.2; **6m**), 5.34 (1H, d, *J* 6.2; **7m**), 6.95–7.33 (7H, m; **6**,**7m**), 8.38 (d, *J* 5.9; **6m**) and 8.49 (2H, d, *J* 6.0; **7m**); *m*/*z* (EI) 257 ($M^+$) (Found: $M^+$, 257.1091. $C_{15}H_{15}O_3N$ requires 257.1052).

### Aldol reaction of the anion of 8

In a similar way to the preparation of **2a** except for the usage of LDA (628 μl, 0.31 mmol) in place of BuLi, 2′-methoxy-1,1′-binaphthalen-2-yl 3-hydroxy-2,3-diphenylpropanoate **9** was obtained from 2′-methoxy-1,1′-binaphthyl phenylacetate **8**[2] (125 mg, 0.30 mmol) and benzaldehyde (31.9 μl, 0.31 mmol, 1.05 equiv.) in 9% yield as a mixture of diastereoisomers. HPLC analysis of the mixture (on a Puresil $C_{18}$ column with 22% $H_2O$–MeOH at a flow rate of 0.5 ml $min^{-1}$) suggested a ratio of 50 : 39 : 11 for *anti* : *anti* : *syn*.

Compound **9**: 9% combined yield; mixture of diastereoisomers; amorphous solid; $\nu_{max}/cm^{-1}$ 3587, 3080–2840, 1746 and 1150; $\delta_H$(400 MHz) 2.19 (br d; *syn*), 2.36 (d, *J* 5.1; *anti*-minor), 2.79 (1H, d, *J* 3.9; *anti*-major), 3.51 (s; *syn*), 3.56 (3H, s; *anti*-major), 3.58 (s; *anti*-minor), 3.64 (d, *J* 9.4; *anti*-minor), 3.73 (d, *J* 8.5; *syn*), 3.74 (1H, d, *J* 9.4; *anti*-major), 4.73 (dd, *J* 9.3 and 3.8; *anti*-minor), 4.80 (1H, dd, *J* 9.3 and 3.5; *anti*-major), 4.87 (br d, *J* 7.5; *syn*) and 6.43–7.98 (22H, m); *m*/*z* (EI) 524 ($M^+$) (Found: $M^+$, 524.1995. $C_{36}H_{28}O_4$ requires 524.1988).

### Michael reaction of the anion of (*S*)-1 with di-*tert*-butyl methylenemalonate

In the same manner as the preparation of **2a**, 2′-hydroxy-1,1′-binaphthalen-2-yl 2-phenyl-4,4-di-*tert*-butoxycarbonylbutanoate **10** was furnished in the yields shown in Table 4 from (*S*)-**1** and di-*tert*-butyl methylenemalonate (1.2 equiv.) with the action of BuLi (2.1 equiv.) as a mixture of two diastereoisomers. The products were analyzed by HPLC with silica gel column.

Compound **10**: amorphous solid; $[\alpha]_D^{19}$ −37.0 (*c* 1.1, in $CHCl_3$, 65% de) (Found: C, 75.96; H, 6.40. Calc. for $C_{40}H_{40}O_7$: C, 75.93; H, 6.37%); $\nu_{max}/cm^{-1}$ 3530, 3080–2880, 1760, 1740 and 1220–1140; $\delta_H$(400 MHz) 1.39 (d, *J* 5.5; minor), 1.41 (18H, s; major), 2.04 (1H, m; major), 2,04 (m; minor), 2.25 (m; minor), 2.33 (1H, m; major), 2.80 (dd, *J* 8.2 and 6.8; minor), 2.85 (1H, dd, *J* 8.4 and 7.0; major), 3.51 (t, *J* 7.9; minor), 3.85 (1H, t, *J* 7.9; major), 5.24 (1H, s; major), 5.30 (s; minor) and 6.63–8.05 (17H, m).

**Methyl 2-phenyl-4,4-di-*tert*-butoxycarbonylbutanoate 11.** According to the general procedure for the transesterification

mentioned above, the methyl ester **11** was obtained in 84% yield from **10** of 65% de as an amorphous solid together with (*S*)-BINOL (82% yield, −100% ee). The optical yield of **11** was determined by HPLC using a reversed-phase chiral column of Ceramospher chiral Ru-1 under the conditions of 0.5 ml $min^{-1}$ of flow rate of MeOH detected at 235 nm. Compound **11**; $[\alpha]_D^{19}$ +35.1 (*c* 0.9 $CHCl_3$, 64% ee); $\nu_{max}/cm^{-1}$ 3040–2950, 1732 and 1160–1140; $\delta_H$(200 MHz) 1.44 (9H, s), 1.47 (9H, s), 2.29 (1H, m), 2.54 (1H, m), 3.02 (1H, dd, *J* 8.3 and 7.0), 3.65 (1H, m, no resolution), 3.66 (3H, s) and 7.28–7.34 (5H, m); *m*/*z* (EI) 378 ($M^+$) (Found: $M^+$, 378.2032. $C_{21}H_{30}O_6$ requires 378.2043).

**Conjugate addition of the anion of 1 to DBAD**

In the same manner as the preparation of **2a**, 2′-hydroxy-1,1′-binaphthalen-2-yl *N*,*N*′-bis(*tert*-butoxycarbonyl)hydrazinophenylacetate **12** (310 mg, 75% de) was furnished from (*S*)-**1** (204 mg, 0.5 mmol) and di-*tert*-butyl azodicarboxylate (581 mg, 2.52 mmol, 5 equiv.) by the action of BuLi (2.1 equiv.) as a mixture of two diastereoisomers. The products were analyzed by reversed-phase HPLC using a flow rate of 0.5 $cm^3$ $min^{-1}$ of 15% $H_2O$ in MeOH.

Compound **12**: 97% yield; amorphous solid; $[\alpha]_D^{20}$ +6.7 (*c* 1.5, in $CHCl_3$, 75% de); $\nu_{max}/cm^{-1}$ 3550, 3400, 3070–2930, 1750–1700 and 1160; $\delta_H$(400 MHz, in $C_6D_6$, at 70 °C) 1.12 (br s; minor), 1.15 (9H, br s; major), 1.40 (s; minor), 1.41 (9H, s; major), 5.15 (s; minor), 5.31 (1H, br s; major), 6.03 (br s; minor), 6.17 (1H, br s; major), 6.40 (1H, s) and 6.70–7.70 (17H, m); *m*/*z* (EI) 634 ($M^+$) (Found: $M^+$, 643.2734. $C_{38}H_{38}N_2O_7$ requires 643.2679).

**Methyl *N*,*N*′ bis(*tert*-butoxycarbonyl)hydrazinophenylacetate 13.** A mixture of **12** (200 mg, 0.32 mmol; 75% de), $LiOH·H_2O$ (27 mg, 0.63 mmol, 2 equiv.) and THF–$H_2O$ (3 : 1; 10 $cm^3$) was stirred for 8 h at 0 °C and for 14 h at room temperature. After additional $LiOH·H_2O$ (27 mg, 0.63 mmol, 2 equiv.) had been added, the resulting mixture was further stirred for 3 h at room temperature and then poured into cold 1 M aq. HCl. The mixture was extracted with AcOEt, washed with water, dried and evaporated under reduced pressure. Without isolation and purification, the residual carboxylic acid was immediately methylated with an excess of $CH_2N_2$ in ether at 0 °C to give **13** (95 mg; 26% ee) in 79% yield concomitant with (*S*)-BINOL (97 mg, 99% yield; 100% ee). The optical yield of **13** was determined by HPLC using a reversed-phase chiral column of Ceramospher chiral Ru-1 under the conditions of 0.5 ml $min^{-1}$ of flow rate of MeOH detected at 225 nm. Compound **13**: amorphous solid; $[\alpha]_D^{22}$ +52.5 (*c* 1.26, in $CHCl_3$, 26% ee); $\nu_{max}/cm^{-1}$ 3400, 3040–2950, 1745, 1710 and 1160; $\delta_H$(200 MHz, at 60 °C) 1.19 (9H, br s), 1.48 (9H, s), 3.74 (3H, s), 5.96 (1H, br s), 6.43 (1H, br s) and 7.31 (5H, s); *m*/*z* (EI) 380 ($M^+$) (Found: $M^+$, 380.1956. $C_{19}H_{28}N_2O_6$ requires 380.1948).

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