Pergamon

Tetrahedron: *Asymmetry* 13 (2002) 729–734

TETRAHEDRON: *ASYMMETRY*

Asymmetric construction of novel bicyclo[4.4.0] and [4.3.0]ring systems via intramolecular Horner–Wadsworth–Emmons reactions

Jiro Yamazaki,[a] Ashutosh V. Bedekar,[a] Toshiyuki Watanabe,[a] Kiyoshi Tanaka,[a,*] Joshu Watanabe[b] and Kaoru Fuji[b]

[a]*School of Pharmaceutical Sciences, University of Shizuoka, Shizuoka 422-8526, Japan*
[b]*Institute for Chemical Research, Kyoto University, Uji 611-0011, Japan*

Received 11 March 2002; accepted 1 April 2002

Abstract—Novel perhydro-indanones and -naphthalenones having a quaternary stereogenic carbon and tetrasubstituted olefinic linkage were prepared via asymmetric intramolecular Horner–Wadsworth–Emmons reactions. The optically active binaphthyl phosphonates were connected with the 2-substituted cyclopenta- or cyclohexa-1,3-dione through the linker arm and the successive base treatment of the products with diethylzinc led to cyclization reactions with concomitant differentiation of diastereotopic carbonyl groups to afford the non-racemic title compounds in good enantiomeric excess. The absolute structure of the cyclized product was determined by X-ray analysis of its derived bromide.

1. Introduction

In the preceding paper, we described the asymmetric construction of a fused tetracyclic ring system by intramolecular Wittig-type reactions. In these reactions, the generated carbanions efficiently attack the electrophilic carbonyl carbon center without any influence from steric hindrance and discriminate the diastereotopic carbonyl groups in the same molecules to give the desired cyclic compounds with rather high enantiomeric excess. As another variation of this strategy, we report herein an intramolecular cyclization to fused carbocyclic systems having a quaternary carbon center as well as a tetrasubstituted olefinic linkage using the Horner–Wadsworth–Emmons reaction.

The Horner–Wadsworth–Emmons (HWE) reaction[1] between nucleophilic phosphorous-stabilized carbanions and carbonyl components is a widely used synthetic tool for the construction of carbon–carbon double bonds. The transformation generally occurs at low temperature and covers a large number of carbonyl compounds without incurring any problems with isolation of by-products originating from the reactants. Substantial progress has been made recently in the development of direct syntheses of optically active olefinic compounds from achiral or racemic carbonyl compounds by using HWE reactions.[2] One of the approaches includes differentiation of enantiotopic or diastereotopic carbonyl groups of dicarbonyl compounds. This approach was realized by use of optically active phosphonate reagents as chiral HWE agents possessing axially dissymmetric binaphthol moieties, such as (*S*)-**1**.[3] Despite the inherent low atom economy of the Wittig-type reactions from the viewpoint of so-called green chemistry,[4] the asymmetric HWE reactions of these reagents seem to be effective transformation methods, because they proceed with concomitant elimination of the phosphonate group, resulting in direct production of optically active olefins in a predictable manner. Taking the less accessibility of steric hindrance in intramolecular reactions[5] into account, we first prepared the 1,3-dicarbonyl substrates for intramolecular HWE asymmetrization. In these substrates, the 1,3-dicarbonyl moiety was tethered to the axially chiral 1,1′-binaphthalene-2,2′-diol molecules through an appropriate linker arm and phosphate linkage.

* Corresponding author. Tel.: +81 54 264 5746; fax: +81 54 264 5745; e-mail: tanakaki@u-shizuoka-ken.ac.jp

0957-4166/02/$ - see front matter
PII: S0957-4166(02)00177-5

2. Results and discussion

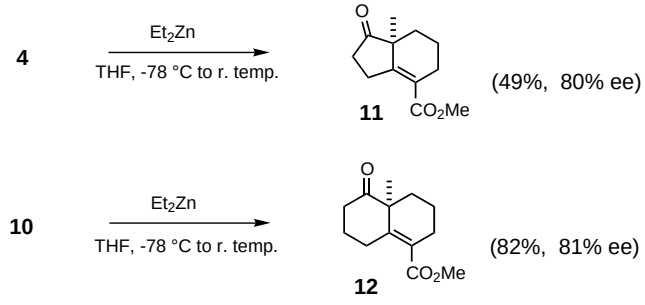
The substrates **4** and **10** for the intramolecular HWE reactions were first prepared. The cyclopentadione **4** was obtained by coupling of the diacetal **2**, which was derived from cyclopenta-1,3-dione according to the reported procedure,[6] with the anion of the HWE reagent (*S*)-**1** as a mixture of diastereomers at the α-carbon of the phosphate to give **3** followed by acidic hydrolysis of the acetals (Scheme 1). In a similar way, the cyclohexadione derivative **10** was also prepared as a mixture of diastereomers. Thus, the *C*-alkylation[7] of cyclohexa-1,3-dione gave **5**, which was transformed stepwise into the diacetal **7** through two different acetalization procedures via the monoacetal **6**. Hydroboration and successive treatment with iodine afforded the iodide **8**, which was then coupled with the anion of (*S*)-**1** to yield **9**. Finally, the acetal was hydrolyzed under acidic conditions to furnish the substrate **10** (Scheme 1).

The reaction conditions for the cyclization of substrates **4** and **10** were then examined using different kinds of bases and solvents. We recently reported the use of diethylzinc as a base for reactions involving active methylene compounds, such as asymmetric catalytic allylic substitution mediated by a palladium complex[8] as well as asymmetric HWE reactions.[9] After several trials of cyclization reactions of **4** and **10**, the effectiveness of diethylzinc as a base was again proven here. Thus, the best results were obtained by diethylzinc in terms of chemical and optical yields. The cyclized products **11** and **12** were obtained in 49 and 82% yield with 80 and 81% e.e., respectively (Scheme 2).

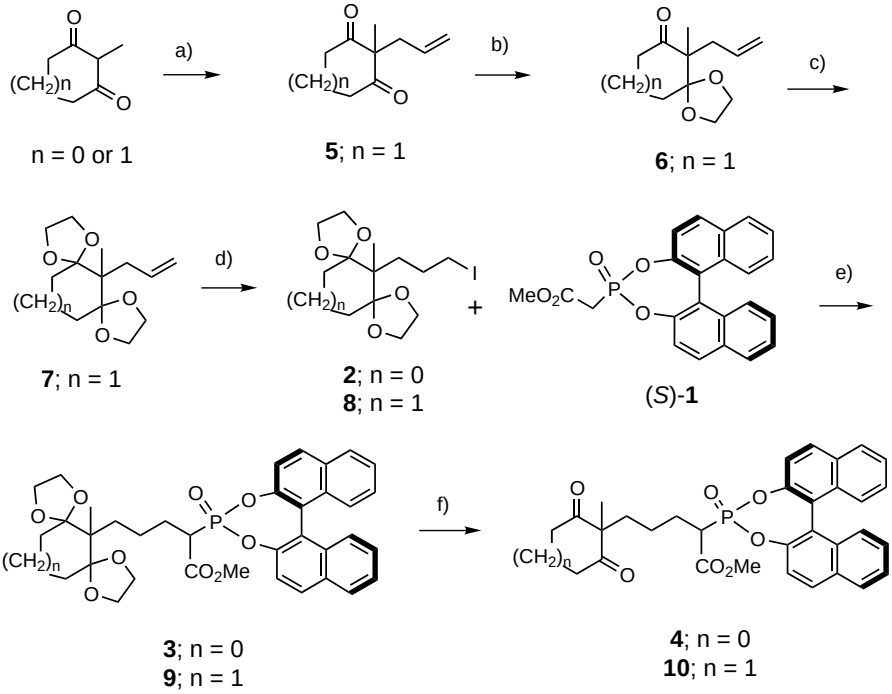
The absolute structures of the cyclized products **11** and **12** were determined or deduced as follows. The CD spectra of the two compounds show a similar curve to each other (Fig. 1) suggesting the same configuration at the stereogenic carbon center.

The cyclized product **12** was converted to the diol **13** stereoselectively by reduction with DIBAL-H, and the diol **13** was acylated by treatment with *p*-bromobenzoyl chloride in pyridine to give the diacylated derivative **14** as a crystalline compound. Recrystallization of **14** from a mixture of ethyl acetate–hexane gave us a single crystal suitable for X-ray analysis (Scheme 3).

In this way, using anomalous dispersion of the bromine atom in X-ray analysis, the absolute stereostructure of the product **14** was clearly elucidated to have *S*-configuration at the stereogenic carbon center. Therefore, the stereochemistry of the other related product **11** was deduced to have the same configuration taking into



Scheme 2.



Scheme 1. *Reagents and conditions*: (a) DBU, allyl bromide, LiI, THF, reflux; (b) ethyleneglycol, $BF_3{\cdot}Et_2O$, CH_2Cl_2, rt; (c) ethylene glycol, *p*-TsOH·H_2O, benzene, reflux; (d) i. $BH_3{\cdot}SMe_2$, THF, ii. MeOH, iii. NaOMe, I_2, rt; (e) NaH, DMF, rt; (f) 60% $HClO_4$, MeOH, H_2O, 40°C.

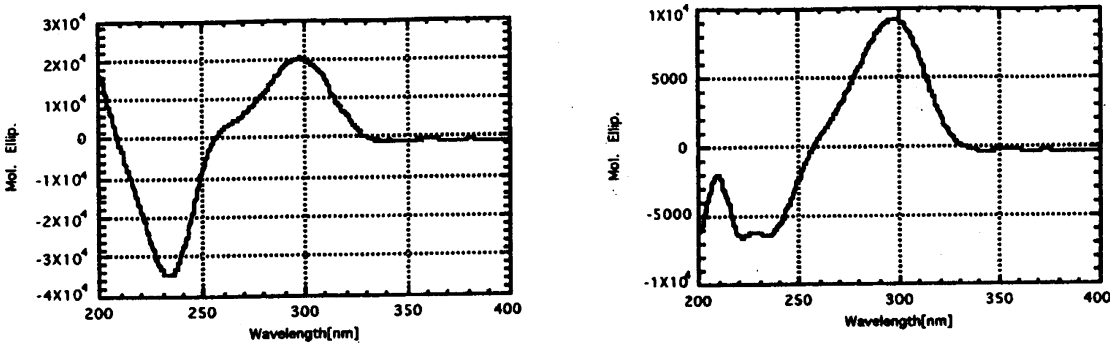
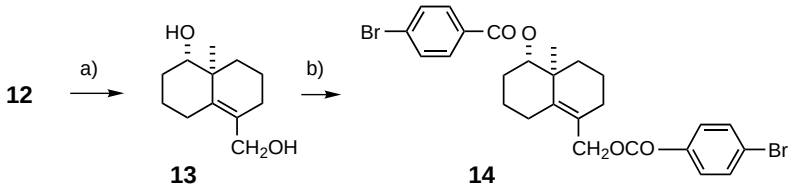


Figure 1. CD spectra of the compounds **11** (left) and **12** (right).



Scheme 3. *Reagents and conditions*: (a) DIBAL-H, THF, −78°C to rt; (b) *p*-bromobenzoyl chloride, pyridine, rt.

consideration the result of this X-ray analysis as well as the reaction mechanism involving the anion of **4** as described below (Fig. 2).

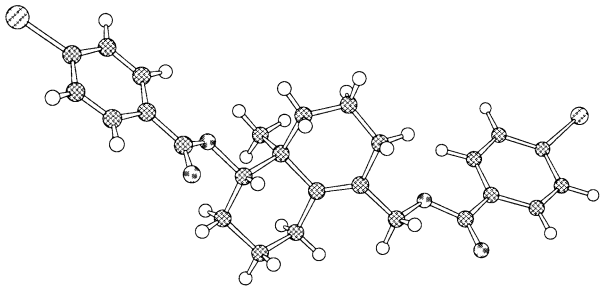


Figure 2. Crystal structure of **14**.

The preferential formation of the enantiomers **11** and **12** can be explained if the following mechanistic explanation is considered. Thus, the intramolecular nucleophilic attack of the carbanion to the carbonyl group occurs from the favored face opposite the methyl substituent ((**a**) *anti*-attack in Fig. 3). Unlike the anion of the Horner–Emmons type reaction in the preceding paper, the anions of **4** and **10** with zinc as a counter cation might form a chelated structure.

With respect to the π-face of the carbanion to be selected, approach to the *si*-face is sterically favored in the case of the *S*-configured chiral auxiliary (**b**). Therefore, by considering a combination of the two possible approaches to the carbonyls, either *si* or *re* approach, and the above-mentioned (**a**) and (**b**), the pair of plausible transition state models (**c**) and (**d**) becomes feasible. Comparison of these two models clearly led to a conclusion that the model (**c**) of *si*/*anti*-*si* is more energetically favorable than the model (**d**) of *si*/*anti*-*re*, because the latter is subject to unfavorable steric interactions. In this way, the observed stereochemistry of the products was straightforwardly explicable.

3. Conclusion

In summary, we have enantioselectively constructed two novel fused bicyclic compounds **11** and **12**. These bicyclo[4.4.0] and [4.3.0] derivatives contain not only a quaternary carbon center and a tetrasubstituted olefinic bond, but also carbonyl and ester functionalities. Consequently, these molecules can be regarded as interesting building blocks for asymmetric synthesis of useful compounds.

4. Experimental

4.1. General

Melting points are uncorrected. Proton nuclear magnetic resonance (^{1}H NMR) spectra were taken at 200 or 270 MHz in $CDCl_3$ with chemical shifts being reported as δ ppm from tetramethylsilane as an internal standard and couplings are expressed in hertz. Infrared (IR) spectra were measured in $CHCl_3$ solution. THF was distilled from sodium benzophenone ketyl and dichloromethane was from calcium hydride. Unless otherwise noted, all reactions were run under an argon atmosphere. All extractive 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 F_{254} plates (Merck) were used for preparative TLC (p-TLC).

4.2. HPLC analysis of derivatives (*S*)-1, 4, 10, 11 and 12

HPLC analyses were performed using a solvent system of hexane/2-PrOH at the flow rate indicated below and

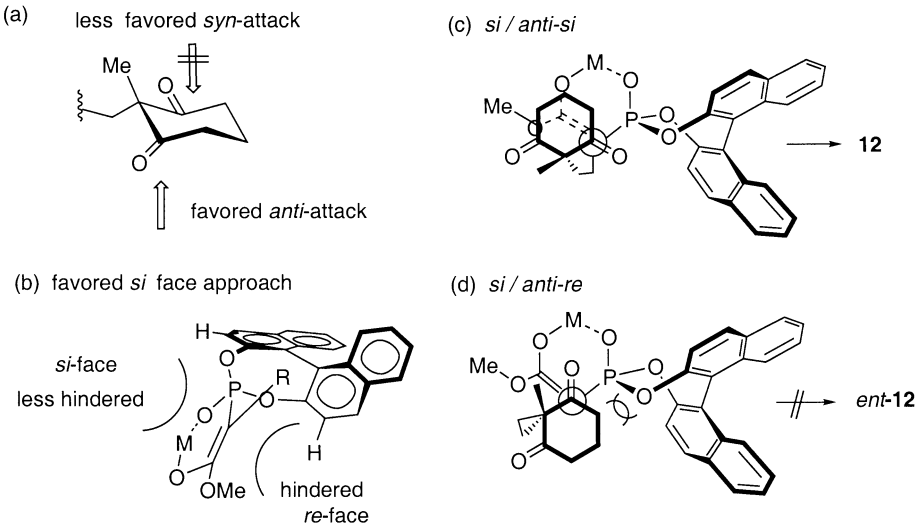


Figure 3. Possible mechanistic explanation for formation of **12**.

each peak was detected at 254 nm. Either silica or chiral column with the following solvent ratio for 2-PrOH in hexane was used. Chiralpak AD, 20%, 1.0 mL/min for (*S*)-**1**; Shim-pack PREP SIL(H), 3.0%, 0.5 mL/min for **4** and **10**; Chiralpak AS (Daicel Chemical Ind. Ltd) 5.0%, 1.0 mL/min for **11**; Chiralpak AS, 1.0%, 0.5 mL/min for **12**.

4.3. 2-Allyl-3-ethylenedioxy-2-methylcyclohexanone 6

A mixture of **5** (2.26 g, 13.6 mmol), ethylene glycol (7.0 mL, 101 mmol, 7.4 equiv.), boron trifluoride etherate solution (0.84 mL, 6.83 mmol, 0.5 equiv.) and CH_2Cl_2 (30 mL) was stirred for 7 h at room temperature. The reaction mixture was poured into satd aqueous $NaHCO_3$ solution and extracted with AcOEt. The extracts were washed successively with water and brine and then dried. Concentration under reduced pressure left a residue, which was subjected to column chromatography on silica gel with hexane/AcOEt (7/3) to give **6** as a colorless oil (2.50 g, 89%). ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.64 (m, 1H), 5.07 (brd, 1H, $J=6.3$ Hz), 5.00 (s, 1H), 3.97 (s, 4H), 2.62 (dd, 1H, $J=10.5$, 5.1 Hz), 2.45–2.31 (m, 3H), 2.04 (m, 1H), 1.89–1.71 (m, 3H), 1.61 (s, 3H); IR (neat) 3075, 2960, 2880, 1710, 1640, 1592, 1450, 1070 cm^{-1}. Anal. calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 68.18; H, 8.59%.

4.4. 2-Allyl-1,3-bis(ethylenedioxy)-2-methylcyclohexane 7

A mixture of **6** (475 mg, 2.26 mmol), ethylene glycol (1.3 mL, 22 mmol, 10 equiv.), *p*-TsOH·H_2O (38.9 mg, 0.23 mmol, 0.1 equiv.) and benzene (50 mL) was heated under reflux for 3.5 h with azeotropic removal of water using a Dean–Stark apparatus. The reaction mixture was poured into sat. aqueous $NaHCO_3$ solution and extracted with AcOEt. The extracts were washed successively with water and brine, and then dried. Concentration under reduced pressure yielded the residue, which was subjected to column chromatography on silica gel with hexane/AcOEt (7/3) to give **7** as a colorless oil (449 mg, 78%). ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.01 (m, 1H), 4.95 (m, 2H), 4.07–3.86 (m, 8H), 2.37 (brd, 1H, $J=7.3$ Hz), 1.68–1.56 (m, 6H, overlapped), 1.17 (s, 3H); IR (neat) 3075, 2960, 2880, 1635, 1460, 1440, 1340, 1230, 1190, 1080, 1030 cm^{-1}. Anal. calcd for $C_{14}H_{22}O_4$: C, 66.12; H, 8.72. Found: C, 66.08; H, 8.79%.

4.5. 1,3-Bis(ethylenedioxy)-2-(1-iodopropyl)-2-methylcyclohexane 8

To a stirred solution of **7** (220 mg, 0.87 mmol) in THF (10 mL) was added dropwise BH_3·SMe_2 complex (0.2 mL, 2.0M in THF, 0.43 mmol, 0.5 equiv.), and the resulting mixture was stirred for 3 h at room temperature. MeOH was added to the mixture until gas formation ceased. The mixture was treated with NaOMe (0.32 mL, 4.0 M in MeOH, 1.21 mmol, 1.4 equiv.) and I_2 (307 mg, 1.30 mmol, 1.5 equiv.) and the mixture was then stirred for 24 h at room temperature. The reaction mixture was poured into sat. aqueous $Na_2S_2O_3$ and extracted with EtOAc. The extracts were washed with water and brine, dried and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with a solvent system of hexane/AcOEt (3/1) to give **8** as a colorless oil (169 mg, 51%). ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.04–3.89 (m, 8H), 3.17 (t, 2H, $J=6.9$ Hz), 1.97 (m, 2H), 1.72–1.59 (m, 8H), 1.12 (s, 3H); IR (neat) 2960, 2880, 1470, 1455, 1440, 1380, 1340, 1230, 1195, 1150, 1050, 1035 cm^{-1}. Anal. calcd for $C_{14}H_{23}IO_4$: C, 43.99; H, 6.06. Found: C, 44.01; H, 6.17%.

4.6. Coupling reaction of 2 and 8 with the anion of (*S*)-1

To a stirred suspension of NaH (23.9 mg, 0.6 mmol, 2.1 equiv.) and DMF (10 mL) was added a solution of (*S*)-**1** (254 mg, 0.63 mmol, 2.3 equiv.) in DMF (5 mL) at 0°C. The mixture was stirred for a further 30 min at

the same temperature. A solution of **8** (106 mg, 0.28 mmol) in DMF (5 mL) was added and the mixture was stirred for 48 h at an ambient temperature. The reaction mixture was poured into water and extracted with Et_2O. The Et_2O layer was successively washed with water and brine, and then dried. Evaporation of the solvent under reduced pressure left a residue, which was purified by p-TLC on silica gel with hexane/AcOEt (1/1) to afford **9** as an amorphous solid (97.1 mg, 53%). **9**: $[\alpha]_D^{18}$ +236 (*c* 0.75, $CHCl_3$, inseparable mixture of diastereomers (ca. 1:1)); ^1H NMR (200 MHz, $CDCl_3$) δ 8.15–7.96 (m, 8H), 7.64–7.49 (m, 8H), 7.36–7.28 (m, 8H), 4.00–3.79 (m, 16H), 3.84 (s, 3H), 3.61 (s, 3H), 3.31–3.08 (m, 2H), 2.39–1.88 (m, 4H), 1.73–1.49 (m, 20H), 1.12 (s, 3H), 1.05 (s, 3H); IR (KBr) 2960, 2880, 1740, 1590, 1510, 1465, 1435, 1325, 1290, 1225, 1155, 1065, 1035 cm^{-1}; MS (*m*/*z*) 658 (M^+); HRMS (*m*/*z*) calcd for $C_{37}H_{39}O_9P$ (M^+) 658.2331, found: 658.2361.

In the same way as above for the preparation of **9**, **3** was provided from **2** and (*S*)-**1** as an inseparable mixture of diastereomers in 48% yield after purification by p-TLC on silica gel with hexane/AcOEt (1/2).

Compound 3: amorphous; $[\alpha]_D^{18}$ +229 (*c* 0.46, $CHCl_3$, inseparable mixture of diastereomers (ca. 1:1)); ^1H NMR (270 MHz, $CDCl_3$) δ 8.57–7.28 (m, 24H), 4.00–3.75 (m, 16H), 3.72 (s, 3H), 3.62 (s, 3H), 3.54–3.30 (m, 2H), 2.27–1.84 (m, 12H), 1.53–1.17 (m, 8H), 1.13 (s, 3H), 1.07 (s, 3H); IR ($CHCl_3$) 3002, 2982, 2957, 1759, 1747, 1743, 1739, 1728, 1722, 1512, 1504, 1462, 1435, 1323, 1286, 1240, 1161, 1074, 1039 cm^{-1}. Anal. calcd for $C_{36}H_{37}O_9P$: C, 67.87; H, 5.78. Found: C, 66.78; H, 6.03%.

4.7. Acidic hydrolysis of 3 and 9 to 4 and 10

A solution of **9** (183 mg, 0.28 mmol) and $HClO_4$ (0.3 mL, 70% in H_2O) in MeOH/H_2O (4/1, 5 mL) was stirred for 1 h at 40°C, and then poured into satd aq. $NaHCO_3$ solution at 0°C. The mixture was extracted with AcOEt and the extracts were washed with water and brine. Drying and following evaporation of the solvent gave the residue, which was subjected to p-TLC (hexane/AcOEt, 1/2). Compound **10** was obtained as an inseparable mixture of diastereomers (100 mg, 63% yield)

Compound 10: amorphous; $[\alpha]_D^{18}$ +244 (*c* 0.77, $CHCl_3$, inseparable mixture of diastereomers (ca. 1:1)); ^1H NMR (200 MHz, $CDCl_3$) δ 8.09–7.98 (m, 8H), 7.63–7.49 (m, 8H), 7.37–7.28 (m, 8H), 3.75 (s, 3H), 3.59 (s, 3H), 3.29–3.00 (m, 2H), 2.64 (dd, 8H, $J=15.0$, 6.7, overlapped), 2.34–1.73 (m, 16H), 1.40–1.00 (m, 4H, overlapped), 1.20 (s, 3H); IR ($CHCl_3$) 3010, 2960, 2880, 1730, 1695, 1590, 1510, 1465, 1435, 1325, 1290, 1225, 1155, 1065, 1035 cm^{-1}; MS (*m*/*z*) 570 (M^+); HRMS (*m*/*z*) calcd for $C_{33}H_{31}O_7P$ (M^+) 570.1784, found: 570.1838. Anal. calcd for $C_{33}H_{31}O_7P$: C, 69.47; H, 5.48. Found: C, 69.75; H, 5.53%.

Similarly, **4** was obtained from **3** as an inseparable mixture of diastereomers in 47% yield.

Compound 4: amorphous; $[\alpha]_D^{18}$ +306 (*c* 0.34, $CHCl_3$, inseparable mixture of diastereomers (ca. 1:1)); ^1H NMR (270 MHz, $CDCl_3$) δ 7.99–7.86 (m, 8H), 7.52–7.37 (m, 8H), 7.30–7.08 (m, 8H), 3.65 (s, 3H), 3.49 (s, 3H), 3.13–2.91 (m, 2H), 2.74–2.60 (m, 8H), 2.10–1.84 (m, 4H), 1.60–1.48 (m, 4H), 1.60–0.97 (m, 4H, overlapped), 1.03 (s, 3H), 0.97 (s, 3H); IR ($CHCl_3$) 3021, 2960, 2880, 1725, 1590, 1465, 1435, 1288, 1225, 1194, 1072, 963 cm^{-1}; MS (*m*/*z*) 556 (M^+); HRMS (*m*/*z*) calcd for $C_{23}H_{29}O_7P$ (M^+) 556.1651, found: 556.1630.

4.8. Cyclization of 4 and 10 to 11 and 12

A solution of **10** (19.5 mg, 0.03 mmol) in THF (4.0 mL) was treated with a solution of Et_2Zn (0.05 mL, 1.0 M in hexane, 0.05 mmol, 1.4 equiv.) at −78°C and the mixture was initially stirred at −78°C and then allowed to warm to room temperature over 17 h under Ar with stirring. The mixture was poured into cold saturated aq. NH_4Cl solution and extracted with AcOEt. The extracts were washed with water and brine. Drying and successive evaporation of the solvent gave the residue, which was subjected to p-TLC (hexane/AcOEt, 3/1). The cyclized compound **12** was obtained as an oil (6.2 mg, 82%). The optical purity of the sample was analyzed by HPLC.

Compound 12: colorless oil; $[\alpha]_D^{18}$ +114 (*c* 0.40, $CHCl_3$, 81% e.e.); ^1H NMR (200 MHz, $CDCl_3$) δ 3.68 (s, 3H), 3.05 (brd, 1H, $J=14.6$ Hz), 2.70–2.52 (m, 1H), 2.43–2.16 (m, 4H), 2.06–1.82 (m, 2H), 1.69–1.55 (m, 4H), 1.29 (s, 3H); IR ($CHCl_3$) 3020, 2935, 1705, 1435, 1230, 1085, 1010 cm^{-1}; CD (MeOH) see Fig. 1; UV (MeOH) λ_{max} 228.6 nm (ε 5850). Anal. calcd for $C_{13}H_{18}O_3$: C, 70.25; H, 8.16. Found: C, 69.96; H, 8.27%.

In the same way as above for the cyclization of **10**, compound **11** was formed as an oil in 49% yield after purification by p-TLC on silica gel with hexane/AcOEt (3/1).

Compound 11: colorless oil; $[\alpha]_D^{18}$ +251 (*c* 0.60, $CHCl_3$, 80% e.e.); ^1H NMR (270 MHz, $CDCl_3$) δ 3.75 (s, 3H), 3.45 (dd, 1H, $J=15.8$, 9.9 Hz), 2.92–2.82 (m, 1H), 2.76–2.64 (m, 1H), 2.35–1.18 (m, 3H), 1.85–1.64 (m, 3H), 1.41–1.25 (m, 1H), 1.20 (s, 3H); IR ($CHCl_3$) 3025, 2950, 1738, 1705, 1651, 1437, 1271, 1114, 1024 cm^{-1}; CD (MeOH) see Fig. 1; UV (MeOH) λ_{max} 232.6 nm (ε 900); MS (*m*/*z*) 208 (M^+); HRMS (*m*/*z*) calcd for $C_{12}H_{16}O_3$ (M^+) 208.1100. Found: 208.1096.

4.9. Dibenzoate 14

To a stirred solution of **12** (12.0 mg, 0.05 mmol) in THF (5.0 mL) was added a solution of DIBAL-H (0.14 mL, 1.5 M in toluene, 0.21 mmol, 4.0 equiv.) at −78°C and the mixture was further stirred for 1.5 h at the same temperature and for 1 h at 0°C. The mixture was poured into cold sat. aqueous NH_4Cl solution and extracted with AcOEt. Washing with water and brine, drying and evaporation left the residue (10.6 mg) con-

taining the diol **13**, which was used for next acylation without further purification. A mixture of the residue (10.6 mg), *p*-bromobenzoyl chloride (40.0 mg, 0.18 mmol, 3.4 equiv.) and pyridine (0.5 mL) was stirred at room temperature. After 19 h, the mixture was poured into cold 10% HCl and extracted with Et_2O. The ethereal extract was washed with water and brine, dried, and then concentrated under reduced pressure to give the residue, which was purified by p-TLC (hexane/AcOEt 5/1). Dibenzoate **14** was obtained as crystals (26.0 mg, 82%).

Compound 14: mp 111–113°C; colorless prisms (from AcOEt/hexane); $[\alpha]_D^{18}$ +50.2 (*c* 0.50, $CHCl_3$, >99% e.e.); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.88 (d, 4H, $J=8.6$ Hz), 7.58 (d, 4H, $J=8.6$ Hz), 4.91–4.76 (m, 3H), 2.71–2.57 (m, 1H), 2.23–1.36 (m, 8H), 1.28 (s, 3H); IR ($CHCl_3$) 2940, 1710, 1590, 1270, 1172, 1115, 1100 cm^{-1}; MS (*m*/*z*) 560, 562 (M^+); HRMS (*m*/*z*) calcd for $C_{13}H_{18}O_3$ (M^+) 560.0198, 562.0177. Found: 560.0197, 562.0176. Crystallized as orthorhombic, space group $P2_12_12_1$ with $a=11.866$ (9), $b=26.483$ (2), $c=7.781$ (1) Å, $V=2445.1$ (4) Å^3, $Z=8$, $D_c=1.527$ g/cm^3. The structure was refined to $R=0.066$, $R_w=0.089$, goodness of fit = 1.21. The structure elucidated was supported by comparison with the *R* factor of *ent*-**14** ($R=0.070$) and furthermore, by the Flack parameter[10] of **14** ($x=-0.0222$). Crystallographic data for the structure **14** have been deposited with Cambridge Crystallographic Data Centre (deposition number 183968).

Acknowledgements

We thank the Ministry of Education, Science, Sports and Culture, Japan for financial support. One of the authors (A.V.B.) is grateful to JSPS for financial support. The authors are also grateful to Drs. Y. Hata, Y. Kawai and T. Fujii (Kyoto University) for their helpful advice on X-ray analysis.

References

1. Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863 and references cited therein.
2. (a) Hanessian, S.; Beaudoin, S. *Tetrahedron Lett.* **1992**, *33*, 7655; (b) Narasaka, K.; Hidai, E.; Hayashi, Y.; Gras, J.-L. *J. Chem. Soc., Chem. Commun.* **1993**, 102; (c) Denmark, S. E.; Rivera, I. *J. Org. Chem.* **1994**, *59*, 6887; (d) Rein, T.; Kreuder, R.; von Zezschwitz, P.; Wulff, C.; Reiser, O. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1023; (e) Tanaka, K.; Otsubo, K.; Fuji, K. *Tetrahedron Lett.* **1996**, *37*, 3735; (f) Yamazaki, J.; Watanabe, T.; Tanaka, K. *Tetrahedron: Asymmetry* **2001**, *12*, 669.
3. (a) Tanaka, K.; Ohta, Y.; Fuji, K.; Taga, T. *Tetrahedron Lett.* **1993**, *34*, 4017; (b) Tanaka, K.; Watanabe, T.; Ohta, Y.; Fuji, K. *Tetrahedron Lett.* **1997**, *38*, 8943.
4. Anastas, P. T.; Warner, J. C. *Green Chemistry: Theory and Practice*; Oxford University Press: Oxford, 1998.
5. References cited in the preceding paper.
6. Mandai, T.; Kaihara, Y.; Tsuji, J. *J. Org. Chem.* **1994**, *59*, 5847.
7. Bedekar, A. V.; Watanabe, T.; Tanaka, K.; Fuji, K. *Synthesis* **1995**, 1069.
8. Fuji, K.; Kinoshita, N.; Tanaka, K. *Chem. Commun.* **1999**, 1895.
9. Tanaka, K.; Watanabe, T.; Shimamoto, K.; Sahakitpichan, P.; Fuji, K. *Tetrahedron Lett.* **1999**, *40*, 6599.
10. Flack, H. D. *Acta Crystallogr., Sect. A* **1983**, *37*, 734.