A Novel Synthesis of Racemic and Enantiomeric Forms of Prostaglandin B_1 Methyl Ester†

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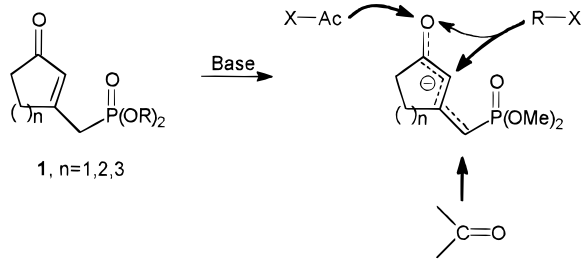
3-(Dimethoxyphosphorylmethyl)cyclopent-2-enone was converted into (±)-prostaglandin B_1 methyl ester in two steps involving regioselective alkylation at C(2) with methyl 7-iodoheptanoate and subsequent Horner−Wittig reaction with dimer of 2-hydroxyheptanal (42% overall yield). The use of (*R*)- and (*S*)-2-(*tert*-butyldimethylsilyloxy)heptanal for the Horner olefination reaction gave, after deprotection of the hydroxy group, the enantiopure forms of the title compound in 28% overall yield.

Introduction

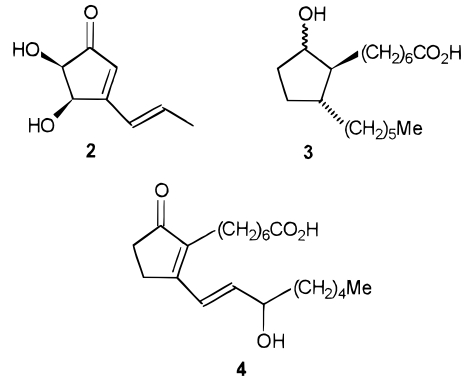
The cyclopentenone moiety is a characteristic unit of several biologically active compounds, among them jasmonoids, retrolons, cyclopentanoid antibiotics, and prostaglandins.[1] Moreover, some suitably substituted cyclopentenones may be transformed into the corresponding cyclopentanones, which also occur in nature. The discovery of prostaglandins, which constitute one of the most exciting groups of highly potent biologically active compounds, has given enormous impetus for the development of methods for the formation of such systems. In the course of our studies on the synthesis of jasmones and cyclopentanoid antibiotics using organophosphorus and organosulfur reagents,[2] the cyclopentenone skeleton was constructed by base-catalyzed cyclization of 1,4-dicarbonyl compounds or by carbenoid cyclization of α-diazo-*β*-ketophosphonates. Our further studies directed toward the synthesis of functionalized cyclopentenones resulted in the development of a general synthesis of 3-(phosphorylmethyl)cycloalk-2-enones **1** involving the reaction of dicarboxylic acid esters with α-phosphonate carbanions followed by base-catalyzed cyclization.[3] The structure of **1** offers new possibilities for further functionalization of the carbocylic ring, mainly due to the presence of the 3-phosphorylmethyl moiety. Particularly interesting is the reactivity of the anion derived from **1** because its negative charge is distributed among several atoms as revealed by hydrogen−deuterium exchange experiments. It was demonstrated that alkylation of this anion occurs preferentially at the α-carbonyl carbon atom, acylation takes place at oxygen, and carbonyl electrophiles react

Scheme 1



at the α-phosphonate carbon atom, giving the Horner−Wittig olefination products (see Scheme 1).[3]

It was realized that alkylation in combination with the Horner−Wittig reaction opens a new way for the synthesis of variously 2,3-disubstituted cycloalkenones. To date 3-(phosphorylmethyl)cyclopent-2-enones **1** ($n = 1$) have been successfully used in the total synthesis of both enantiomers of isoterrein **2**,[4] a member of the cyclopentanoid family, and racemic rosaprostol **3**,[5] an antiulcer drug. In this paper we demonstrate that this new



methodology for the synthesis of disubstituted cyclopentenones turns out to be effective in the synthesis of

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† This paper is dedicated to Professor Wojciech J.Stec on the occasion of his 60th birthday.

(1) (a) Brettle, R. In *Comprehensive Organic Chemistry*; Barton, D. H. R., Ollis, W. D., Eds.; Pergamon Press: Oxford, New York, Toronto, Sydney, Paris, Frankfurt, 1979; Vol. 1, pp 1062−1064 and references therein. (b) Welch, S. C.; Assercq, J.-M.; Loh, J.-P.; Glase, S. A. *J. Org. Chem.* **1987**, *52*, 1440−1450 and references therein. (c) Collins, P. W.; Djuric, S. W. *Chem. Rev.* **1993**, *93*, 1533−1564.

(2) For a recent summary see: (a) Mikołajczyk, M. *Rev. Heteroatom. Chem.* **1989**, *2*, 19−39. (b) Mikołajczyk, M. *S. Afr. J. Chem.* **1994**, *47*, 103−111.

(3) Mikołajczyk, M.; Mikina, M. *J. Org. Chem.* **1994**, *59*, 6760−6765.

(4) Mikołajczyk, M.; Mikina, M.; Wieczorek, M. W.; Błaszczyk, J. *Angew. Chem.* **1996**, *108*, 1645−1647; *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1560−1562.

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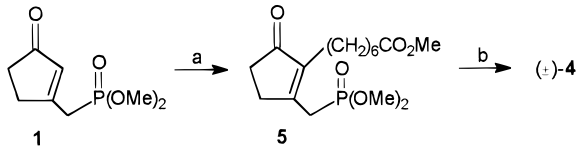
Scheme 2[a]



[a] Reagents and conditions: (a) NaH, $I(CH_2)_6CO_2Me$, DMSO; (b) (±)-$[Me(CH_2)_4CH(OH)CHO]_2$, MeONa, MeOH, rt, 1 h.

racemic and optically active methyl ester of prostaglandin B_1 (PGB_1) **4**. In this context, it is interesting to point out that among numerous reported syntheses of PGB_1 and its esters,[6] only two of them are directed at the optically active compound.[6g,h]

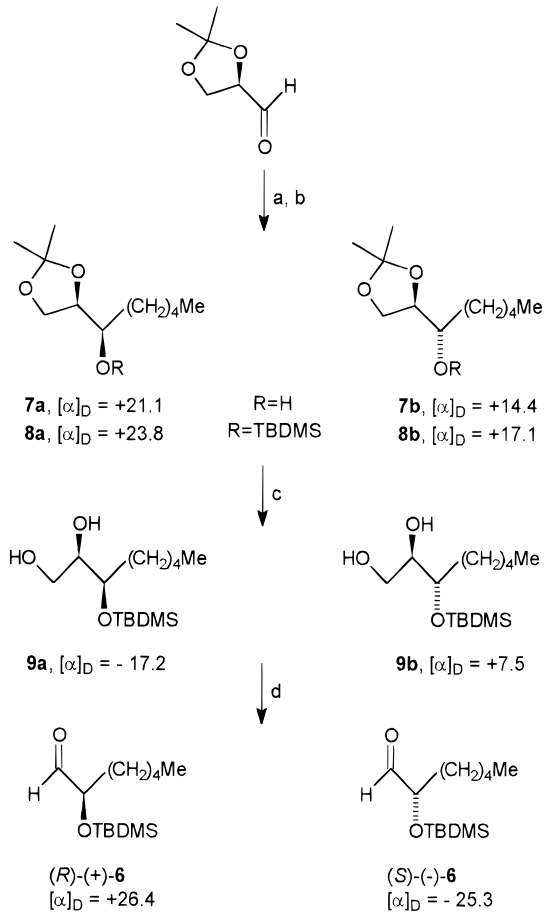
Results and Discussion

The synthesis of racemic methyl ester of PGB_1 **4** was accomplished in two steps starting from readily available 3-(dimethoxyphosphorylmethyl)cyclopent-2-enone **1**[3] (see Scheme 2). The first reaction was alkylation of the anion of **1** with methyl 7-iodoheptanoate carried out in a DMSO solution according to the procedure described in our previous paper.[5] Then, the Horner−Wittig reaction of the cyclopentenone **5** formed with racemic 2-hydroxyheptanal, which exists in a cyclic dimeric form, was carried out under standard conditions (MeONa in MeOH) to afford (±)-**4** in 90% yield.

The above approach is also suitable for the preparation of optically active methyl ester of PGB_1 **4**. It requires, however, the use of enantiomeric 2-hydroxyheptanals as the Horner−Wittig reaction components. Actually, the enantiomers **6** of *O*-*tert*-butyldimethylsilyl protected 2-hydroxyheptanal were used in the present work in order to avoid racemization and side reactions of unprotected aldehyde that could occur under basic reaction conditions. The required chiral reagents (*S*)-(−)-**6** and (*R*)-(+)-**6** were obtained from enantiopure 2,3-(isopropylidene)-D-glyceraldehyde[7] according to a modification of the procedure reported recently by Chattopadhyay and Mamdapur,[8] who used (*R*)-2,3-*O*-(cyclohexylidene)-glyceraldehyde as a substrate (see Scheme 3). The synthesis of enantiomeric aldehydes **6** is shown in Scheme 3 and briefly discussed below.

Addition of *n*-pentylmagnesium bromide to D-glyceraldehyde isopropylidene ketal carried out in THF solution at −78 °C afforded a mixture of two diastereomeric adducts **7a** and **7b**[9] in a 22:78 ratio and in 82% yield. The resulting alcohols **7** were separated by column chromatography and treated with *tert*-butyldimethylsilyl chloride in the presence of imidazole to give the fully protected triols **8a** and **8b** in almost quantitative yield. Then, the isopropylidene moiety in **8a** and **8b** was removed upon treatment with pyridinium *p*-toluenesulfonate (PPTS) in methanol (yield 80%), and the diols **9a** and **9b** were subsequently cleaved with sodium metaperiodate. The enantiomeric (*R*)-(+)- and (*S*)-(−)-(*tert*-butyldimethylsilyloxy)heptanals **6** were obtained in 95% yield.

Scheme 3[a]



[a] Reagents and conditions: (a) $Me(CH_2)_4MgBr$, THF, −78 °C → rt; aq. NH_4Cl; separation; (b) *t*-$BuMe_2SiCl$, imidazole, DMF, rt, 15 h; (c) PPTS, MeOH, rt, 1 h; Et_3N; (d) $NaIO_4$, $MeCN/H_2O$, rt, 1 h.

With the enantiomerically pure aldehydes **6** in hand, the Horner−Wittig reaction with the cyclopentenone **5** could be executed. We found that it can efficiently be performed under the conditions described by Masamune et al., i.e., in the presence of DBU and $LiClO_4$ as a base system.[10,11] The enantiomeric cyclopentenones **10** obtained in 80% yield were in the last step of the synthesis treated with tetrabutylammonium fluoride to give the corresponding enantiomeric methyl esters of PGB_1

(6) (a) Hardegger, E.; Schenk, H. P.; Broger, E. *Helv. Chim. Acta* **1967**, *50*, 2501−2504. (b) Nugteren, D. H.; Vonkeman, H.; Van Dorp, D. A. *Recl. Trav. Chim. Pays-Bas* **1967**, *86*, 1237−1245. (c) Klok, R.; Pabon, H. J. J.; Van Dorp, D. A. *Rec. Trav. Chim. Pays-Bas* **1968**, *87*, 813−823. (d) Holden, K. G.; Hwang, B.; Williams, K. R.; Weinstock, J.; Harman, M.; Weisbach, J. A. *Tetrahedron Lett.* **1968**, 1569−1574. (e) Yura, J.; Ide, J. *Chem. Pharm. Bull.* **1969**, *17*, 408−410. (f) Miyano, M. *J. Org. Chem.* **1970**, *35*, 2314−2318. (g) Pappo, R.; Collins, P.; Jung, C. *Ann. N.Y. Acad. Sci.* **1971**, *180*, 64−75. (h) Hirayama, F.; Uekama, K. *Chem. Pharm. Bull.* **1979**, *27*, 435−441. (i) Marino, J. P.; Kelly, M. G. *J. Org. Chem.* **1981**, *46*, 4389−4393. (j) Naora, H.; Ohnuki, T.; Nakamura, A. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 2859−2863. (k) Stille, J. K.; Sweet, M. P. *Tetrahedron Lett.* **1989**, *30*, 3645−3648; *Organometallics* **1990**, *9*, 3189−3191. (l) Hyuga, S.; Hara, S.; Suzuki, A. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 2303−2305.

(7) Schmid, C. R.; Bryant, J. D.; Dowlatzedah, M.; Philips, J. L.; Prather D. E.; Schantz, R. D.; Sear, N. L. Vianco, C. S. *J. Org. Chem.* **1991**, *56*, 4056−4058.

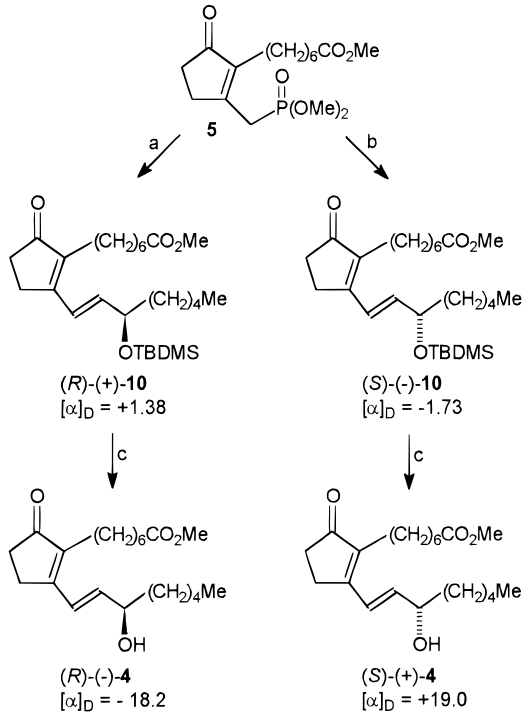
(8) Chattopadhyay, A.; Mamdapur, V. R. *J. Org. Chem.* **1995**, *60*, 585−587.

(9) The absolute configuration (*S*) at the carbon atom C(2) in **7b** was established by its conversion into the known (2*S*)-(benzoyloxy)-heptanal according to the procedure described in ref 8.

(10) Blanchette, M. A.; Choy, W.; Davis, J. T.; Essenfeld, A. P.; Masamune, S.; Roush, W. R.; Sakai, T. *Tetrahedron Lett.* **1984**, *25*, 2183−2186.

(11) When the Horner−Wittig reaction between **5** and optically active aldehydes **6** was carried out in a benzene solution using sodium hydride as a base, the olefination products **10** were formed in a low yield (28%). Moreover, their desilylation gave the corresponding optically active esters **4** exhibiting 63−64% enantiomeric purity.

Scheme 4[a]



[a] Reagents and conditions: (a) (*R*)-(+)-**6**, DBU, $LiClO_4$, THF, rt, 2 h; (b) (*S*)-(−)-**6**, and as in (a); (c) $Bu_4N^+F^-$, THF, rt, 1 h.

(*R*)-(−)-**4**, $[\alpha]_D = -18.2$ and (*S*)-(+)-**4**, $[\alpha]_D = 19.0$ in ca. 75% yield (see Scheme 4).

In view of a very small difference in the optical rotation values of the enantiomers of **4** obtained in this way, it was desirable to confirm their enantiomeric purity. The NMR method using (*R*)-(+)-*tert*-butylphenylphosphinothioic acid **11** as a chiral solvating agent, which is especially useful for the ee determination of alcohols and diols,[12] allowed us to solve this problem in a satisfactory manner. We found that a diagnostic value has the olefinic proton at C(14), which appears in the ^{1}H NMR spectrum of the racemic ester **4** as a double doublet at δ 6.25 ppm (J = 15.8 and 5.9 Hz) and in the presence of (*R*)-(+)-**11** as two well separated double doublets ($\Delta\delta$ = 2.5 Hz) (See Figure 1). Since in the ^{1}H NMR spectra of both optically active esters **4** measured in the presence of (*R*)-(+)-**11** only one double doublet of the methine proton at C(14) was observed, one can conclude that the products are enantiomerically pure within the limits of detection by ^{1}H NMR (diastereomeric solvate quantification ca. 1%).

In summary, we have developed a short and efficient synthesis of racemic and enantiomeric forms of methyl ester of prostaglandin B_1 from the easily accessible 3-(dimethoxyphosphorylmethyl)cyclopent-2-enone. Our synthesis compares favorably in terms of the use of simple reagents and transformations with the majority of the previously reported syntheses. Enantiomers of *tert*-butylphenylphosphinothioic acid have been found to be useful chiral solvating agents for the ^{1}H NMR determination of enantiomeric purity of the title compound.

Experimental Section

General Procedures. All bp values are uncorrected. Tetrahydrofuran was distilled over potassium/benzophenone, and benzene was distilled over Na wire, both immediately prior use. Methylene chloride was distilled over P_2O_5 and stored over anhydrous Na_2CO_3. NMR spectra were recorded at 200 MHz for ^{1}H, 81 MHz for ^{31}P, and 50 MHz for ^{13}C with $CDCl_3$ as solvent, unless otherwise noted. High-resolution mass spectra were recorded using EI or CI technique. IR spectra were recorded with IR−FT apparatus. Optical rotations were measured at 20 °C using a photopolarimeter with the ±0.002° accuracy in CH_2Cl_2, unless otherwise stated. Column chromatography was done on Merck $60F_{254}$ silica gel (70−230 mesh), and flash column chromatography was carried out on Merck $60F_{254}$ silica gel (230−400 mesh). Reactions were analyzed by TLC using Merck $60F_{254}$ TLC plates. All anhydrous reactions were carried out under argon atmosphere. The cyclopentenone **5** was obtained in 47% yield as described in our previous paper.[5] 2-Hydroxypentanal dimer was prepared according to the procedure described by Royals and Robinson.[13]

(±)-Methyl Ester of PGB_1 (4). To a magnetically stirred solution of the cyclopentenone **5** (0.345 g, 1 mmol) and dimer of 2-hydroxypentanal (0.23 g, 1 mmol) in methanol (5 mL) was added sodium hydride (0.024 g, 1 mmol) at room temprature. The mixture was stirred for 1 h and then quenched by addition of aqueous ammonium chloride. After removal of methanol under vacuum, the aqueous solution was extracted with CH_2Cl_2. The combined organic extracts were dried over anhydrous $MgSO_4$ and concentrated under vacuum. The residue was purified by column chromatography (benzene/acetone, 5:1) affording (±)-**4** (0.314 g, 90%) as a colorless oil; HRMS (EI) (M^+) calcd for $C_{21}H_{34}O_4$ 350.2457, obsd 350.2444. The ^{1}H NMR spectral data were fully consistent with those reported in ref 6l.

1,2-*O*-(Isopropylidene)-octane-1,2,3-triol (7a and 7b). To a suspension of magnesium (3.84 g, 0.16 mol) in THF (15 mL) was added a solution of pentyl bromide (22.6 g, 0.15 mol) in THF (200 mL). The mixture was stirred under reflux for 20 min. Then, after cooling to −78 °C, a solution of 2,3-*O*-(isopropylidene)-D-glyceraldehyde (7.8 g, 0.06 mol) in THF (120 mL) was added, and the mixture was stirred at room temperature overnight. Saturated aqueous NH_4Cl was added, followed by extraction with ether. The organic extract was dried over anhydrous Na_2SO_4 and evaporated. The residue was column chromatographed (petroleum ether/ethyl acetate, 9:1), resulting in separation of the diastereomerically pure adducts **7a** (2.2 g, 18%) and **7b** (7.8 g, 64%).

(2*R*,3*R*)-7a: $[\alpha]_{589} = +17.8$, $[\alpha]_{546} = +21.1$ (*c* 5.05, CH_2Cl_2); ^{1}H NMR δ 3.92−4.05 (m, 2H), 3.65−3.79 (m, 1H), 3.40−3.55 (m, 1H), 2.17 (brd, J = 5.0 Hz, 1H), 1.20−1.60 (m, 8H), 1.43 (s, 3H), 1.36 (s, 3H), 0.83−0.92 (m, 3H); ^{13}C NMR δ 109.2, 79.1, 72.1, 66.0, 33.5, 31.7, 26.5, 25.2, 25.1, 22.5, 13.9. Anal. Calcd for $C_{11}H_{22}O_3$: C, 65.31; H, 10.96. Found: C, 65.45; H, 10.89.

(2*R*,3*S*)-7b: $[\alpha]_{589} = +12.1$, $[\alpha]_{546} = +14.4$ (*c*, 4.19, CH_2Cl_2); ^{1}H NMR δ 3.85−4.17 (m, 3H), 3.72−3.82 (m, 1H), 1.95−2.05 (m, 1H), 1.23−1.55 (m, 8H), 1.42 (s, 3H), 0.84−0.91 (m, 3H); ^{13}C NMR δ 108.8, 78.7, 70.6, 64.6, 32.6, 31.7, 26.4, 25.3, 25.2, 22.5, 13.9. Anal. Calcd. for $C_{11}H_{22}O_3$: C, 65.31; H, 10.96. Found: C, 65.38; H, 10.91.

1,2-*O*-(Isopropylidene)-3-*O*-(*tert*-butyldimethylsilyl)octane-1,2,3-triol (8a and 8b). A solution of **7a** or **7b** (4.04 g, 20 mmol), *tert*-butyldimethylsilyl chloride (7.55 g, 50 mmol), and imidazole (6.80 g, 100 mmol) in anhydrous DMF (16 mL) was stirred for 15 h at room temperature. The reaction mixture was chromatographed on silica gel (petroleum ether/ethyl acetate, 19:1), affording the protected triol **8a** or **8b** in almost quantitative yield.

(2*R*,3*R*)-8a: $[\alpha]_{589} = +23.8$, $[\alpha]_{546} = +28.0$ (*c*, 10.4, hexane); ^{1}H NMR δ 3.87−4.15 (m, 2H), 3.60−3.75 (m, 2H), 1.20−1.45 (m, 8H), 1.41 (s, 3H), 1.34 (s, 3H), 0.85−0.95 (m, 3H), 0.88 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR δ 109.0, 78.8, 73.3, 65.6, 32.3, 31.9, 26.4, 25.9, 25.7, 25.3, 22.6, 14.0, −4.3, −4.7. Anal. Calcd for $C_{17}H_{36}SiO_3$: C, 64.50; H, 11.46. Found: C, 64.57; H, 11.32.

(12) Omelańczuk, J.; Mikołajczyk, M. *Tetrahedron: Asymmetry* **1996**, *7*, 2687−2694.

(13) Royals, E. E.; Robinson, A. G., III. *J. Am. Chem. Soc.* **1956**, *78*, 4161.

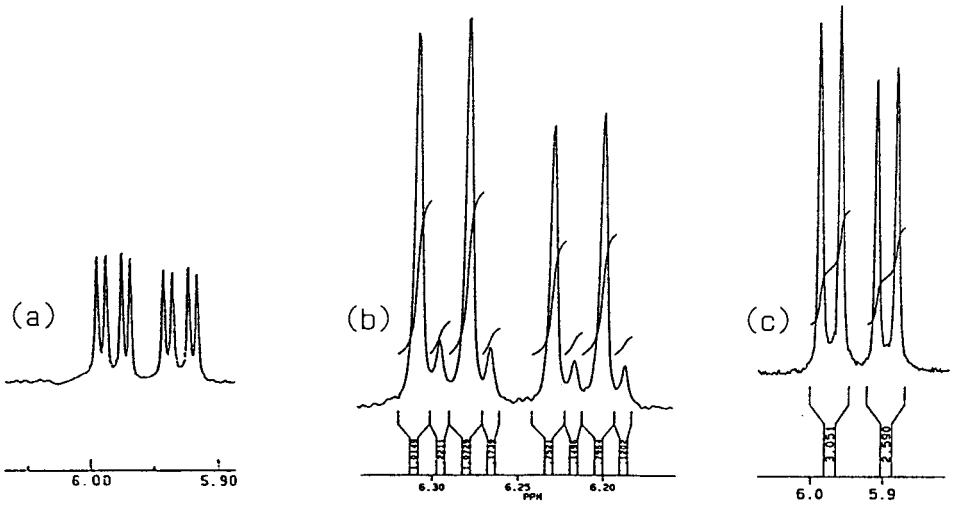


Figure 1. ^{1}H NMR spectra [C(14) vinyl proton region] of the racemic **4** (a), enriched in (+)-enantiomer **4** (b), and (+)-**4**, $[\alpha]_{589} = +19.0$ (c) in the presence of (*R*)-(+)-*tert*-butylphenylphosphinothioic acid **11**.

(2*R*,3*S*)-8b: $[\alpha]_{589} = +17.1$, $[\alpha]_{546} = +20.3$ (*c* 9.91, hexane); ^{1}H NMR δ 3.90−4.05 (m, 2H), 3.68−3.88 (m, 2H), 1.20−1.58 (m, 8H), 1.39 (s, 3H), 1.34 (s, 3H), 0.84−0.93 (m, 3H), 0.88 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR δ 108.8, 78.1, 72.4, 66.4, 34.5, 32.1, 26.7, 25.8, 25.7, 25.5, 24.0, 22.6, 14.0, −4.2, −4.4. Anal. Calcd for $C_{17}H_{36}SiO_3$: C, 64.50; H, 11.46. Found C, 64.63; H, 11.39.

3-(*tert*-Butyldimethylsilyl)-octane-1,2,3-triol (9a and 9b). A solution of **8a** or **8b** (3.16 g, 10 mmol) and pyridinium *p*-toluenesulfonate (2.51 g, 10 mmol) in methanol (50 mL) was stirred for 1 h. After addition of triethylamine (5.3 mL), methanol was evaporated under vacuum. The residue was chromatographed (petroleum ether/ethyl acetate, 4:1), giving the diol **9** (1.30 g) and the unreacted substrate **8** (1.60 g). The latter and a new portion of **8** (2.53 g, 8 mmol) were once again subjected to reaction with pyridinium *p*-toluenesulfonate, and after column chromatography 1.51 g of **9** and 1.69 g of **8** were obtained. This procedure afforded 2.81 g of the diol **9** in 80% yield calculated in respect to the consumed substrate **8**.

(2*R*,3*R*)-9a: $[\alpha]_{589} = -17.2$, $[\alpha]_{546} = -20.3$ (*c* 4.68, CH_2Cl_2); ^{1}H NMR δ 3.72−3.62 (m, 2H), 3.55−3.60 (m, 2H), 2.40−2.50 (m, 1H), 2.10−2.20 (m, 1H), 1.55−1.75 (m, 2H), 1.20−1.50 (m, 6H), 0.82−0.95 (m, 3H), 0.90 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H); ^{13}C NMR δ 73.1, 72.5, 33.6, 31.9, 25.8, 24.7, 22.5, 18.0, 13.9, −4.3, −4.8. Anal. Calcd for $C_{14}H_{32}SiO_3$: C, 60.82; H, 11.67. Found: C, 60.88; H, 11.60.

(2*R*,3*S*)-9b: $[\alpha]_{589} = +7.5$ $[\alpha]_{546} = +8.9$ (*c* 4.88, CH_2Cl_2); ^{1}H NMR δ 3.75−3.90 (m, 2H), 3.55−3.75 (m, 2H), 2.2−2.6 (m, 2H), 1.15−1.70 (m, 8H), 0.88−0.93 (m, 3H), 0.90 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H); ^{13}C NMR δ 74.5, 73.3, 63.2, 33.1, 31.9, 25.7, 24.6, 22.5, 17.9, 13.9, −4.6, −4.7. Anal. Calcd for $C_{14}H_{32}SiO_3$: C, 60.82; H, 11.67. Found: C, 60.91; H, 11.59.

Enantiomeric 2-(*tert*-Butyldimethylsilyloxy)-heptanals (6). To a stirred solution of the diol **9a** or **9b** (2.76 g, 10 mmol) in a mixture of acetonitrile (9 mL) and water (6 mL) was added at 0 °C in portions sodium metaperiodate (4.28 g, 20 mmol) within 1 h. After 1 h of stirring at room temperature, the reaction solution was extracted with $CHCl_3$. The combined organic extracts were dried over anhydrous $MgSO_4$ and concentrated in a vacuum, furnishing the enantiomeric aldehydes **6** in almost quantitative yield.

(*R*)-(+)-6: $[\alpha]_{589} = +26.4$, $[\alpha]_{546} = +31.8$ (*c* 4.24, CH_2Cl_2).

(*S*)-(−)-6: $[\alpha]_{589} = -25.3$, $[\alpha]_{546} = -30.8$ (*c* 4.10, CH_2Cl_2); ^{1}H NMR δ 9.59 (d, $J = 1.5$ Hz, 1H), 3.96 (dt, $J = 6.2$ Hz, $J = 1.5$ Hz, 1H), 1.55−1.70 (m, 2H), 1.20−1.50 (m, 6H), 0.80−0.95 (m, 3H), 0.92 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}C NMR δ 204.1, 77.6, 32.5, 31.6, 25.7, 24.2, 22.4, 18.1, 13.9, −4.7, −5.0.

Enantiomeric Methyl Esters of 15-(*tert*-Butyldimethylsilyl)-prostaglandin B_1 (10). To a closed reaction vessel (5 mL) containing the cyclopentenone **5** (87 mg, 0.25 mmol) and $LiClO_4$ (27 mg, 0.25 mmol) was added anhydrous THF (0.15 mL) with a syringe. To the stirred mixture was added a solution of DBU (38 mg, 0.25 mmol) and (*R*)- or (*S*)-aldehyde **6** (61 mg, 0.25 mmol) in THF (0.1 mL). After 2 h of stirring at room temperature, the reaction mixture was column chromatographed (petroleum ether/acetone, 4:1), affording **10** (93 mg, 80%) as an oil.

(*R*)-(+)-10: $[\alpha]_{589} = +1.38$, $[\alpha]_{546} = +1.02$ (*c* 4.19, CH_2Cl_2); ^{1}H NMR δ 6.67 (dd, $J = 15.6$ Hz, $J = 1.1$ Hz, 1H), 6.23 (dd, $J = 15.6$ Hz, $J = 5.2$ Hz, 1H), 4.30 (dq, $J = 5.2$ Hz, $J = 1.1$ Hz, 1H), 3.65 (s, 3H), 2.55−2.70 (m, 2H), 2.35−2.45 (m, 2H), 2.15−2.35 (m, 4H), 1.20−1.70 (m, 16H), 0.92 (s, 9H), 0.09 (s, 3H), 0.07 (s, 3H); ^{13}C NMR δ 209.5, 174.1, 163.6, 141.2, 140.6, 122.8, 72.6, 51.3, 37.8, 33.9, 33.7, 31.7, 29.2, 28.9, 28.8, 25.7, 24.8, 22.9, 22.5, 18.1, 13.9, −4.6, −4.9; IR (film) 1740, 1696, 1642, 970 cm^{-1}. Anal. Calcd for $C_{27}H_{48}SiO_4$: C, 69.78; H, 10.41. Found: C, 69.91; H, 10.32.

(*S*)-(−)-10: $[\alpha]_{589} = -1.73$, $[\alpha]_{546} = -1.27$ (*c* 4.33, CH_2Cl_2). Anal. Calcd for $C_{27}H_{48}SiO_4$: C, 69.78; H, 10.41. Found: C, 69.85; H, 10.29.

Enantiomeric Methyl Esters of Prostaglandin B_1 (4). To a stirred solution of tetrabutylammonium fluoride (0.392 g, 1.5 mmol) in THF (1 mL) was added (*R*)-**10** or (*S*)-**10** (0.232 g, 0.5 mmol) in THF (1.5 mL). Stirring was continued for 1 h, and the reaction solution was filtered on silica gel (5 g), which was washed with THF. The solvent was removed under vacuum, and the crude product was purified by column chromatography (petroleum ether/ethyl acetate, 5:1), yielding 0.131 g (ca 75%) of **4** as a white solid.

(*R*)-(−)-4: mp 51−52 °C, $[\alpha]_{589} = -18.2$, $[\alpha]_{546} = -22.4$ (*c* 3.58, CH_2Cl_2); ^{1}H NMR δ 6.79 (d, $J = 15.8$ Hz, 1H), 6.25 (dd, $J = 15.8$ Hz, $J = 5.9$ Hz, 1H), 4.25−4.40 (m, 1H), 3.65 (s, 3H), 2.60−2.68 (m, 2H), 2.35−2.45 (m, 2H), 2.28 (t, $J = 7.3$ Hz, 2H), 2.25 (t, $J = 7.3$ Hz, 2H), 1.5−1.7 (m, 4H), 1.2−1.5 (m, 12H), 0.88 (t, $J = 6.4$ Hz, 3H); ^{13}C NMR δ 209.6, 174.4, 163.2, 141.2, 140.3, 123.7, 72.3, 51.5, 37.2, 34.0, 33.8, 31.7, 29.0, 28.7, 28.4, 25.6, 25.0, 24.7, 22.8, 22.5, 14.0; IR (film) 3438, 1738, 1691, 1638, 969. Anal. Calcd for $C_{21}H_{34}O_4$: C, 71.96; H, 9.78. Found: C, 72.06; H, 9.59.

(*S*)-(+)-4: mp 51−52 °C, $[\alpha]_{589} = +19.0$, $[\alpha]_{546} = +23.5$ (*c* 3.40, CH_2Cl_2). Anal. Calcd for $C_{21}H_{34}O_4$: C, 71.96; H, 9.78. Found: C, 72.11; H, 9.62.

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