JOC Article

# A New Method for Installation of Aryl and Alkenyl Groups onto a Cyclopentene Ring and Synthesis of Prostaglandins

Yuichi Kobayashi,* Modachur G. Murugesh, Miwa Nakano, Eisuke Takahisa, Shahid B. Usmani, and Takayuki Ainai

*Department of Biomolecular Engineering, Tokyo Institute of Technology, 4259 Nagatsuta-cho, Midori-ku, Yokohama 226-8501, Japan*

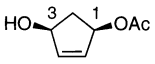
*ykobayas@bio.titech.ac.jp*

*Received June 3, 2002*

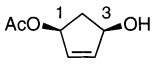
To construct a new strategy for synthesis of cyclopentanoids, the transition metal-catalyzed coupling reaction of cis 4-cyclopentene-1,3-diol monoacetate **1** with hard nucleophiles, $R^T-m$, was investigated (eq 1 in Chart 1). Although preliminary experiments using PhZnCl, $PhSnMe_3$, [Ph-B(Me)(OCH-(Me)CH(Me)O)]-$Li^+$ (**6a**) (derived from boronate ester **4a** ($R^T$ = Ph) and MeLi) in the presence of a palladium or a nickel catalyst resulted in production of unidentified compounds, enone **16**, and/or ketone **17** or recovery of **1**, a new borate **5a** (derived from **4a** and *n*-BuLi) in the presence of a nickel catalyst ($NiCl_2(PPh_3)_2$) in THF at room temperature furnished the trans coupling products **2a** ($R^T$ = Ph) and **3a** ($R^T$ = Ph) in high combined yield, but with a low product ratio of 0.9:1. The ratio was improved to 13:1 by addition of *t*-BuCN and NaI into the reaction mixture. This is the first successful example of the reaction of **1** with a hard nucleophile, and the increase in the ratio, realized with the additives, is unprecedented. This reagent system (borate **5** (1.2−1.8 equiv), $NiCl_2$-$(PPh_3)_2$ (5−10 mol %), *t*-BuCN (2−5 equiv), NaI (0.5−1 equiv), THF, room temp) was further investigated with aryl borates **5b**−**g** and alkenyl borates **5h**−**n** to afford **2b**−**n** in moderate to good yields (52−89%) with practically acceptable levels of the regioselectivity (5 ∼ 21:1), thus establishing the generality of the reaction (Table 2, eqs 6 and 7). Starting with the products of the coupling reaction, syntheses of the prostaglandin intermediates **13** and **14** (for 11-deoxy-$PGE_2$ and $PGA_2$) and $\Delta^7$-$PGA_1$ methyl ester (**15**) were accomplished efficiently. During these investigations, LDA, LiCA, and LHMDS were found to be equally efficient bases for aldol reaction at the α′ (α prime) position of cyclopentenones **39**, **40**, and **41** (Table 3).

## Introduction

Installation of a "carbon-based nucleophile" onto a preexisting cyclopentene (or -ane) ring is a key step in building complex molecules in which the cyclopentane ring acts as a major component of the compound (cyclopentanoids). Cyclopentanone, 2-cyclopenten-1-one, and derivatives possessing a functional group on these compounds have been utilized most frequently as starting substrates. Efficient reactions with these compounds and methodologies therefrom have been developed with great success and exploited in synthesis of the cyclopentanoids.[1] These achievements, however, certainly imply the difficulty in planning a conceptually new strategy for synthesis of the cyclopentanoids, and thence we felt it necessary to find a new reaction using another starting substrate. Monoacetate of cis 4-cyclopentene-1,3-diol (i.e., **1**) is one such compound as the convenient methods to obtain both the enantiomers (>95% ee) have been published.[2,3] Moreover, monoacetate **1** is of excellent chemical




(1*R*,3*S*)-**1**




(1*S*,3*R*)-**1**

stability, thus allowing easy handling. However, it was surprising to learn that only a few types of reactions have successfully been applied to **1**. These are the Claisen rearrangement,[2b,c,4] the intramolecular radical reaction,[5] the palladium-initiated intramolecular reaction,[6] and the palladium-catalyzed reaction with soft nucleophiles furnishing cis 1,4-products.[7−11] We were interested in reac-

(1) (a) Collins, P. W.; Djuric, S. W. *Chem. Rev.* **1993**, *93*, 1533−1594. (b) Crimmins, M. T. *Tetrahedron* **1998**, *54*, 9229−9272. (c) Noyori, R.; Suzuki, M. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 847−876. (d) Noyori, R.; Suzuki, M. *Science* **1993**, *259*, 44−45. (e) Harre, M.; Raddatz, P.; Walenta, R.; Winterfeldt, E. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 480−492.

(2) (1*R*,3*S*)-**1**: (a) Sugai, T.; Mori, K. *Synthesis* **1988**, 19−22. (b) Laumen, K.; Schneider, M. P. *J. Chem. Soc., Chem. Commun.* **1986**, 1298−1299. (1*S*, 3*R*)-**1**: (c) Laumen, K.; Schneider, M. *Tetrahedron Lett.* **1984**, *25*, 5875−5878. (d) Wang, Y.-F.; Chen, C.-S.; Girdaukas, G.; Sih, C. J. *J. Am. Chem. Soc.* **1984**, *106*, 3695−3696. Related literatures: ref 2 of ref 12.

(3) (a) Certainly, acetylation and desilylation of enantiomerically enriched 4-silyloxy-2-cyclopenten-1-ol[3b−d] would afford the enantiomers of monoacetate **1**. (b) Bhuniya, D.; DattaGupta, A.; Singh, V. K. *J. Org. Chem.* **1996**, *61*, 6108−6113. (c) Asami, M.; Inoue, S. *Tetrahedron* **1995**, *51*, 11725−11730. (d) Asami, M. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 1402−1408.

(4) Nara, M.; Terashima, S.; Yamada, S. *Tetrahedron* **1980**, *36*, 3161−3170.

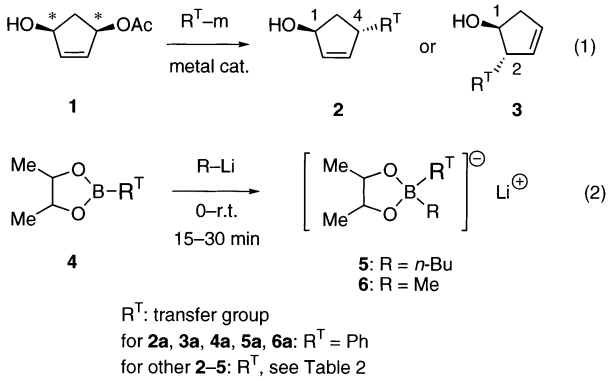
(5) (a) Stork, G.; Sher, P. M.; Chen, H.-L. *J. Am. Chem. Soc.* **1986**, *108*, 6384−6385. (b) Keck, G. E.; Burnett, D. A. *J. Org. Chem.* **1987**, *52*, 2958−2960. (c) Larock, R.; Lee, N. H. *J. Org. Chem.* **1991**, *56*, 6253−6254. (d) Busato, S.; Tinembart, O.; Zhang, Z.; Scheffold, R. *Tetrahedron* **1990**, *46*, 3155−3166.

(6) Larock, R.; Lee, N. H. *J. Am. Chem. Soc.* **1991**, *113*, 7815−7816.

(7) Deardorff, D. R.; Linde, R. G., II; Martin, A. M.; Shulman, M. J. *J. Org. Chem.* **1989**, *54*, 2759−2762.

10.1021/jo020375y CCC: $22.00 
Published on Web 09/11/2002

**CHART 1. Equation 1: The Purpose of the Present Investigation. Regioselective and Stereospecific Formation of 2 Have Been Attained by Using Modified Borates 5 in the Presence of *t*-BuCN and NaI in THF. Equation 2: Preparation of the Modified and Original Borates 5 and 6**




tion with hard nucleophiles $R^T-m$ ($R^T$: transfer group) (eq 1 of Chart 1) because it is, in principle, possible to install a wide range of $R^T$ (especially $sp^2$-carbon) on the cyclopentene ring, and in the trans orientation.[12] The reaction was, however, suffering from low efficiency because of, at least, two reasons pointed out in the next paragraph.

On the basis of the general consideration for the intermediates produced from allylic acetates and transition metal complexes,[13] $\pi$-allylmetal complex **7** would be a plausible intermediate generated from **1** (Figure 1). Since a soft nucleophile (Nu) attacks the $\pi$-allyl moiety from the outside, the steric repulsion of the hydroxyl group results in the regioselective formation of cis 1,4-isomer **8** as is observed in practice.[7,8] On the contrary, a hard nucleophile ($R^T-m$) reacts with the central metal of **7** to produce the advanced $\pi$-allylmetal complex **9**, in which the hydroxyl group is placed on the opposite side of the ring, and thence a mixture of regioisomers **2** and **3** would be produced with low regioselectivity, but with high trans stereoselectivity. In addition to this expectation, $\beta$-hydride elimination of the $\pi$-allylmetal complex

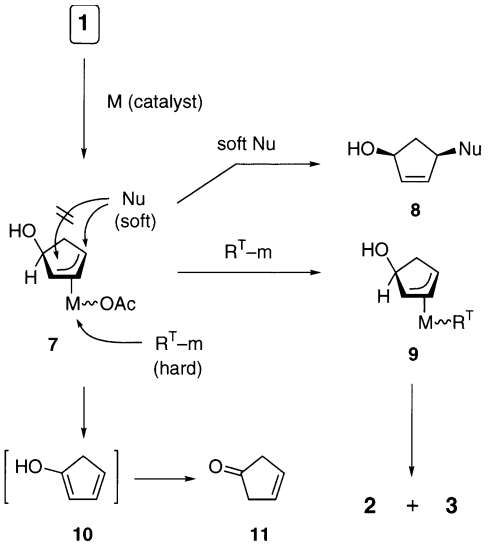



**FIGURE 1.** Plausible intermediates and products.

**7** is a likely process to furnish enol **10** which undergoes tautomerization to ketone **11**. In fact, a poor regioselectivity and facile production of ketone **11** have been reported in the palladium-catalyzed reaction with cyclopentadiene monoepoxide (**12**) where a similar $\pi$-allylpalladium is formed from the monoepoxide.[14,15] Although these results and the above consideration contradict the proposed reaction (Chart 1, eq 1), we dared to start an investigation with the hope that an unauthorized intermediate and/or an unexpected conformational bias in the transient complex(s) may control the regioselectivity. Herein, we report the installation of aryl and alkenyl groups, for the first time, by using new reagents, the lithium borates **5** shown in eq 2 of Chart 1. A practical level of the regioselectivity in obtaining 1,4-isomers **2** is realized by the addition of *t*-BuCN and NaI, the additive effect being unprecedented.[16] Moreover, synthesis of the prostaglandin intermediates (for 11-deoxy-$PGE_2$ and $PGA_2$) and $\Delta^7$-$PGA_1$ methyl ester was achieved efficiently by using the products of this reaction (Figure 2). Regarding the latter synthesis, a significant advancement in aldol reaction was made as well.

## Results and Discussion

**A. Examination of Organometallics.** On the basis of the high reactivity in the coupling reaction with secondary allylic substrates, $R^TZnX$/ Pd or Ni cat.,[17] $R^T$-$SnR_3$/ Pd cat.,[14,18] and the lithium borate (**6**)/ Ni cat.[19] were chosen for the present investigation. The last reagent, developed by us, is prepared in situ from the boronate ester **4** and MeLi (eq 2). Initially, phenylation

(8) (a) Knight, S. D.; Overman, L. E.; Pairaudeau, G. *J. Am. Chem. Soc.* **1995**, *117*, 5776−5788. (b) Deardorff, D. R.; Savin, K. A.; Justman, C. J.; Karanjawala, Z. E.; Sheppeck, J. E., II.; Hager, D. C.; Aydin, N. *J. Org. Chem.* **1996**, *61*, 3616−3622.

(9) Recently, the asymmetric reaction of the 4-cyclopentene-1,3-diol diacetate with soft nucleophiles in the presence of a palladium catalyst and a chiral ligand has been reported: (a) Yoshizaki, H.; Satoh, H.; Sato, Y.; Nukui, S.; Shibasaki, M.; Mori, M. *J. Org. Chem.* **1995**, *60*, 2016−2021. (b) Trost, B. M.; Van Vranken, D. L.; Bingel, C. *J. Am. Chem. Soc.* **1992**, *114*, 9327−9343. (c) Mori, M.; Nukui, S.; Shibasaki, M. *Chem. Lett.* **1991**, 1797−1800.

(10) (a) The same products have been synthesized by the palladium-catalyzed reaction of cyclopentadiene monoepoxide (**12**) with soft nucleophiles.[10b−d] However, the methods suffer from a chemical instability of **12**. (b) Trost, B. M.; Molander, G. A. *J. Am. Chem. Soc.* **1981**, *103*, 5969−5972. (c) Deardorff, D. R.; Shulman, M. J.; Sheppeck, J. E., II. *Tetrahedron Lett.* **1989**, *30*, 6625−6628. (d) Mazón, A.; Nájera, C.; Ezquerra, J.; Pedregal, C. *Tetrahedron Lett.* **1997**, *38*, 2167−2170.

(11) Surman, M. D.; Mulvihill, M. J.; Miller, M. J. *J. Org. Chem.* **2002**, *67*, 4115−4121.

(12) Recently, we have succeeded in alkylation: Ito, M.; Matsuumi, M.; Murugesh, M. G.; Kobayashi, Y. *J. Org. Chem.* **2001**, *66*, 5881−5889.

(13) (a) Tsuji, J. *Palladium Reagents and Catalysts*; Wiley: New York, 1995. (b) Frost, C. G.; Howarth, J.; Williams, J. M. J. *Tetrahedron Asymm.* **1992**, *3*, 1089−1122. (c) Trost, B. M. *Chem. Rev.* **1996**, *96*, 395−422. (d) Numata, S.; Kurosawa, H. *J. Organomet. Chem.* **1977**, *131*, 301−308.

(14) (a) Echavarren, A. M.; Tueting, D. R.; Stille, J. K. *J. Am. Chem. Soc.* **1988**, *110*, 4039−4041. (b) Tueting, D. R.; Echavarren, A. M., Stille, J. K. *Tetrahedron* **1989**, *45*, 979−992.

(15) Suzuki, M.; Oda, Y.; Noyori, R. *J. Am. Chem. Soc.* **1979**, *101*, 1623−1625.

(16) Preliminary works: (a) Kobayashi, Y.; Takahisa, E.; Usmani, S. B. *Tetrahedron Lett.* **1998**, *39*, 597−600. (b) Usmani, S. B.; Takahisa, E.; Kobayashi, Y. *Tetrahedron Lett.* **1998**, *39*, 601−604. (c) Kobayashi, Y. Murugesh, M. G.; Nakano, M. *Tetrahedron Lett.* **2001**, *42*, 1703−1707.

(17) (a) Matsushita, H.; Negishi, E. *J. Chem. Soc., Chem. Commun.* **1982**, 160−161. (b) Hayashi, T.; Yamamoto, A.; Hagihara, T. *J. Org. Chem.* **1986**, *51*, 723−727.

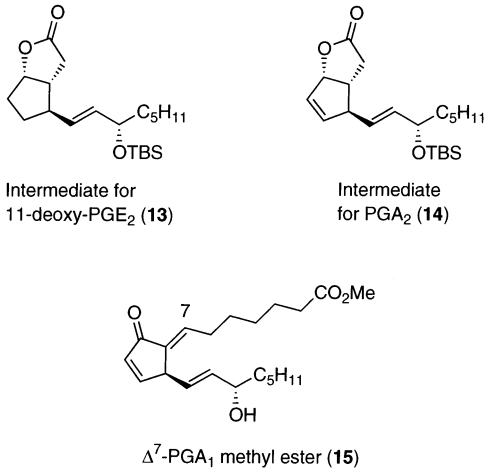



**FIGURE 2.** Target compounds synthesized from the products of the coupling reaction (eqs 6 and 7).

of racemic acetate **1**[20] was investigated. Reactions run with PhZnCl (prepared from PhLi and $ZnCl_2$) in the presence of $Pd(PPh_3)_4$, $PdCl_2(PPh_3)_2$, $NiCl_2(PPh_3)_2$, or $NiCl_2$-(dppf) in THF at room temperature furnished less than 5% of the desired coupling products **2a** and/or **3a** ($R^T$ = Ph). Similar results were also obtained in $Et_2O$ and with PhZnCl prepared from PhMgBr and $ZnCl_2$. Attempted palladium-catalyzed reaction with $PhSnMe_3$ in the presence of $PdCl_2(MeCN)_2$ in DMF and $H_2O$ at 50 °C for 20 h resulted in recovery of **1**. These conditions were once used by Stille in the reaction of cyclopentadiene monoepoxide (**12**) with $PhSnMe_3$, giving **2a** and **3a** with a 1.7:1 ratio.[14] The result of Stille and our finding presented in later paragraphs are discussed in subsection D.

Next, lithium phenylborate **6a** ($R^T$ = Ph, R = Me) was tested in THF in the presence of a Ni(0) species, derived from $NiCl_2(PPh_3)_2$ and MeLi, at room temperature to produce 2-cyclopenten-1-one (**16**) and 3-phenylcyclopentan-1-one (**17**) with a combined yield of <50%. Enone **16** must be the isomerization product of **11**, and the formation of **17** is a result of a nickel-catalyzed 1,4-addition of the remaining borate **6a** to enone **16**.[21,22] The above result clearly indicates that the transmetalation of the supposed intermediate **7** of M = Ni (Figure 1) with **6a** is a slower process than the $\beta$-hydride elimination to **11**,[15] thus suggesting that use of a borate with a more electron-donating alkyl ligand (R) than the methyl ligand would alter the reaction pathway in the desired direction. New borates possessing the *n*-Bu, $TMSCH_2$, or *t*-Bu group as the alkyl ligand were prepared from boronate ester **4a** and the corresponding alkyllithium according to eq 2 and

**TABLE 1. Additive Effect on the Ratio of 2a and 3a**

| entry | additive[a] | ratio of **2a**:**3a**[b] | yield, %[c] |
|---|---|---|---|
| 1 | *t*-BuCN | 6.6:1 | – |
| 2 | MeCN | 5.2:1 | – |
| 3 | PhCN | 4.0:1 | – |
| 4 | AIBN[d] | 6.0:1 | – |
| 5 | NaI[e] | 4.9:1 | – |
| 6 | *t*-BuCN + NaI | 13:1 | 84 |
| 7 | *t*-BuCN + KI | 11:1 | 81 |

[a] THF (solvent): additive = 10:1 (2−6 equiv). [b] Determined by $^1H$ NMR spectroscopy. [c] Not determined in entries 1−5. [d] Unidentified products were coproduced. [e] 1 equiv.

submitted to the reaction under the same conditions mentioned above. Among them, borate **5a** with the *n*-Bu ligand *did* provide **2a** and **3a** with 82% combined yield, for the first time. However, the product ratio of **2a**/**3a** was miserably 0.9:1.

To improve the product ratio of **2a**/**3a**, other ligands for $NiCl_2$ were investigated. However, ligands such as dppf, dppp, dppe, $PBu_3$, and $AsPh_3$ did not provide better results. Next, aprotic polar compounds and inorganic salts were added into the THF solution. While the reaction did not proceed with bipyridine and TMEDA, unifunctional compounds such as DMF, DMSO, $NEt_3$, pyridine, quinoline, *t*-BuCN, and even $H_2O$ increased the selectivity for the 1,4-isomer **2a**. Among them, *t*-BuCN (2 equiv) furnished the highest selectivity of 6.6:1 for **2a**/**3a** (Table 1, entry 1).

However, other nitriles such as MeCN, EtCN, PhCN, and AIBN resulted in lower ratios (entries 2−4). As for inorganic salts such as LiCl, LiBr, NaBr, and NaI, the best result of 4.9:1 was provided by NaI (1 equiv) (entry 5). To the best of our knowledge, the enhancement we encountered is unprecedented for the nickel catalyst.[23] Since a deeper shade of brown was observed in entry 5, the independent roles of *t*-BuCN and NaI were inferred, prompting the cooperative effect of *t*-BuCN and NaI on the ratio. In fact, a higher ratio of 13:1 was observed with 84% isolated yield when the reaction was run with *t*-BuCN and NaI (entry 6). A similar result was also obtained with KI and *t*-BuCN (entry 7).

**B. Scope and Limitation of the New Borates.** To determine the efficiency (the reactivity and the regioselectivity) of the reaction conditions found above for the phenylation, different kinds of aryl and alkenyl borates **5b**−**n** were submitted to the reaction, and the results are summarized in Table 2. For comparison, the result of the phenylation mentioned above is listed again in entry 1. The boronate esters **4b**−**i** were synthesized[19,24] by esterification of the corresponding boronic acids which in turn were prepared by the method of Brown.[24a] Boronate esters **4j**−**l**, the PG $\omega$-chains, were synthesized from

(18) (a) Sheffy, F. K.; Godschalx, J. P.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 4833−4840. (b) Kang, S.-K.; Yamaguchi, T.; Kim, J.-S.; Choi, S.-C. *Synth. Commun.* **1997**, *27*, 1267−1271.

(19) Kobayashi, Y.; Mizojiri, R.; Ikeda, E. *J. Org. Chem.* **1996**, *61*, 5391−5399.

(20) (a) Deardorff, D. R.; Myles, D. C.; MacFerrin, K. D. *Tetrahedron Lett.* **1985**, *26*, 5615−5618. (b) Deardorff, D. R.; Myles, D. C. In *Organic Syntheses*; Freeman, J. P., Ed.; Wiley: New York, 1993; Collect. Vol. 8, pp 13−16.

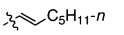
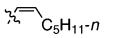
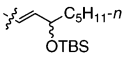
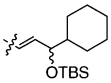
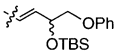
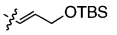
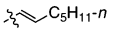
(21) The 1,4-addition reaction was confirmed by an experiment separately examined with enone **16** as a substrate under the same reaction conditions.

(22) Related reactions: (a) Takaya, Y.; Ogasawara, M.; Hayashi, T.; Sakai, M.; Miyaura, N. *J. Am. Chem. Soc.* **1998**, *120*, 5579−5580. (b) Grisso, B. A.; Johnson, J. R.; Mackenzie, P. B. *J. Am. Chem. Soc.* **1992**, *114*, 5160−5165.

(23) Acceleration of the reaction rate with inorganic salts in the palladium-catalyzed coupling of aryl and alkenyl halides with organostannanes ($sp^2$−$sp^2$ coupling): (a) Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc.* **1987**, *109*, 5478−5486. (b) Farina, V.; Krishnan, B. *J. Am. Chem. Soc.* **1991**, *113*, 9585−9595. (c) Farina, V.; Krishnan, B.; Marshall, D. R.; Roth, G. P. *J. Org. Chem.* **1993**, *58*, 5434−5444. (d) Farina, V.; Krishnamurthy, V.; Scott, W. J. In *Organic Reactions*; Paquette, L. A., Ed.; Wiley: New York, 1997; Vol. 50, pp 1−652.

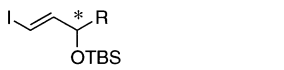
(24) (a) Brown, H. C.; Cole, T. E. *Organometallics* **1983**, *2*, 1316−1319. (b) For **4e**−**g**, see ref 19. (c) For **4h**, see Kobayashi, Y.; Nakayama, Y.; Mizojiri, R. *Tetrahedron* **1998**, *54*, 1053−1062.

**TABLE 2. Coupling of 1, 29, and 30 with Borates 5a−n[a]**

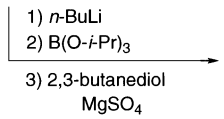
| entry | substrate[b] | $R^T$ of **2**–**5** | suffix for **2**–**5** | with the additives: yield,% | with the additives: **2** : **3**[c,d] | without: **2** : **3**[c] |
|---|---|---|---|---|---|---|
| 1 | **1** | Ph | **a** | 84 | 13 : 1 | 0.9 : 1 |
| 2 | **1** | *o*-$MeC_6H_4$ | **b** | 52[e] | 7 : 1 | 1.1 : 1 |
| 3 | **1** | *m*-$MeC_6H_4$ | **c** | 83 | 7 : 1 | 1.2 : 1 |
| 4 | **1** | *p*-$MeC_6H_4$ | **d** | 82 | 12 : 1 | 1.5 : 1 |
| 5 | **1** | *m*-$MeOC_6H_4$ | **e** | 84 | 6 : 1 | 0.7 : 1 |
| 6 | **1** | *p*-$MeOC_6H_4$ | **f** | 81 | 9 : 1 | —[f] |
| 7 | **1** |  | **g** | 63 | 8 : 1 | —[f] |
| 8 | **1** |  | **h** | 89 | 6 : 1 | 3 : 1 |
| 9 | **1** |  | **i** | 85 | 5 : 1 | 1.3 : 1 |
| 10 | **1** |  | **j** | 70 | 15 : 1 | 5.4 : 1 |
| 11 | **1** |  | **k** | 85 | 15 : 1 | 5.5 : 1 |
| 12 | **1** |  | *l* | 81 | 17 : 1 | 8 : 1 |
| 13 | **1** |  | **m** | 72 | 8 : 1 | 3 : 1 |
| 14 | **1** |  | **n** | 85 | 6 : 1 | 2.5 : 1 |
| 15 | **29** | Ph | **a** | 81 | 16 : 1 | —[f] |
| 16 | **29** |  | **h** | 87 | 6 : 1 | —[f] |
| 17 | **30** | Ph | **a** | 98 | 9 : 1 | —[f] |
| 18 | **30** |  | **h** | 88 | 5 : 1 | —[f] |

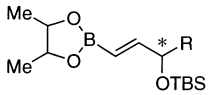
[a] Reactions were carried out with $NiCl_2(PPh_3)_2$ (5−10 mol %) in the presence or absence of additives (*t*-BuCN (2−5 equiv) and NaI (0.5−1 equiv)) for 3−10 h. [b] Racemic substrates were used. [c] Ratios were determined by $^1H$ NMR spectroscopy. [d] Ratios given in entries 15 and 16 are for MOM ethers of **2a**/**3a** and **2h**/**3h**, and those in entries 17 and 18 are for TBS ethers of **2a**/**3a** and **2h**/**3h**, respectively. [e] Recovered **1** in 24% yield. [f] Not determined.

iodides **18**−**20** (eq 3) in a way similar to that for the above



**18** (racemic): R = *n*-$C_5H_{11}$
(*S*)-**18** (*S*-isomer): R = *n*-$C_5H_{11}$
**19** (racemic): R = *c*-$C_6H_{11}$
**20** (racemic): R = $CH_2OPh$

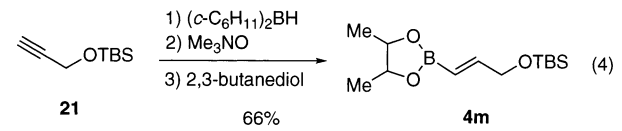


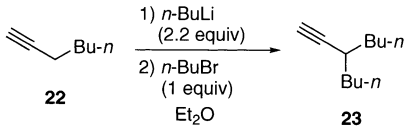



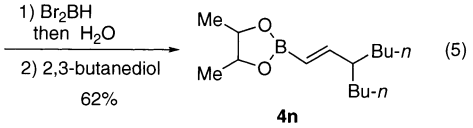
(3)

**4j** (racemic): R = *n*-$C_5H_{11}$
(*S*)-**4j** (*S*-isomer): R = *n*-$C_5H_{11}$
**4k** (racemic): R = *c*-$C_6H_{11}$
**4***l* (racemic): R = $CH_2OPh$

boronate esters. Other boronate esters **4m**[25] and **4n** were derived from acetylenes **21** and **22**, respectively, through hydroborations (eqs 4 and 5). Since we were aware of the




stability of borate **5a** toward $H_2O$ (vide supra), we deduced the same propensity toward the hydroxyl group in monoacetate **1**. Consequently, 1.2−1.8 equiv of borates per **1** were used for the investigation and found to be sufficient: a given boronate ester **4** and $NiCl_2(PPh_3)_2$ (5−10 mol %) were converted into the corresponding borate **5** and a Ni(0) species by addition of *n*-BuLi (0 °C to rt, 15−30 min, THF), and the coupling reaction was carried out with racemic monoacetate **1** at room temperature in the presence of 2−5 equiv of *t*-BuCN and 0.5−1 equiv of NaI. For comparison, the inherent regioselectivities, elucidated in most cases by running the reactions without the additives, are also given in the table.

First, tolylborates **6b**−**d** were examined. In all three cases, addition of *t*-BuCN and NaI furnished good regioselectivities (entries 2−4). However, reaction did not complete with **6b** (entry 2), indicating a substituent at the ortho position is not compatible with the coupling reaction. On the other hand, the methyl groups at the meta and para positions, respectively, did not interfere the efficiency (entries 3 and 4). Regarding the regioselectivity recorded with the additives, **5d** furnished a better result than **5b** and **5c**. Next investigated were methoxyborates **5e** and **5f**. A similar tendency for the reactivity and the regioselectivity was observed (entries 5 and 6). Furyl coupling was also successful as shown in entry 7.

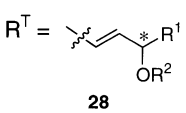
Regarding the alkenyl coupling, as expected from the aryl coupling shown above, good yields with moderate to good regioselectivities were obtained (entries 8−14). In the case of the simple alkenyl borates **5h** and **5i**, the olefinic geometry did not reflect upon either the yield or the regioselectivity (entries 8 and 9), and the regioselectivities are among the lowest of those in Table 2.

The regioselectivity obtained with the alkenyl borate **5j**, the $\omega$-chain of the primary PGs, is especially noteworthy (entry 10). Even without the additives, a moder-

(25) (a) Although the procedure[25b,c] ((i) $(Ipc)_2BH$; (ii) MeCHO; (iii) butanediol) furnished an inseparable mixture of **4m** and IpcOH in our hand, the method of Hoffmann[25d] cleanly afforded **4m** as shown in eq 4. (b) Moriya, T.; Suzuki, A.; Miyaura, N. *Tetrahedron Lett.* **1995**, *36*, 1887−1888. (c) Kamabuchi, A.; Moriya, T.; Miyaura, N.; Suzuki, A. *Synth. Commun.* **1993**, *23*, 2851−2859. (d) Hoffmann, R. W.; Dresely, S. *Synthesis* **1988**, 103−106.

ate selectivity of 5.4:1 for **2j** was observed and was raised to 15:1 by the addition of the additives. Such an unexpectedly high regioselectivity was also observed with **5k** and **5l** (entries 11 and 12), while **5m** and **5n** showed somewhat lower selectivities (entries 13 and 14) than **5j**−**l**.

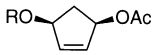
To check the relationship between the regioselectivity and the chiral center present in borates **5j**−**l**, reactions of (*S*)-**5j** with (1*R*,3*S*)-**1** or (1*S*,3*R*)-**1** were examined under the conditions used in entry 10 of Table 2. The enantiomerically enriched boronate ester (*S*)-**4j**, the precursor of borate (*S*)-**5j**, was prepared from the TBS ether (*S*)-**18** of (*S*,*E*)-1-iodo-1-octen-3-ol[26] (> 99% ee) according to eq 3, and converted into (*S*)-**5j**. Without isolation, reaction with (1*R*,3*S*)-**1**[2a,b] (95% ee by the MTPA method) and (1*S*,3*R*)-**1**,[2c,d] (> 95% ee), furnished **24** and **26** as major products as shown in eqs 6 and 7, respectively, with similar ratios and yields to those obtained with racemic **1** and **5j** (Table 2, entry 10). Consequently, it is obvious to generalize that optically active alkenyl groups of the general structure **28** with either the *R* or *S* configuration



**28**

will be installed onto the ring of **1** with a practically high level of the regioselectivity (∼ 15:1), and that a series of artificial prostaglandins can be synthesized as optically active forms from **2** by using the methods described later, or the methods previously reported by other groups[27a−c] where **2j** and the related compounds had been synthesized as racemic forms from cyclopentadiene monoepoxide (**12**).

Next, the regioselectivity for MOM ether **29** and TBS ether **30** was investigated. Although moderate to good



**29**: R = MOM
**30**: R = TBS

levels of the selectivities were obtained with phenyl- and heptenyborates **5a** and **5h** (Table 2, entries 15−18), we found no synthetic advantage in using these ethers because chromatographic separation of the regioisomers was unsuccessful due to the same mobilities and thence we did not continue further investigations with these ethers.

**C. Determination of the Stereochemistry.** The $^1$H NMR spectra of the 1,4-isomers **2a** and **2j** were consistent with the data reported by Stille[14b] and Marino,[27a,c] who have elucidated the stereochemistry of **2a**,**j** on the basis of the difference in chemical shift between the geminal protons at the C(5) position. In general, the differences established for trans and cis isomers are <0.3 ppm and >1 ppm, respectively.[28] As for other major products **2b**−**i**, **2k**−**n**, the trans stereochemistry was determined by this principle (<0.25 ppm). On the other hand, the stereochemistry of the minor products **3a**−**n** was assigned by consideration of the stereochemistry of the major products **2**.

**D. Merits of the Present Reaction.** Some of cyclopentenes **2** with an aryl or alkenyl group as $R^T$ have been synthesized from cyclopentadiene monoepoxide (**12**) by using $R^TSnMe_3$/ Pd catalyst,[14b] $R^THgCl/PdCl_2$,[29] $R^TCu(CN)Li$,[27a,c] $(R^T)(R^R)CuLi$,[27d] and, recently, the reagent derived from $(R^T)_2Te$ and (2-Th)Cu(CN)Li$_2$.[27e] The regioselectivities, however, were < 2:1 for **2a**/**3a** ($R^T$ = Ph),[14b,27a,29] 4:1 for **2j**/**3j** ($R^T$ = (*E*)-CH=CH−CH(OTBS)-$C_5H_{11}$),[27a] 1.2:1 for **2**/**3** of $R^T$ = −CH=CH$_2$,[14b] 1.35:1 for **2**/**3** of $R^T$ = (*E*)-CH=CH−CH(OTBS)$(CH_2)_6CO_2Me$,[14b] < 2.5:1 for **2**/**3** of $R^T$ = −C(CH(OEt)$_2$)=CH$_2$,[27d] and < 3.6:1 for **2**/**3** of $R^T$ = (*Z*)-CH=CHR.[27e] In addition to these low regioselectivities, monoepoxide **12** suffers from a chemical instability. Recently, asymmetric synthesis of **12** has been reported with moderate to high enantiomeric excesses.[30] These reactions, however, seem unattractive as a starting compound due to the disadvantages mentioned above. On the contrary, the present reaction (eq 1 with borates **5**) furnishes good regioselectivity and stereospecificity and

(26) Kitano, Y.; Matsumoto, T.; Wakasa, T.; Okamoto, S.; Shimazaki, T.; Kobayashi, Y.; Sato, F.; Miyaji, K.; Arai, K. *Tetrahedron Lett.* **1987**, *28*, 6351−6354.

(27) (a) Marino, J. P.; Fernández de la Pradilla, R.; Laborde, E. *J. Org. Chem.* **1987**, *52*, 4898−4913. (b) Marino, J. P.; Fernández de la Pradilla, R.; Laborde, E. *J. Org. Chem.* **1984**, *49*, 5279−5280. (c) Marino, J. P.; Kelly, M. G. *J. Org. Chem.* **1981**, *46*, 4389−4393. (d) Marino, J. P.; Farina, J. S. *J. Org. Chem.* **1976**, *41*, 3213−3215. (e) Tucci, F. C.; Chieffi, A.; Comasseto, J. V.; Marino, J. P. *J. Org. Chem.* **1996**, *61*, 4975−4989.

(28) Trost, B. M.; Verhoeven, T. R. *J. Am. Chem. Soc.* **1980**, *102*, 4730−4743.

(29) Larock, R. C.; Ilkka, S. *Tetrahedron Lett.* **1986**, *27*, 2211−2214.

(30) (a) Chang, S.; Heid, R. M.; Jacobsen, E. N. *Tetrahedron Lett.* **1994**, *35*, 669−672. (b) Mikame, D.; Hamada, T.; Irie, R.; Katsuki, T. *Synlett* **1995**, 827−828. (c) Zaidlewicz, M.; Krzeminski, M. *Tetrahedron Lett.* **1996**, *37*, 7131−7134.

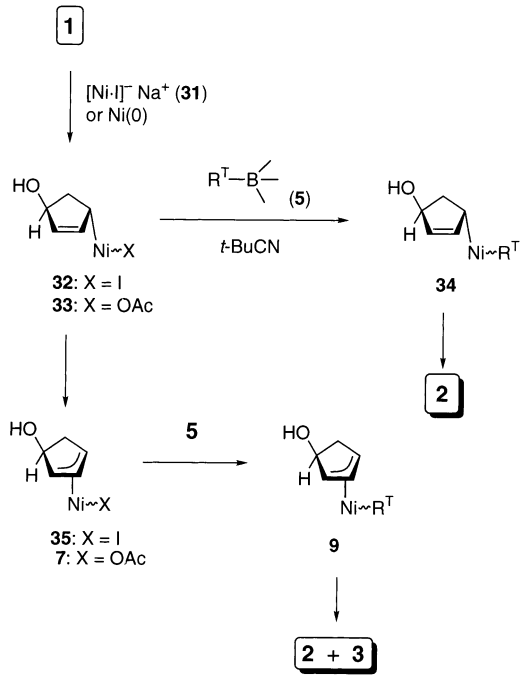
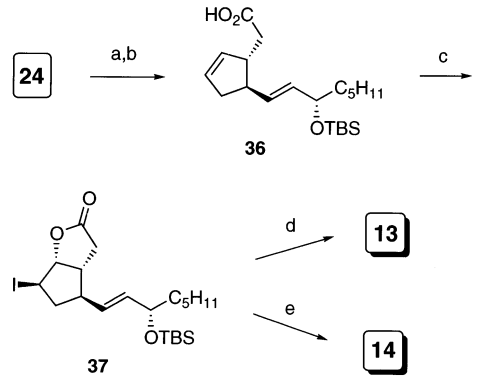



**FIGURE 3.** Plausible intermediates giving **2** and/or **3**.

is applicable to synthesis of the enantiomerically enriched compounds **2** as are demonstrated in eqs 6 and 7. From a synthetic point of view, the use of 1.2−1.8 equiv of borates **5** per monoacetate **1** is convenient, especially in the case that boronate precursors **4** are prepared by multistep procedures. In addition, boronate esters **4** are also chemically stable. Regarding purification of the 1,4-products **2**, separation of the minor 1,2-isomers **3** is easily accomplished by routine chromatography on silica gel ($\Delta R_f$ = ca. 0.2, hexane/$Et_2O$ or EtOAc).

**E. Consideration of the Regioselectivity.** Since the hydroxyl group on the ring does not seem to influence the favoring of compound **2**, the raise in the regioselectivity is best understood by introducing new complexes, $[Ni{\cdot}I]^-Na^+$ (**31**) and $\sigma$-allylnickel iodide **32**, to the well-established catalytic cycle that consists of $\pi$-allylnickels **7** and **9** (Figure 1, M = Ni). The critical steps involving these species are compiled in Figure 3. Although the formation of **31** from Ni(0) species and NaI is speculation from $[Pd{\cdot}I]^-Na^+$ (ref 31), the deeper brown color observed with NaI indirectly suggests the formation of **31**. The participation of the $\sigma$-allyl species (palladium[32] and rhodium[33] species) has recently been argued to explain the results obtained in the coupling reaction of allylic compounds with soft nucleophiles. Accordingly, the key $\sigma$-allylnickel **32** initially formed from acetate **1** and complex **31** undergoes transmetalation with borate **5** to afford the advanced $\sigma$-allylnickel **34**, which then produces 1,4-isomer **2** regioselectively. On the other hand, conversion of $\sigma$-allylnickel **32** to the $\pi$-allylnickel **35** and then

**SCHEME 1**[a]




[a] Reagents and conditions: (a) $MeC(OEt)_3$, PhOH (0.2 equiv), 80%; (b) LiOH, $H_2O$/MeOH, 73%; (c) $KI_3$, $NaHCO_3$, 83%; (d) $Bu_3SnH$, AIBN, 81%; (e) AgOAc, DMSO, 82%.

to **9** is a competitive process with the transmetalation to **34**, eventually producing a mixture of **2** and **3**. Similar competitive reactions are likely for **33** which is produced from acetate **1** and Ni(0) in the absence of NaI. Among the key intermediates **32** and **33** with the iodo and the acetoxy ligands, respectively, it is quite reasonable to think that transmetalation of **32** to **34** takes place faster than that of **33**. As for *t*-BuCN, it is probable that *t*-BuCN simply accelerates the transmetalation of **32** as well as **33** to **34**.

The higher regioselectivity observed with the PG borates **5j**−**l** can be understood similarly (Table 2, entries 10−12). Thus, the inherent selectivity built in **5j**−**l** is increased furthermore by the additives in the manner described above. The origin for the inherent high regioselectivity is, however, not clear at the moment.

**F. Synthesis of the Prostaglandin Intermediates.** As an extension of the present investigation, synthesis of **13**[34] and **14**,[35] which are the intermediates of 11-deoxy-$PGE_2$ and $PGA_2$, respectively (Figure 2), was explored by a route summarized in Scheme 1 starting with **24**, which is the product of eq 6. The Johnson−Claisen rearrangement **24** and subsequent hydrolysis afforded acid **36** which, upon iodolactonization with $KI_3$ and $NaHCO_3$, furnished lactone **37** in good overall yield from **24**. Deiodination of **37** with $Bu_3SnH$ and AIBN produced lactone **13** ($[\alpha]^{21}_D = +4.4$ (*c* 0.95, $CHCl_3$) in 81% yield, while reaction with AgOAc afforded olefin **14** ($[\alpha]^{21}_D = +159$ (*c* 0.85, $CHCl_3$); lit.[35b] $[\alpha]^{22}_D = +161.5$ (*c* 2.8, $CHCl_3$)) in 82% yield.

Previously, **13** was synthesized as a mixture of the diastereomers.[34] However, application of the method to synthesis of the optically active **13** seems difficult. As for **14**, the asymmetric synthesis reported previously[35] is lengthy and less efficient than the present synthesis.

**G. Synthesis of $\Delta^7$-$PGA_1$ Methyl Ester.** The artificial prostaglandin **15** (Figure 2) synthesized by the Noyori

(31) Negishi, E.; Takahashi, T.; Akiyoshi, K. *J. Chem. Soc., Chem. Commun*. **1986**, 1338−1339.

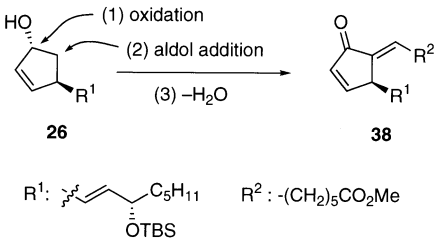
(32) (a) Fiaud, J. C.; Malleron, J. L. *Tetrahedron Lett*. **1981**, *22*, 1399−1402. (b) Trost, B. M.; Bunt, R. C. *J. Am. Chem. Soc*. **1996**, *118*, 235−236.

(33) (a) Evans, P. A.; Nelson, J. D. *J. Am. Chem. Soc*. **1998**, *120*, 5581−5582. (b) Evans, P. A.; Nelson, J. D. *Tetrahedron Lett*. **1998**, *39*, 1725−1728. Cf. (c) Evans, P. A.; Robinson, J. E.; Nelson, J. D. *J. Am. Chem. Soc*. **1999**, *121*, 6761−6762.

(34) Dixon, A. J.; Taylor, R. J. K.; Newton, R. F. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1407−1410.

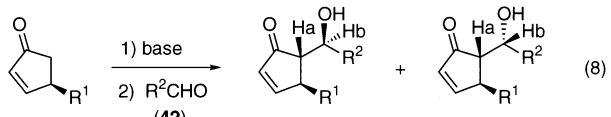
(35) (a) Chapleo, C. B.; Finch, M. A. W.; Lee, T. V.; Roberts, S. M.; Newton, R. F. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2084−2087. (b) Newton, R. F.; Reynolds, D. P.; Davies, J.; Kay, P. B.; Roberts, S. M.; Wallace, T. W. *J. Chem. Soc., Perkin Trans. 1* **1983**, 683−685.

**SCHEME 2**[a]




group[36] has attracted much attention not only because of its unique structure but also because of its antitumor activity.[37] The key structure responsible for the biological activity, according to the group, is the alkylidene cyclopentenone chromophore,[38,39] which is constructed by the 1,4-addition of organo copper reagents onto 4-silyloxy-2-cyclopenten-1-one followed by aldol reaction with the α chain-aldehyde and the subsequent dehydration.[36]

Another method we have planned for synthesis of the α-alkylidene core structure **38** is shown in Scheme 2, which involves oxidation of alcohol **26** (the product of eq 7) to the enone and subsequent installation of the C(1)−C(7) side chain by aldol reaction at the α′ (α prime) position of the enone. Although the α′ enolates from cyclohexenones have been explored well,[40] a few reports related to our investigation have been published. That is reactions with unsubstituted cyclopentenone **41** ($R^1$ = H).[41] What is worse, the conditions elucidated for the enolate preparation are different. For example, Brown used LDA to prepare the enolate from **41**,[41a] while Shibasaki found that Zr(O-*i*-Pr)$_4$ is a better base than LDA though the yield was moderate in his case.[41b] Consequently, we undertook an investigation of the aldol reaction of substituted enones **39** ($R^1$ = (*E*)-CH=CHC$_5$H$_{11}$) and **40** ($R^1$ = Ph) with several aldehydes **42a**−**d** in order to find suitable conditions for synthesis of **15** (eq 8). These




for $R^1$ in **39**–**41**, **43**–**48**:
**39**,**43**,**46**: $R^1$ = (*E*)-CH=CHC$_5$H$_{11}$
**40**,**44**,**47**: $R^1$ = Ph
**41**,**45**,**48**: $R^1$ = H

for $R^2$ in **42**, **43**–**48**:
**a**, (CH$_2$)$_2$Ph; **b**, *i*-Pr; **c**, Ph; **d**, (*E*)-CH=CHPh

enones were prepared by PCC oxidation of **2h** and **2a** in 71% and 65% yields, respectively.

The investigation was initiated with enone **39**, which, after treatment with convenient amides such as LDA, LiCA (LiN(*i*-Pr)(*c*-C$_6$H$_{11}$)), and LHMDS (LiN(TMS)$_2$) at −78 °C for 20−30 min in THF, was submitted to an aldol reaction with aldehyde **42a** ($R^2$ = (CH$_2$)$_2$Ph) at the same temperature (eq 8). The enone disappeared completely and furnished a mixture of the anti and syn aldols **43a** and **46a** in reasonable yields (Table 3, entries 1−3). The aldols were separated easily by routine chromatography. It should be noted that longer reaction times (>60 min) and/or higher temperatures (>−50 °C) for the anion generation decreased the yield of the aldols. These results suggest a somewhat unstable nature of the enolate derived from **39**, and account for a failure in alkylation with MeI at a higher temperature of 0 °C. The anti and syn stereochemistries for the major and minor aldols **43a** and **46a** were determined, respectively, on the basis of the coupling constants between Ha and Hb of **43a** ($J_{a,b}$ = 8.7 Hz) and **46a** ($J_{a,b}$ = 3 Hz) in the $^1$H NMR spectra.[42] In addition, the selective production of the anti isomer **43a** was consistent with the chairlike cyclic transition state involving the lithium α′ enolate and aldehyde **42a**.

Since the yields of entries 1−3 in Table 3 are comparable to each other, the conditions of entry 1 were applied to the aldol reaction with other aldehydes, **42b** ($R^2$ = *i*-Pr), **42c** ($R^2$ = Ph), and **42d** ($R^2$ = (*E*)-CH=CHPh), and all of the reactions uniformly furnished anti aldols as the major products in reasonable yields after chromatography (entries 4−6). The stereochemistry of the aldols was determined by the method described above: anti isomers **43b**−**d**, $J_{a,b}$ = 9.0−9.6 Hz; syn isomers **46b**−**d**, $J_{a,b}$ = ca. 3 Hz.[43] The aldol products were fairly stable and the corresponding dehydration-products were not detected by either TLC or $^1$H NMR spectroscopy even in the cases of the products of entries 5 and 6.

Next, aldol reaction of enone **40** ($R^1$ = Ph) with aldehydes **42a**−**c** ($R^2$ = (CH$_2$)$_2$Ph, *i*-Pr, Ph) was examined under the conditions of entry 1 and found to furnish similar anti/syn ratios and yields (entries 7−9).[43] The unsubstituted enone **41** ($R^1$ = H) also produced aldols **45a**−**c** and **48a**−**c** with similar ratios and yields (entries 10−12).[43]

In conclusion, LDA, LiCA, and LHMDS were found to be equally practical bases for formation of the α′ enolates from the cyclopentenones. Although the α′ enolates were found to be somewhat unstable, aldol reactions were conducted successfully (Table 3).

(36) (a) Sugiura, S.; Toru, T.; Tanaka, T.; Hazato, A.; Okamura, N.; Bannai, K.; Manabe, K.; Kurozumi, S.; Noyori, R. *Chem. Pharm. Bull.* **1984**, *32*, 4658−4661. (b) Suzuki, M.; Morita, Y.; Koyano, H.; Koga, M.; Noyori, R. *Tetrahedron* **1990**, *46*, 4809−4822.

(37) (a) Kato, T.; Fukushima, M.; Kurozumi, S.; Noyori, R. *Cancer Res.* **1986**, *46*, 3538−3542. (b) Noyori, R.; Suzuki, M. *Science* **1993**, *259*, 44−45. (c) Suzuki, M.; Kiho, T.; Tomokiyo, K.; Furuta, K.; Fukushima, S.; Takeuchi, Y.; Nakanishi, M.; Noyori, R. *J. Med. Chem.* **1998**, *41*, 3084−3090.

(38) Suzuki, M.; Mori, M.; Niwa, T.; Hirata, R.; Furuta, K.; Ishikawa, T.; Noyori, R. *J. Am. Chem. Soc.* **1997**, *119*, 2376−2385.

(39) Noyori, R.; Koyano, H.; Mori, M.; Hirata, R.; Shiga, Y.; Kokura, T.; Suzuki, M. *Pure Appl. Chem.* **1994**, *66*, 1999−2005.

(40) For example: (a) Trost, B. M.; Krische, M. J. *J. Am. Chem. Soc.* **1999**, *121*, 6131−6141. (b) Spitzner, D.; Engler, A. In *Organic Syntheses*; Freeman, J. P., Ed.; Wiley: New York, 1993; Collect. Vol. 8, pp 219−222. (c) Gesson, J.-P.; Jacquesy, J.-C.; Renoux, B. *Tetrahedron* **1989**, *45*, 5853−5866.

(41) (a) Brown, D. W.; Campbell, M. M.; Taylor, A. P.; Zhang, X. *Tetrahedron Lett.* **1987**, *28*, 985−988. (b) Sasaki, H.; Kirio, Y.; Shibasaki, M. *J. Org. Chem.* **1990**, *55*, 5306−3508. Cf: (c) Wender, P. A.; Nuss, J. M.; Smith, D. B.; Suárez-Sobrino, A.; Vagberg, J.; Decosta, D.; Bordner, J. *J. Org. Chem.* **1997**, *62*, 4908−4909. (d) Roulland, E.; Monneret, C.; Florent, J.-C. *J. Org. Chem.* **2002**, *67*, 4399−4406.

(42) (a) House, H. O.; Crumrine, D. S.; Teranishi, A. Y.; Olmstead, H. D. *J. Am. Chem. Soc.* **1973**, *95*, 3310−3324. (b) Mukaiyama, T.; Banno, K.; Narasaka, K. *J. Am. Chem. Soc.* **1974**, *96*, 7503−7509.

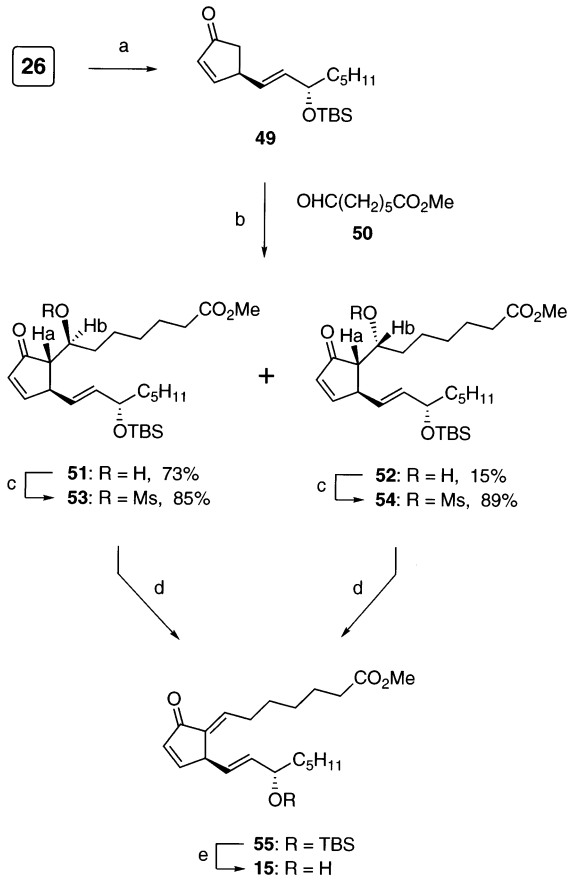
(43) The aldol products and the coupling constants measured are as follows: **43a**, 8.7 Hz; **46a**, 3 Hz; **43b**, 9.3 Hz; **46b**, ca. 3 Hz; **43c**, 9.6 Hz; **46c**, 3 Hz; **43d**, 9.0 Hz; **46d**, 3 Hz; **44a**, 8.4 Hz; **47a**, 3 Hz; **44b**, 9.0 Hz; **47b**, ca. 3 Hz; **44c**, 9.6 Hz; **47c**, ca. 3 Hz. However, coupling constants of **45a**−**c** and **48a**−**c** could not be determined because of overlap of the diagnostic signals.

**TABLE 3. Aldol Reaction between Enones 39−41 and Aldehydes 42a−d[a]**

| entry | enone | $R^1$ for **39**−**41**, **43**−**48** | base | aldehyde | $R^2$ for **42**, **43**−**48** | products anti,*syn*[b,c] | total yield, % | ratio[d] anti/syn |
|---|---|---|---|---|---|---|---|---|
| 1 | **39** | (*E*)-CH=CH−$C_5H_{11}$ | LDA | **42a** | $(CH_2)_2$Ph | **43a**,**46a** | 85 | 2:1 |
| 2 | **39** | (*E*)-CH=CH−$C_5H_{11}$ | LiCA[e] | **42a** | $(CH_2)_2$Ph | **43a**,**46a** | 88 | 4.8:1 |
| 3 | **39** | (*E*)-CH=CH−$C_5H_{11}$ | LHMDS[f] | **42a** | $(CH_2)_2$Ph | **43a**,**46a** | 86 | 3.5:1 |
| 4 | **39** | (*E*)-CH=CH−$C_5H_{11}$ | LDA | **42b** | *i*-Pr | **43b**,**46b** | 66 | >20:1[g] |
| 5 | **39** | (*E*)-CH=CH−$C_5H_{11}$ | LDA | **42c** | Ph | **43c**,**46c** | 75 | 1.6:1 |
| 6 | **39** | (*E*)-CH=CH−$C_5H_{11}$ | LDA | **42d** | (*E*)-CH=CHPh | **43d**,**46d** | 65 | 1.7:1 |
| 7 | **40** | Ph | LDA | **42a** | $(CH_2)_2$Ph | **44a**,**47a** | 83 | 4.2:1 |
| 8 | **40** | Ph | LDA | **42b** | *i*-Pr | **44b**,**47b** | 72 | >20:1[g] |
| 9 | **40** | Ph | LDA | **42c** | Ph | **44c**,**47c** | 74 | 2.5:1 |
| 10 | **41** | H | LDA | **42a** | $(CH_2)_2$Ph | **45a**,**48a** | 72 | 2.4:1 |
| 11 | **41** | H | LDA | **42b** | *i*-Pr | **45b**,**48b** | 75 | 13:1[g] |
| 12 | **41** | H | LDA | **42c** | Ph | **45c**,**48c** | 77 | 1.5:1[g] |

[a] At −78 °C for 15−30 min in THF. [b] The stereochemistry of the aldol isomers **43a**−**d**, **46a**−**d**, **44a**−**c**, and **47a**−**c** was determined by the coupling constants between Ha and Hb of the isomers (see ref 43 in detail), while that of **45a**−**c** and **48a**−**c** was speculated on the basis of chemical shifts of Hb and mobilities on TLC. [c] Both stereoisomers were separated easily by silica gel chromatography (Δ $R_f$ = ca. 0.2). [d] Calculated from the isolated yields unless otherwise noted. [e] LiN(*i*-Pr)(*c*-$C_6H_{11}$). [f] LiN(TMS)$_2$. [g] Determined by $^1$H NMR spectroscopy.

**SCHEME 3[a]**




[a] Reagents and conditions: (a) PCC, 91%; (b) LDA, −78 °C, 20 min; **51** (73%), **52** (15%); (c) MsCl, $Et_3N$, $CH_2Cl_2$; **53** (85%) from **51**; **54** (89%) and **55** (11%) from **52**; (d) $Al_2O_3$, $CH_2Cl_2$; 92% from **53**, 88% from **54**; (e) NBS, DMSO/$H_2O$, 80%.

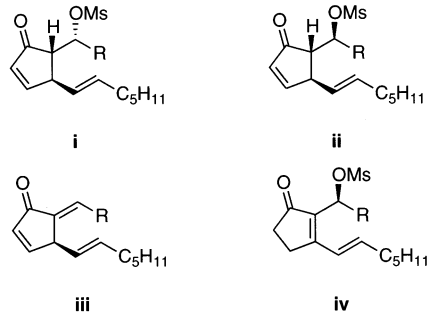
With the above results in mind, synthesis of prostaglandin **15** was investigated and the successful result is presented in Scheme 3. Oxidation of **26** with PCC afforded enone **49** in 91% yield and subsequent aldol reaction with aldehyde **50**[44] under the conditions mentioned above (Table 3, entry 1) produced a mixture of anti aldol **51** and syn aldol **52** in 73% and 15% yields, respectively, after chromatography. Mesylation of **51** under the usual conditions furnished **53** in good yield. On the other hand, the same reaction with **52** produced mesylate **54** in 89% yield and, concomitantly, the subsequent product **55** (= **38** of Scheme 2) in 11% yield. After several trials,[45] elimination of the mesylates **53** and **54** was effected cleanly with $Al_2O_3$[46] to produce **55** in good yields in both cases. Finally, deprotection[47] of the TBS group with NBS[48] in aqueous DMSO furnished the target compound **15** in 80% yield: $[\alpha]^{26}_D = +165$ (*c* 0.13, $CHCl_3$). The $^1$H NMR spectrum of the synthetic PG **15** was identical with that of the enantiomer reported by Suzuki.[37b]

## Conclusions

We have presented a new reaction for installation of aryl and alkenyl groups onto the readily available monoacetate **1** using lithium borates **5** and the nickel catalyst in the presence of *t*-BuCN and NaI to afford trans 1,4-isomers **2** with practically acceptable levels of regioselectivity (eq 1 in Chart 1 and Table 2). Among the

(44) Suzuki, M.; Kawagishi, T.; Yanagisawa, A.; Suzuki, T.; Okamura, N.; Noyori, R. *Bull. Chem. Soc. Jpn*. **1988**, *61*, 1299−1312. Cold MeOH was added to an ice-cold mixture of 1-methoxy-1-cycloheptene and pyridine (0.3 equiv), and the MeOH solution (1.2 M) was submitted to ozonolysis at −78 °C to afford aldehyde **50** in 91% yield.

(45) Although $Et_3N$ in $CH_2Cl_2$ furnished the desired olefin **iii** from a model syn mesylate **i** efficiently, anti mesylate **ii** with $Et_3N$ produced **iii** and **iv** with different ratios depending on the conditions employed. Other amines did not improve the result.




R = $(CH_2)_5CO_2Me$

(46) (a) We used Alumina N − Super I from ICN: Posner, G. H.; Gurria, G. M.; Babiak, K. A. *J. Org. Chem*. **1977**, *42*, 3173−3180. (b) Yamada, K.; Arai, T.; Sasai, H.; Shibasaki, M. *J. Org. Chem*. **1998**, *63*, 3666−3672.

(47) Attempted desilylation with $Bu_4NF$ in THF resulted in production of several unidentified compounds.

(48) Batten, R. J.; Dixon, A. J.; Taylor, R. J. K.; Newton, R. F. *Synthesis* **1980**, 234−236.

entries of Table 2, a series of borates corresponding to the PG $\omega$ chain of the natural and artificial forms furnished **2** with the unexpectedly high levels of the regioselectivity. Then, syntheses of the PG intermediates and $\Delta^7$-$PGA_1$ methyl ester were accomplished quite efficiently starting with the coupling products. The aldol reaction of cyclopentenones at the $\alpha'$ position proceeded efficiently under the conditions we have found and was applied successfully to the synthesis of $\Delta^7$-$PGA_1$ methyl ester. We would like to emphasize that the convenient availability of **2**, which had previously been inaccessible, was all which led to the success in efficient synthesis of these target molecules. It is no doubt that new strategies for synthesis of other cyclopentanoids such as egregiachloride E, hitachimycin, hybridalactone, coronatine, etc., will be proposed with compounds **2** and derivatives thereof quite easily.

## Experimental Section

**General Information.** Infrared (IR) spectra are reported in wavenumbers ($cm^{-1}$). Unless otherwise noted, $^1H$ NMR (300 MHz) and $^{13}C$ NMR (75 MHz) spectra were measured in $CDCl_3$ using $SiMe_4$ ($\delta = 0$ ppm) and the center line of $CDCl_3$ triplet ($\delta = 77.1$ ppm) as internal standards, respectively. The $^{13}C$ NMR spectra of the boronate esters **4a**−**n** were, however, not measured because they are a mixture of *dl*- and meso-isomers concerning the diol ligand and because the signals corresponding to the carbon bearing the boron atom are not identified due to the boron quadrapole.[49] The following solvents were distilled before use: THF (from Na/benzophenone), $Et_2O$ (from Na/benzophenone), and $CH_2Cl_2$ (from $CaH_2$). Racemic acetate **1**,[20] (1*R*,3*S*)-**1**[2a,b] ($[\alpha]^{20}_D = +75$ (*c* 1.02, $CHCl_3$)) of 95% ee (checked by the MTPA method) for eq 6, (1*S*,3*R*)-**1**[2c,d] ($[\alpha]^{20}_D = -74$ (*c* 1.03, $CHCl_3$)) of >95% ee for eq 7 and of >99% ee for Scheme 3, and the boronate esters **4a**,[19] **4e**,[19] **4g**,[19] and **4h**[24c] were prepared according to the procedures indicated. (*S*,*E*)-1-Iodo-1-octen-3-ol of > 99% ee, the precursors of (*S*)-**4j**, was kindly provided by Professor F. Sato.[26] Routinely, organic extracts were concentrated by using a rotary evaporator, and residues were purified by chromatography on silica gel.

**(1*R**,4*S**)-4-Methoxymethoxy-2-cyclopentenyl Acetate (29).** A solution of acetate **1** (1.71 g, 12.1 mmol), MOMCl (1.84 mL, 24.2 mmol), and *i*-$Pr_2NEt$ (10.5 mL, 60.3 mmol) in $CH_2Cl_2$ (15 mL) was stirred at room temperature for 6 h and poured into a mixture of saturated $NaHCO_3$ and $Et_2O$. The mixture was stirred for 30 min vigorously, the layers were separated, and the aqueous layer was extracted with $Et_2O$. The combined extracts were dried ($MgSO_4$) and concentrated to leave a residual oil, which was purified by chromatography to afford MOM ether **29** (2.05 g, 91%): Bp 95 °C (1.5 Torr); IR (neat) 3068, 1738, 1240, 1043 $cm^{-1}$; $^1H$ NMR $\delta$ 1.74 (dt, $J$ = 14, 4 Hz, 1 H), 2.06 (s, 3 H), 2.80 (dt, $J$ = 14, 7 Hz, 1 H), 3.39 (s, 3 H), 4.54−4.60 (m, 1 H), 4.71 (s, 2 H), 5.48−5.54 (m, 1 H), 6.00 (dm, $J$ = 6 Hz, 1 H), 6.12 (dm, $J$ = 6 Hz, 1 H). Anal. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 57.74; H, 7.57.

**(1*R**,4*S**)-4-[(*tert*-Butyldimethylsilyl)oxy]-2-cyclopentenyl Acetate (30).** A solution of acetate **1** (1.42 g, 10.0 mmol), TBSCl (1.81 g, 12.0 mmol), and imidazole (1.16 g, 17.0 mmol) in DMF (10 mL) was stirred at room temperature for 3 h and poured into a mixture of saturated $NaHCO_3$ and hexane. The resulting mixture was stirred for 1 h vigorously, and the phases were separated. The aqueous phase was extracted with hexane twice. The combined extracts were dried ($MgSO_4$) and concentrated to leave a residue, which was purified by chromatography to afford silyl ether **30** (2.35 g, 92%): Bp 155−165 °C (0.5 Torr); IR (neat) 3066, 1738, 1250, 837, 777 $cm^{-1}$. $^1H$ NMR $\delta$ 0.069 (s, 3 H), 0.074 (s, 3 H), 0.88 (s, 9 H), 1.59 (dt, $J$ = 14, 5 Hz, 1 H), 2.03 (s, 3 H), 2.79 (dt, $J$ = 14, 7 Hz, 1 H), 4.70 (tm, $J$ = 6 Hz, 1 H), 5.45 (tm, $J$ = 7 Hz, 1 H), 5.87 (dt, $J$ = 6, 2 Hz, 1 H), 5.96 (dt, $J$ = 6, 2 Hz, 1 H). Anal. Calcd for Calcd for $C_{13}H_{24}O_3Si$: C, 60.89; H, 9.43. Found: C, 61.12; H, 9.36.

**4,5-Dimethyl-2-(2-methylphenyl)-1,3,2-dioxaborolane (4b).** To a solution of 2-bromotoluene (5.50 mL, 45.7 mmol) and bipyridine (ca. 10 mg) in THF (50 mL) was added *n*-BuLi (18.0 mL, 2.5 M in hexane, 45 mmol) at −78 °C. After being stirred at −78 °C for 4 h, B(O-*i*-Pr)$_3$ (10.5 mL, 45.5 mmol) dissolved in $Et_2O$ (10 mL) was added slowly. The solution was allowed to warm to room-temperature slowly, stirred overnight, and poured into a mixture of EtOAc and 3 N HCl with vigorous stirring. After separation of the organic layer, the aqueous layer was extracted with EtOAc twice, and the combined extracts were dried ($MgSO_4$) and concentrated. To the crude boronic acid in benzene (100 mL) were added 2,3-butanediol (4.1 mL, 45.5 mmol) and $MgSO_4$ (10 g), and the resulting mixture was stirred at room temperature and filtered through a pad of Celite with benzene. The filtrate was concentrated to leave an oil, which was purified by chromatography to afford **4b** (6.87 g, 79%): Bp 145 °C (2 Torr); IR (neat) 1601, 1082, 899 $cm^{-1}$: $^1H$ NMR $\delta$ 1.29 and 1.36 (2d, $J$ = 6 and 6 Hz, 6 H (7:1)), 2.54 (s, 3 H), 4.15−4.22 and 4.62−4.75 (2m, 2 H (1:7)), 7.04−7.38 (m, 3 H), 7.79 (d, $J$ = 8 Hz, 1 H). Anal. Calcd for $C_{11}H_{15}BO_2$: C, 69.52; H, 7.96. Found: C, 69.78; H, 7.83.

**4,5-Dimethyl-2-(3-methylphenyl)-1,3,2-dioxaborolane (4c).** According to the above procedure, the title compound **4c** was prepared from 3-bromotoluene (5.5 mL, 45.3 mmol) in 72% yield: Bp 140 °C (2 Torr); IR (neat) 1608, 1585, 1223, 1207, 1103, 1083 $cm^{-1}$: $^1H$ NMR $\delta$ 1.30 and 1.40 (2d, $J$ = 6 and 6 Hz, 6 H (10:1)), 2.36 (s, 3 H), 4.14−4.23 and 4.64−4.76 (2m, 2 H (1:10)), 7.27−7.30 (m, 2 H), 7.58−7.66 (m, 2 H). Anal. Calcd for $C_{11}H_{15}BO_2$: C, 69.52; H, 7.96. Found: C, 69.83; H, 7.91.

**4,5-Dimethyl-2-(4-methylphenyl)-1,3,2-dioxaborolane (4d).** According to the preparation of **4b**, the title compound **4d** was prepared from 4-bromotoluene (5.5 mL, 44.7 mmol) in 76% yield: Bp 130 °C (2 Torr); IR (neat) 1612, 1221, 1095 $cm^{-1}$; $^1H$ NMR $\delta$ 1.29 and 1.39 (2d, $J$ = 6 and 6 Hz, 6 H (6:1)), 2.37 (s, 3 H), 4.12−4.21 and 4.63−4.74 (2m, 2 H (1:6)), 7.20 (d, $J$ = 8 Hz, 2 H), 7.71 (d, $J$ = 8 Hz, 2 H). Anal. Calcd for $C_{11}H_{15}BO_2$: C, 69.52; H, 7.96. Found: C, 69.46; H, 7.88.

**4,5-Dimethyl-2-(4-methoxyphenyl)-1,3,2-dioxaborolane (4f).** According to the preparation of **4b**, the title compound **4f** was prepared from 4-bromoanisole (5.63 mL, 45.0 mmol) in 78% yield. The $^1H$ NMR spectrum of **4f** was identical with that reported.[19]

**(*Z*)-4,5-Dimethyl-2-(1′-heptenyl)-1,3,2-dioxaborolane (4i).** To a solution of (*Z*)-1-iodoheptene (3.39 g, 15.1 mmol) and bipyridine (ca. 10 mg) in $Et_2O$ (30 mL) was added *t*-BuLi (18.3 mL, 1.64 M in pentane, 30 mmol) at −78 °C slowly. The solution was stirred at −78 °C for 3 h and B(O-*i*-Pr)$_3$ (3.50 mL, 15.2 mmol) was added to it. The solution was warmed to 0 °C slowly, stirred overnight, and poured into 1 N HCl with EtOAc. The mixture was extracted with EtOAc three times, and the combined extracts were dried ($MgSO_4$) and concentrated to furnish the corresponding boronic acid, which was used for the next reaction without further purification.

A mixture of the above boronic acid, 2,3-butanediol (1.38 mL, 15.5 mmol), and $MgSO_4$ (ca. 5 g) in benzene (30 mL) was stirred overnight and filtered through a pad of Celite. The filtrate was concentrated to leave an oil, which was purified by chromatography to furnish **4i** (1.92 g, 65%): Bp 85 °C (0.5 Torr); IR (neat) 1630, 1261, 1074, 760 $cm^{-1}$; $^1H$ NMR $\delta$ 0.88 (t, $J$ = 7 Hz, 3 H), 1.07−1.44 (m, 12 H), 2.39 (dq, $J$ = 1, 7.5 Hz, 2 H), 3.98−4.08 and 4.52−4.60 (2m, 2 H (2:7)), 5.34 (dt, $J$ = 13, 1 Hz, 1 H), 6.46 (dt, $J$ = 13, 7.5 Hz, 1 H). Anal. Calcd for $C_{11}H_{21}BO_2$: C, 67.38; H, 10.79. Found: C, 67.33; H 10.78.

(49) Pergament, I.; Srebnik, M. *Tetrahedron Lett.* **2001**, *42*, 8059−8062.

**(*E*)-2-(3′-[(*tert*-Butyldimethylsilyl)oxy]-1′-octenyl)-4,5-dimethyl-1,3,2-dioxaborolane (4j).** To a solution of racemic iodide **18**[50] (3.65 g, 9.92 mmol) and bipyridine (ca. 10 mg) in THF (33 mL) was added *n*-BuLi (6.40 mL, 2.33 M in hexane, 14.9 mmol) at −78 °C dropwise. The solution was stirred for 30 min at −78 °C, and B(O-*i*-Pr)$_3$ (3.66 mL, 15.9 mmol) was added to it. The resulting solution was gradually warmed to 0 °C, stirred overnight and poured into an ice-cold mixture of saturated $NH_4Cl$ and EtOAc. The resulting mixture was stirred vigorously for 30 min. The layers were separated, and the aqueous layer was extracted twice. The combined extracts were dried ($MgSO_4$) and concentrated to give the corresponding boronic acid, which was used for the next reaction without further purification.

A mixture of the above boronic acid, 2,3-butanediol (1.0 mL, 11 mmol), and $MgSO_4$ (20 g) in $Et_2O$ (200 mL) was stirred at room temperature for 2 h and filtered through a pad of Celite with EtOAc. Evaporation of the filtrate and chromatography of the residue afforded boronate ester **4j** (3.12 g, 92%): Bp 130−140 °C (1 Torr); IR (neat) 1645, 1072, 837, 779 cm$^{-1}$; $^1$H NMR $\delta$ 0.005 (s, 3 H), 0.022 (s, 3 H), 0.86 (t, $J$ = 7 Hz, 3 H), 0.88 (s, 9 H), 1.1−1.5 (m, 14 H), 3.98−4.05 and 4.48−4.60 (2m, 2 H) (4:7)), 4.11−4.19 (m, 1 H), 5.59 (d, $J$ = 18 Hz, 1 H), 6.58 (d, $J$ = 18 Hz, 1 H). Anal. Calcd for $C_{18}H_{37}BO_3Si$: C, 63.52; H, 10.96. Found: C, 63.26; H, 10.87.

**(*E*)-2-(3′-[(*tert*-Butyldimethylsilyl)oxy]-3′-cyclohexyl-1′-propenyl)-4,5-dimethyl-1,3,2-dioxaborolane (4k).** According to the above procedure, iodide **19**[51] (1.20 g, 3.15 mmol) was converted into the corresponding boronic acid by using THF (15 mL), *n*-BuLi (1.73 mL, 2.72 M in hexane, 4.71 mmol) (−78 °C, 30 min), and B(O-*i*-Pr)$_3$ (1.09 mL, 4.72 mmol) (−78 °C to room temperature, 4 h). The boronic acid thus prepared was esterified with 2,3-butanediol (0.43 mL, 4.7 mmol) and $MgSO_4$ (5 g) in benzene (50 mL) overnight to afford **4k** (701 mg, 63%): Bp 150 °C (2 Torr); IR (neat) 1642, 1075, 838, 777 cm$^{-1}$; $^1$H NMR $\delta$ 0.00 (s, 3 H), 0.03 (s, 3 H), 0.92 (s, 9 H), 0.95−1.43 (m, 12 H), 1.60−1.80 (m, 5 H), 3.88−3.96 (m, 1 H), 3.98−4.08 and 4.51−4.63 (2m, 2 H (3:4)), 5.57 (dt, $J$ = 18, 4.5 Hz, 1 H), 6.58 (dm, $J$ = 18 Hz, 1 H). Anal. Calcd for $C_{19}H_{37}BO_3Si$: C, 64.76; H, 10.58. Found: C, 64.77; H, 10.56.

**(*E*)-2-(3′-[(*tert*-Butyldimethylsilyl)oxy]-4′-phenyloxy-1′-butenyl)-4,5-dimethyl-1,3,2-dioxaborolane (4l).** According to the preparation of **4j**, iodide **20**[51] (1.0 g, 2.47 mmol) was converted into the corresponding boronic acid by using THF (10 mL), *n*-BuLi (1.31 mL, 2.72 M, 3.56 mmol) (−78 °C, 30 min), and B(O-*i*-Pr)$_3$ (0.72 mL, 3.1 mmol) (−78 °C to room temperature, 3 h). The acid was esterified with 2,3-butanediol (0.32 mL, 3.5 mmol) and $MgSO_4$ (5 g) in benzene (50 mL) to afford **4l** (604 mg, 65%): Bp 240 °C (2 Torr); IR (neat) 1638, 1075, 838, 777 cm$^{-1}$; $^1$H NMR $\delta$ 0.09 (s, 6 H), 0.92 (s, 9 H), 1.23 and 1.36 (2d, $J$ = 7 and 7 Hz, 6 H (7:2)), 3.79−3.95 (m, 2 H), 4.01−4.08 and 4.50−4.64 (2m, 2 H (2:7), 5.88 (dm, $J$ = 18 Hz, 1 H), 6.72 (dd, $J$ = 18, 4 Hz, 1 H), 6.84−6.97 (m, 3 H), 7.23−7.32 (m, 2 H). Anal. Calcd for $C_{20}H_{33}BO_4Si$: C, 63.82; H, 8.84. Found: C, 63.73; H, 8.77.

**(*E*)-2-(3′-[(*tert*-Butyldimethylsilyl)oxy]-1′-propenyl)-4,5-dimethyl-1,3,2-dioxaborolane (4m).** To an ice-cold mixture of $BH_3$·$SMe_2$ (3.23 mL, 2 M in THF, 6.46 mmol) and DME (10 mL) was added cyclohexene (1.31 mL, 12.9 mmol). After 15 min, the ice bath was removed, and the solution was stirred at room temperature for 1.5 h to give a white precipitate of ($c$-$C_6H_{11}$)$_2$BH. The mixture was cooled to 0 °C and acetylene **21** (1.00 g, 5.87 mmol) was added. Stirring was continued for 3 h during which time the solid (($c$-$C_6H_{11}$)$_2$BH) disappeared. To this solution was added a solution of anhydrous $Me_3N$−O in $CHCl_3$ (11.8 mL, 1 M, 11.8 mmol). After an exothermic reaction ceased, the solution was stirred at room temperature for further 1 h and then 2,3-butanediol (0.53 mL, 5.85 mmol) was added. The resulting solution was stirred at room-temperature overnight and concentrated to afford a residue, which was purified by chromatography to afford **4m** (1.10 g, 66%): Bp 130 °C (2 Torr); IR (neat) 1645, 1072, 837, 779 cm$^{-1}$; $^1$H NMR $\delta$ 0.04 (s, 6 H), 0.89 (s, 9 H), 1.18 and 1.28 (2d, $J$ = 6 and 6 Hz, 6 H (9:7)), 3.95−4.04 and 4.46−4.59 (2m, 2 H (7:9)), 4.21−4.25 (m, 2 H), 5.74 (dt, $J$ = 18, 2 Hz, 1 H), 6.66 (dt, $J$ = 18, 4 Hz, 1 H). Anal. Calcd for $C_{13}H_{27}BO_3Si$: C, 57.78; H, 10.07. Found: C, 58.04; H, 9.53.

**3-Butyl-1-heptyne (23).**[52] A solution of 1-heptyne (**22**) (1.36 mL, 10.4 mmol) and *n*-BuLi (8.42 mL, 2.72 M in hexane, 22.9 mmol) in $Et_2O$ (20 mL) was stirred at 0 °C for 5 h and *n*-BuBr (1.11 mL, 10.3 mmol) was added. The resulting solution was stirred at the same temperature overnight and poured into a mixture of brine and EtOAc with vigorous stirring. The layers were separated and the aqueous layer was extracted with EtOAc. The combined extracts were dried ($MgSO_4$) and concentrated to leave an oil, which was distilled to afford acetylene **23** (1.02 g, 65%): Bp 110 °C (22 Torr); IR (neat) 3311, 2112 cm$^{-1}$; $^1$H NMR $\delta$ 0.90 (t, $J$ = 7 Hz, 6 H), 1.2−1.6 (m, 12 H), 2.03 (d, $J$ = 2.4 Hz, 1 H), 2.24−2.36 (m, 1 H); $^{13}$C NMR $\delta$ 88.3, 68.8, 34.6, 31.4, 29.4, 22.5, 13.9. Anal. Calcd for $C_{11}H_{20}$: C, 86.76; H, 13.24. Found: C, 86.99; H, 13.26.

**(*E*)-2-(3′-Butyl-1′-heptenyl)-4,5-dimethyl-1,3,2-dioxaborolane (4n).** To an ice-cold solution of acetylene **23** (3.65 mL, 19.7 mmol) in $CH_2Cl_2$ (40 mL) was added $Br_2BH$·$SMe_2$ (19.7 mL, 1 M in $CH_2Cl_2$, 19.7 mmol). The solution was stirred at room temperature for 6 h and poured into an ice-cold mixture of $H_2O$ (3.55 mL, 197 mmol) and $Et_2O$ (10 mL) with vigorous stirring. The layers were separated and the organic layer was dried ($MgSO_4$) and concentrated. To this boronic acid were added benzene (150 mL), 2,3-butanediol (2.67 mL, 29.3 mmol), and $MgSO_4$ (10 g). The mixture was stirred at room temperature overnight and filtered through a pad of Celite. The filtrate was concentrated, and distillation of the crude product afforded **4n** (3.11 g, 62%): Bp 110 °C (2 Torr); IR (neat) 1638, 1075, 1000, 924 cm$^{-1}$; $^1$H NMR $\delta$ 0.85 (t, $J$ = 7 Hz, 6 H), 1.1−1.5 (m, 18 H), 1.94−2.07 (m, 1 H), 3.94−4.04 and 4.50−4.58 (2m, 2 H (2:5)), 5.36 (d, $J$ = 18 Hz, 1 H), 6.37 (dd, $J$ = 18, 9 Hz, 1 H). Anal. Calcd for $C_{15}H_{29}BO_2$: C, 71.44; H, 11.59. Found: C, 71.37; H, 11.50.

**General Procedure for the Nickel-Catalyzed Coupling Reaction of Monoacetate 1 and Lithium Borate 5.** To an ice-cold suspension of the boronate ester **4** (1.2−1.8 equiv), $NiCl_2(PPh_3)_2$ (10 mol %), and NaI (0.5−1 equiv) in THF was added *n*-BuLi (1.2−1.8 equiv, ca. 2 M in hexane) dropwise. The cooling bath was removed, and the mixture was stirred for 15−30 min at room temperature. Then *t*-BuCN (2−5 equiv) and monoacetate **1** (50−100 mg, 0.352−0.704 mmol) were added. The resulting mixture was stirred at room temperature for several hours or overnight and poured into saturated $NaHCO_3$ solution. The product was extracted with EtOAc or $Et_2O$ several times and the combined extracts were dried ($MgSO_4$) and concentrated to give an oil, which was subjected to chromatography on silica gel. The regioisomer **3** and the major product **2** were eluted in this order.

The yields and the regioselectivities of the products synthesized by this procedure are listed in Table 2, while their spectral and physical data are presented below.

**(1*S**,4*S**)-4-Phenyl-2-cyclopenten-1-ol (2a).** Entry 1: The $^1$H NMR spectra of **2a** and regioisomer **3a** were identical with those reported.[14b]

**(1*S**,4*S**)-4-(2′-Methylphenyl)-2-cyclopenten-1-ol (2b).** Entry 2: IR (neat) 3336, 1489, 1025, 754 cm$^{-1}$; $^1$H NMR $\delta$ 1.6 (br s, 1 H), 1.98 (ddd, $J$ = 14, 7, 6 Hz, 1 H), 2.32 (ddd, $J$ = 14, 8, 2.5 Hz, 1 H), 2.36 (s, 3 H), 4.36 (ddd, $J$ = 8, 6, 2 Hz, 1 H), 5.03 (d, $J$ = 7 Hz, 1 H), 6.07 (br s, 2 H), 6.97−7.18 (m, 4 H); $^{13}$C NMR $\delta$ 143.0, 138.8, 135.6, 134.1, 130.2, 126.20, 126.17, 125.5, 77.5, 46.1, 42.8, 19.8.

(50) Luo, F.-T.; Negishi, E. *J. Org. Chem*. **1985**, *50*, 4762−4766.
(51) Kobayashi, Y.; Shimazaki, T.; Taguchi, H.; Sato, F. *J. Org. Chem*. **1990**, *55*, 5324−5335.
(52) Bhanu, S.; Khan, E. A.; Scheinmann, F. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1609−1612.

Regioisomer **3b**: IR (neat) 3369, 1052 $cm^{-1}$; $^1H$ NMR $\delta$ 1.8 (br s, 1 H), 2.35 (br d, $J$ = 17 Hz, 1 H), 2.45 (s, 3 H), 2.79 (ddq, $J$ = 17, 7, 2.5 Hz, 1 H), 4.03 (br s, 1 H), 4.22−4.29 (m, 1 H), 5.78 (dq, $J$ = 6, 2 Hz, 1 H), 5.96 (dq, $J$ = 6, 2 Hz, 1 H), 6.97−7.24 (m, 4 H); $^{13}C$ NMR $\delta$ 140.1, 136.4, 132.1, 130.4, 129.7, 126.4, 126.13, 126.06, 80.0, 57.2, 41.7, 20.1.

**(1*S**,4*S**)-4-(3′-Methylphenyl)-2-cyclopenten-1-ol (2c).** Entry 3: IR (neat) 3350, 1606, 1111, 1030 $cm^{-1}$; $^1H$ NMR $\delta$ 1.82 (br s, 1 H), 2.09 (ddd, $J$ = 14, 7, 6 Hz, 1 H), 2.27 (ddd, $J$ = 14, 8, 3 Hz, 1 H), 2.32 (s, 3 H), 4.07−4.14 (m, 1 H), 5.02−5.07 (m, 1 H), 5.96−6.06 (m, 2 H), 6.91−7.22 (m, 4 H); $^{13}C$ NMR $\delta$ 144.8, 139.3, 138.2, 133.9, 128.5, 127.9, 127.1, 124.1, 77.4, 49.7, 43.9, 21.3. Anal. Calcd for $C_{12}H_{14}O$: C, 82.7**2**; H, 8.10. Found: C, 82.51; H, 8.07.

Regioisomer **3c**: IR (neat) 3344, 1606, 1051 $cm^{-1}$; $^1H$ NMR $\delta$ 1.96 (br s, 1 H), 2.33 (s, 3 H), 2.37 (br d, $J$ = 17 Hz, 1 H), 2.80 (ddq, $J$ = 17, 7, 2 Hz, 1 H), 3.72 (m, 1 H), 4.22−4.36 (m, 1 H), 5.76 (dq, $J$ = 6, 2 Hz, 1 H), 5.89 (dq, $J$ = 6, 2 Hz, 1 H), 6.92−7.26 (m, 4 H); $^{13}C$ NMR $\delta$ 142.6, 138.3, 132.4, 129.4, 128.6, 128.2, 127.4, 124.4, 81.0, 60.6, 41.2, 21.3.

**(1*S**,4*S**)-4-(4′-Methylphenyl)-2-cyclopenten-1-ol (2d).** Entry 4: IR (neat) 3338, 1041, 889 $cm^{-1}$; $^1H$ NMR $\delta$ 1.96−2.17 (br peak, 1 H), 2.11 (ddd, $J$ = 14, 7, 5 Hz, 1 H), 2.29 (ddd, $J$ = 14, 8, 3 Hz, 1 H), 2.32 (s, 3 H), 4.08−4.14 (m, 1 H), 5.02−5.08 (m, 1 H), 5.99−6.06 (m, 2 H), 7.03 (d, $J$ = 8 Hz, 2 H), 7.10 (d, $J$ = 8 Hz, 2 H); $^{13}C$ NMR $\delta$ 141.8, 139.3, 135.9, 133.8, 129.2, 126.9, 77.3, 49.4, 44.0, 20.8. Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.54; H, 8.14.

Regioisomer **3d**: IR (neat) 3350, 1513, 1052, 811 $cm^{-1}$; $^1H$ NMR $\delta$ 1.84 (br s, 1 H), 2.36 (s, 3 H), 2.37 (br d, $J$ = 17 Hz, 1 H), 2.79 (ddq, $J$ = 17, 6, 2 Hz, 1 H), 3.71−3.76 (m, 1 H), 4.21−4.31 (m, 1 H), 5.77 (dq, $J$ = 6, 2 Hz, 1 H), 5.89 (dq, $J$ = 6, 2 Hz, 1 H), 7.05−7.16 (m, 4 H).

**(1*S**,4*S**)-4-(3′-Methoxyphenyl)-2-cyclopenten-1-ol (2e).** Entry 5: IR (neat) 3383, 1601, 1047 $cm^{-1}$; $^1H$ NMR $\delta$ 1.92 (br s, 1 H), 2.10 (ddd, $J$ = 14, 7, 5 Hz, 1 H), 2.27 (ddd, $J$ = 14, 8, 3 Hz, 1 H), 3.79 (s, 3 H), 4.08−4.16 (m, 1 H), 5.01−5.08 (m, 1 H), 6.04 (br s, 2 H), 6.66−6.79 (m, 3 H), 7.21 (t, $J$ = 8 Hz, 1 H); $^{13}C$ NMR $\delta$ 159.9, 146.6, 139.0, 134.2, 129.6, 119.5, 112.9, 111.5, 77.4, 55.1, 49.8, 43.9. Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.41; H, 7.12.

Regioisomer **3e**: IR (neat) 3390, 3055, 1601, 1583, 1049 $cm^{-1}$; $^1H$ NMR $\delta$ 1.98 (br s, 1 H), 2.36 (dm, $J$ = 17 Hz, 1 H), 2.80 (ddq, $J$ = 17, 7, 2 Hz, 1 H), 3.71−3.76 (m, 1 H), 3.80 (s, 3 H), 4.21−4.33 (m, 1 H), 5.77 (dq, $J$ = 6, 2 Hz, 1 H), 5.89 (dq, $J$ = 6, 2 Hz, 1 H), 6.71−6.82 (m, 3 H), 7.23 (t, $J$ = 8 Hz, 1 H).

**(1*S**,4*S**)-4-(4′-Methoxyphenyl)-2-cyclopenten-1-ol (2f).** Entry 6: IR (neat) 3365, 1610, 1511, 1248 $cm^{-1}$; $^1H$ NMR $\delta$ 1.95 (br peak, 1 H), 2.06 (ddd, $J$ = 14, 7, 5 Hz, 1 H), 2.26 (ddd, $J$ = 14, 8, 3 Hz, 1 H), 3.80 (s, 3 H), 4.08−4.17 (m, 1 H), 5.04 (d, $J$ = 7 Hz, 1 H), 6.02 (s, 2 H), 6.82 (d, $J$ = 8 Hz, 2 H), 7.02 (d, $J$ = 8 Hz, 2 H); $^{13}C$ NMR $\delta$ 158.2, 139.4, 136.9, 133.7, 128.0, 113.9, 77.3, 55.2, 49.0, 44.1. Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.53; H, 7.63.

Regioisomer **3f**: IR (neat) 3404, 1510, 1248 $cm^{-1}$; $^1H$ NMR $\delta$ 1.84 (br peak, 1 H), 2.26−2.40 (m, 1 H), 2.72−2.82 (m, 1 H), 3.68−3.75 (m, 1 H), 3.80 (s, 3 H), 4.22 (dt, $J$ = 7, 4 Hz, 1 H), 5.75 (dq, $J$ = 6, 2 Hz, 1 H), 5.87 (dq, $J$ = 6, 2 Hz, 1 H), 6.82 (d, $J$ = 8 Hz, 2 H), 7.10 (d, $J$ = 8 Hz, 2 H).

**(1*S**,4*S**)-4-(2′-Furyl)-2-cyclopenten-1-ol (2g).** Entry 7: IR (neat) 3410, 3055, 1601, 779, 696 $cm^{-1}$; $^1H$ NMR $\delta$ 1.57 (br s, 1 H), 2.16 (ddd, $J$ = 14, 8, 3 Hz, 1 H), 2.32 (ddd, $J$ = 14, 7, 5 Hz, 1 H), 4.16−4.23 (m, 1 H), 4.99−5.06 (m, 1 H), 5.97−6.06 (m, 3 H), 6.28 (dd, $J$ = 3, 2 Hz, 1 H), 7.31 (dd, $J$ = 2, 1 Hz, 1 H); $^{13}C$ NMR $\delta$ 157.5, 141.5, 136.0, 134.7, 110.3, 104.2, 77.1, 43.4, 40.3. Anal. Calcd for $C_9H_{10}O_2$: C, 71.98; H, 6.71. Found: C, 71.80; H, 6.68.

Regioisomer **3g**: IR (neat) 3340, 1645, 1595, 837 $cm^{-1}$; $^1H$ NMR $\delta$ 1.94 (br s, 1 H), 2.36 (dm, $J$ = 17 Hz, 1 H), 2.80 (dm, $J$ = 17 Hz, 1 H), 3.82−3.88 (m, 1 H), 4.43−4.52 (m, 1 H), 5.75 (dq, $J$ = 6, 2 Hz, 1 H), 5.87 (dq, $J$ = 6, 2 Hz, 1 H), 6.01 (d, $J$ = 3 Hz, 1 H), 6.29 (dd, $J$ = 3, 2 Hz, 1 H), 7.34 (dd, $J$ = 2, 1 Hz, 1 H).

**(1*S**,4*R**,1′*E*)-4-(1′-Heptenyl)-2-cyclopenten-1-ol (2h).** Entry 8: IR (neat) 3336, 3055, 1024 $cm^{-1}$; $^1H$ NMR $\delta$ 0.90 (t, $J$ = 7 Hz, 3 H), 1.1−1.5 (m, 7 H), 1.78−1.97 (m, 4 H), 3.47 (q, $J$ = 7 Hz, 1 H), 4.85−4.91 (m, 1 H), 5.22 (dd, $J$ = 15, 8 Hz, 1 H), 5.44 (dt, $J$ = 15, 7 Hz, 1 H), 5.82 (br s, 2 H); $^{13}C$ NMR $\delta$ 139.3, 133.1, 132.8, 130.2, 77.1, 47.0, 41.2, 32.2, 31.2, 29.0, 22.4, 13.9. Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.79; H, 11.24.

Regioisomer **3h**: IR (neat) 3386, 1610, 1510 $cm^{-1}$; $^1H$ NMR $\delta$ 0.87 (t, $J$ = 7 Hz, 3 H), 1.1−1.5 (m, 6 H), 1.70 (br d, $J$ = 5 Hz, 1 H), 1.97 (q, $J$ = 7.0 Hz, 2 H), 2.26 (br d, $J$ = 17 Hz, 1 H), 2.68 (ddq, $J$ = 17, 7, 2 Hz, 1 H), 3.09−3.18 (m, 1 H), 4.10−4.18 (m, 1 H), 5.32 (dd, $J$ = 15, 8 Hz, 1 H), 5.49 (dt, $J$ = 15, 7 Hz, 1 H), 5.61 (dq, $J$ = 6, 2 Hz, 1 H), 5.70 (dq, $J$ = 6, 2 Hz, 1 H).

**(1*S**,4*R**,1′*Z*)-4-(1′-Heptenyl)-2-cyclopenten-1-ol (2i).** Entry 9: IR (neat) 3367, 1595, 1232 $cm^{-1}$; $^1H$ NMR $\delta$ 0.91 (t, $J$ = 7 H, 3 H), 1.2−1.5 (m, 6 H), 1.6 (br s, 1 H), 1.85 (ddd, $J$ = 14, 7, 5 Hz, 1 H), 2.01 (ddd, $J$ = 14, 8, 2.5 Hz, 1 H), 2.08 (q, $J$ = 7 Hz, 2 H), 3.78−3.89 (m, 1 H), 4.86−4.94 (m, 1 H), 5.09 (tt, $J$ = 10, 1.5 Hz, 1 H), 5.38 (dt, $J$ = 10, 7 Hz, 1 H), 5.80 (dd, $J$ = 5.5, 2 Hz, 1 H), 5.87 (dt, $J$ = 5.5, 2 Hz, 1 H); $^{13}C$ NMR $\delta$ 140.0, 133.1, 132.5, 130.4, 77.2, 41.9, 41.4, 31.3, 29.3, 27.3, 22.4, 13.9. Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.81; H, 10.97.

Regioisomer **3i**: IR (neat) 3390, 1594 $cm^{-1}$; $^1H$ NMR $\delta$ 0.90 (t, $J$ = 7 Hz, 3 H), 1.2−1.5 (m, 6 H), 1.7 (br s, 1 H), 2.14 (q, $J$ = 7 Hz, 2 H), 2.30 (br d, $J$ = 17 Hz, 1 H), 2.72 (ddq, $J$ = 17, 7, 2 Hz, 1 H), 3.44−3.55 (m, 1 H), 4.11−4.19 (m, 1 H), 5.11 (t, $J$ = 11 Hz, 1 H), 5.47 (dt, $J$ = 11, 7 Hz, 1 H), 5.55 (dq, $J$ = 6, 2 Hz, 1 H), 5.72 (dq, $J$ = 6, 2 Hz, 1 H).

**(1*S**,4*S**,1′*E*)-4-[{3′-(*tert*-Butyldimethylsilyl)oxy}-1′-octenyl]-2-cyclopenten-1-ol (2j).** Entry 10: The IR and $^1H$ NMR spectra of **2j** and the regioisomer **3j** were identical with those reported.[27a] The $^{13}C$ NMR spectrum of the optically active **2j** (i.e. **24** and **26**) are presented below. Anal. Calcd for $C_{19}H_{36}O_2Si$: C, 70.31; H, 11.18. Found: C, 70.30; H, 11.28.

**(1*S**,4*S**,1′*E*)-4-[{3′-(*tert*-Butyldimethylsilyl)oxy}-3′-cyclohexyl-1′-propenyl]-2-cyclopenten-1-ol (2k).** Entry 11: IR (neat) 3421, 835, 775 $cm^{-1}$; $^1H$ NMR $\delta$ −0.03 (s, 3 H), 0.003 (s, 3 H), 0.87 (s, 9 H), 1.05−1.88 (m, 12 H), 1.88−2.04 (m, 2 H), 3.46−3.56 (m, 1 H), 3.69 (dt, $J$ = 2, 7 Hz, 1 H), 4.84−4.94 (m, 1 H), 5.31 (dd, $J$ = 15, 7 Hz, 1 H), 5.38 (dd, $J$ = 15, 7 Hz, 1 H), 5.83−5.89 (m, 2 H); $^{13}C$ NMR $\delta$ 138.8, 138.6, 133.60, 133.56, 133.51, 132.1, 78.1, 77.18, 77.15, 46.7, 44.4, 41.0, 40.9, 29.0, 28.6, 28.5, 26.6, 26.17, 26.12, 25.8, 18.1, −4.1, −4.9. Anal. Calcd for $C_{20}H_{36}O_2Si$: C, 71.37; H, 10.78. Found: C, 71.40; H, 10.55.

Regioisomer **3k**: IR (neat) 3367, 1595, 1252 $cm^{-1}$; $^1H$ NMR $\delta$ −0.035, −0.021, 0.003 and 0.011 (4s, 6 H), 0.865 and 0.874 (2s, 9 H), 1.0−1.9 (m, 12 H), 2.27 (d, $J$ = 17 Hz, 1 H), 2.69 (dm, $J$ = 17 Hz, 1 H), 3.14−3.20 (m, 1 H), 3.70−3.75 (m, 1 H), 4.11−4.18 (m, 1 H), 5.34−5.49 (m, 2 H), 5.59−5.65 (m, 1 H), 5.72−5.77 (m, 1 H).

**(1*S**,4*S**,1′*E*)-4-[{3′-(*tert*-Butyldimethylsilyl)oxy}-4′-phenyloxy-1′-butenyl]-2-cyclopenten-1-ol (2l).** Entry 12: IR (neat) 3346, 1601, 1496, 1248 $cm^{-1}$; $^1H$ NMR $\delta$ 0.09 (s, 6 H), 0.90 (s, 9 H), 1.87−2.06 (m, 3 H), 3.56 (q, $J$ = 6 Hz, 1 H), 3.84 (d, $J$ = 6 Hz, 2 H), 4.46 (q, $J$ = 6 Hz, 1 H), 4.88−4.91 (m, 1 H), 5.55 (dd, $J$ = 15, 6 Hz, 1 H), 5.63 (ddd, $J$ = 15, 6, 2 Hz, 1 H), 5.83−5.91 (m, 2 H), 6.87−6.95 (m, 3 H), 7.24−7.31 (m, 2 H); $^{13}C$ NMR $\delta$ 158.9, 138.23, 138.20, 134.95, 134.91, 133.8, 129.4, 129.06, 129.03, 120.6, 114.5, 76.90, 76.89, 72.2, 71.67, 71.63, 46.62, 46.59, 40.77, 40.74, 25.7, 18.2, −4.77, −4.83. Anal. Calcd for $C_{21}H_{32}O_3Si$: C, 69.95; H, 8.94. Found: C, 69.49; H, 8.84.

Regioisomer **3l**: IR (neat) 3369, 1595 $cm^{-1}$; $^1H$ NMR $\delta$ 0.08 (s, 6 H), 0.89 (s, 9 H), 1.72 (br s, 1 H), 2.27, (d, $J$ = 17 Hz, 1 H), 2.69 (dd, $J$ = 17, 6 Hz, 1 H), 3.17−3.25 (m, 1 H), 3.84 (d,

$J$ = 6 Hz, 2 H), 4.13−4.20 (m, 1 H), 4.48 (q, $J$ = 6 Hz, 1 H), 5.56−5.79 (m, 4 H), 6.84−6.97 (m, 3 H), 7.22−7.32 (m, 2 H).

**(1*S**,4*S**,1′*E*)-4-[{3′-(*tert*-Butyldimethylsilyl)oxy}-1′-propenyl]-2-cyclopenten-1-ol (2m).** Entry 13: IR (neat) 3369, 1255, 837, 775 cm$^{-1}$; $^1$H NMR $\delta$ 0.06 (s, 6 H), 0.89 (s, 9 H), 1.5 (br s, 1 H), 1.87−2.03 (m, 2 H), 3.49−3.59 (m, 1 H), 4.12 (d, $J$ = 4.5 Hz, 1 H), 4.84−4.93 (m, 1 H), 5.48 (dd, $J$ = 16, 7 Hz, 1 H), 5.56 (dt, $J$ = 16, 4.5 Hz, 1 H), 5.87 (br s, 2 H); $^{13}$C NMR $\delta$ 138.7, 133.6, 133.5, 128.9, 77.1, 63.7, 46.6, 40.9, 25.9, 18.3, −5.3. Anal. Calcd for $C_{14}H_{26}O_2Si$: C, 66.09; H, 10.30. Found: C, 66.12; H, 10.30.

Regioisomer **3m**: IR (neat) 3398, 837, 775 cm$^{-1}$; $^1$H NMR $\delta$ 3.15−3.22 (m, 1 H), 5.57−5.66 (m, 3 H), 5.72−5.77 (m, 1 H).

**(1*S**,4*R**,1′*E*)-4-(3′-Butyl-1′-heptenyl)-2-cyclopenten-1-ol (2n).** Entry 14: IR (neat) 3350, 3055, 1022 cm$^{-1}$; $^1$H NMR $\delta$ 0.86 (t, $J$ = 7 Hz, 6 H), 1.1−1.4 (m, 12 H), 1.64 (br s, 1 H), 1.77−1.88 (m, 1 H), 1.90 (ddd, $J$ = 14, 7, 5 Hz, 1 H), 1.98 (ddd, $J$ = 14, 8, 3 Hz, 1 H), 3.44−3.52 (m, 1 H), 4.86−4.92 (m, 1 H), 5.07−5.21 (m, 2 H), 5.82−5.88 (m, 2 H); $^{13}$C NMR $\delta$ 139.4, 134.8, 133.0, 132.5, 77.1, 47.1, 42.5, 41.3, 34.98, 34.92, 29.3, 22.64, 22.62, 13.9. Anal. Calcd for $C_{16}H_{28}O$: C, 81.29; H, 11.94. Found: C, 81.10; H, 11.73.

Regioisomer **3n**: IR (neat) 3365, 3057 cm$^{-1}$; $^1$H NMR $\delta$ 0.87 (t, $J$ = 7 Hz, 6 H), 1.1−1.4 (m, 12 H), 1.62−1.92 (m, 2 H), 2.25 (dm, $J$ = 17 Hz, 1 H), 2.68 (ddq, $J$ = 17, 6, 3 Hz, 1 H), 3.09−3.16 (m, 1 H), 4.13 (dt, $J$ = 6, 3 Hz, 1 H), 5.18 (dd, $J$ = 15, 8 Hz, 1 H), 5.24 (dd, $J$ = 15, 7 Hz, 1 H), 5.62 (dq, $J$ = 6, 2 Hz, 1 H), 5.72 (dq, $J$ = 6, 2 Hz, 1 H).

**(1*S**,4*S**)-1-Methoxymethoxy-4-phenyl-2-cyclopentene (MOM Ether of 2a).** Entry 15: IR (neat) 3060, 3026, 1043 cm$^{-1}$; $^1$H NMR $\delta$ 2.05 (ddd, $J$ = 14, 7, 5 Hz, 1 H), 2.38 (ddd, $J$ = 14, 8, 3 Hz, 1 H), 3.39 (s, 3 H), 4.08−4.16 (m, 1 H), 4.70 (d, $J$ = 7 Hz, 1 H), 4.72 (d, $J$ = 7 Hz, 1 H), 4.88−4.94 (m, 1 H), 6.03−6.10 (m, 2 H), 7.11−7.33 (m, 5 H); $^{13}$C NMR $\delta$ 145.0, 139.8, 132.3, 128.7, 127.2, 126.5, 95.8, 82.9, 55.3, 49.9, 41.3. Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.89. Found: C, 76.43; H, 7.89.

Regioisomer (MOM ether of **3a**): IR (neat) 3059, 3028, 1045 cm$^{-1}$; $^1$H NMR $\delta$ 2.43 (dm, $J$ = 17 Hz, 1 H), 2.79 (ddq, $J$ = 17, 7, 2 Hz, 1 H), 3.30 (s, 3 H), 3.88−3.93 (m, 1 H), 4.21 (dt, $J$ = 7, 4 Hz, 1 H), 4.65 (s, 2 H), 5.74 (dq, $J$ = 6, 2 Hz, 1 H), 5.90 (dq, $J$ = 6, 2 Hz, 1 H), 7.18−7.38 (m, 5 H).

**(1*S**,4*R**,1′*E*)-4-(1′-Heptenyl)-1-methoxymethoxy-2-cyclopentene (MOM Ether of 2h).** Entry 16: IR (neat) 3053, 1043 cm$^{-1}$; $^1$H NMR $\delta$ 0.88 (t, $J$ = 7 H, 1 H), 1.2−1.4 (m, 6 H), 1.84 (ddd, $J$ = 14, 7, 5 Hz, 1 H), 1.97 (q, $J$ = 7 Hz, 1 H), 2.08 (ddd, $J$ = 14, 8, 3 Hz, 1 H), 3.37 (s, 3 H), 3.40−3.51 (m, 1 H), 4.67 (d, $J$ = 7 Hz, 1 H), 4.69 (d, $J$ = 7 Hz, 1 H), 4.73−4.79 (m, 1 H), 5.24 (dd, $J$ = 15, 8 Hz, 1 H), 5.44 (dt, $J$ = 15, 7 Hz, 1 H), 5.84−5.92 (m, 2 H); $^{13}$C NMR $\delta$ 139.9, 132.9, 131.2, 130.3, 95.7, 82.6, 55.2, 47.1, 38.4, 32.3, 31.3, 29.1, 22.4, 14.0. Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. Found: C, 74.71; H, 10.49.

Regioisomer (MOM ether of **3h**): IR (neat) 3057, 1047 cm$^{-1}$; $^1$H NMR $\delta$ 0.88 (t, $J$ = 7 H, 1 H), 1.2−1.5 (m, 6 H), 1.99 (q, $J$ = 7 Hz, 1 H), 2.33 (dm, $J$ = 17 Hz, 1 H), 2.67 (ddq, $J$ = 17, 7, 2 Hz, 1 H), 3.22−3.32 (m, 1 H), 3.37 (s, 1 H), 4.08 (dt, $J$ = 7, 4 Hz, 1 H), 4.66 (d, $J$ = 7 Hz, 1 H), 4.69 (d, $J$ = 7 Hz, 1 H), 5.37 (dd, $J$ = 15, 8 Hz, 1 H), 5.50 (dt, $J$ = 15, 7 Hz, 1 H), 5.59 (dq, $J$ = 6, 2 Hz, 1 H), 5.70 (dq, $J$ = 6, 2 Hz, 1 H).

**(1*S**,4*S**)-1-[(*tert*-Butyldimethylsilyl)oxy]-4-phenyl-2-cyclopentene (TBS Ether of 2a).** Entry 17: IR (neat) 3060, 3028, 1603, 1053 cm$^{-1}$; $^1$H NMR $\delta$ 0.16 (s, 6 H), 0.98 (s, 9 H), 2.12 (ddd, $J$ = 14, 7, 5 Hz, 1 H), 2.30 (ddd, $J$ = 14, 8, 3 Hz, 1 H), 4.15−4.23 (m, 1 H), 5.09−5.19 (m, 1 H), 5.97 (dt, $J$ = 6, 2 Hz, 1 H), 6.03 (dd, $J$ = 6, 2 Hz, 1 H), 7.11−7.39 (m, 5 H); $^{13}$C NMR $\delta$ 145.4, 137.5, 134.6, 128.5, 127.1, 126.2, 77.8, 50.0, 44.1, 25.9, 18.2, −4.7. Anal. Calcd for $C_{17}H_{26}OSi$: C, 74.39; H, 9.55. Found: C, 74.52; H, 9.19.

Regioisomer (TBS ether of **3a**): IR (neat) 3059, 3028, 1254 cm$^{-1}$; $^1$H NMR $\delta$ −0.12 (s, 6 H), 0.84 (s, 9 H), 2.30−2.41 (m, 1 H), 2.64−2.76 (m, 1 H), 3.69−3.78 (m, 1 H), 4.21 (dt, $J$ = 7, 5 Hz, 1 H), 5.72 (dq, $J$ = 6, 2 Hz, 1 H), 5.85 (dq, $J$ = 6, 2 Hz, 1 H), 7.15−7.35 (m, 5 H).

**(1*S*,4*S*,1′*E*,3′*S*)-4-[{3′-(*tert*-Butyldimethylsilyl)oxy}-1′-octenyl]-2-cyclopenten-1-ol (24).** The TBS ether (*S*)-**18** was prepared from (*S*,*E*)-1-iodo-1-octen-3-ol[26] (>99% ee) and then converted into the boronate ester (*S*)-**4j** according to the procedure described for preparation of racemic **4j**. According to the procedure for the coupling reaction, reaction of (1*R*,3*S*)-**1** (95% ee, 200 mg, 1.41 mmol) and (*S*)-**4j** (575 mg, 1.69 mmol) with $NiCl_2(PPh_3)_2$ (92 mg, 0.141 mmol), NaI (212 mg, 1.41 mmol), THF (6 mL), *n*-BuLi (0.85 mL, 2.5 M in hexane, 2.13 mmol), and *t*-BuCN (0.78 mL, 7.06 mmol) at room temperature for 4 h gave a 19:1 mixture of **24** and the regioisomer **25** by $^1$H NMR spectroscopy. Chromatography of the mixture afforded **25** (19 mg, 4%) first and then **24** (360 mg, 79%). The IR and $^1$H NMR spectra of **24** and **25** were superimposed with those of the diastereomeric mixtures **2j** and **3j**, respectively, which were synthesized from the racemic partners **1** and **4j**. Additional data of **24**: $[\alpha]^{20}_D$ = −153 (*c* 0.98, $CHCl_3$); $^{13}$C NMR $\delta$ 138.7, 133.53, 133.46, 132.5, 77.1, 73.4, 46.6, 40.9, 38.2, 31.6, 25.8, 24.9, 22.5, 18.1, 13.9, −4.3, −4.9.

**(1*R*,4*R*,1′*E*,3′*S*)-4-[{3′-(*tert*-Butyldimethylsilyl)oxy}-1′-octenyl]-2-cyclopenten-1-ol (26).** According to the procedure for the coupling reaction, (1*S*,3*R*)-**1** (> 95% ee, 50 mg, 0.352 mmol), $NiCl_2(PPh_3)_2$ (23 mg, 0.035 mmol), NaI (53 mg, 0.353 mmol), (*S*)-**4j** (143 mg, 0.420 mmol), *n*-BuLi (0.21 mL, 2.5 M in hexane, 0.53 mmol), *t*-BuCN (0.19 mL, 1.76 mmol), and THF (2 mL) at room temperature for 3 h afforded the regioisomer **27** (4 mg, 3.6%) and the desired product **26** (87 mg, 76%) after chromatography (**26**: **27** = 21:1). The IR and $^1$H NMR spectra of **26** and **27** were superimposed with those of the diastereomeric mixtures **2j** and **3j**, respectively. Additional data of **26**: $[\alpha]^{21}_D$ = +152 (*c* 0.728, $CHCl_3$); $^{13}$C NMR $\delta$ 138.7, 133.53, 133.51, 132.5, 77.2, 73.5, 46.6, 41.0, 38.2, 31.7, 25.8, 24.9, 22.5, 18.1, 13.9, −4.3, −4.9.

**Carboxylic Acid 36.** A solution of **24** (300 mg, 0.926 mmol), $MeC(OEt)_3$ (1.16 mL, 6.33 mmol), and phenol (17 mg, 0.18 mmol) in xylene (7 mL) was stirred at 140 °C for 2 h and diluted with EtOAc. The resulting solution was washed with 1 N NaOH, dried ($MgSO_4$), and concentrated. The residual oil was purified by chromatography to furnish the ethyl ester of **36** (292 mg, 80%): IR (neat) 3053, 1738, 835, 775 cm$^{-1}$; $^1$H NMR $\delta$ −0.003 (s, 3 H), 0.02 (s, 3 H), 0.87 (s, 12 H), 1.1−1.6 (m, 11 H), 2.10−2.22 (m, 2 H), 2.30−2.58 (m, 3 H), 2.76−2.82 (m, 1 H), 4.01 (q, $J$ = 6 Hz, 1 H), 4.13 (q, $J$ = 7 Hz, 2 H), 5.39 (dd, $J$ = 16, 7 Hz, 1 H), 5.56 (dd, $J$ = 16, 6 Hz, 1 H), 5.64−5.75 (m, 2 H); $^{13}$C NMR $\delta$ 172.9, 134.0, 133.2, 132.8, 130.3, 73.6, 60.1, 48.1, 47.9, 38.7, 38.3, 31.7, 25.8, 25.0, 22.5, 18.1, 14.1, 13.9, −4.3, −4.9.

A mixture of the above ester (250 mg, 0.634 mmol) and 1 N LiOH (3.2 mL, 3.2 mmol) in MeOH (5 mL) was stirred at 40 °C overnight and poured into the phosphate buffer (pH 3.6), which had been prepared by mixing $Na_2HPO_4{\cdot}12H_2O$ (2.31 g) and citric acid (1.31 g) in $H_2O$ (98.6 g). Ethyl acetate was added to it and the resulting mixture was stirred for 30 min vigorously. The organic layer was separated and the aqueous layer was extracted with EtOAc. The combined extracts were dried ($MgSO_4$) and concentrated to give an oil, which was purified by chromatography to furnish acid **36** (170 mg, 73%): $[\alpha]^{20}_D$ = +33 (*c* 0.94, $CHCl_3$); IR (neat) 3404, 1709, 835, 775 cm$^{-1}$; $^1$H NMR $\delta$ 0.01 (s, 3 H), 0.03 (s, 3 H), 0.88 (s, 12 H), 1.2−1.6 (m, 8 H), 2.13−2.30 (m, 2 H), 2.31−2.60 (m, 3 H), 2.76−2.85 (m, 1 H), 4.01 (q, $J$ = 7 Hz, 1 H), 5.42 (dd, $J$ = 15, 7 Hz, 1 H), 5.56 (dd, $J$ = 15, 8 Hz, 1 H), 5.65−5.77 (m, 2 H), 10.5 (br peak, 1 H); $^{13}$C NMR $\delta$ 179.5, 134.3, 132.9, 132.5, 130.7, 73.6, 48.0, 47.7, 38.7, 38.5, 38.3, 31.7, 25.8, 25.0, 22.5, 18.2, 13.9, −4.3, −4.9. Anal. Calcd for $C_{21}H_{38}O_3Si$: C, 68.80; H, 10.45. Found: C, 68.63; H, 10.39.

**Iodolactone 37.** An ice-cold mixture of acid **36** (150 mg, 0.409 mmol) and $NaHCO_3$ (0.5 mL) in $Et_2O$ (4 mL) and THF (4 mL) was stirred for 20 min, and then iodine (125 mg, 0.493 mmol) was added to it. The resulting dark brown mixture was

stirred at room temperature for 24 h. Aqueous $Na_2S_2O_3$ was added to the mixture and the product was extracted with $Et_2O$ three times. The combined ethereal solutions were dried ($MgSO_4$) and concentrated. The residue was purified by chromatography to afford iodolactone **37** (167 mg, 83%): $[\alpha]^{20}_D = -14$ (*c* 1.30, $CHCl_3$); IR (neat) 1788, 1155 $cm^{-1}$; $^1H$ NMR $\delta$ −0.01 (s, 3 H), 0.02 (s, 3 H), 0.87 (s, 12 H), 1.1−1.5 (m, 8 H), 2.01 (dt, *J* = 13, 10 Hz, 1 H), 2.16−2.30 (m, 1 H), 2.37 (d, *J* = 16 Hz, 1 H), 2.54−2.76 (m, 3 H), 3.98−4.07 (m, 1 H), 4.13 (ddd, *J* = 10, 7, 3 Hz, 1 H), 5.13 (q, *J* = 3.5 Hz, 1 H), 5.43−5.55 (m, 2 H); $^{13}C$ NMR $\delta$ 175.5, 136.2, 128.3, 94.0, 72.7, 49.1, 45.7, 44.7, 38.1, 33.5, 31.6, 25.8, 24.8, 22.5, 21.4, 18.1, 13.9, −4.4, −4.9.

**Intermediate of 11-Deoxy-PGE$_2$ (13).** A solution of **37** (150 mg, 0.305 mmol), $Bu_3SnH$ (265 mg, 0.911 mmol), and a catalytic amount of AIBN in benzene (10 mL) was stirred at 80 °C for 1 h and concentrated to give an oil, which was diluted with $Et_2O$ and saturated aqueous NaF. The resulting mixture was stirred vigorously at room temperature, the layers were separated, and the aqueous layer was extracted with $Et_2O$. The combined extracts were dried ($MgSO_4$) and concentrated to give an oil, which was purified by chromatography to furnish lactone **13** (91 mg, 81%): $[\alpha]^{21}_D = +4.4$ (*c* 0.95, $CHCl_3$); IR (neat) 1776, 835, 775 $cm^{-1}$; $^1H$ NMR $\delta$ −0.02 (s, 3 H), 0.01 (s, 3 H), 0.86 (s, 12 H), 1.18−1.54 (m, 8 H), 1.82−2.02 (m, 2 H), 2.10−2.30 (m, 3 H), 2.33 (dd, *J* = 18, 2 Hz, 1 H), 2.36−2.47 (m, 1 H), 2.70 (dd, *J* = 18, 9 Hz, 1 H), 3.96−4.05 (m, 1 H), 4.94 (dt, *J* = 3, 7 Hz, 1 H), 5.36−5.50 (m, 2 H); $^{13}C$ NMR $\delta$ 177.2, 134.8, 130.3, 85.8, 73.1, 48.5, 45.2, 38.2, 33.9, 31.8, 31.6, 31.5, 25.7, 24.9, 22.5, 18.1, 13.8, −4.4, −4.9. The above IR and $^1H$ NMR spectra were identical with those reported previously.[34]

**Intermediate of PGA$_2$ (14).** A mixture of **37** (150 mg, 0.305 mmol) and AgOAc (76 mg, 0.455 mmol) in DMSO (10 mL) was stirred at 140 °C for 1 h and poured into brine with $Et_2O$. The product was extracted with $Et_2O$ three times. The combined ethereal solutions were dried ($MgSO_4$) and concentrated to leave an oil, which was purified by chromatography to afford **14** (91 mg, 82%): $[\alpha]^{21}_D = +159$ (*c* 0.85, $CHCl_3$); lit.[35b] $[\alpha]^{22}_D = +161.5$ (*c* 2.8, $CHCl_3$): IR (neat) 1780, 835, 775 $cm^{-1}$; $^1H$ NMR $\delta$ −0.01 (s, 3 H), 0.02 (s, 3 H), 0.87 (s, 12 H), 1.15−1.55 (m, 8 H), 2.36−2.43 (m, 1 H), 2.70−2.88 (m, 2 H), 3.18−3.22 (m, 1 H), 3.98−4.06 (m, 1 H), 5.43 (m, 2 H), 5.51 (dt, *J* = 7, 2 Hz, 1 H), 5.91, (dt, *J* = 6, 2 Hz, 1 H), 5.97 (dd, *J* = 6, 2.5 Hz, 1 H); $^{13}C$ NMR $\delta$ 176.9, 140.3, 135.0, 130.0, 129.2, 89.0, 73.0, 55.1, 42.8, 38.1, 34.9, 31.6, 25.7, 24.7, 22.5, 18.1, 13.9, −4.4, −4.9. The above IR and $^1H$ NMR spectra were identical with those reported previously.[35a] Anal. Calcd for $C_{21}H_{36}O_3Si$: C, 69.18; H, 9.95. Found: C, 69.23; H, 9.88.

**(*E*)-4-(1′-Heptenyl)-2-cyclopenten-1-one (39).** To a mixture of racemic alcohol **2h** (936 mg, 5.19 mmol) and Celite (1.7 g) in $CH_2Cl_2$ (26 mL) was added PCC (1.68 g, 7.75 mmol) in portions. The mixture was stirred vigorously at room temperature for 1 h, and diluted with hexane. The resulting mixture was filtered through a pad of Celite with hexane. The filtrate was washed with water and the aqueous layer was extracted with hexane twice. The combined organic solutions were dried ($MgSO_4$) and concentrated to give an oil, which was purified by chromatography (hexane/EtOAc) to afford enone **39** (660 mg, 71%): Bp 90 °C (1 Torr); IR (neat) 1716, 1180, 970, 785 $cm^{-1}$; $^1H$ NMR $\delta$ 0.87 (t, *J* = 7 Hz, 3 H), 1.18−1.42 (m, 6 H), 2.00 (q, *J* = 7 Hz, 2 H), 2.11 (dd, *J* = 19, 2.5 Hz, 1 H), 2.61 (dd, *J* = 19, 7 Hz, 1 H), 3.49−3.57 (m, 1 H), 5.30 (ddt, *J* = 15, 8, 1.5 Hz, 1 H), 5.55 (ddt, *J* = 15, 1.5, 7 Hz, 1 H), 6.15 (dd, *J* = 6, 2 Hz, 1 H), 7.52 (dd, *J* = 6, 3 Hz, 1 H); $^{13}C$ NMR $\delta$ 210.1, 167.5, 133.7, 132.9, 129.6, 44.2, 41.6, 32.4, 31.3, 28.9, 22.5, 14.0. Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.68; H, 10.32.

**4-Phenyl-2-cyclopenten-1-one (40).** According to the above procedure, racemic alcohol **2a** (161 mg, 1.00 mmol) was transformed into enone **40** (103 mg, 65%) by using Celite (324 mg), PCC (324 mg, 1.50 mmol), and $CH_2Cl_2$ (5 mL) at room temperature for 1 h. **40**: IR (neat) 3028, 1712 $cm^{-1}$; $^1H$ NMR $\delta$ 2.32 (dd, *J* = 19, 2.5 Hz, 1 H), 2.88 (dd, *J* = 19, 7 Hz, 1 H), 4.17 (dq, *J* = 7, 2.5 Hz, 1 H), 6.32 (dd, *J* = 6, 2 Hz, 1 H), 7.10−7.38 (m, 5 H), 7.66 (dd, *J* = 6, 2.5 Hz, 1 H); $^{13}C$ NMR $\delta$ 210.1, 166.8, 141.5, 134.1, 129.1, 127.3, 127.2, 46.6. 43.9. Anal. Calcd for $C_{11}H_{10}O$: C, 83.51; H, 6.37. Found: C, 83.85; H, 6.53.

**General Procedure for the Aldol Reaction: Reaction between 39 ($R^1 = -CH{=}CHC_5H_{11}$) and Dihydrocinnamaldehyde (42a) ($R^2 = -(CH_2)_2Ph$).** To an ice-cold solution of *i*-$Pr_2NH$ (0.079 mL, 0.56 mmol) in THF (4 mL) was added *n*-BuLi (0.17 mL, 2.47 M in hexane, 0.42 mmol) dropwise. The solution was stirred at 0 °C for 15 min and cooled to −78 °C. To this solution was added enone **39** (50 mg, 0.28 mmol) dissolved in THF (1 mL). The solution was stirred further 30 min at −78 °C and then aldehyde **42a** (0.050 mL, 0.38 mmol) was added dropwise. After 30 min at −78 °C, the solution was poured into an ice-cold mixture of $Et_2O$ and saturated $NH_4Cl$ with vigorous stirring. The ethereal solution was separated and the aqueous layer was extracted with $Et_2O$ twice. The combined extracts were dried ($MgSO_4$) and concentrated to give a stereoisomeric mixture of the aldols, which was separated by chromatography (hexane/EtOAc) to afford anti aldol **43a** (49 mg, 57%) and syn aldol **46a** (25 mg, 28%). Anti aldol **43a**: IR (neat) 3855, 3469, 1689, 972 $cm^{-1}$; $^1H$ NMR $\delta$ 0.87 (t, *J* = 7 Hz, 3 H), 1.14−2.41 (m, 6 H), 1.75−2.10 (m, 4 H), 2.17 (dd, *J* = 8.7, 2.7 Hz, 1 H), 2.61−2.94 (m, 2 H), 3.16 (dq, *J* = 8, 2.5 Hz, 1 H), 3.68−3.80 (m, 1 H), 4.25 (br s, 1 H), 5.35 (ddt, *J* = 15, 8, 2 Hz, 1 H), 5.59 (dt, *J* = 15, 6 Hz, 1 H), 6.16 (dd, *J* = 6, 2 Hz, 1 H), 7.10−7.34 (m, 5 H), 7.51 (dd, *J* = 6, 2.5 Hz, 1 H); $^{13}C$ NMR $\delta$ 213.2, 167.8, 142.2, 134.0, 132.8, 128.74, 128.68, 128.5, 125.9, 71.4, 56.3, 48.1, 37.2, 32.4, 31.3, 31.1, 28.8, 22.4, 14.0. Anal. Calcd for $C_{21}H_{28}O_2$: C, 80.73; H, 9.03. Found: C, 80.44; H, 9.32. The Ha signal for *syn* isomer **46a**: $\delta$ 2.24 (t, *J* = 3 Hz).

**(4*S*,1′*E*,3′*S*)-4-[3′-{*tert*-Butyldimethylsilyl}oxy]-1′-octenyl]-2-cyclopenten-1-one (49).** A mixture of alcohol **26** (234 mg, 0.721 mmol), Celite (233 mg), and PCC (233 mg, 1.08 mmol) in $CH_2Cl_2$ (4 mL) was stirred vigorously at room temperature for 1 h, and diluted with hexane. The resulting mixture was filtered through a pad of Celite with hexane and $Et_2O$. The filtrate was washed with water and the aqueous layer was extracted with hexane twice. The combined organic solutions were dried ($MgSO_4$) and concentrated to give an oil, which was purified by chromatography (hexane/EtOAc) to afford enone **49** (211 mg, 91%): $[\alpha]^{22}_D = +143$ (*c* 0.66, $CHCl_3$); IR (neat) 1718, 1254, 835, 775 $cm^{-1}$; $^1H$ NMR $\delta$ −0.001 (s, 3 H), 0.026 (s, 3 H), 0.87 (br s, 12 H), 1.19−1.58 (m, 8 H), 2.10 (dd, *J* = 19, 2 Hz, 1 H), 2.64 (dd, *J* = 19, 7 Hz, 1 H), 3.52−3.61 (m, 1 H), 4.05 (q, *J* = 6 Hz, 1 H), 5.44 (dd, *J* = 16, 7 Hz, 1 H), 5.55 (dd, *J* = 16, 6 Hz, 1 H), 6.18 (dd, *J* = 6, 2 Hz, 1 H), 7.53 (dd, *J* = 6, 3 Hz, 1 H); $^{13}C$ NMR $\delta$ 209.8, 166.8, 135.9, 134.1, 129.1, 73.0, 43.7, 41.3, 38.2, 31.8, 25.9, 24.9, 22.6, 18.2, 14.0, −4.3, −4.8. Anal. Calcd for $C_{19}H_{34}O_2Si$: C, 70.75; H, 10.62. Found: C, 70.47; H, 10.87.

**Aldol Reaction between Enone 49 and Aldehyde 50.** A solution of LDA in THF was prepared from *i*-$Pr_2NH$ (0.054 mL, 0.38 mmol), *n*-BuLi (0.14 mL, 2.26 M in hexane, 0.32 mmol), and THF (7.4 mL) as usual, and enone **49** (95.0 mg, 0.295 mmol) dissolved in THF (2 mL) was added to it at −78 °C. The solution was stirred for 10 min at −78 °C and then aldehyde **50** (56 mg, 0.37 mmol) was injected. After 20 min at −78 °C, the solution was poured into an ice-cold mixture of $Et_2O$ and saturated $NH_4Cl$ with vigorous stirring. The organic layer was separated and the aqueous layer was extracted with $Et_2O$ twice. The combined extracts were dried ($MgSO_4$) and concentrated to afford an anti and syn aldol mixture, which was separated by chromatography (hexane/EtOAc) to furnish anti aldol **51** (103 mg, 73%) and syn aldol **52** (21 mg, 15%).

Major aldol **51**: $[\alpha]^{22}_D = +117$ (*c* 0.35, $CHCl_3$); IR (neat) 3483, 1739, 1693, 836, 775 $cm^{-1}$; $^1H$ NMR $\delta$ 0.007 (s, 3 H), 0.036 (s, 3 H), 0.88 (br s, 12 H), 1.2−1.7 (m, 16 H), 2.10 (dd, *J* = 9, 3 Hz, 1 H), 2.30 (t, *J* = 8 Hz, 2 H), 3.19−3.27 (m, 1 H),

3.66 (s, 3 H), 3.68−3.76 (m, 1 H), 4.04−4.13 (m, 2 H, C(15)−H and OH), 5.49 (dd, $J$ = 16, 8 Hz, 1 H), 5.60 (dd, $J$ = 16, 6 Hz, 1 H), 6.18 (dd, $J$ = 6, 2 Hz, 1 H), 7.52 (dd, $J$ = 6, 2 Hz, 1 H); $^{13}$C NMR $\delta$ 212.9, 174.4, 167.1, 136.8, 133.2, 128.2, 72.8, 72.1, 56.4, 51.5, 47.7, 38.2, 35.5, 34.0, 31.8, 29.1, 25.9, 24.87, 24.83, 22.6, 18.2, 14.0, −4.3, −4.8. Anal. Calcd for $C_{27}H_{48}O_5Si$: C, 67.45; H, 10.06. Found: 67.52; H, 10.20.

Minor aldol **52**: IR (neat) 3462, 1739, 1712, 837, 775 cm$^{-1}$; $^1$H NMR $\delta$ 0.005 (s, 3 H), 0.033 (s, 3 H), 0.88 (br s, 12 H), 1.1−1.7 (m, 16 H), 1.84−1.90 (m, 1 H), 2.17 (t, $J$ = 3 Hz, 1 H), 2.30 (t, $J$ = 8 Hz, 2 H), 3.66 (s, 3 H), 3.58−3.70 (m, 1 H), 4.07 (q, $J$ = 6 Hz, 1 H), 4.12−4.24 (m, 1 H), 5.50 (dd, $J$ = 15, 8 Hz, 1 H), 5.60 (dd, $J$ = 15, 6 Hz, 1 H), 6.18 (dd, $J$ = 6, 2 Hz, 1 H), 7.55 (dd, $J$ = 6, 3 Hz, 1 H); $^{13}$C NMR $\delta$ 211.0, 174.4, 167.6, 136.4, 133.7, 129.1, 73.0, 70.4, 57.6, 51.5, 44.9, 38.2, 34.8, 34.0, 31.8, 28.9, 25.87, 25.81, 24.88, 24.82, 22.6, 18.2, 14.0, −4.3, −4.8.

***anti* Mesylate 53.** To an ice-cold solution of alcohol **51** (46 mg, 0.096 mmol) and $Et_3N$ (0.13 mL, 0.96 mmol) in $CH_2Cl_2$ (1 mL) was added MsCl (0.055 mL, 0.71 mmol). After 40 min at the same temperature, the solution was poured into EtOAc and saturated $NaHCO_3$. The product was extracted with EtOAc several times. The combined extracts were dried ($MgSO_4$) and concentrated. The residue was purified by chromatography (hexane/EtOAc) to furnish mesylate **53** (47 mg, 85%): IR (neat) 1738, 1712, 1174, 837, 777 cm$^{-1}$; $^1$H NMR $\delta$ −0.005 (s, 3 H), 0.025 (s, 3 H), 0.87 (br s, 12 H), 1.2−1.9 (m, 16 H), 2.29 (t, $J$ = 8 Hz, 2 H), 2.58 (dd, $J$ = 4, 3 Hz, 1 H), 2.99 (s, 3 H), 3.58−3.63 (m, 1 H), 3.65 (s, 3 H), 4.08 (q, $J$ = 6 Hz, 1 H), 4.97−5.04 (m, 1 H), 5.50 (dd, $J$ = 15, 8 Hz, 1 H), 5.63 (dd, $J$ = 15, 6 Hz, 1 H), 6.15 (dd, $J$ = 6, 2 Hz, 1 H), 7.55 (dd, $J$ = 6, 2 Hz, 1 H); $^{13}$C NMR $\delta$ 206.5, 174.2, 166.4, 137.0, 133.7, 127.8, 81.3, 72.8, 54.9, 51.5, 46.5, 38.6, 38.1, 33.8, 31.8, 31.0, 28.6, 25.9, 25.4, 24.8, 24.6, 22.6, 18.2, 14.0, −4.3, −4.8.

**Enone 55 (= 38).** From anti mesylate **53**: To a solution of mesylate **53** (33 mg, 0.058 mmol) in $CH_2Cl_2$ (2 mL) was added $Al_2O_3$ (50 mg). The mixture was stirred at room temperature for 16 h, during which time additional $Al_2O_3$ (2 × 50 mg) was added after 4 and 12 h. After the reaction, the mixture was filtered through a pad of Celite with EtOAc. The filtrate was concentrated and the residue was purified by chromatography (hexane/EtOAc) to afford enone **55** (25 mg, 92%): $[\alpha]^{27}_D = +156$ ($c$ 0.31, $CHCl_3$); IR (neat) 1741, 1707, 1655, 837, 775 cm$^{-1}$; $^1$H NMR $\delta$ −0.006 (s, 3 H), 0.024 (s, 3 H), 0.87 (br s, 12 H), 1.1−1.7 (m, 14 H), 2.21 (q, $J$ = 8 Hz, 2 H), 2.30 (t, $J$ = 8 Hz, 2 H), 3.66 (s, 3 H), 4.00 (d, $J$ = 8 Hz, 1 H), 4.06 (q, $J$ = 7 Hz, 1 H), 5.32 (ddd, $J$ = 16, 8, 1 Hz, 1 H), 5.64 (ddd, $J$ = 16, 7, 1 Hz, 1 H), 6.33 (dd, $J$ = 6, 2 Hz, 1 H), 6.60 (t, $J$ = 8 Hz, 1 H), 7.35 (ddd, $J$ = 6, 3, 1 Hz, 1 H); $^{13}$C NMR $\delta$ 196.8 174.2, 160.5, 137.2, 137.0, 136.9, 134.9, 127.1, 73.0, 51.5, 46.8, 38.2, 33.9, 31.8, 28.9, 28.8, 28.2, 25.8, 24.8, 24.7, 22.6, 18.2, 14.0, −4.3, −4.8. Anal. Calcd for $C_{27}H_{46}O_4Si$: C, 70.08; H, 10.02. Found: C, 69.85; H, 9.97.

From alcohol **52** (syn aldol): According to the procedure described above, alcohol **52** (20 mg, 0.042 mmol) was submitted to mesylation with MsCl (0.024 mL, 0.31 mmol) and $Et_3N$ (0.059 mL, 0.42 mmol) in $CH_2Cl_2$ (1 mL) at 0 °C for 1.5 h to produce mesylate **54** (21 mg, 89%) and enone **55** (2 mg, 11%) after chromatography. Mesylate **54**: $^1$H NMR $\delta$ 0.88 (br s, 12 H), 1.1−1.7 (m, 16 H), 2.26−2.33 (m, 3 H), 2.86 (s, 3 H), 3.66 (s, 3 H), 3.65−3.75 (m, 1 H), 4.05−4.15 (m, 1 H), 5.06−5.14 (m, 1 H), 5.49 (ddd, $J$ = 15, 8, 1 Hz, 1 H), 5.66 (dd, $J$ = 15, 6 Hz, 1 H), 6.22 (dd, $J$ = 6, 2 Hz, 1 H), 7.56 (dd, $J$ = 6, 3 Hz, 1 H). Next, mesylate **54** (14 mg, 0.027 mmol) was transformed to enone **55** (11 mg, 88%) with $Al_2O_3$ (50 mg X 2) in $CH_2Cl_2$ (1 mL) at room temperature for 2.5 h. The $^1$H NMR spectrum and $R_f$ value on TLC were identical with those of **55** obtained from mesylate **53**.

**$\Delta^7$-PGA$_1$ Methyl Ester (15).** To a solution of enone **55** (25 mg, 0.054 mmol) in DMSO/$H_2O$ (19:1, 1 mL) was added NBS (13 mg, 0.073 mmol). The solution was stirred at room-temperature overnight and poured into a mixture of $Et_2O$ and the phosphate buffer of pH 3.6. The mixture was extracted with $Et_2O$ twice, and the combined extracts were dried ($MgSO_4$) and concentrated to leave an oil, which, upon purification by chromatography (hexane/EtOAc), afforded **15** (15 mg, 80%). The $^1$H NMR (300 MHz) spectrum of synthetic **15** was identical with that (270 MHz) reported for the enantiomer of **15**.[37c] An additional data of **15**: $[\alpha]^{26}_D = +165$ ($c$ 0.13, $CHCl_3$).

**Acknowledgment.** This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports, and Culture, Japan, and the Kurata Foundation. S.B.U. is grateful to the Sasakawa Scientific Research Grant. We thank Professor Fumie Sato of Tokyo Institute of Technology for the generous gift of (*S*,*E*)-1-iodo-1-octen-3-ol and Professor M. Shibasaki for providing us an information about supply of $Al_2O_3$.

**Supporting Information Available:** Experimental data for aldol reaction and $^1$H NMR spectra of compounds lacking elemental analyses (**2b**, **37**, **52**, and **53**). This material is available free of charge via the Internet at http://pubs.acs.org.

JO020375Y