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Syntheses of (5E)-PGE$_2$ and New 6-Functionalized Derivatives by the Use of Palladium-Catalyzed Decarboxylative Allylic Alkylation[1]

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Abstract—(5E)-Prostaglandin E_2 (7) was synthesized from (R)-4-t-butyldimethylsilyloxy-2-cyclopentenone (1) by *in situ* 2-alkenyloxycarbonylation of the organocopper conjugate-addition adduct (3) followed by intramolecular palladium-catalyzed decarboxylative allylic alkylation. The (5E)-prostaglandin E_2 skeleton was also obtained from the 8-keto allylic ester (11) by a similar decarboxylative allylic alkylation. The decarboxylative allylic alkylation of another type of the three-component coupling product (12) gave new 6-methyleneprostaglandin E_1 skeleton (15a), which was converted into new 6-methylprostaglandin I methyl ester (20) *via* 6-methyleneprostaglandin $F_{1\alpha}$ derivative (16) by two different ways. The stereochemistry of this intramolecular decarboxylative allylic alkylation was discussed in the reaction of 2-[(E)- or (Z)-2-butenyloxycarbonyl]cyclopentanone systems.

In the three-component coupling process[2] of prostaglandin (PG) synthesis starting from (R)-4-t-butyldimethylsilyloxy-2-cyclopentenone[3] (1), choice of enolate trapping agent defines the functionalized position of prostanoic acid skeleton to be synthesized. The enolate trapping agents designed so far are carboxylic acid chlorides,[4] methyl or allyl chloroformate,[5,6] diphenyl disulfide or benzenesulfenyl chloride,[7] aldehydes,[8] alkenyl or alkynyl halides,[9] 1,1-bis(methylthio)ethene S-oxide,[10] and nitro olefins.[11] These agents provide two types of products. One is a type of the products possessing the whole prostanoic acid skeleton such as 7-oxo-PGE_1 skeleton[4] from carboxylic acid chloride trapping, 7-hydroxyprostaglandins[8b,c] from aldehydes trapping, E series of prostaglandins[9] from alkenyl or alkynyl halides, and 6-functionalized prostaglandins[11] from nitro-olefin trapping. The other is a type of the products corresponding to new synthons possessing reactive sites to construct a prostaglandin skeleton, such as 8-phenylthio derivative[7] from diphenyl disulfide or benzenesulfenyl chloride trapping, 8-hydroxymethyl one[8a] from formaldehyde trapping, and 6-methylthio-6-methylsulfinyl one[10] from 1,1-bis(methylthio)ethene S-oxide trapping (prostaglandin numbering). Previously, we reported that methyl chloroformate as an enolate trapping agent provided 8-methoxycarbonyl synthon[5] for 11-deoxy-8-methoxycarbonyl-PGE derivatives, and that allyl chloroformate afforded 8-allyloxycarbonyl synthon[6] convertible into prostaglandin derivatives such as 4-thia-PGE_1,[6] 4-thia-PGI_1,[12] carbacyclin,[13,14] and isocarbacyclin derivatives.[14] We also preliminary reported the short synthesis

of (5E)-PGE_2 by trapping of enolate using N-[(Z)-6-methoxycarbonyl-2-hexenyloxycarbonyl]imidazole (4) followed by the palladium-catalyzed decarboxylative allylic alkylation.[15] In this paper, we wish to describe the further studies on the syntheses of (5E)-PGE_2 as well as new prostaglandin derivatives such as 6-methylene-PGE_2 and 6-methyl-PGI_2 by palladium-catalyzed decarboxylative allylic alkylation.

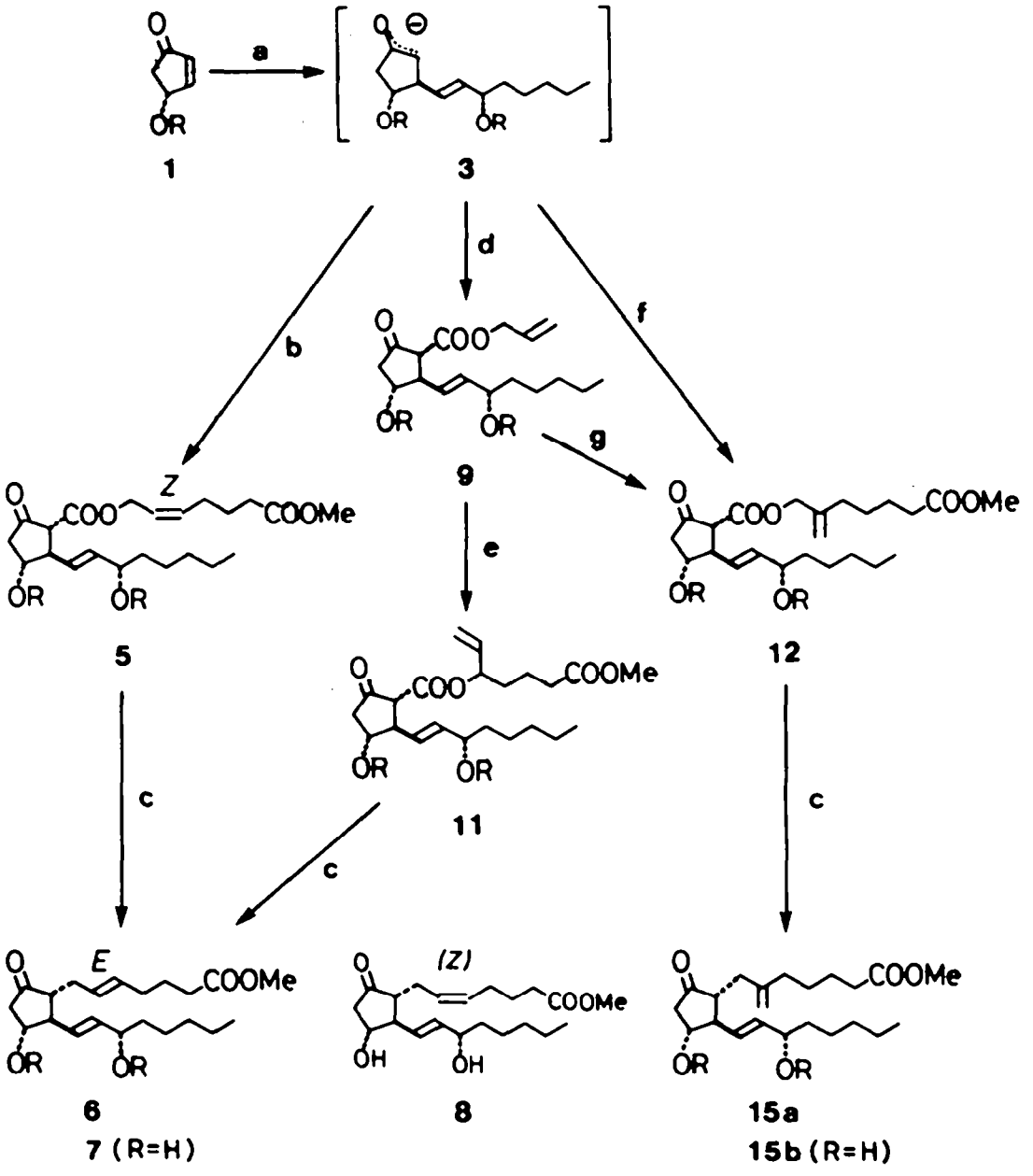
Synthesis of (5E)-PGE_2 Methyl Ester

Construction of (5E)-PGE_2 skeleton by palladium-catalyzed decarboxylative allylic alkylation of three-component coupling product was carried out as follows. The enolate 3 generated by conjugate addition of the organocopper reagent of (S,E)-3-t-butyldimethylsilyloxy-1-lithio-1-octene[16] (2) to the chiral enone 1 was trapped with 1.18 equiv of N-[(Z)-6-methoxycarbonyl-2-hexenyloxycarbonyl]imidazole (4) in THF containing hexamethylphosphoric triamide at -40 °C for 3 h to afford the 2-alkenyloxycarbonylated three-component coupling product 5 in 41% yield. Treatment of the product 5 with 5 mol% of $Pd(PPh_3)_4$[18] in DMF (50 °C, 30 min) provided protected (5E)-PGE_2 derivative (6) (64%), which afforded (5E)-PGE_2 methyl ester (7) (85%) ($[\alpha]_D^{24}$ -62°) after desilylation (Scheme 1). The 5E-geometry of the product was confirmed by the ^{13}C NMR measurement. The product 7 showed the chemical shifts at δ 31.7 and 30.1 ppm corresponding to C-7 and C-4 carbon atoms (PG numbering), respectively, whereas an authentic PGE_2 methyl ester[8c] (8) ($[\alpha]_D^{20}$ - 71.7°) showed the corresponding shifts higher at δ 25.2 and 26.5 ppm. These higher field shifts are considered to be caused by γ-steric compression effect of the carbons with (Z)-geometrical surroundings. This 5E-geometry of 7 was also supported by the fact that 7 was less polar than Z-isomer 8 on a $AgNO_3$-impregnated thin layer chromatoplate.[17] Thus, it was found that the initial Z-double bond of 5 corresponding to 5-position resulted in the exclusive formation of E-double bond of the product 6 through the decarboxylative allylic alkylation reaction.

One more possibility[18] to construct (5E)-PGE_2 skeleton by this palladium-catalyzed decarboxylative allylic alkylation reaction was examined on another type of allyloxycarbonylcyclopentanone derivative (11). The compound 11 is an ester of the α-substituted allyl alcohol, and the preceding synthon 5 was the ester of γ-substituted one. To get the desired product 11 in 58% yield, transesterification of the allyl ester 9 with the corresponding allylic alcohol 10 was carried out in toluene in the presence of 4-dimethylaminopyridine.[19] The product 11 was allowed to react with 3 mol% of $Pd(PPh_3)_4$ in THF (room temperature, 2.5 h). There was obtained (5E)-PGE_2 derivative 6 (78%) with no detectable formation of 5Z-isomer (Scheme 1). The desilylated product of 6 was also identical with the (5E)-PGE_2 methyl ester 7 obtained from the γ-substituted allylic isomer 5 as mentioned above. It was concluded that both palladium-catalyzed decarboxylative allylic alkylation of α-substituted allyl ester synthon 11 and γ-substituted one 5 afforded the same and single product 6. Since the natural abundance of (5E)-PGE_2 is very little and its known syntheses so far were possible by derivation from naturally occurring (5E)-PGA_2 resource[20] or by photo-isomerization[17] of natural PGE_2 having (5Z)-geometry, the present synthetic method might be practically useful to get (5E)-PGE_2 derivatives for their further pharmacological evaluation.

Synthesis of New 6-Methylene-PGE_1 Methy Ester and 6-Methyl-PGI_1 Methyl Ester

Further examination of the palladium-catalyzed decarboxylative allylic alkylation reaction was carried out on the β-substituted allylic ester (12). The



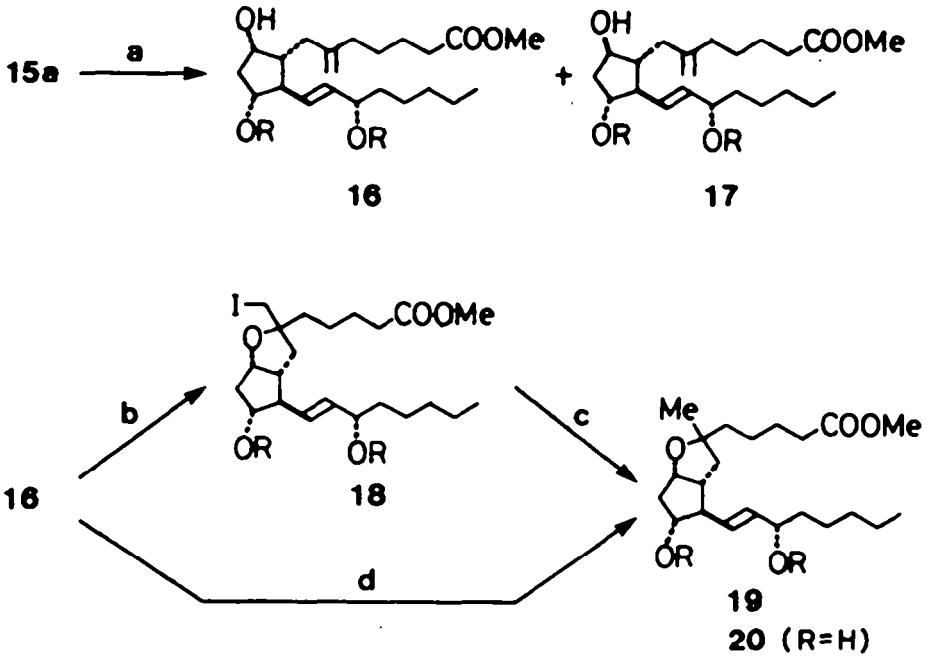
(a), Li–⟨OR⟩ **2**, $CuC{\equiv}C^{n}Pr,(Me_2N)_3P$; (b), ⟨N⟩NCOO– –COOMe **4**;

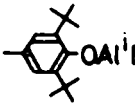
(c), $Pd(PPh_3)_4$; (d), ClCOO– ⟨⟩; (e), HO– –COOMe **10**, Me_2N–⟨⟩N;

(f), ⟨N⟩NCOO– –COOMe **14**; (g), HO– –COOMe **13**, Me_2N–⟨⟩N.

Scheme 1

R=$SiMe_2{}^{t}Bu$



Scheme 2 (a), $NaBH_4$ or  ; (b), I_2, K_2CO_3; R=$SiMe_2{}^tBu$ (c), $^nBu_3SnH$, AIBN; (d), $Hg(OCOCF_3)_2$.

starting compound 12 was obtained *via* two different routes employing three-component coupling process. In the first route, the enolate 3 formed from 2 by conjugate addition of the organocopper reagent to the chiral enone 1 was trapped with *N*-(6-methoxycarbonyl-2-methylenehexyloxycarbonyl)imidazole (14) in the presence of hexamethylphosphoric triamide to afford the three-component coupling product 12 in 31% yield. Alternatively, the same product 12 was obtained in 74% yield by transesterification[19] of the above-mentioned allyl ester 9 with methyl 7-hydroxy-6-methyleneheptanonate[21] (13). The palladium-catalyzed decarboxylative allylic alkylation of thus obtained β-substituted product 12 resulted in the formation of protected 6-methylene-PGE_1 derivative (15a) (51%) which afforded novel 6-methylene-PGE_1 methyl ester[29] (15b) (84%) after desilylation (Scheme 1).

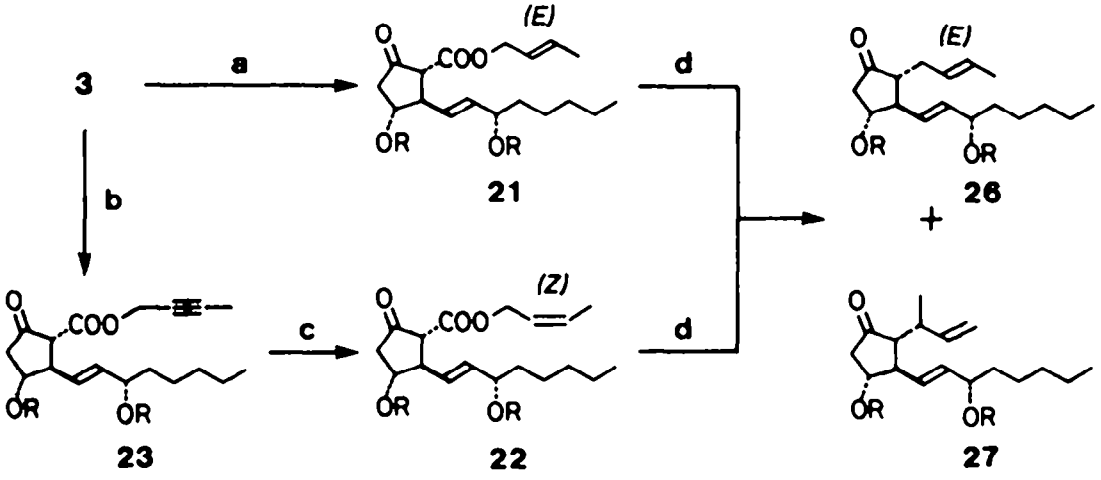
Thus obtained 6-methylene-PGE_1 derivative 15a was submitted to further conversion into new kinds of prostaglandin skeletons as follows. Reduction of the 9-oxo function of 15a with diisobutylaluminum 2,6-di-*t*-butyl-4-methylphenoxide[23] in toluene gave a desired 9α-alcohol of 6-methylene-$PGF_{1\alpha}$ (16) (66%) accompanied by 9β-isomer (17) (11%), while sodium borohydride reduction of 15a gave a mixture of 16 (68%) and 17 (19%). Since the product 16 possessed a 4-alkenol moiety in the molecule similar to that in $PGF_{2\alpha}$, intramolecular iodoetherization[24] of 16 was examined using iodine in the presence of potassium carbonate. There was obtained a product of 6-iodomethyl-PGI_1 derivative (18) (72%) which was allowed to react with tributyltin hydride[25] in the presence of azobisisobutyronitrile, and gave 6-methyl-PGI_1 derivative (19) in 75% yield. This product 19 was also accessible from 16 in a single pot reaction by intramolecular oxymercuration[24c,25,26] with mercuric trifluoroacetate followed by sodium borohydride reduction in 51% yield. Desilylation of the product 19 with tetrabutylammonium fluoride produced new

6-methyl-PGI$_1$ methyl ester[29] (20) as an approximately equal portion mixture of diastereomeric isomers at 6-position. Thus no stereoselectivity was observed in these two cyclization reaction of 16 (Scheme 2).

Stereochemical Consideration on the Intramolecular Decarboxylative Allylic Alkylation Product

We studied on the stereochemistry of this intramolecular decarboxylative allylic alkylation although it is already proposed that palladium-catalyzed decarboxylative allylic alkylation reaction of general β-keto allyl esters proceeded via π-allylpalladium intermediate.[18,27] Our present results in the case of 3,4-substituted 2-allyloxycarbonylcyclopentanone systems indicated that the reaction would also proceed via a similar π-allylpalladium intermediate because either γ-substituted allyl ester synthon 5 or α-substituted one 11 afforded the same product 6 possessing 5E-geometry. To confirm this idea, we prepared both (E)- and (Z)-2-butenyl β-keto esters (21) and (22), and their palladium-catalyzed decarboxylative allylic alkylations were studied on both compounds.

Both (E)- and (Z)-2-butenyl β-keto esters were prepared as follows. An (E)-2-butenyloxycarbonylation of the corresponding enolate 3 with N-[(E)-2-butenyloxycarbonyl]imidazole (24) gave the E-isomer 21 (40%). Another alkynyloxycarbonylation of the enolate 3 with N-(2-butynyloxycarbonyl)imidazole (25) afforded the



Scheme 3 (a),  24; (b), 25;

R=SiMe$_2$^{t}Bu (c), H_2 / Pd-$BaSO_4$, quinoline; (d), $Pd(PPh_3)_4$.

acetylenic product (23) (46%), which was hydrogenated by using of 5% Pd-$BaSO_4$ in methanol containing quinoline to give the Z-isomer 22 (76%). Treatment of E-isomer 21 with a catalytic (5 mol%) of $Pd(PPh_3)_4$ in DMF (50 °C, 1 h) resulted in the formation of (E)-2-butenylated 26 (58%) as a main product accompanied by a minor product 27 (9%). Similar treatment (25°C, 2 h) of Z-isomer 22 gave the same products of 26 (63%) and 27 (8%) (Scheme 3). In the ^{13}C NMR spectrum of 26, signals corresponding to C-1 and C-4 carbons of (E)-2-butenyl group were observed at δ 30.5 and 17.9 ppm, respectively. These observations suggested that the reactions proceeded *via* the same π-allylpalladium species, and the coupling of the five membered ring with allylic cation occurred predominantly at the less hindered site to afford the product with more favorable E olefin geometry. Formation of a by-product 27 (8-9%) also indicated that π-allylpalladium intermediate reacted at the more hindered site during the reaction. These stereochemical results of intramolecular decarboxylative allylic alkylation are significant in comparison with those in the reported intermolecular allylic alkylation[28] of enolates.

Experimental

IR spectra were recorded on a JASCO A102 spectrometer. ^1H- and ^{13}C-NMR spectra were obtained on a JEOL JNM-GX400 (400 MHz), a JEOL JNM-PS-100 (100 MHz), or a Varian EM 360A (60 MHz) spectrometer. Chemical shifts and coupling constants (J) are given in δ(ppm) relative to internal tetramethylsilane and Hz, respectively. The following abbreviations are used: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), b (broad). Mass spectra (MS) were taken at 70 or 20 eV on a HITACHI M-80B (FD-MS and high-resolution MS), a JEOL JMS D 300 (high-resolution MS), or a LKB-9000 (EI-MS) mass spectrometer. Optical rotations were measured on a Union Giken PM-101 automatic polarimeter. For high pressure liquid chromatography (HPLC) analysis, a Shimadzu Model LC-6A equipped with a Shimadzu SPD-6A UV detector and a Shimadzu C-R3A chromatopac was employed. Thin layer chromatography (TLC) was performed using Merck silica gel (Kiesel gel 60 F_{254}) analytical or preparative plates. Column chromatography was carried out on Wako gel C-300 or Daiso gel IR-60 silica gel. All reactions were carried out under argon or nitrogen. Solvents for reactions were purified if necessary before use by distillation from suitable drying agents. Solvents for extraction and chromatography were GR grades.

Synthesis of (5E)-PGE_2 Methyl Ester (7)

Preparation of N-[(Z)-6-methoxycarbonyl-2-hexenyloxycarbonyl]imidazole (4)

To a stirred solution of 5% Pd-$BaSO_4$ (200 mg) and quinoline (200 mg) in MeOH (8 ml) was added a solution of methyl 7-hydroxy-5-heptynoate (5.045 g, 32.3 mmol) in MeOH (2 ml), and the mixture was stirred under hydrogen atmosphere at r.t. for 2 days. After filtered off the catalyst through Celite and washed the catalyst with ethyl acetate, filtrate and washings were concentrated *in vacuo* to give a crude product (5.5 g), which was chromatographed on silica gel (200 g) with hexane-ethyl acetate (2:1) to afford methyl (Z)-7-hydroxy-5-heptenoate (4.877 g, 30.9 mmol, 96%): IR (neat), 3420, 3030, 1730, 1650, 1250, 1220, 1160, 1100, 1030, and 1005 cm^{-1}; NMR ($CDCl_3$), δ 1.2-1.6 (6H, m), 3.18 (1H, bs), 3.56 (3H, s), 4.02 (2H, d, J=5 Hz), 5.0-5.75 (2H, m); ^{13}C-NMR ($CDCl_3$, multiplicity), δ 24.7 (t), 26.6 (t), 33.3 (t), 51.6 (q), 58.3 (t), 129.8 (d), 131.3 (d), 174.1 (s).

A solution of methyl (Z)-7-hydroxy-5-heptenoate (2.134 g, 13.5 mmol) and 1,1'-carbonyldiimidazole (6.56 g, 40.5 mmol) in THF (20 ml) was stirred at r.t. for 1 h. After evaporation of the solvent, the resulting residue was taken up in ethyl acetate (100 ml) for extraction, and the separated aqueous layer was extracted with ethyl acetate (3 × 100 ml). The combined organic layers were washed with water (100 ml) and then brine (100 ml), and dried over $MgSO_4$. Removal of the solvent afforded an oily crude product (4.48 g), which was purified by silica gel (100 g) column chromatography using hexane : ethyl acetate (3:2) as eluant to give N-[(Z)-6-methoxycarbonyl-2-hexenyloxycarbonyl]imidazole (4; 2.492 g, 9.89 mmol, 73%): IR (neat), 3450, 3150, 3040, 1760, 1735, 1650, 1390, 1320, 1290, 1240, 1170, 1095, 1000, and 770 cm^{-1}; NMR ($CDCl_3$), δ 1.3-2.1 (2H, m), 1.9-2.4 (4H, m), 3.54 (3H, s), 4.7-4.9 (2H, m), 5.45-5.7 (2H, m), 6.87 (1H, m), 7.23 (1H, m), 7.93 (1H, m); EI-MS (m/z), 252 (M^+), 177, 141 (100), 109 (100), 99, 81, 69, 67, 41; High-resolution MS for $C_{12}H_{16}N_2O_4$: Calcd m/z: 252.1108; Found: 252.1021.

Synthesis of (2R,3R,4R)-2-[(Z)-6-methoxycarbonyl-2-hexenyloxycarbonyl]-3-[(S,E)-3-t-butyldimethylsilyloxy-1-octenyl]-4-t-butyldimethylsilyloxycyclopentanone (5)

A 1.9 M pentane solution of t-butyllithium (8.34 ml, 16.6 mmol) was added at -78°C to a stirred solution of (S,E)-3-t-butyldimethylsilyloxy-1-iodo-1-octene

(3.054 g, 8.3 mmol) in dry ether (30 ml), and the mixture was stirred at -78°C for 2 h. A solution of 1-pentynylcopper (I) (1.083 g, 8.3 mmol) and hexamethylphosphorous triamide (2.71 g, 16.6 mmol) in dry ether (10 ml) was then added at -78°C, and the resulting mixture was stirred at -78°C for 1 h. Then, a solution of (R)-4-t-butyldimethylsilyloxy-2-cyclopentenone (1; 1.484 g, 7.0 mmol) in dry ether (20 ml) was added at -78°C, and the resulting mixture was stirred at -78°C for 15 min, then at -40°C for 2 h. A solution of N-(E)-6-methoxycarbonyl-2-hexenyloxycarbonyl]imidazole (4; 2.094 g, 8.3 mmol) in THF (40 ml) and hexamethylphosphoric triamide (10 ml) was added at -78°C and the whole mixture was stirred at -40°C for 3 h. The reaction mixture was poured into an aq. 4.0 M acetate buffer solution (200 ml). The organic layer was taken up to hexane (150 ml), and the separated aqueous layer was extracted with hexane (3 × 100 ml). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo to afford 3.954 g of a crude oily product. Separation of the products by silica gel (360 g) column chromatography (hexane : ethyl acetate = 9:1) provided the enolate-trapping product 5 (1.83 g, 2.87 mmol, 41%): $[\alpha]_D^{22}$ - 27.8 (c 0.58, MeOH); IR (neat), 2870, 1765, 1740, 1645, 1245, 1120, 965, 845, 835, and 775 cm^{-1}; NMR ($CDCl_3$), δ 0.03 (6H, s), 0.06 (6H, s), 0.87 (21H), 1.1-1.5 (8H, m), 1.6-2.6 (8H, m), 3.0-3.2 (2H, m), 3.60 (3H, s), 3.8-4.2 (2H, m), 4.60 (2H, d, J=5 Hz), 5.3-5.6 (4H, m); FD-MS (m/z), 639 (M+1), 581 (M-57); EI-MS (m/z), 581 (M-57), 481, 423, 323, 265, 195, 141 (100), 75; ^{13}C-NMR ($CDCl_3$), -4.8, -4.3, 14.0, 18.0, 18.2, 22.6, 24.6, 25.0, 25.9, 26.9, 31.8, 33.6, 38.4, 47.4, 51.5, 51.7, 60.5, 61.2, 72.6, 124.2, 126.7, 134.1, 136.9, 167.7, 173.8, 206.5; High-resolution MS for $C_{33}H_{53}O_7Si_2$ (M-^{t}Bu): Calcd m/z: 581.3327; Found: 581.3332.

Synthesis of (5E)-PGE$_2$ Methyl Ester (7) from 5

Tetrakis(triphenylphosphine)palladium(0) (13 mg, 0.0112 mmol) was added to a solution of the above ester 5 (143 mg, 0.224 mmol) in N,N-dimethylformamide (1 ml) under an argon atmosphere, and the reaction mixture was stirred at 50°C for 30 min. Brine (30 ml) was added and the resulting mixture was extracted with ethyl acetate (4 × 50 ml). The separated organic layer was washed with brine, dried ($MgSO_4$), and concentrated in vacuo to afford a crude product (136 mg). Purification of the crude product by silica gel (20 g) column chromatography (hexane : ethyl acetate = 19:1 up to 4:1) gave protected (5E)-PGE$_2$ (6: 85 mg, 0.143 mmol, 64%): $[\alpha]_D^{22}$ - 42° (c 0.81, MeOH); IR (neat), 1745, 1250, 1095, 1005, 965, 927, 835, and 775 cm^{-1}; NMR ($CDCl_3$), δ 0.03 (6H, s), 0.06 (6H, s), 0.8-1.0 (21H), 1.1-1.5 (8H, m), 1.5-2.8 (12H, m), 3.53 (3H, s), 3.7-4.2 (2H, m), 5.1-5.3 (2H, m), 5.3-5.5 (2H, m); FD-MS (m/z), 537 (M-57); EI-MS (m/z), 579 (M-15), 538 (100), 537, 512, 463, 405, 379, 337, 277, 245, 215, 161, 73; ^{13}C-NMR ($CDCl_3$), δ -4.6, -4.2, 14.1, 18.1, 18.3, 22.7, 24.6, 25.1, 25.9, 30.4, 31.9, 33.4, 38.6, 47.7, 51.4, 52.1, 53.9, 72.8, 73.4, 127.4, 128.6, 132.2, 136.5, 174.0, 215.4: High-resolution MS for $C_{29}H_{53}O_5Si_2$ (M-^{t}Bu): Calcd m/z: 537.3427; Found; 537.3388.

A stirred solution of the bis-silyl ether 6 (51 mg, 0.086 mmol) in acetonitrile (3 ml) was treated with hydrogen fluoride-pyridine (0.1 ml) at r.t. for 3 h. The reaction mixture was neutralized with saturated aq. $NaHCO_3$, and extracted with ethyl acetate (4 × 50 ml). The combined extracts were washed with brine, and dried over $MgSO_4$. Removal of the solvents in vacuo left a crude product, which was purified by silica gel (5 g) column chromatography using hexane-ethyl acetate (1:1 up to 1:4) for elution to give (5E)-PGE$_2$ methyl ester (7; 27 mg, 73 mmol, 85%): $[\alpha]_D^{24}$ - 62° (c 0.90, MeOH); IR (neat), 3410, 1740, 1245, 1160, 1075, 1015, 965, 910, and 730 cm^{-1}; NMR ($CDCl_3$), δ 0.85 (3H, m), 1.0-2.9 (22H, m), 3.54 (3H, s), 3.65-4.20 (2H, m), 5.05-5.30 (2H, m), 5.30-5.50 (2H, m); FD-MS (m/z), 367 (M+1), 349 (M-17); EI-MS (m/z), 348 (M-18), 330, 317, 299, 277, 245, 208, 190(100), 164, 141, 133, 119, 109, 108, 107, 99; ^{13}C-NMR ($CDCl_3$), δ 14.0, 22.6, 24.5, 25.2, 30.1, 31.7, 31.8, 33.4, 37.4, 46.3, 51.5, 53.2, 54.6, 72.1, 72.8, 127.2, 130.5, 132.5, 137.3, 174.1, 213.9; High-resolution MS for $C_{21}H_{32}O_4$ (M-H_2O): Calcd m/z: 348.2298; Found: 348.2263.

Alternative Synthesis of (5E)-PGE$_2$ Methyl Ester (7) from 11

Preparation of Methyl 5-Hydroxy-6-heptenoate (10)

To a stirred solution of methyl 5-oxopentanoate (5.0 g, 38.5 mmol) in THF (30 ml), a 1.15 M THF solution of vinylmagnesium bromide (33.5 ml, 38.5 mmol) was added at -78°C, the mixture was stirred at -78°C for 1 h. The resulting mixture was poured into saturated aq. NH_4Cl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (4 × 100 ml). The combined organic layers were washed with brine, dried and concentrated in vacuo to provide an oily crude product (4.4 g), which was chromatographed on silica gel (200 g) with methylene chloride to give 10 (1.003 g, 6.35 mmol, 16%) and its lactonized product, 5-vinyl-δ-valerolactone (1.658 g, 13.2 mmol, 34%). This lactone (1.658 g, 13.2 mmol) was easily coverted into 10 (1.368 g, 8.66 mmol, 66%) by treatment with MeOH in the presence of a catalytic amount of pyridinium-p-toluenesulfonate at r.t. for 1 h: IR (neat); 3450, 3100, 1740, 1640, 1240, 1200, 1170, 1120, 1065, 990, and 920 cm^{-1}; NMR ($CDCl_3$), δ 1.3-1.9 (4H, m), 2.1-2.5 (2H, m), 2.47 (1H, bs), 3.55 (3H, s), 4.0 (1H, m), 4.8-5.1 (2H, m), 5.45-6.05 (1H, ddd, J= 5.5, 10 & 17 Hz); FD-MS (m/z), 141 (M-17), 57.

Synthesis of (2R,3R,4R)-2-(4-methoxycarbonyl-1-vinylbutyloxycarbonyl)-3-[(S,E)-3-t-butyldimethylsilyloxy-1-octenyl]-4-t-butyldimethylsilyloxycyclopentanone (11)

A solution of (2R,3R,4R)-2-allyloxycarbonyl-3-[(S,E)-3-t-butyldimethylsilyloxy-1-octenyl]-4-t-butyldimethylsilyloxycyclopentanone (9; 241 mg, 0.448 mmol) and 10 (212 mg, 1.344 mmol) in toluene (5 ml) in the presence of 4-dimethylaminopyridine (55 mg, 0.448 mmol) was refluxed with stirring for 2 h. Aq. NH_4Cl solution was added and the resulting mixture was extracted with ethyl acetate (3 × 30 ml). The combined organic layers were washed with aq. potassium bisulfate solution, then brine, and dried ($MgSO_4$). Evaporation of the solvent left an oily residue, which was purified by silica gel (40 g) column chromatography (hexane : ethyl acetate = 12:1) to yield 11 (166 mg, 0.260 mmol, 58%): IR (neat), 3080, 1760, 1740, 1660, 1255, 1120, 965, 855, 835, and 775 cm^{-1}; NMR ($CDCl_3$), δ 0.06 (12H, s), 0.87 (21H), 1.1-1.9 (12H, m), 1.9-2.8 (5H, m), 3.15 (1H, m), 3.75 (3H, s), 3.9-4.45 (3H, m), 5.15-6.10 (3H, m), 5.65-5.85 (2H, m); FD-MS (m/z), 639 (M+1), 581 (M-57); EI-MS (m/z), 581 (M-57); High-resolution MS for $C_{30}H_{53}O_7Si_2$ (M-^{t}Bu): Calcd m/z: 581.3327; Found: 581.3294.

Synthesis of (5E)-PGE$_1$ Methyl Ester (7) from 11

Tetrakis(triphenylphosphine)palladium(0) (9 mg, 0.008 mmol) was added to a solution of the ester 11 (159 mg, 0.25 mmol) in THF (3 ml) under an argon atmoshere, and the mixture was stirred at r.t. for 2.5 h. Removal of the solvent left a crude reaction mixture, which was separated by silica gel (20 g) column chromatography (hexane : ethyl acetate = 25:1) to give 6 (116 mg, 0.195 mmol, 78%), which showed the same spectral data (IR, NMR, ^{13}C-NMR, FD-MS, and EI-MS) as the product obtained from 5.

A similar desilylation (r.t., 3 h) of this ester 6 (111 mg, 0.187 mmol) using hydrogen fluoride-pyridine (0.4 ml) in acetonitrile (5 ml), and work-up gave 7 (30 mg, 0.082 mmol, 44%), which was also identical (IR, NMR, MS, TLC, and HPLC) with the product 7 obtained from 5.

Synthesis of 6-Methylene-PGE$_1$ Methyl Ester (15b)

Preparation of Methyl 7-Hydroxy-6-methyleneheptanoate (13) and N-(6-methoxycarbonyl-2-methylenehexyloxycarbonyl)imidazole (14)

According to the cited procedure,[22] 1,1,3,3-tetramethylguanidine (104 mg, 0.91 mmol) was added to a stirred solution of methyl 6-nitro-6-heptanoate (4.82 g, 25.8 mmol), thiophenol (3.67 g, 33.4 mmol), and 37% aq. formaldehyde (3 g, 35 mmol) in acetonitrile (15 ml) at r.t. and the resulting mixture was stirred at r.t. for 24 h. To the mixture was added a mixture of acetic anhydride (5.1 g, 50 mmol) and pyridine (5.9 g, 75 mmol) and the whole mixture was stirred at r.t. for additional 18 h. Ethanol (10 ml) and ethyl acetate (100 ml) were added and the organic layer was washed with aq. potassium bisulfate solution, aq. $NaHCO_3$ solution, and then brine. The organic layer was separated and the aqueous layers were extracted twice with ethyl acetate (100 ml). The collected organic layers were dried ($MgSO_4$) and concentrated in vacuo to afford a crude product (11.2 g). Column chromatographic separation of the product on silica gel (200 g) using hexane : ethyl acetate = 4:1 as an eluant gave methyl 6-acetoxy-6-nitro-7-phenylthioheptanoate (7.81 g, 21.2 mmol, 82%): IR (neat), 3060, 2880, 1740, 1580, 1545, 1225, 1170, 1050, 845, 740, and 690 cm^{-1}; NMR ($CDCl_3$), δ 0.9-1.7 (6H, m), 1.7-2.4 (2H, m), 1.82 (3H, s), 3.55 (2H, m), 3.62 (3H, s), 4.40 (2H, s), 7.1-7.6 (5H, m).

A solution of the above nitro sulfide (7.33 g, 19.9 mmol) and tributyltin hydride (13 g, 44.8 mmol) in benzene (45 ml) containing azobisisobutyronitrile (856 mg, 5.2 mmol) was refluxed with stirring for 3 h. Evaporation of the solvent afforded a crude residue, which was purified by column chromatography on silica gel (180 g) (hexane : ethyl acetate = 6:1) to give a crude methyl 7-acetoxy-6-methyleneheptanoate (4.35 g). Alcoholysis (reflux, 5 h) of the crude acetoxy product in MeOH (500 ml) containing p-toluenesulfonic acid (0.2 g) provided a crude 13 (3.517 g), which was purified by column chromatography (hexane : ethyl acetate = 4:1) to give a pure 13 for the use of transesterification reaction: NMR ($CDCl_3$), 1.2-1.8 (4H, m), 1.8-2.4 (4H, m), 2.93 (1H, t, J=5 Hz), 3.60 (3H, s). 3.96(2H, d, J=5 Hz), 4.77 (1H, m), 4.95 (1H, m).

To a solution of the above alcohol (3.517 g) in THF (20 ml), was added 1,1'-carbonyldiimidazole (4.54 g, 28 mmol) and the resulting mixture was stirred at r.t. for 1 h. Ethyl acetate (200 ml) was added for extraction and the resulting organic layer was washed with water and then brine. The separated organic layer was dried ($MgSO_4$) and concentrated in vacuo to give an oily product (5.468 g), which was ohromatographed on silica gel (100 g) (hexane : ethyl acetate = 2:1) to yield 14 (3.787 g, 14.2 mmol, 74% from the nitro sulfide): IR (KBr), 3140, 3030, 1765, 1740, 1660, 1245, 1180, 1005, 900, and 769 cm^{-1}; NMR ($CDCl_3$), δ 1.3-1.8 (4H, m), 1.9-2.4 (4H, m), 3.60 (3H, s), 4.78 (2H, s), 5.06 (2H, d, J=5 Hz), 7.00 (1H, m), 7.40 (1H, m), 8.10 (1H, m).

Synthesis of (2R,3R,4R)-2-(6-methoxycarbonyl-2-methylenehexyloxycarbonyl)-3-[(S,E)-3-t-butyldimethylsilyloxy-1-octenyl]-4-t-butyldimethylsilyloxycyclopentanone (12)

A 2.0 M pentane solution of t-butyllithium (5.5 ml, 11.0 mmol) was added at -78°C to a stirred solution of (S,E)-3-t-butyldimethylsilyloxy-1-iodo-1-octene (2.024 g, 5.5 mmol) in ether (15 ml), and the mixture was stirred at -78°C for 2 h.

To the mixture was added a solution of 1-pentynylcopper (I) (718 mg, 5.5 mmol) and hexamethylphosphorous triamide (1.79 g, 11.0 mmol) in ether (10 ml) at -78°C for 1 h. Then, a cooled solution of **1** (1.06 g, 5.0 mmol) in ether (10 ml) was added at -78°C, and the resulting mixture was stirred at -78°C for 15 min, then at -40°C for 1 h. A solution of **14** (2.188 g, 8.23 mmol) in THF (30 ml) and hexamethylphosphoric triamide (10 ml) was added at -78°C and the whole mixture was stirred at -40°C for 3 h. The reaction mixture was poured into an aq. 4.0 M acetate buffer solution (150 ml). The organic layer was taken up in hexane (100 ml), and the separated aqueous layer was extracted twice with hexane (100 ml). The combined organic layers were washed with aq. NH_4Cl, then brine, and dried ($MgSO_4$). Evaporation of the solvents left a crude product (3.370 g), which was purified by column chromatography on silica gel (200 g) using hexane-ethyl acetate (9:1) to produce **12** (1.00 g, 1.535 mmol, 31%); $[\alpha]_D^{23}$ -27.5° (c 0.81, MeOH); IR (neat), 3090, 1760, 1740, 1650, 1255, 1120, 1080, 965, 835, and 775 cm^{-1}; NMR ($CDCl_3$), δ 0.06 (12H, s), 0.85 (21H), 1.0-1.8 (12H, m), 1.8-2.6 (7H, m), 3.03 (1H, m), 3.54 (3H, s), 3.7-4.2 (2H, m), 4.45 (2H, bs), 4.87 (2H, bd, J=6 Hz), 5.4-5.6 (2H, m); FD-MS (m/z), 595 (M-57); EI-MS (m/z), 595 (M-57), 521, 481, 423, 323, 291, 265, 215, 185, 155 (100), 147, 123; ^{13}C-NMR ($CDCl_3$), δ -4.8, -4.7, -4.6, -4.3, 14.0, 18.0, 18.2, 22.6, 24.6, 25.0, 25.7, 25.9, 26.9, 31.9, 32.7, 33.9, 38.4, 47.4, 51.4, 51.7, 60.6, 67.6, 72.6, 112.9, 126.7, 137.0, 142.9, 167.6, 174.0, 206.4; High-resolution MS for $C_{31}H_{55}O_7Si_2$ (M-^{t}Bu): Calcd m/z: 595.3483; Found: 596.3471.

Alternatively, a similar transesterification of **9** (280 mg, 0.52 mmol) with the alcohol **13** (179 mg, 1.04 mmol) under a refluxing condition (1.5 h) in toluene (5 ml) in the presence of 4-dimethylaminopyridine (32 mg, 0.26 mmol) gave the same product **12** (250 mg, 0.38 mmol, 74%) after usual work-up and purification. The product **12** was identical with the three-component coupling product **12** obtained as mentioned above.

Synthesis of 6-Methylene-PGE$_1$ Methyl Ester (15b)

Tetrakis(triphenylphosphine)palladium(0) (27 mg, 0.023 mmol) was added to a solution of the ester **12** (300 mg, 0.495 mmol) in N,N-dimethylformamide (2 ml), and the mixture was stirred at r.t. for 2 h. Brine (50 ml) was added and the resulting mixture was extracted with ethyl acetate (4 × 50 ml). The separated organic layer was collected, dried ($MgSO_4$), and concentrated *in vacuo* to give a crude product (292 mg). Separation of the crude products by silica gel (20 g) column chromatography (hexane : ethyl acetate = 9:1) gave the decarboxylative allylic alkylation product **15a** (142 mg, 0.233 mmol, 51%): $[\alpha]_D^{21}$ - 36° (c 0.42, MeOH); IR (neat), 3080, 1745, 1640, 1255, 1120, 1090, 1005, 970, 870, 835, and 775 cm^{-1}; NMR ($CDCl_3$), δ 0.05 (12H, s), 0.85 (21H), 1.0-2.8 (22H, m), 3.55 (3H, s), 3.8-4.2 (2H, m), 4.55 (2H, m), 5.3-5.5 (2H, m); FD-MS (m/z), 609 (M+1), 551 (M-57); EI-MS (m/z), 551 (M-57, 100), 419, 345, 327, 313, 295, 241, 219, 215, 175, 147, 101; ^{13}C-NMR ($CDCl_3$), δ -4.7, -4.2, 14.0, 18.0, 18.2, 22.6, 24.6, 25.0, 25.8, 25.9, 27.1, 31.9, 33.9, 35.7, 38.5, 47.3, 51.4, 51.7, 52.8, 72.9, 73.8, 111.7, 129.0, 136.0, 146.4, 174.0, 216.9: High-resolution MS for $C_{30}H_{55}O_5Si_2$ (M-^{t}Bu): Calcd m/z: 551.3585; Found: 551.3579.

A stirred solution of **15a** (142 mg, 0.233 mmol) in acetonitrile (2 ml) was treated with pyridine (0.05 ml) and hydrogen fluoride-pyridine (0.1 ml) at r.t. for 4 h. A similar work-up and chromatographic separation (silica gel 20g, hexane : ethyl acetate = 1:3) gave 6-methylene-PGE$_1$ methyl ester (**15b**, 74 mg, 0.195 mmol, 84%): $[\alpha]_D^{20}$ - 55° (c 1.10, MeOH); IR (neat), 3400, 3090, 1740, 1640, 1160, 1075, 965, and 890 cm^{-1}; NMR ($CDCl_3$), δ 0.85 (3H, m), 1.0-1.7 (12H, m), 1.7-2.9 (12H, m), 3.54 (3H, s), 3.7-4.2 (2H, m), 4.60 (2H, bs), 5.25-5.5 (2H, m); FD-MS (m/z), 380 (M$^+$), 362 (M-18); EI-MS (m/z), 363 (M-17), 362, 345, 313, 291, 259, 241, 225, 208, 193, 190, 155, 133, 119, 107 (100); ^{13}C-NMR ($CDCl_3$), δ 14.0, 22.6, 24.6, 25.1, 26.9, 31.8, 33.9, 34.6, 35.6, 37.3, 45.7, 51.5, 52.7, 54.6, 72.0, 73.1, 112.3, 131.7, 136.7, 145.8, 174.2, 214.6; High-resolution MS for $C_{22}H_{34}O_4$ (M-H_2O): Calcd m/z: 362.2455; Found: 362.2463.

Synthesis of 6-Methyl-PGI$_1$ Methyl Ester (20)

Synthesis of 11,15-bis(t-butyldimethylsilyl)-6-methylene-PGF$_{1\alpha}$ Methyl Ester (16)

A 1.5 M toluene solution (1.33 ml, 2.0 mmol) of diisobutylaluminum hydride was added at 4°C to a stirred solution of 2,6-di-t-butyl-4-methylphenol (440 mg, 2.0 mmol) in toluene (5 ml). After the mixture was stirred at 4°C for 1 h, a solution of **15a** (213 mg, 0.35 mmol) in toluene (15 ml) was added at -78°C to the mixture, and the resulting mixture was stirred at -78°C for 30 min, then -20°C for 3 h. Saturated aq. sodium bitartrate solution (50 ml) and ethyl acetate (50 ml) were added to the reaction mixture, and the extracted organic layer was separated. The aqueous layer was extracted twice with ethyl acetate (2 × 50 ml), and the collected organic layers were washed with brine. The filtered organic layer was dried ($MgSO_4$) and concentrated *in vacuo* to give 604 mg of a crude product, which was purified by silica gel (20 g) column chromatography (hexane : ethyl acetate = 10:1 up to 4:1) to give the 9α isomer **16** (140 mg, 0.230 mmol, 66%) and the 9β isomer **17** (23 mg, 0.038 mmol, 11%). **16**: $[\alpha]_D^{22}$ + 6.7° (c 0.57, MeOH); IR (neat), 3430, 3080, 1740, 1635, 1250, 1070, 865, 830, and 770 cm^{-1}; NMR ($CDCl_3$), δ 0.05 (12H, s), 0.86 (21H), 1.0-2.7 (23H, m), 3.54 (3H, s), 3.7-4.3 (3H, m), 4.55-4.85 (2H, m), 5.15-5.40 (2H, m); FD-MS (m/z), 611 (M+1), 553, 115, 57; EI-MS (m/z), 595 (M-15), 553 (100), 535, 521, 461, 421, 397, 329, 297, 215, 201, 171, 159, 149, 147,

131, 115, 101; ^{13}C-NMR ($CDCl_3$), δ -4.7, -4.6, -4.2, 14.0, 17.9, 18.3, 22.7, 24.7, 25.0, 25.8, 25.9, 27.2, 31.9, 34.0, 34.8, 35.8, 38.7, 43.1, 49.4, 51.4, 56.3, 73.2, 74.1, 79.6, 110.4, 130.6, 134.8, 148.3, 174.1; High-resolution MS for C H O Si (M-^{t}Bu); Calcd m/z: 553.3742; Found: 553.3729. **17**: $[\alpha]_D^{22}$ - 14° (c 0.18, MeOH); IR (neat), 3460, 3080, 1740, 1640, 1255, 1060, 835, and 775 cm^{-1}; NMR ($CDCl_3$), δ 0.05 (12H, s), 0.86 (21H), 1.0-2.7 (23H, m), 3.54 (3H, s), 3.7-4.2 (3H, m), 4.55-4.85 (2H, m), 5.1-5.4 (2H, m); FD-MS (m/z); 611 (M+1), 553, 423, 133, 57; EI-MS (m/z), 595 (M-15), 553 (100), 535, 521, 461, 423, 407, 397, 389, 329, 297, 215, 201, 175, 147, 131, 115, 105; ^{13}C-NMR ($CDCl_3$), δ -4.7, -4.5, -4.2, 14.1, 18.1, 18.3, 22.7, 24.6, 25.1, 25.9, 27.1, 31.9, 33.9, 35.2, 38.9, 40.3, 43.2, 49.9, 51.5, 57.0, 73.0, 76.1, 76.5, 111.1, 130.3, 135.5, 149.4, 174.0; High-resolution MS for $C_{30}H_{57}O_5Si_2$ (M-^{t}Bu): Calcd m/z: 553.3742; Found: 553.3755.

Sodium borohydride (130 mg, 3.44 mmol) was added at -40 °C to a stirred solution of **15a** (418 mg, 0.688 mmol) in MeOH (10 ml) and the mixture was stirred at 0 °C for 1 h. Saturated aq. NH_4Cl solution was added and the resulting mixture was extracted with ethyl acetate (3 × 50 ml). The separated organic layers were washed with brine, dried ($MgSO_4$), and concentrated *in vacuo* to afford a crude product (413 mg), which was similarly chromatographed on silica gel (30 g) to give **16** (286 mg, 0.469 mmol, 68%) and **17** (80 mg, 0.131 mmol, 19%).

(a) Synthesis of **20** by Iodoetherization

Anhydrous potassium carbonate (75 mg, 0.54 mmol) was added to a solution of **16** (110 mg, 0.18 mmol) in methylene chloride (10 ml) and the mixture was cooled at -20 °C. To the suspension was added a solution of iodine (55 mg, 0.216 mmol) in methylene chloride (6 ml) and the reaction mixture was stirred at -20°C for 40 min. Methylene chloride (50 ml) was added and the resulting organic layer was washed with 10% Na_2SO_3, then brine, and the separated organic layer was dried over $MgSO_4$. Evapolation of the solvent provided an oily product (140 mg), which was purified by silica gel (20 g) column chromatography (hexane : ethyl acetate = 19:1) to give the iodo ether **18** (96 mg, 0.13 mmol, 72%); IR (neat), 1740, 1255, 1120, 1060, 835, and 775 cm^{-1}; NMR ($CDCl_3$), δ 0.06 (12H, s), 0.83 (21H), 1.0-2.6 (22H, m), 3.08 & 3.20 (2H, s × 2), 3.51 (3H, s), 3.6-4.2 (2H, m), 4.0-4.5 (1H, m), 5.2-5.5 (2H, m); FD-MS (m/z), 721 (M-15), 679 (100), 587, 547, 447, 397, 301, 240, 215, 171, 149; High-resolution MS for $C_{30}H_{56}O_5Si_2$ (M-^{t}Bu): Calcd m/z: 679.2710; Found: 679.2728.

To a stirring solution of **18** (96 mg, 0.13 mmol) in benzene (3 ml), was added tributyltin hydride (524 mg, 1.8 mmol) and azobisisobutyronitrile (5 mg), and the mixture was stirred at r.t. for 2 h. The reaction mixture was chromatographed on silica gel (20 g) using hexane-ethyl acetate (19:1) to yield **19** (60 mg, 0.098 mmol, 75%): IR (neat), 1740, 1255, 1095, 1060, 1025, 835, 800, and 775 cm^{-1}; NMR ($CDCl_3$), δ 0.04 (12H, s), 0.84 (21H), 1.0-2.5 (22H, m), 1.03 & 1.20 (3H, s × 2), 3.53 (3H, s), 3.5-4.4 (3H, m), 5.2-5.4 (2H, m); FD-MS (m/z), 553 (M-57), 57; EI-MS (m/z), 553 (M-57, 100), 495, 461, 421, 397, 329, 321, 303, 241, 215, 159, 147; High-resolution MS for $C_{30}H_{57}O_5Si_2$ (M-^{t}Bu): Calcd m/z: 553.3742; Found: 553.3754.

A 1.0 M THF solution of tetrabutylammonium fluoride (0.44 ml, 0.44 mmol) was added at r.t. to a solution of **19** (53 mg, 0.087 mmol) in THF (2 ml) and the mixture was stirred at r.t. for 4 h. Saturated aq. NH_4Cl solution was added and the resulting mixture was extracted with ethyl acetate (50 ml). The separated organic layer was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo* to leave a crude product (56 mg). Purification of the crude product by silica gel (20 g) column chromatography (hexane : ethyl acetate = 1:2) to yield **20** (29 mg, 0.076 mmol, 87%): IR (neat), 1735, 1245, 1170, 1105, 1055, 965, 880, and 730 cm^{-1}; NMR ($CDCl_3$), δ 0.84 (3H, m), 1.0-2.7 (24H, m), 1.06 & 1.23 (3H, s × 2), 3.54 (3H, s), 3.5-4.5 (3H, m), 5.2-5.5 (2H, m); FD-MS (m/z), 383 (M+1, 100), 365, 308, 267, 247, 183, 122; EI-MS (m/z), 383 (M+1), 367, 320, 292, 267, 249, 231, 208, 182, 181, 177, 107.

(b) Synthesis of **20** by Oxymercuration

To a solution of **16** (196 mg, 0.32 mmol) in THF (10 ml) was added a solution of mercuric trifluoroacetate (172 mg, 0.40 mmol) in THF (3 ml) at 0 °C, and the mixture was stirred at 0 °C for 10 min. To the mixture, MeOH (3 ml) and then sodium borohydride (80 mg, 2.1 mmol) was added at 0 °C and the resulting mixture was stirred at 0 °C for 1 h. Saturated aq. NH_4Cl solution and ether (50 ml) was added for extraction, and the separated organic layer was washed with aq. $NaHCO_3$ solution, then brine, dried ($MgSO_4$), and evaporated to afford a crude product (147 mg), which was purified by silica gel (20 g) column chromatography (hexane : ethyl acetate = 19:1) to give **19** (72 mg, 0.117 mmol, 51%). This product **19** was identical (IR, NMR, MS, and TLC) with the above **19** obtained from **18**.

Intramolecular Decarboxylative Allylic Alkylation

Preparation of E- and Z-(2R,3R,4R)-2-(2-butenyloxycarbonyl)-3-[(S,E)-3-t-butyldimethylsilyloxy-1-octenyl]-4-t-butyldimethylsilyloxycyclopentanone (**21** and **22**)

A solution of (E)-2-buten-1-ol (5.54 g, 77 mmol) and 1,1'-carbonyldiimidazole (25 g, 0.154 mmol) in THF (40 ml) was stirred at r.t. for 1 h. After removal of THF, ethyl acetate (150 ml) was added for extraction. The resulting mixture was washed with ethyl acetate, and then brine. The separated aqueous layer was extracted twice with ethyl acetate (2 × 150 ml), and the combined organic layers were dried over MgSO , and evaporated to give 17.09 g of a crude product, which was purified by silica gel (170 g) column chromatography (hexane : ethyl acetate = 1:1) to yield N-

[(E)-2-butenyloxycarbonyl]imidazole (24; 12.18 g, 73.4 mmol, 95%): IR (neat), 3140, 3040, 1760, 1675, 1470, 1400, 1320, 1280, 1240, 1170, 1095, 1000, 965, 895, 830, 765, and 740 cm^{-1}; NMR ($CDCl_3$), δ 1.68 (3H, dd, J=1 & 6 Hz), 4.72 (2H, dd, J=1 & 5 Hz), 5.3-6.2 (2H, m), 6.96 (1H, m), 7.33 (1H, m), 8.04 (1H, m).

According to the above-mentioned procedure, the enolate 3 was generated by conjugate addition of the mixed cuprate, formed from vinyllithium 2 (5.5 mmol) and 1-pentynylcopper (I) (718 mg, 5.5 mmol) in the presence of hexamethylphosphorous triamide (1.793 g, 11.0 mmol), to 1 (1.06 g, 5.0 mmol) in ether (30 ml). To the solution of enolate 3 was added a solution of 24 (2.74 g, 16.5 mmol) in THF (50 ml) and hexamethylphosphoric triamide (10 ml) at -40 °C, and the mixture was stirred at -40 °C for 3 h. A similar work-up gave an oily crude product (3.589 g), which was chromatographed on silica gel (200 g) with hexane-ethyl acetate (19:1) to afford 21 (1.098 g, 1.99 mmol, 40%); IR (neat), 3040, 1765, 1655, 1255, 1120, 1080, 1000, 965, 850, 835, and 775 cm^{-1}; NMR ($CDCl_3$), δ 0.06 (12H, s), 0.85 (21H), 1.0-1.5 (8H, m), 1.63 (3H, d, J=5 Hz), 1.8-2.7 (3H, m), 3.0 (1H, m), 3.7-4.2 (2H, m), 4.43 (2H, d, J=5 Hz), 5.3-5.7 (4H, m); FD-MS (m/z), 553 (M+1), 495, 394, 133; EI-MS (m/z), 495 (M-57O), 441 (100), 422, 349, 309, 265, 217, 185, 147, 101; ^{13}C-NMR ($CDCl_3$), δ -4.8, -4.7, -4.6, -4.5, -4.3, -4.2, 14.0, 17.7, 18.0, 18.2, 22.6, 25.2, 25.7, 25.8, 25.9, 26.0, 31.8, 38.4, 47.4, 51.8, 60.5, 66.1, 72.6, 124.8, 126.7, 131.6, 136.9, 167.7, 206.5; High-resolution MS for $C_{26}H_{47}O_5Si_2$ (M-^{t}Bu): Calcd m/z: 495.2960; Found: 495.2935.

Similarly, reaction (r.t., 1 h) of 2-butyn-1-ol (5 g, 71.4 mmol) with 1,1'-carbonyldiimidazole (17.4 g, 107.1 mmol) in THF (50 ml) gave N-(2-butynyloxycarbonyl)imidazole (25; 10.8 g, 65.9 mmol, 92%) after usual work-up and chromatographic separation: IR (neat), 3150, 2320, 2250, 1765, 1470, 1400, 1315, 1290, 1240, 1165, 1095, 990, 920, 830, and 765 cm^{-1}; NMR ($CDCl_3$), δ 1.77 (3H, t, J=2.5 Hz), 4.83 (2H, q, J=2.5 Hz), 6.91 (1H, m), 7.27 (1H, m), 7.99 (1H, m).

The enolate 3 formed from the above-mentioned mixed cuprate (11.0 mmol) and 1 (2.12 g, 10.0 mmol) was trapped (-40 °C, 2 h) with 25 (4.10 g, 25 mmol) to give 23 (2.528 g, 4.6 mmol, 46%): IR (neat), 2250, 1765, 1740, 1660, 1620, 1255, 1120, 1080, 965, 850, 835, and 775 cm ; NMR ($CDCl_3$), δ 0.06 (12H, s), 0.85 (21H), 1.0-1.8 (9H, m), 1.73 (3H, t, J=2 Hz), 2.1-2.5 (2H, m), 3.0 (1H, m), 3.8-4.1 (2H, m), 4.53 (2H, q, J=2 Hz), 5.4-5.5 (2H, m), FD-MS (m/z), 551 (M+1), 493, 397, 115, 57; EI-MS (m/z), 493 (M-57), 419, 423, 347, 323, 291, 265, 215, 185, 147, 101; High-resolution MS for $C_{26}H_{45}O_5Si_2$ (M-^{t}Bu): Calcd m/z: 493.2803; Found: 493.2775.

The product 23 (559 mg, 1.02 mmol) was added to a solution of 5% Pd-$BaSO_4$ (20 mg) and quinoline (20 mg) in MeOH (20 ml) and the resulting mixture was stirred at r.t. for 18 h under hydrogen atmosphere. The catalyst was filtered off through Celite and washed with ethyl acetate. Concentration of the filtrate and washings left a crude product (605 mg), which was purified by silica gel (50 g) column chromatography (hexane : ethyl acetate = 19:1) to provide 22 (429 mg, 0.78 mmol, 76%): IR (neat), 3050, 1765, 1735, 1660, 1620, 1255, 1120, 965, 835, and 775 cm^{-1}; NMR ($CDCl_3$), δ 0.06 (12H, s), 0.87 (21H), 1.0-1.5 (8H, m), 1.62 (3H, d, J=5 Hz), 1.7-2.9 (3H, m), 2.9-3.2 (1H, m), 3.7-4.2 (2H, m), 4.56 (2H, d, J=5 Hz), 5.1-5.9 (4H, m); FD-MS (m/z), 553 (M+1), 495, 311, 57; EI-MS (m/z), 553 (M+1), 495, 481, 441, 423, 367, 349, 309, 291, 265, 215, 185 (100), 147, 101; ^{13}C-NMR ($CDCl_3$), δ -4.8, -4.7, -4.6, -4.3, 13.1, 14.0, 18.0, 18.2, 22.6, 25.0, 25.7, 25.9, 31.9, 38.5, 47.5, 51.8, 60.6, 60.7, 72.6, 124.0, 126.7, 129.8, 136.9, 167.8, 206.4; High-resolution MS for $C_{26}H_{47}O_5Si_2$ (M-^{t}Bu): Calcd m/z: 495.2960; Found: 495.2982.

Intramolecular Decarboxylative Allylic Alkylation of 21 and 22

Tetrakis(triphenylphosphine)palladium(0) (21 mg, 0.018 mmol) was added to a solution of 21 (200 mg, 0.362 mmol) in N,N-dimethylformamide (1.5 ml) and the resulting mixture was stirred at 50 °C for 1 h. Similar work-up (extraction, washing, evaporation) and separation by chromatography (hexane : ethyl acetate = 49:1) gave decarboxylative allylic alkylation products, 26 (107 mg, 0.21 mmol, 58%) and 27 (15 mg, 0.029 mmol, 8%). 26: IR (neat), 3040, 1750, 1255, 1110, 1090, 965, 835, and 775 cm^{-1}; NMR ($CDCl_3$), δ 0.06 (12H, s), 0.87 (21H), 1.1-1.5 (8H, m), 1.54 (3H, d, J=4 Hz), 1.75-2.8 (6H, m), 3.7-4.2 (2H, m), 5.1-5.5 (4H, m); FD-MS (m/z), 451 (M-57); EI-MS (m/z), 451 (M-57), 437, 396, 335, 319, 263 (100), 251, 191, 147, 107, 93, 75, 73, 55, 41; ^{13}C-NMR ($CDCl_3$), δ -4.7, -4.6, -4.2, 14.0, 17.9, 18.0, 18.1, 18.3, 22.7, 25.1, 25.9, 26.0, 30.5, 31.9, 38.6, 47.8, 52.2, 54.0, 72.9, 73.4, 127.4, 127.9, 128.7, 136.5, 215.5; High-resolution MS for $C_{25}H_{47}O_3Si_2$ (M-^{t}Bu): Calcd m/z: 451.3061; Found: 451.3058. 27: IR (neat), 3080, 1745, 1640, 1460, 1255, 1115, 1095, 965, 835, and 775 cm^{-1}; NMR ($CDCl_3$), δ 0.06 (12H, s), 0.85 (21H), 1.06 (3H, d, J=6 Hz), 1.0-1.7 (8H, m), 1.7-2.8 (5H, m), 3.6-4.2 (2H, m), 4.6-5.0 (2H, m), 5.0-6.0 (1H, m), 5.2-5.5 (2H, m); EI-MS (m/z), 451 (M-57), 377, 335, 319 (100), 305, 293 (100), 251, 245, 215, 191, 147, 107; High-resolution MS for $C_{25}H_{47}O_3Si_2$ (M-^{t}Bu): Calcd m/z: 451.3061; Found: 451.3052.

Similar decarboxylative allylic alkylation reaction (25 °C, 2 h) of 22 (284 mg, 0.51 mmol) with tetrakis(triphenylphosphine)palladium(0) (30 mg, 0.026 mmol) in N,N-dimethylformamide (3 ml) gave the same products, 26 (163 mg, 0.321 mmol, 63%) and 27 (23 mg, 0.045 mmol, 9%). Each product 26 and 27 obtained from Z-isomer 22 was identical with the products of 26 and 27 from E-isomer 21, respectively.

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