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REGIOSELECTIVE ALLYLATION AND PROPARGYLATION USING ACYLSILANES: FACILE SYNTHESIS OF PGE3 AND F3α METHYL ESTER

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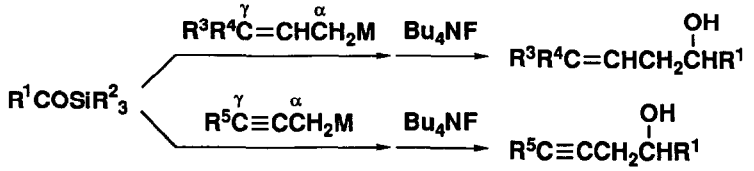
Abstract: *Regioselective allylation and propargylation were achieved using acylsilanes as electrophiles and this methodology was applied to the synthesis of PGE3 and F3α methyl ester.*

The central problem in utilization of an allylmetal reagent for the preparation of homoallylic compounds is the control of regio- and stereochemistry.[1] In general, γ-monosubstituted allylmetals react with carbonyl compounds exclusively at the γ-position, bulky ketones being the only exception.[2] Although work on α-regioselectivity has been reported, no satisfactory method has yet appeared for α-selective allylation.[3,4] Similarly, the regiocontrolled synthesis of homopropargylic alcohols from the corresponding propargylic organometallics remains a challenge in organic synthesis.[5] Here, we disclose a new approach to α-selective allylation and propargylation using acylsilanes as the electrophiles.[6,7] Prostaglandin E_3 (PGE_3) methyl ester and $PGF_{3\alpha}$ methyl ester were efficiently synthesized using this process.

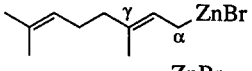
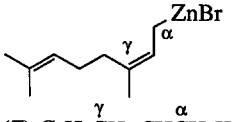


Treatment of the allylic metal with an acylsilane followed by desilylation with tetrabutylammonium fluoride afforded the homoallylic alcohols **1** (α-adduct) and **2** (γ-adduct). Regioselectivity (α/γ) of allylation with various acylsilanes[8] and aldehydes is shown in Table I.

1 **2**

a, R^1 = Ph; R^3 = CH_3; R^4 = H
b, R^1 = Ph; R^3 = R^4 = CH_3
c, R^1 = $^nC_5H_{11}$; R^3 = R^4 = CH_3
d, R^1 = $^nC_5H_{11}$; R^3 = $(CH_3)_2C{=}CHCH_2CH_2$; R^4 = CH_3
e, R^1 = $^nC_5H_{11}$; R^3 = C_2H_5; R^4 = H

Table I. Regioselectivity of Allylation with Carbonyl Compounds

allylic metal	carbonyl	allylation °C, time	allylation yield, %[a]	desilylation method[b]	desilylation yield, %	products	α/γ[c]
$CH_3\overset{\gamma}{C}H{=}CH\overset{\alpha}{C}H_2MgBr$	$PhCOSiMe_3$	0, 20 min	89	A	89	**1a** + **2a**	< 1:99
	$PhCOSi(i\text{-}Pr)_3$	0, 20 min	78	A	> 99	**1a** + **2a**	< 1:99
$CH_3\overset{\gamma}{C}H{=}CH\overset{\alpha}{C}H_2ZnBr$	$PhCOSiMe_3$	0, 30 min	87	A	68	**1a** + **2a**	3:97
	$PhCOSi(i\text{-}Pr)_3$	0, 1 h	78	A	85	**1a** + **2a**	> 99:1[d]
	$PhCOSiPh_3$	0, 1 h	82	A	51	**1a** + **2a**	< 1:99
$(CH_3)_2\overset{\gamma}{C}{=}CH\overset{\alpha}{C}H_2MgCl$	$PhCOSiMe_3$	20, 20 min	96	A	78	**1b** + **2b**	2:98
	$PhCOSi(i\text{-}Pr)_3$	0, 30 min	57	A	> 99	**1b** + **2b**	86:14
	$^nC_5H_{11}CHO$	0, 10 min	94	—	—	**1c** + **2c**	< 1:99
	$^nC_5H_{11}COSiMe_3$	0, 25 min	98	B	99	**1c** + **2c**	2:98
	$^nC_5H_{11}COSi(i\text{-}Pr)_3$	0, 25 min	93	B	94	**1c** + **2c**	87:13
$(CH_3)_2\overset{\gamma}{C}{=}CH\overset{\alpha}{C}H_2ZnBr$	$PhCOSiMe_3$	0, 45 min	85	A	74	**1b** + **2b**	90:10
	$PhCOSi(i\text{-}Pr)_3$	0, 1 h	80	A	72	**1b** + **2b**	> 99:1
	$PhCOSiPh_3$	0, 1 h	76	A	65	**1b** + **2b**	5:95
	$^nC_5H_{11}CHO$	0, 10 min	85	—	—	**1c** + **2c**	< 1:99
	$^nC_5H_{11}COSiMe_3$	0, 2 h	82	B	77	**1c** + **2c**	89:11
	$^nC_5H_{11}COSi(i\text{-}Pr)_3$	40, 1 h	88	B	89	**1c** + **2c**	> 99:1
	$^nC_5H_{11}COSiMe_3$	0, 50 min	99	B	91	**1d** + **2d**	96:4[e]
	$^nC_5H_{11}COSiMe_3$	0, 50 min	> 99	B	78	**1d** + **2d**	95:5[e]
$(Z)\text{-}C_2H_5\overset{\gamma}{C}H{=}CH\overset{\alpha}{C}H_2K$	$^nC_5H_{11}CHO$	-78, 10 min	69	—	—	**1e** + **2e**	46:54[f]
	$^nC_5H_{11}COSiMe_3$	-78, 20 min	81	B	88	**1e** + **2e**	95:5[f]

[a] Isolated yield. [b] Method A: $^nBu_4NF$ (4–5 equiv) in THF at 20 °C for 2–3 h. Method B: $^nBu_4NF$ (4–6 equiv) in DMF at 70 °C for 3–4 h. [c] The α/γ ratios of products were determined by 200 MHz ^1H NMR analysis. [d] *E/Z* ratio of **1a** was 50:50. [e] *E/Z* ratio of **1d** was 85:15. [f] *E/Z* ratio of **1e** was 1:99.

Several characteristic features of the reaction have been noted. (1) Because of the bulk of the triisopropylsilyl group, its use resulted in a greater measure of stereochemical control than the more common trimethylsilyl unit. For example, the condensation of allylic zinc reagents with benzoyltriisopropylsilane produced the α-adduct **1** exclusively (>99:1). With the triphenylsilyl group, however, the γ-adduct **2** was obtained as the major product. (2) In general, the homoallylic alcohol **1** could be obtained in greater quantity from allylic zinc reagents than from the corresponding allylic magnesium reagents. (3) Reaction of benzoylsilane or hexanoylsilane with allylic metals resulted in similar regioselectivities. (4) Noteworthy is the example that condensation of (*Z*)-2-pentenyl potassium[9,10] prepared from (*Z*)-2-pentene, potassium *tert*-butoxide, TMEDA, and a solution of *n*-butyllithium in hexane with hexanoyltrimethylsilane in THF at -78 °C for 20 min followed by desilylation afforded a 95:5 mixture of homoallylic alcohols **1e** and **2e** in 72% overall yield. The desired α-adduct **1e** was formed predominantly as the *Z*-isomer (*E*/*Z* = 1:99).[11] (5) The double bond geometry of the allylic zinc reagent was not retained in the condensation reaction with acylsilanes. The homoallylic alcohol **1d**, derived from neryl bromide, Zn, and hexanoyltrimethylsilane, showed the same stereoselectivity (*E*/*Z* = 85:15) as that from geranyl bromide.

The overall applicability of the process is quite broad. Similar results were obtained using propargylic zinc and magnesium reagents (Table II). For example, treatment of the zinc reagent, derived from 2-octynyl bromide and zinc dust in THF, with benzoyltrimethylsilane followed by desilylation afforded only the homopropargylic alcohol **3g** without contamination of any regioisomer (α/γ >99:1). With benzaldehyde, in contrast, a 35:65 mixture of acetylenic alcohol **3g** and allenic alcohol **4g** was obtained using the same zinc reagent. The combination of propargylic zinc reagent and acylsilane allows easy preparation of various types of homopropargylic alcohol **3f–3i** in high yield with an α/γ ratio of >99:1. Unfortunately, desilylation of the intermediate α-hydroxysilane, prepared from (*E*)-2-hexenoyltrimethylsilane and 2-octynylzinc bromide, resulted in a low yield because of a subsequent allylic rearrangement reaction.

3 **4**

f, $R^1 = Ph$; $R^5 = H$
g, $R^1 = Ph$; $R^5 = {}^nC_5H_{11}$
h, $R^1 = {}^nC_5H_{11}$; $R^5 = {}^nC_5H_{11}$
i, $R^1 = (E)\text{-}CH{=}CHPr^n$; $R^5 = {}^nC_5H_{11}$

The methodology described above was applied to the synthesis of prostaglandins (PGs) in the 3 series. The syntheses of PGE_3 and $PGF_{3\alpha}$ methyl ester (**14** and **17**, respectively) were carried out starting from the readily available aldehyde **5**.[12] Treatment of **5** in THF with the (*E*)-enolate prepared from [(trimethylsilyl)acetyl]trimethylsilane[8f] and lithium diisopropylamide, afforded the (*E*)-α,β-unsaturated acylsilane **6** (68% yield). Acylsilane **6** was converted exclusively (α/γ >99:1) to the desired $PGF_{3\alpha}$ derivative **7** in 92% yield by means of the zinc reagent derived from 2-pentynyl bromide and zinc dust in THF.

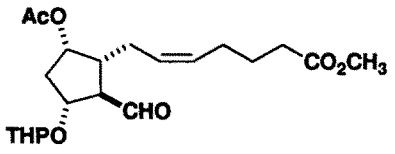
Table II. Regioselectivity of Propargylation with Carbonyl Compounds

propargylic metal	carbonyl	propargylation °C, time	yield, %[a]	desilylation method[b]	yield, %	products	α/γ[c]
$HC\overset{\gamma}{\equiv}C\overset{\alpha}{C}H_2MgBr$	PhCHO	0, 30 min	99	—	—	**3f + 4f**	>99:1
$HC\overset{\gamma}{\equiv}C\overset{\alpha}{C}H_2ZnBr$	PhCHO	20, 20 min	95	—	—	**3f + 4f**	92:8
	$PhCOSiMe_3$	0, 30 min	78	A	68	**3f + 4f**	93:7
	$PhCOSi(i\text{-}Pr)_3$	0, 20 min	66	A	90	**3f + 4f**	>99:1
$^nC_5H_{11}\overset{\gamma}{C}\equiv\overset{\alpha}{C}CH_2MgBr$	PhCHO	0, 2 h	96	—	—	**3g + 4g**	30:70
	$PhCOSiMe_3$	0, 20 min	73	A	>99	**3g + 4g**	41:59
	$PhCOSi(i\text{-}Pr)_3$	0, 20 min	84	A	>99	**3g + 4g**	>99:1
	$^nC_5H_{11}CHO$	0, 25 min	87	—	—	**3h + 4h**	36:64
	$^nC_5H_{11}COSiMe_3$	0, 25 min	73	B	>99	**3h + 4h**	43:57
	$^nC_5H_{11}COSi(i\text{-}Pr)_3$	0, 25 min	91	B	75	**3h + 4h**	96:4
$^nC_5H_{11}\overset{\gamma}{C}\equiv\overset{\alpha}{C}CH_2ZnBr$	PhCHO	20, 45 min	>99	—	—	**3g + 4g**	35:65
	$PhCOSiMe_3$	0, 45 min	81	A	71	**3g + 4g**	>99:1
	$^nC_5H_{11}CHO$	0, 10 min	92	—	—	**3h + 4h**	21:79
	$^nC_5H_{11}COSiMe_3$	0, 45 min	97	B	87	**3h + 4h**	>99:1
	(*E*)-^{n}PrCH=CHCHO	20, 40 min	>99	—	—	**3l + 4l**	16:84
	(*E*)-^{n}PrCH=CHCOSiMe$_3$	0, 45 min	87	A	31	**3l + 4l**	>99:1

[a] Isolated yield. [b] Method A: $^nBu_4NF$ (3–5 equiv) in THF at 20 °C for 1–4 h. Method B: $^nBu_4NF$ (6–10 equiv) in DMF at 70 °C for 5–7 h. [c] The α/γ ratios of products were determined by 200 MHz ^1H NMR analysis.

Formylation of the C-15 hydroxyl group of **7** with acetic-formic anhydride and 4-(dimethylamino)pyridine in dichloromethane gave the formate **8** (84% yield), further transformed into the desilylated compound **9** by reaction with tetrabutylammonium fluoride in THF in 67% yield.[13] $PGF_{3\alpha}$ derivative **9** was converted to the PGE_3 derivative **12** by a three-step sequence: (1) tetrahydropyranyl (THP) protection of the C-15 hydroxyl group giving **10** (77% yield), (2) deacetylation with methanolic sodium methoxide to afford **11** (96% yield), and (3) Jones oxidation of the C-9 hydroxyl group to **12** (67% yield). Hydrolysis of the THP groups with a 3:1:1 mixture of acetic acid, water, and THF led to **13** in 85% yield with a 15α/15β ratio of 54:46. Partial hydrogenation of the triple bond in the 15α isomer of **13**, giving the *Z* double bond, was accomplished on Lindlar catalyst to afford PGE_3 methyl ester (**14**) in 99% yield, $[\alpha]^{21}_D$ -80.0° (*c* 0.64, $CHCl_3$).[14] $PGF_{3\alpha}$ methyl ester (**17**) is also accessible from intermediate **9** in three steps. Removal of the THP group from **9** with a 3:1:1 mixture of acetic acid, water, and THF gave the diol **15** in 89% yield with a 15α/15β ratio of 56:44. Partial hydrogenation of the acetylenic linkage in the 15α isomer of **15** (76% yield) and subsequent treatment with a methanolic sodium methoxide quantitatively formed $PGF_{3\alpha}$ methyl ester (**17**), $[\alpha]^{22}_D$ +22.0° (*c* 0.45, $CHCl_3$). $PGF_{3\alpha}$ methyl ester (**17**) was also obtainable by α-selective reduction of

PGE_3 methyl ester (**14**) with L-Selectride in 46% yield. Finally, alkaline hydrolysis of the ester group of **17** gave $PGF_{3\alpha}$ (**18**) in >99% yield, $[\alpha]^{22}_D$ +31.5° (*c* 0.49, THF).[14c,15]



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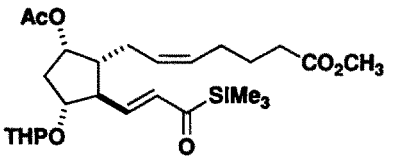

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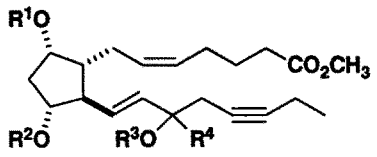
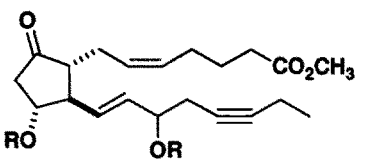
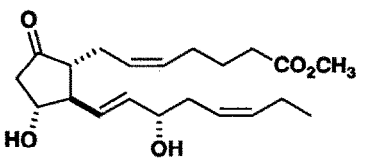


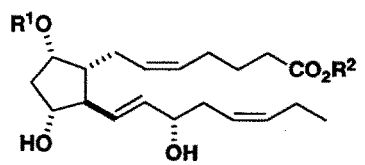
7, R^1 = Ac; R^2 = THP; R^3 = H; R^4 = $SiMe_3$
8, R^1 = Ac; R^2 = THP; R^3 = HCO; R^4 = $SiMe_3$
9, R^1 = Ac; R^2 = THP; R^3 = R^4 = H
10, R^1 = Ac; R^2 = R^3 = THP; R^4 = H
11, R^1 = R^4 = H; R^2 = R^3 = THP
15, R^1 = Ac; R^2 = R^3 = R^4 = H



12, R = THP
13, R = H



14 (PGE_3 methyl ester)



16, R^1 = Ac; R^2 = CH_3
17, R^1 = H; R^2 = CH_3 ($PGF_{3\alpha}$ methyl ester)
18, R^1 = R^2 = H ($PGF_{3\alpha}$)

The above example provides further evidence of the power of this new process and demonstrates that its use can lead to a profound simplification of the problem of synthesis of various derivatives from fatty acid cascades, an increasingly important class of biologically active molecules. The versatility of acylsilanes as electrophiles for ambient nucleophiles has been demonstrated.

Experimental Section

General Methods.

Analytical TLC was done on E. Merck precoated (0.25 mm) silica gel 60 F_{254} plates. Column chromatography was conducted by using silica gel 60 (E. Merck 9385, 230–400 mesh). IR spectra were obtained using a Hitachi 260-10 spectrometer. ^{1}H NMR spectra were obtained using a Varian Gemini-200 (200 MHz) or VXR-

500S (500 MHz) spectrometer. Chemical shifts of ^1H NMR spectra are reported relative to tetramethylsilane (δ 0) or chloroform (δ 7.26). Splitting patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Mass spectra were recorded with a JEOR JMS-D300 mass spectrometer. Optical rotation was measured on a JASCO DIP-140 polarimeter. All experiments were carried out under an atmosphere of dry argon. In experiments requiring dry solvents, ether and tetrahydrofuran (THF) were freshly distilled from sodium metal using benzophenone ketyl as indicator. Methylene chloride (CH_2Cl_2) was stored over 4-Å molecular sieves.

General Procedure for Allylation with Carbonyl Compounds: A. Allylic Grignard Reagent. Mg turnings (122 mg, 5.0 mmol) were placed in a two-necked round bottomed flask (10-mL) and covered with dry ether (2 mL). 1,2-Dibromoethane (0.017 mL, 0.20 mmol) and iodine (12.7 mg, 0.050 mmol) were added and the resulting mixture was heated to reflux for a few minutes. The mixture was cooled to 0 °C (ice bath) and a solution of the allylic halide (1 mmol) in dry ether (1 mL) was added dropwise. The mixture was stirred for 1 h at this temperature and the carbonyl compound (0.3 mmol) was added at 0 or 20 °C. After completion of the reaction, the mixture was quenched with a saturated aqueous NH_4Cl solution (10 mL). Ether (5 mL) was then added and the organic phase was separated. The aqueous phase was extracted with ether (5 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$, and concentrated. The crude product was purified by column chromatography on silica gel to give the allylated α-hydroxysilane.

B. Allylic Zinc Reagent.
A suspension of zinc dust[16] (183 mg, 2.80 mmol) in dry THF (1 mL) containing 1,2-dibromoethane (0.020 mL, 0.23 mmol) was heated to reflux for a few minutes and cooled to 0 °C. To this mixture was added a solution of the allylic bromide (1.5 mmol) in dry THF (1 mL) at this temperature and stirred for 40 min. After the carbonyl compound (0.5 mmol) was added at 0 or 40 °C, the resulting mixture was stirred until disappearance of the starting material. The mixture was poured into a saturated NH_4Cl aqueous solution (10 mL) and extracted with ether (5 mL × 2). The combined organic extracts were dried and concentrated, and the crude product was purified by column chromatography on silica gel to give the homoallylic α-hydroxysilane.

C. (*Z*)-2-Pentenyl Potassium.
A mixture of (*Z*)-2-pentene (0.43 mL, 4.0 mmol), TMEDA (0.15 mL, 1.0 mmol), and powdered *t*-BuOK (112 mg, 1.0 mmol) was placed in a 20-mL Schlenk tube, cooled to -78 °C, and a solution of *n*-BuLi (1.6 M, 0.63 mL, 1.0 mmol) in hexane was added dropwise. This mixture was stirred for 2 h, then the cooling bath was removed, and the temperature was allowed to rise to 0 °C and stirring was continued for 15 min. The suspension was then cooled to -78 °C and a solution of the carbonyl compound (0.36 mmol) in dry THF (1 mL) was added. After stirring for 20 min at this temperature, a saturated NH_4Cl aqueous solution (10 mL) and ether (10 mL) were added to this mixture. The aqueous phase was extracted with ether (5 mL), and the combined organic extracts were dried over $MgSO_4$ and concentrated. The crude product was purified by column chromatography on silica gel to give the homoallylic α-hydroxysilane.

Desilylation of Homoallylic or Homopropargylic Alcohol: Method A.
To a solution of the α-hydroxysilane (0.17–0.5 mmol, 1 equiv) in THF (2 mL) was added a commercial THF solution of tetrabutylammonium fluoride (1 M, 3–5 equiv) at 20 °C, and the mixture was stirred at this temperature for 1–4 h and diluted with THF (5 mL). Saturated brine (5 mL) was added to the mixture with vigorous shaking. Extractive workup with ether (10 mL) followed by column chromatography on silica gel gave the corresponding homoallylic or homopropargylic alcohol.

Method B.
To a solution of the α-hydroxysilane (0.22–0.5 mmol, 1 equiv) in DMF (2 mL) was added a commercial THF solution of tetrabutylammonium fluoride (1 M, 4–10 equiv) at 70 °C, and the mixture was stirred at this temperature for 3–7 h and then treated as described in the method A.

1-Phenyl-3-penten-1-ol (1a): TLC R_f 0.33 (1:5 ethyl acetate/hexane); IR ($CHCl_3$) 3750–3300, 3020, 2930, 1610, 1500, 1455, 1385, 980 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.61 (d, 1.5 H, J = 6.6 Hz, CH_3), 1.69 (d, 1.5 H, J = 6.2 Hz, CH_3), 1.97–2.08 (m, 1 H, OH), 2.30–2.68 (m, 2 H, CH_2), 4.65–4.78 (m, 1 H,

CHO), 5.34–5.73 (m, 2 H, 2 vinyls), 7.21–7.44 (m, 5 H, aromatic). Anal. Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.51; H, 8.95.

4-Methyl-1-phenyl-3-penten-1-ol (1b): TLC R_f 0.37 (1:5 ethyl acetate/hexane); IR ($CHCl_3$) 3620–3300, 2970, 2910, 1670, 1600, 1485, 1440, 1370, 1040, 880 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.61 (s, 3 H, CH_3), 1.73 (s, 3 H, CH_3), 1.78 (br, 1 H, OH), 2.32–2.58 (m, 2 H, CH_2), 4.69 (dd, 1 H, J = 7.7, 5.5 Hz, CHO), 5.18 (t, 1 H, J = 8.1 Hz, vinyl), 7.25–7.43 (m, 5 H, aromatic). Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.98; H, 9.15.

2-Methyl-2-decen-5-ol (1c): TLC R_f 0.42 (1:5 ethyl acetate/hexane); IR ($CHCl_3$) 3700–3300, 2910, 2840, 1440, 1370, 865 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.89 (t, 3 H, J = 6.5 Hz, CH_3), 1.23–1.60 (m, 9 H, $4CH_2$ and OH), 1.65 (s, 3 H, CH_3), 1.75 (s, 3 H, CH_3), 2.16 (t, 2 H, J = 7.1 Hz, CH_2), 3.60 (m, 1 H, CHO), 5.17 (t, 1 H, J = 7.5 Hz, vinyl). Anal. Calcd for $C_{11}H_{22}O$: C, 77.58; H, 13.02. Found: C, 77.15; H, 13.47.

9,13-Dimethyl-8,12-tetradecadien-6-ol (1d): TLC R_f 0.49 (1:5 ethyl acetate/hexane); IR ($CHCl_3$) 3750–3330, 2920, 2850, 1665, 1445, 1380 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.89 (t, 3 H, J = 6.6 Hz, CH_3), 1.20–1.52 (m, 8 H, $4CH_2$), 1.55–1.78 (hidden in this region, 1 H, OH), 1.61 (s, 3 H, CH_3), 1.63 (s, 3 H, CH_3), 1.69 (s, 3 H, CH_3), 1.96–2.23 (m, 6 H, 3 CH_2), 3.59 (m, 1 H, CHO), 5.08 (t, 1 H, J = 6.9 Hz, vinyl), 5.17 (t, 1 H, J = 7.8 Hz, vinyl). Anal. Calcd for $C_{16}H_{30}O$: C, 80.61; H, 12.68. Found: C, 80.20; H, 12.96.

(Z)-3-Undecen-6-ol (1e): TLC R_f 0.44 (1:5 ethyl acetate/hexane); IR ($CHCl_3$) 3750–3300, 2975, 2940, 2870, 1460, 1380, 1070, 870 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.89 (t, 3 H, J = 6.5 Hz, CH_3), 0.97 (t, 3 H, J = 7.5 Hz, CH_3), 1.20–1.63 (m, 9 H, 4 CH_2 and OH), 2.08 (dq, 2 H, J = 7.3, 6.2 Hz, CH_2), 2.22 (dd, 2 H, J = 7.3, 6.0 Hz, CH_2), 3.62 (m, 1 H, CHO), 5.37 (m, 1 H, vinyl), 5.58 (m, 1 H, vinyl). Anal. Calcd for $C_{11}H_{22}O$: C, 77.58; H, 13.02. Found: C, 77.38; H, 13.30.

General Procedure for Propargylation with Carbonyl Compounds: A. Propargylic Grignard Reagent.

A 10-mL, two-necked round bottomed flask was charged with Mg turnings (50 mg, 2.1 mmol) and mercury (II) chloride (1.5 mg, 0.0055 mmol) under Ar atmosphere. In the flask were placed dry ether (2.5 mL) and the propargylic bromide (0.1 mmol) and the resulting mixture was heated to reflux for a few minutes. A solution of the propargylic bromide (0.9 mmol) in dry ether (0.5 mL) was added dropwise at 0 °C. The mixture was stirred for 2 h at 20 °C and the carbonyl compound (0.5 mmol) was added at 0 °C. After completion of the reaction, the mixture was quenched with a saturated NH_4Cl aqueous solution (5 mL). Extractive workup with ether followed by column chromatography on silica gel gave the homopropargylic α-hydroxysilane.

B. Propargylic Zinc Reagent.

A suspension of zinc dust[16] (131 mg, 2.0 mmol) in dry THF (1 mL) containing 1,2-dibromoethane (0.020 mL, 0.23 mmol) was heated to reflux for a few minutes and cooled to 0 °C. To this mixture was added a solution of the propargylic bromide (1 mmol) in dry THF (1 mL) and stirred for 1 h at this temperature. After addition of the carbonyl compound (0.5 mmol) at 0 or 20 °C, the resulting mixture was stirred for 10–45 min and poured into a saturated NH_4Cl aqueous solution (5 mL). Extractive workup with ether followed by column chromatography on silica gel gave the homopropargylic α-hydroxysilane.

1-Phenyl-3-butyn-1-ol (3f): TLC R_f 0.21 (1:5 ethyl acetate/hexane); IR ($CHCl_3$) 3725–3250, 3310, 2960, 2925, 2850, 2105, 1605, 1495, 1450, 1050, 865 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.08 (t, 1 H, J = 2.6 Hz, CH), 2.20 (br, 1 H, OH), 2.65 (dd, 2 H, J = 6.4, 2.6 Hz, CH_2), 4.89 (t, 1 H, J = 6.3 Hz, CHO), 7.25–7.45 (m, 5 H, aromatic). Anal. Calcd for $C_{10}H_{10}O$: C, 82.16; H, 6.89. Found: C, 81.73; H, 7.02.

1-Phenyl-3-nonyn-1-ol (3g): TLC R_f 0.34 (1:5 ethyl acetate/hexane); IR ($CHCl_3$) 3720–3300, 3000, 2930, 2860, 1610, 1500, 1455, 1050 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.90 (t, 3 H, J = 6.8 Hz, CH_3), 1.20–1.58 (m, 6 H, 3 CH_2), 2.10–2.35 (m, 3 H, CH_2 and OH), 2.56–2.65 (m, 2 H, CH_2), 4.81 (dd, 1 H, J = 7.2, 5.5 Hz, CHO), 7.24–7.45 (m, 5 H, aromatic). Anal. Calcd for $C_{15}H_{20}O$: C, 83.29; H, 9.32. Found: C, 83.15; H, 9.51.

8-Tetradecyn-6-ol (3h): TLC R_f 0.42 (1:5 ethyl acetate/hexane); IR ($CHCl_3$) 3725–3325, 2925, 2850, 1455, 1380 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.89 (t, 3 H, J = 6.5 Hz, CH_3), 0.90 (t, 3 H, J = 6.9 Hz, CH_3), 1.18–1.59 (m, 14 H, 7 CH_2), 1.81 (br, 1 H, OH), 2.08–2.49 (m, 4 H, 2 CH_2), 3.69 (m, 1 H, CHO). Anal. Calcd for $C_{14}H_{26}O$: C, 79.94; H, 12.46. Found: C, 79.54; H, 12.73.

(*E*)-4-Tetradecen-8-yn-6-ol (3i): TLC R_f 0.37 (1:5 ethyl acetate/hexane); IR ($CHCl_3$) 3720–3300, 2970, 2930, 2870, 1455, 1275, 965 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.90 (t, 6 H, J = 7.2 Hz, 2 CH_3), 1.17–1.58 (m, 8 H, 4 CH_2), 1.82 (br, 1 H, OH), 2.02 (dt, 2 H, J = 7.5, 6.7 Hz, CH_2), 2.17 (m, 2 H, CH_2), 2.41 (m, 2 H, CH_2), 4.18 (dt, 1 H, J = 6.4, 5.7 Hz, CHO), 5.52 (ddd, 1 H, J = 15.4, 6.4, 1.2 Hz, vinyl), 5.72 (dt, 1 H, J = 15.4, 6.6 Hz, vinyl). Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.40; H, 11.79.

Methyl (1"*E*,5Z)-7-[5'-Acetoxy-2'-(3"-oxo-3"-trimethylsilyl-1"-propenyl)-3'-(tetrahydropyran-2'''-yloxy)-1'-cyclopentanyl]-5-heptenoate (6). To a solution of diisopropylamine (0.13 mL, 0.93 mmol) in THF (1.3 mL) at -78 °C was added a solution of *n*-BuLi (1.6 M, 0.50 mL, 0.80 mmol) in hexane. The mixture was stirred for 15 min at 0 °C, treated at -78 °C with a solution of [(trimethylsilyl)acetyl]-trimethylsilane[8f] (154 mg, 0.82 mmol) in THF (2 mL), and stirred at 0 °C for 30 min. The mixture was treated at -78 °C with a solution of the aldehyde **5**[12] (318 mg, 0.80 mmol) in THF (1.5 mL) over a 10-min period. The resulting mixture was stirred for 20 min at -78 °C, warmed to 0 °C during 20 min, and poured into a saturated aqueous NH_4Cl solution (10 mL). After extraction with ether, the combined organic phases were washed with brine (10 mL) and dried over $MgSO_4$. Column chromatography on silica gel eluted by a 1:2 mixture of ethyl acetate and hexane gave unreacted **5** (45 mg, 14% recovery) and **6** (272 mg, 68% yield, 80% conversion, a yellow oil). **6**: TLC R_f 0.33 (1:2 ethyl acetate/hexane); IR ($CHCl_3$) 2950, 2860, 1725, 1690, 1640, 1590, 1440, 1375, 1240, 1130, 1080, 1020, 975, 910, 850 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.27 (s, 9 H, 3 $SiCH_3$), 1.40–2.83 (m, 16 H, 7 CH_2 and 2 CH), 2.07 (s, 3 H, CH_3), 2.29 (t, 2 H, J = 7.4 Hz, CH_2), 3.43 (m, 1 H, CH_2O), 3.66 (s, 3 H, OCH_3), 3.75 (m, 1 H, CH_2O), 4.07 (m, 1 H, CHO), 4.51–4.63 (m, 1 H, OCHO), 5.11 (m, 1 H, CHO), 5.24–5.43 (m, 2 H, 2 vinyls), 6.34 (d, 0.4 H, J = 16.3 Hz, vinyl), 6.37 (d, 0.6 H, J = 16.0 Hz, vinyl), 6.62 (dd, 0.4 H, J = 16.1, 9.0 Hz, vinyl), 6.67 (dd, 0.6 H, J = 16.2, 8.7 Hz, vinyl); MS (EI, 24 ev) *m/z* (rel) 434 (1.04, M^+–60 [CH_3CO_2H]), 409 (2.62), 393 (2.09), 379 (2.64), 366 (5.76), 350 (11.00), 332 (12.57), 278 (100), 260 (53.93).

9-*O*-Acetyl-17,18-didehydro-11-*O*-(tetrahydropyran-2-yl)-15-trimethylsilyl$PGF_{3\alpha}$ Methyl Ester (7). To a solution of 2-pentynylzinc bromide, prepared from zinc dust[16] (306 mg, 4.7 mmol) and 2-pentynyl bromide (0.5 g, 3.4 mmol) in THF (3.5 mL), was added a solution of **6** (331 mg, 0.67 mmol) in THF (1.5 mL) at 0 °C. The mixture was stirred at this temperature for 1 h and quenched with sat. aq. NH_4Cl solution (10 mL). Extractive workup with ether followed by column chromatography on silica gel eluted by a 1:5 mixture of ethyl acetate and hexane afforded **7** (346 mg, 92% yield) as a colorless oil: TLC R_f 0.30 and 0.39 (1:2 ethyl acetate/hexane); IR ($CHCl_3$) 3550–3300, 2960, 2860, 2250, 1720, 1435, 1375, 1240, 1105, 1020, 965, 900, 840 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.05, 0.06, 0.07, and 0.08 (each s, 9 H, 3 $SiCH_3$), 1.08 and 1.16 (each t, 3 H, CH_3), 1.38–2.70 (m, 21 H, 9 CH_2, 2 CH, and OH), 2.04 (s, 3 H, CH_3), 2.30 (t, 2 H, J = 7.4 Hz, CH_2), 3.47 (m, 1 H, CH_2O), 3.67 (s, 3 H, OCH_3), 3.85 (m, 1 H, CH_2O), 4.06 (m, 0.5 H, 0.5 CHO), 4.59–4.77 (m, 1.5 H, OCHO and 0.5 CHO), 5.05 (m, 1 H, CHO), 5.30–5.51 (m, 3 H, 3 vinyls), 5.64–5.82 (m, 1 H, vinyl); MS (EI, 24 ev) *m/z* (rel) 563 (0.61, M^++1), 534 (0.97), 477 (4.24), 460 (3.21), 445 (2.42), 417 (5.21), 400 (11.52), 259 (100).

9-*O*-Acetyl-17,18-didehydro-15-*O*-formyl-11-*O*-(tetrahydropyran-2-yl)-15-trimethylsilyl-$PGF_{3\alpha}$ Methyl Ester (8). To a solution of **7** (346 mg, 0.61 mmol) in dry CH_2Cl_2 (1.1 mL) were added acetic–formic anhydride (1.20 g, 17.6 mmol) and 4-(dimethylamino)pyridine (0.6 g, 4.9 mmol) at -30 °C, and the mixture was stirred at -30 ~ -20 °C for 2 h. After workup, the mixture was chromatographed on silica gel by using a 1:2 mixture of ethyl acetate and hexane as eluant to give unreacted **7** (55 mg, 16% recovery) and **8** (304 mg, 84% yield, >99% conversion, a colorless oil) **8**: TLC R_f 0.44 (1:2 ethyl acetate/hexane); IR ($CHCl_3$) 2960, 1735, 1610, 1445, 1385, 1260, 1160, 1030, 980, 920, 855 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.15 and 0.16 (each s, 9 H, 3 $SiCH_3$), 1.10 (t, 3 H, J = 7.6 Hz, CH_3), 1.40–3.00 (m, 20 H, 9 CH_2 and 2 CH),

2.05 (s, 3 H, CH_3), 2.30 (t, 2 H, J = 7.6 Hz, CH_2), 3.37–3.54 (m, 1 H, CH_2O), 3.67 (s, 3 H, OCH_3), 3.75–3.93 (m, 1.5 H, CH_2O and 0.5 CHO), 4.03 (m, 0.5 H, 0.5 CHO), 4.62 (m, 1 H, OCHO), 5.06 (m, 1 H, CHO), 5.25–5.49 (m, 3 H, 3 vinyls), 5.63–5.92 (m, 1 H, vinyl), 8.28 (m, 1 H, HCO); MS (EI, 24 ev) *m/z* (rel) 590 (0.18, M^+), 576 (0.33), 562 (0.48), 545 (1.10), 530 (1.21), 516 (1.18), 505 (3.60), 382 (20.07), 259 (100).

9-*O*-Acetyl-17,18-didehydro-11-*O*-(tetrahydropyran-2-yl)PGF$_{3\alpha}$ Methyl Ester (9). To a solution of **8** (102 mg, 0.17 mmol) in THF (0.5 mL) was added a 1 M THF solution of tetrabutylammonium fluoride (1.2 mL, 1.2 mmol) at 0 °C. The mixture was stirred at this temperature for 4 h and then at 20 °C for 40 min. After dilution with THF (5 mL), H_2O (5 mL) was added to the mixture. Extractive workup with ether (5 mL × 2) followed by column chromatography on silica gel eluted by a 1:1 mixture of ethyl acetate and hexane gave **9** (57 mg, 67% yield) as a colorless oil: TLC R_f 0.31 and 0.37 (1:1 ethyl acetate/hexane); IR ($CHCl_3$) 3700–3250, 2925, 1720, 1430, 1270, 1240, 1125, 1070, 1015, 960, 900, 860 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.12 (t, 3 H, J = 7.7 Hz, CH_3), 1.38–2.73 (m, 21 H, 9 CH_2, 2 CH, and OH), 2.05 (s, 3 H, CH_3), 2.30 (t, 2 H, J = 7.3 Hz, CH_2), 3.37–3.55 (m, 1 H, CH_2O), 3.67 (s, 3 H, OCH_3), 3.73–4.08 (m, 2 H, CH_2O and CHO), 4.24 (m, 1 H, CHO), 4.50–4.70 (m, 1 H, OCHO), 5.06 (m, 1 H, CHO), 5.27–5.46 (m, 2 H, 2 vinyls), 5.55–5.83 (m, 2 H, 2 vinyls); MS (EI, 24 ev) *m/z* (rel) 472 (1.98, M^+-18 [H_2O]), 434 (4.32), 374 (46.05), 368 (27.41), 339 (27.16), 328 (100), 321 (33.09).

9-*O*-Acetyl-17,18-didehydro-11,15-*O*-bis(tetrahydropyran-2-yl)PGF$_{3\alpha}$ Methyl Ester (10). To a solution of **9** (133 mg, 0.27 mmol) in dry CH_2Cl_2 (0.5 mL) were added 3,4-dihydro-2*H*-pyran (0.12 mL, 1.3 mmol) and pyridinium *p*-toluenesulfonate (50 mg, 0.20 mmol) at 0 °C, and the mixture was stirred at 20 °C for 24 h. After being diluted with ether (5 mL), sat. aq. $NaHCO_3$ solution (5 mL) was added to the mixture with vigorous stirring. Extractive workup with ether (5 mL × 2) followed by column chromatography on silica gel eluted by a 1:2 mixture of ethyl acetate and hexane and then a 1:1 mixture of ethyl acetate and hexane gave unreacted **9** (23 mg, 17% recovery) and **10** (120 mg, 77% yield, 93% conversion, a colorless oil). **10**: TLC R_f 0.67 (1:1 ethyl acetate/hexane); IR ($CHCl_3$) 2950, 1730, 1440, 1380, 1250, 1135, 1080, 1025, 980, 915, 875 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.05–1.14 (m, 3 H, CH_3), 1.38–2.66 (m, 26 H, 12 CH_2 and 2 CH), 2.05 (s, 3 H, CH_3), 2.30 (t, 2 H, J = 7.7 Hz, CH_2), 3.37–3.55 (m, 2 H, CH_2O), 3.67 (s, 3 H, OCH_3), 3.73–4.10 (m, 3 H, CH_2O and CHO), 4.22 (m, 1 H, CHO), 4.54–4.92 (m, 2 H, 2 OCHO), 5.05 (m, 1 H, CHO), 5.33 (m, 2 H, 2 vinyls), 5.45–5.84 (m, 2 H, 2 vinyls); MS (EI, 24 ev) *m/z* (rel) 473 (0.72, M^+-101 [$C_5H_9O_2$]), 423 (2.02), 412 (3.71), 389 (3.05), 371 (2.39), 339 (100), 328 (98.14), 321 (55.17), 310 (34.48).

17,18-Didehydro-11,15-*O*-bis(tetrahydropyran-2-yl)PGF$_{3\alpha}$ Methyl Ester (11). The compound **10** (108 mg, 0.19 mmol) was dissolved in a methanolic sodium methoxide solution (1 M, 0.64 mL, 0.64 mmol), and the mixture was stirred at 20 °C for 2 h. This solution was carefully neutralized with 1 N HCl solution and then diluted with ether (10 mL). Extractive workup with ether (5 mL × 2) followed by column chromatography on silica gel eluted by a 2:3 mixture of ethyl acetate and hexane gave **11** (96 mg, 96% yield) as a colorless oil: TLC R_f 0.49 (1:1 ethyl acetate/hexane); IR ($CHCl_3$) 3700–3300, 2930, 1720, 1600, 1430, 1110, 1075, 1020, 965, 865 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.05–1.14 (m, 3 H, CH_3), 1.35–2.60 (m, 27 H, 12 CH_2, 2 CH, and OH), 2.32 (t, 2 H, J = 7.7 Hz, CH_2), 3.39–3.55 (m, 2 H, CH_2O), 3.67 (s, 3 H, OCH_3), 3.74–4.27 (m, 5 H, CH_2O and 3 CHO), 4.68 (m, 1.5 H, 1.5 OCHO), 4.87 (m, 0.5 H, 0.5 OCHO), 5.29–5.70 (m, 4 H, 4 vinyls); MS (EI, 24 ev) *m/z* (rel) 431 (0.79, M^+-101 [$C_5H_9O_2$]), 412 (0.57), 399 (0.63), 391 (5.08), 363 (2.74), 358 (9.24), 347 (5.05), 328 (9.46), 297 (100), 279 (64.04), 274 (61.20).

17,18-Didehydro-11,15-*O*-bis(tetrahydropyran-2-yl)PGE$_3$ Methyl Ester (12). The compound **11** (89 mg, 0.17 mmol) was dissolved in acetone (1 mL) and cooled to -20 °C. Jones reagent (0.27 M, 0.96 mL, 0.26 mmol) was added slowly to the mixture at -20 °C, and the mixture was stirred at this temperature for 15 min. Ether (10 mL) and sat. aq. $NaHCO_3$ solution (10 mL) were added to the mixture. The organic layer was separated, and then the aqueous layer was extracted with ether (5 mL × 2), and the combined extracts were dried and evaporated. Column chromatography on silica gel eluted by a 2:3 mixture of ethyl acetate and hexane gave unreacted **11** (10 mg, 11% recovery) and **12** (60 mg, 67% yield, 76% conversion, a colorless oil). **12**:

TLC R_f 0.68 (1:1 ethyl acetate/hexane); IR ($CHCl_3$) 2930, 1730, 1600, 1435, 1120, 1070, 1020, 965, 865 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.06–1.14 (m, 3 H, CH_3), 1.35–2.88 (m, 26 H, 12 CH_2 and 2 CH), 2.32 (t, 2 H, J = 7.6 Hz, CH_2), 3.41–3.57 (m, 2 H, CH_2O), 3.67 (s, 3 H, OCH_3), 3.73–4 32 (m, 4 H, CH_2O and 2 CHO), 4.65–4.79 (m, 1.5 H, 1.5 OCHO), 4.88 (m, 0.5 H, 0.5 OCHO), 5.24–5.82 (m, 4 H, 4 vinyls); MS (EI, 24 ev) *m/z* (rel) 428 (3.38, M^+–102 [$C_5H_{10}O_2$]), 415 (0.78), 397 (2.05), 379 (6.23), 344 (10.78), 326 (11.73), 313 (5.20), 295 (100), 277 (36.83).

17,18-DidehydroPGE$_3$ Methyl Ester (13). The compound **12** (52 mg, 0.097 mmol) was dissolved in a 3:1:1 mixture of acetic acid, water, and THF (3 mL), and the mixture was stirred at 40 °C for 4.5 h. The mixture was concentrated in vacuo followed by the azeotropic evaporation with toluene (two times). Column chromatography on silica gel eluted with a 10:1 mixture of ethyl acetate and hexane and then ethyl acetate gave **13** (30 mg, 85% yield, 15α/15β = 54:46) as a colorless oil. **13α**: TLC R_f 0.44 (ethyl acetate); IR ($CHCl_3$) 3725–3240, 2910, 1735, 1600, 1430, 1315, 1140, 1075, 965 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.13 (t, 3 H, J = 7.5 Hz, CH_3), 1.55–2.52 (m, 15 H, 6 CH_2, CH, and 2 OH), 2.32 (t, 2 H, J = 7.3 Hz, CH_2), 2.76 (ddd, 1 H, J = 18.4, 7.5, 1.1 Hz, CH), 3.67 (s, 3 H, OCH_3), 4.09 (m, 1 H, CHO), 4.28 (m, 1 H, CHO), 5.38 (m, 2 H, 2 vinyls), 5.72 (m, 2 H, 2 vinyls); $[\alpha]^{22}_D$ -82.8° (*c* 0.72, $CHCl_3$); MS (EI, 24 ev) *m/z* (rel) 344 (4.67, M^+–18 [H_2O]), 326 (6.95), 315 (5.72), 313 (5.65), 295 (60.11), 277 (62.50), 263 (32.16), 245 (100).

PGE$_3$ Methyl Ester (14). To a solution of the 15α isomer of **13** (13 mg, 0.036 mmol) in a 5:5:1 mixture of benzene, cyclohexane, and cyclohexene (1.7 mL) was added Lindlar catalyst (7 mg). The mixture was stirred at 20 °C for 20 min under hydrogen atmosphere (1 atm). The catalyst was filtered through Celite pad, and the filtrate was evaporated. Column chromatography on silica gel eluted by a 5:1 mixture of ethyl acetate and acetone gave **14** (13 mg, 99% yield) as a colorless oil: TLC R_f 0.41 (ethyl acetate); IR ($CHCl_3$) 3730–3100, 2950, 1735, 1600, 1435, 1240, 1160, 1080, 975, 870 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.98 (t, 3 H, J = 7.5 Hz, CH_3), 1.67 (m, 2 H, CH_2), 1.80–2.53 (m, 13 H, 5 CH_2, CH, and 2 OH), 2.31 (t, 2 H, J = 7.4 Hz, CH_2), 2.75 (dd, 1 H, J = 18.0, 7.3 Hz, CH), 3.67 (s, 3 H, OCH_3), 4.03–4.23 (m, 2 H, 2 CHO), 5.26–5.79 (m, 6 H, 6 vinyls); $[\alpha]^{21}_D$ -80.0° (*c* 0.64, $CHCl_3$); MS (EI, 24 ev) *m/z* (rel) 364 (17.75, M^+), 346 (4.50), 328 (13.77), 295 (8.21), 277 (21.19), 261 (30.40), 249 (99.34), 248 (100).

9-*O*-Acetyl-17,18-didehydroPGF$_{3\alpha}$ Methyl Ester (15). The compound **9** (46 mg, 0.094 mmol) was dissolved in a 3:1:1 mixture of acetic acid, water, and THF (3 mL), and the mixture was stirred at 50 °C for 2.5 h. The mixture was concentrated in vacuo, and the residual material was subjected to azeotropic evaporation with toluene. Column chromatography on silica gel eluted by a 5:1 mixture of ethyl acetate and hexane and then ethyl acetate gave **15** (34 mg, 89% yield, 15α/15β = 56:44) as a colorless oil. **15α**: TLC R_f 0.42 (ethyl acetate); IR ($CHCl_3$) 3720–3200, 2930, 1720, 1430, 1370, 1240, 1030, 965 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.12 (t, 3 H, J = 7.5 Hz, CH_3), 1.67 (m, 4 H, 2 CH_2), 1.89–2.60 (m, 12 H, 4 CH_2, 2 CH, and 2 OH), 2.06 (s, 3 H, CH_3), 2.30 (t, 2 H, J = 7.3 Hz, CH_2), 3.67 (s, 3 H, OCH_3), 3.91 (m, 1 H, CHO), 4.25 (m, 1 H, CHO), 5.11 (m, 1 H, CHO), 5.33 (m, 2 H, 2 vinyls), 5.50–5.77 (m, 2 H, 2 vinyls); $[\alpha]^{22}_D$ +40.5° (*c* 0.68, $CHCl_3$); MS (EI, 24 ev) *m/z* (rel) 406 (0.39, M^+), 388 (1.52), 370 (1.39), 339 (5.30), 328 (29.48), 321 (20.96), 310 (83.91), 261 (100).

9-*O*-AcetylPGF$_{3\alpha}$ Methyl Ester (16). To a solution of the 15α isomer of **15** (18.1 mg, 0.0445 mmol) in a 6:6:1 mixture of benzene, cyclohexane, and cyclohexene (0.9 mL) was added Lindlar catalyst (8 mg). The mixture was stirred at 20 °C for 40 min under hydrogen atmosphere (1 atm). The catalyst was filtered through Celite pad, and the filtrate was evaporated. Column chromatography on silica gel eluted by ethyl acetate gave **16** (13.9 mg, 76% yield) as a colorless oil: TLC R_f 0.40 (ethyl acetate); IR ($CHCl_3$) 3750–3300, 3030, 1730, 1425, 1215, 1045, 930 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.98 (t, 3 H, J = 7.5 Hz, CH_3), 1.48–1.80 (m, 6 H, 2 CH_2 and 2 OH), 1.88–2.57 (m, 10 H, 4 CH_2 and 2 CH), 2.06 (s, 3 H, CH_3), 2.30 (t, 2 H, J = 7.5 Hz, CH_2), 3.67 (s, 3 H, OCH_3), 3.93 (m, 1 H, CHO), 4.17 (m, 1 H, CHO), 5.12 (m, 1 H, CHO), 5.27–5.75 (m, 6 H, 6 vinyls); $[\alpha]^{23}_D$ +33.0° (*c* 0.61, $CHCl_3$); MS (EI, 24 ev) *m/z* (rel) 390 (0.95, M^+–18 [H_2O]), 372 (5.12), 339 (3.27), 330 (41.97), 321 (14.08), 312 (100).

PGF$_{3\alpha}$ Methyl Ester (17). The compound **16** (10.4 mg, 0.0255 mmol) was dissolved in a methanolic sodium methoxide solution (0.86 M, 0.36 mL, 0.31 mmol), and the mixture was stirred at 20 °C for 40 min.

This reaction mixture was quenched with sat. aq. NH_4Cl solution (5 mL). Extractive workup with ether (5 mL × 2) followed by column chromatography on silica gel eluted by a 1:1 mixture of ethyl acetate and acetone gave **17** (9.4 mg, >99% yield) as a colorless oil: TLC R_f 0.18 (ethyl acetate); IR ($CHCl_3$) 3750–3200, 2960, 2870, 1725, 1450, 1365, 1230, 1165, 1060, 970, 900 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.97 (t, 3 H, J = 7.5 Hz, CH_3), 1.20–1.85 (m, 6 H, 2 CH_2 and 2 OH), 1.96–2.44 (m, 11 H, 4 CH_2, 2 CH, and OH), 2.33 (t, 2 H, J = 7.3 Hz, CH_2), 3.67 (s, 3 H, OCH_3), 3.86–4.36 (m, 3 H, 3 CHO), 5.26–5.79 (m, 6 H, 6 vinyls); $[\alpha]^{22}_D$ +22.0° (*c* 0.45, $CHCl_3$); MS (EI, 24 ev) *m/z* (rel) 348 (4.64, M^+-18 [H_2O]), 330 (19.49), 312 (39.28), 297 (11.01), 279 (49.37), 261 (66.24), 255 (100).

The compound **17** was also synthesized by α-selective reduction of **14** (12.0 mg, 0.0329 mmol) with a THF solution of L-Selectride (1 M, 0.035 mL, 0.035 mmol) in THF (1 mL) at -78 °C for 15 min. Column chromatography on silica gel with a 2:1 mixture of ethyl acetate and acetone as eluant afforded **17** (5.5 mg, 46%).

$PGF_{3\alpha}$ (18). The compound **17** (10.0 mg, 0.0273 mmol) was dissolved in MeOH (0.2 mL) and cooled to 0 °C. To this was added 0.6 M aq. NaOH solution (0.20 mL, 0.12 mmol). The mixture was stirred at 20 °C for 4.5 h and then acidified by adding 2 N HCl solution (0.060 mL, 0.12 mmol) at 0 °C. The reaction mixture was concentrated in vacuo, and the residual material was subjected to column chromatography on silica gel using a 1:1 mixture of acetone and methanol to give **18** (9.8 mg, >99% yield): TLC R_f 0.03 (ethyl acetate); IR (THF) 3700–3000, 1740, 1580, 1410, 1305, 970, 730 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.97 (t, 3 H, J = 7.5 Hz, CH_3), 1.05–2.40 (m, 20 H, 7 CH_2, 2 CH, 3 OH, and CO_2H), 4.00–4.30 (m, 3 H, 3 CHO), 5.27–5.69 (m, 6 H, 6 vinyls); $[\alpha]^{22}_D$ +31.5° (*c* 0.49, THF).

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References and Notes

1. Reviews: (a) Yamamoto, Y.; Maruyama, K. *Heterocycles* **1982**, *18*, 357. (b) Hoffmann, R. W. *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 555.
2. (a) Courtois, G.; Miginiac, L. *J. Organomet. Chem.* **1974**, *69*, 1. (b) Benkeser, R. A.; Siklosi, M. P.; Mozdzen, E. C. *J. Am. Chem. Soc.* **1978**, *100*, 2134.
3. Recent approaches to α-selective allylation: (a) Yamamoto, Y.; Maruyama, K. *J. Org. Chem.* **1983**, *48*, 1564. (b) Yamamoto, Y.; Maeda, N.; Maruyama, K. *J. Chem. Soc., Chem. Commun.* **1983**, 742. (c) Clarembeau, M.; Krief, A. *Tetrahedron Lett.* **1984**, *25*, 3629. (d) Araki, S.; Hatano, M.; Ito, H.; Butsugan, Y. *J. Organomet. Chem.* **1987**, *333*, 329. (e) Araki, S.; Butsugan, Y. *Chem. Lett.* **1988**, 457. (f) Iqbal, J.; Joseph, S. P. *Tetrahedron Lett.* **1989**, *30*, 2421.
4. Highly stereocontrolled α-selective allylation of aldehydes using allylceriums has been reported; see: Guo, B. -S.; Doubleday, W.; Cohen, T. *J. Am. Chem. Soc.* **1987**, *109*, 4710.
5. Recent methods of regiospecific synthesis of homopropargyl alcohols: (a) Daniels, R. G.; Paquette, L. A. *Tetrahedron Lett.* **1981**, *22*, 1579. (b) Corey, E. J.; Rücker, C. *Tetrahedron Lett.* **1982**, *23*, 719. (c) Ishiguro, M.; Ikeda, N.; Yamamoto, H. *J. Org. Chem.* **1982**, *47*, 2225. (d) Furuta, K.; Ishiguro, M.; Haruta, R.; Ikeda, N.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 2768. (e) Danheiser, R. L.; Carini, D. J.; Kwasigroch, C. A. *J. Org. Chem.* **1986**, *51*, 3870. Review: Epsztein, R. *Comprehensive Carbanion Chemistry*; Buncel, E., Durst, T., Eds.; Elsevier: New York, 1984; Part B, Chapter 3.
6. A preliminary communication of this work has appeared: Yanagisawa, A.; Habaue, S.; Yamamoto, H. *J. Org. Chem.* **1989**, *54*, 5198.

7. For other examples of the use of acylsilanes to control the regiochemistry of allylic carbanions, see: (a) [3-methylpentadienyllithium] Wilson, S. R.; Hague, M. S.; Misra, R. N. *J. Org. Chem.* **1982**, *47*, 747. (b) [allenyltin/alkyllithium] Suzuki, M.; Morita, Y.; Noyori, R. *J. Org. Chem.* **1990**, *55*, 441.
8. Acylsilanes can be prepared by the following methods: (a) 1,3-dithians: Brook, A. G.; Duff, J. M.; Jones, P. F.; Davis, N. R. *J. Am. Chem. Soc.* **1967**, *89*, 431. Corey, E. J.; Seebach, D.; Freedman, R. *J. Am. Chem. Soc.* **1967**, *89*, 434. (b) Acyl chlorides: Yamamoto, K.; Hayashi, A.; Suzuki, S.; Tsuji, J. *Organometallics* **1987**, *6*, 974. Kang, J.; Lee, J. H.; Kim, K. S.; Jeong, J. U.; Pyun, C. *Tetrahedron Lett.* **1987**, *28*, 3261. Capperucci, A.; Degl'Innocenti, A.; Faggi, C.; Ricci, A. *J. Org. Chem.* **1988**, *53*, 3612. Furstner, A.; Weidmann, H. *J. Organomet. Chem.* **1988**, *354*, 15. (c) (α-Hydroxyalkyl)silanes: Danheiser, R. L.; Fink, D. M.; Okano, K.; Tsai, Y. -M.; Szczepanski, S. W. *J. Org. Chem.* **1985**, *50*, 5393. Linderman, R. J.; Suhr, Y. *J. Org. Chem.* **1988**, *53*, 1569. (d) Alkoxyallenes: Clinet, J. -C.; Linstrumelle, G. *Tetrahedron Lett.* **1980**, *21*, 3987. Reich, H. J.; Kelly, M. J. *J. Am. Chem. Soc.* **1982**, *104*, 1119. Ricci, A.; Degl'Innocenti, A.; Capperucci, A.; Faggi, C.; Seconi, G.; Favaretto, L. *Synlett* **1990**, 471. (e) Thiocarboxylic acid *S*-esters: Kuwajima, I.; Mori, A.; Kato, M. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 2634. (f) Alkynylsilanes: Miller, J. A.; Zweifel, G. *Synthesis* **1981**, 288. Miller, J. A.; Zweifel, G. *J. Am. Chem. Soc.* **1981**, *103*, 6217. (g) 1-Methoxypropene: Schinzer, D. *Synthesis* **1989**, 179. (h) (α-Phosphonoacyl)silane: Nowick, J. S.; Danheiser, R. L. *J. Org. Chem.* **1989**, *54*, 2798. (i) Methoxybis(trimethylsilyl)methane: Yoshida, J.; Matsunaga, S.; Ishichi, Y.; Maekawa, T.; Isoe, S. *J. Org. Chem.* **1991**, *56*, 1307. For reviews of preparation of acylsilanes, see: Colvin, E. W. *Silicon Reagents in Organic Synthesis*; Academic Press: London, 1988; Chapter 12. Ricci, A.; Degl'Innocenti, A. *Synthesis*, **1989**, 647. Page, P. C. B.; Klair, S. S.; Rosenthal, S. *Chem. Soc. Rev.* **1990**, *19*, 147.
9. (a) Schlosser, M.; Hartmann, J.; David, V. *Helv. Chim. Acta* **1974**, *57*, 1567. (b) Schlosser, M.; Hartmann, J. *J. Am. Chem. Soc.* **1976**, *98*, 4674. (c) Stähle, M.; Hartmann, J.; Schlosser, M. *Helv. Chim. Acta* **1977**, *60*, 1730.
10. Brandsma, L.; Verkruijsse, H. D. *Preparative Polar Organometallic Chemistry*; Springer-Verlag: New York, 1986.
11. The *E*/*Z* ratio was determined by 500-MHz ^{1}H NMR assay.
12. The aldehyde **5** was generously supplied by Ono Pharmaceutical Co.
13. A definite but not unexpected limitation of the new method has been found to occur in cases where allylic alcohol was produced. Thus the desilylation of the unprotected **7** caused an allylic rearrangement reaction. This limitation was circumvented by a simple formylation followed by desilylation.
14. (a) Samuelsson, B. *J. Am. Chem. Soc.* **1963**, *85*, 1878. (b) Axen, U.; Thompson, J. L.; Pike, J. E. *J. Chem. Soc., Chem. Commun.* **1970**, 602. (c) Corey, E. J.; Shirahama, H.; Yamamoto, H.; Terashima, S.; Venkateswarlu, A.; Schaaf, T. K. *J. Am. Chem. Soc.* **1971**, *93*, 1490.
15. Reported optical rotation value of **18**: $[\alpha]^{26}_{D}$ +29.6° (*c* 0.54, THF).[14c]
16. Zinc dust (guaranteed reagent, >90% purity) was purchased from Wako Pure Chemical Industries, Ltd., Japan and activated with dilute HCl rinse.[17] The activated zinc was dried with a heat gun under reduced pressure (5 Torr) prior to use.
17. Shriner, R. L.; Neumann, F. W. *Org. Synth. Coll. Vol. III*, **1955**, 73.