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Highly efficient total synthesis of Δ^{12}-PGJ_2, 15-deoxy-$\Delta^{12,14}$-PGJ_2, and their analogues

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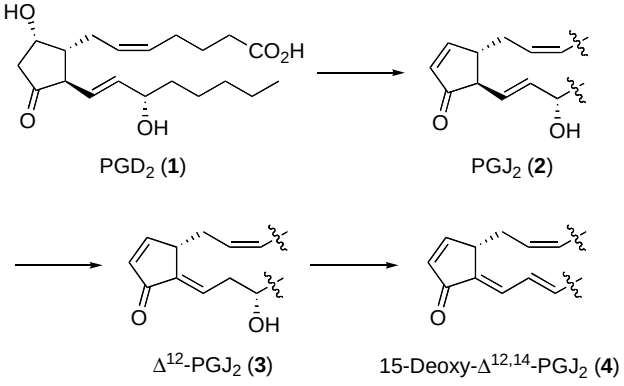
Abstract—Palladium-catalyzed reaction of TBS ether of 4-cyclopentene-1,3-diol monoacetate (>95% ee) with an anion derived from methyl malonate and a base such as *t*-BuOK and LDA proceeded highly efficiently and reproducibly. The product obtained in >90% isolated yield was transformed in five steps into the key cyclopentenone possessing the α-chain at the γ position. Aldol reaction of this enone with the ω-chain aldehyde afforded the aldol adduct, and exposure of the derived mesylate to Al_2O_3 furnished the cross-conjugated dienone of the full structure. Finally, functional group manipulation furnished Δ^{12}-PGJ_2 efficiently. Similarly, 15-deoxy-$\Delta^{12,14}$-PGJ_2, 5,6-acetylene analogues, and a 5,6-dihydro analogue were synthesized.

1. Introduction

In the 1980s, Fitzpatrick and Wyland reported[1] albumin-catalyzed metabolism of PGD_2 in vitro to afford Δ^{12}-PGJ_2 and 15-deoxy-$\Delta^{12,14}$-PGJ_2 (Scheme 1, Fig. 1). Later, Hayashi et al. extracted Δ^{12}-PGJ_2 from normal human urine to support the existence of albumin-catalyzed metabolism in vivo.[2] In contrast with other PGs, which elicit a biological response through binding to G-protein coupled receptors, these metabolites interact with other specific cellular targets such as signaling molecules and transcriptional factors directly.[3,4] For example, 15-deoxy-$\Delta^{12,14}$-PGJ_2 represents the most potent natural ligands reported to date for PPARγ, a receptor that has been linked to non-insulin dependent diabetes mellitus (NIDDM or type II diabetes), obesity, hypertension, and atherosclerosis.[5] Inhibition of the NF-κB-mediated transcription is another property of 15-deoxy-$\Delta^{12,14}$-PGJ_2, and is responsible for anti-inflammatory activity. On the other hand, Δ^{12}-PGJ_2 exhibits strong antitumor effects by incorporating into tumor cells and transferring into nuclei, activating the gadd45 promoter independently of p53[6] and inhibiting topoisomerase.[7]



Scheme 1. Biosynthesis of Δ^{12}-PGJ_2 and 15-deoxy-$\Delta^{12,14}$-PGJ_2.

Although the fundamental profiles of these Δ^{12}-PGs **3** and **4** have been thus elucidated, more than 50 publications using these PGs have emerged every year in the last several years indicating importance of their property in life science. PGs **3** and **4** in those studies have been purchased from a company or gifted by another company. According to a recent review,[8] the former company produces PG **4**[9] by base-catalyzed decomposition of PGD_2 (**1**), while the method for synthesis of **3** is not disclosed. On the other hand, **3** and **4** are synthesized from a $PGF_{2\alpha}$ derivative in the latter company.[10] Consequently, we felt it important to establish a chemical method for synthesizing not only these PGs but also analogues thereof for further biological study (Fig. 1).

Keywords: Aldol reaction; Cyclopentenone; Palladium; PPARγ; Δ^{12}-PGJ_2; 15-Deoxy-$\Delta^{12,14}$-PGJ_2.
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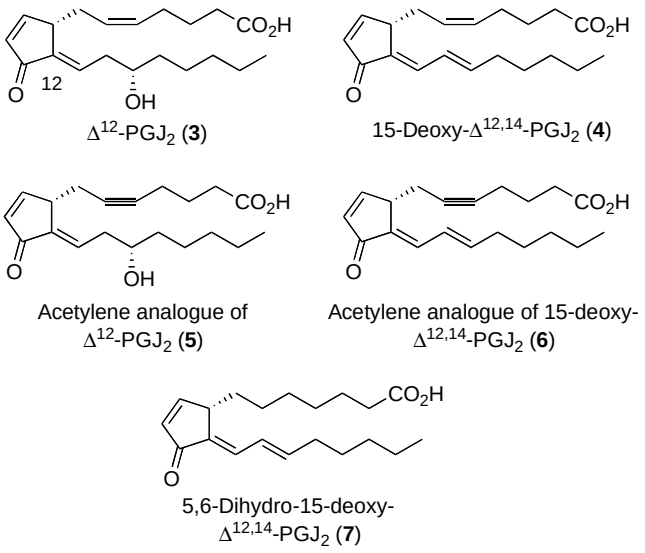


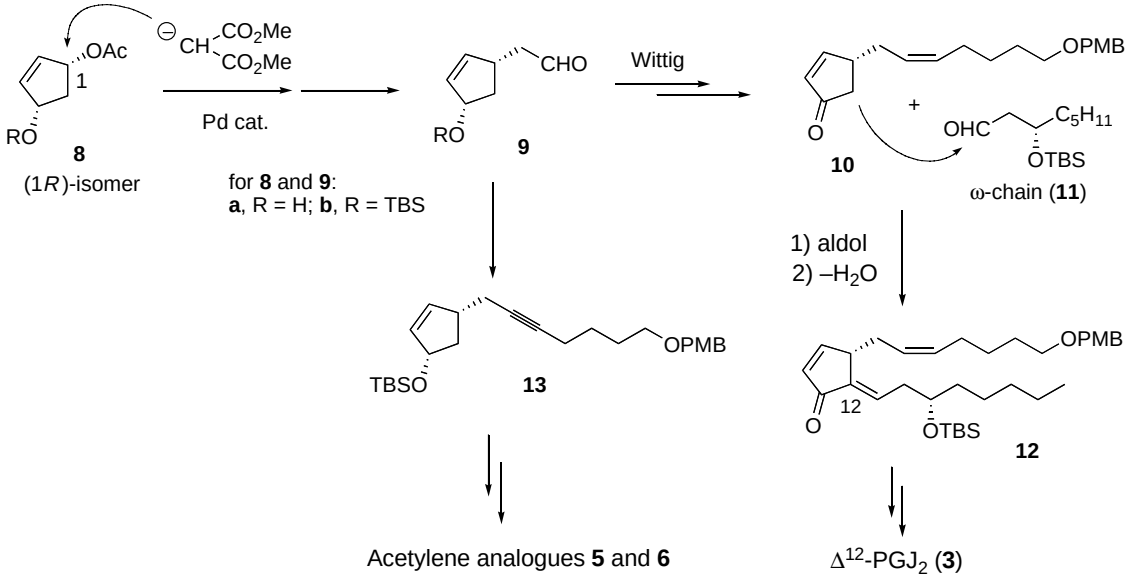
Figure 1. Δ^{12}-PGJ_2 and related PGs we have synthesized.

Among these targets, **4** was synthesized by Sutton in 2003, for the first time.[11] Meinwald rearrangement[12] of the norbornadiene was utilized to construct the core cyclopentenone structure, and was coupled with asymmetric acetylation using enzyme in two stages to accomplish resolutions at the stereocenters on the ω chain and on the cyclopentene ring. Later, **4** was again synthesized as a racemate by Brummond through a silicon-tethered allenic [2+2+1] cycloaddition.[13] At the same time we reported another approach to optically active PGs (**3** and **4**) and the acetylene analogue **5** as a communication.[14] The former two syntheses by Sutton and Brummond, however, seem to present little advantage over our method with respect to the product selectivity, efficiency, and, in particular, diastereoselectivity in the former rearrangement.[15] Furthermore, the reaction conditions would be hardly applicable to synthesis of **3**, the parent compound of this class. These limited syntheses prompted us to publish a full account of the synthesis of **3**–**5** as well as other analogues **6** and **7**. The acetylene analogues **5** and **6** would be precursors of radio labeled **3** and **4**. On the other hand, **5**–**7** would allow access to the structure–activity relation. In addition, **7** is formally the metabolite of PGD_1 derived from bishomo-γ-linolenic acid (5-dihydro derivative of arachidonic acid) though isolation of **7** is not yet reported.

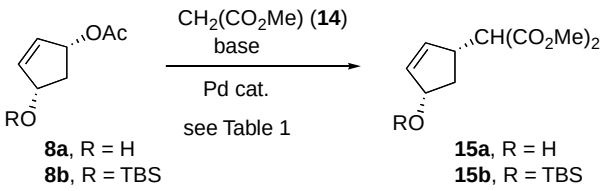
2. Results and discussion

We envisioned that the cross-conjugated dienone structure of **3**–**7** will be constructed by aldol condensation between cyclopentenone possessing the α chain and an aldehyde of the ω chain. For example, aldol reaction between cyclopentenone **10** and aldehyde **11** would furnish **12** with the Δ^{12}-PGJ_2 structure (Scheme 2). Likewise, simply changing the aldehyde partner would produce analogue **4**. It should be mentioned at this stage that γ-substituted cyclopentenones such as **10** were compounds for which an efficient method has not been established. In this investigation, we contemplated a sequence, which consists of palladium-catalyzed reaction[16] of cyclopentene monoacetate **8** with malonate anion and subsequent Wittig reaction of the derived aldehyde **9**. On the other hand, we envisaged that Corey–Fuchs[17] reaction of aldehyde **9** followed by alkylation of the derived acetylene would produce acetylene **13**, which would be transformed to 5,6-dehydro derivatives **5** and **6** by the aldol strategy. Concerning a synthesis of 5,6-dihydro analogue **7**, we decided to apply a copper-catalyzed S_N2 type reaction[18] of *ent*-**8** and RMgBr to construct the necessary enone intermediate (vide infra).

When 0.5–2 g of racemic monoacetate **8a** (R=H) was subjected several times to the reaction with methyl malonate (**14**) (2–2.5 equiv), NaH (2 equiv), and $Pd(PPh_3)_4$ (5 mol%) in THF at room temperature−50 °C according to the reported protocol[16] (Scheme 3), yields of product **15a** observed were among 50–70% (the best yield is shown in entry 1 of Table 1), which were lower than that (86%) reported for 100 mg-scale.[19] Since this step was strategically very important, this



Scheme 2. Our approach to Δ^{12}-PGJ_2 and the acetylene analogues through Aldol reaction.



Scheme 3. Palladium-catalyzed reaction of **8a**,**b** with malonate anion.

Table 1. Palladium-catalyzed reaction of **8a**,**b** with **14** (Scheme 3)[a]

Entry	Substrate	Base	Time (h)	Temperature (°C)	Yield (%)
1	**8a**	NaH	2	rt	69[b,c]
2	**8a**	MeONa	2	rt	71[b]
3	**8a**	LDA	1.5	rt	83[b]
4	**8a**	*t*-BuOK	2	rt	90
5	**8b**	NaH	4	50[d]	66
6	**8b**	MeONa	3	50[d]	87
7	**8b**	LDA	3	rt	91
8	**8b**	*t*-BuOK	3	50[d]	93

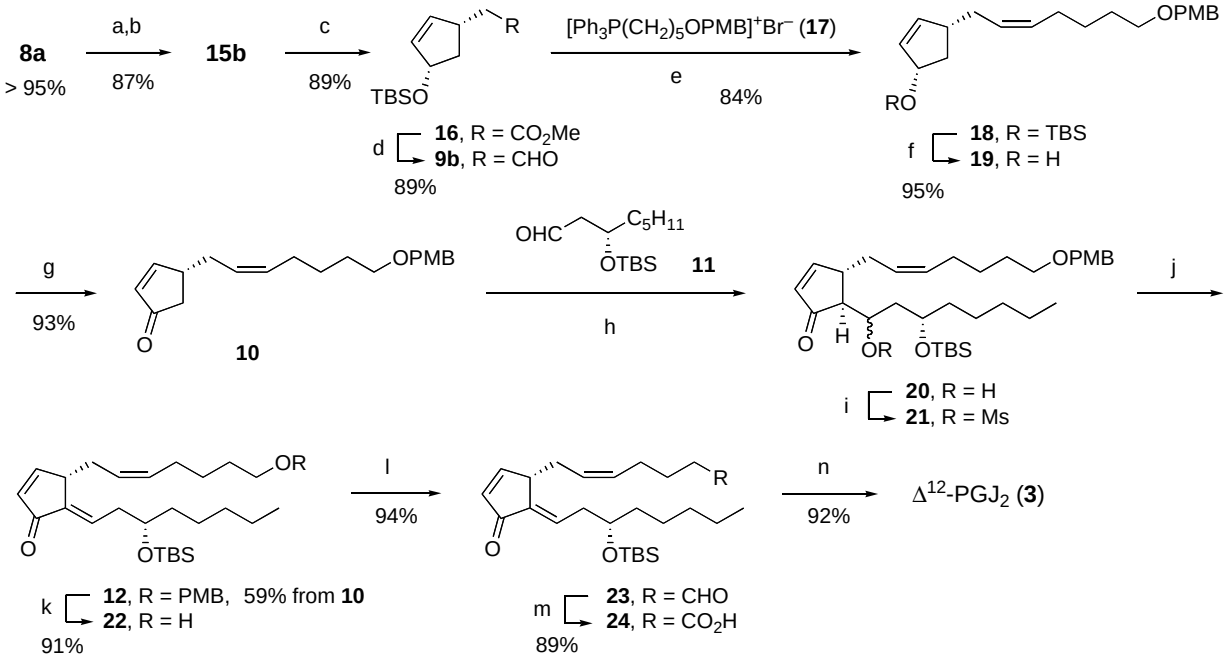
[a] Reactions were carried out with malonate anions (2.2 equiv) in the presence of $Pd(PPh_3)_4$ (5 mol%) in THF.
[b] An unidentified by-product was also produced.
[c] The maximum yield among several runs is given. See the text for more information.
[d] No reaction at room temperature was monitored by TLC.

reaction was re-investigated under various conditions. We first focused on the loading of $Pd(PPh_3)_4$ (5–20%) and the PPh_3 ligand (2–6 equiv of Pd), use of polar solvents, etc. These changes, however, resulted in no improvement. Next, malonate anion generated from **14** (2.2 equiv) and a base (2.0 equiv) was subjected to the reaction with 5 mol% $Pd(PPh_3)_4$. Among the bases listed in Table 1, LDA and *t*-BuOK provided substantially higher yields of **15a** than NaH (entries 3 and 4).

Next, these bases were applied to TBS ether of **8a**, that is, **8b** (R=TBS). Reaction with LDA proceeded at room temperature, while *t*-BuOK required a higher temperature of 50 °C (entries 7 and 8). Except for the difference in the reaction temperatures, both entries produced **15b** in >90% yields (entries 7 and 8). Of the two bases, we have routinely used the latter base for the present investigation because of easy handling. In several 2–3 g-scale reactions, yields constantly exceeded 90% (see Section 4).

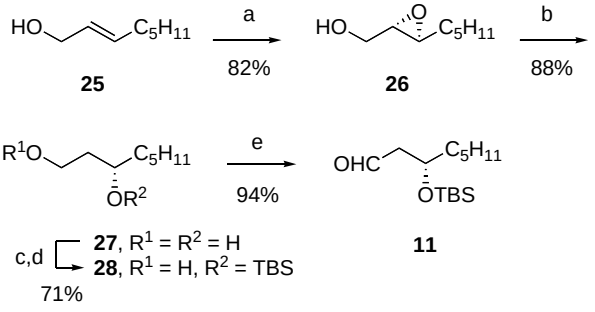
The above reaction was repeated with **8b** derived from **8a**[20] of >95% ee to obtain optically active **15b**. Transformation of **15b** to the key enone **10**, aldol reaction thereof, and further transformation to Δ^{12}-PGJ_2 (**3**) are delineated in Scheme 4. Decarboxylation of **15b** with KI in wet DMI proceeded well at 130 °C to afford ester **16** in 89% isolated yield after chromatography. Ester **16** was also synthesized from alcohol **15a** by decarboxylation using KI in wet DMF followed by silylation with TBSCl. Of the two routes to **16**, the former sequence had the advantage of easily purifying the crude TBS ether **16** containing DMI, because of the sufficiently different R_f values thereof. Aldehyde **9b** synthesized in 89% yield by DIBAL reduction of **16** was subjected to Wittig reaction with the ylide derived from $[Ph_3P(CH_2)_5OPMB]^+Br^-$ (**17**) and $NaN(TMS)_2$ first at −70 °C then at room temperature according to the literature procedure[21] to afford *cis* olefin **18** exclusively in 84% yield.[22] The TBS group was removed and the resulting alcohol **19** was oxidized to the key intermediate **10** in good yield.

Aldehyde **11**, the aldol partner of enone **10**, was synthesized from alcohol **25** through epoxy alcohol **26** in five steps in 48% overall yield (Scheme 5). Thus, epoxy alcohol **26** ($[\alpha]_D^{24}$ −43 (*c* 0.45, $CHCl_3$); lit.[23] $[\alpha]_D^{25}$ −42.7 (*c* 4.7, $CHCl_3$) for >98% ee), synthesized by the Sharpless asymmetric epoxidation[23,24] of **25**, was subjected to



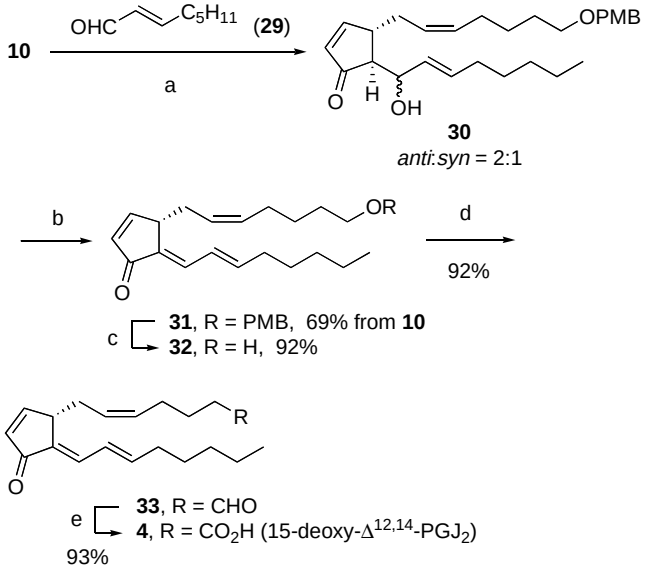
Scheme 4. Synthesis of Δ^{12}-PGJ_2: (a) TBSCl, imidazole; (b) $CH_2(CO_2Me)_2$, *t*-BuOK, $Pd(PPh_3)_4$ (cat.); (c) KI, DMI–H_2O (10:1), 130 °C; (d) DIBAL, CH_2Cl_2, −78 °C; (e) **17**, $NaN(TMS)_2$, −70 °C to rt; (f) TBAF; (g) PCC; (h) LDA (2.0 equiv), −78 °C, THF then **11** (1.2 equiv), −78 °C; (i) MsCl, Et_3N, 0 °C; (j) Al_2O_3; (k) DDQ, CH_2Cl_2–H_2O (19:1); (l) PCC; (m) $NaClO_2$, MeCH=C(Me)$_2$, *t*-BuOH, phosphate buffer (pH 3.6); (n) HF–MeCN (1:19).

reduction with Red-Al to produce 1,3-diol **27** in good yield with 22:1 regioselection over the 1,2-isomer by ^{1}H NMR spectroscopy. Diol **27** was converted to the bis-silyl ether, and exposed to PPTS (1.2 equiv) in EtOH–CH_2Cl_2 (1:1) to afford, after easy chromatography, mono alcohol **28** and unwanted diol **27** in 71 and 26% yield, respectively. Diol **27** was recycled. Finally, PCC oxidation of **28** afforded aldehyde **11** ($[\alpha]_D^{27}$ +6.7 (*c* 0.21, $CHCl_3$); lit.[25] $[\alpha]_D^{24}$ −5.0 (*c* 1.0, $CHCl_3$) for the enantiomer of >98% ee).[26]



Scheme 5. Preparation of aldehyde **11**: (a) *t*-BuOOH, L-(+)-DIPT (0.3 equiv), $Ti(i\text{-}PrO)_4$ (0.25 equiv), MS 4 Å; (b) Red-Al, THF; (c) TBSCl, imidazole; (d) PPTS, EtOH–CH_2Cl_2 (1:1); (e) PCC.

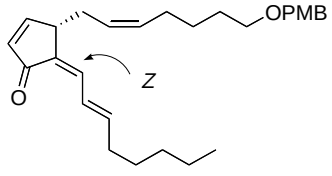
According to the protocol[27] for aldol reaction of cyclopentenone with aldehyde, the lithium enolate of enone **10** was prepared by using LDA at −78 °C for 20 min, and subjected to aldol reaction with aldehyde **11**. After 30 min at −78 °C, the reaction was quenched to afford aldol **20** as a 3:1 mixture of the *anti* and *syn* isomers by ^{1}H NMR spectroscopy.[28] Without separation, the aldol mixture was converted to mesylates with MsCl and Et_3N. During the mesylation, elimination of the derived mesylate to dienone **12** did not take place (cf. Scheme 6 for the aldol **30** derived from enal **29**). After filtration through a silica gel pad, the mesylate was exposed to Al_2O_3 at room temperature, which assisted stereoselective and exclusive formation of dienone **12** in 59% yield from enone **10**. The corresponding (*Z*)-olefin isomer of **12** (structure not shown) was not detected at the expected 0.5 ppm up field region in the ^{1}H NMR spectrum of the crude dienone **12**.[29] The selective formation of the (*E*)-olefin by using Al_2O_3 is consistent with the original dehydration of an aldol,[30] though the reason for the selectivity is still a matter of conjecture.[31]



Scheme 6. Synthesis of 15-deoxy-$\Delta^{12,14}$-PGJ_2: (a) LDA (2.0 equiv), −78 °C, THF then **29** (1.2 equiv), −78 °C; (b) MsCl, Et_3N, −15 °C; (c) DDQ, CH_2Cl_2–H_2O (19:1); (d) PCC; (e) $NaClO_2$, $MeCH{=}C(Me)_2$, *t*-BuOH, phosphate buffer (pH 3.6).

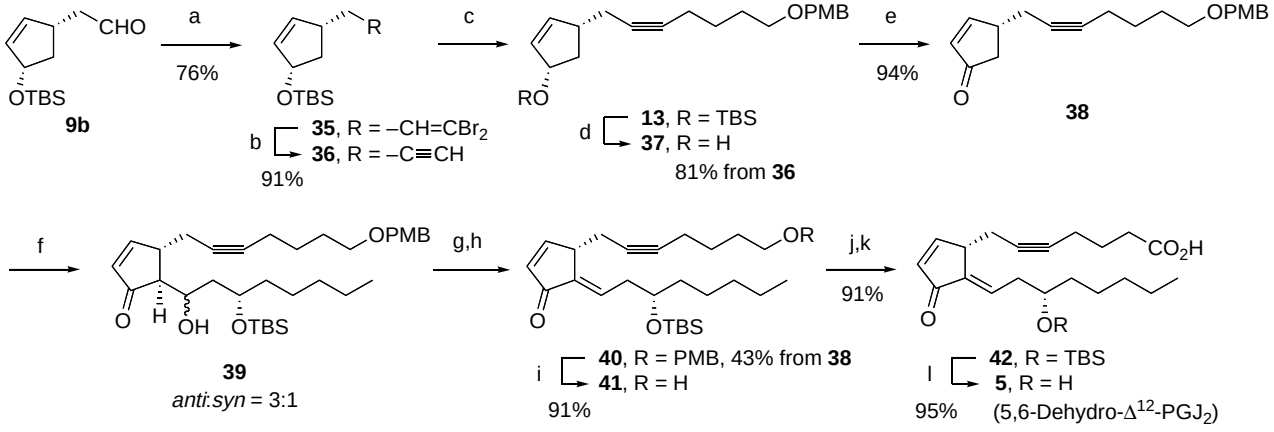
The remaining transformation of **12** to Δ^{12}-PGJ_2 (**3**) was accomplished efficiently as presented in Scheme 4. The PMB group of **12** was removed with DDQ in wet CH_2Cl_2 without affecting the dienone moiety. The resulting alcohol **22** was converted to acid **24** by two-step oxidation through aldehyde **23** in 84% yield. Direct oxidation of **22** with PDC in DMF produced a mixture of products. Finally, deprotection of the TBS group with HF in MeCN afforded Δ^{12}-PGJ_2 (**3**) in 92% yield.[32] The ^{1}H NMR spectrum of synthetic **3** was identical with that reported (δ 5–8 ppm)[1] and that provided by Ono Pharmaceutical Co., Ltd.

As illustrated in Scheme 6, the above enone **10** was next converted to 15-deoxy-$\Delta^{12,14}$-PGJ_2 (**4**). Thus, aldol reaction between enone **10** and *trans*-2-octenal (**29**) afforded aldol **30** as a 2:1 mixture of the *anti* and *syn* isomers.[28] Without separation, the mixture was treated with MsCl at 0 °C. In contrast to the above case, elimination of the mesylate took place simultaneously to produce dienone **31** and its (*Z*)-isomer **34** in a 4:1 ratio.[33] Fortunately, this low product selectivity was improved to 14:1 by simply conducting the reaction at −15 °C to furnish dienone **31** in 69% from enone **10** after chromatography. Following the procedure described above in Scheme 4, the CH_2OPMB group of **31** was converted to the carboxylic acid moiety of 15-deoxy-$\Delta^{12,14}$-PGJ_2 (**4**) in 79% yield from the PMB ether **31**. The structure of **4** thus synthesized was confirmed by comparison of the ^{1}H NMR (500 MHz, δ 5–8 ppm)[1] and ^{13}C NMR (75 MHz, all peaks)[11] spectra with those reported. These spectra were also consistent with those reported by Brummond.[13]



34: (*Z*)-Isomer of **31**

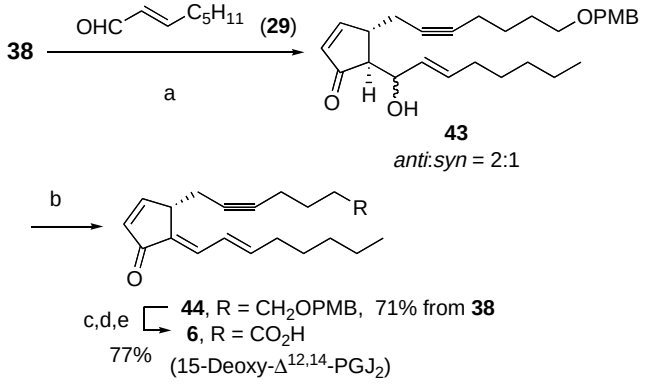
Synthesis of acetylene analogue **5** was accomplished through a sequence delineated in Scheme 7. Initially, aldehyde **9b** was converted to acetylene **36**[34] by the Corey–Fuchs method.[17] Alkylation of **36** with $Br(CH_2)_4$-OPMB proceeded in THF–DMPU (4:1), and the silyl group of **13** thus produced was removed by using TBAF to afford alcohol **37** in 81% yield from acetylene **36**. Oxidation of **37** to the key enone **38** followed by aldol reaction with aldehyde **11** furnished **39**, which upon mesylation and elimination with Al_2O_3 gave dienone **40** exclusively. Finally, the C(1) carbon was oxidized to the carboxylic



Scheme 7. Synthesis of acetylene analogue of Δ^{12}-PGJ$_2$: (a) PPh_3, CBr_4, 0 °C; (b) *n*-BuLi, −78 °C; (c) *n*-BuLi, $PMBO(CH_2)_4Br$, THF–DMPU (4:1), −78 °C to rt; (d) TBAF; (e) PCC; (f) LDA then **11**, −78 °C; (g) MsCl, Et_3N, 0 °C; (h) Al_2O_3; (i) DDQ; (j) PCC; (k) $NaClO_2$, $MeCH{=}C(Me)_2$, *t*-BuOH, phosphate buffer (pH 3.6); (l) HF–MeCN (1:19).

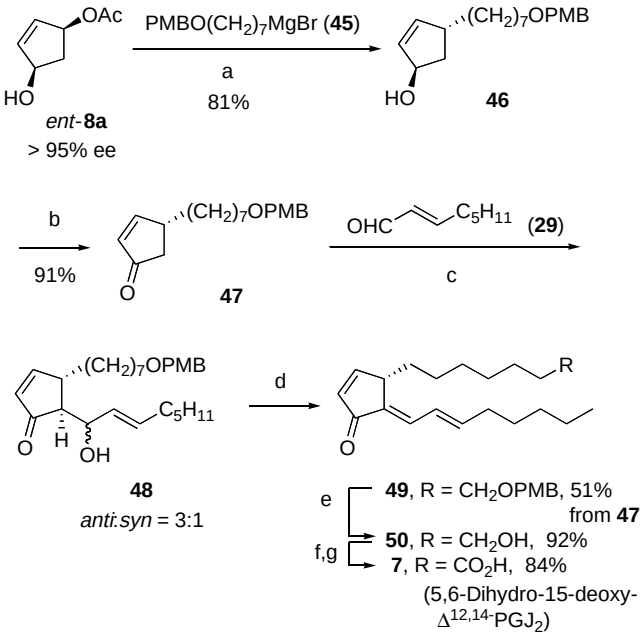
acid moiety, and the protective group of the C(15)–OH was removed to furnish 5,6-dehydro-Δ^{12}-PGJ$_2$ (**5**) in good yield.

Synthesis of another acetylene analogue **6** is summarized in Scheme 8. Aldol **43** was derived from enone **38** and aldehyde **29** with similar efficiency. Subsequently, mesylation with MsCl and Et_3N at −15 °C produced dienone **44** in good yield with high product selectivity (**44**:(*Z*)-isomer = 12:1).

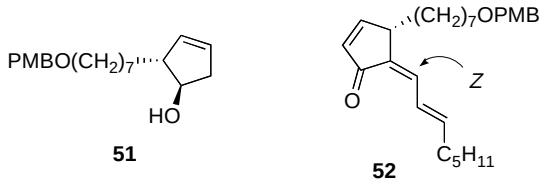


Scheme 8. Synthesis of 5,6-dehydro-15-deoxy-$\Delta^{12,14}$-PGJ$_2$: (a) LDA, −78 °C, THF then **29**, −78 °C; (b) MsCl, Et_3N, −15 °C; (c) DDQ, CH_2Cl_2–H_2O (19:1); (d) PCC; (e) $NaClO_2$, $MeCH{=}C(Me)_2$, *t*-BuOH, phosphate buffer (pH 3.6).

Recently, the S_N2 type reaction of 4-cyclopentene-1,3-diol monoacetate **8a** with RMgBr (R = aryl, alkenyl) was attained with the CuCN catalyst and the LiCl additive.[18] We envisioned that this reaction with an *alkyl* Grignard reagent of the α-chain would afford **46** and that transformation of **46** along the present strategy would produce 5,6-dihydro-15-deoxy-$\Delta^{12,14}$-PGJ$_2$ (**7**) (Scheme 9). To this end, the required *ent*-**8a** of >95% ee was prepared by the literature method[35] and subjected to the CuCN-catalyzed reaction with $PMBO(CH_2)_7MgBr$ (3 equiv) in the presence of LiCl (4 equiv) to afford S_N2 product **46** and *anti* S_N2' product **51** in a 92:8 ratio. The isomers were easily separated by chromatography and alcohol **46** thus isolated in 81% yield was oxidized to the key enone **47** with PCC.



Scheme 9. Synthesis of 5,6-dihydro-15-deoxy-$\Delta^{12,14}$-PGJ$_2$: (a) **45** (3 equiv), CuCN (0.3 equiv), LiCl (4.0 equiv), THF, −10 °C; (b) PCC; (c) LDA, −78 °C, THF then **29**, −78 °C; (d) MsCl, Et_3N, −20 °C; (e) DDQ, CH_2Cl_2–H_2O (19:1); (f) SO_3·pyridine, DMSO, Et_3N; (g) $NaClO_2$, $MeCH{=}C(Me)_2$, *t*-BuOH, phosphate buffer (pH 3.6).



Aldol reaction between the key enone **47** and *trans*-2-octenal (**29**) furnished aldol **48** as a mixture of *anti* and *syn* isomers in a 3:1 ratio.[28] Upon treatment with MsCl and Et_3N at −20 °C, aldol **48** underwent mesylation/elimination smoothly as in the above cases (see Schemes 6 and 8) to produce dienone **49** and the (*Z*)-isomer **52** in 51 and 5% yields, respectively, from enone **47**. Finally, dienone **49** was

converted into 5,6-dihydro-15-deoxy-$\Delta^{12,14}$-PGJ_2 (**7**) in good yield.

3. Conclusion

In summary, total synthesis of Δ^{12}-PGJ_2 (**3**) was accomplished through aldol reaction between cyclopentenone **10** and aldehyde **11** (Schemes 2 and 3). Cyclopentenone **10** was prepared from monoacetate **8b**, and the first step, that is, the palladium-catalyzed reaction of **8a** and malonate anion, was improved with *t*-BuOK, which was found to generate the highly reactive malonate anion. The synthesis of 15-deoxy-$\Delta^{12,14}$-PGJ_2 (**4**) and Δ^{12}-PGJ_2 analogues **5**–**7** was carried out with similar efficiency, thus demonstrating flexibility and reliability of the aldol strategy using γ-substituted cyclopentenones for construction of the cross-conjugated cyclopentadienone structures. We believe that the biological investigation of Δ^{12}-PGJ_2 and 15-deoxy-$\Delta^{12,14}$-PGJ_2 would be spurred by these analogues.

4. Experimental

4.1. General methods

Infrared (IR) spectra are reported in wave numbers (cm^{-1}). The ^1H NMR (300 and 500 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 following solvents were distilled before use: THF (from Na/benzophenone), Et_2O (from Na/benzophenone), and CH_2Cl_2 (from CaH_2). Purity of the title compounds were confirmed by elemental analysis in most of cases or by the spectral method (^1H and ^{13}C NMR) in the case the satisfactory results were not recorded.

4.2. Synthesis of the key enone 10

4.2.1. (1*R*,4*S*)-4-[(*tert*-Butyldimethylsilyl)oxy]-2-cyclopenten-1-yl acetate (8b). According to the literature method,[20] a solution of **8a** (1.52 g, 10.7 mmol, 96% ee by ^1H NMR spectroscopy of the derived MTPA ester), TBSCl (2.42 g, 16.1 mmol), and imidazole (1.46 g, 21.4 mmol) in DMF (22 mL) was stirred at room temperature for 2 h to afford silyl acetate **8b** (2.58 g, 94% yield) after chromatography (hexane/EtOAc). The ^1H and ^{13}C NMR spectra were identical with those reported.[36]

4.2.2. Dimethyl (1*R*,4*S*)-4-[(*tert*-Butyldimethylsilyl)oxy]-2-cyclopenten-1-yl malonate (15b). To an ice-cold slurry of *t*-BuOK (2.19 g, 19.5 mmol) in THF (18 mL) was added methyl malonate (**14**) (2.46 mL, 21.4 mmol) in a dropwise manner. After being stirred vigorously at room temperature for 30 min, $Pd(PPh_3)_4$ (564 mg, 0.49 mmol) and a solution of **8b** (2.50 g, 9.76 mmol) in THF (2 mL) were added into the mixture. The resulting mixture was stirred vigorously at 50 °C for 3 h. The reaction was quenched by adding saturated NH_4Cl and hexane with vigorous stirring. The organic layer was separated and the aqueous layer was extracted by using hexane three times. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure to afford an yellow oily residue, which was purified by chromatography (hexane/EtOAc) to furnish **15b** (2.98 g, 93% yield): bp 130 °C (1 mmHg); IR (neat) 1738, 1252, 837, 777 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.06 (s, 6H), 0.88 (s, 9H), 1.40 (ddd, $J=14$, 7, 5 Hz, 1H), 2.44 (dt, $J=14$, 7 Hz, 1H), 3.15–3.26 (m, 1H), 3.37 (d, $J=10$ Hz, 1H), 3.74 (s, 6H), 4.77–4.84 (m, 1H), 5.80 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.61, −4.58, 18.2, 25.9, 39.0, 43.5, 52.52, 52.54, 57.3, 76.8, 133.6, 136.3, 168.98, 169.04. Anal. Calcd for $C_{16}H_{28}O_5Si$: C, 58.50; H, 8.59. Found: C, 58.49; H, 8.49.

4.2.3. Methyl (1*S*,4*S*)-4-[(*tert*-butyldimethylsilyl)oxy]-2-cyclopenten-1-yl acetate (16). A slurry of **15b** (2.80 g, 8.52 mmol), KI (11.32 g, 68.2 mmol), DMI (30 mL), and water (3 mL) was vigorously stirred at 130 °C for 10 h and diluted with water and hexane. The organic layer was separated and the aqueous layer was extracted four times with hexane. The combined organic layers were dried over $MgSO_4$ and concentrated to furnish an oily residue, which was purified by chromatography (hexane/EtOAc) to afford **16** (2.05 g, 89% yield): $[\alpha]_D^{31}$ −19 (*c* 0.56, $CHCl_3$); bp 115 °C (1 mmHg); IR (neat) 1742, 1252, 1085, 836, 776 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.07 (s, 6H), 0.89 (s, 9H), 1.30 (ddd, $J=13$, 6, 5 Hz, 1H), 2.38 (dd, $J=16$, 8 Hz, 1H), 2.46 (dt, $J=13$, 7.5 Hz, 1H), 2.48 (dd, $J=16$, 7 Hz, 1H), 2.86–3.00 (m, 1H), 3.68 (s, 3H), 4.78–4.86 (m, 1H), 5.74 (dt, $J=6$, 2 Hz, 1H), 5.80 (dt, $J=6$, 2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.6, 18.2, 26.0, 40.4, 40.6, 40.8, 51.5, 77.3, 135.0, 135.7, 173.1. Anal. Calcd for $C_{14}H_{26}O_3Si$: C, 62.18; H, 9.69. Found: C, 61.86; H, 9.70.

4.2.4. (1*S*,4*S*)-4-[(*tert*-Butyldimethylsilyl)oxy]-2-cyclopenten-1-yl ethanal (9b). To a stirred solution of **16** (1.80 g, 6.66 mmol) in CH_2Cl_2 (26 mL) at −78 °C was added $(i\text{-Bu})_2AlH$ (7.98 mL, 0.95 M in hexane, 7.59 mmol) dropwise. After 45 min the solution was poured into a flask containing water (2.5 mL, 140 mmol) and ether with vigorous stirring. The mixture was stirred with NaF (2.8 g, 67 mmol) at room temperature for 30 min, and filtered through a pad of Celite. The filtrate was concentrated and purified by chromatography (hexane/EtOAc) to afford aldehyde **9b** (1.42 g, 89% yield) and the corresponding alcohol (138 mg, 9% yield): $[\alpha]_D^{30}$ −23 (*c* 0.38, $CHCl_3$); IR (neat) 1726, 1251, 836, 775 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.05 (s, 6H), 0.87 (s, 9H), 1.29 (ddd, $J=13$, 6, 5 Hz, 1H), 2.41–2.68 (m, 3H), 2.92–3.04 (m, 1H), 4.78–4.85 (m, 1H), 5.71–5.80 (m, 2H), 9.79 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.44, −4.42, 18.3, 26.1, 38.1, 40.9, 50.6, 77.2, 135.0, 135.4, 201.6. Anal. Calcd for $C_{13}H_{24}O_2Si$: C, 64.95; H, 10.06. Found: C, 64.96; H, 9.80.

4.2.5. (1*S*,4*R*,2′*Z*)-1-[(*tert*-Butyldimethylsilyl)oxy]-4-[7′-(4-methoxybenzyloxy)-2′-heptenyl]-2-cyclopentene (18). To an ice-cold slurry of $[PPh_3P(CH_2)_5OPMB]^+Br^-$ (**17**) (2.05 g, 3.73 mmol) in THF (25 mL) was added $NaN(TMS)_2$ (5.0 mL, 1.0 M in THF, 5.0 mmol) dropwise. After being stirred for 30 min at room temperature, the mixture was cooled to −70 °C and aldehyde **9b** (0.60 g, 2.50 mmol) was added to it. The temperature was kept at −70 °C for 1 h, and then allowed to increase gradually to room temperature over 2 h. The mixture was stirred overnight at ambient temperature and diluted with saturated

NH_4Cl and hexane. The organic layer was separated and the aqueous layer was extracted with hexane twice. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure to obtain an yellow oil, which was purified by chromatography (hexane/EtOAc) to afford **18** (0.90 g, 84% yield): IR (neat) 1612, 1513, 1249 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.07 (s, 6H), 0.89 (s, 9H), 1.22–1.32 (m, 1H), 1.35–1.48 (m, 2H), 1.54–1.66 (m, 2H), 1.98–2.25 (m, 4H), 2.36 (dt, $J=13$, 7 Hz, 1H), 2.46–2.58 (m, 1H), 3.43 (t, $J=7$ Hz, 2H), 3.78 (s, 3H), 4.42 (s, 2H), 4.78–4.86 (m, 1H), 5.33–5.46 (m, 2H), 5.70 (dt, $J=6$, 2 Hz, 1H), 5.78 (dt, $J=6$, 2 Hz, 1H), 6.87 (d, $J=9$ Hz, 2H), 7.26 (d, $J=9$ Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.34, −4.31, 18.4, 26.2, 26.5, 27.3, 29.6, 34.0, 40.8, 44.5, 55.4, 70.1, 72.6, 77.7, 113.8, 128.1, 129.2, 130.5, 130.8, 134.1, 136.7, 159.0. Anal. Calcd for $C_{26}H_{42}O_3Si$: C, 72.51; H, 9.83. Found: C, 72.84; H, 9.86.

4.2.6. (1*S*,4*R*,2′*Z*)-4-[7′-(4-Methoxybenzyloxy)-2′-heptenyl]-2-cyclopenten-1-ol (19). To an ice-cold solution of silyl ether **18** (1.21 g, 2.81 mmol) in THF (28 mL) was added TBAF (3.36 mL, 1.0 M in THF, 3.36 mmol). The solution was stirred at room temperature for 5 h and diluted with saturated NH_4Cl and EtOAc. The organic layer was separated and the aqueous layer was extracted with EtOAc twice. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure to obtain an oily residue, which was purified by chromatography (hexane/EtOAc) to afford **19** (835 mg, 95% yield): $[\alpha]_D^{26}$ +51 (*c* 0.51, $CHCl_3$); IR (neat) 3409, 1613, 1513, 1247 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.27 (dt, $J=14$, 5 Hz, 1H), 1.36–1.48 (m, 2H), 1.55–1.68 (m, 2H), 1.93 (br s, 1H), 1.98–2.25 (m, 4H), 2.43 (dt, $J=14$, 8 Hz, 1H), 2.56–2.68 (m, 1H), 3.43 (t, $J=6$ Hz, 2H), 3.79 (s, 3H), 4.42 (s, 2H), 4.71–4.82 (m, 1H), 5.30–5.52 (m, 2H), 5.74–5.81 (m, 1H), 5.82–5.88 (m, 1H), 6.87 (d, $J=9$ Hz, 2H), 7.26 (d, $J=9$ Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.3, 27.2, 29.4, 33.7, 39.8, 44.5, 55.3, 70.0, 72.5, 77.2, 113.7, 127.6, 129.2, 130.6, 131.1, 133.4, 138.1, 159.0. Anal. Calcd for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92. Found: C, 75.85; H, 9.12.

4.2.7. (4*R*,2′*Z*)-4-[7′-(4-Methoxybenzyloxy)-2′-heptenyl]-2-cyclopenten-1-one (10). A mixture of alcohol **19** (750 mg, 2.37 mmol) and PCC (1.02 g, 4.73 mmol) in CH_2Cl_2 (23 mL) was stirred vigorously at room temperature for 3 h and diluted with ether. The resulting mixture was filtered through a short pad of Celite. The filtrate was concentrated to furnish an yellow residue, which was purified by chromatography (hexane/EtOAc) to afford enone **10** (693 mg, 93% yield): $[\alpha]_D^{29}$ +106 (*c* 0.39, $CHCl_3$); IR (neat) 1711, 1612, 1586, 1512, 1247 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.36–1.49 (m, 2H), 1.54–1.67 (m, 2H), 1.95–2.08 (m, 3H), 2.12–2.34 (m, 2H), 2.50 (dd, $J=19$, 6 Hz, 1H), 2.93–3.03 (m, 1H), 3.43 (t, $J=6$ Hz, 2H), 3.79 (s, 3H), 4.42 (s, 3H), 5.28–5.40 (m, 1H), 5.43–5.56 (m, 1H), 6.15 (dd, $J=6$, 2 Hz, 1H), 6.87 (d, $J=9$ Hz, 2H), 7.26 (d, $J=9$ Hz, 2H), 7.61 (dd, $J=6$, 2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.3, 27.2, 29.5, 32.0, 40.6, 41.5, 55.3, 69.9, 72.6, 113.7, 125.7, 129.2, 130.6, 132.4, 134.0, 159.0, 167.9, 209.6. Anal. Calcd for $C_{13}H_{26}O_3$: C, 76.40; H, 8.33. Found: C, 76.12; H, 8.30.

4.3. Synthesis of aldehyde 11

4.3.1. (2*S*,3*S*)-2,3-Epoxy-1-octanol (26). (*E*)-Octen-1-ol (**25**) (1.20 g, 9.36 mmol) was subjected to Sharpless epoxidation by using Ti(*i*-PrO)$_4$ (0.69 mL, 2.33 mmol), L-(+)-DIPT (0.59 mL, 2.78 mmol), *t*-BuOOH (2.3 mL, 5.71 M in CH_2Cl_2, 13.1 mmol) over activated 4 Å molecular sieves (600 mg) at −20 °C for 9 h. After the reaction, H_2O (1.7 mL) and NaF (4.0 g, 95 mmol) were added. The resulting mixture was stirred vigorously for 30 min at room temperature and filtered through a pad of Celite. The filtrate was concentrated to obtain an yellow residue, which was diluted with CH_2Cl_2 (10 mL). Brine and 30% NaOH (4 mL) were added to the solution, and the mixture was stirred at room temperature for 20 min. The phases were separated and the aqueous layer was extracted with CH_2Cl_2 two times. The combined organic layers were dried over $MgSO_4$ and concentrated to afford an oil, which was purified by chromatography (hexane/EtOAc) to furnish epoxy alcohol **26** (1.11 g, 82% yield): $[\alpha]_D^{24}$ −43 (*c* 0.45, $CHCl_3$); lit.[24] $[\alpha]_D^{25}$ −42.7 (*c* 4.7, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, $J=7$ Hz, 3H), 1.24–1.66 (m, 8H), 1.73 (br t, $J=6$ Hz, 1H), 2.90–3.00 (m, 2H), 3.58–3.70 (m, 1H), 3.87–3.97 (m, 1H). Anal. Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.85; H, 11.31.

4.3.2. (*S*)-1,3-Octanediol (27). To an ice-cold solution of epoxy alcohol **26** (150 mg, 1.04 mmol) in THF (4 mL) was added Red-Al (0.65 mL, 65% in toluene, 2.09 mmol) in a dropwise manner. After being stirred at 0 °C for 1 h and then at room temperature for 10 h, the solution was poured into a flask containing water (0.4 mL, 22 mmol) and ether (10 mL) at 0 °C with vigorous stirring. The mixture was stirred vigorously with NaF (350 mg, 8.3 mmol) for 30 min at ambient temperature, and filtered through a pad of Celite. The filtrate was concentrated and the residue was purified by chromatography (hexane/EtOAc) to afford 1,3-diol **27** (134 mg, 88% yield): IR (neat) 3350, 1055 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, $J=7$ Hz, 3H), 1.22–1.54 (m, 8H), 1.58–1.78 (m, 2H), 2.61 (br s, 1H), 2.70 (br s, 1H), 3.76–3.94 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.7, 25.3, 31.9, 37.8, 38.3, 61.9, 72.4. Anal. Calcd for $C_8H_{18}O_2$: C, 65.71; H, 12.41. Found: C, 65.95; H, 12.39.

4.3.3. (*S*)-3-[(*tert*-Butyldimethylsilyl)oxy]-octan-1-ol (28). A solution of diol **27** (1.70 g, 11.6 mmol), TBSCl (5.25 g, 34.8 mmol), and imidazole (3.16 g, 46.4 mmol) in DMF (22 mL) was stirred at room temperature for 3 h, and diluted with saturated $NaHCO_3$ and hexane with vigorous stirring. The organic layer was separated and the aqueous layer was extracted with hexane several times. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure to obtained an oily residue, which was purified by chromatography (hexane/EtOAc) to obtain the corresponding disilyl ether (3.64 g, 94% yield): ^1H NMR (300 MHz, $CDCl_3$) δ 0.04 (s, 12H), 0.88 (s, 9H), 0.89 (s, 9H), 0.86–0.90 (m, 3H), 1.20–1.48 (m, 9H), 1.64 (q, $J=6$ Hz, 1H), 3.62–3.73 (m, 2H), 3.79 (quintet, $J=6$ Hz, 1H).

A solution of the above disilyl ether (380 mg, 1.14 mmol) and PPTS (342 mg, 1.36 mmol) in EtOH (6 mL) and CH_2Cl_2 (6 mL) was stirred for 14 h at room temperature,

and diluted with saturated NH_4Cl and EtOAc. The phases were separated and the aqueous layer was extracted with EtOAc twice. The combined organic portions were dried over $MgSO_4$ and concentrated under reduced pressure to obtained an oily residue, which was purified by chromatography (hexane/EtOAc) to afford alcohol **28** (226 mg, 76% yield) and diol **27** (26 mg, 16% yield). Diol **27** was recycled. Alcohol **28**: $[\alpha]_D^{27}$ +18 (*c* 0.62, $CHCl_3$); IR (neat) 3350, 1255, 1058, 836, 774 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.07 (s, 3H), 0.08 (s, 3H), 0.89 (br s, 9H), 0.85–0.91 (m, 3H), 1.20–1.36 (m, 6H), 1.45–1.56 (m, 2H), 1.57–1.70 (m, 1H), 1.74–1.87 (m, 1H), 2.55 (br s, 1H), 3.65–3.76 (m, 1H), 3.77–3.95 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.5, −4.2, 14.2, 18.2, 22.8, 25.2, 26.0, 32.1, 36.9, 37.8, 60.4, 72.1. Anal. Calcd for $C_{14}H_{32}O_2Si$: C, 64.55; H, 12.38. Found: C, 64.40; H, 12.27.

4.3.4. (*S*)-3-[(*tert*-Butyldimethylsilyl)oxy]octanal (11). A mixture of alcohol **28** (1.18 g, 4.53 mmol) and PCC (1.95 g, 9.05 mmol) in CH_2Cl_2 (45 mL) was stirred vigorously at room temperature for 3 h and diluted with ether. The resulting mixture was filtered through a pad of Celite and the filtrate was concentrated under reduced pressure. An yellow oil obtained was purified by chromatography (hexane/EtOAc) to afford aldehyde **11** (1.10 g, 94% yield): $[\alpha]_D^{27}$ +6.7 (*c* 0.21, $CHCl_3$); lit.[26] $[\alpha]_D^{24}$ −5.0 (*c* 1.0, $CHCl_3$) for the enantiomer of >98% ee; IR (neat) 1713, 1256, 1095, 836, 776 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.05 (s, 3H), 0.07 (s, 3H), 0.87 (br s, 9H), 0.84–0.92 (m, 3H), 1.18–1.40 (m, 6H), 1.45–1.60 (m, 2H), 2.51 (dd, *J*=6, 2 Hz, 2H), 4.17 (quintet, *J*=6 Hz, 1H), 9.81 (t, *J*=2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.5, −4.2, 14.2, 18.2, 22.8, 25.0, 31.9, 38.0, 51.0, 68.4, 202.3.

4.4. Synthesis of Δ^{12}-PGJ$_2$ (3)

4.4.1. Dienone 12. To an ice-cold solution of $(i\text{-Pr})_2NH$ (0.15 mL, 1.07 mmol) in THF (4 mL) was added *n*-BuLi (0.37 mL, 1.90 M in hexane, 0.703 mmol). The solution was stirred at 0 °C for 20 min to generate LDA and then cooled to −78 °C. A solution of enone **10** (109 mg, 0.347 mmol) in THF (2 mL) was added into the LDA solution. After 20 min of stirring at the same temperature, aldehyde **11** (108 mg, 0.418 mmol) dissolved in THF (1 mL) was added. The solution was stirred for 30 min at the same temperature, and poured into a flask containing saturated NH_4Cl and ether with vigorous stirring. After 15 min, the organic layer was separated and the aqueous layer was extracted with EtOAc twice. The combined extracts were dried over $MgSO_4$ and concentrated to afford aldol **20** as a mixture of *anti* and *syn* isomers. The ratio of the mixture was ca. 3:1 by ^1H NMR spectroscopy (δ 2.78–2.92 (m) and 3.00–3.11 (m) for *anti* and *syn* isomers, respectively) and TLC analysis. After being passed through a short column of silica gel (hexane/EtOAc), the crude aldol was used for the next reaction.

To an ice-cold solution of the above aldol **20** dissolved in CH_2Cl_2 (3.5 mL) were added Et_3N (0.24 mL, 1.72 mmol) and MsCl (0.053 mL, 0.685 mmol). The solution was stirred for 45 min at the same temperature, and diluted with saturated $NaHCO_3$. The product was extracted with EtOAc repeatedly. The combined organic layers were dried over $MgSO_4$ and concentrated to furnish mesylate **21** as an yellow oil. After being passed through a short column of silica gel (hexane/EtOAc), the crude mesylate was subjected to the next reaction.

To a slurry of activated alumina (350 mg, ICN, N-Super I, activated by heating on a heater for 20 min under vacuum) in CH_2Cl_2 (5 mL) was added a solution of the crude mesylate **21** in CH_2Cl_2 (2 mL). The mixture was stirred vigorously at room temperature for 10 h and filtered through a pad of Celite with CH_2Cl_2. The filtrate was concentrated under reduced pressure to furnish an yellow oil, which was purified by chromatography (hexane/EtOAc) to afford dienone **12** (114 mg, 59% yield from enone **10**): $[\alpha]_D^{26}$ +96 (*c* 0.43, $CHCl_3$); IR (neat) 1705, 1657, 1513, 1249 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.04 (s, 3H), 0.05 (s, 3H), 0.80–0.96 (m, 12H), 1.20–1.64 (m, 12H), 2.00 (q, *J*=7 Hz, 2H), 2.17 (dt, *J*=15, 9 Hz, 1H), 2.39–2.46 (m, 2H), 2.55–2.67 (m, 1H), 3.43 (t, *J*=7 Hz, 3H), 3.80 (s, 3H), 3.78–3.88 (m, 1H), 4.42 (s, 2H), 5.28–5.40 (m, 1H), 5.42–5.56 (m, 1H), 6.32 (dd, *J*=6, 1.5 Hz, 1H), 6.60 (t, *J*=8 Hz, 1H), 6.87 (d, *J*=8 Hz, 2H), 7.25 (d, *J*=8 Hz, 2H), 7.49 (dd, *J*=6, 2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.4, −4.2, 14.2, 18.3, 22.8, 25.1, 26.0, 26.4, 27.3, 29.6, 30.7, 32.1, 37.4, 37.5, 43.6, 55.4, 70.0, 71.6, 72.6, 113.8, 125.1, 129.2, 130.7, 132.45, 132.51, 134.8, 138.7, 159.0, 161.5, 196.2.

4.4.2. Aldehyde 23. To an ice-cold solution of dienone **12** (108 mg, 0.195 mmol) in CH_2Cl_2 (3.8 mL) and water (0.2 mL) was added DDQ (66 mg, 0.29 mmol). The mixture was stirred at 0 °C for 45 min and filtered through a pad of Celite using ether. The filtrate was concentrated, and a reddish brown residue produced was purified by chromatography (hexane/EtOAc) to furnish alcohol **22** (77 mg, 91% yield): IR (neat) 3441, 1701, 1654, 1075 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.04 (s, 3H), 0.05 (s, 3H), 0.80 (br s, 12H), 1.2–1.7 (m, 12H), 1.95–2.30 (m, 3H), 2.39–2.46 (m, 2H), 2.55–2.67 (m, 1H), 3.43–3.48 (m, 1H), 3.65 (t, *J*=7 Hz, 2H), 3.78–3.90 (m, 1H), 5.28–5.40 (m, 1H), 5.42–5.56 (m, 1H), 6.32 (dd, *J*=6, 1.5 Hz, 1H), 6.60 (t, *J*=8 Hz, 1H), 7.49 (dd, *J*=6, 2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.4, −4.2, 14.2, 18.3, 22.8, 25.1, 25.9, 26.0, 27.3, 30.8, 32.1, 32.5, 37.5, 43.6, 62.8, 71.7, 125.3, 132.4, 132.6, 134.8, 138.7, 161.5, 196.2.

A mixture of alcohol **22** (45 mg, 0.104 mmol) and PCC (45 mg, 0.209 mmol) in CH_2Cl_2 (1 mL) was stirred for 2.5 h at room temperature, diluted with ether, and filtered through a short pad of Celite. The filtrate was concentrated, and an yellow residue obtained was purified by chromatography (hexane/EtOAc) to afford aldehyde **23** (42 mg, 94% yield): $[\alpha]_D^{29}$ +57 (*c* 0.14, $CHCl_3$); IR (neat) 1709, 1649, 836, 775 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.04 (s, 3H), 0.05 (s, 3H), 0.87 (s, 9H), 0.83–0.91 (m, 3H), 1.16–1.52 (m, 8H), 1.60–1.76 (m, 2H), 2.04 (q, *J*=7 Hz, 2H), 2.12–2.26 (m, 1H), 2.30–2.54 (m, 4H), 2.56–2.68 (m, 1H), 3.40–3.52 (m, 1H), 3.78–3.90 (m, 1H), 5.30–5.53 (m, 2H), 6.33 (dd, *J*=6, 2 Hz, 1H), 6.60 (t, *J*=8 Hz, 1H), 7.48 (dd, *J*=6, 2.5 Hz, 1H), 9.76 (t, *J*=1.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.4, −4.2, 14.2, 18.3, 22.0, 22.8, 25.1, 26.0, 26.8, 30.7, 32.1, 37.4, 37.5, 43.40, 43.44, 71.6, 126.2, 131.2, 132.7, 135.0, 138.5, 161.2, 196.1, 201.9.

4.4.3. Acid 24. To a slurry of aldehyde **23** (42 mg, 0.097 mmol) in *t*-BuOH (1.3 mL), phosphate buffer of pH 3.6 (0.61 mL), and 2-methyl-2-butene (0.105 mL, 0.99 mmol) was added $NaClO_2$ (17 mg, 0.15 mmol, purity 80%) in water (0.5 mL) and the resulting mixture was stirred at room temperature. After 3 h, *t*-BuOH was removed by using a vacuum pump and the phosphate buffer (pH 3.6) was added to the residue. The product was extracted with EtOAc several times. The combined organic layers were dried over $MgSO_4$ and concentrated to afford an oily residue, which was purified by chromatography (CH_2Cl_2/EtOH) to furnish acid **24** (39 mg, 89% yield): IR (neat) 3100, 1710, 1652, 1252, 836, 775 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.05 (s, 6H), 0.84–0.92 (m, 12H), 1.18–1.52 (m, 8H), 1.69 (quintet, $J=7$ Hz, 2H), 2.00–2.22 (m, 3H), 2.34 (t, $J=7$ Hz, 2H), 2.40–2.48 (m, 2H), 2.60–2.70 (m, 1H), 3.41–3.50 (m, 1H), 3.78–3.90 (m, 1H), 5.32–5.56 (m, 2H), 6.33 (dd, $J=6$, 1 Hz, 1H), 6.60 (t, $J=8$ Hz, 1H), 7.50 (dd, $J=6$, 2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.4, −4.2, 14.2, 18.3, 22.8, 24.6, 25.1, 26.0, 26.8, 30.7, 32.0, 33.3, 37.4, 37.5, 43.6, 71.8, 126.2, 131.3, 132.7, 134.9, 138.6, 161.5, 178.1, 196.3.

4.4.4. Δ^{12}-PGJ$_2$ (3). To an ice-cold flask containing acid **24** (9 mg, 0.020 mmol) was added a solution of HF in MeCN (0.2 mL), which had been prepared by mixing 55% HF and MeCN in a 1:19 ratio. The solution was stirred at 0 °C for 15 min and poured into brine. The product was extracted with EtOAc several times. The combined extracts were dried over $MgSO_4$ and concentrated to leave an oil, which was purified by chromatography (CH_2Cl_2/EtOH) to furnish Δ^{12}-PGJ$_2$ (**3**) (6.2 mg, 92% yield): IR (neat) 3409, 1699, 1653 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.88 (t $J=7$ Hz, 3H), 1.20–1.80 (m, 10H), 2.06–2.18 (m, 3H), 2.26–2.63 (m, 4H), 2.66–2.78 (m, 1H), 3.42–3.54 (m, 1H), 3.78–3.92 (m, 1H), 5.1–5.9 (br s, 4H), 6.35 (dd, $J=6$, 2 Hz, 1H), 6.59 (t, $J=8$ Hz, 1H), 7.56 (dd, $J=6$, 2 Hz, 1H). The ^1H NMR spectrum was identical with that provided by Ono Pharmaceutical Co., Ltd.

4.5. Synthesis of 15-deoxy-$\Delta^{12,14}$-PGJ$_2$ (4)

4.5.1. Dienone 31 through aldol 30. To a solution of *i*-Pr_2NH (0.22 mL, 1.57 mmol) in THF (10 mL) at 0 °C was added *n*-BuLi (0.58 mL, 2.20 M in hexane, 1.28 mmol). The solution was stirred at the same temperature for 20 min to prepare LDA, and cooled to −78 °C. A solution of enone **10** (200 mg, 0.636 mmol) in THF (3 mL) was added into the LDA solution dropwise, and the solution was stirred for 20 min. (*E*)-2-Octenal (**29**) (0.115 mL, 0.771 mmol) was added to the solution. After 20 min at the same temperature, the solution was poured into a flask containing saturated NH_4Cl and ether with vigorous stirring. The organic layer was separated and the aqueous layer was extracted with EtOAc. The combined organic extracts were dried over $MgSO_4$ and concentrated to afford aldol **30** as a mixture of the *anti* and *syn* isomers in a 2:1 ratio by ^1H NMR spectroscopy (*anti* isomer, δ 4.14 (t, $J=$ 8 Hz); *syn* isomer, δ 4.49–4.58 (m)). The aldol product **30** was subjected to the next reaction after filtration through a short column of silica gel (hexane/EtOAc).

The aldol reaction was repeated, and the stereoisomers were separated by chromatography on silica gel (hexane/EtOAc). *anti* Isomer: ^1H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, $J=7$ Hz, 3H), 1.16–1.48 (m, 8H), 1.52–1.66 (m, 2H), 1.94–2.14 (m, 5H), 2.15–2.37 (m, 2H), 2.64–2.72 (m, 1H), 3.43 (t, $J=7$ Hz, 2H), 3.80 (s, 3H), 3.95 (br s, 1H), 4.14 (t, $J=8$ Hz, 1H), 4.42 (s, 2H), 5.26–5.37 (m, 1H), 5.39–5.58 (m, 2H), 5.73 (dt, $J=15$, 7 Hz, 1H), 6.14 (dd, $J=6$, 2 Hz, 1H), 6.87 (d, $J=9$ Hz, 2H), 7.25 (d, $J=9$ Hz, 2H), 7.62 (dd, $J=6$, 2 Hz, 1H). *syn* Isomer: ^1H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, $J=7$ Hz, 3H), 1.16–1.50 (m, 7H), 1.53–1.76 (m, 3H), 1.94–2.14 (m, 4H), 2.15–2.38 (m, 3H), 2.59 (d, $J=6$ Hz, 1H), 2.82–2.94 (m, 1H), 3.43 (t, $J=7$ Hz, 2H), 3.80 (s, 3H), 4.42 (s, 2H), 4.49–4.59 (m, 1H), 5.28–5.57 (m, 3H), 5.73 (dt, $J=15$, 7 Hz, 1H), 6.15 (dd, $J=6$, 2 Hz, 1H), 6.87 (d, $J=9$ Hz, 2H), 7.25 (d, $J=9$ Hz, 2H), 7.63 (dd, $J=6$, 2 Hz, 1H).

To a solution of the above aldol **30** in CH_2Cl_2 (6 mL) and Et_3N (0.88 mL, 6.31 mmol) at −15 °C was added MsCl (0.20 mL, 2.58 mmol) dropwise. After 45 min at the same temperature, the reaction was quenched by addition of saturated $NaHCO_3$. The organic layer was separated and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over $MgSO_4$ and concentrated to furnish an yellow residue, which was subjected to chromatography (hexane/EtOAc) to afford dienone **31** (185 mg, 69% yield from enone **10**) and its (*Z*)-isomer **34** (14 mg, 5%). Dienone **31**: IR (neat) 1685, 1631, 1512, 1248 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.89 (t, $J=$ 7 Hz, 3H), 1.1–1.6 (m, 10H), 2.01 (q, $J=7$ Hz, 2H), 2.16–2.35 (m, 3H), 2.58 (dt, $J=14$, 6 Hz, 1H), 3.42 (t, $J=6$ Hz, 2H), 3.51–3.60 (m, 1H), 3.80 (s, 3H), 4.42 (s, 2H), 5.27–5.39 (m, 1H), 5.41–5.53 (m, 1H), 6.15–6.39 (m, 3H), 6.87 (d, $J=8$ Hz, 2H), 6.94 (d, $J=11$ Hz, 1H), 7.25 (d, $J=8$ Hz, 2H), 7.46 (dd, $J=6$, 2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 22.6, 26.4, 27.3, 28.6, 29.6, 31.0, 31.5, 33.6, 43.7, 55.4, 70.0, 72.6, 113.8, 125.1, 125.7, 129.2, 130.6, 131.6, 132.5, 135.1, 135.2, 146.7, 159.0, 160.7, 197.2. (*Z*)-Isomer **34**: IR (neat) 1684, 1634, 1512, 1248 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, $J=7$ Hz, 3H), 1.20–1.66 (m, 10H), 2.01 (q, $J=7$ Hz, 2H), 2.16–2.36 (m, 3H), 2.44 (dt, $J=14$, 7 Hz, 1H), 3.29–3.38 (m, 1H), 3.42 (t, $J=6$ Hz, 2H), 3.80 (s, 3H), 4.42 (s, 2H), 5.28–5.56 (m, 2H), 6.06 (dt, $J=$ 15, 7 Hz, 1H), 6.28 (dd, $J=6$, 2 Hz, 1H), 6.43 (d, $J=11$ Hz, 1H), 6.87 (d, $J=9$ Hz, 2H), 7.25 (d, $J=9$ Hz, 2H), 7.37 (dd, $J=6$, 2 Hz, 1H), 7.66 (ddt, $J=15$, 11, 2 Hz, 1H).

4.5.2. Aldehyde 33 through alcohol 32. To an ice-cold solution of PMB ether **31** (53 mg, 0.125 mmol) in CH_2Cl_2 (1.2 mL) and water (0.1 mL) was added DDQ (43 mg, 0.19 mmol). After 45 min, the reaction was quenched by addition of saturated $NaHCO_3$ and ether. The organic layer was separated and the aqueous layer was extracted with ether twice. The combined organic fractions were dried over $MgSO_4$ and concentrated to obtained an yellow residue, which was purified by chromatography (hexane/EtOAc) to furnish alcohol **32** (35 mg, 92% yield): IR (neat) 3421, 1685, 1629 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, $J=7$ Hz, 3H), 1.1–1.7 (m, 11H), 2.02 (q, $J=7$ Hz, 2H), 2.16–2.38 (m, 3H), 2.54–2.66 (m, 1H), 3.50–3.70 (m, 3H), 5.25–5.60 (m, 2H), 6.16–6.31 (m, 2H), 6.32–6.40 (m, 1H), 6.95 (d, $J=11$ Hz, 1H), 7.48 (dd, $J=6$, 2 Hz, 1H).

To an ice-cold solution of alcohol **32** (35 mg, 0.116 mmol) in CH_2Cl_2 (1.2 mL) was added PCC (37 mg, 0.17 mmol).

The mixture was stirred vigorously at room temperature for 2.5 h, and diluted with Et_2O. The resulting mixture was filtered through a short pad of Celite. The filtrate was concentrated, and the residue was purified by chromatography (hexane/EtOAc) to afford aldehyde **33** (32 mg, 92% yield): IR (neat) 1727, 1695, 1632, 1206 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.89 (t, $J=7$ Hz, 3H), 1.20–1.72 (m, 8H), 2.02 (q, $J=7$ Hz, 2H), 2.16–2.44 (m, 5H), 2.58 (dt, $J=15$, 5 Hz, 1H), 3.54–3.62 (m, 1H), 5.28–5.52 (m, 2H), 6.14–6.40 (m, 3H), 6.94 (d, $J=11$ Hz, 1H), 7.45 (dd, $J=6$, 3 Hz, 1H), 9.75 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 22.0, 22.7, 26.8, 28.7, 30.9, 31.6, 33.6, 43.4, 43.6, 125.6, 126.1, 131.3, 131.6, 135.0, 135.3, 146.9, 160.4, 197.1, 202.0.

4.5.3. 15-Deoxy-$\Delta^{12,14}$-PGJ_2 (4). To a slurry of aldehyde **33** (32 mg, 0.106 mmol) in *t*-BuOH (1.4 mL), phosphate buffer of pH 3.6 (0.66 mL), and 2-methyl-2-butene (0.11 mL, 1.04 mmol) was added $NaClO_2$ (18 mg, 0.16 mmol, 80% purity) in water (0.53 mL). The mixture was stirred at ambient temperature for 3 h, and concentrated by using a vacuum pump. Phosphate buffer of pH 3.6 was added to the residue, and the mixture was extracted with EtOAc several times. The combined organic layers were dried over $MgSO_4$ and concentrated to afford an oily residue, which was purified by chromatography (CH_2Cl_2/EtOH) to furnish 15-deoxy-$\Delta^{12,14}$-PGJ_2 (**4**) (31 mg, 93% yield): $[\alpha]_D^{26}$ +193 (*c* 0.17, $CHCl_3$) (lit.[13] $[\alpha]_D$ +194.3 (*c* 0.7, $CHCl_3$)); IR (neat) 3303, 1707, 1628, 1209 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.89 (t, $J=7$ Hz, 3H), 1.15–1.54 (m, 6H), 1.67 (quintet, $J=7$ Hz, 2H), 2.05 (q, $J=7$ Hz, 2H), 2.16–2.40 (m, 5H), 2.54–2.66 (m, 1H), 3.54–3.62 (m, 1H), 3.6–5.0 (br s, 2H), 5.28–5.56 (m, 2H), 6.16–6.42 (m, 3H), 6.96 (d, $J=11$ Hz, 1H), 7.47 (dd, $J=6$, 2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 22.6, 24.6, 26.7, 28.6, 30.9, 31.6, 33.4, 33.6, 43.6, 125.6, 126.1, 131.3, 131.9, 135.0, 135.3, 147.0, 160.7, 178.5, 197.5.

The following ^1H NMR spectrum, measured at 500 MHz, unambiguously indicated the trans olefin geometry at C(14)–C(15): ^1H NMR (500 MHz, $CDCl_3$) δ 0.89 (t, $J=7$ Hz, 3H), 1.22–1.36 (m, 4H), 1.39–1.49 (m, 2H), 1.62–1.72 (m, 2H), 2.04 (q, $J=7$ Hz, 2H), 2.22 (q, $J=7$ Hz, 2H), 2.26–2.37 (m, 3H), 2.56–2.62 (m, 1H), 3.56–3.61 (m, 1H), 5.33–5.40 (m, 1H), 5.42–5.49 (m, 1H), 6.23 (dt, $J=15$, 7 Hz, 1H), 6.31 (ddt, $J=15$, 11, 1 Hz, 1H), 6.36 (dd, $J=6$, 2 Hz, 1H), 6.95 (d, $J=11$ Hz, 1H), 7.47 (ddd, $J=6$, 2.5, 1 Hz, 1H).

These spectra were in good agreement with the reported IR,[13] ^1H NMR (600 MHz),[13] and ^{13}C NMR (150, 75 MHz) spectra.[11,13]

4.6. Synthesis of 5,6-dehydro-Δ^{12}-PGJ_2 (5)

4.6.1. (1*S*,4*R*)-1-[(*tert*-Butyldimethylsilyl)oxy]-4-[3′,3′-dibromo-2′-propenyl]-2-cyclopentene (35). To an ice-cold solution of PPh_3 (436 mg, 1.66 mmol) in CH_2Cl_2 (3 mL) was added CBr_4 (276 mg, 0.832 mmol) portionwise. After vigorous stirring for 10 min, aldehyde **9b** (100 mg, 0.416 mmol) dissolved in CH_2Cl_2 (1.5 mL) was added slowly. The solution was stirred at 0 °C for 30 min and diluted with hexane. The resulting mixture was filtered through a pad of Celite with hexane and the filtrate was concentrated under reduced pressure to leave an oil, which was purified by chromatography (hexane) to afford dibromide **35** (125 mg, 76% yield): IR (neat) 3058, 1256, 1086, 836, 775 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.08 (s, 6H), 0.89 (s, 9H), 1.31 (dt, $J=13$, 5 Hz, 1H), 2.08–2.32 (m, 2H), 2.39 (dt, $J=13$, 8 Hz, 1H), 2.66 (quintet, $J=7$ Hz, 1H), 4.78–4.85 (m, 1H), 5.75 (s, 2H), 6.45 (t, $J=7$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.3, 18.4, 26.1, 39.2, 40.3, 42.8, 77.3, 89.3, 135.1, 135.5, 137.0. Anal. Calcd for $C_{14}H_{24}Br_2OSi$: C, 42.44; H, 6.11. Found: C, 42.93; H, 6.52.

4.6.2. (1*S*,4*R*)-1-[(*tert*-Butyldimethylsilyl)oxy]-4-(2′-propynyl)-2-cyclopentene (36). To a solution of **35** (115 mg, 0.290 mmol) in THF (3 mL) at −78 °C was added *n*-BuLi (0.32 mL, 2.25 M in hexane, 0.72 mmol) dropwise. After being stirred at −78 °C for 30 min, the reaction flask was immersed into an ice-water bath (0 °C). The reaction was continued for 30 min and quenched by addition of saturated NH_4Cl and hexane. The phases were separated and the aqueous layer was extracted with hexane. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure to leave an oil, which was purified by chromatography (hexane/EtOAc) to furnish acetylene **36** (62 mg, 91% yield): IR (neat) 3313, 1256, 1079, 836, 775 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.08 (s, 6H), 0.90 (s, 9H), 1.37 (ddd, $J=13$, 6, 5 Hz, 1H), 1.96 (t, $J=2.5$ Hz, 1H), 2.26 (d, $J=2.5$ Hz, 1H), 2.28 (d, $J=2.5$ Hz, 1H), 2.44 (dt, $J=13$, 8 Hz, 1H), 2.66–2.78 (m, 1H), 4.79–4.87 (m, 1H), 5.76 (dt, $J=6$, 2 Hz, 1H), 5.87 (dt, $J=6$, 2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.5, 18.3, 25.3, 26.0, 40.4, 43.4, 68.8, 77.4, 83.3, 135.2, 135.5. Anal. Calcd for $C_{14}H_{24}OSi$: C, 71.12; H, 10.23. Found: C, 71.22; H, 10.51.

4.6.3. (1*S*,4*R*)-4-[7′-(4-Methoxybenzyloxy)-2′-heptynyl]-2-cyclopenten-1-ol (37). To a solution of acetylene **36** (180 mg, 0.761 mmol) in THF (6 mL) at −78 °C was added *n*-BuLi (0.76 mL, 1.90 M in hexane, 1.44 mmol) dropwise. After 20 min of stirring at the same temperature, DMPU (1.5 mL) and $PMBO(CH_2)_4Br$ (250 mg, 0.915 mmol) were added. The reaction was conducted at −78 °C for 1 h, and then gradually warmed to room temperature over 10 h. The mixture was diluted with saturated NH_4Cl and hexane. The organic layer was separated and the aqueous layer was extracted with hexane twice. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure to obtain an oil containing acetylene **13** and $PMBO(CH_2)_4Br$. This residue was passed through a short pad of silica gel for the next reaction: ^1H NMR (300 MHz, $CDCl_3$) (characteristic peaks only) δ 3.40–3.52 (m, 2H), 3.80 (s, 3H), 4.42 (s, 2H), 4.78–4.87 (m, 1H), 5.73 (dt, $J=6$, 2 Hz, 1H), 5.86 (dt, $J=6$, 2 Hz, 1H), 6.87 (d, $J=9$ Hz, 2H), 7.26 (d, $J=9$ Hz, 2H).

To an ice-cold solution of the above product dissolved in THF (8 mL) was added *n*-Bu_4NF (1.14 mL, 1.0 M in THF, 1.14 mmol). The solution was stirred at room temperature for 3 h and diluted with saturated NH_4Cl and EtOAc. The organic layer was separated, and the aqueous layer was extracted with EtOAc three times. The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure to leave an oil, which was purified by chromatography (hexane/EtOAc) to afford alcohol **37** (193 mg, 81% yield in two steps): $[\alpha]_D^{28}$ +50 (*c* 0.31, $CHCl_3$); IR (neat) 3420, 1612, 1513, 1248 cm^{-1}; ^1H NMR

(300 MHz, $CDCl_3$) δ 1.42 (dt, $J=14$, 4 Hz, 1H), 1.50–1.75 (m, 4H), 1.89–1.97 (m, 1H), 2.12–2.22 (m, 2H), 2.28–2.36 (m, 2H), 2.45 (dt, $J=14$, 8 Hz, 1H), 2.74–2.84 (m, 1H), 3.44 (t, $J=6$ Hz, 2H), 3.80 (s, 3H), 4.42 (s, 2H), 4.73 (br s, 1H), 5.83 (dd, $J=6$, 2 Hz, 1H), 5.88 (dt, $J=6$, 2 Hz, 1H), 6.87 (d, $J=9$ Hz, 2H), 7.26 (d, $J=9$ Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.6, 25.1, 25.9, 29.0, 39.1, 43.5, 55.3, 69.6, 72.6, 76.9, 79.2, 81.7, 113.7, 129.2, 130.6, 134.3, 137.0, 159.0. Anal. Calcd for $C_{20}H_{26}O_3$: C, 76.40; H, 8.33. Found: C, 76.25; H, 8.12.

4.6.4. (*R*)-4-[7′-(4-Methoxybenzyloxy)-2′-heptynyl]-2-cyclopenten-1-one (38). A mixture of alcohol **37** (190 mg, 0.604 mmol) and PCC (195 mg, 0.905 mmol) in CH_2Cl_2 (6 mL) was stirred for 1 h, diluted with ether, and filtered through a pad of Celite. The filtrate was concentrated to obtain an yellow residue, which was purified by chromatography (hexane/EtOAc) to furnish enone **38** (177 mg, 94% yield): $[\alpha]_D^{28}$ +107 (*c* 0.62, $CHCl_3$); IR (neat) 1714, 1612, 1512, 1247 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.50–1.72 (m, 4H), 2.08–2.21 (m, 3H), 2.34–2.44 (m, 2H), 2.52 (dd, $J=19$, 7 Hz, 1H), 3.06–3.16 (m, 1H), 3.45 (t, $J=6$ Hz, 2H), 3.80 (s, 3H), 4.43 (s, 2H), 6.20 (dd, $J=6$, 2 Hz, 1H), 6.87 (d, $J=8$ Hz, 2H), 7.26 (d, $J=8$ Hz, 2H), 7.63 (dd, $J=6$, 3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.6, 24.0, 25.8, 29.0, 40.2, 40.6, 55.4, 69.6, 72.6, 76.4, 82.4, 113.7, 129.2, 130.6, 134.6, 159.0, 166.7, 209.2. Anal. Calcd for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74. Found: C, 76.52; H, 8.99.

4.6.5. Dienone 40. According to the aldol reaction of enone **10** and aldehyde **11**, a solution of LDA was prepared (0 °C, 20 min) from *i*-Pr_2NH (0.23 mL, 1.64 mmol) and *n*-BuLi (0.67 mL, 1.90 M in hexane, 1.27 mmol) in THF (9 mL) and used for preparation of the anion from enone **38** (200 mg, 0.64 mmol) in THF (2 mL) at −78 °C for 20 min. Aldehyde **11** (199 mg, 0.77 mmol) in THF (2 mL) was added to the solution, and, after 20 min, the solution was poured into a flask containing saturated NH_4Cl and ether with vigorous stirring. Aldol **39**, thus synthesized as a mixture of the *anti* and *syn* isomers (ca. 3:1 by TLC), was subjected to the next reaction after filtration through a short column of silica gel (hexane/EtOAc).

According to the conversion of aldol **20** to dienone **12**, the above aldol **39** in CH_2Cl_2 (6.5 mL) was converted into the mesylate with MsCl (0.10 mL, 1.29 mmol) and Et_3N (0.45 mL, 3.23 mmol) at 0 °C for 45 min. This mesylate, after being passed through a short column of silica gel (hexane/EtOAc), was dissolved in CH_2Cl_2 (2 mL) and the solution was added to a slurry of alumina (496 mg, ICN Alumina N-Super I, activated by heating on a heater for 20 min under vacuum) in CH_2Cl_2 (7 mL). After 13 h at room temperature, the mixture was filtered through a pad of Celite, and the filtrate was concentrated to furnish an yellow residue, which was purified by chromatography (hexane/EtOAc) to afford dienone **40** (151 mg, 43% yield from enone **38**): $[\alpha]_D^{28}$ +98 (*c* 0.38, $CHCl_3$); IR (neat) 1708, 1662, 1515, 1246 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.04 (s, 3H), 0.05 (s, 3H), 0.88 (s, 9H), 0.84–0.92 (m, 3H), 1.16–1.74 (m, 12H), 2.10–2.28 (m, 3H), 2.35–2.44 (m, 2H), 2.70–2.82 (m, 1H), 3.45 (t, $J=6$ Hz, 2H), 3.48–3.58 (m, 1H), 3.80 (s, 3H), 3.70–3.92 (m, 1H), 4.42 (s, 2H), 6.37 (dd, $J=6$, 1.5 Hz, 1H), 6.61 (t, $J=8$ Hz, 1H), 6.87 (d, $J=8$ Hz, 2H), 7.26 (d, $J=8$ Hz, 2H), 7.65 (dd, $J=6$, 2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.4, −4.1, 14.2, 18.3, 18.7, 22.8, 23.2, 25.1, 25.8, 26.0, 29.1, 32.1, 37.4, 37.5, 43.0, 55.4, 69.7, 71.6, 72.7, 76.5, 82.8, 113.8, 129.2, 130.6, 133.0, 135.3, 137.9, 159.0, 161.0, 195.8.

4.6.6. Alcohol 41. A solution of dienone **40** (102 mg, 0.184 mmol) in CH_2Cl_2 (2 mL) and water (0.1 mL) was treated with DDQ (63 mg, 0.278 mmol) at 0 °C for 45 min, and diluted with saturated $NaHCO_3$ and ether to obtain an yellow residue, which was purified by chromatography (hexane/EtOAc) to furnish alcohol **41** (73 mg, 91% yield): $[\alpha]_D^{29}$ +158 (*c* 0.61, $CHCl_3$); IR (neat) 3441, 1703, 1653 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.03 (s, 3H), 0.04 (s, 3H), 0.87 (s, 9H), 0.82–0.90 (m, 3H), 1.1–1.7 (m, 12H), 1.87 (br s, 1H), 2.10–2.20 (m, 2H), 2.28–2.48 (m, 3H), 2.72 (ddt, $J=17$, 4, 2 Hz, 1H), 3.50–3.59 (m, 1H), 3.61 (t, $J=6$ Hz, 2H), 3.82 (quintet, $J=6$ Hz, 1H), 6.39 (dd, $J=6$, 2 Hz, 1H), 6.61 (t, $J=8$ Hz, 1H), 6.59 (dd, $J=6$, 2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.4, −4.2, 14.2, 18.2, 18.6, 22.8, 22.9, 25.1, 25.2, 26.0, 31.9, 32.0, 37.3, 37.4, 42.8, 62.5, 71.5, 76.3, 82.9, 133.1, 135.4, 137.8, 160.9, 196.2.

4.6.7. Acid 42. A mixture of alcohol **41** (20 mg, 0.046 mmol) and PCC (15 mg, 0.069 mmol) in CH_2Cl_2 (1 mL) was stirred vigorously at room temperature for 2 h, and diluted with ether to afford the corresponding aldehyde (18 mg, 90% yield) after chromatography (hexane/EtOAc): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.04 (s, 3H), 0.05 (s, 3H), 0.88 (s, 9H), 0.84–0.92 (m, 3H), 1.16–1.50 (m, 8H), 1.72–1.84 (m, 2H), 2.16–2.50 (m, 5H), 2.53 (dt, $J=1.5$, 7 Hz, 2H), 2.75 (ddt, $J=17$, 4.5, 3 Hz, 1H), 2.68–2.82 (m, 1H), 3.50–3.60 (m, 1H), 3.83 (quintet, $J=6$ Hz, 1H), 6.39 (dd, $J=6$, 1.5 Hz, 1H), 6.61 (t, $J=8$ Hz, 1H), 7.60 (dd, $J=6$, 2 Hz, 1H), 9.79 (t, $J=1.5$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.4, −4.1, 14.2, 18.26, 18.32, 21.5, 22.8, 23.0, 25.1, 26.0, 32.1, 37.4, 37.5, 42.7, 42.9, 71.6, 77.4, 81.8, 133.1, 135.4, 137.8, 160.6, 195.7, 201.7.

A mixture of the above aldehyde (18 mg, 0.042 mmol) in *t*-BuOH (0.55 mL), phosphate buffer of pH 3.6 (0.26 mL), and 2-methyl-2-butene (0.045 mL, 0.42 mmol) was treated with $NaClO_2$ (8 mg, 0.071 mmol, 80% purity) in water (0.21 mL) at ambient temperature for 3 h to afford acid **42** (17.5 mg, 91% yield) after chromatography (CH_2Cl_2/EtOH): IR (neat) 3100, 1707, 1653, 813, 775 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.04 (s, 3H), 0.05 (s, 3H), 0.88 (s, 9H), 0.84–0.92 (m, 3H), 1.16–1.54 (m, 8H), 1.79 (quintet, $J=7$ Hz, 2H), 2.12–2.60 (m, 7H), 2.76 (dm, $J=17$ Hz, 1H), 3.52–3.62 (m, 1H), 3.84 (quintet, $J=6$ Hz, 1H), 4.4–5.6 (br s, 1H), 6.41 (dd, $J=6$, 2 Hz, 1H), 6.62 (t, $J=8$ Hz, 1H), 7.63 (dd, $J=6$, 2 Hz, 1H).

4.6.8. 5,6-Dehydro-Δ^{12}-PGJ_2 (5). To a flask containing acid **42** (17 mg, 0.039 mmol) was added a solution (0.39 mL) of 55% HF and MeCN in a ratio of 1:19. The solution was stirred at 0 °C for 15 min and diluted with brine to furnish 5-dehydro-Δ^{12}-PGJ_2 (**5**) (12 mg, 95% yield) after chromatography (CH_2Cl_2/EtOH): $[\alpha]_D^{26}$ +199 (*c* 0.14, $CHCl_3$); IR (neat) 3417, 1699, 1652 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.89 (t, $J=7$ Hz, 3H), 1.20–1.60

(m, 8 H), 1.77 (quintet, $J=7$ Hz, 2H), 2.16–2.28 (m, 2H), 2.38–2.56 (m, 5H), 2.68–2.82 (m, 1H), 3.56–3.64 (m, 1H), 3.83 (quintet, $J=6$ Hz, 1H), 3.2–4.2 (br s, 2H), 6.43 (dd, $J=6$, 2 Hz, 1H), 6.66 (t, $J=8$ Hz, 1H), 7.59 (dd, $J=6$, 2 Hz, 1H).

4.7. Synthesis of 5,6-dehydro-15-deoxy-$\Delta^{12,14}$-PGJ$_2$ (6)

4.7.1. Dienone 44 through aldol 43. To a solution of *i*-Pr_2NH (0.17 mL, 1.21 mmol) in THF (8 mL) at 0 °C was added *n*-BuLi (0.44 mL, 2.20 M in hexane, 0.97 mmol). The solution was stirred at the same temperature for 20 min to prepare LDA, and cooled to −78 °C. Enone **38** (150 mg, 0.48 mmol) dissolved in THF (2 mL) was added into the LDA solution dropwise, and the solution was stirred for 20 min. (*E*)-2-Octenal (**29**) (0.086 mL, 0.58 mmol) was added to the solution. After being stirred for further 20 min at the same temperature, the solution was poured into a flask containing saturated NH_4Cl and ether with vigorous stirring. The organic layer was separated and the aqueous layer was extracted with EtOAc. The combined organic extracts were dried over $MgSO_4$ and concentrated to afford aldol **43** as the *anti* and *syn* isomers in a 2:1 ratio by ^{1}H NMR spectroscopy (*anti* isomer, δ 4.19 (q, $J=8$ Hz); *syn* isomer, δ 4.55–4.62 (m)). The aldol **43** was subjected to the next reaction after being passed through a short column of silica gel. The aldol reaction was repeated, and the stereoisomers were separated by chromatography (hexane/EtOAc). *anti* Isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, $J=7$ Hz, 3H), 1.1–1.8 (m, 11H), 1.96–2.56 (m, 7H), 2.72–2.80 (m, 1H), 3.44 (t, $J=7$ Hz, 2H), 3.80 (s, 3H), 4.19 (q, $J=8$ Hz, 1H), 4.42 (s, 2H), 5.44 (ddt, $J=16$, 8, 1 Hz, 1H), 5.74 (dt, $J=16$, 8 Hz, 1H), 6.18 (dd, $J=6$, 2 Hz, 1H), 6.87 (d, $J=9$ Hz, 2H), 7.25 (d, $J=9$ Hz, 2H), 7.66 (dd, $J=6$, 2 Hz, 1H). *syn* Isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, $J=7$ Hz, 3H), 1.1–1.8 (m, 11H), 2.03 (q, $J=7$ Hz, 2H), 2.08–2.22 (m, 2H), 2.28–2.40 (m, 2H), 2.44–2.52 (m, 1H), 2.95–3.04 (m, 1H), 3.44 (t, $J=7$ Hz, 2H), 3.80 (s, 3H), 4.42 (s, 2H), 4.55–4.62 (m, 1H), 5.46 (ddt, $J=16$, 7, 1.5 Hz, 1H), 5.74 (dt, $J=16$, 7 Hz, 1H), 6.19 (dd, $J=6$, 2 Hz, 1H), 6.87 (d, $J=9$ Hz, 2H), 7.25 (d, $J=9$ Hz, 2H), 7.66 (dd, $J=6$, 2 Hz, 1H).

To a solution of the crude aldol **43** in CH_2Cl_2 (5 mL) and Et_3N (0.67 mL, 4.8 mmol) at −15 °C was added MsCl (0.15 mL, 1.94 mmol) dropwise. After 45 min at the same temperature, the reaction was quenched by addition of saturated $NaHCO_3$. The mixture was extracted with EtOAc three times. The combined organic layers were dried over $MgSO_4$ and concentrated to furnish an yellow residue, which was purified by chromatography (hexane/EtOAc) to afford dienone **44** (143 mg, 71% yield from enone **38**) and (*Z*)-isomer (12 mg, 6% yield). Dienone **44**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, $J=7$ Hz, 3H), 1.22–1.75 (m, 10H), 2.10–2. 28 (m, 5H), 2.70–2.82 (m, 1H), 3.46 (t, $J=6$ Hz, 2H), 3.58–3.67 (m, 1H), 3.80 (s, 3H), 4.43 (s, 2H), 6.16–6.35 (m, 2H), 6.40 (dd, $J=7$, 2 Hz, 1H), 6.88 (d, $J=8$ Hz, 2H), 6.95 (d, $J=11$ Hz, 1H), 7.26 (d, $J=8$ Hz, 2H), 7.64 (dd, $J=6$, 2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 18.7, 22.6, 23.6, 25.8, 28.7, 29.1, 31.6, 33.6, 43.2, 55.4, 69.7, 72.7, 77.2, 82.9, 113.8, 125.4, 129.2, 130.7, 132.0, 134.3, 135.6, 147.3, 159.1, 160.2, 196.8. (*Z*)-Isomer of **44**: ^{1}H NMR (300 MHz, $CDCl_3$) (characteristic signals) δ 6.06 (dt, $J=15$, 8 Hz, 1H), 6.33 (dd, $J=6$. 2 Hz, 1H), 6.49 (d, $J=11$ Hz, 1H), 7.49 (dd, $J=6$, 2 Hz, 1H), 7.26–7.68 (m, 1H).

4.7.2. 5,6-Dehydro-15-deoxy-$\Delta^{12,14}$-PGJ$_2$ (6). To an ice-cold solution of dienone **44** (55 mg, 0.13 mmol) in CH_2Cl_2 (1.2 mL) and water (0.1 mL) was added DDQ (45 mg, 0.198 mmol). After 45 min, the reaction was quenched by addition of saturated $NaHCO_3$ and ether. The organic layer was separated and the aqueous layer was extracted with ether twice. The combined organic fractions were dried over $MgSO_4$ and concentrated to obtained an yellow residue, which was purified by chromatography (hexane/EtOAc) to furnish the corresponding alcohol (36 mg, 92% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, $J=7$ Hz, 3H), 1.20–1.83 (m, 11H), 2.10–2.30 (m, 5H), 2.37 (ddt, $J=16$, 9, 2 Hz, 1H), 2.74 (ddt, $J=16$, 4, 3 Hz, 1H), 3.64, (t, $J=7$ Hz, 2H), 3.58–3.72 (m, 1H), 6.22–6.32 (m, 2H), 6.42 (dd, $J=6$, 1.5 Hz, 1H), 6.72 (d, $J=11$ Hz, 1H), 7.59 (dd, $J=6$, 3 Hz, 1H).

To an ice-cold solution of the above alcohol (35 mg, 0.116 mmol) in CH_2Cl_2 (1 mL) was added PCC (38 mg, 0.176 mmol). The mixture was stirred vigorously at room temperature for 2 h and diluted with ether. The resulting mixture was filtered through a short pad of Celite. The filtrate was concentrated, and the residue was purified by chromatography (hexane/EtOAc) to afford the corresponding aldehyde (32 mg, 92% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, $J=7$ Hz, 3H), 1.16–1.52 (m, 6H), 1.80 (quintet, $J=7$ Hz, 2H), 2.10–2.40 (m, 5H), 2.53 (t, $J=7$ Hz, 2H), 2.75 (ddt, $J=17$, 4.5, 2 Hz, 1H), 3.60–3.69 (m, 1H), 6.17–6.34 (m, 2H), 6.41 (dd, $J=6$, 1.5 Hz, 1H), 6.96 (d, $J=11$ Hz, 1H), 7.59 (dd, $J=6$, 3 Hz, 1H), 9.79 (t, $J=2$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 18.3, 21.5, 22.6, 23.4, 28.6, 31.6, 33.6, 42.8, 42.9, 77.3, 81.8, 125.3, 132.0, 134.2, 135.8, 147.4, 159.8, 196.7, 201.8.

To a slurry of the above aldehyde (25 mg, 0.084 mmol) in *t*-BuOH (1.1 mL), phosphate buffer of pH 3.6 (0.53 mL), and 2-methyl-2-butene (0.09 mL, 0.85 mmol) was added $NaClO_2$ (14 mg, 0.12 mmol, 80% purity) in water (0.42 mL). The mixture was stirred at ambient temperature for 3 h, and concentrated by using a vacuum pump. Phosphate buffer of pH 3.6 was added to the residue, and the mixture was extracted with EtOAc several times. The combined organic layers were dried over $MgSO_4$ and concentrated to afford an oily residue, which was purified by chromatography (CH_2Cl_2/EtOH) to furnish the title acid **6** (24 mg, 91% yield): $[\alpha]_D^{27}$ +157 (*c* 0.22, $CHCl_3$); IR (neat) 3100, 1699, 1630, 1209 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, $J=7$ Hz, 3H), 1.20–1.56 (m, 6H), 1.79 (quintet, $J=7$ Hz, 2H), 2.14–2.38 (m, 5H), 2.45 (t, $J=7$ Hz, 2H), 2.70–2.84 (m, 1H), 3.60–3.70 (m, 1H), 6.15–6.36 (m, 2H), 6.42 (dd, $J=6$, 2 Hz, 1H), 6.96 (d, $J=11$ Hz, 1H), 7.61 (dd, $J=6$, 2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 18.3, 22.6, 23.4, 23.9, 28.6, 31.6, 32.8, 33.7, 43.0, 77.4, 81.7, 125.3, 132.3, 134.2, 135.7, 147.6, 160.2, 178.1, 197.1.

4.8. Synthesis of 5,6-dihydro-15-deoxy-$\Delta^{12,14}$-PGJ$_2$ (7)

4.8.1. (1*R*,4*R*)-4-[7′-(4-Methoxybenzyloxy)heptyl]-2-cyclopenten-1-ol (46). To an ice-cold slurry of LiCl (180 mg, 4.25 mmol) and $PMBO(CH_2)_7MgBr$ (**45**) (9.10 mL, 0.35 M in THF, 3.19 mmol) was added CuCN

(29 mg, 0.323 mmol). After 30 min at −10 °C, monoacetate *ent*-**8a** (150 mg, 1.06 mmol, >95% ee) in THF (2 mL) was added. The mixture was stirred at the same temperature for 3 h, and the solution was diluted with saturated NH_4Cl, few drops of 28% NH_3, and EtOAc. The organic layer was separated and the aqueous layer was extracted with EtOAc twice. The combined organic fractions were dried over $MgSO_4$ and concentrated to obtain an yellow oil, which was a mixture of 1,4-isomer **46** and 1,2-isomer **51** in a 92:8 ratio by ^1H NMR spectroscopy. The mixture was separated by chromatography (hexane/EtOAc). Alcohol **46** (272 mg, 81% yield): IR (neat) 3398, 1613, 1513, 1248 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.16–1.48 (m, 8H), 1.52–1.70 (m, 5H), 1.75 (ddd, J=14, 7, 5 Hz, 1H), 1.89 (ddd, J=14, 7, 3 Hz, 1H), 2.78–2.90 (m, 1H), 3.43 (t, J=7 Hz, 2H), 3.79 (s, 3H), 4.42 (s, 2H), 4.79–4.87 (m, 1H), 5.80 (dt, J=5, 2 Hz, 1H), 5.93 (dd, J=5, 2 Hz, 1H), 6.87 (d, J=9 Hz, 2H), 7.26 (d, J=9 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.2, 27.9, 29.4, 29.70, 29.75, 35.9, 40.6, 44.1, 55.3, 70.2, 72.5, 77.1, 113.7, 129.2, 130.8, 132.4, 140.2, 159.1. Regioisomer **51**: ^1H NMR (300 MHz, $CDCl_3$) δ 1.10–1.46 (m, 8H), 1.50–1.65 (m, 5H), 2.25 (dm, J=18 Hz, 1H), 2.46–2.56 (m, 1H), 2.70 (dd, J=18, 7 Hz, 1H), 3.43 (t, J=7 Hz, 2H), 3.79 (s, 3H), 4.04–4.12 (m, 1H), 4.42 (s, 2H), 5.61–5.73 (m, 2H), 6.87 (d, J=9 Hz, 2H), 7.26 (d, J=9 Hz, 2H).

4.8.2. (*R*)-4-[7′-(4-Methoxybenzyloxy)heptyl]-2-cyclopenten-1-one (47). To a solution of alcohol **46** (250 mg, 0.79 mmol) in CH_2Cl_2 (8 mL) was added PCC (254 mg, 1.18 mmol). After being stirred vigorously for 1 h, the mixture was diluted with ether and filtered through a pad of Celite. The filtrate was concentrated to obtain an yellow residue, which was purified by chromatography (hexane/EtOAc) to furnish enone **47** (226 mg, 91% yield) as an oil: ^1H NMR (300 MHz, $CDCl_3$) δ 1.1–1.7 (m, 12H), 1.99 (dd, J=19, 2 Hz, 1H), 2.52 (dd, J=19, 7 Hz, 1H), 2.84–2.96 (m, 1H), 3.42 (t, J=7 Hz, 2H), 3.79 (s, 3H), 4.42 (s, 2H), 6.13 (dd, J=6, 2 Hz, 1H), 6.87 (d, J=9 Hz, 2H), 7.25 (d, J=9 Hz, 2H), 7.62 (dd, J=6, 2 Hz, 1H).

4.8.3. Dienone 49. To an ice-cold solution of *i*-Pr_2NH (0.27 mL, 1.93 mmol) in THF (9 mL) was added *n*-BuLi (0.67 mL, 1.90 M in hexane, 1.27 mmol). The solution was stirred at the same temperature for 20 min to prepare LDA and cooled to −78 °C. To this solution were added enone **47** (200 mg, 0.63 mmol) dissolved in THF (3 mL) and, after 20 min, *trans*-2-octenal (**29**) (0.14 mL, 0.94 mmol). The solution was stirred for further 30 min at the same temperature, and poured into a flask containing saturated NH_4Cl and ether with vigorous stirring. After 30 min, the organic layer was separated and the aqueous layer was extracted with EtOAc twice. The combined organic extracts were dried over $MgSO_4$ and concentrated to afford aldol **48** as the *anti* and *syn* isomers in a 3:1 ratio by TLC analysis, which was used for the next reaction after filtration through a short column of silica gel: ^1H NMR (300 MHz, $CDCl_3$) (characteristic peaks only) δ 5.38–5.50 (m, 1H), 5.64–5.78 (m, 1H), 6.12 (dd, J=6, 2 Hz, 1H), 6.87 (d, J=9 Hz, 2H), 7.25 (d, J=9 Hz, 2H), 7.65–7.72 (m, 1H).

To a solution of the above aldol **48** in CH_2Cl_2 (6 mL) and Et_3N (0.88 mL, 6.31 mmol) at −20 °C was added MsCl (0.195 mL, 2.52 mmol) dropwise. After 45 min at the same temperature, the reaction was quenched by addition of saturated $NaHCO_3$. The mixture was extracted with EtOAc three times. The combined organic layers were dried over $MgSO_4$ and concentrated to furnish an yellow residue, which was subjected to chromatography (hexane/EtOAc) to afford dienone **49** (136 mg, 51% yield from enone **47**) and (*Z*)-isomer **52** (14 mg, 5% yield). Dienone **49**: IR (neat) 1694, 1633, 1513, 1248, 1099 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.89 (t, J=7 Hz, 3H), 1.2–1.7 (m, 17H), 1.75–1.95 (m, 1H), 2.22 (q, J=7 Hz, 2H), 3.41 (t, J=7 Hz, 2H), 3.49–3.56 (m, 1H), 3.79 (s, 3H), 4.42 (s, 2H), 6.14–6.30 (m, 2H), 6.34 (dd, J=6, 2 Hz, 1H), 6.87 (d, J=9 Hz, 2H), 6.92 (d, J=10 Hz, 1H), 7.25 (d, J=9 Hz, 2H), 7.51 (dd, J=6, 2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.5, 26.0, 26.2, 28.5, 29.4, 29.76, 29.78, 31.4, 33.0, 33.5, 43.6, 55.3, 70.2, 72.6, 113.8, 125.7, 129.3, 130.8, 131.3, 135.2, 135.7, 146.6, 159.1, 161.2, 197.7. (*Z*)-Isomer **52**: ^1H NMR (300 MHz, $CDCl_3$) (characteristic signals) δ 6.07 (dt, J=15, 8 Hz, 1H), 6.28 (dd, J=6, 2 Hz, 1H), 6.38 (d, J=11 Hz, 1H), 7.42 (dd, J=6, 2 Hz, 1H), 7.60–7.74 (m, 1H).

4.8.4. Alcohol 50. To an ice-cold solution of dienone **49** (135 mg, 0.317 mmol) in CH_2Cl_2 (3 mL) and water (0.2 mL) was added DDQ (108 mg, 0.476 mmol). After 45 min, the reaction was quenched by addition of saturated $NaHCO_3$ and ether. The organic layer was separated and the aqueous layer was extracted with ether twice. The combined organic fractions were dried over $MgSO_4$ and concentrated to obtained an yellow residue, which was purified by chromatography (hexane/EtOAc) to furnish alcohol **50** as an oil (90 mg, 92% yield): IR (neat) 3417, 1695, 1630, 1213 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, J=7 Hz, 3H), 1.1–1.7 (m, 18H), 1.80–1.94 (m, 1H), 2.22 (q, J=7 Hz, 2H), 3.50–3.59 (m, 1H), 3.63 (t, J=7 Hz, 2H), 6.15–6.31 (m, 2H), 6.35 (dd, J=6, 2 Hz, 1H), 6.92 (d, J=11 Hz, 1H), 7.51 (dd, J=6, 2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.6, 25.7, 26.0, 28.5, 29.4, 29.8, 31.5, 32.8, 33.0, 33.5, 43.6, 63.1, 125.7, 131.4, 135.2, 135.7, 146.7, 161.2, 197.8.

4.8.5. 5,6-Dihydro-15-deoxy-$\Delta^{12,14}$-PGJ$_2$ (7). To an ice-cold solution of alcohol **50** (90 mg, 0.296 mmol) in CH_2Cl_2 (5 mL), DMSO (1.5 mL), and Et_3N (0.29 mL, 2.1 mmol) was added SO_3·pyridine (141 mg, 0.89 mmol). The solution was stirred vigorously at the same temperature for 1.5 h, and diluted with ether and cold water. The resulting mixture was stirred vigorously at room temperature for 20 min. The phases were separated and the aqueous layer was extracted with ether twice. The combined organic layers were dried over $MgSO_4$ and concentrated to obtain an yellow residue, which was purified by column chromatography (hexane/EtOAc) to afford the corresponding aldehyde (83 mg, 93% yield): IR (neat) 1725, 1694, 1634, 1205 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, J=7 Hz, 3H), 1.1–1.7 (m, 17H), 1.78–1.92 (m, 1H), 2.22 (q, J=7 Hz, 2H), 2.41 (dt, J=1.5, 7 Hz, 2H), 3.50–3.58 (m, 1H), 6.14–6.30 (m, 2H), 6.35 (dd, J=6, 2 Hz, 1H), 6.92 (d, J=10 Hz, 1H), 7.51 (dd, J=6, 2 Hz, 1H), 9.76 (t, J=1.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.0, 22.5, 25.8, 28.5, 29.0, 29.6, 31.4, 32.9, 33.5, 43.5, 43.9, 125.7, 131.4, 135.3, 135.6, 146.7, 161.1, 197.8, 202.7.

To a slurry of the above aldehyde (80 mg, 0.264 mmol) in *t*-BuOH (3.5 mL), phosphate buffer of pH 3.6 (1.7 mL), and 2-methyl-2-butene (0.26 mL, 2.45 mmol) was added $NaClO_2$ (45 mg, 0.398 mmol, purity 80%) in water

(1.3 mL). The resulting mixture was stirred at room temperature for 1 h, and connected to a vacuum pump to remove volatile compounds (*t*-BuOH). The phosphate buffer of pH 3.6 was added to the residue, and the mixture was extracted with EtOAc several times. The combined organic layers were dried over $MgSO_4$ and concentrated to afford an oily residue, which was purified by chromatography (CH_2Cl_2/EtOH) to furnish acid **7** (76 mg, 90% yield): IR (neat) 3000, 1708, 1697, 1206 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.89 (t, $J=7$ Hz, 3H), 1.1–1.7 (m, 17H), 1.78–1.94 (m, 1H), 2.22 (q, $J=7$ Hz, 2H), 2.33 (t, $J=7.5$ Hz, 2H), 3.50–3.58 (m, 1H), 6.15–6.34 (m, 2H), 6.35 (dd, $J=6$, 2 Hz, 1H), 6.93 (d, $J=11$ Hz, 1H), 7.51 (dd, $J=6$, 2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.6, 24.6, 25.8, 28.5, 29.0, 29.5. 31.4, 32.9, 33.5, 33.9, 43.6, 125.7, 131.5, 135.3, 135.6, 146.8, 161.2, 179.1, 197.8.

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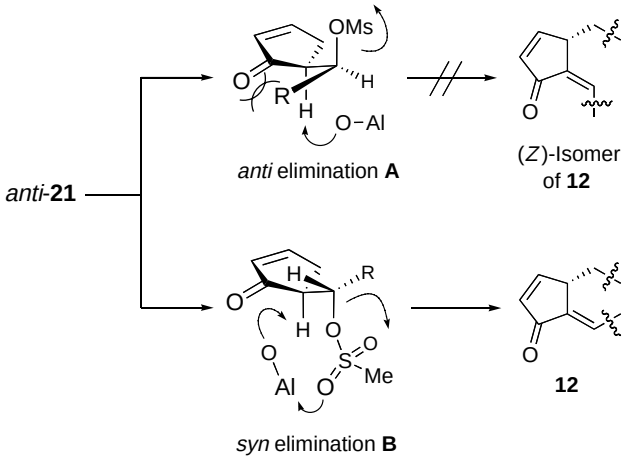

32. Deprotection of the TBS group with TBAF in THF and with NBS in wet DMSO was unsuccessful.
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