SYNTHESIS OF 14,15-EPOXYISOPROSTANE A₂ PHOSPHORYLCHOLINE†

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Abstract – The product of the copper-promoted allylic substitution of the 4-hydroxycyclopent-2-enyl ester with TMS-C≡CCH₂MgBr was converted to the cyclopentenone with the PMBO(CH₂)₄CH=CHCH₂ side chain. Aldol reaction of the enone with the epoxy aldehyde derived from (E)-oct-2-en-1-ol through the Sharpless asymmetric epoxidation gave the full structure of the isoprostane. Dehydration, conversion of the PMBOCH₂ moiety to CO₂H, and condensation with lysophosphorylcholine produced the title molecule.

The cross-conjugated dienone core and a (Z)-allylic side chain are unique characteristics of the epoxy-isoprostane phosphorylcholines (1a and 2a)¹² and several prostaglandins shown in Figure 1. To construct such a dienone structure, we developed an aldol strategy using enone and aldehyde, and its efficiency was demonstrated by the syntheses of methyl ester of Δ²-PGA₂ (5).³ Later, the approach has been applied to the dienones 1a–4a possessing the allylic side chain and some of their acetylene analogues.⁴–⁶ The allylic and propargylic side chains on the key enones 8 and 9 have been constructed through palladium-catalyzed allylation of the monoester of 4-cyclopentene-1,3-diol (6) with a malonate anion, which proceeds efficiently under the modified conditions⁶ to produce 7 in good yield (Scheme 1).

Recently, we communicated a Hg-free preparation of the propargylic Grignard reagents including 11,⁷ which had been prepared by using a mercury salt as a catalyst. Furthermore, we found regio- and stereoselective allylic substitution of monoester 6 (R = Me, t-Bu) with the copper complex derived from

† This paper is dedicated to Professor Ryoji Noyori on the occasion of his 70th birthday.
Figure 1. Isoprostanes and prostaglandins with the cross-conjugated dienone structure.\textsuperscript{a}

\textsuperscript{a} IPA\textsubscript{2}-PC, isoprostane A\textsubscript{2} phosphorylcholine.

Scheme 1. Preparation of enones 8 and 9 through Pd-catalyzed allylic substitution of monoester 6 with malonate anion

Scheme 2. Preparation of acetylene 12 through Cu-promoted allylic substitution of monoester 6 with the propargyl-MgBr (11)
anion 11 and CuCN in the presence of excess MgCl₂ (Scheme 2). The product 12 was utilized for synthesis of 1a and 1b through enone 8 (R = C₆H₁₁). Herein, we describe another utilization of 12 for synthesis of 14,15-epoxy-IPA₂-PC (2a)² through the key enone 16. In addition, 16 is also the intermediate leading to Δ¹²-PGJ₂ (3a) and the deoxy derivative 4a.

First, alcohol 12 was protected as the TBS ether and the TMS group at the acetylene carbon was removed to produce 13 in 90% yield (Scheme 3). The PMBO(CH₂)₄ group was attached to the acetylene terminus by alkylation with PMBO(CH₂)₄Br to afford 14 in good yield. Lindlar hydrogenation of 14 and subsequent deprotection of the TBS group produced alcohol 15, which upon oxidation with PCC furnished the key enone 16 (= 8 with PMBO(CH₂)₂ as R).

**Scheme 3. Synthesis of 14,15-epoxy-IPA₂-PC (2a)**

Optically active epoxy aldehyde 17, the aldol partner, was prepared from (E)-oct-2-en-1-ol by the Sharpless epoxidation⁵ followed by oxidation with SO₃•pyridine. Aldol reaction of 16 with the aldehyde was carried out at −78 °C to afford a mixture of anti and syn aldols 18 in a 2 : 1 ratio by TLC analysis. Without separation, the mixture was converted to the mesylates, which upon exposure to Al₂O₃ produced the cross-conjugated dienone 19. The stereoisomer at the newly formed olefin was not detected by ¹H NMR spectroscopy. The PMB group was removed with DDQ and the resulting alcohol was converted to 14,15-epoxy-IPA₂ (20) by the two-step oxidation. Finally, condensation of acid 20 with lyso-PC (21) according to the protocol⁹ using the Yamaguchi reagent furnished 2a in 50% yield.

Similarly, the synthetic intermediate 14 was converted into enone 22 with the propargylic side chain on the cyclopentane ring (corresponding to acetylene 9) as delineated in Scheme 4. The enone was
previously converted to acetylene analogues 3b and 4b.\(^6\)

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\text{Scheme 4. Synthesis of the key intermediate 22 leading to 3b and 4b}
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In summary, enone 16 was synthesized by a new route through 12 and converted to 14,15-epoxy-IPA\(_2\)-PC (2a), in which aldol reaction with epoxy aldehyde 17 played a key role for construction of the cross-conjugated dienone structure of 2a.

**EXPERIMENTAL**

**General.** Infrared (IR) spectra are reported in wave numbers (cm\(^{-1}\)). The \(^1\)H NMR (300 MHz) and \(^{13}\)C NMR (75 MHz) spectra were measured in CDCl\(_3\) using SiMe\(_4\) (\(\delta = 0\) ppm) and the center line of CDCl\(_3\) triplet (\(\delta = 77.1\) ppm) as internal standards, respectively. Signal patterns are indicated as br s, broad singlet; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Coupling constants (\(J\)) are given in hertz (Hz). In some cases chemical shifts of carbons accompany plus (for C and CH\(_2\)) and minus (for CH and CH\(_3\)) signs of APT experiments. After the reactions, organic extracts were concentrated by using a rotary evaporator and residues were purified by chromatography on silica gel (Merck, silica gel 60).

**Acetylene 13.** A solution of alcohol 12 (> 95% ee, 110 mg, 0.57 mmol), TBSCI (130 mg, 0.86 mmol), and imidazole (80 mg, 1.14 mmol) in DMF (6 mL) was stirred at rt for 1 h and diluted with saturated aqueous NaHCO\(_3\) and hexane with vigorous stirring. The layers were separated, and the aqueous layer was extracted with hexane three times. The combined organic layers were dried over MgSO\(_4\) and concentrated to afford a residue, which was purified by chromatography to give the TBS ether of 12 (164 mg, 93%). A mixture of the TBS ether and K\(_2\)CO\(_3\) (215 mg, 1.56 mmol) in MeOH (5 mL) was stirred at rt for 3 h and diluted with saturated aqueous NH\(_4\)Cl and Et\(_2\)O with vigorous stirring. The phases were separated, and the aqueous phase was extracted with Et\(_2\)O three times. The combined organic layers were dried over MgSO\(_4\) and concentrated. The residue was purified by chromatography to produce acetylene 13 (121 mg, 90% from 12): \([\alpha]_D^{27} +142\) (c 0.166, CHCl\(_3\)); IR (neat) 3313, 1252, 1070, 837 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta \) 0.08 (s, 6 H), 0.89 (s, 9 H), 1.89–1.95 (m, 3 H), 2.22 (dd, \(J = 7, 3\) Hz, 2 H), 3.04–3.16 (m, 1 H), 4.86–5.00 (m, 1 H), 5.79 (dt, \(J = 5, 1\) Hz, 1 H), 5.84–5.92 (m, 1 H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta \) −4.5 (−), 18.4 (+), 24.7 (+), 26.0 (−), 40.0 (+), 43.5 (−), 68.9 (+), 77.5 (−), 83.0 (+), 134.7
Acetylene 14. To a solution of acetylene 13 (150 mg, 0.634 mmol) in THF (4 mL) at −78 °C was added n-BuLi (0.35 mL, 2.50 M in hexane, 0.88 mmol) dropwise. After 30 min of stirring at −78 °C, HMPA (1.5 mL) and a solution of PMBO(CH$_2$)$_2$Br (210 mg, 0.77 mmol) in THF (1 mL) were added. The solution was stirred at −78 °C for 2 h, gradually warmed to rt over 9 h, and diluted with saturated aqueous NH$_4$Cl 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 to leave an oil, which was purified by chromatography to afford 14 (242 mg, 89%): [α]$_D^{25}$ +105 (c 0.762, CHCl$_3$); IR (neat) 1513, 1249, 1069, 836 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) δ 0.07 (s, 6 H), 0.89 (s, 9 H), 1.48–1.75 (m, 4 H), 1.85–1.92 (m, 2 H), 2.11–2.19 (m, 4 H), 2.96–3.08 (m, 1 H), 3.45 (t, J = 7 Hz, 2 H), 3.80 (s, 3 H), 4.43 (s, 2 H), 4.85–4.99 (m, 1 H), 5.72–5.77 (m, 1 H), 5.84–5.90 (m, 1 H), 6.87 (d, J = 9 Hz, 2 H), 7.25 (d, J = 9 Hz, 2 H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ −4.5, 18.6, 25.1, 25.9, 28.9, 40.1, 44.1, 55.3, 69.7, 72.6, 77.7, 78.8, 80.7, 113.8, 129.3, 130.7, 134.3, 137.3, 159.2.

Alcohol 15. A mixture of acetylene 14 (270 mg, 0.63 mmol), quinoline (0.04 mL), and Pd/BaSO$_4$ (10 mg) in MeOH (8 mL) was stirred under argon for 20 min, and hydrogen was flushed into the flask. After 20 min of vigorous stirring, hydrogen uptake was stopped. The mixture was diluted with hexane and filtered through a pad of Celite. The filtrate was concentrated and the residue was passed through a short pad of silica gel to afford the TBS ether of 15 (266 mg, 98%): [α]$_D^{25}$ +91.4 (c 0.672, CHCl$_3$); IR (neat) 1513, 1249, 1041, 836 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) δ 0.07 (s, 6 H), 0.89 (s, 9 H), 1.34–1.47 (m, 2 H), 1.54–1.66 (m, 2 H), 1.72–1.90 (m, 2 H), 1.94–2.14 (m, 4 H), 2.84–2.96 (m, 1 H), 3.43 (t, J = 6 Hz, 2 H), 3.78 (s, 3 H), 4.42 (s, 2 H), 4.86–4.94 (m, 1 H), 5.34–5.46 (m, 2 H), 5.66–5.73 (dm, J = 5 Hz, 2 H), 5.81–5.88 (dm, J = 5 Hz, 1 H), 6.87 (d, J = 8 Hz, 2 H), 7.25 (d, J = 8 Hz, 2 H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ −4.5 (−), 18.4, 26.0 (+), 26.1 (−), 26.3 (+), 27.2 (+), 29.5 (+), 33.3 (+), 40.2 (+), 44.4 (−), 55.3 (−), 70.1 (+), 72.6 (+), 77.7 (−), 113.8 (−), 128.0 (−), 129.3 (−), 130.8 (−), 133.4 (−), 138.3 (−), 159.2 (+).

To an ice-cold solution of the above TBS ether (115 mg, 0.27 mmol) in THF (3 mL) was added n-Bu$_4$NF (0.42 mL, 0.95 M in THF, 0.40 mmol). The solution was stirred at rt for 1.5 h and diluted with saturated aqueous NH$_4$Cl 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 to afford alcohol 15 (80 mg, 94%): [α]$_D^{25}$ +116 (c 0.42, CHCl$_3$); IR (neat) 3384, 1513, 1248 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) δ 1.35–1.48 (m, 2 H), 1.54–1.67 (m, 2 H), 1.74–1.92 (m, 2 H), 1.96–2.16 (m, 4 H), 2.84–2.98 (m, 1 H), 3.43 (t, J = 7 Hz, 2 H), 3.80 (s, 3 H), 4.42 (s, 2 H), 4.80–4.88 (m, 1 H), 5.28–5.47 (m, 2 H), 5.82 (dt, J = 5, 2 Hz, 1 H), 5.92 (dd, J = 5, 2 Hz, 1 H), 6.87 (d, J = 8 Hz, 2 H), 7.25 (d, J = 8 Hz, 2 H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 26.3, 27.2, 29.4, 33.1, 40.1, 44.3, 55.3, 70.0, 72.6, 77.2, 113.8, 127.6, 129.3, 130.8, 131.0,
133.0, 139.7, 159.2.

**Enone 16.** A mixture of alcohol 15 (80 mg, 0.25 mmol) and PCC (82 mg, 0.38 mmol) in CH$_2$Cl$_2$ (3 mL) was stirred vigorously for 1 h and diluted with Et$_2$O. The resulting mixture was filtered through a pad of Celite. The filtrate was concentrated and the residue was purified by chromatography to furnish enone 16 (69 mg, 90%). The $^1$H and $^{13}$C NMR spectra of 16 were consistent with those reported previously.$^6$

**Dienone 19.** To a solution of $i$-Pr$_2$NH (0.26 mL, 1.86 mmol) in THF (12 mL) at 0 °C was added n-BuLi (0.80 mL, 2.0 M in hexane, 1.60 mmol). The solution was stirred at 0 °C for 20 min, and then cooled to −78 °C. A solution of enone 16 (250 mg, 0.80 mmol) in THF (2 mL) was added to the LDA solution dropwise, and the solution was stirred for 20 min. Then, a solution of epoxy aldehyde 17 (226 mg, 1.59 mmol) in THF (2 mL) was added to the solution. After 20 min at −78 °C, the solution was poured into a flask containing saturated aqueous NH$_4$Cl and Et$_2$O with vigorous stirring. The phases were separated and the aqueous layer was extracted with EtOAc. The combined organic extracts were dried over MgSO$_4$ and concentrated to afford a mixture of anti and syn aldols 18 (2 : 1 ratio by TLC), which was subjected to chromatography to afford a mixture of aldol products 18 (240 mg, 66%) as an oil: $^1$H NMR (300 MHz, CDCl$_3$) (characteristic peaks only) δ 3.45 (t, $J = 6$ Hz, 2 H), 3.50–3.60 (m, 1 H for anti–), 3.65 (br s, 1 H for anti–), 3.80 (s, 3 H), 4.42 (s, 2 H), 5.32–5.44 (m, 1 H), 5.48–5.60 (m, 1 H), 6.16 (dd, $J = 6$, 2 Hz, 1 H), 6.87 (d, $J = 9$ Hz, 2 H), 7.25 (d, $J = 9$ Hz, 2 H), 7.66 (dd, $J = 6$, 2 Hz, 1 H). To an ice-cold solution of 18 (240 mg, 0.526 mmol) and Et$_3$N (0.90 mL, 6.5 mmol) in CH$_2$Cl$_2$ (5 mL) was added MsCl (0.20 mL, 2.6 mmol). After 45 min of stirring at 0 °C, the solution was diluted with saturated aqueous NaHCO$_3$ and EtOAc. The phases were separated and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over MgSO$_4$ and concentrated to furnish the corresponding mesylates, which was subjected to the next reaction without further purification: $^1$H NMR (300 MHz, CDCl$_3$) (characteristic peaks only) δ 3.45 (t, $J = 6$ Hz, 2 H), 3.80 (s, 3 H), 4.42 (s, 2 H), 5.30–5.43 (m, 1 H), 5.48–5.60 (m, 1 H), 6.16 (dd, $J = 6$, 2 Hz, 1 H), 6.87 (d, $J = 9$ Hz, 2 H), 7.25 (d, $J = 9$ Hz, 2 H), 7.66 (dd, $J = 6$, 2 Hz, 1 H). To a slurry of alumina (ICN, N–Super I, 540 mg, 5.30 mmol) in CH$_2$Cl$_2$ (3 mL) was added a solution of the mesylates in CH$_2$Cl$_2$ (2 mL). The mixture was stirred vigorously at rt for 6 h, and filtered through a pad of Celite. The filtrate was concentrated and the residue was subjected to chromatography to afford dienone 19 (210 mg, 91% from 16): $^1$H NMR (300 MHz, CDCl$_3$) δ 0.89 (t, $J = 7$ Hz, 3 H), 1.20–1.75 (m, 12 H), 1.97 (q, $J = 6$ Hz, 2 H), 2.22–2.40 (m, 1 H), 2.48–2.64 (m, 1 H), 2.99 (dt, $J = 1.5$, 5 Hz, 1 H), 3.37 (dd, $J = 8$, 1.5 Hz, 1 H), 3.42 (t, $J = 6$ Hz, 2 H), 3.62–3.70 (m, 1 H), 3.80 (s, 3 H), 4.42 (s, 2 H), 5.28–5.40 (m, 1 H), 5.44–5.56 (m, 1 H), 6.19 (d, $J = 8$ Hz, 1 H), 6.34 (dd, $J = 6$, 2 Hz, 1 H), 6.87 (d, $J = 9$ Hz, 2 H), 7.25 (d, $J = 9$ Hz, 2 H), 7.52 (dd, $J = 6$, 2 Hz, 1 H).

**14,15-Epoxy-IPA$_2$ (20).** To an ice-cold solution of dienone 19 (110 mg, 0.251 mmol) in CH$_2$Cl$_2$ (4.7 mL) and H$_2$O (0.3 mL) was added DDQ (85 mg, 0.374 mmol). The mixture was stirred vigorously for 45 min
and diluted with saturated aqueous NaHCO₃ and Et₂O. The organic layer was separated and the aqueous layer was extracted with Et₂O twice. The combined organic fractions were dried over MgSO₄ and concentrated to obtain an yellow residue, which was purified by chromatography to furnish the corresponding alcohol (71 mg, 89%): ¹H NMR (300 MHz, CDCl₃) δ 0.89 (t, J = 7 Hz, 3 H), 1.2–1.7 (m, 13 H), 2.02 (q, J = 7 Hz, 2 H), 2.31 (dt, J = 15, 8 Hz, 1 H), 2.55 (dt, J = 15, 6 Hz, 1 H), 2.98 (dt, J = 1.5, 5 Hz, 1 H), 3.37 (dd, J = 8, 1.5 Hz, 1 H), 3.63 (t, J = 6 Hz, 2 H), 3.57–3.72 (m, 1 H), 5.28–5.41 (m, 1 H), 5.46–5.57 (m, 1 H), 6.21 (d, J = 8 Hz, 1 H), 6.35 (dd, J = 6, 2 Hz, 1 H), 7.54 (dd, J = 6, 2 Hz, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 14.0, 22.6, 25.68, 25.75, 27.1, 31.7, 31.9, 32.0, 32.4, 43.3, 55.3, 60.6, 62.7, 124.9, 131.5, 132.9, 134.6, 140.8, 161.9, 195.9. To an ice-cold solution of the above alcohol (15 mg, 0.047 mmol) and Et₃N (0.065 mL, 0.47 mmol) in CH₂Cl₂ (3 mL) and DMSO (1 mL) was added SO₃•pyridine (23 mg, 0.144 mmol). The solution was stirred vigorously at the same temperature for 2 h and poured into cold water and Et₂O. The resulting mixture was stirred vigorously at rt for 20 min. The phases were separated and the aqueous layer was extracted with Et₂O twice. The combined organic layers were dried over MgSO₄ and concentrated to obtain a residue, which was purified by chromatography to afford the corresponding aldehyde as (13 mg, 88%): ¹H NMR (300 MHz, CDCl₃) δ 0.89 (t, J = 7 Hz, 3 H), 1.2–1.8 (m, 10 H), 2.04 (q, J = 6 Hz, 2 H), 2.24–2.38 (m, 1 H), 2.43 (dt, J = 1.5, 7 Hz, 2 H), 2.51–2.62 (m, 1 H), 2.97 (dt, J = 2, 5 Hz, 1 H), 3.36 (dd, J = 8, 2 Hz, 1 H), 3.64–3.72 (m, 1 H), 5.32–5.54 (m, 2 H), 6.22 (d, J = 8 Hz, 1 H), 6.35 (dd, J = 6, 2 Hz, 1 H), 7.52 (dd, J = 6, 2 Hz, 1 H), 9.76 (t, J = 1.5 Hz, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 14.4, 22.3, 22.6, 25.68, 25.75, 27.1, 31.7, 31.9, 32.0, 32.4, 43.6, 43.7, 55.6, 61.0, 126.3, 131.9, 132.2, 135.1, 141.0, 162.1, 196.2, 202.6. To an ice-cold slurry of the above aldehyde (13 mg, 0.041 mmol) and 2-methyl-2-buten (0.044 mL, 0.414 mmol) in t-BuOH (0.53 mL) and phosphate buffer of pH 7 (0.25 mL) was added aqueous solution of NaClO₂ (7 mg, 0.062 mmol, purity 80%) in H₂O (0.2 mL). After 45 min of stirring, brine and EtOAc were added to the mixture. The organic layer was separated and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over MgSO₄ and concentrated to afford an oily residue, which was purified by chromatography to give acid 20 (13 mg, 95%): ¹H NMR (500 MHz, CDCl₃) δ 0.89 (t, J = 7 Hz, 3 H), 1.2–1.8 (m, 10 H), 1.98–2.14 (m, 2 H), 2.24–2.38 (m, 3 H), 2.48–2.64 (m, 1 H), 2.97 (dt, J = 1.5, 5 Hz, 1 H), 3.36 (dd, J = 8, 1.5 Hz, 1 H), 3.63–3.73 (m, 1 H), 5.32–5.58 (m, 2 H), 6.22 (d, J = 8 Hz, 1 H), 6.36 (dd, J = 6, 2 Hz, 1 H), 7.53 (dd, J = 6, 2.5 Hz, 1 H).

Methyl Ester of 14,15-IPA₂. The above acid 20 was converted to the methyl ester with excess CH₂N₂ in Et₂O at 0 °C for 30 min in 96% to confirm the structure by ¹H NMR spectroscopy: ¹H NMR (500 MHz, CDCl₃) δ 0.90 (t, J = 7 Hz, 3 H), 1.2–1.8 (m, 10 H), 1.98–2.12 (m, 2 H), 2.24–2.48 (m, 3 H), 2.50–2.64 (m, 1 H), 2.97 (dt, J = 2, 6 Hz, 1 H), 3.36 (dd, J = 8, 2 Hz, 1 H), 3.62–3.72 (m, 1 H), 3.67 (s, 3 H), 5.33–5.56 (m, 2 H), 6.22 (d, J = 9 Hz, 1 H), 6.35 (dd, J = 6, 2 Hz, 1 H), 7.53 (dd, J = 6, 2 Hz, 1 H).
14,15-Epoxy-IPA₂-PC (2a). To a solution of lyso-PC (21) (10 mg, 0.020 mmol), 14,15-epoxyisoprostane A₂ (20) (20 mg, 0.060 mmol), DMAP (44 mg, 0.36 mmol), and Et₃N (0.084 mL, 0.60 mmol) in CH₂Cl₂ (2 mL) was added 2,4,6-Cl₃C₆H₂COCl (0.019 mL, 0.12 mmol). After being conducted at rt for 26 h, the reaction was quenched by addition of a few drops of H₂O. The mixture was concentrated, and the residue was subjected to chromatography (SiO₂, CH₂Cl₂/MeOH) to give a mixture of 2a and DMAP. The mixture was then subjected to a reversed phase chromatography by using Et₂O/CH₂Cl₂ as an eluent to separate 2a (8 mg, 50%): ¹H NMR (500 MHz, CDCl₃) δ 0.90 (t, J = 7 Hz, 6 H), 1.1–1.7 (m, 38 H), 1.9–2.8 (m, 6 H), 2.94–3.02 (m, 1 H), 3.20–3.50 (m, 10 H), 3.60–4.45 (m, 9 H), 5.18–5.28 (m, 1 H), 5.30–5.60 (m, 2 H), 6.21 (d, J = 8 Hz, 1 H), 6.35 (dd, J = 6, 2 Hz, 1 H), 7.54 (dd, J = 6, 2 Hz, 1 H).

Alcohol Derivative of 14. To an ice-cold solution of the TBS ether 14 (236 mg, 0.551 mmol) in THF (6 mL) was added n-Bu₄NF (1.0 mL, 0.95 M in THF, 0.95 mmol). The solution was stirred at rt for 2 h and diluted with saturated aqueous NH₄Cl and EtOAc. The organic layer was separated, and the aqueous layer was extracted with EtOAc three times. The combined organic extracts were dried over MgSO₄ and concentrated under reduced pressure to leave an oil, which was purified by chromatography to afford the corresponding alcohol (156 mg, 90%): [α]D²⁵ +89 (c 0.438, CHCl₃); IR (neat) 3398, 1513, 1248, 1036 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 1.48–1.75 (m, 4 H), 1.88–1.94 (m, 2 H), 2.10–2.21 (m, 4 H), 2.98–3.10 (m, 1 H), 3.45 (t, J = 7 Hz, 2 H), 3.79 (s, 3 H), 4.42 (s, 2 H), 4.84–4.92 (m, 1 H), 5.83–5.88 (m, 1 H), 5.92–5.97 (m, 1 H), 6.87 (d, J = 8.5 Hz, 2 H), 7.25 (d, J = 8.5 Hz, 2 H); ¹³C NMR (75 MHz, CDCl₃) δ 18.6, 24.9, 25.8, 28.9, 39.9, 43.9, 55.3, 69.6, 72.6, 77.3, 78.5, 80.9, 113.8, 129.3, 130.7, 133.8, 138.8, 159.2.

Enone 22. A mixture of the above alcohol (50 mg, 0.16 mmol) and PCC (52 mg, 0.24 mmol) in CH₂Cl₂ (2 mL) was stirred vigorously for 1 h and diluted with Et₂O. The resulting mixture was filtered through a pad of Celite. The filtrate was concentrated, and the residue was purified by chromatography to furnish enone 22 (47 mg, 95%). The ¹H and ¹³C NMR spectra of 22 were consistent with those reported previously.⁶

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REFERENCES AND NOTES


