Supporting Information

A Detachable Ester Bond enables Perfect Z-Alkylations of Olefins for the Synthesis of Tri- and Tetrasubstituted Olefins

Takashi Nishikata*, Kimiaki Nakamura, Yuki Inoue and Shingo Ishikawa
Graduate School of Science and Engineering, Yamaguchi University, Ube, Yamaguchi, 755-8611, Japan
E-mail: nisikata@yamaguchi-u.ac.jp

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1. General Information

Product Characterization

All reactions were carried out under nitrogen (99.95%) atmosphere. For TLC analyses precoated Kieselgel 60 F254 plates (Merck, 0.25 mm thick) were used; for column chromatography Silica Flash® P60 (SiliCycle, 40-63 μm) was used. Visualization was accomplished by UV light (254 nm). $^1$H and $^{13}$C NMR spectra were obtained using a JEOL 500 MHz NMR spectrometer. Chemical shifts for $^1$H NMR were described in parts per million (chloroform as an internal standard $\delta = 7.26$) in CDCl$_3$, unless otherwise noted. Chemical shifts for $^{13}$C NMR were expressed in parts per million in CDCl$_3$ as an internal standard ($\delta = 77.16$), unless otherwise noted. High resolution mass analyses were obtained using an ACQUITY UPLC/TOF-MS for ESI. Anhydrous toluene were purchased from Kanto Chemical Co., Ltd. Other chemicals were purchased from TCI, Aldrich and Wako and directly used from the bottles. Copper salts were purchased from TCI and Wako.

Table S1 Starting materials.

Styrenes

![Styrene structures](image)

Alkyl Bromides $Ar = \text{C}_6\text{H}_4(\text{CO}_2\text{Me}-4)$

![Alkyl bromide structures](image)
2. Olefinations

General Procedure

A. Olefination:

Cu salt (0.05 mmol), ligand (0.05 mmol), and BnBu3NBr (0.1 mmol) were sequentially added under air to a dram vial equipped with a stir bar and a screw cap. 1 (0.5 mmol), 2 (0.75 mmol), amine (0.75 mmol) and dried toluene (1.0 mL) were added by syringe and the resulting mixture vigorously stirred under nitrogen atmosphere (purity 99.95%) for 20 h at the temperature shown in tables. After this time, the contents of the flask were filtered through the plug of silica gel, and then concentrated by rotary evaporation. The residue was purified by flash chromatography, eluting with hexane/EtOAc to afford the cyclic product 4 with inseparable isomer 4’. (The ratios of proximal:distal were determined by 1H NMR of the crude product.) We tried to isolate pure 4 but it was impossible even by GPC we have.

B. Hydrolysis:

After the isolation of 4, 1,4-dioxane (1mL), and 0.5M NaOHaq (0.2 mL) were sequentially added to the product 4 and the resulting solution was stirred for 4 h at 80 °C. After this time, the contents of the flask were diluted with water and extracted with EtOAc. The solution obtained was dried over anhydrous MgSO4, filtered, and concentrated by rotary evaporation. The residue was purified by flash chromatography eluting with hexane/EtOAc to afford the product 5.

Following the general procedure A, using 1a (0.5 mmol, 67 mg), 2a (0.75 mmol, 225.8 mg), CuOAc (0.05 mmol, 6.1 mg), Hex3N (0.75 mmol, 101 mg), BnBu3NBr (0.1 mmol, 36.5 mg), TPMA (0.5 mmol, 14.5 mg), and dried toluene (1.0 mL) at 120 °C, yielded the product 4a with an inseparable isomer (89 mg, 86% (proximal:distal=95:<5 (this ratio is from crude mixture)));

IR (neat) ν 2975, 1745, 1437, 1203, 1102, 761 cm⁻¹. 1H NMR (500 MHz, CDCl3) δ: 1.18 (s, 6H), 2.18 (s, 3H), 5.61 (d, J = 7.4 Hz, 1H), 7.14 (dd, J = 1.1 and 8.1 Hz, 1H), 7.18 (dd, J = 1.2 and 8.7 Hz, 1H), 7.32 (dd, J = 1.5 and 8.6 Hz, 1H), 7.43 (dd, J = 1.5 and 8.0 Hz, 1H). 13C NMR (126 MHz, CDCl3) δ: 22.05, 24.14, 42.93, 119.90, 124.46, 126.94, 129.03, 129.47, 132.12, 134.42, 150.25, 172.69. HRESIMS calcd. for C13H14O2Na (M+Na⁺): 225.0891; found 225.0891.
Following the general procedure B, using 1,4-dioxane (1 mL) and 0.5 M NaOH aq (0.2 mL) at 80 °C, yielded the product 5a (94 mg, 96%);

IR (neat) ν 3485, 3402, 3000-2500(br), 1702, 1686, 1483, 1157 cm⁻¹. ¹H NMR (500 MHz, CDCl₃) δ: 1.17-1.36 (brs, 6H), 1.99 (s, 3H), 5.75 (s, 1H), 6.83-6.88 (m, 2H), 7.00 (dd, J = 1.7 and 7.5 Hz, 1H), 7.14 (ddd, J = 1.7, 7.5 and 15.4 Hz, 2H). ¹³C NMR (126 MHz, CDCl₃) δ: 27.61, 44.18, 115.91, 120.50, 128.13, 129.02, 129.33, 134.02, 152.05, 182.91. HRESIMS calcd. for C₁₃H₁₆O₃Na (M+Na⁺): 243.0997; found 243.0997.

Following the general procedure A, using 1a (0.5 mmol, 67 mg), 2b (0.75 mmol, 236.4 mg), CuOAc (0.05 mmol, 6.1 mg), Hex₃N (0.75 mmol, 101 mg), BnBu₃NBr (0.1 mmol, 36.5 mg), TPMA (0.5 mmol, 14.5 mg), and dried toluene (1.0 mL) at 120 °C, yielded the product 4b with an inseparable isomer (96 mg, 89% (proximal:distal=95:<5 (this ratio is from crude mixture)));

IR (neat) ν 2974, 1745, 1437, 1207, 1102 cm⁻¹. ¹H NMR (500 MHz, CDCl₃) δ: 0.79 (t, J = 7.4 Hz, 3H), 1.29-1.36 (m, 1H), 1.30 (s, 3H), 1.39-1.47 (m, 1H), 2.20 (s, 3H), 5.59 (s, 1H), 7.16 (dd, J = 1.2 and 8.1 Hz, 1H), 7.20 (dd, J = 1.3, 7.5, and 7.5 Hz, 1H), 7.33 (dd, J = 1.6, 7.5, and 7.5 Hz, 1H), 7.43 (dd, J = 1.5 and 7.8 Hz, 1H). ¹³C NMR (126 MHz, CDCl₃) δ: 9.00, 22.09, 22.64, 27.34, 47.59119.67, 124.42, 126.77, 129.01, 131.42, 134.30, 149.98, 172.03. HRESIMS calcd. for C₁₄H₁₆O₂Na (M+Na⁺): 239.1048; found 239.1048.

Following the general procedure B, using 1,4-dioxane (1 mL) and 0.5 M NaOH aq (0.2 mL) at 80 °C, yielded the product 5b (100 mg, 96%);

IR (neat) ν 3500-2500(br), 3401, 2968, 1691, 1447, 1222, 1150 cm⁻¹. ¹H NMR (500 MHz, CDCl₃) δ: 0.83-0.92 (m, 3H), 1.00-1.17 (m, 3H), 1.56-1.76 (m, 2H), 2.89 (s, 3H), 5.70 (s, 1H), 6.81-6.85 (m, 2H), 6.99 (dd, J = 1.4, and 7.5 Hz, 1H), 7.33 (dd, J = 1.5, 7.5 and 7.5 Hz, 1H), 8.13 (brs, 1H). ¹³C NMR (126 MHz, CDCl₃) δ: 9.00, 22.09, 22.64, 27.34,
Following the general procedure A, using 1a (0.5 mmol, 67 mg), 2c (0.75 mmol, 246.9 mg), CuOAc (0.05 mmol, 6.1 mg), Hex3N (0.75 mmol, 101 mg), BnBu3NBr (0.1 mmol, 36.5 mg), TPMA (0.5 mmol, 14.5 mg), and dried toluene (1.0 mL) at 120 °C, yielded the product 4c with an inseparable isomer (98 mg, 85% (proximal:distal=95:<5 (this ratio is from crude mixture)));

**IR** (neat) $\nu$ 2965, 1742, 1437, 1207, 1100 cm$^{-1}$.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$: 0.84 (t, $J = 7.4$ Hz, 6H), 1.50-1.63 (m, 4H), 2.22 (d, $J = 9.9$ and 13.0 Hz, 3H), 5.61 (dd, $J = 6.8$ and 13.0 Hz, 1H), 7.16 (dd, $J = 1.2$ and 8.1 Hz, 1H), 7.19 (dddd, $J = 1.2$, 7.8, 8.9 and 9.5 Hz, 1H), 7.31 (dddd, $J = 1.7$, 8.0, 8.9 and 9.5 Hz, 1H), 7.43 (dd, $J = 1.6$ and 7.8 Hz, 1H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$: 8.61, 22.47, 24.67, 26.84, 51.52, 119.70, 124.43, 126.82, 129.37, 130.03, 134.55, 150.12, 171.63. 

HRESIMS calcd. for C$_{15}$H$_{19}$O$_2$Na (M+Na$^+$): 231.1385; found 231.1385.

Following the general procedure B, using 1,4-dioxane (1 mL) and 0.5 M NaOH aq (0.2 mL) at 80 °C, yielded the product 5c (102 mg, 97%);

**IR** (neat) $\nu$ 3500-2600(br), 3402, 2965, 1696, 1438, 1206, 1104 cm$^{-1}$. 

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$: 0.80-0.82 (brs, 6H), 1.50-1.82 (brs, 4H), 2.01 (d, $J = 1.4$ Hz, 3H), 5.67 (d, $J = 1.4$ Hz, 1H), 6.82 (dd, $J = 0.6$ and 8.0 Hz, 1H), 6.85 (ddd, $J = 1.1$, 7.5 and 7.5 Hz, 1H), 6.98 (dd, $J = 1.7$ and 6.5 Hz, 2H), 7.13 (dd, $J = 1.7$ and 7.5 Hz, 1H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$: 8.54, 27.86, 51.99, 116.02, 120.45, 128.47, 128.85, 128.99, 132.33, 134.80, 152.04, 182.63. 

HRESIMS calcd. for C$_{15}$H$_{21}$O$_3$ (M+H$^+$): 249.1490; found 249.1491.

Following the general procedure A, using 1a (0.5 mmol, 67 mg), 2d (0.75 mmol, 255.9 mg), CuOAc (0.05 mmol, 6.1 mg), Hex3N (0.75 mmol, 101 mg), BnBu3NBr (0.1 mmol, 36.5 mg), TPMA (0.5 mmol, 14.5 mg), and dried toluene (1.0 mL) at 120 °C, yielded the product 4c with an inseparable isomer (98 mg, 85% (proximal:distal=95:<5 (this ratio is from crude mixture));

**IR** (neat) $\nu$ 2965, 1742, 1437, 1207, 1100 cm$^{-1}$.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$: 0.84 (t, $J = 7.4$ Hz, 6H), 1.50-1.63 (m, 4H), 2.22 (d, $J = 9.9$ and 13.0 Hz, 3H), 5.61 (dd, $J = 6.8$ and 13.0 Hz, 1H), 7.16 (dd, $J = 1.2$ and 8.1 Hz, 1H), 7.19 (dddd, $J = 1.2$, 7.8, 8.9 and 9.5 Hz, 1H), 7.31 (dddd, $J = 1.7$, 8.0, 8.9 and 9.5 Hz, 1H), 7.43 (dd, $J = 1.6$ and 7.8 Hz, 1H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$: 8.61, 22.47, 24.67, 26.84, 51.52, 119.70, 124.43, 126.82, 129.37, 130.03, 134.55, 150.12, 171.63. 

HRESIMS calcd. for C$_{15}$H$_{19}$O$_3$Na (M+Na$^+$): 257.1153; found 257.1151.
36.5 mg), TPMA (0.5 mmol, 14.5 mg), and dried toluene (1.0 mL) at 120 °C, yielded the product 4d with an inseparable isomer (101 mg, 82% (proximal:distal=95:<5 (this ratio is from crude mixture)));

**IR** (neat) ν 2925, 1739, 1437, 1207, 1094 cm⁻¹. **¹H NMR** (500 MHz, CDCl₃) δ: 1.33-1.45 (m, 4H), 1.52-1.56 (m, 4H), 1.67-1.73 (m, 2H), 2.22 (d, J = 0.4 Hz, 3H), 5.55 (d, J = 1.4 Hz, 1H), 7.13 (dd, J = 1.3 and 8.2 Hz, 1H), 7.17 (ddd, J = 1.3, 7.6 and 7.6 Hz, 1H), 7.32 (ddd, J = 1.7, 7.3 and 7.3 Hz, 1H), 7.43 (dd, J = 1.7, 7.9 and 7.9 Hz, 1H). **¹³C NMR** (126 MHz, CDCl₃) δ: 22.36, 22.58, 25.63, 31.84, 47.83, 119.40, 124.23, 126.92, 128.75, 129.35, 130.31, 134.09, 150.28, 170.89. **HRESIMS** calcd. for C₁₆H₁₉O₂ (M+H⁺): 243.1385; found 243.1385.

Following the general procedure B, using 1,4-dioxane (1 mL) and 0.5 M NaOH aq (0.2 mL) at 80 °C, yielded the product 5d (101 mg, 95%);

**IR** (neat) ν 3500-2600(br), 3498, 3371, 2930, 1685, 1449, 1174 cm⁻¹. **¹H NMR** (500 MHz, CDCl₃) δ: 1.29-1.66 (m, 8H), 1.69-1.82 (m, 1H), 1.84-1.96 (m, 1H), 2.02 (s, 3H), 5.62 (d, J = 1.3 Hz, 1H), 6.81 (d, J = 8.0 Hz, 1H), 6.85 (t, J = 7.5 Hz, 1H), 7.00 (dd, J = 1.6 and 7.5 Hz, 1H), 7.12 (ddd, J = 1.5, 7.7 and 7.7 Hz, 1H). **¹³C NMR** (126 MHz, CDCl₃) δ: 22.50, 25.45, 28.01, 48.57, 115.83, 120.42, 128.11, 128.97, 129.09, 132.92, 134.95, 151.99, 182.92. **HRESIMS** calcd. for C₁₆H₂₀O₃Na (M+Na⁺): 283.1310; found 283.1316.

Following the general procedure A, using 1a (0.5 mmol, 67 mg), 2e (0.75 mmol, 255.9 mg), CuOAc (0.05 mmol, 6.1 mg), Hex₃N (0.75 mmol, 101 mg), BnBu₃NBr (0.1 mmol, 36.5 mg), TPMA (0.5 mmol, 14.5 mg), and dried toluene (1.0 mL) at 120 °C, yielded the product 4e with an inseparable isomer (84 mg, 83% (proximal:distal=95:<5 (this ratio is from crude mixture)));

**IR** (neat) ν 2963, 1739, 1437, 1201, 1102 cm⁻¹. **¹H NMR** (500 MHz, CDCl₃) δ: 0.97 (t, J = 7.4 Hz, 3H), 1.74-1.83 (m, 1H), 1.99-2.08 (m, 1H), 2.20 (s, 3H), 2.46-2.57 (m, 1H), 5.51 (dd, J = 1.3 and 5.1 Hz, 1H), 7.23 (dt, J = 1.5 and 8.0 Hz, 2H), 7.36 (dt, J = 1.6 and 8.1 Hz, 2H).
Hz, 1H), 7.49 (dd, J = 1.6 and 8.0 Hz, 2H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$: 11.78, 20.82, 22.66, 44.57, 121.10, 124.89, 126.10, 127.22, 129.25, 130.46, 135.18, 149.57, 171.08. HRESIMS calcd. for C$_{13}$H$_{14}$O$_2$Na (M+Na$^+$): 225.0891; found 225.0893.

Following the general procedure B, using 1,4-dioxane (1 mL) and 0.5 M NaOH aq (0.2 mL) at 80 °C, yielded the product 5e (88 mg, 96%); IR (neat) $\nu$ 3500-2500(br), 2964, 1699, 1446, 1198 cm$^{-1}$. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$: 0.82 (t, J = 7.5 Hz, 3H), 1.51 (q, J = 7.5 Hz, 1H), 1.75 (q, J = 7.5 Hz, 1H), 2.05 (d, J = 7.4 Hz, 3H), 2.82-2.87 (m, 1H), 5.63 (d, J = 10.1 Hz, 1H), 6.90-6.94 (m, 2H), 7.00 (dd, J = 0.9 and 7.5 Hz, 1H), 7.19 (ddd, J = 1.6, 7.5 and 7.5 Hz, 1H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$: 11.41, 25.55, 47.08, 116.14, 120.88, 127.39, 127.57, 128.93, 129.05, 136.58, 152.01, 180.54. HRESIMS calcd. for C$_{13}$H$_{16}$O$_3$Na (M+Na$^+$): 243.0997; found 243.0991.

Following the general procedure A, using 1a (0.5 mmol, 67 mg), 2f (0.75 mmol, 246.9 mg), CuOAc (0.05 mmol, 6.1 mg), Hex$_3$N (0.75 mmol, 101 mg), BnBu$_3$NBr (0.1 mmol, 36.5 mg), TPMA (0.5 mmol, 14.5 mg), and dried toluene (1.0 mL) at 120 °C, yielded the product 4f with an inseparable isomer (87 mg, 76% (proximal:distal=94:6 (this ratio is from crude mixture))); IR (neat) $\nu$ 2929, 1761, 1437, 1203, 1103 cm$^{-1}$. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$: 0.86-0.90 (m, 3H), 1.28-1.35 (m, 4H), 1.72-1.79 (m, 1H), 1.97-2.03 (m, 1H), 2.19 (s, 3H), 2.52-2.56 (m, 1H), 5.51 (dd, J = 1.2 and 5.4 Hz, 1H), 7.22 (d, J = 8.2 Hz, 1H), 7.25 (dd, J = 1.2 and 8.1 Hz, 1H), 7.34-7.38 (m, 1H), 7.49 (dd, J = 1.7 and 7.9 Hz, 1H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$: 14.01, 20.82, 22.68, 29.18, 29.40, 42.98, 121.08, 124.88, 126.31, 127.22, 129.25, 130.45, 135.06, 149.56, 171.18. HRESIMS calcd. for C$_{15}$H$_{18}$O$_3$Na (M+Na$^+$): 253.1204; found 253.1209.
Following the general procedure B, using 1,4-dioxane (1 mL) and 0.5 M NaOH aq (0.2 mL) at 80 °C, yielded the product 5f (86 mg, 99%);

IR (neat) ν 3500-2500(br), 3029, 2929, 1699, 1446, 1200 cm⁻¹. ¹H NMR (500 MHz, CDCl₃) δ: 0.83 (t, J = 7.2 Hz, 3H), 1.14-1.29 (m, 4H), 1.40-1.54 (m, 1H), 1.66-1.79 (m, 1H), 2.04 (s, 3H), 2.90 (brs, 1H), 5.62 (d, J = 9.3 Hz, 1H), 6.90-6.94 (m, 2H), 7.00 (d, J = 7.4 Hz, 1H), 7.19 (dd, J = 1.6 and 8.0 Hz, 1H). ¹³C NMR (126 MHz, CDCl₃) δ: 13.92, 22.41, 25.54, 28.92, 116.22, 120.28, 120.86, 127.39, 129.05, 129.15, 136.29, 152.03, 181.88. HRESIMS calcd. for C₁₅H₂₁O₃ (M+H⁺): 249.1490; found 249.1494.

Following the general procedure A, using 1b (0.5 mmol, 74 mg), 2a (0.75 mmol, 225.8 mg), CuOAc (0.05 mmol, 6.1 mg), Hex₃N (0.75 mmol, 101 mg), BnBu₃NBr (0.1 mmol, 36.5 mg), TPMA (0.5 mmol, 14.5 mg), and dried toluene (1.0 mL) at 120 °C, yielded the product 4h with an inseparable isomer (90mg, 86% (proximal:distal=81:19 (this ratio is from crude mixture)));

IR (neat) ν 2968, 1746, 1439, 1202, 1105, 763 cm⁻¹. ¹H NMR (500 MHz, CDCl₃) δ: 1.06 (t, J = 7.4 Hz, 3H), 1.19 (s, 6H), 2.57 (q, J = 7.4 Hz, 2H), 5.60 (s, 1H), 7.19 (dd, J = 1.2 and 7.0 Hz, 1H), 7.20 (ddd, J = 1.3, 7.7 and 7.7 Hz, 1H), 7.34 (ddd, J = 1.6, 8.2 and 8.2 Hz, 1H), 7.45 (dd, J = 1.6 and 7.8 Hz, 1H). ¹³C NMR (126 MHz, CDCl₃) δ: 13.43, 24.25, 28.40, 42.88, 52.55, 120.11, 124.55, 126.76, 128.30, 129.41, 130.79, 140.35, 150.84, 173.12. HRESIMS calcd. for C₁₄H₁₆O₂Na (M+Na⁺): 239.1048; found 239.1051.

Following the general procedure B, using 1,4-dioxane (1 mL) and 0.5 M NaOH aq (0.2 mL) at 80 °C, yielded the product 5h (94 mg, 97%);

IR (neat) ν 3500-2600(br), 3402, 2965, 1693, 1447, 1283, 1212, 1166 cm⁻¹. ¹H NMR (500 MHz, CDCl₃) δ: 0.99 (t, J = 7.4 Hz, 3H), 1.12 (brs, 3H), 1.29 (brs, 3H), 2.27 (q, J = 7.4 Hz, 2H), 5.69 (s, 1H), 6.83 (dd, J = 1.7 and 8.2 Hz, 1H), 6.85 (dd, J = 0.9 and 7.4 Hz, 1H), 6.95 (dd, J = 1.6 and 7.5 Hz, 1H), 7.13 (ddd, J = 1.7, 8.0 and 8.0 Hz, 1H). ¹³C NMR (126 MHz, CDCl₃) δ: 12.73, 33.92, 44.14, 50.07, 115.73, 120.21, 127.08, 129.02, 129.99, 132.91, 139.50, 152.56, 183.54. HRESIMS calcd. for C₁₅H₁₉O₃ (M+H⁺): 235.1334; found 235.1339.
Following the general procedure A, using 1c (0.5 mmol, 98 mg), 2a (0.75 mmol, 225.8 mg), CuOAc (0.05 mmol, 6.1 mg), Hex3N (0.75 mmol, 101 mg), BnBu3NBr (0.1 mmol, 36.5 mg), TPMA (0.5 mmol, 14.5 mg), and dried toluene (1.0 mL) at 120 °C, yielded the product 4i (125 mg, 95%);

**IR** (neat) ν 2930, 1741, 1439, 1206, 1094 cm⁻¹. **¹H NMR** (500 MHz, CDCl₃) δ: 1.29 (s, 6H), 5.88 (s, 1H), 7.09-7.10 (m, 2H), 7.23 (d, J = 8.3 Hz, 1H), 7.28-7.30 (m, 2H), 7.34-7.39 (m, 4H). **¹³C NMR** (126 MHz, CDCl₃) δ: 44.6, 116.0, 120.4, 125.64, 126.72, 127.96, 128.58, 129.80, 131.33, 136.24, 137.20, 141.28, 153.32, 182.84. **HRESIMS** calcd. for C₁₈H₁₇O₂ (M+H⁺): 265.1228; found 265.1224.

Following the general procedure B, using 1,4-dioxane (1 mL) and 0.5 M NaOH aq (0.2 mL) at 80 °C, yielded the product 5i (128 mg, 96%);

**IR** (neat) ν 3550, 3500-2400(br), 1695, 1445, 1193 cm⁻¹. **¹H NMR** (500 MHz, CDCl₃) δ: 1.18-1.43 (m, 6H), 6.33 (s, 1H), 6.86 (d, J = 8.1 Hz, 1H), 6.90 (ddd, J = 0.8, 7.5 and 14.9 Hz, 1H), 7.06 (dd, J = 1.3 and 17.5 Hz, 1H), 7.20 (ddd, J = 1.7, 8.0 and 15.0 Hz, 1H), 7.22-7.28 (m, 5H). **¹³C NMR** (126 MHz, CDCl₃) δ: 8.89, 9.01, 21.20, 29.50, 31.05, 41.61, 49.42, 80.43, 122.71, 123.34, 125.58, 128.66, 129.41, 137.92, 138.34, 147.81, 166.69. **HRESIMS** calcd. for C₁₈H₁₉O₃ (M+H⁺): 283.1334; found 283.1340.

Following the general procedure A, using 1d (0.5 mmol, 91 mg), 2a (0.75 mmol, 225.8 mg), CulMe₂S (0.05 mmol, 12 mg), Hex3N (0.75 mmol, 101 mg), BnBu3NBr (0.1 mmol, 36.5 mg), TPMA (0.5 mmol, 14.5 mg), and dried toluene (1.0 mL) at 120 °C, yielded the product 4j with an inseparable isomer (98 mg, 78% (proximal:distal=95:<5 (this ratio is from crude mixture)));

**IR** (neat) ν 2917, 1750, 1389, 1107, 903 cm⁻¹. **¹H NMR** (500 MHz, CDCl₃) δ: 1.20 (s, 6H),
2.15 (s, 3H), 2.38 (s, 3H), 5.61 (d, J = 1.4 Hz, 1H), 7.03 (s, 1H), 7.39 (s, 1H).  
\[ ^{13}C \text{ NMR} \] (126 MHz, CDCl\textsubscript{3}) \( \delta \): 19.92, 22.01, 24.25, 42.98, 122.00, 127.00, 128.08, 130.08, 132.43, 133.53, 137.73, 148.56, 172.19.  

HRESIMS calcd. for C\textsubscript{14}H\textsubscript{16}ClO (M+H\textsuperscript{+}): 251.0838; found 251.0838.

Following the general procedure B, using 1,4-dioxane (1 mL) and 0.5 M NaOH aq (0.2 mL) at 80 °C, yielded the product 5j (100 mg, 95%);  

IR (neat) \( \nu \): 3490, 3414, 3000-2500(br), 1706, 1672, 1393, 1144 cm\textsuperscript{-1}.  
\[ ^{1}H \text{ NMR} \] (500 MHz, CDCl\textsubscript{3}) \( \delta \): 1.13-1.26 (brs, 6H), 1.95 (d, J = 1.3 Hz, 3H), 2.26 (s, 3H), 5.70 (d, J = 1.3 Hz, 1H), 6.71 (s, 1H), 6.96 (s, 1H).  
\[ ^{13}C \text{ NMR} \] (126 MHz, CDCl\textsubscript{3}) \( \delta \): 19.97, 27.56, 44.28, 118.22, 125.43, 127.10, 129.13, 132.88, 134.55, 136.58, 150.62, 183.63.

HRESIMS calcd. for C\textsubscript{14}H\textsubscript{17}ClO\textsubscript{3}Na (M+Na\textsuperscript{+}): 291.0763; found 291.0770.

Following the general procedure A, using 1e (0.5 mmol, 107 mg), 2a (0.75 mmol, 225.8 mg), Cul (0.05 mmol, 9.5 mg), Hex\textsubscript{3}N (0.75 mmol, 101 mg), BnBu\textsubscript{3}NBr (0.1 mmol, 36.5 mg), TPMA (0.5 mmol, 14.5 mg), and dried toluene (1.0 mL) at 120 °C, yielded the product 4k with an inseparable isomer (108 mg, 77% (proximal:distal=95:<5 (this ratio is from crude mixture)));  

IR (neat) \( \nu \): 2975, 1747, 1472, 1391, 1204, 1102, 812 cm\textsuperscript{-1}.  
\[ ^{1}H \text{ NMR} \] (500 MHz, CDCl\textsubscript{3}) \( \delta \): 1.20 (s, 6H), 2.17 (s, 3H), 5.67 (d, J = 1.4 Hz, 1H), 7.04 (d, J = 8.3 Hz, 1H), 7.44 (dd, J = 8.3 Hz, 1H), 7.55 (d, J = 8.3 Hz, 1H).  
\[ ^{13}C \text{ NMR} \] (126 MHz, CDCl\textsubscript{3}) \( \delta \): 22.04, 24.23, 43.06, 117.42, 121.75, 129.76, 131.00, 132.41, 133.48, 149.31, 168.48.

HRESIMS calcd. for C\textsubscript{13}H\textsubscript{13}BrO\textsubscript{2}Na (M+Na\textsuperscript{+}): 302.9996; found 303.0000.

Following the general procedure B, using 1,4-dioxane (1 mL) and 0.5 M NaOH aq (0.2 mL) at 80 °C, yielded the product 5k (113 mg, 99%);  

IR (neat) \( \nu \): 3474, 3389, 3000-2500(br), 1705, 1669, 1396, 1272, 1123 cm\textsuperscript{-1}.  
\[ ^{1}H \text{ NMR} \] (500 MHz, CDCl\textsubscript{3}) \( \delta \): 1.16-1.27 (brs, 6H), 1.95 (d, J = 1.3 Hz, 3H), 2.25 (s, 3H), 5.70 (d, J = 1.3 Hz, 1H), 6.74 (s, 1H), 7.07 (s, 1H).  
\[ ^{13}C \text{ NMR} \] (126 MHz, CDCl\textsubscript{3}) \( \delta \): 19.97, 27.56, 44.28, 118.22, 125.43, 127.10, 129.13, 132.88, 134.55, 136.58, 150.62, 183.63.

HRESIMS calcd. for C\textsubscript{14}H\textsubscript{17}ClO\textsubscript{3}Na (M+Na\textsuperscript{+}): 291.0763; found 291.0770.
MHz, CDCl₃ δ: 1.11-1.36 (m, 6H), 1.97 (s, 3H), 5.72 (d, J = 1.3 Hz, 1H), 6.73 (d, J = 8.7 Hz, 1H), 7.12 (d, J = 2.5 Hz, 2H), 7.22 (dd, J = 2.5 and 8.7 Hz, 2H). ¹³C NMR (126 MHz, CDCl₃) δ: 27.51, 44.35, 112.40, 117.78, 130.24, 131.71, 131.75, 132.64, 134.63, 151.36, 183.46. HRESIMS calcd. for C₁₃H₁₅BrO₃Na (M+Na⁺): 323.0081; found 323.0075.

Following the general procedure A, using 1f (0.5 mmol, 84 mg), 2a (0.75 mmol, 225.8 mg), CuI (0.05 mmol, 9.5 mg), Hex₃N (0.75 mmol, 101 mg), BnBu₃NBr (0.1 mmol, 36.5 mg), TPMA (0.5 mmol, 14.5 mg), and dried toluene (1.0 mL) at 120 °C, yielded the product 4l with an inseparable isomer (92 mg, 78% (proximal:distal=95:<5 (this ratio is from crude mixture)));

IR (neat) ν 2977, 1751, 1596, 1486, 1390, 1204, 1096, 944 cm⁻¹. ¹H NMR (500 MHz, CDCl₃) δ: 1.20 (s, 6H), 2.17 (s, 3H), 5.63 (d, J = 1.4 Hz, 1H), 7.17-7.19 (m, 2H), 7.37 (d, J = 8.9 Hz, 1H). ¹³C NMR (126 MHz, CDCl₃) δ: 22.09, 24.20, 43.08, 120.17, 124.79, 127.70, 127.94, 132.50, 133.76, 134.57, 150.51, 171.87. HRESIMS calcd. for C₁₃H₁₃ClO₂Na (M+Na⁺): 259.0501; found 259.0495.

Following the general procedure B, using 1,4-dioxane (1 mL) and 0.5 M NaOH aq (0.2 mL) at 80 °C, yielded the product 5l (97 mg, 98%);

IR (neat) ν 3455, 3000-2500(br), 1691, 1595, 1404, 1252, 1089 cm⁻¹. ¹H NMR (500 MHz, CDCl₃) δ: 1.08-1.35 (m, 6H), 1.96 (s, 3H), 5.72 (s, 1H), 6.83-6.85 (m, 2H), 6.91 (d, J = 8.7 Hz, 1H). ¹³C NMR (126 MHz, CDCl₃) δ: 27.43, 44.30, 116.43, 120.43, 126.73, 130.12, 132.85, 134.10, 134.93, 152.93, 183.06. HRESIMS calcd. for C₁₃H₁₆ClO₃ (M+H⁺): 255.0788; found 255.0790.

Following the general procedure A, using 1g (0.5 mmol, 74 mg), 2a (0.75 mmol, 225.8 mg), CuI · Me₂S (0.05 mmol, 12 mg), Hex₃N (0.75 mmol, 101 mg), BnBu₃NBr (0.1 mmol, 36.5 mg), TPMA (0.5 mmol, 14.5 mg), and dried toluene (1.0 mL) at 120 °C, yielded the
product 4m with an inseparable isomer (84 mg, 78% (proximal:distal=95:<5 (this ratio is from crude mixture)));

IR (neat) ν 2975, 1744, 1391, 1206, 1165, 1135, 1103, 826 cm⁻¹. ¹H NMR (500 MHz, CDCl₃) δ: 1.19 (s, 6H), 2.16 (s, 3H), 2.37 (s, 3H), 5.56 (d, J = 1.4 Hz, 1H), 6.97 (d, J = 0.7 Hz, 1H), 7.01 (dd, J = 1.0 and 7.9 Hz, 1H), 7.31 (d, J = 7.9 Hz, 1H). ¹³C NMR (126 MHz, CDCl₃) δ: 21.07, 22.10, 24.18, 42.92, 120.23, 125.40, 126.24, 126.73, 131.22, 134.43, 140.02, 150.13, 172.71. HRESIMS calcd. for C₁₄H₁₆O₂Na (M+Na⁺): 239.1048; found 239.1051.

Following the general procedure B, using 1,4-dioxane (1 mL) and 0.5 M NaOH aq (0.2 mL) at 80 °C, yielded the product 5m (89 mg, 98%);

IR (neat) ν 3401, 3000-2500(br), 1695, 1412, 1288, 1165 cm⁻¹. ¹H NMR (500 MHz, CDCl₃) δ: 1.08-1.36 (brs, 6H), 1.98 (s, 3H), 2.25 (s, 3H), 5.71 (d, J = 1.5 Hz, 1H), 6.66 (s, 1H), 6.68 (d, J = 7.7 Hz, 1H), 6.88 (d, J = 7.7 Hz, 1H). ¹³C NMR (126 MHz, CDCl₃) δ: 21.28, 27.71, 44.15, 116.49, 121.34, 125.13, 129.12, 134.06, 134.28, 139.16, 151.88, 182.87. HRESIMS calcd. for C₁₄H₁₉O₃ (M+H⁺): 235.1334; found 235.1331.

Following the general procedure A, using 1h (0.5 mmol, 67 mg), 2a (0.75 mmol, 246.9 mg), CuOAc (0.05 mmol, 6.1 mg), Hex₅N (0.75 mmol, 101 mg), BnBu₃NBr (0.1 mmol, 36.5 mg), TPMA (0.5 mmol, 14.5 mg), and dried toluene (1.0 mL) at 120 °C, yielded the product 4p with an inseparable isomer (84 mg, 84% (proximal:distal=30:70 (this ratio is from crude mixture)));

IR (neat) ν 2971, 1720, 1463, 1148, 1058 cm⁻¹. ¹H NMR (500 MHz, CDCl₃) δ: 1.43 (s, 6H), 5.24 (d, J = 1.3 Hz, 2H), 5.98 (s, 1H), 7.31-7.39 (m, 5H). ¹³C NMR (126 MHz, CDCl₃) δ: 26.79, 38.01, 69.67, 125.23, 128.56, 128.96, 129.25, 131.57, 135.81, 175.20. HRESIMS calcd. for C₁₃H₁₄O₂Na (M+H⁺): 225.0891; found 225.0892.
CDCl₃ δ: 25.10, 36.38, 37.36, 118.02, 125.27, 127.81, 128.98, 136.55, 137.46, 173.76.  
HRESIMS calcd. for C₁₁H₁₄O₂Na (M+H⁺): 225.0891; found 225.0943.

3. Miscellaneous
3-1. Methylation

5a (0.5 mmol), and MeI (2.5 mmol), K₂CO₃ (1.5 mmol) were sequentially added under air to a dram vial equipped with a stir bar and a screw cap. Acetone (2 mL) were added by syringe and the resulting mixture vigorously stirred under nitrogen atmosphere for 6 h at 80 °C. After this time, the contents of the flask were filtered through the plug of silica gel, and then concentrated by rotary evaporation. The residue was purified by flash chromatography eluting with Hexane/EtOAc to afford the product 5a-Me (0.48 mmol, 95 %).

IR (neat) ν 2917, 1729, 1431, 1242, 1136, 1027 cm⁻¹. ¹H NMR (500 MHz, CDCl₃) δ: 1.17 (s, 6H), 1.96 (s, 3H), 3.33 (s, 3H), 3.81 (s, 3H), 5.57 (s, 1H), 6.84 (d, J = 8.3 Hz, 1H), 6.85 (t, J = 7.5 Hz, 1H), 6.95 (dd, J = 1.7 and 7.5 Hz, 1H), 7.22 (dd, J = 1.8 and 7.5 Hz, 1H). ¹³C NMR (126 MHz, CDCl₃) δ: 26.72, 29.72, 43.56, 51.49, 55.25, 110.40, 120.18, 128.44, 129.90, 130.24, 132.19, 134.94, 156.30, 177.22. HRESIMS calcd. for C₁₅H₂₁O₃ (M+H⁺): 249.1490; found 249.1485.

3-2. Nitrogen-containing trisubstituted alkene

4a (0.5 mmol), and NBS (0.75 mmol) were sequentially added under air to a dram vial equipped with a stir bar and a screw cap. DMF (1 mL) were added by syringe and the resulting mixture vigorously stirred under nitrogen atmosphere for 2 h at 50 °C. After this time, the contents of the flask were filtered through the plug of silica gel, and then concentrated by rotary evaporation. The residue was purified by flash chromatography eluting with Hexane/EtOAc to afford the product 4a-Br (0.38 mmol, 75%).
IR (neat) ν 2976, 1735, 1438, 1201, 1104 cm⁻¹. ¹H NMR (500 MHz, CDCl₃) δ: 1.21 (s, 6H), 4.38 (s, 2H), 6.02 (s, 1H), 7.19 (dd, J = 0.8 and 8.2 Hz, 1H), 7.25 (dd, J = 1.3 and 7.9 Hz, 1H), 7.40 (dd, J = 1.4 and 7.8 Hz, 1H), 7.60 (dd, J = 1.3 and 7.9 Hz, 1H). ¹³C NMR (126 MHz, CDCl₃) δ: 23.86, 33.41, 43.26, 120.34, 124.80, 125.80, 126.47, 130.41, 135.30, 136.45, 150.95, 172.04. HRESIMS calcd. for C₁₃H₁₃O₂BrNa (M+Na⁺): 302.9996; found 302.9996.

4a-Br (0.2 mmol), and N-Methylbenzylamine (0.3 mmol) were sequentially added under air to a dram vial equipped with a stir bar and a screw cap. DMF (0.2 mL) and THF (0.2 mL) were added by syringe and the resulting mixture vigorously stirred under nitrogen atmosphere for 4 h at room temperature. After this time, the contents of the flask were filtered through the plug of silica gel, and then concentrated by rotary evaporation. The residue was purified by flash chromatography eluting with Hexane/EtOAc to afford the product 4a-N (0.16 mmol, 81%).

IR (neat) ν 2976, 2785, 1745, 1439, 1202, 1101, 1022 cm⁻¹. ¹H NMR (500 MHz, CDCl₃) δ: 1.20 (s, 6H), 2.12 (s, 3H), 2.01 (s, 2H), 3.47 (s, 2H), 5.80 (s, 1H), 7.15-7.18 (m, 2H), 7.21 (d, J = 7.9 Hz, 2H), 7.24 (d, J = 7.9 Hz, 1H), 7.28-7.31 (m, 2H), 7.34 (ddd, J = 1.7, 8.9 and 8.9 Hz, 1H), 7.49 (dd, J = 1.0 and 7.9 Hz, 1H). ¹³C NMR (126 MHz, CDCl₃) δ: 24.18, 42.17, 43.08, 61.82, 62.12, 119.89, 124.29, 127.26, 127.43, 127.96, 128.35, 129.26, 129.59, 134.43, 136.36, 138.99, 150.88, 173.01. HRESIMS calcd. for C₂₁H₂₃NO₂Na (M+Na⁺): 344.1625; found 344.1619.

Following the general procedure B, using 1,4-dioxane (1 mL) and 0.5 M NaOH aq (0.2 mL) at 80 °C, yielded the product 5-N (0.14 mmol, 90%);

IR (neat) ν 3400-2400(br), 2919, 1706, 1554, 1448, 1255, 1103 cm⁻¹. ¹H NMR (500 MHz, CDCl₃) δ: 1.22 (s, 6H), 1.25 (s, 3H), 2.39 (s, 2H), 3.40 (s, 2H), 3.83 (s, 2H), 5.87 (s, 1H), 6.76 (t, J = 7.4 Hz, 1H), 6.89 (d, J = 8.0 Hz, 1H), 6.94 (d, J = 7.4 Hz, 1H), 7.15 (t, J = 8.0 Hz, 1H), 7.29-7.33 (m, 5H). ¹³C NMR (126 MHz, CDCl₃) δ: 26.82, 29.80, 39.98, 44.40,
3-3. Tetrasubstituted alkene

\[
\begin{align*}
\text{4j} & \text{ (0.5 mmol), and NBS (0.75 mmol) were sequentially added under air to a dram vial equipped with a stir bar and a screw cap. DMF (1 mL) were added by syringe and the resulting mixture vigorously stirred under nitrogen atmosphere for 2 h at 50 °C. After this time, the contents of the flask were filtered through the plug of silica gel, and then concentrated by rotary evaporation. The residue was purified by flash chromatography eluting with Hexane/EtOAc to afford the product 4j-Br (0.19 mmol, 93%).}
\end{align*}
\]

**IR** (neat) \( \nu \) 2931, 1744, 1436, 1209, 1111 cm\(^{-1}\).  \( ^1H \text{ NMR} \) (500 MHz, CDCl\(_3\)) \( \delta \): 1.46 (s, 6H), 6.87 (dd, \( J = 1.6 \) and 8.0 Hz, 1H), 7.02 (ddd, \( J = 1.3, 7.3\) and 7.3 Hz, 1H), 7.19-7.21 (m, 3H), 7.33-7.43 (m, 4H).  \( ^{13}C\text{ NMR} \) (126 MHz, CDCl\(_3\)) \( \delta \): 26.74, 49.25, 119.61, 124.63, 126.72, 128.06, 128.63, 129.22, 129.80, 130.19, 130.80, 141.41, 150.16, 169.84.  

**HRESIMS** calcd. for C\(_{18}\)H\(_{15}\)O\(_2\)BrNa (M+Na\(^+\)) : 365.0153; found 365.0147.

Suzuki-Miyaura coupling followed by hydrolysis

\[
\begin{align*}
\text{4j-Br (0.2 mmol), p-tolyboronic acid (0.6 mmol), and PdCl\(_2\)(dppf)\(_2\) HCCl\(_3\) (0.025 mmol) were sequentially added under nitrogen atmosphere to a reaction tube equipped with a stir bar and a septum. toluene (0.4 mL) and Cs\(_2\)CO\(_3\) (0.4 mmol) was added by syringe and vigorously stirred for 13 h at 120 °C. After the reaction, the mixture was extracted with EtOAc and then filtered through a plug of silica gel and concentrated by rotary evaporation. The residue (4j-Suzuki) was then subjected to the following hydrolysis.}
\end{align*}
\]
IR (neat) ν 2920, 1735, 1434, 1209, 1109 cm\(^{-1}\). \(^1\)H NMR (500 MHz, CDCl\(_3\)) δ: 1.18 (s, 6H), 2.21 (s, 3H), 6.80 (d, \(J = 8.0\) Hz, 2H), 6.88-6.93 (m, 5H), 7.01 (ddd, \(J = 1.2, 7.3\) and 7.3 Hz, 1H), 7.04-7.09 (m, 3H), 7.23 (dd, \(J = 1.1\) and 8.2 Hz, 1H), 7.33 (ddd, \(J = 1.7, 7.4\) and 7.4 Hz, 1H). \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) δ: 21.19, 25.11, 46.99, 119.10, 124.01, 126.60, 127.64, 128.29, 129.58, 129.96, 130.59, 130.83, 131.08, 136.31, 136.96, 138.71, 141.59, 143.03, 150.50, 171.53. HRESIMS calcd. for C\(_{25}\)H\(_{22}\)O\(_2\)Na (M+Na\(^+\)): 377.1517; found 377.1508.

1,4-dioxane (1 mL), and 0.5 M NaOHaq (0.2 mL) were sequentially added to the crude 4j-Suzuki and the resulting solution was stirred for 4 h at 80 °C. After this time, the contents of the flask were diluted with water and extracted with EtOAc. The solution obtained was dried over anhydrous MgSO\(_4\), filtered, and concentrated by rotary evaporation. The residue was purified by flash chromatography eluting with hexane/EtOAc to afford the product 6 (70% yield for 2 steps).

Final product 6

IR (neat) ν 3500-2500(br), 3454, 2973, 1701, 1444, 1173 cm\(^{-1}\). \(^1\)H NMR (500 MHz, CDCl\(_3\)) δ: 1.22 (3H), 1.38 (s, 3H), 2.22 (s, 3H), 6.80 (d, \(J = 8.4\) Hz, 1H), 6.89-7.04 (m, 10H), 7.15 (t, \(J = 7.3\) Hz, 1H), 7.36 (d, \(J = 7.8\) Hz, 1H). \(^{13}\)C NMR (126 MHz, DMSO-d) δ: 20.66, 25.65, 28.23, 46.88, 115.46, 118.64, 125.08, 127.00, 127.63, 129.11, 129.79, 130.32, 130.45, 134.49, 138.18, 138.54, 143.25, 144.52, 154.30, 178.34. HRESIMS calcd. for C\(_{25}\)H\(_{24}\)O\(_3\)Na (M+Na\(^+\)): 395.1623; found 395.1628.
4. Spectral Data for New Compounds
nOe analysis of 5a
nOe analysis of 5i