Pinacol Coupling Reaction of β -Halo- α,β -Unsaturated Aldehydes Promoted by TiI_4

Makoto Shimizu,* Hiroshi Goto, and Ryuuichirou Hayakawa

Department of Chemistry for Materials, Mie University, Tsu, Mie 514-8507, Japan

Experimental

General Aspects

Infrared spectra were determined on a JASCO IR-810 spectrometer. ^1H - and ^{13}C -NMR spectra were recorded with JNM EX-270 and JEOL α -500 spectrometers using tetramethylsilane as an internal standard. Exact mass spectra were taken on a Waters micromass ZQ. Propionitrile was distilled from calcium hydride. Purification of products was performed by column chromatography on silica gel (Merck Silica Gel-60) and/or preparative TLC on silica gel (Merck Kiesel Gel PF254).

Pinacol coupling reaction of unsaturated aldehydes using TiI_4 .

dl-(*E,E*)-3,4-Dihydroxy-1,6-diphenylhexa-1,5-diene (2a).^{1,2}

Propionitrile (1.0 mL) was added to TiI_4 (555.5 mg, 1.0 mmol) at ambient temperature under an argon atmosphere. The solution was stirred for 10 min, and to it was added a propionitrile (1.0 mL) solution of cinnamaldehyde (66.1 mg, 0.5 mmol) at -78°C . After being stirred at -78°C to -20°C , the reaction was quenched with sat. aqueous NaHCO_3 , 10% aqueous NaHSO_3 , and triethylamine. The whole mixture was filtered through a Celite pad and extracted with ethyl acetate (10 mL x 3). The combined organic extracts were dried over anhydrous Na_2SO_4 , and concentrated *in vacuo*. Purification by preparative TLC on silica gel (*n*-hexane : ethyl acetate = 2 : 1 as an eluent) gave *dl*-(*E, E*)-3,4-dihydroxy-1,6-diphenylhexa-1,5-diene (55.1 mg, 83%).

^1H NMR (CDCl_3) δ 2.65 (brs, 2H), 4.26 (d, J = 5.0 Hz, 2H), 6.25 (dd, J = 5.0 and 15.8 Hz, 2H), 6.71 (d, J = 15.8 Hz, 2H), 7.21-7.39 (m, 10H).

^{13}C NMR (CDCl_3) δ 75.8, 126.6, 127.5, 127.9, 128.6, 132.7, 136.3.

IR (CHCl_3) 3440, 2870, 1615, 1510, 1465, 1400, 1105, 985, 700 cm^{-1} .

HRMS calcd for $\text{C}_{18}\text{H}_{15} [\text{M}-\text{H}_2\text{O}-\text{OH}]^+$ 231.12, found 231.14.

The spectral data are in accordance with those in the literature.^{1,2}

dl-(*Z,Z*)-1,6-Dichloro-3,4-dihydroxy-1,6-diphenylhexa-1,5-diene (2b).

^1H NMR (CDCl_3) δ 2.76 (s, 2H), 4.83 (d, J = 6.9 Hz, 2H), 6.27 (dd, J = 6.9 and 2.0 Hz, 2H), 7.31-7.39 (m, 6H), 7.53-7.61 (m, 4H).

^{13}C NMR (CDCl_3) δ 79.3, 124.1, 128.2, 128.4, 129.1, 131.5, 134.7.

IR (CHCl_3) 3525, 3300, 1640, 1500, 1460, 1100, 880, 600 cm^{-1} .

HRMS calcd for $\text{C}_{18}\text{H}_{15}\text{OCl}_2 [\text{M}-\text{OH}]^+$ 317.05, found 317.20.

***dl*-(Z,Z)-1,6-Dibromo-3,4-dihydroxy-1,6-diphenylhexa-1,5-diene (2c).**

^1H NMR (CDCl_3) δ 2.68 (s, 2H), 4.76-4.83 (m, 2H), 6.36-6.47 (m, 2H), 7.26-7.36 (m, 6H), 7.51-7.56 (m, 4H).

^{13}C NMR (CDCl_3) δ 78.3, 124.0, 128.2, 128.4, 129.1, 131.5, 134.7.

IR (CHCl_3) 3550, 3350, 1630, 1500, 1460, 1300, 1015, 880, 660, 600 cm^{-1} .

HRMS calcd for $\text{C}_{18}\text{H}_{17}\text{O}_2\text{Br}_2$ $[\text{M}+\text{H}]^+$ 422.96, found 422.90.

***dl*-(Z,Z)-3,4-Dihydroxy-1,6-diiodo-1,6-diphenylhexa-1,5-diene (2d).**

^1H NMR (CDCl_3) δ 3.03 (s, 2H), 4.63 (d, J = 6.6 Hz, 2H), 6.39-6.45 (m, 2H), 7.27-7.33 (m, 6H), 7.44-7.48 (m, 4H).

^{13}C NMR (CDCl_3) δ 79.8, 108.0, 128.3, 128.6, 128.9, 135.5, 142.4.

IR (CHCl_3) 3570, 3400, 1660, 1525, 1480, 1420, 1040, 930, 900, 720, 675 cm^{-1} .

HRMS calcd for $\text{C}_{18}\text{H}_{16}\text{O}_2\text{I}_2$ $[\text{M}]^+$ 517.92, found 517.90.

***dl*-(Z,Z)-2,5-Dibromo-3,4-dihydroxy-1,6-diphenylhexa-1,5-diene (2e).**

^1H NMR (CDCl_3) δ 3.05 (brs, 2H), 4.62 (s, 2H), 7.19 (s, 2H), 7.25-7.37 (m, 6H), 7.51-7.55 (m, 4H).

^{13}C NMR (CDCl_3) δ 75.1, 127.7, 128.3, 128.6, 128.9, 129.2, 139.0.

IR (CHCl_3) 3530, 3350, 1660, 1510, 1460, 1400, 1110, 880 cm^{-1} .

HRMS calcd for $\text{C}_{18}\text{H}_{17}\text{O}_2\text{Br}_2$ $[\text{M}+\text{H}]^+$ 422.96, found 422.90.

***dl*-(E,E)-6,7-Dihydroxydodeca-4,8-diene (2f).**

^1H NMR (CDCl_3) δ 0.89 (t, J = 6.9 Hz, 6H), 1.33-1.46 (m, 4H), 2.02 (q, J = 7.3 Hz, 4H), 2.21 (s, 2H), 3.92 (d, J = 5.3 Hz, 2H), 5.44 (dd, J = 5.3 and 15.5 Hz, 2H), 5.68-5.80 (m, 2H).

^{13}C NMR (CDCl_3) δ 13.6, 22.2, 34.4, 76.0, 128.6, 134.5.

IR (CHCl_3) 3410, 2920, 1730, 1470, 1315, 1115, 985 cm^{-1} .

HRMS calcd for $\text{C}_{12}\text{H}_{21}\text{O}$ $[\text{M}-\text{OH}]^+$ 181.10, found 181.16.

***dl*-(Z,Z)-4,9-Dibromo-6,7-dihydroxydodeca-4,8-diene (2g).**

^1H NMR (CDCl_3) δ 0.90 (t, J = 7.3 Hz, 6H), 1.52-1.61 (m, 4H), 2.45 (q, J = 7.6 Hz, 4H), 2.66 (s, 2H), 4.31 (d, J = 5.9 Hz, 2H), 5.65 (d, J = 5.9 Hz, 2H).

^{13}C NMR (CDCl_3) δ 12.9, 22.8, 47.5, 71.8, 132.6, 138.

IR (CHCl_3) 3350, 2900, 1650, 1470, 1400, 1100, 1010, 900, 600 cm^{-1} .

HRMS calcd for $\text{C}_{12}\text{H}_{22}\text{OBr}$ $[\text{M}+\text{H}_2-\text{BrO}]^+$ 261.08, found 260.98.

***dl*-(Z,Z)-6,7-Dihydroxy-4,9-diiodododeca-4,8-diene (2h).**

^1H NMR (CDCl_3) δ 0.88 (t, J = 7.2 Hz, 6H), 1.47-1.64 (m, 4H), 2.51 (q, J = 7.9 Hz, 4H), 2.60 (s, 2H), 4.34 (d, J = 4.6 Hz, 2H), 5.44 (d, J = 4.6 Hz, 2H).

^{13}C NMR (CDCl_3) δ 12.8, 22.8, 47.5, 78.9, 110.7, 138.7.

IR (CHCl_3) 3400, 2900, 1650, 1470, 1400, 1130, 1020, 900, 610 cm^{-1} .

HRMS calcd for $\text{C}_{12}\text{H}_{21}\text{O}_2\text{I}_2$ $[\text{M}+\text{H}]^+$ 450.97, found 451.68.

***dl*- and *meso*-(*Z,Z*)-3,8-Dichloro-5,6-dihydroxy-2,2,9,9-tetramethyldeca-3,7-diene (2j).**

¹H NMR (CDCl₃) δ 1.16 (s, 18H), 2.57 (brs, 2H), 4.57 (d, *J* = 6.9 Hz, 1.86H, *dl*), 4.79 (d, *J* = 6.9 Hz, 0.14H, *meso*), 5.59-5.62 (m, 2H).

¹³C NMR (CDCl₃) δ 28.7, 38.9, 72.6, 120.8, 148.7.

IR (CHCl₃) 3550, 3400, 2960, 1670, 1500, 1385, 1305, 1040, 865, 670 cm⁻¹.

HRMS calcd for C₁₄H₂₆O₂Cl₂ [M+H₂]⁺ 296.14, found 296.19.

***dl*- and *meso*-1,2-Di(2-chlorocyclohex-1-enyl)-1,2-dihydroxyethane (2l).**

¹H NMR (CDCl₃) δ 1.58-1.78 (m, 8H), 2.30-2.35 (m, 8H), 2.59 (brs, 2H), 4.79 (s, 1.94H, *dl*), 4.98 (s, 0.06H, *meso*).

¹³C NMR (CDCl₃) δ 21.8, 23.6, 25.3, 34.4, 72.3, 130.2, 131.2.

IR (CHCl₃) 3530, 3380, 2920, 2850, 1745, 1675, 1465, 1390, 1355, 1285, 1000, 835 cm⁻¹.

HRMS calcd for C₁₄H₁₉OCl₂ [M-OH]⁺ 273.08, found 273.10.

***dl*-(*E,E*)-3,4-Dihydroxy-1,6-diiodo-1,6-diphenylhexa-1,5-diene (2m).**

¹H NMR (CDCl₃) δ 3.03 (s, 2H), 4.63 (d, *J* = 6.6 Hz, 2H), 6.16 (d, *J* = 6.6 Hz, 2H), 7.24-7.30 (m, 6H), 7.44-7.46 (m, 4H).

¹³C NMR (CDCl₃) δ 79.8, 128.3, 128.6, 128.9, 135.9, 143.3.

IR (CHCl₃) 3550, 3350, 1660, 1525, 1460, 1420, 1140, 900, 720, 660 cm⁻¹.

HRMS calcd for C₁₈H₁₅OI [M-I-OH]⁺ 374.01, found 373.99.

***dl*-3,4-Dihydroxy-1,6-diphenylhexa-1,5-diyne (6).**

¹H NMR (CDCl₃) δ 2.95 (s, 2H), 4.75 (s, 2H), 7.25-7.35 (m, 6H), 7.44-7.48 (m, 4H).

¹³C NMR (CDCl₃) δ 66.8, 80.0, 97.2, 128.3, 128.6, 128.8, 131.9.

IR (CHCl₃) 3540, 3350, 1745, 1610, 1505, 1455, 1395, 1295, 1085, 975, 700 cm⁻¹.

HRMS calcd for C₁₈H₁₃O₂ [M-H]⁺ 261.09, found 261.10.

***dl*-6,7-Dihydroxydodecane (8, R¹ = *n*-Pr).^{1,2}**

A suspension of 10% Pd/C (31.8 mg, 0.03 mmol) in ethanol (1.0 mL) was stirred at ambient temperature under a hydrogen atmosphere (1 atm). To the suspension was added a solution of *dl*-(*Z,Z*)-4,9-dibromo-6,7-dihydroxydodeca-4,8-diene (55.0 mg, 0.15 mmol) in ethanol (1.0 mL). After being stirred for 12 hr, the mixture was filtered through a Celite pad and concentrated in vacuo. Purification by silica gel chromatography (*n*-hexane : ethyl acetate = 2 : 1 as an eluent) gave *dl*-6,7-dihydroxydodecane (21.9 mg, 72%).

¹H NMR (CDCl₃) δ 0.90 (t, *J* = 7.0 Hz, 6H) 1.19-1.39 (m, 8H) 1.40-1.51 (m, 8H) 2.10 (brs, 2H) 3.41 (unresolved d, *J* = 5.5 Hz, 2H).

¹³C NMR (CDCl₃) δ 14.0, 22.6, 25.3, 31.8, 33.6, 74.5.

IR (CHCl₃) 3540, 1610, 1500, 1450, 1380, 1150, 1010, 970 cm⁻¹.

The spectral data are in accordance with those in the literature.^{1,2}

***dl*-1,6-Diphenylhexane-3,4-diol (8, R¹ = Ph).^{1,2}**

^1H NMR (CDCl_3) δ 1.74-1.83 (m, 4H), 2.02 (d, J = 5.0 Hz, 2H), 2.62-2.87 (m, 4H), 3.43-3.48 (m, 2H), 7.16-7.21 (m, 6H), 7.27-7.31 (m, 4H).

^{13}C NMR (CDCl_3) δ 31.9, 35.3, 73.9, 125.9, 128.4, 128.5, 141.8.

IR (CHCl_3) 2900, 1505, 1465, 1400, 1300, 1075, 930 cm^{-1} .

The spectral data are in accordance with those in the literature.^{1,2}

***dl*-4,5-Bis-[(*Z,E*)-4-*t*-butoxycarbonyl-2-propyl-1,3-butadienyl]-2,2-dimethyl-1,3-dioxolane (9).**

A solution of *dl*-(*Z,Z*)-3,4-dihydroxy-1,6-diiodo-1,6-diphenylhexa-1,5-diene (**2d**) (189.0 mg, 0.42 mmol), 2,2-dimethoxypropane (437.4 mg, 4.2 mmol), and PPTS (32.7 mg, 0.13 mmol) in toluene (2 mL) was heated to 70 °C for 3h under an argon atmosphere. After cooling, the mixture was concentrated in vacuo. Purification on preparative silica gel TLC (*n*-hexane : ethyl acetate = 10 : 1 as an eluent) gave *dl*-4,5-bis-[(*Z*)-2-iodo-1-pentenyl]-2,2-dimethyl-1,3-dioxolane (191.5 mg, 93%) as a colorless oil. A solution of *dl*-4,5-bis-[(*Z*)-2-iodo-1-pentenyl]-2,2-dimethyl-1,3-dioxolane (39.8 mg, 0.08 mmol), *t*-butyl acrylate (61.5 mg, 0.48 mmol), bis(triphenylphosphine)dichloropalladium (Ö†) (11.2 mg, 0.016 mmol), and diisopropylethylamine (62.0 mg, 0.48 mmol) in DMF (2 mL) was heated to 130 °C for 2 h under an argon atmosphere. After cooling, the reaction mixture was extracted with ethyl acetate. The organic phase was washed with sat. aqueous NaHCO_3 and brine, dried over anhydrous Na_2SO_4 , and concentrated *in vacuo*. Purification on silica gel preparative TLC (*n*-hexane : ethyl acetate = 10 : 1 as an eluent) gave *dl*-4,5-bis-[(*Z,E*)-4-*t*-butoxycarbonyl-2-propyl-1,3-butadienyl]-2,2-dimethyl-1,3-dioxolane (**9**) (24.7 mg, 63%) as a colorless oil.

^1H NMR (CDCl_3) δ 0.87 (t, J = 8.0 Hz, 6H) 1.40-1.51 (m, 28H) 2.13 (t, J = 8.0 Hz, 4H) 4.63-4.70 (m, 2H) 5.63 (d, J = 7.3 Hz, 2H) 5.81 (d, J = 15.8 Hz, 2H) 7.39 (d, J = 15.8 Hz, 2H).

^{13}C NMR (CDCl_3) δ 14.4, 22.0, 27.6, 28.6, 36.1, 77.9, 80.9, 110.2, 121.7, 131.1, 139.1, 141.1, 166.8.

IR (CHCl_3) 2900, 1710, 1620, 1465, 1380, 1320, 1160, 1060, 985, 880 cm^{-1} .

HRMS calcd for $\text{C}_{29}\text{H}_{46}\text{O}_6$ $[\text{M}]^+$ 490.33, found 490.31.

1) Mukaiyama, T.; Yoshimura, N.; Igarashi, K.; Kagayama, A. *Tetrahedron* **2001**, 57, 2499-2506.

2) Hirao, T.; Asahara, M.; Muguruma, Y.; Ogawa, A. *J. Org. Chem.* **1998**, 63, 2812-2813.