

Supporting Information

Highly Stereoselective Coupling Reaction of Acrolein or Vinyl Ketone with Aldehydes

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Instrumentation and Materials

^1H NMR (300 MHz) and ^{13}C NMR (75.3 MHz) spectra were taken on a Varian GEMINI 300 spectrometer in CDCl_3 as a solvent, and chemical shifts were given in δ value with tetramethylsilane as an internal standard. IR spectra were determined on a JASCO IR-810 spectrometer. TLC analyses were performed on commercial glass plates bearing 0.25 mm layer of Merk Silica-gel 60F₂₅₄. Column chromatography was done with silica-gel (Wakogel 200 mesh). The analyses were carried out at the Elemental Analysis Center of Kyoto University. Unless otherwise noted, materials obtained from commercial suppliers were used without further purification, however aldehydes including acrolein were distilled and stocked under argon. Dichloromethane was dried with molecular sieves 4A.

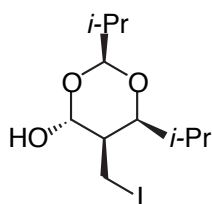
Experimental

General Procedure for Acrolein with Aldehydes into 4-Hydroxy-1,3-dioxane.

To a solution of TiCl_4 (2.0 mmol) in CH_2Cl_2 (5 mL) was added a solution of $n\text{-Bu}_4\text{NI}$ (2.0 mmol) in CH_2Cl_2 (3 mL) at 0 °C. After being stirred for 10 min at 0 °C, a resulting dark-red solution was cooled to -78 °C and 2-methylpropanal (3.0 mmol) and a solution of acrolein (1.0 mmol) in

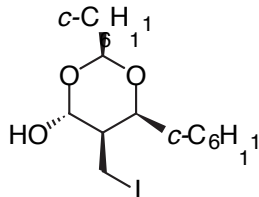
CH₂Cl₂ (2 mL) were successively added. The reaction mixture was stirred for 30 min at -78 °C and then the whole mixture was poured into saturated aqueous ammonium chloride. The mixture was extracted by ether (30 ml × 3) and the organic layer was washed with brine and dried over anhydrous Na₂SO₄. Concentration under reduced pressure and purification by silica-gel column chromatography afforded 4-hydroxy-2,6-diisopropyl-5-iodomethyl-1,3-dioxane (**2a**, 0.22 g) in 68% yield.

(2*S,4*S**,5*R**,6*S**)-4-hydroxy-2,6-diisopropyl-5-iodomethyl-1,3-dioxane (**2a**):**



IR (neat) 3402, 2958, 1725, 1468, 1257, 1141, 1106, 1074, 1045, 1016, 990 cm⁻¹; ¹H NMR (CDCl₃) δ 0.85 (d, *J* = 6.9 Hz, 3H), 0.91 (d, *J* = 6.9 Hz, 3H), 0.92 (d, *J* = 6.9 Hz, 3H), 0.99 (d, *J* = 6.3 Hz, 3H), 1.68–1.84 (m, 2H), 1.93 (dddd, *J* = 2.4, 3.0, 3.0, 11.4 Hz, 1H), 2.76 (bs, 1H), 3.27 (dd, *J* = 10.2, 11.4 Hz, 1H), 3.38 (dd, *J* = 3.0, 10.2 Hz, 1H), 3.46 (dd, *J* = 2.4, 10.2 Hz, 1H), 4.84 (d, *J* = 5.1 Hz, 1H), 5.56 (d, *J* = 3.0 Hz, 1H); ¹³C NMR (CDCl₃) δ 2.39, 16.42, 16.98, 17.23, 19.42, 29.16, 32.21, 42.16, 80.10, 94.35, 98.33. Found: C, 40.09; H, 6.56%. Calcd for C₁₁H₂₁IO₃: C, 40.26; H, 6.45%.

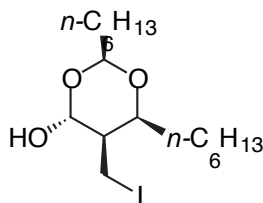
(2*S,4*S**,5*R**,6*S**)-2,6-dicyclohexyl-4-hydroxy-5-iodomethyl-1,3-dioxane (**2b**):**



Mp. 114–116 ° C; IR (neat) 3330, 1152, 1121, 1060, 1006, 984, 952 cm⁻¹; ¹H NMR (CDCl₃) δ 0.75–1.96 (m, 22H), 2.05 (ddd, *J* = 2.1, 3.6, 10.2 Hz, 1H), 3.14 (d, *J* = 2.7 Hz, 1H), 3.27 (dd, *J* = 10.2, 10.2 Hz, 1H), 3.35 (dd, *J* = 3.6, 10.2 Hz, 1H), 3.56 (dd, *J* = 2.1, 9.9 Hz, 1H), 4.84 (d, *J* = 8.7 Hz, 1H),

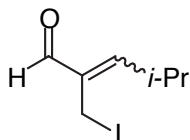
5.53 (d, $J = 2.7$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 2.70, 13.98, 22.52, 25.40, 25.58, 25.62, 26.32, 26.88, 27.19, 27.33, 29.86, 31.46, 38.32, 41.79, 79.92, 94.36, 97.75. Found: C, 49.91; H, 6.99%. Calcd for $\text{C}_{17}\text{H}_{29}\text{IO}_3$: C, 50.01; H, 7.16%.

(2*S,4*S**,5*R**,6*S**)-4-hydroxy-5-iodomethyl-2,6-dinonyl-1,3-dioxane (2c):**



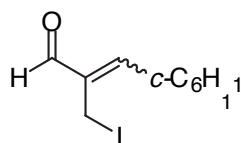
IR (neat) 3376, 2920, 2850, 1467, 1377, 1142, 950 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.87 (t, $J = 6.3$ Hz, 6H), 1.10–1.46 (m, 28H), 1.53–1.65 (m, 4H), 1.75–1.83 (m, 1H), 3.01 (bs, 1H), 3.29 (dd, $J = 10.2, 11.4$ Hz, 1H), 3.42 (dd, $J = 3.3, 10.2$ Hz, 1H), 3.92–4.00 (m, 1H), 5.15 (t, $J = 5.1$ Hz, 1H), 5.53 (d, $J = 3.0$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 2.59, 13.98, 22.55, 23.78, 25.38, 29.19, 29.34, 29.37, 29.41, 29.44, 29.47, 31.78, 32.10, 34.43, 43.99, 74.38, 94.40, 94.80. Found: C, 55.53; H, 9.39%. Calcd for $\text{C}_{23}\text{H}_{45}\text{IO}_3$: C, 55.64; H, 9.14%.

2-Iodomethyl-4-methyl-2-pentanone (4a, $E/Z = 46/54$):



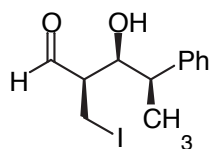
IR (neat) 2962, 1687, 1637, 1467, 1364, 1316, 1237, 1161, 1086, 856 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.13 (d, $J = 6.6$ Hz, 6H), 2.80–3.06 (m, 1H), 3.97 (s, 1.08H), 4.21 (s, 0.92H), 6.38 (d, $J = 10.5$ Hz, 0.54H), 6.49 (d, $J = 10.5$ Hz, 0.46H), 9.35 (s, 0.54H), 9.37 (s, 0.46H); ^{13}C NMR (CDCl_3) δ -9.89, 20.63, 21.59, 28.59, 28.67, 33.33, 137.32, 138.60, 162.54, 164.90, 192.46, 192.58. Found: C, 35.39; H, 4.72%. Calcd for $\text{C}_7\text{H}_{11}\text{IO}$: C, 35.32; H, 4.66%.

2-Iodomethyl-3-cyclohexyl-2-propenone (4b, *E/Z* = 34/66):



IR (neat) 2922, 2848, 1689, 1637, 1449, 1270, 1252, 1160, 1115, 969, 904, 855, 721 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.08–1.95 (m, 11H), 3.98 (s, 1.32H), 4.22 (s, 0.68H), 6.41 (d, $J = 10.2$ Hz, 0.66H), 6.51 (d, $J = 10.2$ Hz, 0.34H), 9.35 (s, 0.66H), 9.37 (s, 0.34H); ^{13}C NMR (CDCl_3) δ -9.61, 24.94, 24.96, 25.43, 25.48, 30.45, 31.46, 33.47, 38.30, 38.47, 137.68, 138.94, 161.08, 163.44, 192.53, 192.66. Found: C, 48.25; H, 5.49%. Calcd for $\text{C}_{10}\text{H}_{15}\text{IO}$: C, 43.18; H, 5.44%.

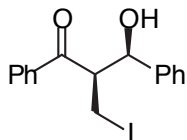
(2*S,3*S**,4*R**)-2-iodomethyl-3-hydroxy-4-phenyl-1-pentanal (1e):**



IR (neat) 3182, 2930, 1720, 1602, 1454, 1184, 1049, 971, 763, 702 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.37 (d, $J = 6.9$ Hz, 3H), 2.05 (d, $J = 3.9$ Hz, 1H), 2.67 (dddd, $J = 1.2, 4.5, 4.8, 8.4$ Hz, 1H), 2.94 (qd, $J = 6.9, 7.5$ Hz, 1H), 3.36 (dd, $J = 4.5, 10.2$ Hz, 1H), 3.41 (dd, $J = 8.4, 10.2$ Hz, 1H), 4.11 (ddd, $J = 3.9, 4.8, 7.5$ Hz, 1H), 7.20–7.38 (m, 5H), 9.64 (d, $J = 1.2$ Hz, 1H); ^{13}C NMR (CDCl_3) δ -2.82, 16.51, 43.04, 55.05, 75.73, 127.29, 127.55, 129.12, 142.96, 203.07. Analytically pure sample could not be obtained because of its instability. Thus, the analysis was carried out after reduction into its diol upon treatment with NaBH_4 . 3-(1-phenylethyl)-2-iodomethyl-1,3-propanediol: Mp. 90–91 $^\circ\text{C}$; IR (neat) 3182, 2930, 1720, 1602, 1454, 1184, 1049, 971, 763, 702 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.36 (d, $J = 6.6$ Hz, 3H), 1.56 (m, 1H), 2.16 (d, $J = 3.6$ Hz, 1H), 2.77 (d, $J = 3.3$ Hz, 1H), 2.91 (qd, $J = 6.9, 7.5$ Hz, 1H), 3.41 (dd, $J = 9.0, 9.9$ Hz, 1H), 3.47 (dd, $J = 3.6, 9.9$ Hz, 1H), 3.74 (ddd, $J = 3.6, 3.6, 10.8$ Hz, 1H), 3.89–3.99 (m, 2H), 7.18–7.35 (m, 5H); ^{13}C NMR (CDCl_3) δ 4.65, 17.03, 43.09, 43.63, 65.01, 78.60, 126.83, 127.51,

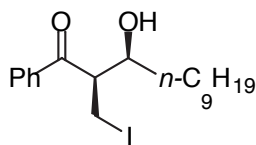
128.90, 143.91. Found: C, 44.90; H, 5.26%. Calcd for C₁₂H₁₇IO₂: C, 5.35; H, 45.02%.

Syn-3-hydroxy-2-iodomethyl-1,3-diphenyl-1-propanone (9a):



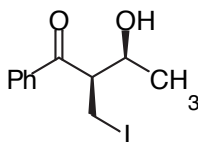
IR (neat) 3386, 3060, 1672, 1597, 1449, 1252, 1044, 889, 787 cm⁻¹; ¹H NMR (CDCl₃) δ 2.75 (d, *J* = 2.1 Hz, 1H), 3.43 (dd, *J* = 3.6 Hz, 9.6 Hz, 1H), 3.66 (dd, *J* = 9.6 Hz, 10.5 Hz, 1H), 4.25 (ddd, *J* = 3.6 Hz, 5.4 Hz, 10.5 Hz, 1H), 4.94 (dd, *J* = 2.1 Hz, 5.4 Hz, 1H), 7.20–7.60 (m, 8H), 7.85 (d, *J* = 7.2 Hz, 2H); ¹³C NMR (CDCl₃) δ 0.30, 55.81, 75.10, 126.20, 128.14, 128.59, 128.59, 128.65, 133.64, 136.62, 140.67, 201.65. Found: C, 52.75; H, 4.14%. Calcd for C₁₆H₁₅IO₂: C, 52.48; H, 4.13%.

Syn-3-hydroxy-2-iodomethyl-1-phenyl-1-dodecanone (9b):



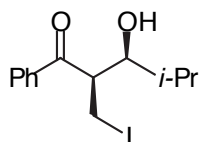
IR (neat) 3412, 2922, 2850, 1677, 1597, 1460, 1255, 1090, 702 cm⁻¹; ¹H NMR (CDCl₃) δ 0.82 (t, *J* = 6.6 Hz, 3H), 1.10–1.60 (m, 16H), 2.41 (s, 1H), 3.48 (dd, *J* = 3.6 Hz, 9.9 Hz, 1H), 3.58 (dd, *J* = 9.9 Hz, 9.9 Hz, 1H), 3.82 (ddd, *J* = 3.6 Hz, 9.9 Hz, 9.9 Hz, 1H), 3.99 (dt, *J* = 9.9 Hz, 4.5 Hz, 1H), 7.45–7.68 (m, 3H), 7.95–8.06 (m, 2H); ¹³C NMR (CDCl₃) δ 0.43, 13.94, 22.49, 25.79, 29.10, 29.20, 29.32, 31.70, 34.94, 53.93, 73.09, 128.74, 128.89, 133.84, 136.64, 201.96. Found: C, 54.99; H, 7.17%. Calcd for C₁₈H₂₉IO₂: C, 54.81; H, 7.02%.

Syn-3-hydroxy-2-iodomethyl-1-phenyl-1-butanone (9c):



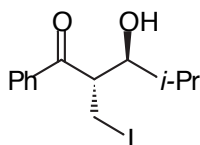
IR (neat) 3412, 2968, 1675, 1597, 1448, 1256, 1218, 699 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.24 (d, $J = 6.3$ Hz, 3H), 2.35 (s, 1H), 3.50 (dd, $J = 3.9$ Hz, 9.6 Hz, 1H), 3.57 (dd, $J = 9.6$ Hz, 9.6 Hz, 1H), 3.95 (ddd, $J = 3.9$ Hz, 5.4 Hz, 9.6 Hz, 1H), 4.04 (qd, $J = 6.3$ Hz, 5.4 Hz, 1H), 7.45–7.68 (m, 3H), 7.93–8.05 (m, 2H); ^{13}C NMR (CDCl_3) δ 0.48, 21.26, 55.02, 69.35, 128.79, 128.93, 133.90, 136.77, 201.89. Found: C, 43.62; H, 4.29%. Calcd for $\text{C}_{11}\text{H}_{13}\text{IO}_2$: C, 43.44; H, 4.31%.

Syn-3-hydroxy-2-iodomethyl-4-methyl-1-phenyl-1-pentanone (9d):



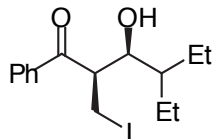
IR (neat) 3434, 2958, 1678, 1597, 1448, 1359, 1255, 994, 702 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.93 (d, $J = 6.9$ Hz, 3H), 0.99 (d, $J = 6.9$ Hz, 3H), 1.75 (m, 1H), 2.40 (d, $J = 3.9$ Hz, 1H), 3.47 (dd, $J = 9.9$ Hz, 3.3 Hz, 1H), 3.51 (ddd, $J = 3.9$ Hz, 4.8 Hz, 6.3 Hz, 1H), 3.60 (dd, $J = 9.9$ Hz, 9.9 Hz, 1H), 4.15 (ddd, $J = 3.3$ Hz, 4.8 Hz, 9.9 Hz, 1H), 7.48–7.65 (m, 3H), 7.98–8.00 (m, 2H); ^{13}C NMR (CDCl_3) δ 0.35, 17.51, 19.56, 31.12, 51.32, 77.90, 128.73, 128.95, 133.89, 136.42, 202.09. Found: C, 47.04; H, 5.09%. Calcd for $\text{C}_{13}\text{H}_{17}\text{IO}_2$: C, 47.00; H, 5.16%.

Anti-3-hydroxy-2-iodomethyl-4-methyl-1-phenyl-1-pentanone (9d'):



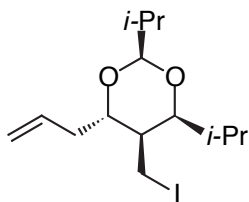
IR (neat) 3434, 2958, 1679, 1597, 1449, 1360, 1255, 999, 700 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.85 (d, $J = 6.6$ Hz, 3H), 1.01 (d, $J = 6.6$ Hz, 3H), 1.65 (m, 1H), 2.99 (d, $J = 9.6$ Hz, 1H), 3.44–3.65 (m, 3 H), 4.00 (ddd, $J = 4.2$ Hz, 6.9 Hz, 6.9 Hz, 1H), 7.49–7.66 (m, 3H), 7.98–8.00 (m, 2H); ^{13}C NMR (CDCl_3) δ 2.68, 18.11, 19.44, 32.21, 49.57, 79.16, 128.62, 128.99, 134.11, 136.77, 203.59. Found: C, 47.04; H, 5.05%. Calcd for $\text{C}_{13}\text{H}_{17}\text{IO}_2$: C, 47.00; H, 5.16%.

Syn-4-ethyl- 3-hydroxy-2-iodomethyl-1-phenyl-1-hexanone (9e):



IR (neat) 3404, 2958, 1673, 1597, 1449, 999 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.70 (t, $J = 7.5$ Hz, 3H), 0.88 (t, $J = 7.5$ Hz, 3H), 1.17–1.61 (m, 5H), 2.37 (bs, 1H), 3.49 (dd, $J = 9.6$ Hz, 3.3 Hz, 1H), 3.60 (dd, $J = 9.6$ Hz, 10.2 Hz, 1H), 3.74 (dd, $J = 5.4$ Hz, 9.0 Hz, 1H), 4.18 (ddd, $J = 3.3$ Hz, 5.4 Hz, 10.2 Hz, 1H), 7.47–7.64 (m, 3H), 7.97–7.99 (m, 2H); ^{13}C NMR (CDCl_3) δ 1.27, 10.72, 10.87, 20.59, 21.99, 43.53, 51.43, 74.43, 128.65, 128.90, 133.80, 136.69, 202.27. Found: C, 50.31; H, 5.60%. Calcd for $\text{C}_{15}\text{H}_{21}\text{IO}_2$: C, 50.01; H, 5.88%.

4-Allyl-5-iodomethyl-2,6-diisopropyl-1,3-dioxan (12):



IR (neat) 2958, 1473, 1279, 1147, 1093, 916 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.83 (d, $J = 6.6$ Hz, 3H), 0.89 (d, $J = 6.9$ Hz, 3H), 0.90 (d, 6.9 Hz, 3H), 1.00 (d, 6.6 Hz, 3H), 1.67–1.83 (m, 3H), 2.31–2.41 (m, 1H), 2.67–2.77 (m, 1H), 3.22 (dd, $J = 2.4$, 10.2 Hz, 1H), 3.42 (d, $J = 10.2$ Hz, 1H), 3.48 (d, $J = 10.2$ Hz, 1H), 4.31 (dd, $J = 7.8$ Hz, 7.8 Hz, 1H), 4.39 (d, $J = 5.4$ Hz, 1H), 5.08–5.15 (m, 2H), 5.73–5.87 (m, 1H); ^{13}C NMR (CDCl_3) δ 6.30, 16.68, 17.02, 17.33, 19.59, 29.52, 32.64, 34.54, 40.41, 74.97, 80.63, 99.50, 117.42, 134.23. Found: C, 47.67; H, 7.36%. Calcd for $\text{C}_{14}\text{H}_{25}\text{IO}_2$: C, 47.74; H, 7.15%.