Supporting Information

$TiCl_4$–*n*-Bu_4NX (X = Cl, Br, and I) Combination-Induced Coupling of α,β-Unsaturated Ketones with Aldehydes

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Instrumentation and Materials

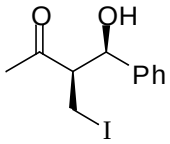
^{1}H NMR (300 MHz) and ^{13}C NMR (75.3 MHz) spectra were taken on a Varian GEMINI 300 spectrometer in $CDCl_3$ as a solvent, and chemical shifts were given in δ value with tetramethylsilane as an internal standard. IR spectra were determined on a JASCO IR-810 spectrometer. TLC analyses were performed on commercial glass plates bearing 0.25 mm layer of Merk Silica-gel $60F_{254}$. Purification by 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. Aldehydes and methyl vinyl ketone were distilled and stocked under argon. Dichloromethane was dried with molecular sieves 4A.

Experimental

General Procedure for the Coupling between Vinyl ketones and Aldehydes with $TiCl_4$–*n*-Bu_4NI. To a solution of $TiCl_4$ (2.0 mL, 1.0 M solution in CH_2Cl_2, 2.0 mmol) in CH_2Cl_2 (5 mL) was added a solution of *n*-Bu_4NI (739 mg, 2.0 mmol) in CH_2Cl_2 (3 mL) at 0 °C. After stirring for 10 min at 0 °C, a resulting dark-red solution was cooled to –78 °C, and a solution of phenyl vinyl ketone (132 mg, 1.0 mmol) in CH_2Cl_2 (2.0 mL) was added dropwise. The reaction mixture was stirred for 1 h at –78 °C, and benzaldehyde (0.15 mL, 1.5 mmol) was introduced via a syringe. The reaction mixture was

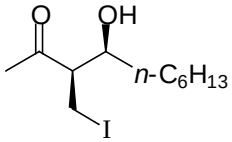
stirred for 2 h at –78 °C. The whole mixture was poured into saturated aqueous ammonium chloride. The mixture was extracted by hexane and the organic layer was washed with brine and dried over anhydrous Na_2SO_4. Concentration under reduced pressure and purification by silica gel column chromatography afforded 3-hydroxy-2-iodomethyl-1,3-diphenylpropan-1-one (**1a**, 326 mg) in 89% yield. The compound data of **1a**–**e** can be found in the literature.[1]

***syn*-4-Hydroxy-3-iodomethyl-4-phenylbutan-2-one (1f)**



IR (neat) 3418, 1711, 1360, 1168, 1027, 763, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.88 (s, 3H), 2.68 (bs, 1H), 3.35 (m, 3H), 4.64 (d, *J* = 6.0 Hz, 1H), 7.22–7.40 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 0.14, 31.76, 62.25, 75.24, 126.19, 128.38, 128.73, 140.98, 209.81. The titled compound was relatively unstable and not suitable for the elemental analysis. The compound was converted into 2-(1-hydroxycyclohexyl)-1-phenylpropan-1-one by treatment with *n*-Bu_3SnH (0.29 g, 1.0 mmol) and Et_3B (0.1 mmol) in hexane at 25 °C. After stirring for 30 min, the solvent was removed under reduced pressure and the residue was dissolved with ethyl acetate (20 mL). Potassium fluoride (1.0 g) and a saturated aqueous solution of KF (2 mL) were added and the mixture was vigorously stirred for 2 h. The mixture was filtered through a pad of Celite and the filtrate was concentrated. The residue was purified by silica gel to provide the reduction product of which spectral data was identical with the authentic sample.

***syn*-4-Hydroxy-3-iodomethyldecan-2-one (1g)**

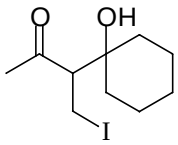


IR (neat) 3426, 2924, 1710, 1359, 1246, 1171, 1042 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87 (t, *J* = 6.9 Hz 3H), 1.20–1.60 (m, 10H), 2.05 (bs, 1H), 2.30 (s, 3H), 3.07 (m, 1H), 3.32 (m, 2H), 3.76 (m, 1H); ^{13}C NMR

[1] Uehira, S.; Han, Z.; Shinokubo, H.; Oshima, K.*Org. Lett*. **1999**, *1*, 1383.

($CDCl_3$) δ –0.70, 13.89, 22.42, 25.73, 28.93, 31.47, 31.58, 34.56, 60.03, 72.40, 210.17. The titled compound was relatively unstable and not suitable for the elemental analysis. The reduction product with *n*-Bu_3SnH was identical with the authentic sample.

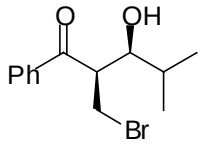
3-(1-Hydroxycyclohexyl)-4-iodo-2-butanone (1h)



IR (neat) 3456, 2928, 1705, 1358, 1167, 1149, 963 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10–1.80 (m, 10H), 2.34 (s, 3H), 2.52 (bs, 1H), 3.14 (dd, *J* = 3.9, 8.7 Hz, 1H), 3.32 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 0.13, 21.32, 21.52, 25.24, 34.33, 34.74, 36.75, 62.93, 74.26, 213.49. The titled compound was relatively unstable and not suitable for the elemental analysis. The reduction product with *n*-Bu_3SnH was identical with the authentic sample.

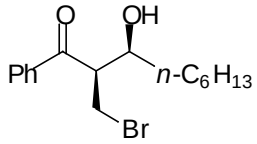
General Procedure for the Coupling between Vinyl ketones and Aldehydes with $TiCl_4$–*n*-Bu_4NBr. To a solution of $TiCl_4$ (2.0 mL, 1.0 M solution in CH_2Cl_2, 2.0 mmol) in CH_2Cl_2 (5 mL) was added a solution of *n*-Bu_4NBr (645 mg, 2.0 mmol) in CH_2Cl_2 (3 mL) at 0 °C. After stirring for 10 min at 0 °C, a resulting red solution was cooled to –78 °C, and a solution of phenyl vinyl ketone (132 mg, 1.0 mmol) in CH_2Cl_2 (2.0 mL) was added dropwise. The reaction mixture was stirred for 1 h at –78 °C, and 2-methylpropanal (0.14 mL, 1.5 mmol) was introduced via a syringe. The reaction mixture was allowed to warm up to –40 °C during a period of 2 h. The whole mixture was poured into saturated aqueous ammonium chloride. The mixture was extracted by hexane and the organic layer was washed with brine and dried over anhydrous Na_2SO_4. Concentration under reduced pressure and purification by silica gel column chromatography afforded *syn*-2-bromomethyl-3-hydroxy-4-methyl-1-phenylpentan-1-on**e** (**3a**, 171 mg) in 60% yield.

***syn*-2-Bromomethyl-3-hydroxy-4-methyl-1-phenylpentan-1-one (3a)**



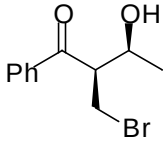
IR (neat) 3483, 2962, 1678, 1448, 1265, 1001, 706 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.92 (d, *J* = 6.8 Hz, 3H), 1.00 (d, *J* = 6.8 Hz, 3H), 1.75 (dqq, *J* = 6.8, 6.8, 6.8 Hz, 1H), 2.25 (bs, 1H), 3.57 (dd, *J* = 4.8, 6.8 Hz, 1H), 3.73 (dd, *J* = 3.9, 9.9 Hz, 1H), 3.87 (dd, *J* = 9.9, 9.9 Hz, 1H), 4.18 (ddd, *J* = 3.9, 4.8, 9.9 Hz, 1H), 7.51–8.09 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 17.45, 19.51, 29.32, 31.14, 50.90, 77.13, 128.75, 128.95, 133.91, 136.74, 201.92. The titled compound was relatively unstable and not suitable for the elemental analysis.. The reduction product with *n*-Bu_3SnH was identical with the authentic sample.

***syn*-2-Bromomethyl-3-hydroxy-1-phenylnonan-1-one (3b)**



IR (neat) 3475, 2929, 1678, 1448, 1222, 1265, 1043, 706 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.85 (t, *J* = 6.6 Hz, 3H), 1.20–1.60 (m, 10H), 2.3 (bs, 1H), 3.73 (dd, *J* = 3.9, 9.9 Hz, 1H), 3.86 (m, 2H), 4.01 (m, 1H), 7.52–7.99 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 13.87, 22.39, 25.73, 28.88, 29.29, 31.56, 35.02, 53.58, 72.25, 128.77, 128.91, 133.89, 136.92, 201.80. The titled compound was relatively unstable and not suitable for the elemental analysis. The reduction product with *n*-Bu_3SnH was identical with the authentic sample.

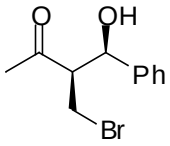
***syn*-2-Bromomethyl-3-hydroxy-1-phenylbutan-1-one (3c)**



IR (neat) 3348, 2914, 1668, 1446, 1221, 924, 702 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.26 (d, *J* = 6.0 Hz, 3H), 2.2 (bs, 1H), 3.76 (dd, *J* = 3.9, 9.9 Hz, 1H), 3.85 (dd, *J* = 9.9, 9.9 Hz, 1H), 3.99 (ddd, *J* = 3.9, 6.0, 9.9 Hz, 1H), 4.11 (dq, *J* = 6.0, 6.0 Hz, 1H), 7.50–8.00 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 21.36, 29.46, 54.84,

68.46, 128.75, 128.87, 133.85, 137.03, 201.62. Found: C, 51.67; H, 5.20%. Calcd for $C_{11}H_{13}BrO_2$: C, 51.38; H, 5.10%.

3-Bromomethyl-4-hydroxy-4-phenylbutan-2-one (3d)



IR (neat) 3435, 2910, 1712, 1361, 1041, 702 cm^{-1}; ^1H NMR (CDCl3): δ 1.18 (s, 3H), 2.4 (bs, 1H), 3.38 (ddd, *J* = 3.9, 7.2, 9.9 Hz, 1H), 3.61 (ddd, *J* = 3.9, 9.9 Hz, 1H), 3.71 (dd, *J* = 9.9, 9.9 Hz, 1H), 4.81 (d, *J* = 7.2 Hz, 1H), 7.35 (m, 5H); ^{13}C NMR ($CDCl_3$): δ 29.18, 32.10, 61.63, 74.27, 125.18, 128.39, 128.78, 128.98, 209.50. The titled compound was unstable to obtain the analytically pure sample. The reduction product with *n*-Bu_3SnH was identical with the authentic sample.

General Procedure for the Coupling between Vinyl ketones and Aldehydes with $TiCl_4$–*n*-Bu_4NCl. To a solution of $TiCl_4$ (2.0 mL, 1.0 M solution in CH_2Cl_2, 2.0 mmol) in CH_2Cl_2 (5 mL) was added a solution of *n*-Bu_4NCl (556 mg, 2.0 mmol) in CH_2Cl_2 (3 mL) at 0 °C. After stirring for 10 min at 0 °C, a resulting yellow solution was cooled to –78 °C, and a solution of methyl vinyl ketone (70 mg, 1.0 mmol) in CH_2Cl_2 (2.0 mL) was added dropwise. The reaction mixture was stirred for 1 h at –78 °C, and benzaldehyde (1.5 mL, 1.5 mmol) was introduced via a syringe. The reaction mixture was allowed to warm up to –20 °C during a period of 2 h. The whole mixture was poured into saturated aqueous ammonium chloride. The mixture was extracted by hexane and the organic layer was washed with brine and dried over anhydrous Na_2SO_4. Concentration under reduced pressure and purification by silica gel column chromatography afforded 3-chloromethyl-4-hydroxy-4-phenylbutan-2-one (**4a**, 130 mg) in 61% yield. The compound data of **4a**, **4b**, and **4c** can be found in the literature.[2]

[2] Shi, M.; Feng, Y.-S. *J. Org. Chem.* **2001**, *66*, 406.