Supporting Information

High Turnover Frequency Observed in Catalytic Enantioselective Additions of Enecarbamates and Enamides to Iminophosphonates

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General.

^1H and ^{13}C NMR spectra were recorded on an ECX 400 (400 MHz for ^1H and 100 MHz for ^{13}C NMR) spectrometer in CDCl_3 unless otherwise noted. Tetramethylsilane (TMS) served as internal standard ($\delta = 0$) for ^1H NMR, and CDCl_3 was used as internal standard ($\delta = 77.0$) for ^{13}C NMR. IR spectra were measured with a JASCO FT/IR-610 spectrometer. Optical rotations were measured with a JASCO P-1010 polarimeter. High-performance liquid chromatography was carried out using following apparatuses; SHIMADZU LC-10AT (liquid chromatograph), SHIMADZU SPD-10A (UV detector), and SHIMADZU C-R6A Chromatopac. Column chromatography was conducted on Silica gel 60 (Merck) and preparative thin-layer chromatography was carried out using Wakogel B-5F. All reactions were carried out under argon atmosphere in a dried glassware. All solvents were dried and distilled by standard procedures. Enecarbamates **2a**, **2c**, **2d**, **2e**, **2f**, and **2g** were prepared from the corresponding nitriles by standard protocols by using MeMgBr and CbzCl .¹ Enecarbamate **2j** was prepared from acrylic acid according to the reported methods.² Enamides **2b**, **2h**, and **2i** were prepared from the corresponding nitriles by using MeMgCl and PhCOOEt .

Preparation of enamide (2b)

Benzonitrile (1.53 g, 15 mmol) and methyl magnesium chloride in THF (3.0 M, 5.5 mL, 16.5 mmol, Aldrich) were mixed under argon atmosphere, followed by heating to reflux for 30 min. After cooling to rt, the magnesium amide solution thus obtained was added to a solution of ethyl benzoate (2.70 g, 18 mmol) in THF (5.0 mL) at 0 °C. After 4 h of reaction, ether (20 mL) and water (10 ml) were added. After vigorous stirring for 5 min, the mixture was filtered through Celite pad. Organics were extracted with EtOAc (2 times) from the filtrate, and the combined organics were then washed with 10% NaCl aqueous solution (3 times). The organics were dried over sodium sulfate, and the inorganic salts were removed by filtration. After removal of solvents *in vacuo*, the residual crude mixture was purified by column chromatography (neutral silica gel, Hex/EtOAc) to afford yellowish product. The solid thus obtained was triturated in CH₂Cl₂ and Hex to give pure enamide **2b** (530 mg, 16% yield).

Experimental procedure for comparison of enecarbamate vs. silicon enolate

To a mixture of $\text{Cu}(\text{OTf})_2$ (7.2 mg, 0.020 mmol) and ligand (*R,R*)-**3a** (10.8 mg, 0.022 mmol) in CH_2Cl_2 (2.0 mL) under argon atmosphere. The suspension was mildly stirred for 10 h to give a transparent green solution, and it was cooled to 0 °C. Nucleophile (0.30 mmol, 1.5 equiv) in CH_2Cl_2 (1.0 mL) was added, followed by slow addition of an iminophosphonate solution (0.10 M, 2.0 mL). After completion of slow addition, saturated NaHCO_3 aqueous solution was added to quench the reaction. Organics were extracted with CH_2Cl_2 4 times and then the combined organic phase was washed with brine. The organic phase was dried over anhydrous sodium sulfate. After removal of the solvents *in vacuo*, the crude imine products were obtained.

In a case of enecarbamate addition, EtOH (3.0 mL) and 47% HBr aq (1.0 mL) were added. The mixture was stirred for 5 min, cooled to 0 °C, and a saturated NaHCO_3 aqueous solution was added. Organics were extracted with CH_2Cl_2 4 times and then the combined organic phase was washed with brine. After removal of the solvents *in vacuo*, the crude mixture was purified by chromatography on silica gel.

In a case of silicon enolate addition, the previously reported work-up procedure was conducted.³

Typical procedure for the reactions of enecarbamates

To a mixture of $\text{Cu}(\text{OTf})_2$ (7.2 mg, 0.020 mmol) and ligand (*R,R*)-**3a** (10.8 mg, 0.022 mmol) in CH_2Cl_2 (2.0 mL) under argon atmosphere. The suspension was mildly stirred for 4 h to give a transparent green solution. An aliquot of the solution (1.0 mL, 0.010 mmol of Cu) was transferred to another flask containing a solution of enecarbamate (61.5 mg, 0.24 mmol) in CH_2Cl_2 (1.0 mL) under Ar, then the mixed solution was cooled to $-10\text{ }^\circ\text{C}$. Iminophosphonate solution (0.10 M, 2.0 mL, 0.20 mmol) was slowly added to the solution of the catalyst and enecarbamate over 30 min. A saturated NaHCO_3 aqueous solution was added. Organics were extracted with CH_2Cl_2 4 times and then the combined organic phase was washed with brine. The organic phase was dried over anhydrous sodium sulfate. After removal of the solvents *in vacuo*, EtOH (3.0 mL) and 47% HBr aq (1.0 mL) were added then the mixture was stirred for 10 min, cooled to $0\text{ }^\circ\text{C}$. A saturated NaHCO_3 aqueous solution was added, and organics were extracted with CH_2Cl_2 4 times. The combined organic phase was washed with brine. After removal of the solvents *in vacuo*, the crude mixture was purified by chromatography on silica gel to give **4a** (70.6 mg, 77% yield).

Typical procedure for the reactions of enamides

To a mixture of $\text{Cu}(\text{OTf})_2$ (7.2 mg, 0.020 mmol) and ligand (*R,R*)-**3a** (10.8 mg, 0.022 mmol) in CH_2Cl_2 (2.0 mL) under argon atmosphere. The suspension was mildly stirred for 4 h to give a transparent green solution. An aliquot of the solution (0.30 mL, 0.0030 mmol of Cu) was transferred to another flask containing a solution of enamide (54.3 mg, 0.24 mmol) in CH_2Cl_2 (1.7 mL) under Ar at $-10\text{ }^\circ\text{C}$. Iminophosphonate solution (0.10 M, 2.0 mL, 0.20 mmol) was slowly added to the solution of catalyst and enecarbamate over 30 min. A saturated NaHCO_3 aqueous solution was added. Organics were extracted with CH_2Cl_2 4 times and then the combined organic phase was washed with brine. The organic phase was dried over anhydrous sodium sulfate. After removal of the solvents *in vacuo*, EtOH (5.0 mL) and 47% HBr aq (0.5 mL) were added then the mixture was stirred for 3 min, cooled to $0\text{ }^\circ\text{C}$. A saturated NaHCO_3 aqueous solution was added, and organics were extracted with CH_2Cl_2 4 times. The combined organic phase was washed with brine. After removal of the solvents *in vacuo*, the crude mixture was purified by chromatography on silica gel to give **4a** (74.3 mg, 81% yield).

Physical data

2a, 2c, 2d, 2f, 2g, and **4a-e** have already been reported in the previous report.^{1,2,3}

N-(1-phenylvinyl)benzamide (**2b**)

M.p. 92.8-93.0 °C; ¹H NMR (C₆D₆) δ = 7.60-7.50 (2H, Ar-H), 7.25-6.95 (9H, Ar-H and N-H), 6.46 (1H, s), 5.15 (1H, s) ppm; ¹³C NMR (C₆D₆, C₆D₆ as an internal standard: δ = 128.0 ppm): δ = 165.6, 141.3, 139.4, 135.5, 131.4, 128.9, 128.69, 128.66, 127.3, 126.4, 102.7 ppm; IR (KBr): 3307, 3057, 1639, 1519, 1484, 1288, 891, 767, 698, 603 cm⁻¹; HRMS (FAB); Exact mass calcd for C₁₅H₁₄NO⁺ [M+H]⁺, 224.1070. Found 224.1073.

N-(1-*p*-chlorophenylvinyl)benzamide (**2e**)

M.p. 130.5-131.1 °C; ¹H NMR (C₆D₆) δ = 7.55-7.50 (2H, Ar-H), 7.08-6.85 (8H, Ar-H and N-H), 6.80 (1H, 1s), 6.33 (1H, s), 5.00 (1H, s) ppm; ¹³C NMR (C₆D₆, C₆D₆ as an internal standard: δ = 128.0 ppm): δ = 165.4, 140.2, 137.6, 135.3, 134.5, 131.6, 129.0, 128.7, 127.7, 127.2, 103.4 ppm; IR (KBr): 3293, 1650, 1514, 1482, 1277, 1092, 894, 833, 697 cm⁻¹; HRMS (FAB); Exact mass calcd for C₁₅H₁₃ClNO⁺ [M+H]⁺, 258.0680. Found 258.0674.

N-(1-*m*-tolylvinyl)benzamide (**2h**)

M.p. 72.1-72.4 °C; ¹H NMR (C₆D₆) δ = 7.60-7.50 (2H, Ar-H), 7.16-6.90 (8H, Ar-H and N-H), 6.54 (1H, d, *J* = 3.7 Hz), 5.18 (1H, s), 2.06 (3H, s) ppm; ¹³C NMR (C₆D₆, C₆D₆ as an internal standard: δ = 128.0 ppm): δ = 165.5, 141.4, 139.6, 138.52, 135.5, 131.4, 129.5, 128.9, 128.7, 127.21, 127.19, 123.6, 102.3, 21.3 ppm; IR (KBr): 3267, 3038, 1644, 1518, 1373, 1335, 1287, 1079, 870, 795, 705 cm⁻¹; HRMS (ESI); Exact mass calcd for C₁₆H₁₆NO⁺ [M+H]⁺, 238.1226. Found 238.1234.

3-oxo-3-*m*-tolyl-1-(2,2,2-trichloroethoxy)carbonylaminopropane phosphonic acid diethyl ester

$[\alpha]_D^{24} -3.9$ (87% ee, c 1.89, CHCl_3); ^1H NMR (CDCl_3) $\delta = 7.80\text{--}7.70$ (2H, Ar-H), 7.454–7.25 (3H, Ar-H), 5.90–5.50 (1H, m), 4.80–4.70 (1H, m), 4.80 (1H, d, $J = 11.9$ Hz), 4.67 (1H, d, $J = 11.9$ Hz), 4.18 (2H, q, $J = 6.6$ Hz),

4.16 (2H, q, $J = 6.7$ Hz), 3.55–3.35 (2H, m), 2.41 (3H, s), 1.33 (3H, t, $J = 6.6$ Hz), 1.30 (3H, t, $J = 6.6$ Hz) ppm; ^{13}C NMR (CDCl_3): $\delta = 196.3$ (d, $J_{\text{c-p}} = 10.5$ Hz), 154.0 (d, $J_{\text{c-p}} = 4.8$ Hz), 138.6, 136.3, 134.4, 128.7, 128.6, 125.4, 95.3, 74.8, 63.2 (d, $J_{\text{c-p}} = 6.7$ Hz), 62.9 (d, $J_{\text{c-p}} = 6.7$ Hz), 44.6 (d, $J_{\text{c-p}} = 160.1$ Hz), 38.4 (d, $J_{\text{c-p}} = 3.8$ Hz), 21.3, 16.4 (d, $J_{\text{c-p}} = 5.8$ Hz), 16.3 (d, $J_{\text{c-p}} = 5.8$ Hz) ppm; IR (neat): 3236, 3046, 2984, 1740, 1686, 1680, 1540, 1259, 1150, 1032, 969, 815, 730, 549, 424 cm^{-1} ; HRMS (ESI); Exact mass calcd for $\text{C}_{17}\text{H}_{24}\text{Cl}_3\text{NO}_6\text{P}^+ [\text{M}+\text{H}]^+$, 474.0401. Found 474.0405.; Chiral HPLC: Daicel Chiralcel AD, hexane/ i PrOH = 4/1, flow rate = 1.0 mL/min, $t_R = 7.9$ min (*R*), $t_R = 9.7$ min (*S*).

Reference:

- (1) Matsubara, R.; Nakamura, Y.; Kobayashi, S. *Angew. Chem. Int. Ed.* **2004**, *43*, 1679. (2) Matsubara, R.; Kawai, N.; Kobayashi, S. *Angew. Chem. Int. Ed.* **2006**, *45*, 3814. (3) Kobayashi, S.; Kiyohara, H.; Nakamura, Y.; Matsubara, R. *J. Am. Chem. Soc.* **2004**, *124*, 6558.

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