Highly Enantioselective Copper-Catalyzed Conjugate Addition of Diethylzinc to Nitroalkenes

Hojae Choi, Zihao Hua and Iwao Ojima*

Department of Chemistry, State University of New York at Stony Brook,

Stony Brook, New York 11794-3400

iojima@notes.cc.sunysb.edu

Supplementary material

General methods and material: All solvents were purified using Solvent Purification System 400-4 from Innovative Technology, Inc. All reactions were carried out under argon atmosphere. ^1H , ^{13}C NMR spectra were measured on a Varian Inova-400 NMR or a Varian Gemini-2300 spectrometer in a deuterated solvent. The reactions were monitored by using GC/MS (Agilent GC6890 series with 5973N mass selective detector). The enantiomeric excess was determined by Analytical gas chromatography (Hewlett-Packard 5890 Series II gas chromatograph (FID) with a Hewlett-Packard HP 3396A integrator using a Supelco Beta Dex-120 column or Lipodex E column) and HPLC (Waters M45 system with Waters 484 detector, DIACEL OD-H column). Optical rotations were measured on a Perkin-Elmer Model 241 polarimeter. TLC was performed on Merck DC-alufolien with Kieselgel 60F-254 and column chromatography was carried out on silica gel 60 (Merck; 230-400 mesh ASTM). High-resolution mass spectrometric analyses were carried out at the Mass Spectrometry Laboratory, University of Illinois Urbana-Champaign, Urbana, IL. Ligands L3-L6^{1,2} and nitroalkenes 1a-11^{3,4} were prepared by previously reported methods.

General procedure for the asymmetric conjugate addition of diethylzinc to nitroalkenes. In a Schlenk tube with a magnetic stirring bar under argon atmosphere, a mixture of 0.005 mmol of $\text{Cu}(\text{OTf})_2$ and 0.01 mmol of a phosphoramidite ligand was dissolved in 5 mL of toluene, and the solution was stirred at room temperature for 30 min. To this solution was added 0.5 mmol of a nitroalkene. The mixture was cooled to $-65\text{ }^\circ\text{C}$ and 0.75 mmol of Et_2Zn (1.0M solution in toluene) was added slowly via syringe, and then kept at this temperature for 6 h with stirring. The reaction mixture was poured into saturated aqueous NH_4Cl and extracted three times with ether, and the combined organic layers were dried over MgSO_4 . The crude product was concentrated under reduced pressure and purified by column chromatography on silica gel using hexanes/ethyl acetate as eluent.

2-Phenyl-1-nitrobutane (2a):

Lipodex E column (25 m x 0.25 mm), $100\text{ }^\circ\text{C}$, $1\text{ }^\circ\text{C}/\text{min}$, $130\text{ }^\circ\text{C}$, $R_t = 37.6\text{ min (S)} / 38.2\text{ min (R)}$. ^1H NMR (300 MHz, CDCl_3) δ 7.25-7.45 (m, 5H), 4.64 (m, 2H), 3.44 (m, 1H), 1.79 (m, 2H), 0.92 (t, $J = 7.5\text{ Hz}$, 3H), ^{13}C NMR (75 MHz, CDCl_3) δ 139.2, 129.1, 128.8, 127.5, 80.7, 45.9, 26.1, 11.5. GC-MS: $m/z = 179\text{ [M}^+]$, 132, 117, 104, 91. All spectral data are consistent with the literature values.⁷

2-(4-Methylphenyl)-1-nitrobutane (2b):

Lipodex E column (25 m x 0.25 mm), 100 °C, 1 °C/min, 150 °C, R_t = 35.9 min (-) / 36.4 min (+). ^1H NMR (300 MHz, CDCl_3) δ 7.13 (d, J = 8.1 Hz, 2H), 7.05 (d, J = 8.1 Hz, 2H), 4.52 (m, 2H), 3.31 (m, 1H), 2.31 (s, 3H), 1.70 (m, 2H), 0.82 (t, J = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 137.2, 136.1, 129.5, 127.4, 80.9, 45.6, 26.1, 21.0, 11.5. GC-MS: m/z = 193 [M^+], 146, 131, 118, 105 (100). All spectral data are consistent with the literature values.³

2-(4-Methoxyphenyl)-1-nitrobutane (2c):

Lipodex E column (25 m x 0.25 mm), 100 °C, 1 °C/min, 120 °C, R_t = 111.7 min (-) / 114.8 min (+). ^1H NMR (300 MHz, CDCl_3) δ 7.08 (d, J = 8.7 Hz, 2H), 6.85 (d, J = 8.7 Hz, 2H), 4.51 (m, 2H), 3.77 (s, 3H), 3.29 (m, 1H), 1.67 (m, 2H), 0.81 (t, J = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 158.8, 131.1, 128.5, 114.2, 81.0, 55.2, 45.3, 26.2, 11.5. GC-MS: m/z = 209 [M^+], 162, 134, 121(100). All spectral data are consistent with the literature values.⁵

2-(3-Methoxyphenyl)-1-nitrobutane (2d):

DAICEL OD-H, 0.5mL/min, hexanes:2-propanol = 90:10, R_t = 23.7 min (+) / 47.6 min (-). ^1H NMR (300 MHz, CDCl_3) δ 7.24 (m, 1H), 6.70-6.81 (m, 3H), 4.53 (m, 2H), 3.78 (s, 3H), 3.31 (m, 1H), 1.68 (m, 2H), 0.83 (t, J = 7.4 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 159.8, 140.8, 129.8, 119.7, 113.7, 80.7, 55.1, 45.9, 26.1, 11.5. GC-MS: m/z = 209 [M^+], 162, 134, 121(100). All spectral data are consistent with the literature values.⁵

2-(2-Methoxyphenyl)-1-nitrobutane (2e):

DAICEL OD-H, 0.3mL/min, hexanes: 2-propanol = 90:10, R_t = 20.7 min (+) / 23.3 min (-). ^1H NMR (300 MHz, CDCl_3) δ 7.24 (m, 1H), 7.01 (m, 1H), 6.90 (m, 2H), 4.63 (m, 2H), 3.82 (s, 3H), 3.68 (m, 1H), 1.75 (m, 2H), 0.82 (t, J = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 157.5, 128.8, 128.4, 127.0, 120.7, 110.9, 79.3, 55.3, 41.1, 24.3, 11.7. GC-MS: m/z = 209 [M^+], 162, 134, 121(100) 91. All spectral data are consistent with the literature values.⁶

2-(4-Fluorophenyl)-1-nitrobutane (2f):

Supelco Beta β -120 column (30 m x 0.25 mm), 100 °C, 1 °C/min, 120 °C, R_t = 138.0 min (-) / 138.8 min (+). ^1H NMR (300 MHz, CDCl_3) δ 7.13 (m, 2H), 7.01 (m, 2H), 4.52 (m, 2H), 3.34 (m, 1H), 1.68 (m, 2H), 0.81 (t, J = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 163.5 (d), 134.9, 129.0 (d), 115.8 (d), 80.7, 45.2, 26.2, 11.5. GC-MS: m/z = 197 [M^+], 150, 135, 122, 109 (100). All spectral data are consistent with the literature values.³

2-(3-Fluorophenyl)-1-nitrobutane (2g):

Lipodex E column (25 m x 0.25 mm), 100 °C, 1 °C/min, 130 °C, R_t = 37.1 min (+) / 38.9 min (-). ^1H NMR (400 MHz, CDCl_3) δ 7.29 (m, 1H), 6.88-6.99 (m, 3H), 4.55 (m, 2H), 3.37 (m, 1H), 1.71 (m, 2H), 0.85 (t, J = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 163.0 (d), 141.9 (d), 130.4 (d), 123.3 (d), 114.6 (d), 114.4 (d), 80.4, 45.7, 26.1, 11.4, HRMS calcd for $\text{C}_{10}\text{H}_{12}\text{NO}_2\text{F}$ [M]⁺ 197.0852. Found 197.0854 (Δ = 1.5 ppm).

2-(2-Fluorophenyl)-1-nitrobutane (2h):

Supelco β -Dex-120 column (30 m x 0.25 mm), 100 °C, 1 °C/min, 120 °C, R_t = 91.1 min (-) / 93.4 min (+). ^1H NMR (400 MHz, CDCl_3) δ 7.03-7.28 (m, 4H), 4.65 (m, 2H), 3.64 (m, 1H), 1.78 (m, 2H), 0.87 (t, J = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 161.1 (d), 129.4 (d), 126.1 (d), 124.4 (d), 116.0 (d), 79.1, 40.7, 25.1, 11.6, HRMS Calcd for $\text{C}_{10}\text{H}_{12}\text{NO}_2\text{F}$ [M]⁺ 197.0852. Found 197.0855 (Δ = 1.5 ppm).

2-(4-Trifluoromethylphenyl)-1-nitrobutane (2i):

DAICEL OD-H, 0.3mL/min, hexanes: 2-propanol = 90:10, R_t = 23.9 min (+) / 27.1 min (-). ^1H NMR (300 MHz, CDCl_3) δ 7.59 (d, J = 8.1 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 4.58 (m, 2H), 3.43 (m, 1H), 1.73 (m, 2H), 0.83 (t, J = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 143.4, 128.0 (d), 125.9, 125.8, 125.7, 80.1, 45.7, 26.1, 11.4. GC-MS: m/z = 247 [M^+], 200, 159 (100). All spectral data are consistent with the literature values.³

2-(2-Trifluoromethylphenyl)-1-nitrobutane (2j):

Lipodex E column (25 m x 0.25 mm), 100 °C, 1 °C/min, 130 °C, R_t = 28.1 min (-) / 29.5 min (+). ^1H NMR (300 MHz, CDCl_3) δ 7.68 (m, 1H), 7.56 (m, 1H), 7.38 (m, 2H), 4.54 (d, J = 7.2 Hz, 2H), 3.87 (m, 1H), 1.81 (m, 2H), 0.81 (t, J = 7.5 Hz, 3H), ^{13}C NMR (75 MHz, CDCl_3) δ 132.3, 127.5, 127.5, 126.5, 126.4, 122.3, 80.2, 40.5, 26.4, 11.2. GC-MS: m/z = 247 [M^+], 200, 159 (100). All spectral data are consistent with the literature values.³

2-(Furan-2-yl)-1-nitrobutane (2k):

Lipodex E column (25 m x 0.25 mm), 100 °C, 1 °C/min, 120 °C, R_t = 42.0 min (-) / 42.7 min (+). ^1H NMR (300 MHz, CDCl_3) δ 7.34 (s, 1H), 6.29 (dd, 2H), 6.14 (d, 1H), 4.56 (m, 2H), 3.51 (m, 1H), 1.73 (m, 2H), 0.90 (t, J = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 152.4, 142.1, 110.2, 107.3, 78.2, 39.4, 24.1, 11.2. GC-MS: m/z = 169 [M^+], 122 (100), 107, 94, 81. All spectral data are consistent with the literature values.⁷

2-(Thiophen-2-yl)-1-nitrobutane (2l):

Lipodex E column (25 m x 0.25 mm), 100 °C, 1 °C/min, 130 °C, R_t = 33.7 min (-) / 34.9 min (+). ^1H NMR (300 MHz, CDCl_3) δ 7.23 (m, 1H), 6.95 (m, 1H), 6.88 (m, 1H), 4.55 (m, 2H), 3.71 (m, 1H), 1.75 (m, 2H), 0.92 (t, J = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 142.3, 126.9, 125.4, 123.4, 81.0, 41.3, 27.3, 11.4. GC-MS: m/z = 185 [M^+], 138 (100), 123, 110, 97. All spectral data are consistent with the literature values.⁵

2-Dimethoxymethyl-1-nitrobutane (2m):

Supelco β -Dex-120 column (30 m x 0.25 mm), 110 °C isothermic, R_t = 33.5 min (+) / 34.3 min (-). ^1H NMR (300 MHz, CDCl_3) δ 4.56 (m, 1H), 4.31 (m, 2H), 3.38 (s, 3H), 3.37 (s, 3H), 2.50 (m, 1H), 1.64 (m, 1H), 1.43 (m, 1H), 0.99 (t, J = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 105.3, 75.2, 55.9, 54.7, 42.0, 20.4, 10.9. All spectral data are consistent with the literature values.⁷

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