Supporting Information

Copper-Catalyzed Asymmetric Reduction of 3,3-Diarylacrylonitriles

Daehyung Lee, Youngmin Yang, and Jaesook Yun^{*}

Department of Chemistry and Institute of Basic Science, Sungkyunkwan University,
Suwon 440-746, Korea

E-mail: jaesook@skku.edu Tel: +82-31-299-4561; Fax: +82-31-290-7075

Experimental section

General Methods. Toluene was distilled from sodium benzophenone ketyl under nitrogen. Cu(OAc)₂, hydrosilanes, and other commercial substrates were purchased and used as received. Nitrile substrates (**1a–1h**) were prepared by chromatographic purification following standard Horner–Wadsworth–Emmons (HWE) of the corresponding ketones with diethyl cyanomethylphosphonate¹ or by the stereospecific coupling reaction (Heck reaction) of 3-arylacrylonitriles with aryl iodides.² All reactions were carried out under a nitrogen atmosphere, in an oven-dried Schlenk tube and run two or more times. Flash chromatography was performed on silica gel from Merck (70–230 mesh). All ¹H NMR spectra were obtained on Varian Mercury 300 systems and reported in parts per million (ppm) downfield from tetramethylsilane. ¹³C NMR spectra are reported in ppm referenced to deuteriochloroform (77.2 ppm). Infrared spectra (IR) were obtained on a Nicolet 205 FT-IR instrument. HPLC analysis was performed on a Younglin Acme 9000 series. Low resolution MS were recorded using a Varian 4000 GC/MS. High resolution mass spectra (HRMS) were obtained at Korea Basic Science Institute (Daegu, Korea) and reported in the form of m/z (intensity relative to base peak = 100).

Preparation of α,β -unsaturated nitriles by HWE reaction (1a–1g**):** NaH (15 mmol, 360 mg) was placed in an oven-dried 250 mL two-neck round-bottomed flask and THF (40 mL) were added under nitrogen. The reaction mixture was cooled to 0 °C and diethyl cyanomethylphosphonate (12 mmol, 1.89 mL) was added dropwise with stirring. The reaction mixture was allowed to warm to room temperature and stirred for 5 min until gas evolution had ceased. And then, ketone (10 mmol) was added dropwise to the yellow solution, maintained below 25 °C. During the addition, a gummy precipitate appeared. The solution was stirred at room temperature until no starting material was detected by TLC. The reaction mixture was extracted with ethyl acetate (3 x 50 mL). The combined organic layers were washed with brine, dried over Na₂SO₄, and concentrated. The (*E*)- and (*Z*)- products were isolated by column chromatography.

Preparation of α,β -unsaturated nitriles by Heck reaction (1h**):** Cinnamonnitrile (0.28 mL, 2.24 mmol) was added to a mixture of 4-iodotoluene (0.93 g, 4.27 mmol), KOAc (0.55 g, 5.60 mmol), Pd(OAc)₂ (25 mg, 0.11 mmol), and tetrabutylammonium bromide (0.79 g, 2.45 mmol) in anhydrous DMF (8 mL). The reaction mixture was heated at 80 °C, and monitored by TLC and GC. After completion of the reaction, the resulting

solution was cooled to room temperature, and then H₂O (5 mL) was added. The reaction mixture was extracted with ethyl acetate (3 × 20 mL) and the combined organic layers were washed with brine, dried over Na₂SO₄, and concentrated. The residue was purified by column chromatography (95 % *n*-hexane/ 5 % ethyl acetate) to afford **1h** (428 mg, 1.95 mmol).

The stereochemical assignments of the unsaturated nitrile compounds **1a**, **1b**, and **1f–1h** were made by comparison of the NMR spectra of the compounds reported previously in literature. In the cases of **1c** and **1d**, the structures were assigned by analogy with **1a**; the vinyl proton of the (*E*)-isomer was shifted to downfield in comparison with that of the (*Z*)-isomer due to the anisotropy effect of the near pyridyl *N*-atom.³ The structural assignment of **1e** were determined by an NOE study.

(*E*)-3-Phenyl-3-(pyridin-2-yl)acrylonitrile (1a**).**³ Yellow solid; ¹H NMR (300 MHz, CDCl₃) δ 8.69–8.67 (m, 1H), 7.65 (dt, *J* = 7.8 Hz, 1.8 Hz, 1H), 7.51–7.41 (m, 5H), 7.35–7.26 (m, 1H), 7.11 (d, *J* = 7.9 Hz, 1H), 6.70 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 160.3, 154.4, 150.0, 136.9, 135.7, 130.0, 129.3, 129.0, 124.9, 124.2, 118.0, 99.0; IR (neat) 2211 cm⁻¹.

(*Z*)-3-Phenyl-3-(pyridin-2-yl)acrylonitrile (1a**).**³ Yellow solid; ¹H NMR (300 MHz, CDCl₃) δ 8.79–8.77 (m, 1H), 7.81 (dt, *J* = 7.8 Hz, 1.7 Hz, 1H), 7.51–7.27 (m, 7H), 5.88 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 161.3, 155.2, 150.1, 137.8, 136.9, 130.7, 129.0, 128.5, 125.1, 124.5, 117.6, 97.4; IR (neat) 2211 cm⁻¹.

(*E*)-3-(3,4-Difluorophenyl)-3-(pyridin-2-yl)acrylonitrile (1b**).**⁴ Yellow solid; ¹H NMR (300 MHz, CDCl₃) δ 8.70–8.68 (m, 1H), 7.69 (dt, *J* = 7.8 Hz, 1.8 Hz, 1H), 7.38–7.21 (m, 4H), 7.11 (d, *J* = 8.0 Hz, 1H), 6.70 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 158.2, 153.7, 151.4 (dd, *J* = 252.1 Hz, 12.2 Hz), 150.5 (dd, *J* = 250.4 Hz, 12.7 Hz), 150.3, 137.1, 132.5 (t, *J* = 5.0 Hz), 126.1 (dd, *J* = 6.6 Hz, 3.9 Hz), 125.2, 123.9, 118.8 (d, *J* = 18.2 Hz), 117.8 (d, *J* = 17.7 Hz), 117.4, 100.0; IR (neat) 2217 cm⁻¹.

(E)-3-(4-Chlorophenyl)-3-(pyridin-2-yl)acrylonitrile (1c).

White solid; ^1H NMR (300 MHz, CDCl_3) δ 8.70–8.68 (m, 1H), 7.67 (dt, $J = 7.7$ Hz, 1.7 Hz, 1H), 7.50–7.32 (m, 5H), 7.10 (d, $J = 8.0$ Hz, 1H), 6.69 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 159.2, 154.0, 150.2, 137.0, 136.2, 134.1, 130.8, 129.4, 125.1, 124.0, 117.7, 99.5; IR (neat) 2211 cm^{-1} .

(E)-3-(4-Methoxyphenyl)-3-(pyridin-2-yl)acrylonitrile (1d).

Yellow solid; ^1H NMR (300 MHz, CDCl_3) δ 8.67–8.65 (m, 1H), 7.64 (dt, $J = 7.9$ Hz, 1.8 Hz, 1H), 7.40–7.37 (m, 2H), 7.31 (ddd, $J = 5.3$ Hz, 4.8 Hz, 1.1 Hz, 1H), 7.16 (dd, $J = 7.0$ Hz, 1.1 Hz, 1H), 7.17–6.96 (m, 2H), 6.50 (s, 1H), 3.86 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 160.8, 159.9, 154.9, 149.9, 136.7, 131.0, 127.8, 124.7, 124.2, 118.3, 114.2, 97.7, 55.6; IR (neat) 2211 cm^{-1} ; HRMS(EI) calcd for $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_1$ 236.0950, Found 236.0948.

(Z)-3-(4-Methoxyphenyl)-3-(pyridin-2-yl)acrylonitrile (1d).

Yellow solid; ^1H NMR (300 MHz, CDCl_3) δ 8.78–8.75 (m, 1H), 7.81 (dt, $J = 7.8$ Hz, 1.8 Hz, 1H), 7.53–7.49 (m, 1H), 7.38 (ddd, $J = 7.6$ Hz, 4.8 Hz, 1.0 Hz, 1H), 7.25–7.22 (m, 2H), 6.91–6.87 (m, 2H), 5.80 (s, 1H), 3.83 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 161.5, 160.6, 155.3, 149.9, 136.7, 129.9, 129.8, 125.0, 124.3, 117.8, 114.2, 95.0, 55.6; IR (neat) 2211 cm^{-1} ; Anal. Calcd for $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_1$: C, 76.25; H, 5.12. Found: C, 76.19; H, 5.23.

(Z)-3-(Pyridin-2-yl)-3-o-tolylacrylonitrile (1e).

Yellow solid; ^1H NMR (300 MHz, CDCl_3) δ 8.78–8.76 (m, 1H), 7.69 (dt, $J = 7.8$ Hz, 1.8 Hz, 1H), 7.67–7.21 (m, 6H), 5.63 (s, 1H), 1.99 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 161.3, 154.6, 149.9, 138.4, 136.8, 136.3, 130.9, 129.7, 129.6, 126.4, 124.6, 124.0, 117.5, 99.7, 20.3; IR (neat) 2217 cm^{-1} ; Anal. Calcd for $\text{C}_{15}\text{H}_{12}\text{N}_2$: C, 81.79; H, 5.49; N, 12.72. Found: C, 81.79; H, 5.52; N, 12.50. The (Z)-isomer was assigned by a nuclear Overhauser enhancement (NOE) study; irradiation of the vinyl hydrogen at δ 5.63 gave a 1.75 % enhancement of the methyl hydrogens.

(*E*)-3-(Pyridin-2-yl)-3-*o*-tolylacrylonitrile (1e). White solid; ^1H NMR (300MHz, CDCl_3) δ 8.69–8.67 (m, 1H), 7.61 (dt, $J = 7.8$ Hz, 1.8 Hz, 1H), 7.40–7.22 (m, 5H), 6.94 (s, 1H), 6.89 (d, $J = 7.9$ Hz, 1H), 2.13 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 160.4, 153.3, 150.1, 137.2, 136.1, 135.3, 130.9, 129.6, 129.2, 126.5, 124.9, 123.4, 117.6, 100.1, 19.7; IR (neat) 2211 cm^{-1} ; Anal.Calcd for $\text{C}_{15}\text{H}_{12}\text{N}_2$: C, 81.79; H, 5.49. Found: C, 81.73; H, 5.51. The (*E*)-isomer was assigned by a nuclear Overhauser enhancement (NOE) study; irradiation of the vinyl hydrogen at δ 6.94 gave no enhancement of the methyl hydrogens.

(*E*)-3-Phenyl-3-(pyridin-3-yl)acrylonitrile (1f).^{2a,3} Yellow solid; ^1H NMR (300 MHz, CDCl_3) δ 8.70 (dd, $J = 5.0$ Hz, 1.6 Hz, 1H), 8.62 (dd, $J = 1.4$ Hz, 1.6 Hz, 1H), 7.70 (d, $J = 1.8$ Hz, 1H), 7.53–7.42 (m, 6H), 5.81 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 160.0, 151.4, 149.1, 136.1, 135.9, 134.9, 130.7, 129.5, 129.0, 123.5, 117.4, 96.4; IR (neat) 2211 cm^{-1} .

(E)-3-Phenyl-3-(pyridin-4-yl)acrylonitrile (1g).³ Yellow solid; ¹H NMR (300 MHz, CDCl₃) δ 8.67 (d, *J* = 5.3 Hz, 2H), 7.51–7.40 (m, 5H), 7.19, (d, *J* = 5.7 Hz, 2H), 5.87 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 160.5, 150.6, 143.1, 135.6, 130.8, 129.5, 129.0, 122.6, 117.1, 98.0; IR (neat) 2217 cm⁻¹.

(Z)-3-Phenyl-3-(pyridin-4-yl)acrylonitrile (1g).³ Yellow solid; ¹H NMR (300 MHz, CDCl₃) δ 8.76 (d, *J* = 5.7 Hz, 2H), 7.51–7.25 (m, 7H), 5.90 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 160.5, 150.6, 144.8, 137.3, 131.2, 129.2, 128.3, 123.8, 117.0, 97.0; IR (neat): 2217 cm⁻¹.

(E)-3-(4-Methylphenyl)-3-Phenyl-2-propenenitrile (1h).^{2a} Yellow solid; ¹H NMR (300 MHz, CDCl₃) δ 7.47–7.41(m, 5H), 7.19 (s, 4H), 5.72 (s, 1H), 2.39 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 163.1, 141.0, 137.3, 136.1, 130.0, 129.6, 129.5, 128.6, 128.5, 118.2, 94.0, 21.4; IR (neat): 2213 cm⁻¹

General Procedure for the enantioselective reduction of 3,3-diarylacrylonitriles: Cu(OAc)₂ (1.82 mg, 0.010 mmol) and Josiphos ligand (6.41 mg, 0.010 mmol, ethanol adduct) were placed in an oven-dried Schlenk tube and toluene (0.5 mL) were added under nitrogen. The reaction mixture was stirred for 10 min at room temperature. PMHS (0.12 mL, 2.0 mmol) was added to the reaction mixture and stirred for 5 min for catalyst activation. The reaction tube was placed in a bath of indicated temperatures and unsaturated nitrile (0.5 mmol) and toluene (0.5 mL) were added, followed by *t*-BuOH (0.191 mL, 2.0 mmol). The reaction was sealed, and stirred until the starting material was completely consumed as judged by TLC. The reaction mixture was quenched with water and transferred to a round-bottomed flask with an aid of Et₂O (10 mL), and NaOH (2.5 M, 1.2 mL) was added. The biphasic mixture was stirred vigorously for 0.5 h. The layers were separated and the aqueous layer was extracted with Et₂O (3 x 20 mL). The combined organic layers were washed with brine, dried over MgSO₄, and concentrated. The product was purified by chromatography on silica gel or Kugelrohr distillation.

3-Phenyl-3-(2-pyridyl)propionitrile (2a, Table 1, entry 1).³ The title compound was isolated as a yellow oil in 90% yield. ¹H NMR (300 MHz, CDCl₃) δ 8.62–8.60 (m, 1H), 7.60 (dt, *J* = 7.7 Hz, 1.8 Hz, 1H), 7.34–7.27 (m, 5H), 7.18 (ddd, *J* = 7.6 Hz, 5.0 Hz, 1.1 Hz, 1H), 7.13 (d, *J* = 7.8 Hz, 1H), 4.44 (t, *J* = 7.5 Hz, 1H), 3.41 (dd, *J* = 16.7 Hz, 7.6 Hz, 1H), 3.09 (dd, *J* = 16.7 Hz, 7.6 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 159.7, 149.4, 141.0, 136.9, 129.1, 128.0, 127.8, 123.6, 122.4, 119.2, 49.4, 23.3; IR (neat) 2245 cm⁻¹; MS, *m/z*: 208 (50) [M⁺], 207 (100) [M-H]⁺, 168 (38), 167 (62). The ee (96% ee) was measured by chiral HPLC on an OD-H column (*i*PrOH:hexane = 5:95, 1.0 mL/min): major isomer *t*_r = 12.1 min and minor isomer *t*_r = 13.5 min.

(S)-3-(3,4-Difluorophenyl)-3-(2-pyridyl)propionitrile (2b, Table 2, entry 2).⁴ The title compound was isolated as a yellow oil in 95% yield. ¹H NMR (300 MHz, CDCl₃) δ 8.62 (d, *J* = 4.1 Hz, 1H), 7.63 (dt, *J* = 7.7 Hz, 1.8 Hz, 1H), 7.22 (ddd, *J* = 7.6 Hz, 4.9 Hz, 1.1 Hz, 1H), 7.19–7.07 (m, 4H), 4.38 (t, *J* = 7.6 Hz, 1H), 3.32 (dd, *J* = 16.7 Hz, 7.2 Hz, 1H), 3.09 (dd, *J* = 16.7 Hz, 8.1 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 158.7, 150.6 (dd, *J* = 249.6 Hz, 13.0 Hz), 150.0 (dd, *J* = 248.8 Hz, 12.2 Hz), 149.7, 137.8, 137.1, 124.2 (dd, *J* = 6.4 Hz, 3.6 Hz), 123.5, 122.8, 118.7, 117.8 (d, *J* = 17.1 Hz), 117.0 (d, *J* = 17.7 Hz), 48.5, 23.5; IR (neat): 2245 cm⁻¹. The ee (91% ee) was measured by chiral HPLC on an AS-H column (*i*PrOH:hexane = 10:90, 0.5 mL/min): (*S*) isomer *t*_r = 22.3 min and (*R*) isomer *t*_r = 26.5 min. [α]_D²⁰ = +72.8° (c 0.31, CHCl₃).

3-(4-Chlorophenyl)-3-(2-pyridyl)propionitrile (2c, Table 2, entry 5).⁵ The title compound was isolated as a yellow oil in 89% yield. ¹H NMR (300 MHz, CDCl₃) δ 8.61 (d, *J* = 4.1 Hz, 1H), 7.61 (dt, *J* = 7.7 Hz, 1.8 Hz, 1H), 7.32–7.17 (m, 5H), 7.11 (d, *J* = 7.8 Hz, 1H), 4.40 (t, *J* = 7.6 Hz, 1H), 3.35 (dd, *J* = 16.7 Hz, 7.3 Hz, 1H), 3.09 (dd, *J* = 16.7 Hz, 7.9 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 159.0, 149.4, 139.3, 136.9, 133.5, 129.3, 129.1, 123.4, 122.5, 118.8, 48.5, 23.1; IR (neat) 2245 cm⁻¹; MS, *m/z*: 244 (27) [M⁺(³⁷Cl)], 243 (43) [M(³⁷Cl)-H]⁺, 242 (80) [M⁺(³⁵Cl)], 241 (100) [M(³⁵Cl)-H]⁺, 168 (66). The ee (93% ee) was measured by chiral HPLC on an AS-H column (*i*PrOH:hexane = 10:90, 0.5 mL/min): major isomer *t*_r = 24.0 min and minor isomer *t*_r = 27.5 min.

3-(4-Methoxyphenyl)-3-(2-pyridyl)propionitrile (2d, Table 2, entry 8). The title compound was isolated as a yellow oil in 93% yield. ^1H NMR (300 MHz, CDCl_3) δ 8.60 (d, $J = 4.8$ Hz, 1H), 7.59 (dt, $J = 7.7$ Hz, 1.8 Hz, 1H), 7.24–7.10 (m, 4H), 6.87–6.83 (m, 2H), 4.39 (t, $J = 7.6$ Hz, 1H), 3.78 (s, 3H), 3.36 (dd, $J = 16.6$ Hz, 7.3 Hz, 1H), 3.06 (dd, $J = 16.7$ Hz, 7.8 Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 159.9, 159.0, 149.2, 136.7, 133.0, 128.9, 123.4, 122.2, 119.3, 114.3, 55.3, 48.4, 23.3; IR (neat) 2250 cm^{-1} ; Anal. Calcd for $\text{C}_{15}\text{H}_{14}\text{N}_2\text{O}_1$: C, 75.61; H, 5.92; N, 11.76. Found: C, 75.66; H, 6.04; N, 11.45. The ee (95% ee) was measured by chiral HPLC on an AS-H column (*i*PrOH:hexane = 5:95, 0.5 mL/min): major isomer $t_r = 43.7$ min and minor isomer $t_r = 47.9$ min.

3-(2-pyridyl)-3-o-tolylpropionitrile (2e, Table 2, entry 11). The title compound was isolated as a yellow oil in 86% yield. ^1H NMR (300 MHz, CDCl_3) δ 8.62–8.60 (m, 1H), 7.56 (dt, $J = 7.7$ Hz, 5.9 Hz, 1H), 7.25–7.15 (m, 5H), 7.13 (d, $J = 7.9$ Hz, 1H), 4.75 (t, $J = 7.6$ Hz, 1H), 3.41 (dd, $J = 16.7$ Hz, 7.6 Hz, 1H), 3.02 (dd, $J = 16.7$ Hz, 7.6 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 160.0, 149.5, 139.2, 137.0, 136.0, 131.2, 127.7, 127.5, 127.0, 123.5, 122.4, 119.4, 44.9, 22.8, 20.1; IR (neat) 2245 cm^{-1} ; HRMS(EI) calcd for $\text{C}_{15}\text{H}_{14}\text{N}_2$ 222.1157, Found 222.1157. The ee (95% ee) was measured by chiral HPLC on an AS-H column (*i*PrOH:hexane = 10:90, 0.5 mL/min): minor isomer $t_r = 18.5$ min and major isomer $t_r = 21.2$ min.

3-Phenyl-3-(3-pyridyl)propionitrile (2f, Table 2, entry 13).³ The title compound was isolated as a yellow oil in 92% yield. ^1H NMR (300 MHz, CDCl_3) δ 8.58–8.55 (m, 2H), 7.68 (dd, $J = 7.9$ Hz, 1.8 Hz, 1H), 7.41–7.22 (m, 6H), 4.46 (t, $J = 7.6$ Hz, 1H), 3.10 (d, $J = 7.5$ Hz, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 149.1, 148.8, 140.0, 134.9, 129.1, 127.8, 127.5, 117.9, 44.8, 23.9; IR (neat) 2245 cm^{-1} ; MS, m/z : 208 (40) $[\text{M}^+]$, 207 (70) $[\text{M}-\text{H}]^+$, 206 (100). The ee (96% ee) was measured by chiral HPLC on an AS-H column (*i*PrOH:hexane = 10:90, 1.0 mL/min): major isomer $t_r = 37.3$ min and minor isomer $t_r = 46.1$ min.

3-Phenyl-3-(4-pyridyl)propionitrile (2g, Table 2, entry 14).³ The title compound was isolated as a yellow oil in 86% yield. The ee (90% ee) was measured by chiral HPLC on an AS-H column

(*i*PrOH:hexane = 10:90, 1.0 mL/min): minor isomer t_r = 49.8 min and major isomer t_r = 57.5 min.

3-Phenyl-3-(4-pyridyl)propionitrile (2g, Table 2, entry 15).³ The title compound was isolated as a yellow oil in 87% yield. ¹H NMR (300 MHz, CDCl₃) δ 8.60 (d, J = 6.0 Hz, 2H), 7.41–7.20 (m, 7H), 4.40 (t, J = 7.6 Hz, 1H), 3.07 (d, J = 7.6 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 150.1, 149.7, 139.5, 129.1, 127.9, 127.5, 123.5, 117.9, 46.4, 23.3; IR (neat) 2250 cm⁻¹; MS, m/z : 208 (70) [M⁺], 207 (100) [M-H]⁺, 168 (66). The ee (92% ee) was measured by chiral HPLC on an AS-H column (*i*PrOH:hexane = 10:90, 1.0 mL/min): major isomer t_r = 48.1 min and minor isomer t_r = 59.4 min.

3-Phenyl-3-*p*-tolylpropionitrile (2h, Table 2, entry 16). The title compound was isolated as a yellow solid in 94% yield; ¹H NMR (300 MHz, CDCl₃) δ 7.36–7.31 (m, 3H), 7.28–7.22 (m, 2H), 7.13 (dt, J = 8.4 Hz, J = 1.5 Hz, 4H), 4.35 (t, J = 7.8 Hz, 1H), 3.02 (d, J = 7.8 Hz, 2H), 2.32 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 141.6, 138.4, 137.3, 129.7, 129.0, 127.7, 127.6, 127.5, 118.7, 46.9, 24.5, 21.2; IR (neat) 2242 cm⁻¹; MS, m/z : 221 (52) [M⁺], 181 (100), 167 (42), 89 (10); HRMS (EI) calcd for C₁₆H₁₅N 221.1204, Found 221.1207. The ee (94% ee) was measured by chiral HPLC on an OD-H column (*i*PrOH:hexane = 10:90, 0.5 mL/min): major isomer t_r = 47.2 min and minor isomer t_r = 50.9 min.

Eyring diagram⁶ for the reduction of (*E*)-1c

T(°C)	ee (%)
0	79
22	93
40	89
60	85

References

1. Wadsworth, W. S.; Emmons, W. D. *J. Am. Chem. Soc.* **1961**, 83, 1733.
2. (a) Masllorens, J.; Moreno-Mañas, M.; Pla-Quintana, A.; Pleixats, R.; Roglans, A. *Synthesis* **2002**, 13, 1903. (b) Botella, L.; Nájera, C. *J. Org. Chem.* **2005**, 70, 4360.
- 3 Ishikawa, F. *Chem. Pharm. Bull.* **1980**, 28, 1394.
- 4 Wabnitz, T. C.; Rizzo, S.; Götte, C.; Buschauer, A.; Benincori, T.; Reiser, O. *Tetrahedron Lett.* **2006**, 47, 3733.
5. Aslanian, R.; Mutahi, M.; Shih, N.-Y. ; Piwinski, J. J.; West, R.; Williams, S. M.; She, S.; Wu, R.-L.; Hey, J. A. *Bioorg. Med. Chem. Lett.* **2003**, 13, 1959.
6. Eyring, H. *J. Chem. Phys.* **1935**, 3, 107.

(E)-1a

(Z)-1a

(E)-1b

(Z)-1e

(E)-1e

2a, Table 1, entry 1

2b, Table 2, entry 2

2c, Table 2, entry 5

2d, Table 2, entry 8

2e, Table 2, entry 11

2f, Table 2, entry 13

2g, Table 2, entry 15

2h, Table 2, entry 16