Highly Regio- and Enantioselective Palladium-Catalyzed Allylic Alkylation and Amination of Dienyl Esters with 1,1'-*P,N*-Ferrocene Ligands

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General Experimental Conditions. All reactions were performed under an atmosphere of dry argon using oven-dried glassware. Solvents were distilled under an atmosphere of argon before use. Tetrahydrofuran, toluene and ethyl ether were distilled from sodium benzophenone ketal. Dichloromethane and acetonitrile were distilled from calcium hydride. The commercially available reagents were used as received without further purification. Ligands **L1a** and **L2b** were prepared according to the procedures we reported before.¹ Melting points are uncorrected. ¹H NMR spectra were recorded on a Varian MERCURY300 (300 MHz) spectrometer and the chemical shifts were referenced to CHCl₃ (δ 7.27) in CDCl₃. ¹³C NMR

spectra were recorded on a Varian MERCURY300 (300 MHz) spectrometer and the chemical shifts were referenced to CHCl_3 (δ 77.00) in CDCl_3 . The ratio of **linear** and **branched** products was determined by ^1H NMR spectra. Optical rotations were measured using a Perkin-Elmer 341 MC polarimeter with a thermally jacketed 10 cm cell at 25 °C (concentration c given as g/100 mL). IR spectra were measured in cm^{-1} , using a Shimidazu IR-400 infrared spectrophotometer. Mass spectra and high-resolution mass spectra were taken using HP5989A, HP5973N and IonSpec 4.7 Tesla FTMS mass spectrometers, respectively. Elemental analyses were performed on a Foss-Heraeus Vario EL instrument. The ee values were determined by chiral HPLC (Chiralcel OD, OJ-H, AD, AD-H column).

General procedure for the palladium-catalyzed allylic alkylation of 1a~1g:

$[\text{Pd}(\eta^3\text{-C}_3\text{H}_5)\text{Cl}]_2$ (1.8 mg, 0.005 mmol) and ligand **L1a** (7.3 mg, 0.01 mmol) were dissolved in dry solvent (1 mL) in a dried Schlenk tube under argon, and then stirred at room temperature. After 1 h, **1a** or other substrate (0.25 mmol) and potassium acetate (1.5 mg, 0.015 mmol) were added and the mixture was stirred for another 30 min. Finally, the mixture was kept at the proper temperature. To this solution were successively added dimethylmalonate (0.09 mL, 0.78 mmol) and *N,O*-bis (trimethylsilyl)acetamide (0.18 mL, 0.75 mmol). The reaction was monitored by TLC. After completion, the reaction mixture was diluted with CH_2Cl_2 (20 mL) and washed twice with saturated aqueous NaCl. The organic phase was dried over anhydrous Na_2SO_4 and then concentrated under reduced pressure. The residue was purified by preparative TLC (petroleum ether/ethyl acetate 10/1) to give the product. The regioselectivity was determined by 300 MHz ^1H NMR. The enantiomeric purities were determined by HPLC.

2-(3-Phenyl-1-vinyl-allyl)-malonic acid dimethyl ester 4a:² 80% yield, 92% *ee*. ¹H NMR (300 MHz, CDCl₃): δ 3.59 (d, *J* = 9.0 Hz, 1H), 3.65-3.75 (m, 7H), 5.14 (d, *J* = 10.5Hz, 1H), 5.19 (d, *J* = 17.5Hz, 1H), 5.89 (ddd, *J* = 17.4, 10.2, 7.2Hz, 1H), 6.15 (dd, *J* = 15.9, 8.4Hz, 1H), 7.22-7.36 (m, 5H). EI-MS *m/z* (rel int) 274 (M⁺, 5), 215 (26), 214 (38), 199 (14), 182 (32), 155 (78), 143 (100), 128 (84), 115 (35), 91 (20). HPLC (Chiralcel OJ-H column, 254 nm, hexane/isopropanol 90/10, flow = 0.9 mL/min) *t*_R = 16.41, 18.41 min.

2-(3-Phenyl-2-methyl-1-vinyl-allyl)-malonic acid dimethyl ester 4b: 89% yield, 93% *ee*. ¹H NMR (300 MHz, CDCl₃): δ 1.83 (s, 3H), 3.47 (q, *J* = 6.9Hz, 1H), 3.65-3.82 (m, 7H), 5.13 (d, *J* = 10.5Hz, 1H), 5.17 (d, *J* = 17.4Hz, 1H), 5.82 (ddd, *J* = 18.3, 10.2, 4.8Hz, 1H), 6.39 (s, 1H), 7.17-7.33 (m, 5H). ¹³C NMR (300MHz, CDCl₃): δ 168.10, 137.53, 136.56, 136.23, 128.82, 128.03, 127.53, 126.41, 117.18, 55.03, 53.16, 52.54, 52.52, 15.55. EI-MS *m/z* (rel int) 288 (M⁺, 4), 229 (8), 213 (8), 196 (16), 169 (33), 157 (100), 141 (39), 129 (74), 115 (42), 91 (47); IR (film) 3082 (w), 2954 (w), 1760 (s), 1739 (s), 1436 (m), 1319 (m), 1261 (m), 1162 (m), 1028 (m), 702 (m). HRMS Calcd. for C₁₇H₂₀O₄Na: 311.1251 (M + Na)⁺. Found: 311.1254. HPLC (Chiralcel OJ-H column, 254 nm, hexane/isopropanol 90/10, flow = 0.7 mL/min) *t*_R = 10.22, 12.44 min.

2-(3-Phenyl-3-methyl-1-vinyl-allyl)-malonic acid dimethyl ester 4c: 81% yield, 88% *ee*. ¹H NMR (300 MHz, CDCl₃): δ 2.09 (s, 3H), 3.54 (d, *J* = 9.6Hz, 1H), 3.64-3.74 (m, 7H), 5.07 (d, *J* = 9.9Hz, 1H), 5.15 (d, *J* = 17.4Hz, 1H), 5.60 (dd, *J* = 10.2, 1.5Hz, 1H), 5.8 (ddd, *J* = 17.4, 9.6, 6.9Hz), 7.21-7.36 (m, 5H). ¹³C NMR (300MHz, CDCl₃): δ 168.21, 168.18, 143.40, 137.95, 136.57, 128.17, 127.07, 125.86, 125.28, 116.28, 56.65, 52.44, 43.19, 16.22. EI-MS *m/z* (rel int) 288 (M⁺, 2), 228 (21), 213 (11), 196 (25), 169 (39), 157 (100), 141 (39), 129 (93),

115 (35), 91 (40). IR (film) 2957 (w), 1739 (s), 1715 (s), 1436 (m), 1363 (m), 1223 (m), 762 (w). HRMS Calcd. for $C_{17}H_{20}O_4Na$: 311.1261 ($M + Na$)⁺. Found: 311.1254. HPLC (Chiralcel OJ-H column, 254 nm, hexane/isopropanol 90/10, flow = 0.7 mL/min) t_R = 8.22, 10.78 min.

2-(3-(4-Methoxy-phenyl)-1-vinyl-allyl)-malonic acid dimethyl ester 4d: 79% yield, 87% *ee*. ¹H NMR (300 MHz, CDCl₃): δ 3.54-3.71 (m, 7H), 3.79 (s, 3H), 5.11 (d, J = 10.8Hz, 1H), 5.16 (d, J = 17.4Hz, 1H), 5.87 (ddd, J = 7.5, 10.2, 17.4Hz, 1H), 5.99 (dd, J = 8.1, 15.9Hz, 1H), 6.41 (d, J = 15.9Hz, 1H), 6.83 (d, J = 8.7Hz, 2H), 7.26 (d, J = 8.4Hz, 2H). ¹³C NMR (300MHz, CDCl₃): δ 168.13, 159.15, 136.83, 131.64, 129.67, 127.47, 125.47, 116.87, 113.88, 56.66, 55.24, 52.42, 47.11. EI-MS m/z (rel int) 304 (M^+ , 23), 245 (6), 229 (5), 213 (6), 185 (18), 173 (100), 158 (35), 141 (11), 128 (11), 115 (15). IR (film) 2956 (w), 1757 (s), 1737 (s), 1609 (m), 1513 (s), 1252 (s), 911 (m), 734 (s); HRMS Calcd. for $C_{17}H_{20}O_5Na$: 327.1197 ($M + Na$)⁺. Found: 327.1203. HPLC (Chiralcel OD column, 254 nm, hexane/isopropanol 100/2, flow = 0.7 mL/min) t_R = 33.98, 41.63 min.

2-(3-(1'-Naphthyl)-1-vinyl-allyl)-malonic acid dimethyl ester 4e: 86% yield, 87% *ee*. ¹H NMR (300 MHz, CDCl₃): δ 3.65 (d, J = 9.6Hz, 1H), 3.70-3.85 (m, 7H), 5.19 (d, J = 10.5Hz, 1H), 5.27 (dt, J = 17.1, 1.2Hz, 1H), 5.96 (ddd, J = 17.4, 10.2, 7.2Hz, 1H), 6.15 (dd, J = 15.6, 8.4Hz, 1H), 7.40-7.54 (m, 4H), 7.77 (d, J = 8.4Hz, 1H), 7.82-7.85 (m, 1H), 8.03-8.07 (m, 1H). ¹³C NMR (300MHz, CDCl₃): δ 168.18, 168.08, 136.60, 134.76, 133.46, 131.07, 130.99, 129.86, 128.44, 127.91, 126.02, 125.74, 125.55, 123.93, 123.77, 117.31, 56.66, 52.52, 47.42. EI-MS m/z (rel int) 324 (M^+ , 14), 264 (18), 249 (14), 232 (23), 205 (38), 193 (100), 178 (67), 165 (41), 152 (21). IR (film) 2955 (w), 1737 (s), 1714 (s), 1436 (m), 779 (m); HRMS Calcd. for $C_{20}H_{20}O_4Na$: 347.1254 ($M + Na$)⁺. Found: 347.1254. HPLC (Chiralcel OJ column, 254 nm,

hexane/isopropanol 90/10, flow = 0.7 mL/min) t_R = 17.21, 19.21 min.

2-(3,3-Dimethyl-1-vinyl-allyl)-malonic acid dimethyl ester 4f:² 82% yield, 91% *ee*. ¹H NMR (300 MHz, CDCl₃): δ 1.66(d, J = 1.8Hz, 3H), 1.69 (d, J = 1.8Hz, 3H), 3.41(dt, J = 9.3, 1.8Hz, 1H), 3.67-3.74 (m, 7H), 5.01 (d, J = 12.0Hz, 2H), 5.07 (d, J = 17.4Hz, 1H), 5.72 (ddd, J = 17.4, 10.2, 7.5Hz, 1H). ¹³C NMR (300MHz, CDCl₃): δ 168.35, 137.29, 135.10, 122.02, 115.56, 56.76, 52.31, 52.28, 42.83, 25.88, 17.97. EI-MS m/z (rel int) 226 (M^+ , 3), 208 (6), 194 (5), 167 (21), 151 (11), 135 (11), 107 (18), 95 (100), 79 (19), 67 (24). HPLC (Chiralpak AD column, 220 nm, hexane/isopropanol 98/2, flow = 0.7 mL/min) t_R = 13.38, 16.54 min.

2-(3-Phenyl-1-methyl-1-vinyl-allyl)-malonic acid dimethyl ester 4g: 83% yield, 56% *ee*. ¹H NMR (300 MHz, CDCl₃): δ 1.48 (s, 3H), 3.59 (s, 1H), 3.69 (s, 6H), 3.73-3.75 (m, 1H), 5.12 (d, J = 13.8Hz, 1H), 5.17 (d, J = 6.9Hz, 1H), 6.18 (dd, J = 11.1, 17.4Hz, 1H), 6.44 (t, J = 16.5Hz, 2H), 7.21-7.38 (m, 5H). ¹³C NMR (300MHz, CDCl₃): δ 167.84, 142.00, 137.27, 133.84, 129.03, 128.47, 127.33, 126.33, 114.22, 60.33, 52.18, 44.43, 21.78. EI-MS m/z (rel int) 288(6), 157(100), 142(22), 129(59), 115(20), 105(10), 91(33). IR (film) 2954 (w), 1758 (s), 1736 (s), 1436 (m). HRMS Calcd. For C₁₇H₂₀O₄Na: 311.1240(M + Na)⁺. Found: 311.1254. HPLC (Chiralpak AD-H column, 254 nm, hexane/isopropanol 100/1, flow = 0.7 mL/min) t_R = 13.96, 14.71 min.

General procedure for the palladium-catalyzed allylic amination of 2a-2d:
[Pd(η -C₃H₅)Cl]₂ (1.8 mg, 0.005 mmol) and ligand **L2b** (7.2 mg, 0.01 mmol) were dissolved in dry solvent (1 mL) in a dried Schlenk tube under argon, and then stirred at room temperature. After 0.5 h, **2a** or other substrate (0.25 mmol) and benzylamine (0.09 mL, 0.75 mmol) were added. The reaction was monitored by TLC. After completion, the reaction

mixture was diluted with CH₂Cl₂ (20 mL) and washed twice with saturated aqueous NH₄Cl. The organic phase was dried over anhydrous Na₂SO₄ and then concentrated under reduced pressure. The residue was purified by preparative TLC (petroleum ether/ethyl acetate 10/1) to give the product. The regioselectivity was determined by 300 MHz ¹H NMR. The enantiomeric purities were determined by HPLC.

Benzyl-(3-phenyl-1-vinyl-allyl)-amine 9a:³ 85% yield, 90% *ee*. ¹H NMR (300 MHz, CDCl₃): δ 3.82-3.88 (m, 3H), 5.19 (d, *J* = 10.2Hz, 1H), 5.26 (d, *J* = 17.4Hz, 1H), 5.88 (ddd, *J* = 6.9, 9.9, 17.1Hz, 1H), 6.18 (dd, *J* = 7.5, 15.9Hz, 1H), 6.54 (d, *J* = 16.5Hz, *J*=1H), 7.21-7.41(m, 10H). EI-MS *m/z* (rel int) 249 (M⁺, 13), 248 (11), 222 (9), 158 (44), 143 (51), 128 (17), 115 (16), 91 (100). HPLC (Chiralcel OD column, 230 nm, hexane/isopropanol 98/2, flow = 0.7 mL/min) *t_R* = 11.40, 12.96 min.

Benzyl-(3-phenyl-2-methyl-1-vinyl-allyl)-amine 9b: 80% yield, 93% *ee*. ¹H NMR (300 MHz, CDCl₃): δ 1.87 (s, 3H), 3.72-3.82 (m, 3H), 5.17 (d, *J* = 10.2Hz, 1H), 5.28 (d, *J*=17.1Hz, 1H), 5.87 (ddd, *J* = 6.9, 10.5, 17.1Hz, 1H), 6.55 (s, 1H), 7.20-7.37 (m, 10H). ¹³C NMR (300MHz, CDCl₃): δ 140.53, 139.40, 138.64, 137.90, 128.94, 128.36, 128.20, 128.05, 126.87, 126.71, 126.26, 115.61, 68.46, 51.13, 14.15. EI-MS *m/z* (rel int) 263 (M⁺, 3), 262 (3), 248 (5), 236 (5), 172 (20), 146 (25), 129 (10), 115 (11), 91 (100). IR (film) 3026 (w), 2918 (w), 2855 (w), 1494 (m), 1453 (m), 919 (m), 699 (s). HRMS Calcd. For C₁₉H₂₂N: 264.1746(M + H)⁺. Found: 264.1747. HPLC (Chiralcel OD column, 230 nm, hexane/isopropanol 98/2, flow = 0.7 mL/min) *t_R* = 6.92, 7.65 min.

Benzyl-(3-(1'-naphthyl)-1-vinyl-allyl)-amine 9c: 79% yield, 94% *ee*. ¹H NMR (300 MHz, CDCl₃): δ 3.90 (s, 2H), 3.97-4.01 (m, 1H), 5.24 (d, *J* = 10.2Hz, 1H), 5.33 (d, *J* = 17.1Hz,

1H), 5.96 (ddd, $J = 6.6, 9.9, 16.8\text{Hz}$, 1H), 6.21 (dd, $J = 7.2, 15.6\text{Hz}$, 1H), 7.26-7.55 (m, 10H), 7.62 (d, $J = 7.5\text{Hz}$, 1H), 7.77-7.88 (m, 2H), 8.13 (t, $J = 7.2\text{Hz}$, 1H). ^{13}C NMR (300MHz, CDCl_3): δ 140.25, 139.56, 134.70, 134.26, 133.59, 128.51, 128.46, 128.44, 128.34, 128.26, 127.84, 126.99, 125.97, 125.71, 125.61, 123.85, 123.77, 116.09, 63.19, 51.15. EI-MS m/z (rel int) 299 (M^+ , 7), 298 (7), 208 (21), 191(10), 178 (15), 165 (23), 158 (20), 141 (11), 91 (100). IR (film) 3310 (w), 3061 (w), 2926 (w), 1670 (s), 1454 (m), 925 (w), 755 (s). HRMS Calcd. For $\text{C}_{22}\text{H}_{22}\text{N}$: 300.1741($\text{M} + \text{H}$) $^+$. Found: 300.1747. HPLC (Chiralcel OJ-H column, 230 nm, hexane/isopropanol 97/3, flow = 0.7 mL/min) t_R = 23.16, 26.40 min.

Benzyl-(3-methyl-1-vinyl-allyl)-amine 9d: 76% yield, 88% *ee*. ^1H NMR (300 MHz, CDCl_3): δ 1.70 (d, $J = 6.9\text{Hz}$, 3H), 3.58-3.63 (m, 1H), 3.74 (s, 2H), 5.10 (d, $J = 12.0\text{Hz}$, 1H), 5.15 (d, $J = 17.4\text{Hz}$, 1H), 5.41 (ddd, $J = 1.5, 7.2, 15.3\text{Hz}$, 1H), 5.61 (ddd, $J = 0.9, 6.6, 15.3\text{Hz}$, 1H), 5.78 (ddd, $J = 7.5, 10.2, 17.4\text{Hz}$, 1H), 7.21-7.31 (m, 5H). ^{13}C NMR (300MHz, CDCl_3): δ 140.45, 140.16, 132.43, 128.34, 128.15, 127.02, 126.81, 115.21, 62.95, 50.99, 17.82. EI-MS m/z (rel int) 188 ($\text{M}^+ + 1$, 8), 187 (M^+ , 2), 172 (6), 160 (12), 146 (8), 108 (9), 96 (45), 91 (100), 81 (35), 65 (26). IR (film) 2963 (s), 2925 (s), 1454 (m), 1262 (s), 802 (s), 699 (m). HRMS Calcd. For $\text{C}_{13}\text{H}_{18}\text{N}$: 188.1438($\text{M} + \text{H}$) $^+$. Found: 188.1434. HPLC (Chiralcel OD column, 230 nm, hexane/isopropanol 99/1, flow = 0.5 mL/min) t_R = 9.67, 12.38 min.

References:

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