Asymmetric Allylic Alkylation of Ketone Enolates: An Asymmetric Claisen Surrogate.

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Supporting Information

Experimental

Materials. Benzene was dried over sodium metal. All other materials were used as received. β -ketoesters **1a-1h** were prepared by the addition of diketene to the corresponding allylic alcohols.¹ β -ketoester **1f** was prepared by the DMAP catalyzed condensation of β -ketoethyl ester and allylic alcohol.² β -ketoesters **1i-1l** were prepared by the condensation of the corresponding acid chloride with Meldrum's acid³ followed by addition of the appropriate allylic alcohol.⁴ ¹H NMR spectra were obtained on a Bruker Avance 400 or a Bruker Avance 500 DRX spectrometer and referenced to residual protio solvent signals. Structural assignments are based on ¹H, ¹³C, DEPT-135, COSY, and HMQC spectroscopies.

General procedure for catalytic rearrangements: In a Schlenk tube under Ar, allyl- β -ketoester (1.2 mmol) and either Pd(PPh₃)₄ (10 mol %) or the combination of Pd₂(dba)₃ (5 mol %) and Trost ligand (10 mol %) were dissolved in 4 mL of benzene. The reaction was allowed to stir under Ar for the reported time. Following solvent evaporation the crude product was purified via flash chromatography (SiO₂, 10% Et₂O: Hex).

¹ Collado, I.; Pedregal, C.; Mazon, A.; Espinosa, J. F.; Blanco-Urgoiti, J.; Schoepp, D. D.; Wright, R. A.; Johnson, B. G.; Kingston, A. E. *J. Med. Chem.* **2002**, *45*, 3619-3629.

² Gilbert, J. C.; Kelly, T. A. *J. Org. Chem.* **1998**, *53*, 449-450.

³ Svenstrup, N.; Simonsen, K.; Thorup, N.; Brodersen, J.; Dehaen, W.; Becher, J. *J. Org. Chem.* **1999**, *64*, 2814-2820.

⁴ Yuste, F.; Brena, F.; Barrios, H.; Sanchez-Obregon, R.; Ortiz, B.; Walls, F. *Synth. Commun.* **1988**, *18*, 735-739.

2a⁵ yellow oil: ¹H NMR (400 MHz, CDCl₃) δ 7.30 (m, 10H: arom H), 6.38 (m, 2H: ambiguous CH=), 4.12 (app. q, *J* = 7 Hz, 1H: CH), 3.01 (dd, *J* = 7 Hz, 16 Hz, 1H: diastereotopic CH₂) 2.95 (dd, *J* = 7 Hz, 16 Hz, 1H: diastereotopic CH₂), 2.14 (s, 3H: CH₃). ¹³C NMR (75 MHz, CDCl₃) δ 207.36 (C=O), 143.35 (arom. C), 137.49 (arom. C), 132.76 (CH=), 130.39 (CH=), 129.13 (arom. CH), 128.91 (arom. CH), 128.06 (arom. CH), 127.75 (arom. CH), 127.12 (arom. CH), 126.65 (arom. CH), 49.82 (CH₂), 44.36 (CH), 31.20 (CH₃). IR (CH₂Cl₂): ν_{max} 1710, 1490, 1255. HRMS calcd for C₁₈H₁₈O [M⁺] 250.1358, found 250.1352.

⁵ Oi, S.; Honma, Y.; Inoue, Y. *Org. Lett.* **2002**, *4*, 667.

2b⁶ clear oil: ¹H NMR (400 MHz, CDCl₃) δ 5.43 (m, 1H: =CH-CH₃), 5.34 (dd, *J* = 7 Hz, 15 Hz, 1H: =CH-CH), 2.66 (app. sep, *J* = 7 Hz, 1H: =CH-CH), 2.44 (dd, *J* = 7 Hz, 15.6 Hz, 1H: diastereotopic CH₂), 2.34 (dd, *J* = 7 Hz, 15.6 Hz, 1H: diastereotopic CH₂), 2.13 (s, 3H: (C=O)CH₃), 1.64 (d, *J* = 6 Hz, 3H: =CH-CH₃), 1.00 (d, *J* = 7 Hz, 3H: CH-CH₃).

⁶ Tsuji, J.; Yamada, T.; Minami, I.; Yuhara, M.; Nisar, M.; Shimizu, I. *J. Org. Chem.* **1987**, *52*, 2988-95.

^{13}C NMR (75 MHz, CDCl_3) δ 208.92 (C=O), 135.90 (=CH-CH), 124.14 (=CH-CH₃), 51.40 (CH₂), 33.11 (=CH-CH), 30.90 ((C=O)CH₃), 20.93 (CH-CH₃), 18.28 (=CH-CH₃). IR (CDCl_3): ν_{max} 1705, 1454, 1357. HRMS calcd for $\text{C}_8\text{H}_{15}\text{O}$ [M+H] 127.1123, found 127.1105. GC (Chiraldex B-TA : Hold 50°C for 5 min., ramp 1°C /min to 75°C) t_{r} = 27.6, 29.3 min.

2c⁷ clear oil: ^1H NMR (400 MHz, CDCl_3) δ 5.83 (m, 1H: =CH), 5.76 (m, 1H: =CH), 3.11 (m, 1H: CH), 2.54 (dd, J = 7 Hz, 16.5 Hz, 1H: diastereotopic (C=O)CH₂), 2.44 (dd, J = 7

⁷ Hassner, A. Naumann, F. *Chem. Ber.* **1988**, 121, 1823-6.

Hz, 16.5 Hz, 1H: diastereotopic (C=O)CH₂), 2.32 (m, 2H: ambiguous CH₂), 2.16 (s, 3H: CH₃), 2.14 (m, 1H: ambiguous diastereotopic CH₂), 1.38 (m, 1H: ambiguous diastereotopic CH₂). ¹³C NMR (75 MHz, CDCl₃) δ 209.01 (C=O), 134.30 (5.76) (=CH), 131.67 (5.83) (=CH), 50.32 ((C=O)CH₂), 41.36 (CH), 32.21 (ambiguous CH₂), 30.70 (CH₃), 30.20 (ambiguous CH₂). IR (CDCl₃): ν_{max} 1700, 1403, 1362. HRMS calcd for C₈H₁₂O [M+H] 125.0966, found 125.0970. GC (Chiraldex B-TA : Hold 50° C for 5 min., ramp 0.5°C/min to 75°C) t_r = 47.3, 48.5 min.

2d⁸ clear oil: ¹H NMR (400 MHz, CDCl₃) δ 5.71 (m, 1H: =CH), 5.51 (m, 1H: =CH), 2.65 (m, 1H: =CH-CH), 2.46 (dd, *J* = 7 Hz, 16.3 Hz, 1H: diastereotopic (C=O)CH₂), 2.40 (dd, *J* = 7 Hz, 16.3 Hz, 1H: diastereotopic (C=O)CH₂), 2.16 (s, 3H: CH₃), 1.98 (m, 2H: ambiguous CH₂), 1.81 (m, 1H: ambiguous diastereotopic CH₂), 1.69 (m, 1H: ambiguous diastereotopic CH₂), 1.56 (m, 1H: ambiguous diastereotopic CH₂), 1.23 (m, 1H: ambiguous diastereotopic CH₂). ¹³C NMR (75 MHz, CDCl₃) δ 208.81 (C=O), 130.85 (5.51) (=CH), 128.38 (5.71) (=CH), 50.46 ((C=O)CH₂), 31.55 (CH), 30.92 (CH₃), 29.29 (1.81, 1.23) (ambiguous CH₂), 25.43 (1.98) (ambiguous CH₂), 21.43 (1.69, 1.56) (ambiguous CH₂). IR (CDCl₃): ν_{max} 1700, 1450, 1357. HRMS calcd for C₉H₁₅O [M+H] 139.1123, found 139.1129. GC (Chiraldex B-TA : Hold 50° C for 5 min., ramp 0.5° C/min to 85° C) t_r = 71.9, 72.8 min.

⁸ Monti, S.; Cowherd, F. G.; McAninch, T. W. *J. Org. Chem.* **1975**, *40*, 858-62.

2e clear oil: ^1H NMR (400 MHz, CDCl_3) δ 5.78 (m, 1H: =CH-CH₂), 5.45 (dd, J = 4 Hz, 11 Hz, 1H: =CH-CH), 2.81 (m, 1H: CH), 2.55 (dd, J = 7 Hz, 16.4 Hz, 1H: diastereotopic (C=O)CH₂), 2.47 (dd, J = 7 Hz, 16.4 Hz, 1H: diastereotopic (C=O)CH₂), 2.15 (s, 3H: CH₃), 2.15 (m, 2H: ambiguous CH₂), 1.92 (m, 1H: ambiguous diastereotopic CH₂), 1.64 (broad m, 3H), 1.29 (m, 2H: ambiguous CH₂). ^{13}C NMR (75 MHz, CDCl_3) δ 208.86 (C=O), 136.60 (=CH-CH), 132.43 (=CH-CH₂), 51.20 ((C=O)CH₂), 35.93 (CH), 33.88 (1.59, 1.29) (ambiguous CH₂), 30.79 (CH₃), 30.65 (ambiguous CH₂), 29.10 (ambiguous CH₂), 27.20 (ambiguous CH₂). IR (CDCl_3): ν_{max} 1710, 1450, 1357. HRMS calcd for $\text{C}_{10}\text{H}_{17}\text{O}$ [M+H] 153.1279, found 153.1286. GC (Chiraldex B-TA : Hold 80°C) t_r = 76.2, 77.1 min.

2f clear oil: ^1H NMR (400 MHz, CDCl_3) Major Diastereomer: δ 5.37 (overlapping multiplet, 1H: $=\text{CH}-\text{CH}_3$), 5.19 (ddd, $J = 2$ Hz, 8 Hz, 15 Hz, 1H: $=\text{CH}-\text{CH}$), 2.57 (app. hex, $J = 7$ Hz, 1H: $\text{CH}-\text{CH}_3$), 2.27 (overlapping multiplet, cyclohexyl CH_2), 2.12 (m, 1H: $(\text{C}=\text{O})\text{CH}$), 1.93 (overlapping multiplet, cyclohexyl CH_2), 1.92 (overlapping multiplet, cyclohexyl CH_2), 1.65 (overlapping multiplet, $=\text{CH}-\text{CH}_3$), 1.59 (overlapping multiplet, cyclohexyl CH_2), 0.97 (d, $J = 6.6$ Hz, 3H: $\text{CH}-\text{CH}_3$). Minor Diastereomer: δ 5.39 (overlapping multiplet, $=\text{CH}-\text{CH}$), 5.37 (overlapping multiplet, $=\text{CH}-\text{CH}_3$), 2.65 (m, 1H: $\text{CH}-\text{CH}_3$), 2.37 (overlapping multiplet, cyclohexyl CH_2), 2.23 (m, 1H: $(\text{C}=\text{O})\text{CH}$), 1.84 (overlapping multiplet, cyclohexyl CH_2), 1.74 (overlapping multiplet, cyclohexyl CH_2), 1.65 (overlapping multiplet, $=\text{CH}-\text{CH}_3$), 1.59 (overlapping multiplet, cyclohexyl CH_2), 0.99 (d, $J = 6.6$ Hz, 3H: $\text{CH}-\text{CH}_3$). ^{13}C NMR (75 MHz, CDCl_3) Major Diastereomer: δ 214.03 ($\text{C}=\text{O}$), 134.72 ($=\text{CH}-\text{CH}$), 125.39 ($=\text{CH}-\text{CH}_3$), 56.71 ($(\text{C}=\text{O})\text{CH}$), 42.32 (2.27) (cyclohexyl CH_2), 36.26 ($\text{CH}-\text{CH}_3$), 31.32 (1.93) (cyclohexyl CH_2), 28.54 (1.92) (cyclohexyl CH_2), 24.20 (1.59) (cyclohexyl CH_2), 19.47 ($\text{CH}-\text{CH}_3$), 18.36 ($=\text{CH}-\text{CH}_3$). Minor Diastereomer: δ 213.12 ($\text{C}=\text{O}$), 135.35 ($=\text{CH}-\text{CH}$), 124.48 ($=\text{CH}-\text{CH}_3$), 56.16 ($(\text{C}=\text{O})\text{CH}$), 42.51 (2.37) (cyclohexyl CH_2), 35.47 ($\text{CH}-\text{CH}_3$), 29.21 (1.59) (cyclohexyl CH_2), 28.08 (1.74) (cyclohexyl CH_2), 24.69 (1.84) (cyclohexyl CH_2), 18.39 ($=\text{CH}-\text{CH}_3$), 17.00 ($\text{CH}-\text{CH}_3$). IR (CDCl_3): ν_{max} 1700, 1449. HRMS calcd for $\text{C}_{11}\text{H}_{19}\text{O}$ [$\text{M}+\text{H}$] 167.1436, found 167.1431. GC (Chiraldex B-TA : Hold 50°C for 5 min., ramp $1^\circ\text{C}/\text{min}$ to 115°C) Major Diastereomer: $t_r = 67.3, 69.8$ min. Minor Diastereomer: $t_r = 68.5, 68.8$ min.

2h clear oil: ^1H NMR (400 MHz, CDCl_3) δ 7.26 (m, 3H: arom H), 7.11 (d, $J = 8$ Hz, 2H: arom H), 5.77 (m, 1H: =CH), 5.14 (d, $J = 12$ Hz, 1H: =CH(H)_{cis}), 5.14 (d, $J = 17$ Hz, 1H: =CH(H)_{trans}), 2.89 (s, 2H: $\text{CH}_2\text{-Ph}$), 2.38 (dd, $J = 7$ Hz, 15Hz, 1H: diastereotopic $\text{CH}_2\text{-CH=}$), 2.28 (dd, $J = 7$ Hz, 15Hz, 1H: diastereotopic $\text{CH}_2\text{-CH=}$), 2.11 (s, 3H: $(\text{C=O})\text{-CH}_3$), 1.64 (m, 2H: $\text{CH}_2\text{-CH}_3$), 0.90 (t, $J = 7$ Hz, 3H: $\text{CH}_2\text{-CH}_3$). ^{13}C NMR (75 MHz, CDCl_3) δ 213.40 (C=O), 138.01 (arom. C), 134.10 (=CH), 130.45 (arom. CH), 128.58 (arom. CH),

126.82 (arom. CH), 118.72 (=CH₂), 56.42 (C), 39.67 (CH₂-Ph), 37.81 (CH₂=CH-CH₂), 27.31 ((C=O)-CH₃), 27.26 (CH₂-CH₃), 8.96(CH₂-CH₃). IR (CDCl₃): ν_{max} 1699, 1454, 1261, 1269. HRMS calcd for C₁₅H₂₁O [M+H] 217.1592, found 217.1602.

2i⁹ clear oil: ¹H NMR (400 MHz, CDCl₃) δ 7.36 (m, 2H: arom H), 7.30 (m, 1H: arom H), 7.23 (m, 2H: arom H), 5.69 (m, 1H: =CH), 5.48 (m, 1H: =CH), 3.70 (s, 2H: CH₂-Ph), 2.66 (m, 1H: CH-CH=), 2.45 (d, *J* = 7 Hz, 2H: (C=O)CH₂-CH), 1.97 (m, 2H: ambiguous CH₂), 1.77 (m, 1H: ambiguous diastereotopic CH₂), 1.64 (m, 1H: ambiguous diastereotopic CH₂), 1.54 (m, 1H: ambiguous diastereotopic CH₂), 1.14 (m, 1H: ambiguous diastereotopic CH₂). ¹³C NMR (75 MHz, CDCl₃) δ 208.03 (C=O), 134.58 (arom. C), 130.89 (5.47) (=CH), 129.84 (arom. CH), 129.13 (arom. CH), 128.36 (5.68) (=CH), 127.41 (arom. CH), 51.14 (CH₂-Ph), 48.60 ((C=O)CH₂-CH), 31.42 (CH-CH=), 29.20 (1.77, 1.14) (ambiguous CH₂), 25.43 (1.97) (ambiguous CH₂), 21.39 (1.54, 1.64) (ambiguous CH₂). IR (CDCl₃): ν_{max} 1710, 1497, 1454. HRMS calcd for C₁₅H₁₉O [M+H] 215.1436, found 215.1461. HPLC (Diacel Chiralpak AD : 99:1 Hex:IPA, 0.5 mL/min) t_r = 17.0, 19.2 min.

⁹ House, H.; Fischer, W.; Gall, M.; McLaughlin, T.; Peet, N. *J. Org. Chem.* **1971**, 36, 3429-37.

2j clear oil: ^1H NMR (400 MHz, CDCl_3) δ 5.71 (m, 1H: =CH), 5.50 (m, 1H: =CH), 2.68 (m, 1H: =CH-CH), 2.61 (app. pen, $J = 7$ Hz, 1H: $(\text{CH}_3)_2\text{-CH}$), 2.45 (d, $J = 7$ Hz, 2H: $(\text{C=O})\text{CH}_2$), 1.99 (m, 2H: ambiguous CH_2), 1.81 (m, 1H: ambiguous diastereotopic CH_2), 1.69 (m, 1H: ambiguous diastereotopic CH_2), 1.58 (m, 1H: ambiguous

diastereotopic CH₂), 1.20 (m, 1H: ambiguous diastereotopic CH₂), 1.11 (d, $J = 7\text{ Hz}$, 6H: (CH₃)₂). ¹³C NMR (75 MHz, CDCl₃) δ 214.49 (C=O), 131.23 (5.50) (=CH), 128.17 (5.71) (=CH), 47.09 ((C=O)CH₂), 41.61 ((CH₃)₂-CH), 31.37 (CH-CH=), 29.39 (1.81, 1.20) (ambiguous CH₂), 25.49 (1.99) (ambiguous CH₂), 21.48 (1.69, 1.58) (ambiguous CH₂), 18.52 ((CH₃)₂). IR (CDCl₃): ν_{max} 1707, 1265, 1467. HPLC (Diacel Chiralpak AD : 99.5:1 Hex:IPA, 0.5 mL/min) $t_r = 9.7, 10.5$ min.

2k¹⁰ clear oil: ¹H NMR (400 MHz, CDCl₃) δ 7.99 (m, 2H: arom H), 7.59 (m, 1H: arom H), 7.49 (app. t, J = 7 Hz, 2H: arom H), 5.75 (m, 1H: =CH), 5.61 (m, 1H: =CH), 2.98 (d, J = 7 Hz, 1H: diastereotopic (C=O)CH₂), 2.97 (d, J = 7 Hz, 1H: diastereotopic (C=O)CH₂), 2.85 (m, 1H: =CH-CH), 2.02 (m, 2H: ambiguous CH₂), 1.89 (m, 1H: ambiguous diastereotopic CH₂), 1.73 (m, 1H: ambiguous diastereotopic CH₂), 1.61 (m, 1H: ambiguous diastereotopic CH₂), 1.34 (m, 1H: ambiguous diastereotopic CH₂). ¹³C NMR (75 MHz, CDCl₃) δ 200.08 (C=O), 137.72 (arom. C), 133.37 (arom. CH), 131.17 (5.61) (=CH), 128.98 (arom. CH), 128.52 (arom. CH), 128.37 (5.75) (=CH), 45.23 ((C=O)CH₂), 32.02 (CH-CH=), 29.49 (1.89, 1.34) (ambiguous CH₂), 25.53 (2.02) (ambiguous CH₂), 21.50 (1.61, 1.73) (ambiguous CH₂). IR (CDCl₃): ν_{max} 1684, 1448, 1261. HRMS calcd for C₁₄H₁₇O [M+H] 201.1279, found 201.1278. HPLC (Diacel Chiralpak AD : 99:1 Hex:IPA, 0.5 mL/min) t_r = 15.3, 16.0 min.

¹⁰ Fernandez-Mateos, A; Alonso, J.; Gonzalez, R. *Tetrahedron*. **1999**, 55, 847-860.

2l clear oil: ^1H NMR (400 MHz, CDCl_3) δ 5.76 (m, 1H: =CH), 5.65 (m, 1H: =CH), 3.12 (m, 1H: CH-CH=), 2.52 (dd, $J = 7$ Hz, 16.5 Hz, 1H: diastereotopic (C=O)CH₂), 2.43 (overlapping multiplet, 1H: diastereotopic (C=O)CH₂), 2.43 (overlapping multiplet, 2H: CH₂-CH₃), 2.33 (m, 2H: ambiguous CH₂), 2.14 (m, 1H: ambiguous diastereotopic CH₂),

1.38 (m, 1H: ambiguous diastereotopic CH₂), 1.07 (t, $J = 7.3$ Hz, 3H: CH₃). ¹³C NMR (75 MHz, CDCl₃) δ 211.63 (C=O), 134.48 (5.65) (=CH), 131.56 (5.76) (=CH), 48.99 ((C=O)CH₂), 41.43 (CH-CH=), 36.70 (CH₂-CH₃), 32.22 (2.33) (ambiguous CH₂), 30.28 (1.38) (ambiguous CH₂), 8.21 (CH₃) . IR (CDCl₃): ν_{max} 1710, 1460, 1115. HRMS calcd for C₉H₁₄O [M+H] 166.1358, found 166.0780. GC (Chiraldex B-TA : Hold 50° C for 5 min., ramp 0.5° C/min to 75° C) t_r = 60.1, 62.1 min.