Supporting Information

Enantioselective Organocatalytic Mukaiyama-Michael Addition of Silyl Enol Ethers to α , β -Unsaturated Aldehydes

Wei Wang,* Hao Li, and Jian Wang

Department of Chemistry, University of New Mexico, Albuquerque, NM 87131-0001

General Information: Commercial reagents were used as received, unless otherwise stated. Merck 60 silica gel was used for chromatography, and Whatman silica gel plates with fluorescence F₂₅₄ were used for thin-layer chromatography (TLC) analysis. ¹H and ¹³C NMR spectra were recorded on Broker Avance 500, and tetramethylsilane (TMS) was used as a reference. Data for ¹H are reported as follows: chemical shift (ppm), and multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). Data for ¹³C NMR are reported as ppm. Mass Spectra were obtained from Ohio State University Mass Spectral facility.

General Procedure for addition of silyl enol ethers to unsaturated aldehydes: A mixture of an aldehyde (1 equiv.) in the presence of 30 mol % chiral amine **I** and DNBA in 0.5 mL of *t*-BuOH and *i*-PrOH (5/1, v/v) was stirred at rt for 10 min, then 5 equiv. of silyl enol ether was added and stirred for 4-18 h at rt or 0 °C. The solution was concentrated *in vacuo*. The resulting residue was then purified by silica gel chromatography and fractions were collected and concentrated *in vacuo* to provide the desired product.

(R)-5-Oxo-3,5-diphenyl-pentanal (Table 2, entry 1): Yield: 75%; ¹H NMR (500 MHz, CDCl₃): δ 9.62 (s, 1H), 7.83 (d, 2H, *J* = 8.0 Hz), 7.12-7.48 (m, 8H), 3.90 (m, 1H), 3.27 (d, 2H, *J* = 7.0 Hz), 2.71-2.86 (m, 2H); ¹³C NMR (125 MHz, CDCl₃): δ 201.1, 198.1, 143.2, 136.7, 133.2, 128.8, 128.6, 128.0, 127.4, 126.9, 49.5, 44.9, 35.3; [α]_D²⁵ = + 1.4 (*c* = 0.5, CHCl₃); HPLC (Daicel CHIRALPAK AS-H, Hexane/2-PrOH = 90:10, flow rate 1.0 ml/ min, λ = 254 nm); *t*_R = 17.66 (minor), 19.71 (major) min.

(R)-5-(4-Bromophenyl)-5-oxo-3-phenyl-pentanal (Table 2, entry 2): Yield: 58%; ¹H NMR (500 MHz, CDCl₃): δ 9.71 (d, 1H, *J* = 1.6 Hz), 7.76 (d, 2H, *J* = 8.6 Hz), 7.57 (d, 2H, *J* = 8.6 Hz), 7.20-7.32 (m, 5H), 3.95 (m, 1H), 3.30 (d, 2H, *J* = 7.0 Hz), 2.79-2.94 (m, 2H); ¹³C NMR (125 MHz, CDCl₃): δ 200.9, 197.1, 142.9, 135.4, 131.9, 129.5, 128.8, 128.4, 127.3, 127.0, 49.5, 44.8, 35.3. [α]_D²⁵ = + 4.7 (*c* = 1.0, CHCl₃); HPLC (Daicel CHIRALPAK AS-H, Hexane/2-PrOH = 90:10, flow rate 1.0 ml/ min, λ = 254 nm); *t*_R = 20.99 (minor), 23.84 (major) min.

(R)-5-Oxo-3-phenyl-5-*p*-tolyl-pentanal (Table 2, entry 3): Yield: 62%; ¹H NMR (500 MHz, CDCl₃): δ 9.69 (s, 1H), 7.81 (d, 2H, *J* = 8.1 Hz), 7.19-7.31 (m, 7H), 3.97 (m, 1H), 3.31 (d, 2H, *J* = 7.3 Hz), 2.77-2.93 (m, 2H), 2.39 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 201.2, 197.7, 144.1, 143.2, 134.3, 129.3, 128.8, 128.1, 127.3, 126.9, 49.5, 44.8, 35.4, 21.6. [α]_D²⁵ = + 4.1 (*c*

= 1.0, CHCl₃); HPLC (Daicel CHIRALPAK AS-H, Hexane/2-PrOH = 90:10, flow rate 1.0 ml/ min, λ = 254 nm); t_R = 16.50 (minor), 17.55 (major) min.

(R)-5-(4-Methoxyphenyl)-5-oxo-3-phenyl-pentanal (Table 2, entry 4): Yield: 56%; ¹H NMR (500 MHz, CDCl₃): δ 9.70 (s, 1H), 7.89 (d, 2H, J = 8.5 Hz), 7.19-7.32 (m, 5H), 6.90 (d, 2H, J = 8.5 Hz), 3.96 (m, 1H), 3.85 (s, 3H), 3.28 (d, 2H, J = 6.9 Hz), 2.78-2.93 (m, 2H); ¹³C NMR (125 MHz, CDCl₃): δ 201.3, 196.6, 163.6, 143.3, 130.3, 129.8, 128.8, 127.4, 126.9, 113.7, 55.4, 49.5, 44.6, 35.5. $[\alpha]_D^{25}$ = + 4.0 (c = 1.0, CHCl₃); HPLC (Daicel CHIRALPAK AS-H, Hexane/2-PrOH = 90:10, flow rate 1.0 ml/ min, λ = 254 nm); t_R = 35.75 (minor), 38.15 (major) min.

(R)-3-(4-Fluorophenyl)-5-oxo-5-p-tolyl-pentanal (Table 2, entry 5): Yield: 71%; ¹H NMR (500 MHz, CDCl₃): δ 9.69 (s, 1H), 7.80 (d, 2H, J = 8.1 Hz), 7.22-7.26 (m, 4H), 6.98 (t, 2H, J = 8.6 Hz), 3.97 (m, 1H), 3.29 (d, 2H, J = 7.0 Hz), 2.76-2.93 (m, 2H), 2.40 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 200.8, 197.5, 162.6, 160.6, 144.2, 138.9, 134.2, 129.3, 128.9, 128.8, 128.1, 115.6, 115.5, 49.7, 44.8, 34.7, 21.6. $[\alpha]_D^{25}$ = + 2.5 (c = 1.0, CHCl₃); HPLC (CHIRALCEL OJ-H, Hexane/2-PrOH = 90:10, flow rate 1.0 ml/ min, λ = 254 nm); t_R = 45.13 (minor), 48.47 (major) min.

(R)-3-(4-Fluorophenyl)-5-(4-methoxyphenyl)-5-oxo-pentanal (Table 2, entry 6): Yield: 63%; ¹H NMR (500 MHz, CDCl₃): δ 9.62 (s, 1H), 7.81 (d, 2H, J = 9.0 Hz), 7.06 (q, 2H, J = 5.4 Hz, J = 8.4 Hz), 6.90 (t, 2H, J = 8.6 Hz), 6.83 (d, 2H, J = 8.8 Hz), 3.88 (m, 1H), 3.80 (s, 3H), 3.18 (d, 2H, J = 7.0 Hz), 2.68-2.86 (m, 2H); ¹³C NMR (125 MHz, CDCl₃): δ 200.9, 196.4, 163.6, 162.5, 160.6, 139.0, 130.3, 129.7, 128.9, 128.8, 115.6, 115.5, 113.7, 55.4, 49.7, 44.5, 34.7. $[\alpha]_D^{25}$ = + 5.7 (c = 1.0, CHCl₃); HPLC (Daicel CHIRALPAK AS-H, Hexane/2-PrOH = 85:15, flow rate 1.0 ml/ min, λ = 254 nm); t_R = 35.05 (major), 42.22 (minor) min.

(R)-4-[3-Oxo-1-(2-oxo-ethyl)-3-phenyl-propyl]-benzonitrile (Table 2, entry 7): Yield: 59%; ^1H NMR (500 MHz, CDCl_3): δ 9.72 (s, 1H), 7.90 (d, 2H, $J = 7.5$ Hz), 7.41-7.60 (m, 7H), 4.05 (m, 1H), 3.38 (m, 2H), 2.85-3.01 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3): δ 199.7, 197.2, 136.3, 133.4, 132.5, 128.7, 128.3, 127.9, 118.6, 110.7, 49.1, 44.0, 35.0. $[\alpha]_{\text{D}}^{25} = +17.4$ ($c = 1.0$, CHCl_3); HPLC (CHIRALCEL OJ-H, Hexane/2-PrOH = 60:40, flow rate 0.7 ml/min, $\lambda = 254$ nm); $t_{\text{R}} = 37.60$ (minor), 41.58 (major) min.

(R)-4-[3-(4-Methoxyphenyl)-3-oxo-1-(2-oxo-ethyl)-propyl]-benzonitrile (Table 2, entry 8): Yield: 61%; ^1H NMR (500 MHz, CDCl_3): δ 9.71 (s, 1H), 7.88 (d, 2H, $J = 8.8$ Hz), 7.59 (d, 2H, $J = 8.2$ Hz), 7.40 (d, 2H, $J = 8.2$ Hz), 6.91 (d, 2H, $J = 8.8$ Hz), 4.03 (m, 1H), 3.86 (s, 3H), 3.31 (m, 2H), 2.83-3.00 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3): δ 199.8, 195.7, 163.8, 149.0, 132.5, 130.3, 129.5, 128.4, 118.7, 113.8, 110.7, 55.5, 49.2, 43.7, 35.3. $[\alpha]_{\text{D}}^{25} = +26.4$ ($c = 1.0$, CHCl_3); HPLC (CHIRALCEL OJ-H, Hexane/2-PrOH = 60:40, flow rate 0.7 ml/min, $\lambda = 254$ nm); $t_{\text{R}} = 71.74$ (minor), 92.92 (major) min.

(R)-3,5-Bis-(4-methoxyphenyl)-5-oxo-pentanal (Table 2, entry 9): Yield: 63%; ^1H NMR (500 MHz, CDCl_3): δ 9.68 (t, 1H, $J = 1.7$ Hz), 7.90 (d, 2H, $J = 8.9$ Hz), 7.18 (d, 2H, $J = 8.7$ Hz), 6.91 (d, 2H, $J = 8.9$ Hz), 6.83 (d, 2H, $J = 8.7$ Hz), 3.92 (m, 1H), 3.85 (s, 3H), 3.77 (s, 3H), 3.25 (d, 2H, $J = 7.0$ Hz), 2.73-2.91 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3): δ 201.4, 196.7, 163.5, 158.3, 135.2, 130.3, 129.9, 128.3, 114.1, 113.7, 55.4, 55.2, 49.7, 44.8, 34.8. $[\alpha]_{\text{D}}^{25} = +3.6$ ($c = 1.0$, CHCl_3); HPLC (Daicel CHIRALPAK AS-H, Hexane/2-PrOH = 60:40,

flow rate 0.7 ml/ min, λ = 254 nm); t_R = 59.20 (minor), 68.93 (major) min.

(R)-3-Methyl-5-oxo-5-*p*-tolyl-pentanal (Table 2, entry 10): Yield: 60%; ^1H NMR (500 MHz, CDCl_3): δ 9.78 (s, 1H), 7.86 (d, 2H, J = 8.1 Hz), 7.26 (d, 2H, J = 8.1 Hz), 3.00 (q, 1H, J = 6.6 Hz, J = 16.4 Hz), 2.88 (q, 1H, J = 6.9 Hz, J = 16.4 Hz), 2.78 (m, 1H), 2.57 (m, 1H), 2.41 (s, 3H), 2.38 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3): δ 202.0, 198.7, 143.9, 134.4, 129.3, 128.2, 50.5, 44.8, 24.6, 21.6, 20.4. $[\alpha]_D^{25}$ = -9.7 (c = 1.0, CHCl_3); HPLC (CHIRALCEL OJ-H, Hexane/2-PrOH = 95:5, flow rate 1.0 ml/ min, λ = 254 nm); t_R = 15.73 (minor), 16.93 (major) min.

(R)-3-(1,2,3,4-Tetrahydro-1-oxonaphthalen-2-yl)-3-phenylpropanal (Table 2, entry 11): Yield: 87%; ^1H NMR (500 MHz, CDCl_3): δ 9.67 (m, 1H), 8.05 (d, 1H, J = 7.8 Hz), 7.46 (m, 1H), 7.20-7.34 (m, 7H), 4.33 (m, 1H), 2.76-2.95 (m, 5H), 2.08 (m, 1H), 2.191 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3): δ 201.8, 201.1, 199.3, 198.3, 143.8, 143.5, 141.5, 141.3, 133.5, 132.7, 132.4, 128.7, 128.4, 127.6, 127.5, 127.0, 126.9, 126.7, 53.7, 52.0, 48.5, 43.5, 38.2, 38.1, 29.3, 27.3, 25.8, 24.3. $[\alpha]_D^{25}$ = -39.9 (c = 1.0, CHCl_3); HPLC (Daicel CHIRALPAK AS-H, Hexane/2-PrOH = 90:10, flow rate 1.0 ml/ min, λ = 254 nm); t_R = 14.90 (major), 18.24 (minor) min.

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Method Name: C:\EZStart\Projects\Default\Method\WaiWang1.met
Data File: C:\EZStart\Projects\WaiWang\hld73e90e2.dat
Date Acquired: 11/4/2004 2:37:13 PM Date Printed: 01/27/2005 04:51:26 PM
Sample ID: hld73e90e

SPD-10Avp

Ch1-254nm Results

Pk #	RT	Area	Area %
1	17.650	977000	52.269
2	19.660	892191	47.731
Totals		1869191	100.000

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Method Name: C:\EZStart\Projects\Default\Method\WeiWang19.met
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Date Acquired: 11/2/2004 1:31:59 PM Date Printed: 01/27/2005 05:26:20 PM
Sample ID: hld73e

SPD-10Avp

Ch1-254nm Results

PK #	RT	Area	Area %
1	17.650	96157	4.778

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Method Name: C:\EZStart\Projects\Default\Method\WeiWang22.met
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Sample ID: hle17e

SPD-10Avp
Ch1-254nm Results

Pk #	RT	Area	Area %
1	20.850	3025359	51.069
2	23.840	2898695	48.931
Totals		5924054	100.000

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Method Name: C:\EZStart\Projects\Default\Method\WeiWang22.met
Data File: C:\EZStart\Projects\WeiWang\hle18e1.dat
Date Acquired: 11/15/2004 4:08:59 PM Date Printed: 01/27/2005 05:04:25 PM
Sample ID: hle18e

SPD-10Avp
Ch1-254nm Results

Pk #	RT	Area	Area %
1	20.990	510924	6.932
2	23.840	6859611	93.068

Totals		7370535	100.000

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Method Name: C:\EZStart\Projects\Default\Method\WeiWang20.met
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Date Acquired: 11/10/2004 12:54:07 PM Date Printed: 01/27/2005 05:01:11 PM
Sample ID: hle8e

SPD-10Avp

Ch1-254nm Results

Pk #	RT	Area	Area %
1	16.360	3863014	47.261
2	17.540	4310716	52.739

Totals		8173730	100.000

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Method Name: C:\EZStart\Projects\Default\Method\WeiWang20.met
Data File: C:\EZStart\Projects\WeiWang\hle9e1.dat
Date Acquired: 11/10/2004 1:49:49 PM Date Printed: 01/27/2005 05:02:48 PM
Sample ID: hle9e

SPD-10Avp
Ch1-254nm Results

Pk #	RT	Area	Area %
2	16.500	95540	2.444
3	17.550	3560910	91.078

Totals		3656450	93.522

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Method Name: C:\EZStart\Projects\Default\Method\WeiWang20.met
Data File: C:\EZStart\Projects\WeiWang\hle7e1.dat
Date Acquired: 11/9/2004 12:20:45 PM Date Printed: 01/27/2005 04:57:03 PM
Sample ID: hle7e

SPD-10Avp
Ch1-254nm Results

Pk #	RT	Area	Area %
1	35.290	4320126	51.202
2	37.630	4117240	48.798
Totals		8437366	100.000

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Method Name: C:\EZStart\Projects\Default\Method\WeiWang1.met
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Sample ID: hld97e

SPD-10Avp
Ch1-254nm Results

Pk #	RT	Area	Area %
1	35.750	50304	1.675
2	38.150	2953365	98.325
Totals		3003669	100.000

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Method Name: C:\EZStart\Projects\Default\Method\WeiWang28.met
Data File: C:\EZStart\Projects\WeiWang\hle49e4.dat
Date Acquired: 12/3/2004 7:20:40 PM Date Printed: 01/27/2005 05:11:46 PM
Sample ID: hle49e

SPD-10Avp
Ch1-254nm Results

PK #	RT	Area	Area %

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Method Name: C:\EZStart\Projects\Default\Method\WeiWang28.met
Data File: C:\EZStart\Projects\WeiWang\hle50e1.dat
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Sample ID: hle50e

SPD-10Avp
Ch1-254nm Results

PK #	RT	Area	Area %

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Method Name: C:\EZStart\Projects\Default\Method\WeiWang28.met
Data File: C:\EZStart\Projects\WeiWang\hle46e2.dat
Date Acquired: 12/2/2004 1:53:22 PM Date Printed: 01/27/2005 05:14:54 PM
Sample ID: hle46e

SPD-10Avp
Ch1-254nm Results

PK #	RT	Area	Area %

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Sample ID: hle47e

SPD-10Avp

Ch1-254nm Results

PK #	RT	Area	Area %

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Method Name: C:\EZStart\Projects\Default\Method\WeiWang29.met
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Date Acquired: 12/12/2004 2:47:41 PM Date Printed: 01/27/2005 05:16:34 PM
Sample ID: hle60e

SPD-10Avp
Ch1-254nm Results

PK #	RT	Area	Area %

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Method Name: C:\EZStart\Projects\Default\Method\WeiWang29.met
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Date Acquired: 12/13/2004 1:52:16 PM Date Printed: 01/27/2005 05:16:58 PM
Sample ID: hle61e

SPD-10Avp
Ch1-254nm Results

PK #	RT	Area	Area %

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Method Name: C:\EZStart\Projects\Default\Method\WeiWang29.met
Data File: C:\EZStart\Projects\WeiWang\hle62e2.dat
Date Acquired: 12/12/2004 6:01:37 PM Date Printed: 01/27/2005 05:17:46 PM
Sample ID: hle62e

SPD-10Avp
Ch1-254nm Results

Pk #	RT	Area	Area

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Method Name: C:\EZStart\Projects\Default\Method\WeiWang29.met
Data File: C:\EZStart\Projects\WeiWang\hle63e1.dat
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Sample ID: hle63e

SPD-10Avp
Ch1-254nm Results

PK #	RT	Area	Area %

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Method Name: C:\EZStart\Projects\Default\Method\WeiWang28.met
Data File: C:\EZStart\Projects\WeiWang\hle27e8.dat
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Sample ID: hle27e

SPD-10Avp
Ch1-254nm Results

PK #	RT	Area	Area %

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Sample ID: hle28e

SPD-10Avp

Ch1-254nm Results

PK #	RT	Area	Area %

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Sample ID: hle41e

SPD-10Avp

Ch1-254nm Results

Pk #	RT	Area	Area %
1	15.790	295774	50.511
2	17.040	289791	49.489

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Method Name: C:\EZStart\Projects\Default\Method\WeiWang28.met
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Sample ID: hle38e

SPD-10Avp

Ch1-254nm Results

Pk #	RT	Area	Area %
1	15.730	1164319	8.654
2	16.930	12289953	91.346

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Method Name: C:\EZStart\Projects\Default\Method\WeiWang22.met
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Sample ID: hle2e

SPD-10Avp

Ch1-254nm Results

Pk #	RT	Area	Area %
1	15.250	1782282	49.599
2	18.630	1811081	50.401

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Method Name: C:\EZStart\Projects\Default\Method\WeiWang22.met
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Date Acquired: 11/19/2004 6:31:57 PM Date Printed: 02/07/2005 07:06:47 PM
Sample ID: hle23e

SPD-10Avp
Ch1-254nm Results

Pk #	RT	Area	Area %
1	14.900	3134326	92.290
2	18.240	261828	7.710