Supporting Information

Antibody-Catalyzed Asymmetric Intramolecular Michael Addition of Aldehydes and Ketones to Yield the disfavored Cis-Product

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Experimental

General methods. Thin layer chromatography (TLC): silica gel plates Merck 60 F_{254}: compounds were visualized by irradiation with UV light and/or by treatment with a solution of 25 g phosphomolybdic acid, 10 g $Ce(SO_4)_2 \cdot H_2O$, 60 mL conc. H_2SO_4 and 940 mL H_2O followed by heating and/or by staining with a solution of 12 g 2,4-dinitrophenylhydrazine in 60 mL conc. H_2SO_4, 80 mL H_2O and 200 mL 95% EtOH followed by heating. – Flash chromatography (FC): silica gel Merck 60 (particle size 0.040-0.063 mm), eluent given in parentheses. ^{1}H NMR spectra were measured using Bruker Avance operated at 200 MHz or 400MHz as mentioned. ^{13}C NMR spectra were measured using Bruker Avance operated at 50 MHz or 100MHz as mentioned. The chemical shifts are expressed in δ relative to TMS (δ = 0 ppm) and the coupling constants *J* in Hz. The spectra were recorded in $CDCl_3$ as solvent at room temperature

unless stated otherwise. All general reagents, including salts and solvents, were purchased from Aldrich (Milwaukee, MN). All reactions were carried out at room temperature unless stated otherwise.

Abbreviations. OsO_4 – Osmium tetraoxide, NMO – 4-Methylmorpholine N-Oxide, DCM- Dichloromethane, DMF- Dimethylformamide, EtOAc- Ethyl acetate, Hex- n-Hexanes, PBS- Phosphate buffer saline, THF – Tetrahydrofuran, NaOH – Sodium hydroxide.

8-(4-Methoxy-phenyl)-8-oxo-oct-6-enal (4)

(4'-Metoxyphenacyl)triphenylphosphonium bromide (500 mg, 1.02 mmol, 1.02 eq) was dissolved in a mixture of DCM (15 mL) and NaOH 2N (10 mL). The reaction was monitored by TLC (EtOAc:Hex 1:1) until complete disappearance of the phosphonium salt (0.5-3 hours). After completion, EtOAc was added and the solution was washed with brine. The organic phase was dried over sodium-sulphate, filtered and evaporated to yield the phosphonium ylide in an almost quantitative yield. The phosphonium ylide (410 mg, 1.00 mmol, 1 eq) was dissolved in DCM (3mL) in a pressure tube, and Hexanedial (171 mg,1.5 mmol,1.5 eq) was added. The reaction was heated to 50^{o}C and stirred for 3 hours. The reaction was monitored by TLC (EtOAc:Hex 1:2) for disappearance of the phosphonium salt. After completion, the solvent was evaporated and the crude product was purified by FC (EtOAc:Hex 1:2) to yield enone **4** in 53% yield (133 mg, 0.53 mmol). ^{1}H NMR (200MHz,$CDCl_3$): δ = 9.77 (1H, t, *J* = 1.6 Hz), 7.94 (2H, d, *J* = 8.9 Hz), 6.86-6.99 (4H, m), 3.86 (3H, s), 2.48 (2H, dt, *J* = 7.0, 1.5 Hz), 2.33 (2H, q, *J* = 7.0 Hz), 1.52-1.78 (4H, m). ^{13}C NMR

(50MHz,$CDCl_3$): δ = 23.5, 29.6, 34.4, 45.6, 57.4, 115.7, 127.8, 132.6, 132.7, 149.7, 190.9, 204.1. CI-HRMS calcd for $C_{15}H_{18}O_3$ [MH^+] *m/z* 247.1326, found 247.1333.

1-Phenyl-non-2-ene-1,8-dione (6)

Phenacyltriphenylphosphonium bromide (1175 mg, 2.55 mmol, 1.02 eq) was dissolved in a mixture of DCM (15 mL) and NaOH 2N (10 mL). The reaction was monitored by TLC (EtOAc:Hex 1:1) until complete disappearance of the phosphonium salt. After completion, EtOAc was added and the solution was washed with brine. The organic phase was dried over sodium-sulphate, filtered and evaporated to yield the phosphonium ylide in a quantitative yield. The phosphonium ylide (963 mg, 2.53 mmol, 1 eq) was dissolved in DCM (3 mL) in a pressure tube, and 6-Oxo-heptanal (1.5 eq) was added. The reaction was heated to 60°C, stirred for overnight and was monitored by TLC (EtOAc:Hex 1:2) for disappearance of the phosphonium salt. After completion, the solvent was evaporated and the crude product was purified by FC (EtOAc:Hex 1:2) to yield enone **6** in 85% yield (495 mg, 2.15 mmol). ^{1}H NMR (200MHz,$CDCl_3$): δ = 7.92 (2H, d, *J* = 7.9 Hz), 7.41-7.60 (3H, m), 7.04 (1H, dt, *J* = 15.4, 6.4 Hz), 6.88 (1H, d, *J* = 15.4 Hz), 2.47 (2H, t, *J* = 6.8 Hz) , 2.33 (2H, q, *J* = 6.7 Hz), 2.04 (3H, s), 1.51-1.64 (4H, m). ^{13}C NMR (50MHz,$CDCl_3$): δ = 23.2, 27.6, 29.9, 32.5, 43.3, 126.1, 128.4, 132.6, 137.8, 149.1, 190.8, 208.5. CI-HRMS calcd for $C_{15}H_{18}O_2$ [MH^+] *m/z* 231.1377, found 231.1382.

8-Oxo-8-phenyl-oct-6-enal (3)

Aldehyde **3** was prepared in the same manner as **4**, starting from phenacyltriphenylphosphonium bromide (1940 mg, 4.20 mmol, 1.01 eq), to yield 469 mg, 2.29 mmol (55%). Known compound (Registry 190522-49-7).

8-(4-Nitro-phenyl)-8-oxo-oct-6-enal (5)

Aldehyde **5** was prepared in the same manner as **4**, starting from (4'-nitrophenacyl)triphenylphosphonium bromide (1520 mg, 3.00 mmol, 1.00 eq), to yield 510 mg, 1.95 mmol (65%). ^{1}H NMR (400MHz,$CDCl_3$): δ = 9.79 (1H, t, *J* = 1.4 Hz), 8.31 (2H, d, *J* = 8.8 Hz), 8.05 (2H, d, *J* = 8.8 Hz), 7.10 (1H, dd, *J* = 15.4, 6.7 Hz), 6.87 (1H, d, *J* = 15.4 Hz), 2.33-2.54 (4H, m), 1.48-1.66 (4H, m). ^{13}C NMR (50MHz,$CDCl_3$): δ = 21.3, 27.4, 32.6, 43.5, 123.7, 125.7, 129.4, 142.6, 149.9, 151.2, 189.1, 201.9. CI-HRMS calcd for $C_{14}H_{15}NO_4$ [MH^+] *m/z* 262.1071, found 262.1079.

1-(4-Methoxy-phenyl)-non-2-ene-1,8-dione (7)

Ketone **7** was prepared in the same manner as **6**, starting from (4'-metoxyphenacyl)triphenylphosphonium bromide (1823 mg, 3.71 mmol, 1.02 eq), to yield 549 mg, 2.11 mmol (58%). ^{1}H NMR (200MHz,$CDCl_3$): δ = 7.95 (2H, d, *J* = 8.9Hz), 6.85-7.06 (4H, m), 3.87 (3H, s), 2.45 (2H, t, *J* = 6.8 Hz), 2.32 (2H, q, *J* = 6.7 Hz), 2.14 (3H, s), 1.47-1.68 (4H, m). ^{13}C NMR (100MHz,$CDCl_3$): δ = 25.2, 29.6, 31.8, 34.5, 57.4, 115.7, 127.7, 132.7, 150.0, 165.2, 190.9, 210.6. CI-HRMS calcd for $C_{16}H_{20}O_3$ [MH^+] *m/z* 261.1482, found 261.1492.

1-p-Tolyl-non-2-ene-1,8-dione (8)

Ketone **8** was prepared in the same manner as **6**, starting from (4'-methylphenacyl)triphenylphosphonium bromide (600 mg, 1.26 mmol, 1.00 eq), to yield 200 mg, 0.82 mmol (65%). ^{1}H NMR (200MHz,$CDCl_3$): δ = 7.82 (2H, d, *J* = 8.2 Hz), 7.24 (2H, d, *J* = 7.7 Hz), 7.01 (1H, dt, *J* = 15.4, 6.4 Hz), 6.86 (1H, d, *J* = 15.4 Hz), 2.44 (2H, t, *J* = 6.9 Hz), 2.38 (3H, s), 2.30 (2H, q, *J* = 6.6 Hz), 2.12 (3H, s), 1.49-1.62 (4H, m). ^{13}C NMR (50MHz,$CDCl_3$): δ = 21.5, 23.2, 27.6, 29.8, 32.5, 43.3, 126.0,

128.6, 129.1, 135.2, 143.4, 148.5, 190.2, 208.5. CI-HRMS calcd for $C_{16}H_{20}O_2$ [MH^+] *m/z* 245.1533, found 245.1545.

1-(4-Bromo-phenyl)-non-2-ene-1,8-dione (9)

Ketone **9** was prepared in the same manner as **6**, starting from (4'-bromoyphenacyl)triphenylphosphonium bromide (600 mg, 1.11 mmol, 1.05 eq), to yield 227 mg, 0.73 mmol (69%). ^{1}H NMR (400MHz,$CDCl_3$): δ = 7.79 (2H, d, *J* = 8.6 Hz), 7.60 (2H, d, *J* = 8.6 Hz), 7.05 (1H, dt, *J* = 15.4, 6.6 Hz), 6.83 (1H, dt, *J* = 15.4, 1.1 Hz), 2.46 (2H, t, *J* = 6.8 Hz), 2.33 (2H, q, *J* = 6.6Hz), 2.15 (3H, s), 1.48-1.70 (4H, m). ^{13}C NMR (50MHz,$CDCl_3$): δ = 23.9, 29.5, 32.3, 35.1, 45.2, 115.6, 129.6, 131.9, 133.7, 138.5, 151.7, 191.8, 210.4. CI-HRMS calcd for $C_{15}H_{17}O_2Br$ [MH^+] *m/z* 309.0482, found 309.0483.

***cis*-2-[2-(4-Methoxy-phenyl)-2-oxo-ethyl]-cyclopentanecarbaldehyde (4a)**

Aldehye **4** (165 mg, 0.67 mmol, 1 eq) was dissolved in DMF (1 mL), and piperidine (28 mg, 0.33 mmol, 0.5 eq) was added. The reaction was monitored by TLC (EtOAc:Hex 1:2). After completion (2 hours), DMF was removed under reduced pressure and the crude product was purified by FC (EtOAc:Hex 1:2) to yield the intramolecular Michael addition product **4a** in 10% yield (16.5 mg, 0.067 mmol). ^{1}H NMR (200MHz,$CDCl_3$): δ = 9.76 (1H, d, *J* = 2.5 Hz), 7.92 (2H, d, *J* = 8.9 Hz), 6.92 (2H, d, *J* = 8.9 Hz), 3.86 (3H, s), 3.17 (1H, dd, *J* = 17.1, 7.4 Hz), 3.02 (1H, dd, *J* = 17.1, 7.0 Hz), 3.00-3.09 (1H, m), 2.80-2.98 (1H, m), 1.42-1.99 (6H, m). ^{13}C NMR (100MHz,$CDCl_3$): δ = 27.2, 33.5, 36.6, 41.1, 55.5, 57.4, 115.6, 131.8, 132.2, 199.7, 206.9. CI-HRMS calcd for $C_{15}H_{18}O_3$ [MH^+] *m/z* 247.1326, found 247.1334. The anti isomer was yielded as well in 85% yield (140 mg, 0.57 mmol). ^{1}H NMR

(200MHz,$CDCl_3$): δ = 9.66 (1H, d, *J* = 3.2 Hz), 7.92 (2H, d, J = 8.9 Hz), 6.92 (2H, d, *J* = 8.9 Hz), 3.86 (3H, s), 3.09 (1H, dd, *J* = 16.7, 7.1 Hz), 2.99 (1H, dd, *J* = 16.7, 6.7 Hz), 2.71 (1H, sext, *J* = 7.4 Hz), 2.42 (1H, ddd, *J* = 16.0, 8.0, 3.3 Hz), 1.25-2.11 (6H, m). ^{13}C NMR (100MHz,$CDCl_3$): δ = 28.7, 34.9, 38.8, 45.1, 57.4, 59.7, 115.7, 131.8, 132.3, 165.5, 199.6, 205.6. CI-HRMS calcd for $C_{15}H_{18}O_3$ [MH^+] *m/z* 247.1326, found 247.1334.

cis-2-(2-Acetyl-cyclopentyl)-1-phenyl-ethanone (6a)

Ketone **6** (240 mg, 1.05 mmol, 1 eq) was dissolved in DMF (1mL) and piperidine (44 mg, 0.52 mmol, 0.5 eq) was added. The reaction was heated to 60^{o}C, stirred for overnight and was monitored by TLC (EtOAc:Hex 1:2). After completion, DMF was removed under reduced pressure and the crude product was purified by FC (EtOAc:Hex 1:2) to yield the intramolecular Michael addition product **6a** in 40% yield (98 mg, 0.42 mmol). ^{1}H NMR (200MHz,$CDCl_3$): δ = 7.94 (2H, d, *J* = 6.9 Hz), 7.42-7.56 (3H, m), 3.15-3.27 (1H, m), 3.06 (2H, m), 2.65-2.93 (1H, m), 2.15 (3H, s), 1.57-1.93 (6H, m). ^{13}C NMR (50MHz,$CDCl_3$): δ = 24.6, 28.8, 29.6, 32.5, 38.1, 43.9, 58.2, 128.1, 128.5, 133.0, 136.8, 199.6, 210.8. CI-HRMS calcd for $C_{15}H_{18}O_2$ [MH^+] *m/z* 231.1377, found 231.1394. The anti isomer was yielded as well in 45% (115 mg, 0.48 mmol). ^{1}H NMR (200MHz,$CDCl_3$): δ = 7.97 (2H, d, *J* = 6.9 Hz), 7.43-7.57 (3H, m), 3.14 (1H, dd, *J* = 15.8, 6.0 Hz), 2.93 (1H, dd, J = 15.8, 7.3 Hz), 2.58-2.80 (2H, m), 2.20 (3H, s), 1.66-2.07 (6H, m). ^{13}C NMR (50MHz,$CDCl_3$): δ = 24.8, 25.3, 30.1, 34.1, 40.1, 41.4, 55.8, 129.8, 130.5, 135.0, 139.0, 201.9, 214.1. CI-HRMS calcd for $C_{15}H_{18}O_2$ [MH^+] *m/z* 231.1377, found 231.1392.

***cis*-2-(2-Oxo-2-phenyl-ethyl)-cyclopentanecarbaldehyde (3a)**

Aldehyde **3a** was prepared in the same manner as **4a**, starting from aldehyde **3** (145 mg, 0.67 mmol, 1 eq), to yield 24 mg, 0.11 mmol (9%) of **3a**. ^{1}H NMR (200MHz,$CDCl_3$): δ = 9.77 (1H, d, *J* = 2.5 Hz), 7.93 (2H, d, *J* = 6.8 Hz), 7.40-1.60 (3H, m), 3.01-3.30 (2H, m), 2.81 (1H, sext, *J* = 7.1 Hz), 1.39-2.01 (6H, m). ^{13}C NMR (50MHz,$CDCl_3$): δ = 25.4, 32.1, 38.2, 39.5, 53.4, 127.9, 128.5, 133.2, 136.7, 199.2, 204.9. CI-HRMS calcd for $C_{14}H_{16}O_2$ [MH^+] *m/z* 217.1220, found 217.1222. The trans isomer was obtained as well in 17% (13 mg, 0.06 mmol) yield. ^{1}H NMR (200MHz,$CDCl_3$): δ = 9.68 (1H, d, *J* = 3.3 Hz), 7.94 (2H, d, *J* = 6.9 Hz), 7.40-7.60 (3H, m), 3.10 (1H, dd, *J* = 6.8, 4.0 Hz), 2.73 (1H, sext, *J* = 7.6 Hz), 2.43 (1H, dd, *J* = 8.0, 3.2 Hz), 1.97-2.09 (1H, m), 1.83-1.92 (2H, m), 1.65-1.79 (2H, m), 1.37-1.45 (2H, m). ^{13}C NMR (100MHz,$CDCl_3$): δ = 26.7, 28.7, 34.9, 38.6, 45.5, 59.7, 190.0, 130.6, 135.1, 138.7, 201.0, 205.5. CI-HRMS calcd for $C_{14}H_{16}O_2$ [MH^+] *m/z* 217.1220, found 217.1223.

***cis*-2-[2-(4-nitro-phenyl)-2-oxo-ethyl]-cyclopentanecarbaldehyde (5a)**

Aldehyde **5a** was prepared in the same manner as **4a**, starting from aldehyde **5** (70 mg, 0.26 mmol, 1 eq), to yield 5 mg, 0.07 mmol (10%) of **5a**. ^{1}H NMR (200MHz,$CDCl_3$): δ = 9.75 (1H, d, ^{3}J=2.26Hz), 8.27-8.33 (2H, m), 8.06-8.12 (2H, m), 3.28-3.40 (1H, dd, *J* = 18.0, 7.5 Hz), 3.04-3.17 (2H, m), 2.72-2.88 (1H, m), 1.4-2.0 (6H, m). ^{13}C NMR (50MHz,$CDCl_3$): δ = 23.5, 25.7, 32.0, 37.8, 40.2, 53.1, 123.8, 128.9, 141.3, 150.3, 197.8, 204.7. CI-HRMS calcd for $C_{14}H_{15}ONO_4$ [MH^+] *m/z* 262.1071, found 262.1077. The trans isomer was obtained as well in 43% (30 mg, 0.29 mmol) yield. ^{1}H NMR (200MHz,$CDCl_3$): δ = 8.29 (2H, d, *J* = 7.0 Hz), 8.09 (2H, d, *J* = 7.0 Hz), 3.13 (2H, t, *J* = 6.6 Hz), 2.63-2.82 (1H, m), 2.36-2.50 (1H, m), 1.27-

2.12 (6H, m). ^{13}C NMR (100MHz,$CDCl_3$): δ = 28.8, 31.6, 32.9, 34.9, 46.0, 59.6, 125.7, 125.8, 131.0, 143.0, 152.3, 199.5, 208.9. CI-HRMS calcd for $C_{14}H_{15}ONO_4$ [MH^+] *m/z* 262.1071, found 262.1078.

cis-2-(2-Acetyl-cyclopentyl)-1-(4-methoxy-phenyl)-ethanone (7a)

Ketone **7a** was prepared in the same manner as **6a**, starting from ketone **7** (265 mg, 1.02 mmol, 1 eq), to yield 46 mg, 0.17 mmol (17%) of **7a**. ^{1}H NMR (400MHz,$CDCl_3$): δ = 7.91 (2H,d, *J* = 8.9 Hz), 6.91 (2H, d, *J* = 8.9 Hz), 3.86 (3H, s), 3.22 (1H, q, *J* = 7.4 Hz), 3.01 (1H, dd, *J* = 17.2, 7.2 Hz), 2.93 (1H, dd, *J* = 17.2, 7.0 Hz), 2.75-2.83 (1H, m), 2.13 (3H, s), 1.54-1.63 (6H, m). ^{13}C NMR (50MHz,$CDCl_3$): δ = 23.3, 28.0, 31.3, 32.1, 38.4, 39.0, 53.9, 55.4, 113.6, 130.2, 130.3, 163.4, 198.5, 212.2. CI-HRMS calcd for $C_{16}H_{20}O_3$ [MH^+] *m/z* 261.1482, found 261.1495. The trans isomer was obtained as well in 22% (59 mg, 0.23 mmol) yield. ^{1}H NMR (400MHz,$CDCl_3$): δ = 7.94 (2H, d, *J* = 8.9 Hz), 6.93 (2H, d, *J* = 8.9 Hz), 3.86 (3H, s), 3.06 (1H, dd, *J* = 15.5, 6.1 Hz), 2.85 (1H, dd, *J* = 15.5, 7.6 Hz), 2.66-2.75 (1H, m), 2.59-2.65 (1H, m), 2.19 (3H, s), 1.97-2.00 (2H, m), 1.67-1.71 (4H, m). ^{13}C NMR (50MHz,$CDCl_3$): δ = 26.5, 30.8, 31.6, 34.5, 40.4, 45.6, 57.4, 60.3, 115.6, 131.9, 132.4, 165.4, 200.1, 212.9. CI-HRMS calcd for $C_{16}H_{20}O_3$ [MH^+] *m/z* 261.1482, found 261.1495.

cis-2-(2-Acetyl-cyclopentyl)-1-p-tolyl-ethanone (8a)

Ketone **8a** was prepared in the same manner as **6a**, starting from ketone **8** (167 mg, 0.68 mmol, 1.00eq), to yield 41 mg, 0.17 mmol (25%) of **8a**. ^{1}H NMR (400MHz,$CDCl_3$): δ = 7.82 (2H, d, *J* = 8.2 Hz), 7.23 (2H, d, *J* = 8.0), 3.22 (1H, q, *J* = 7.4 Hz), 3.04 (1H, dd, *J* = 17.4, 7.2 Hz), 2.95 (1H, dd, *J* = 17.4, 7.0 Hz), 2.80 (1H,

sept, *J* = 7.1 Hz), 2.39 (3H, s), 2.13 (3H, s), 1.57-1.89 (6H, m). ^{13}C NMR (100MHz,$CDCl_3$): δ = 21.5, 23.3, 29.6, 31.2, 32.1, 38.2, 39.2, 53.8, 128.2, 129.1, 134.6, 143.7, 199.5, 212.1. CI-HRMS calcd for $C_{16}H_{20}O_2$ [MH^+] *m/z* 245.1533, found 245.1550. The trans isomer was obtained as well in 26% (44 mg, 0.18 mmol). ^{1}H NMR (400MHz,$CDCl_3$): δ = 7.86 (2H, d, *J* = 6.6 Hz), 7.25 (2H, d, *J* = 6.6 Hz), 3.08 (1H, dd, *J* = 15.6, 6.0 Hz), 2.88 (1H, dd, *J* = 15.6, 7.3 Hz), 2.56-2.80 (2H, m), 2.40 (3H, s), 2.18 (3H, s), 1.90- 2.01 (2H, m), 1.64-1.72 (4H, m). ^{13}C NMR (50MHz,$CDCl_3$): δ = 21.5, 24.5, 28.8, 29.6, 32.5, 38.2, 43.8, 58.2, 128.2, 129.2, 134.3, 143.7, 199.2, 204.5. CI-HRMS calcd for $C_{16}H_{20}O_2$ [MH^+] *m/z* 245.1533, found 245.1537.

cis-2-(2-Acetyl-cyclopentyl)-1-(4-bromo-phenyl)-ethanone (9a)

Ketone **9a** was prepared in the same manner as **6a**, starting from ketone **9** (320 mg, 1.03 mmol, 1 eq), to yield 126 mg, 0.41 mmol (39%) of **9a**. ^{1}H NMR (200MHz,$CDCl_3$): δ = 7.79 (2H, d, *J* = 8.6 Hz), 7.58 (2H, d, *J* = 8.6 Hz), 3.11 (1H, dd, *J* = 17.4, 7.3 Hz), 2.92 (1H, dd, *J* = 17.4, 6.7 Hz), 2.70-2.85 (1H, m), 2.57-2.66 (1H, m), 2.13 (3H, s), 1.40-2.17 (6H, m). ^{13}C NMR (100MHz,$CDCl_3$): δ = 25.3, 30.2, 31.6, 34.1, 39.9, 41.4, 55.7, 129.6, 131.5, 133.8, 137.7, 200.9, 214.1. CI-HRMS calcd for $C_{15}H_{17}O_2Br$ [MH^+] *m/z* 309.0482, found 309.0493.

The trans isomer was obtained as well in 56% (174 mg, 0.58 mmol) yield. ^{1}H NMR (400MHz,$CDCl_3$): δ = 7.82 (2H, d, *J* = 6.82 Hz), 7.60 (2H, d, *J* = 8.5 Hz), 3.07 (1H, dd, *J* = 15.8, 6.0 Hz), 2.85 (1H, dd, *J* = 15.8, 7.7 Hz), 2.69 (1H, sext, *J* = 7.9 Hz), 2.60 (1H, q, *J* = 7.9 Hz), 2.19 (3H, s), 1.97-2.03 (3H, m) 1.68-1.71 (3H, m). ^{13}C NMR (100MHz,$CDCl_3$): δ = 26.4, 30.8, 31.6, 34.4, 39.9, 45.9, 60.2, 130.1, 131.6, 133.8,

137.4, 200.6, 212.7. CI-HRMS calcd for $C_{15}H_{17}O_2Br$ [MH^+] *m/z* 309.0482, found 309.0483.

Enantiomers separation

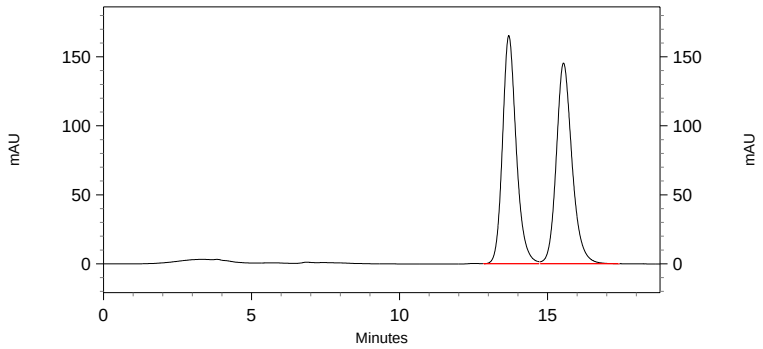
All the *cis*- and *trans*- Michael addition products enantiomers, were separated by RP-HPLC (Hitachi LaChromeELITE equipped with an L-2000 series organizer box, L-2300 column-oven, L-2450 diode array detector, L-2200 autosampler and L-2130) at various $5\mu m$ pump) using CHIRALPAK® AD-RH column (150mm x 4.6mm, proportions of Acetonitrile : Water at 0.5 ml/min flow-rate.

Table 1. Conditions for separation of intra molecular Michael products **3a-9a** enantiomers.

Enone	Solvents ratio Acetonitrile : Water	Retention time *cis* enantiomers (min)	Retention time *trans* enantiomers (min)	[nm] λ Wavelength for monitoring enantiomeric separation
3a	55% : 45%	16.57 , 28.79	17.06 , 17.66	244
4a	55% : 45%	20.76 , 32.71	21.35 , 24.75	274
5a	70% : 30%	15.14 , 22.62	16.12 , 17.14	266
6a	60% : 40%	9.36 , 10.90	No separation. One pick 9.55	243
7a	55% : 45%	13.68 , 15.56	13.06 , 14.80	274
8a	55% : 45%	15.26 , 16.41	15.62 , 17.34	254
9a	60% : 40%	21.25 , 24.15	19.66 , 24.48	256

The enantiomeric excess of all *cis*- products of the reaction of the corresponding ketone or aldehyde with Ab38C2, was determined under the same conditions as mentioned in the appropriate entry in table 1. One example, the *cis*- product of ketone **7** with Ab38C2 (similar to **7a**) was further purified under the same conditions , Acetonitrile $5\mu m$ (LiChroCART 250-4 Purospher® RP-18e column 250mm x 4mm, : Water 55% : 45%) used to separate the *cis-/trans*- stereoisomers. The enantiomeric excess of the purified *cis*- product was then determined.

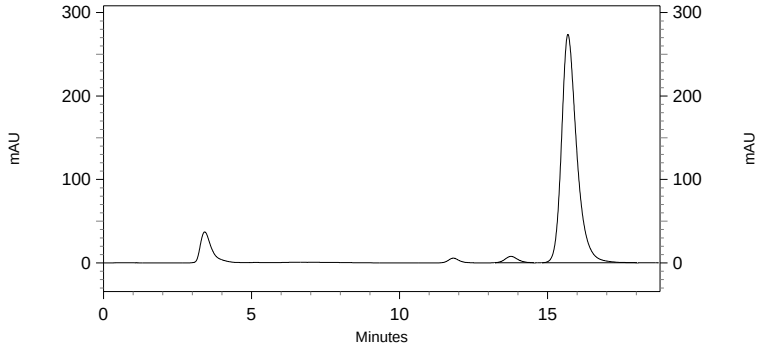
Figure 1. Separation of racemic **7a** enantiomers.



1: 274 nm, 4 nm Results

Retention Time	Area	Area Percent
13.687	21366960	49.8
15.540	21511123	50.2
Totals		
42878083	100.0	

Figure 2. Separation of Ab38C2 reaction product **7a** enantiomres.



1: 274 nm, 4 nm Results

Retention Time	Area	Area Percent
13.767	920136	2.3
15.687	38997299	97.7
Totals		
	39917435	100.0

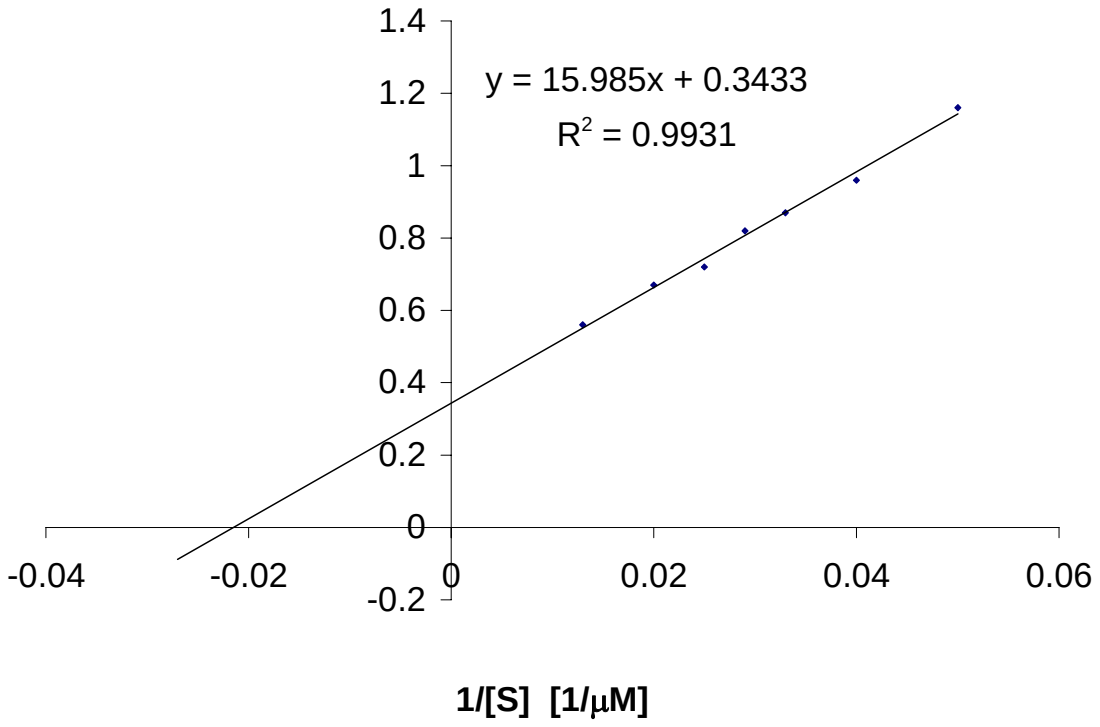
In all other *cis*-enone products, a sample of the crude reaction solution was examined without further purification.

Michaelis-Menten kinetic measurements

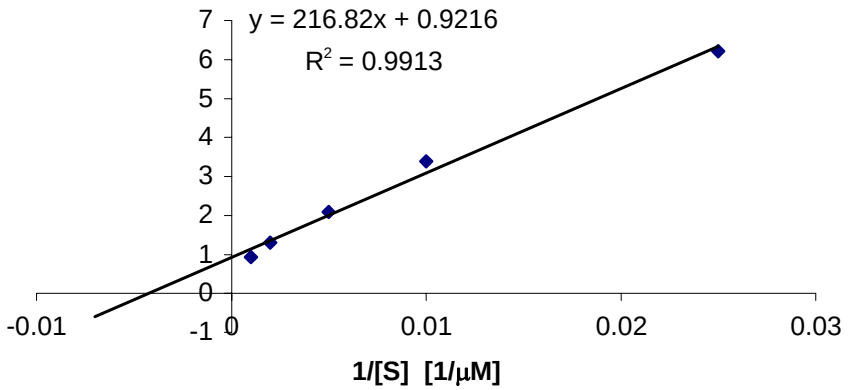
Lineweaver-Burk plots of Ab38C2-catalyzed intramolecular Michael addition of Aldehydes and Ketones

. 25°*C* All reactions were carried out in phosphate buffered saline (PBS), pH 7.4 at . μM Reactions were typically carried out in concentrations ranging between 20-1250 Antibody 38C2 was typically used in concentrations ranging between 0.05-1mg/ml. Antibody catalyzed reactions were monitored by RP-HPLC (Hitachi LaChromeELITE equipped with an L-2000 series organizer box, L-2300 column-oven, L-2450 diode array detector, L-2200 autosampler and L-2130 pump) using) at various $5\mu m$ LiChroCART 250-4 Purospher® RP-18e column (250mm x 4mm, proportions of Acetonitrile : Water (0.1% trifluoroacetic acid) at 1 ml/min flow-rate. Conditions for monitoring the reaction of formyl-enone and methylketone-enone substrates with Ab38C2 were: Acetonitrile : Water (55% : 45%), except for ketone **9**: Acetonitrile : Water (60% : 40%).

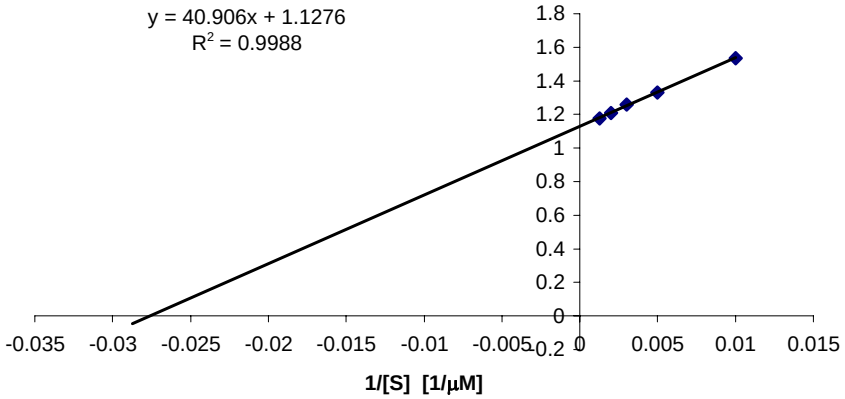
. **3 → 3a Graph 1.** Lineweaver-Burk plot of Ab38C2 catalysis for the reaction



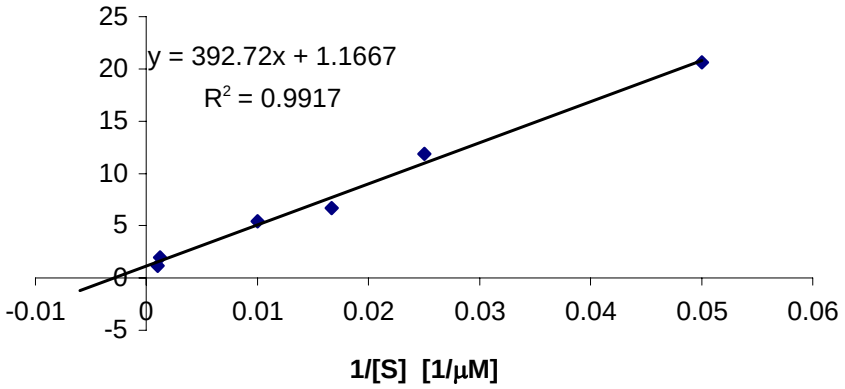
. **4 → 4a Graph 2.** Lineweaver-Burk plot of Ab38C2 catalysis for the reaction



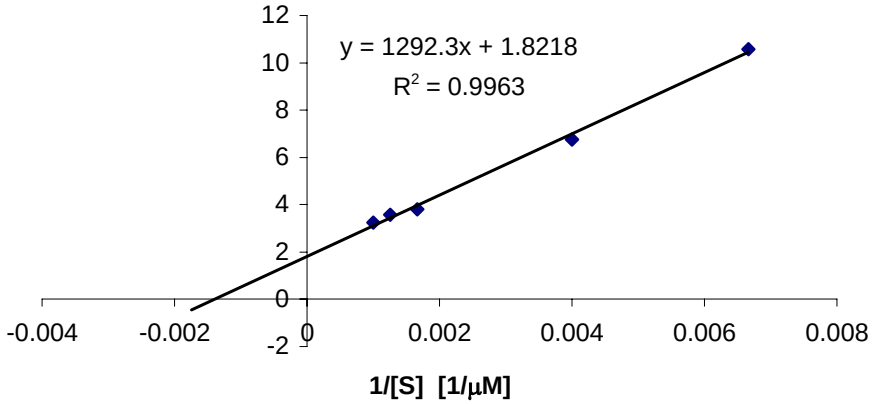
. **5 → 5a Graph 3.** Lineweaver-Burk plot of Ab38C2 catalysis for the reaction



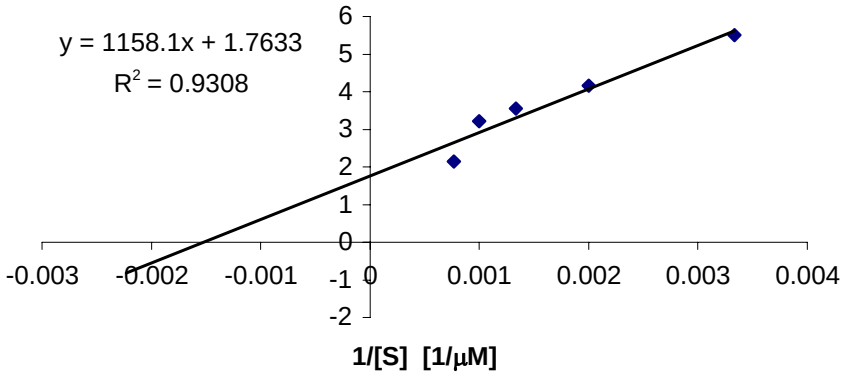
. **6 → 6a Graph 4.** Lineweaver-Burk plot of Ab38C2 catalysis for the reaction



. **7** → **7a Graph 5.** Lineweaver-Burk plot of Ab38C2 catalysis for the reaction



. **8** → **8a Graph 6.** Lineweaver-Burk plot of Ab38C2 catalysis for the reaction



. **9 → 9a Graph 7.** Lineweaver-Burk plot of Ab38C2 catalysis for the reaction

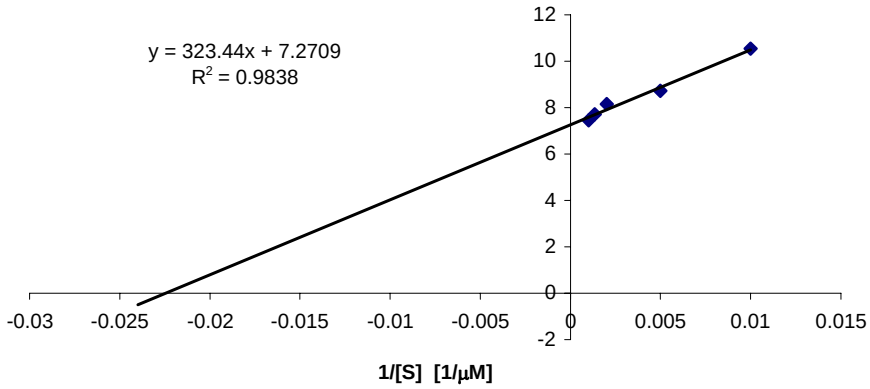


Table 2. K_{uncat} measurements for **3-9** in PBS:

Reaction	K_{uncat} [min^{-1}]
$3 \rightarrow 3a$	$3.5 \cdot 10^{-5}$
$4 \rightarrow 4a$	$5.4 \cdot 10^{-5}$
$5 \rightarrow 5a$	$5.7 \cdot 10^{-5}$
$6 \rightarrow 6a$	$4.0 \cdot 10^{-7}$
$7 \rightarrow 7a$	$3.0 \cdot 10^{-6}$
$8 \rightarrow 8a$	$7.0 \cdot 10^{-7}$
$9 \rightarrow 9a$	$1.0 \cdot 10^{-6}$

K_{uncat} measurements were made with the appropriate aldehyde or ketone at concentration in $500 \mu M$ PBS solution at pH 7.4.