Supporting information

Asymmetric Michael addition between kojic acid derivatives and unsaturated ketoesters promoted by C₂-symmetric organocatalysts


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Contents

1. Synthesis of catalysts **V-VIII** .......................................................... S3
2. Catalytic Michael reaction between **6** and **7** ............................. S11
3. Synthesis of esters **11** and **12** ......................................................... S38
4. HPLC data for Michael adducts **13** ............................................. S43
5. HRMS pictures of catalyst **V** and compounds **11** and **12** ....... S50
6. Literature ....................................................................................... S53
1. Synthesis of catalysts V-VIII (General procedure)

Dimethyl squarate 2 (0.70 g, 4.91 mmol) was added to a solution of corresponding diamine 1 (2.33 mmol) in MeOH (2 mL) in one portion. After 20 h of stirring at ambient temperature, the precipitated product 3 was filtered, washed with Et₂O (3 x 10 mL) and dried in air. Then, it was added without further purification to the solution of 2-(Piperidin-1-yl)cyclohexanamine 4 (0.69 g, 3.77 mmol) in MeOH (2 mL). The reaction mixture was stirred at ambient temperature for 20 h. The precipitate was filtered, washed with Et₂O (3 x 10 mL) and dried under reduced pressure (10 Torr) to afford corresponding catalyst V, VI, VII or VIII. Catalysts III-IV were prepared by known procedures [1].

(R,R)-4,4’-(((1R,2R)-1,2-Di(naphthalen-1-yl)ethane-1,2-diyl)bis(azanediyl))bis(3-(((1R,2R)-2-(piperidin-1-yl)cyclohexyl)amino)cyclobut-3-ene-1,2-dione) (V): Yellow solid (0.72 g, 82%). Mp: >230°C dec. ¹H NMR (300 MHz, DMSO-d₆) δ 8.28 (m, 3H), 8.08 – 6.76 (m, 19H), 3.81 (s, 3H), 3.17 (s, 1H), 2.03 (m, 8H), 1.67 (m, 6H), 1.14 (s, 20H) ppm. ¹³C NMR (75 MHz, DMSO-d₆) δ 183.3, 182.6, 168.7, 167.7, 134.9, 133.8, 130.9, 129.1, 127.2, 126.4, 125.8, 122.8, 68.7, 54.3, 49.7, 35.1, 26.5, 25.2, 24.9, 24.8, 24.0 ppm. HRMS (ESI): m/z M + H⁺ calcd for C₅₂H₆₁N₆O₄⁺ 833.4748, found 833.4760.
(S,S)-4,4’-(((1R,2R)-1,2-Di(naphthalen-1-yl)ethane-1,2-diyl)bis(azanediyl))bis(3-(((1S,2S)-2-(piperidin-1-yl)cyclohexyl)amino)cyclobut-3-ene-1,2-dione) (VI): Yellow solid (0.81 g, 83% yield). Mp: >230°C dec. $^1$H NMR (300 MHz, DMSO-d$_6$) $\delta$ 8.27 (m, 3H), 8.08 – 7.05 (m, 19H), 6.86 (s, 1H), 3.81 (s, 3H), 3.17 (s, 1H), 2.25 – 1.75 (m, 8H), 1.67 (m, 6H), 1.14 (s, 20H) ppm. $^{13}$C NMR (75 MHz, DMSO-d$_6$) $\delta$ 183.3, 182.6, 168.7, 167.7, 134.9, 133.8, 130.9, 129.1, 127.2, 126.4, 125.8, 122.8, 68.7, 54.3, 49.7, 35.1, 26.5, 25.2, 24.9, 24.8, 24.0 ppm. HRMS (ESI): $m/z$ M + H$^+$ calcd for C$_{52}$H$_{61}$N$_6$O$_4$ $^+$ 833.4748, found 833.4741.
(R,R)-4,4′-(((1R,2R)-1,2-Di(quinolin-8-yl)ethane-1,2-diyl)bis(azanediyl))bis(3-(((1R,2R)-2-(piperidin-1-yl)cyclohexylamino)cyclobut-3-ene-1,2-dione) (VII): Yellow solid (0.69 g, 72% yield). Mp 195-197°C. ^1H NMR (300 MHz, DMSO-d$_6$) $\delta$ 8.98 (s, 2H), 8.20 (d, $J$ = 8.3 Hz, 4H), 7.55 (m, 6H), 7.16 (s, 4H), 3.76 (s, 2H), 3.38 (d, $J$ = 7.2 Hz, 2H), 2.34 (m, 4H), 2.22 – 1.86 (m, 6H), 1.69 (s(br), 3H), 1.48 – 0.43 (m, 20H) ppm. $^{13}$C NMR (75 MHz, DMSO-d$_6$) $\delta$ 182.7, 168.9, 149.9, 145.4, 136.9, 128.4, 128.3, 126.1, 121.8, 68.5, 60.9, 60.1, 54.4, 52.3, 51.0, 49.6, 40.8, 40.6, 40.3, 40.0, 39.7, 39.4, 39.2, 31.1, 26.3, 24.3, 22.8, 21.79,182.7, 168.9, 149.9, 145.4, 136.9, 128.4, 128.3, 126.1, 121.8, 68.5, 60.9, 60.1, 54.4, 52.3, 51.0, 49.6, 40.8, 40.6, 40.3, 40.0, 39.7, 39.4, 39.2, 31.1, 26.3, 24.3, 22.8, 21.7 ppm. HRMS (ESI): m/z M + H$^+$ calcd for C$_{50}$H$_{59}$N$_8$O$_4^+$ 835.4654, found 835.4712.
(R,R)-4,4'-(((1S,2S)-1,2-Di(quinolin-8-yl)ethane-1,2-diyl)bis(azanediyl))bis(3-(((1R,2R)-2-(piperidin-1-yl)cyclohexyl)amino)cyclobut-3-ene-1,2-dione) (VIII): Yellow solid (0.74 g, 77% yield). Mp 191-193°C. $^1$H NMR (300 MHz, DMSO-d$_6$) $\delta$ 9.63 (s, 1H), 9.20-8.82 (m, 2H), 8.30-8.03 (m, 5H), 7.99-7.40 (m, 5H), 7.37-7.22 (m, 2H), 7.18-6.68 (m, 5H), 3.90 (s(br), 2H), 2.25-2.06 (m, 5H), 2.04-1.58 (m, 10H), 1.50-0.68 (m, 19H), 0.67-0.30 (m, 3H) ppm. $^{13}$C NMR (75 MHz, DMSO-d$_6$) $\delta$ 182.7, 168.9, 149.9, 145.4, 136.9, 128.4, 128.3, 126.1, 121.8, 68.5, 60.1, 54.3, 49.6, 34.8, 31.1, 26.3, 24.3 ppm. HRMS (ESI): $m/z$ M + H$^+$ calcd for C$_{50}$H$_{59}$N$_8$O$_4^+$ 835.4654, found 835.4776.
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NMR 50122310
2. Catalytic Michael reaction between 6 and 7 (General Procedure)

Kojic acid derivative 6 (0.12 mmol) and β,γ-unsaturated α-ketoester 7 (0.12 mmol) were added to a mixture of catalyst V (1 mg, 0.0012 mmol) and DCM (0.1 mL). After stirring at room temperature for 8 h, the solvent was evaporated under reduced pressure (10 Torr). The residue was extracted with MeOH (2 × 4 mL). The combined extracts were filtered through silica gel to afford pure 8.

(S)-Methyl 2-hydroxy-6-methyl-8-oxo-4-phenyl-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8aa): Yellow oil. $^1$H NMR (300 MHz, DMSO-d$_6$) $\delta$ 8.94 (brs, 1.29H), 8.07 (brs, 1.03H), 7.29 (m, 5H), 6.24 (s, 1.00H), 4.70 (m, 0.32H), 4.30 (m, 0.73H), 3.74 (m, 2.83H), 2.14 (m, 6.61H) ppm. [2,3]
(S)-Methyl 2-hydroxy-6-(methoxymethyl)-8-oxo-4-phenyl-2,3,4,8-tetrahydropyrano-[3,2-b]pyran-2-carboxylate (8ba): Yellow oil. $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 9.17 (brs, 0.87H), 8.10 (m, 0.94H), 7.83-7.78 (m, 0.32H), 7.50 (m, 0.36H), 7.30 (m, 5.14H), 6.39-6.33 (m, 1.18H), 4.74 (s, 0.33H), 4.35 – 4.19 (m, 1.87H), 4.07 (s, 1.7H), 3.79 – 3.67 (m, 3H), 3.19 – 3.09 (s, 2H), 2.43 (m, 0.61H), 2.23 (m, 0.88H) ppm. $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$ 191.4, 172.1, 169.0, 163.3, 150.1, 140.1, 139.8, 139.2, 129.6, 129.1, 128.6, 128.4, 127.8, 127.7, 127.5, 113.2, 112.3, 111.4, 94.7, 69.9, 69.6, 58.4, 53.0, 41.7, 38.3, 37.8 ppm. HRMS (ESI): $m/z$ M + H$^+$ calcd for $C_{18}H_{19}O_7^+$ 347.1125, found 347.1185.
(S)-Methyl 4-(4-cyanophenyl)-2-hydroxy-6-(methoxymethyl)-8-oxo-2,3,4,8-tetrahydro-
pyrano[3,2-b]pyran-2-carboxylate (8bb): Yellow oil. $^1$H NMR (300 MHz, DMSO-d$_6$) $\delta$ 9.15
(brs, 0.87H), 8.32 – 7.97 (m, 1.19H), 7.84 (m, 2.12H), 7.63 – 7.36 (m, 2H), 6.36 (m, 1H), 4.76
(m, 0.32H), 4.46 (m, 0.36H), 4.27 (s, 1.40H), 4.10 (m, 1.11H), 3.78 (m, 3.15H), 3.17 (m, 2.05H),
2.43 (m, 0.41H), 2.32 – 2.14 (m, 0.59H) ppm. $^{13}$C NMR (75 MHz, DMSO-d$_6$) $\delta$ 190.9, 172.0,
164.2, 163.3, 149.0, 146.3, 145.1, 140.1, 133.0, 132.7, 130.0, 129.7, 129.1, 119.1, 113.3, 112.2,
111.5, 110.7, 94.7, 69.9, 69.8, 69.5, 58.5, 58.4, 53.1, 38.3, 37.8, 37.5 ppm. HRMS (ESI): $m/z$ M
+ H$^+$ calcd for C$_{19}$H$_{18}$NO$_7$ 371.1005, found 371.1018.
(S)-Methyl 4-(furan-2-yl)-2-hydroxy-6-(methoxymethyl)-8-oxo-2,3,4,8-tetrahydro-pyran[3,2-b]pyran-2-carboxylate (8bc): Yellow oil. $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 9.20 (s, 0.83H), 8.01 (m, 1.21H), 7.61 (m, 1.10H), 7.19 (m, 0.50H), 7.02 (m, 0.56H), 6.72 (s, 0.57H), 6.38 (m, 2H), 4.47 (t, $J = 8.8$ Hz, 1H), 4.33 – 4.07 (m, 2.28H), 3.85 – 3.66 (m, 3.18H), 3.28 – 3.12 (m, 1.75H), 2.81 (m, 0.38H), 2.40 (d, $J = 8.8$ Hz, 0.64H) ppm. $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$ 190.7, 182.7, 174.1, 164.2, 163.4, 150.6, 148.0, 147.9, 146.3, 143.3, 142.7, 140.1, 133.8, 120.0, 118.1, 114.0, 113.2, 112.2, 111.4, 111.0, 108.8, 106.9, 94.8, 69.9, 69.6, 58.5, 53.1, 34.3, 31.6 ppm. HRMS (ESI): $m/z$ M + H$^+$ calcd for $C_{16}H_{17}O_8^+$ 337.0918, found 337.0922.
KA103Fur.(13C)

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31.67  32.81  34.35  53.18  58.59  69.69  69.93  94.80  106.96  107.88  108.80  111.03  111.44  112.29  113.25  118.11  120.08  133.82  139.26  140.11  142.77  143.30  146.34  147.92  148.05  150.68  150.88  162.83  163.42  163.58  164.26  168.86  172.07  174.16  182.74  190.77
(S)-Methyl 2-hydroxy-8-oxo-4-phenyl-6-((phenylthio)methyl)-2,3,4,8-tetrahydro-
pyrano[3,2-b]pyran-2-carboxylate (8ca): Yellow oil. $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 9.05 (brs, 0.45H), 8.12 (m, 0.67H), 7.47 – 7.08 (m, 10H), 6.21 (m, 1.1H), 4.72 – 4.57 (m, 0.38H), 4.29 – 4.15 (m, 1.1H), 4.06 – 3.92 (m, 1.15H), 3.71 (m, 3.12H), 3.59 – 3.48 (m, 0.42H), 2.40 (m, 0.53H), 2.19 (m, 0.73H) ppm. $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$ 191.2, 172.0, 163.2, 150.1, 141.6, 140.5, 139.6, 139.2, 130.4, 130.2, 129.7, 129.5, 129.1, 129.0, 128.9, 128.6, 128.4, 127.8, 127.7, 127.4, 127.3, 127.2, 126.8, 113.9, 112.0, 94.7, 53.1, 53.0, 41.9, 38.4, 37.8, 34.9, 34.4 ppm. HRMS (ESI): $m/z$ M + H$^+$ calcd for C$_{23}$H$_{21}$O$_6$S$^+$ 425.1053, found 425.1062.
(S)-Methyl 6-(((4-fluorophenyl)thio)methyl)-2-hydroxy-8-oxo-4-phenyl-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8da): Yellow oil. $^1$H NMR (300 MHz, DMSO-$d_6$) \( \delta \) 9.08 (s, 0.48H), 8.21 – 7.97 (m, 71H), 7.53 – 7.00 (m, 9.00H), 6.17 (m, 1.00H), 4.70 – 4.62 (m, 0.29H), 4.18 – 4.07 (m, 1.04H), 3.92 (m, 0.94H), 3.83 – 3.66 (m, 2.56H), 2.45 – 2.33 (m, 0.36H), 2.27 – 2.13 (m, 0.56H) ppm. $^{13}$C NMR (75 MHz, DMSO-$d_6$) \( \delta \) 191.2, 173.6, 171.9, 169.0, 163.1, 160.1, 150.1, 140.5, 140.2, 139.6, 139.2, 133.7, 133.6, 133.5, 133.1, 133.0, 129.1, 128.9, 128.6, 128.4, 127.8, 127.7, 127.5, 126.8, 116.8, 116.7, 116.5, 116.4, 113.9, 113.4 (d, \( J_{C-F} \) = 66.6 Hz), 94.7, 53.1, 53.0, 41.9, 38.4, 37.8, 35.9, 35.5 ppm. HRMS (ESI): \( m/z \) M + H$^+$ calcd for C$_{23}$H$_{20}$FO$_6$S$^+$ 443.0959, found 443.0941.
(S)-Methyl 6-(((2-fluorophenyl)thio)methyl)-2-hydroxy-8-oxo-4-phenyl-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8ea): Yellow oil. $^1$H NMR (300 MHz, DMSO-d$_6$) $\delta$ 9.09 (s, 0.53H), 8.06 (m, 0.66H), 7.57 – 7.03 (m, 8.36H), 6.20 (m, 1.01H), 4.79 – 4.55 (m, 0.31H), 4.35 – 4.08 (m, 1.59H), 3.92 (s, 0.88H), 3.82 – 3.65 (m, 3.16H), 3.12 (m, 0.42H), 2.43-2.36 (m, 0.41H), 2.22-2.14 (m, 0.55H) ppm. $^{13}$C NMR (75 MHz, DMSO-d$_6$) $\delta$ 191.1, 173.6, 171.9, 169.0, 162.8, 162.7, 151.3, 150.1, 146.1, 140.5, 140.2, 139.6, 139.1, 133.5, 133.2, 132.5, 130.4, 130.2, 130.1, 129.9, 129.1, 128.9, 128.6, 128.4, 127.8, 127.6, 127.4, 126.8, 125.5, 125.4, 116.3, 116.0, 113.9, 113.6 (d, $J_{C-F}$ = 63.6 Hz), 94.7, 53.1, 53.0, 41.9, 38.4, 37.7, 34.5, 34.4, 33.8 ppm. HRMS (ESI): m/z M + H$^+$ calcd for C$_{23}$H$_{20}$FO$_6$S$^+$ 443.0959, found 443.0948.
(S)-Methyl 4-(4-cyanophenyl)-6-(((2-fluorophenyl)thio)methyl)-2-hydroxy-8-oxo-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8eb): Yellow oil. $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 7.76 (m, 1.91H), 7.28 (m, 4.87H), 6.20 (s, 0.41H), 4.16 (m, 0.74H), 4.02 (m, 0.59H), 3.74 (m, 1.95H), 3.66 – 3.31 (m, 2H), 2.93 (m, 2H), 1.23 – 1.03 (m, 3.39H) ppm. $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$ 194.5, 172.5, 168.2, 163.0, 140.2, 133.4, 132.9, 131.9, 131.4, 129.8, 129.5, 129.3, 128.9, 119.1, 113.9, 113.5 (d, $J_{C-F} = 60.2$ Hz), 110.6, 94.7, 68.6, 53.1, 37.8, 37.6, 34.8, 34.4 ppm. HRMS (ESI): $m/z$ M + H$^+$ calcd for C$_{24}$H$_{19}$FNO$_6$S$^+$ 468.0912, found 468.0915.
(S)-Methyl 6-(((2,4-difluorophenyl)thio)methyl)-2-hydroxy-8-oxo-4-phenyl-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8fa): Yellow oil. $^1$H NMR (300 MHz, DMSO-$d_6$) δ 9.09 (s, 0.51H), 8.06 (m, 0.68H), 7.47 – 7.12 (m, 7.16H), 6.12 (m, 0.85H), 4.67 (m, 0.29H), 4.24 (m, 0.46H), 4.07 (m, 0.66H), 3.85 (m, 0.83H), 3.78 (s, 1.20H), 3.70 (m, 1.13H), 3.09 (m, 0.21H), 3.09 (s, 0.221H), 2.39 (m, 0.42H), 2.17 (m, 0.54H) ppm. $^{13}$C NMR (75 MHz, DMSO-$d_6$) δ 191.2, 173.9, 171.9, 169.0, 162.8, 162.5, 150.1, 140.2, 139.6, 139.1, 136.1, 135.9, 129.0, 128.9, 128.6, 128.4, 127.8, 127.6, 127.5, 113.8, 113.0, 112.9, 112.6, 112.2, 105.4, 105.1, 104.7, 94.7, 53.0, 41.9, 38.4, 37.8, 35.6, 35.3, 34.9 ppm. HRMS (ESI): $m/z$ M + H$^+$ calcld for C$_{23}$H$_{19}$F$_2$O$_6$S$^+$ 461.0865, found 461.0843.

![Diagram of the molecule](attachment:diagram.png)
(S)-Methyl 4-(4-cyanophenyl)-6-(((2,4-difluorophenyl)thio)methyl)-2-hydroxy-8-oxo-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8fb): Yellow oil. $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 9.73 – 8.67 (m, 0.78H), 8.21 (s, 0.35H), 8.00 (s, 0.32H), 7.78 (m, 1.92H), 7.34 (m, 3.80H), 7.02 (m, 1.11H), 6.14 (s, 1.00H), 4.74 (m, 0.46H), 4.38 (m, 0.61H), 4.17 – 3.60 (m, 4.76H), 3.22 (m, 1.03H), 2.63 (m, 0.54H), 2.28 (m, 1.19H) ppm. $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$ 190.8, 171.9, 168.8, 164.3, 163.0, 161.0, 149.0, 144.9, 140.2, 135.6, 132.9, 132.6, 129.8, 129.6, 129.0, 119.1, 113.9, 112.9, 112.6, 110.6, 105.0, 94.7, 68.5, 53.1, 49.7, 41.3, 38.6, 37.8, 35.6, 35.0, 26.5, 25.0 ppm. HRMS (ESI): $m/z$ M + H$^+$ calcd for C$_{24}$H$_{18}$F$_2$NO$_6$S$^+$ 486.0817, found 486.0841.
(S)-Methyl 6-(((4-chlorophenyl)thio)methyl)-2-hydroxy-8-oxo-4-phenyl-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8ga): Yellow oil. $^1$H NMR (300 MHz, DMSO-d$_6$) $\delta$ 9.08 (brs, 0.62H), 8.06 (m, 0.71H), 7.53 – 7.03 (m, 9.00H), 6.26 (m, 1.03H), 4.70 – 4.59 (m, 0.30H), 4.23 (m, 1.62H), 3.98 (s, 1.05H), 3.85 – 3.42 (m, 3.46H), 3.23 – 2.95 (m, 0.73H), 2.39 (m, 0.50H), 2.29 – 2.10 (m, 0.63H) ppm. $^{13}$C NMR (75 MHz, DMSO-d$_6$) $\delta$ 191.1, 171.9, 163.0, 150.1, 140.2, 139.2, 132.0, 131.9, 131.4, 129.5, 129.4, 129.1, 128.9, 128.6, 128.4, 127.8, 127.6, 127.4, 113.9, 113.1, 112.2, 94.7, 53.1, 53.0, 41.9, 38.4, 37.8, 34.8, 34.3 ppm. HRMS (ESI): $m/z$ M + H$^+$ calcd for C$_{23}$H$_{20}$ClO$_6$S $^+$ 459.0664, found 459.0678.
(S)-Methyl 6-(((4-chlorophenyl)thio)methyl)-4-(4-cyanophenyl)-2-hydroxy-8-oxo-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8gb): Yellow oil. \(^1\)H NMR (300 MHz, DMSO-d\(_6\)) \(\delta\) 9.18 (s, 1H), 8.19 (brs, 0.53H), 8.01 (s, 0.55H), 7.77 (m, 2.03H), 7.51 – 7.14 (m, 8.18H), 6.26 (m, 1.05H), 4.71 (m, 0.62H), 4.38 (m, 0.71H), 4.19 (m, 1.98H), 4.03 (m, 1.48H), 3.88 – 3.66 (m, 3.59H), 3.19 (m, 0.77H), 2.66 (m, 0.73H), 2.45 – 2.10 (m, 1.67H), 1.50 – 1.00 (m, 2.07H) ppm. \(^{13}\)C NMR (75 MHz, DMSO-d\(_6\)) \(\delta\) 190.7, 173.9, 171.9, 163.8, 163.2, 140.2, 133.4, 132.9, 131.9, 131.4, 129.8, 129.5, 129.3, 128.9, 119.1, 113.9, 113.1, 112.3, 110.6, 94.7, 68.6, 53.1, 37.8, 37.6, 34.8, 34.4, 26.7, 24.9 ppm. HRMS (ESI): \(m/z\) M + H\(^+\) calcd for C\(_{24}\)H\(_{19}\)ClNO\(_5\)S\(^+\) 484.0616, found 484.0664.
(S)-Methyl 6-(chloromethyl)-2-hydroxy-8-oxo-4-phenyl-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8ha): Yellow oil. $^1$H NMR (300 MHz, DMSO-d$_6$) δ 9.27 (s, 0.59H), 8.15 (m, 0.81H), 7.30 (m, 5.00H), 6.55 (m, 1.17H), 4.67 (m, 0.99H), 4.47 (m, 0.93H), 3.73 (m, 3.07H), 2.22 (m, 0.66H), 2.08 (s, 0.72H) ppm. $^{13}$C NMR (75 MHz, DMSO-d$_6$) δ 191.2, 172.1, 168.9, 161.2, 161.0, 150.4, 140.5, 140.4, 140.0, 139.1, 129.1, 128.9, 128.6, 128.4, 128.1, 127.9, 127.7, 127.5, 127.4, 127.0, 126.8, 114.5, 113.7, 112.7, 94.8, 53.1, 41.9, 41.7, 41.5, 38.6, 38.4, 37.8, 14.5 ppm. HRMS (ESI): m/z M + H$^+$ calcd for C$_{17}$H$_{16}$ClO$_6$ 351.0630, found 351.0635
(S)-Methyl 2-hydroxy-6-(morpholinomethyl)-8-oxo-4-phenyl-2,3,4,8-tetrahydro-
pyrano[3,2-b]pyran-2-carboxylate (8ia): Yellow oil. $^1$H NMR (300 MHz, DMSO-d$_6$) $\delta$ 8.14 (m, 0.82H), 7.81 (m, 0.44H), 7.31 (m, 5.00H), 6.30 (s, 1.00H), 3.73-3.54 (m, 5.90H), 3.22-3.09 (m, 2.80H), 2.45-2.17 (m, 5.14H), 1.23 (m, 1.07H) ppm. $^{13}$C NMR (75 MHz, DMSO-d$_6$): $\delta$ 172.2, 163.6, 150.2, 139.6, 139.2, 129.1, 128.8, 128.0, 127.5, 126.8, 124.2, 112.6, 110.4, 94.8, 66.5, 58.6, 53.1, 52.9, 46.9, 37.9, 37.8 ppm. HRMS (ESI): $m/z$ M + H$^+$ calcd for C$_{21}$H$_{24}$NO$_7^+$ 402.1547, found 402.1584.
KA03M (13C) NMR/50592399

19.09 37.77 37.91 46.91 52.85 53.10 58.55 66.49 94.79 110.42 112.57 114.24 126.80 127.73 128.82 129.12 139.24 139.58 150.24 163.56 172.18 172.22 180.72 191.36

**Synthesis of 11.** DMAP (cat) was added with stirring to a solution of DCC (22.7 mg, 0.11 mmol), 8ba (34.6 mg, 0.1 mmol) and rac-9 or (S)-9 (20.7 mg, 0.1 mmol) in DCM (3 ml). The reaction mixture was stirred at ambient temperature for 10 h and then washed with water (2 x 1 mL). The organic phase was dried over anhydrous Na$_2$SO$_4$ and evaporated under reduced pressure (10 Torr). The residue was purified by flash chromatography (n-hexane/EtOAc 2:1) to afford compound (S,S)/(S,R)-11 or (S,S)-11 as colorless oil.

**Synthesis of 12.** DMAP (cat) was added with stirring to a solution of DCC (22.7 mg, 0.11 mmol), 8ha (35 mg, 0.1 mmol) and 10 (18.4 mg, 0.1 mmol) in DCM (3 ml). The reaction mixture was stirred at ambient temperature for 10 h. Product 12 was isolated as colorless oil similar to aforementioned procedure.

**Methyl 4-(3-((2-(4-isobutylphenyl)propanoyl)oxy)-6-(methoxymethyl)-4-oxo-4H-pyran-2-yl)-2-oxo-4-phenylbutanoate ((S,S)/(S,R)-11).** Colorless oil (37.8 mg, 70% yield) $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.32 (m, 2.4H), 7.21 (m, 2.3H), 7.07 (m, 2H), 6.99 (m, 1H), 6.87 (m, 1H), 6.37 (m, 1H), 4.58 (s, 1H), 4.38 (m, 0.3H), 4.25 (m, 1H), 3.95 (m, 0.6H), 3.90 – 3.67 (m, 3.6H), 3.53 – 3.34 (m, 2.5H), 3.27 (s, 1H), 2.70 (m, 0.5H), 2.47 (m, 1.3H), 2.37 (m, 0.8H), 2.32 – 2.19 (m, 0.5H), 1.85 (m, 1.9H), 1.76 – 1.55 (m, 2.6H), 1.50 (m, 1.8H), 1.34 (m, 1H), 1.12 (m, 1.3H) ppm. $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 190.2, 171.5, 171.3, 170.9, 166.5, 163.6, 162.8, 159.3, 157.2, 149.2, 140.9, 140.6, 139.2, 137.8, 137.3, 136.9, 136.5, 129.6, 129.4, 129.3, 129.2, 128.9, 128.8, 127.9, 127.8, 127.7, 127.5, 127.2, 126.9, 113.6, 112.7, 94.7, 69.9, 69.6, 58.9, 53.4, 53.1, 49.1, 45.0, 44.9, 44.6, 41.5, 38.9, 37.6, 37.2, 33.8, 30.1, 25.5, 24.9, 22.3, 22.3, 18.4, 17.9, 17.7 ppm. HRMS (ESI): m/z M + Na$^+$ calcd for C$_{31}$H$_{33}$O$_8$Na$^+$ 557.2146, found 557.2146.
(S)-methyl 4-3-((S)-2-(4-isobutylphenyl)propanoyl)oxy)-6-(methoxymethyl)-4-oxo-4H-pyran-2-yl)-2-oxo-4-phenylbutanoate ((S,S)-11). Colorless oil (43.3 mg, 81% yield) $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.38 - 6.84 (m, 9H (Ar)), 6.37 (s, 1H), 4.25 (s, 2H), 4.08-4.01 (m, 1H), 3.85 (s, 3H), 3.51-3.48 (m, 2H), 3.40 (s, 3H), 2.51-2.48 (d, $J$ = 7.0 Hz, 2H), 1.92 - 1.83 (m, 1H), 1.63-1.60 (d, $J$ = 7.0 Hz, 3H), 0.91-0.87 (m, 6H) ppm. $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 190.1, 172.3, 170.9, 163.6, 160.6, 159.6, 141.0, 137.4, 136.9, 129.7 - 127.0 (Ar), 113.7, 70.0, 58.9, 53.0, 45.0, 41.3, 38.8, 33.6, 30.2, 22.3, 18.4 ppm.
(S)-6-(Chloromethyl)-2-(4-methoxy-3,4-dioxo-1-phenylbutyl)-4-oxo-4H-pyran-3-yl undec-10-enoate (12): Colorless oil (41.8 mg, 85% yield) $^1$H NMR (300 MHz, CDCl$_3$) δ 7.37 – 7.28 (m, 5H), 6.42 (m, 1H), 5.91 – 5.76 (m, 1H), 5.04 – 4.93 (m, 2H), 4.75 (m, 1H), 4.33 – 4.15 (m, 4H), 3.88 (m, 2H), 3.64 (t, $J$ = 7.8 Hz, 1H), 2.61 (m, 2H), 2.06 (m, 4H), 1.34 (m, 12H) ppm. $^{13}$C NMR (75 MHz, CDCl$_3$) δ 190.3, 172.1, 169.9, 160.9, 159.7, 139.1, 137.3, 129.1, 128.1, 127.7, 115.0, 114.1, 53.2, 49.1, 41.7, 40.9, 39.1, 33.9, 33.7, 33.6, 29.6, 29.2, 29.1, 29.0, 29.0, 28.9, 25.6, 24.9, 24.7, 14.1 ppm. HRMS (ESI): m/z M + NH$_4^+$ calcd for C$_{28}$H$_{33}$ClO$_7$NH$_4^+$ 534.2254, found 534.2243.

\[
\begin{align*}
\text{12}
\end{align*}
\]
4. HPLC data for adducts 8

(S)-Methyl 2-hydroxy-6-methyl-8-oxo-4-phenyl-2,3,4,8-tetrahydropyano[3,2-b]pyran-2-carboxylate (8aa): CHIRALPAC OD-H, n-hexane-iPrOH 90/10, 1 mL/min, 220 nm, $t_{\text{major}} = 7.3$ min, $t_{\text{minor}} = 12.1$ min

Rac  

Chiral 8aa

(S)-Methyl 2-hydroxy-6-(methoxymethyl)-8-oxo-4-phenyl-2,3,4,8-tetrahydropyano[3,2-b]pyran-2-carboxylate (8ba): CHIRALPAC OD-H, n-hexane-iPrOH 90/10, 1 mL/min, 220 nm, $t_{\text{minor}} = 15.8$ min, $t_{\text{major}} = 23.0$ min.

Rac  

Chiral 8ba
(S)-Methyl 4-(4-cyanophenyl)-2-hydroxy-6-(methoxymethyl)-8-oxo-2,3,4,8-tetrahydropyran-2-carboxylate (8bb): CHIRALPAC OJ-H, n-hexane-iPrOH 70/30, 1 mL/min, 220 nm, $t_{\text{major}} = 12.6$ min, $t_{\text{minor}} = 15.1$ min

Rac

Chiral 8bb

(5)-Methyl 4-(furan-2-yl)-2-hydroxy-6-(methoxymethyl)-8-oxo-2,3,4,8-tetrahydropyran-2-carboxylate (8bc): CHIRALPAC OJ-H, n-hexane-iPrOH 70/30, 1 mL/min, 220 nm, $t_{\text{major}} = 11.5$ min, $t_{\text{minor}} = 16.2$ min

Rac

Chiral 8bc
(S)-Methyl 2-hydroxy-8-oxo-4-phenyl-6-((phenylthio)methyl)-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8ca): CHIRALPAC OJ-H, \( n \)-hexane-PrOH 70/30, 1 mL/min, 220 nm, \( t_{\text{major}} = 5.6 \) min, \( t_{\text{minor}} = 17.9 \) min

**Rac**

**Chiral 8ca**

(Rac)

(Chiral 8ca)

(S)-Methyl 6-(((4-fluorophenyl)thio)methyl)-2-hydroxy-8-oxo-4-phenyl-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8da): CHIRALPAC OJ-H, \( n \)-hexane-PrOH 70/30, 1 mL/min, 220 nm, \( t_{\text{minor}} = 23.1 \) min, \( t_{\text{major}} = 35.1 \) min

**Rac**

**Chiral 8da**

(Rac)

(Chiral 8da)
(S)-Methyl 6-(((2-fluorophenyl)thio)methyl)-2-hydroxy-8-oxo-4-phenyl-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8ea): CHIRALPAC OJ-H, \( n \)-hexane-\( i \)PrOH 70/30, 1 mL/min, 220 nm, \( t_{\text{major}} = 22.8 \) min, \( t_{\text{minor}} = 26.8 \) min

\[ \text{Rac} \quad \text{Chiral 8ea} \]

(S)-Methyl 4-(4-cyanophenyl)-6-(((2-fluorophenyl)thio)methyl)-2-hydroxy-8-oxo-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8eb): CHIRALPAC OJ-H, \( n \)-hexane-\( i \)PrOH 70/30, 1 mL/min, 220 nm, \( t_{\text{major}} = 20.0 \) min, \( t_{\text{minor}} = 22.8 \) min

\[ \text{Rac} \quad \text{Chiral 8eb} \]
(S)-Methyl 6-(((2,4-difluorophenyl)thio)methyl)-2-hydroxy-8-oxo-4-phenyl-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8fa): CHIRALPAC OJ-H, \( n \)-hexane-PrOH 70/30, 1 mL/min, 220 nm, \( t_{\text{minor}} = 7.3 \) min, \( t_{\text{major}} = 8.8 \) min

\( \text{Rac} \quad \text{Chiral 8fa} \)

(\( S \))-Methyl 4-(4-cyanophenyl)-6-(((2,4-difluorophenyl)thio)methyl)-2-hydroxy-8-oxo-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8fb): CHIRALPAC OJ-H, \( n \)-hexane-PrOH 70/30, 1 mL/min, 220 nm, \( t_{\text{major}} = 17.3 \) min, \( t_{\text{minor}} = 20.0 \) min

\( \text{Rac} \quad \text{Chiral 8fb} \)
(S)-Methyl 6-(((4-chlorophenyl)thio)methyl)-2-hydroxy-8-oxo-4-phenyl-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8ga): CHIRALPAC OJ-H, *n*-hexane-PrOH 70/30, 1 ml/min, 220 nm, *t*\(_{\text{minor}}\) = 8.2 min, *t*\(_{\text{major}}\) = 11.3 min

Rac

Chiral 8ga

(S)-Methyl 6-(((4-chlorophenyl)thio)methyl)-4-(4-cyanophenyl)-2-hydroxy-8-oxo-2,3,4,8-tetrahydropyrano[3,2-b]pyran-2-carboxylate (8gb): CHIRALPAC OJ-H, *n*-hexane-PrOH 70/30, 1 mL/min, 220 nm, *t*\(_{\text{major}}\) = 20.7 min, *t*\(_{\text{minor}}\) = 25.2 min

Rac

Chiral 8gb
(S)-Methyl 6-(chloromethyl)-2-hydroxy-8-oxo-4-phenyl-2,3,4,8-tetrahydropyra[3,2-b]pyran-2-carboxylate (8ha): CHIRALPAC OD-H, n-hexane-iPrOH 90/10, 1 mL/min, 220 nm, $t_{\text{minor}} = 21.0$ min, $t_{\text{major}} = 29.2$ min

\[ \text{Rac} \quad \text{Chiral 8ha} \]

(5)-Methyl 2-hydroxy-6-(morpholinomethyl)-8-oxo-4-phenyl-2,3,4,8-tetrahydropyra[3,2-b]pyran-2-carboxylate (8ia): CHIRALPAC OD-H, n-hexane-iPrOH 90/10, 1 mL/min, 220 nm, $t_{\text{minor}} = 16.1$ min, $t_{\text{major}} = 20.2$ min

\[ \text{Rac} \quad \text{Chiral 8ha} \]
5. HRMS pictures of catalyst V and compounds 11 and 12

Freshly prepared catalyst V
Catalyst V after regeneration
HRMS data for compound 11
6. Literature