Supporting Information

Towards a universal organocatalyst for the synthesis of enantioenriched phenylalanine derivatives by enantioselective decarboxylative protonation

Morgane Pigeaux[a], Romain Laporte[a], David C. Harrowven[b], Jérôme Baudoux[a,*], Jacques Rouden[a,*]

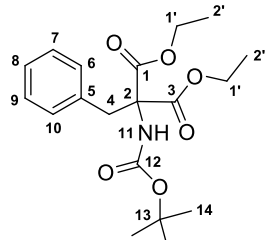
[a] *Normandie Univ., LCMT, ENSICAEN, UNICAEN, CNRS, 6 Boulevard du Maréchal Juin, 14000-France*
[b] *Department of Chemistry, University of Southampton, Highfield, Southampton SO17 1BJ, United Kingdom*

jerome.baudoux@ensicaen.fr ; Jacques.rouden@ensicaen.fr

General information. All reagents were purchased from Acros Organics, Sigma Aldrich, Alfa Aesar, TCI or Fluka and were used without further purification and used as received. Solvents were used in RPE grade without further purification. Anhydrous solvents were obtained from a PURESOLV SPS400 apparatus developed by Innovative Technology Inc. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX 400 MHz or a Bruker DRX 500 MHz spectrometer. Samples were dissolved in an appropriate deuterated solvent ($CDCl_3$, acetone-d6, MeOD, D_2O). The chemical shifts (δ) are expressed in ppm relative to internal tetramethylsilane for ^{1}H and ^{13}C nuclei, and coupling constants are indicated in Hz. Abbreviations for signal coupling are as follows: s = singlet; d = doublet; dd = doublet of doublets; t = triplet; q = quartet; quin = quintet; m = multiplet; br = broad signal. To assign the signals to the different proton and carbon atoms, as well as the relative stereochemistry of the cycloadducts, additional 2D NMR experiments (COSY, HSQC, HMBC) and NOESY experiments were performed. Mass spectra were obtained on a GC/MS Saturn 2000 spectrometer. High-resolution mass spectra (HRMS) were performed on Q-TOF Micro WATERS by electrospray ionisation (ESI). Infrared (IR) spectra were recorded with a Perkin Elmer 16 PC FT-IR ATR spectrometer, using the pure product (oil or solid). Thin Layer Chromatography (TLC) was run on pre-coated aluminum plates of silica gel 60 F-254 (Merck). Flash chromatography was performed on silica gel column (Merck silica gel, 40-63 µm) using air pressure. Some compounds (**3a** and **3b**) were known in literature and synthesized as described below.[1]

1) Synthesis of malonates

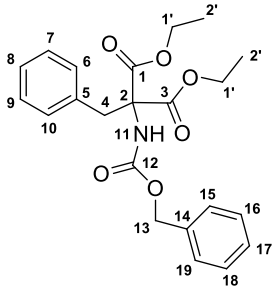
2-(*N*-(tert-butoxycarbonyl)amino)-2-benzyl-propanedioic diethyl ester



To a solution of diethyl 2-[(tert-butoxycarbonyl)amino]malonate (1.0 g, 3.63 mmol, 1 eq) in DMF (50 mL) was added sodium hydride (60% in oil, 0.113 g, 8.61 mmol, 1.3 eq) portionwise. Then, benzyl bromide (0.932 g, 9.94 mmol, 1.5 eq) was added dropwise and the solution was stirred for 24h at room temperature. Water (200 mL) was added and the mixture was extracted with diethyl ether (3*50 mL). The combined organic layers were dried over $MgSO_4$ and the volatiles were removed under reduced pressure. The purification of the crude product by flash chromatography on silica gel with cyclohexane/ethyl acetate (9/1) afforded the diester as colorless oil in 68 % yield (662 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (t, $^{3}J_{HH}$ = 7.1 Hz, 6H, $H^{2'}$), 1.48 (s, 9H, H^{14}), 3.62 (s, 2H, H^{4}), 4.17-4.35 (m, 4H, $H^{1'}$), 5.74 (br s, 1H, H^{11}), 7.04-7.06 (m, 2H, H^{6}+H^{10}), 7.21-7.30 (m, 3H, H^{7}+H^{8}+H^{9}). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0 ($C^{2'}$), 28.2 (C^{14}), 38.3 (C^{4}), 62.5 ($C^{1'}$), 67.1 (C^{2}), 80.17 (C^{13}), 127.1 (C^{8}), 128.2 (C^{7}+C^{9}), 130.0 (C^{6}+C^{10}), 135.3 (C^{5}), 153.8 (C^{12}), 167.6 (C^{1}+C^{3}). HRMS (ESI) calculated for $C_{19}H_{28}NO_6$ MH^+ 366.1917; found 366.1916. IR (cm^{-1}) ν 3434, 1740, 1714, 1484, 1158, 700.

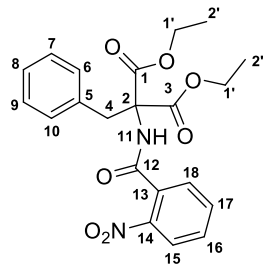
[1] M.-Y. Chang, C.-Y. Lin, P.-P. Sun *J. Chin. Chem. Soc.*, **2005**, *52*, 1061-1067. A. Kumar, G. Oehme, J.-P. Roque, M. Schwarze, R. Selke *Angew. Chem.*, **1994**, *106*, 2272-2275. X. Lv, Y. Yu, M. Zhou, C. Hu, F. Gao, J. Li, X. Liu, K. Deng, P. Zheng, W. Gong, A. Xia, J. Wang *J. Am. Chem. Soc.*, **2015**, *137*, 7270-7273. I. S. R. Stenhagen, A. K. Kirjavainen, S. J. Forsback, C. G. Jorgensen, E. G. Robins, S. K. Luthra, O. Solin, V. Gouverneur *Chem. Commun.*, **2013**, *49*, 1386-1388.

2-(*N*-(benzyloxycarbonyl)amino)-2-benzyl-propanedioic diethyl ester



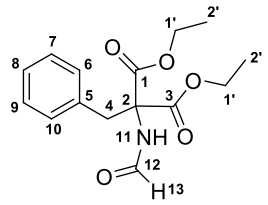
To a solution of diethyl 2-(benzyloxycarbonyl)aminomalonate (3.00 g, 9.69 mmol, 1 eq) in DMF (30 mL) was added sodium hydride (60% in oil, 0.504 g, 12.6 mmol, 1.3 eq) by small portions. Then, benzyl bromide (2.48 g, 14.54 mmol, 1.5 eq) was added dropwise and the solution was stirred for 24h at room temperature. Water (200 mL) was added and the mixture was extracted with diethyl ether (3*50 mL). The combined organic layers were dried over $MgSO_4$ and the volatile compounds were removed under reduced pressure. The purification of the crude product by flash chromatography on silica gel with cyclohexane/ethyl acetate (9/1) afforded the title compound as colorless oil in 88 % yield (3.44 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (t, $^3J_{HH}$ = 7.1 Hz, 6H, $H^{2'}$), 3.64 (s, 2H, H^4), 4.20-4.33 (m, 4H, $H^{1'}$), 5.18 (s, 2H, H^{13}), 5.99 (s, 1H, H^{11}), 6.95-6.98 (m, 2H, H^6+H^{10}), 7.20-7.22 (m, 3H, H^7+H^8+H^9), 7.33-7.41 (m, 5H, H^{15}-H^{19}). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9 ($C^{2'}$), 38.1 (C^4), 62.6 ($C^{1'}$), 66.8 (C^2), 67.3 (C^{13}), 127.1 (C^7+C^8+C^9), 128.2 (C^{15}+C^{19}), 128.4 (C^6+C^{10}), 129.9 (C^{16}+C^{17}+C^{18}), 134.9 (C^5), 136.3 (C^{14}), 154.3 (C^{12}), 167.3 (C^1+C^3). HRMS (ESI) calculated for $C_{22}H_{26}NO_6$ MH^+ 400.1760; found 400.1764. IR (cm^{-1}) ν 2982, 1722, 1489, 1197, 1027, 700.

2-(*N*-(2-nitrobenzoyl)amino)-2-benzyl-propanedioic diethyl ester



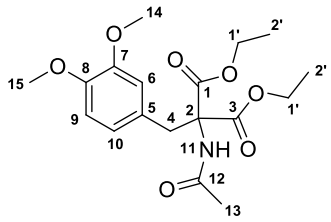
To a solution of diethyl 2-(2-nitrobenzoyl)aminomalonate (8.5 g, 26.2 mmol, 1 eq) in DMF (40 mL) was added sodium hydride (60% in oil, 1.37 g, 34.0 mmol, 1.3 eq) portionwise. Then, benzyl bromide (4.67 mL, 39.3 mmol, 1.5 eq) was added dropwise and the solution was stirred for 24h at room temperature. Water (200 mL) was added and the mixture was extracted with diethyl ether (3*50 mL). The combined organic layers were dried over $MgSO_4$ and the volatile compounds were removed under reduced pressure. The purification of the crude product by flash chromatography on silica gel with cyclohexane/ethyl acetate (8/2) afforded the title compound as a solid in 80 % yield (8.68 g). Mp 94-95 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (t, $^3J_{HH}$ = 7.1 Hz, 6H, $H^{2'}$), 3.79 (s, 2H, H^4), 4.27-4.35 (m, 4H, $H^{1'}$), 7.05 (s Br, 1H, H^{11}), 7.18-7.22 (m, 2H, H^7+H^9), 7.24-7.29 (m, 3H, H^6+H^{10}+H^8), 7.38-7.40 (m, 1H, H^{18}), 7.54-7.62 (m, 2H, H^{17}+H^{16}), 7.96-7.98 (m, 1H, H^{15}). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9 ($C^{2'}$), 37.9 (C^4), 62.9 ($C^{1'}$), 67.6 (C^2), 124.6 (C^{15}), 127.3 (C^8), 128.3 (C^7+C^9), 128.5 (C^{18}), 130.0 (C^6+C^{10}), 131.0 (C^{16}), 131.4 (C^{13}), 133.2 (C^{17}), 134.9 (C^5), 147.3 (C^{14}), 164.6 (C^{12}), 167.1 (C^1+C^3). HRMS (ESI) calculated for $C_{21}H_{23}N_2O_7$ MH^+ 415.1505; found 415.1492. IR (cm^{-1}) ν 3357, 1763, 1732, 1660, 1513, 1209.

2-(*N*-formamido)-2-benzyl-propanedioic diethyl ester



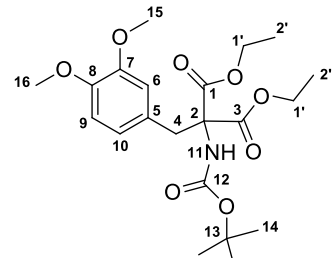
To a solution of formamidomalonate (3.0 g, 14.7 mmol, 1 eq) in DMF (40 mL) was added sodium hydride (60% in oil, 0.76 g, 19.2 mmol, 1.3 eq) portionwise. Then, benzyl bromide (2.77 g, 16.2 mmol, 1.1 eq) was added dropwise and the solution was stirred for 24h at room temperature. Water (200 mL) was added and the mixture was extracted with diethyl ether (3*50 mL). The combined organic layers were dried over $MgSO_4$ and the volatiles were removed under reduced pressure. Purification of the crude product by flash chromatography on silica gel with cyclohexane/ethyl acetate (9/1) afforded the diethyl ester as a white solid in 77% yield (3.366g). Mp 99 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (t, $^3J_{HH}$ = 7.1 Hz, 6H, $H^{2'}$), 3.68 (s, 2H, H^4), 4.25-4.34 (m, 4H, $H^{1'}$), 6.73 (br s, 1H, H^{11}), 7.04-7.06 (m, 2H, H^6+H^{10}), 7.26 (d, 2H, $^3J_{HH}$ = 1.9 Hz H^7+H^9), 7.27-7.28 (m, 1H, H^8), 8.19 (s, 1H, H^{13}). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9 ($C^{2'}$), 37.8 (C^4), 62.8 ($C^{1'}$), 66.6 (C^2), 127.3 (C^8), 128.3 (C^7+C^9), 129.9 (C^6+C^{10}), 134.7 (C^5), 159.8 (C^{12}), 167.1 (C^1+C^3). HRMS (ESI) calculated for $C_{15}H_{19}NO_5Na$ [M+Na^+] 316.1161; found 316.1158. IR (cm^{-1}) ν 2905, 1736, 1653, 1190, 700.

2-(*N*-acetylamino)-2-(3,4-diméthoxybenzyl)-propanedioic diethyl ester



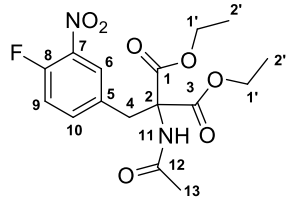
To a solution of acetamidomalonate (4.0 g, 18.4 mmol, 1 eq) in DMF (50 mL) was added sodium hydride (60% in oil, 0.883 g, 22.0 mmol, 1.2 eq) portionwise. Then, 3,4-diméthoxybenzyl chloride (5.15 g, 27.6 mmol, 1.5 eq) was added dropwise and the solution was stirred for 24h at room temperature. Water (200 mL) was added and the mixture was extracted with diethyl ether (3*50 mL). The combined organic layers were dried over $MgSO_4$. After removal of the volatiles under reduced pressure the crude product was purified by flash chromatography on silica gel with cyclohexane/ethyl acetate (7/3) afforded the diester as a white solid in 77 % yield (5.20 g). Mp 73 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27 (t, $^3J_{HH}$ = 7.1 Hz, 6H, $H^{2'}$), 2.00 (s, 3H, H^{13}), 3.57 (s, 2H, H^4), 3.78 (s, 3H, H^{14}), 3.82 (s, 3H, H^{15}), 4.20-4.29 (m, 4H, $H^{1'}$), 4.59 (s, 1H, H^{11}), 6.50-6.54 (m, 3H, H^6+H^9+H^{10}), ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0 ($C^{2'}$), 23.0 (C^{13}), 37.4 (C^4), 55.8 (C^{14}+C^{15}), 62.6 ($C^{1'}$), 67.3 (C^2), 111.8 (C^9), 113.1 (C^6), 121.9 (C^{10}), 127.6 (C^5), 148.2 (C^8), 148.6 (C^7), 167.5 (C^1+C^3), 169.0 (C^{12}). HRMS (ESI) calculated for $C_{18}H_{25}NO_7Na$ [M+Na^+] 390.1529; found 390.1547. IR (cm^{-1}) ν 3283, 2979, 1743, 1645, 1188.

2-(*N*-(tert-butoxycarbonyl)amino)-2-(3,4-diméthoxybenzyl)-propanedioic diethyl ester



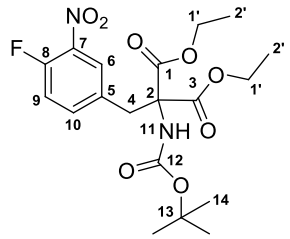
To a solution of diethyl 2-[(tert-butoxycarbonyl)amino]malonate (5.22 g, 18.99 mmol, 1 eq) in DMF (80 mL) was added sodium hydride (60% in oil, 0.911 g, 22.79 mmol, 1.2 eq) portionwise. Then, 3,4-diméthoxybenzyl chloride (5.30 g, 28.40 mmol, 1.5 eq) was added dropwise and the solution was stirred for 24h at room temperature. Water (200 mL) was added and the mixture was extracted with diethyl ether (3*50 mL). The combined organic layers were dried over $MgSO_4$ and the volatiles were removed under reduced pressure. The purification of the crude product by flash chromatography on silica gel with cyclohexane/ethyl acetate (9/1) afforded the diester as pale yellow oil in 84 % yield (6.77 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25 (t, $^3J_{HH}$ = 7.1 Hz, 6H, $H^{2'}$), 1.44 (s, 9H, H^{14}), 3.52 (s, 2H, H^4), 3.80 (s, 3H, H^{15}), 3.81 (s, 3H, H^{16}), 4.14-4.32 (m, 4H, $H^{1'}$), 5.73 (br s, 1H, H^{11}), 6.55 (s, 1H, H^6), 6.56 (d, $^3J_{HH}$ = 7.9 Hz, 1H, H^{10}), 6.73 (d, $^3J_{HH}$ = 7.9 Hz, 1H, H^9). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0 ($C^{2'}$), 28.3 (C^{14}), 37.9 (C^4), 55.7 (C^{15}+C^{16}), 62.4 ($C^{1'}$), 67.2 (C^2), 80.1 (C^{13}), 110.9 (C^9), 113.4 (C^6), 121.9 (C^{10}), 127.7 (C^5), 148.1 (C^8), 148.5 (C^7), 158.8 (C^{12}), 167.6 (C^1+C^3). HRMS (ESI) calculated for $C_{21}H_{31}NO_8$ [M+Na]$^+$ 448.1947; found 448.1927. IR (cm^{-1}) ν 3436, 2981, 1732, 1712, 1252, 1158.

2-(*N*-acetylamino)-2-(4-fluoro-3-nitrobenzyl)propanedioic diethyl ester



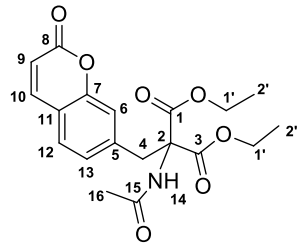
To a solution of acetamidomalonate (1.16 g, 5.34 mmol, 1 eq) in DMF (20 mL) was added sodium hydride (60% in oil, 0.298 g, 1.4 eq) by small portion. Then, 4-fluoro-3-nitrobenzyl bromide (1.5 g, 1.2 eq) was added portionwise and the solution was stirred for 24h at room temperature. Water (70 mL) was added and the mixture was extracted with diethyl ether (3*20 mL). The combined organic layers were dried over $MgSO_4$ and the volatiles were removed under reduced pressure. The purification of the crude product by flash chromatography on silica gel with petroleum ether/ethyl acetate (6/4) afforded the diester as a slightly yellow solid in 74 % yield (1.75 g). Mp 123 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32 (t, $^3J_{HH}$ = 7.2 Hz, 6H, $H^{2'}$), 2.07 (s, 3H, H^{13}), 3.73 (s, 2H, H^4), 4.29 (q, $^3J_{HH}$ = 7.2 Hz, 4H, $H^{1'}$), 6.58 (br s, 1H, H^{11}), 7.20 (dd, $^3J_{HF}$ = 10.2 Hz, $^3J_{HH}$ = 8.4, 1H, H^9), 7.28-7.33 (m, 1H, H^6), 7.73 (dd, $^3J_{HH}$ = 7.3, $^4J_{HH}$ = 2.2 Hz, 1H, H^{10}). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.0 ($C^{2'}$), 23.0 (C^{13}), 36.7 (C^4), 63.1 ($C^{1'}$), 66.9 (C^2), 118.4 (d, $^2J_{CF}$ = 20.7 Hz, C^9), 127.0 (C^{10}), 132.5 (C^5), 136.9 (C^6), 137.0 (C^7), 155.0 (d, $^1J_{CF}$ = 265.2 Hz, C^8), 167.0 (C^1+C^3), 169.5 (C^{12}). ^{19}F NMR ($CDCl_3$) δ -119.52. HRMS (ESI) calculated for $C_{16}H_{19}N_2O_7FNa$ [M+Na^+] 393.1074; found 393.1059. IR (cm^{-1}) ν 3242, 1741, 1641, 1193, 817.

2-(*N*-Boc-amino)-2-(4-fluoro-3-nitrobenzyl)propanedioic diethyl ester



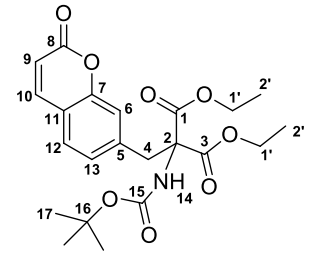
To a solution of diethyl *N*-Boc-aminomalonate (1.5 g, 5.45 mmol, 1 eq) in freshly distilled DMF (20 mL) was added sodium hydride (60% in oil, 0.261 g, 1.2 eq) portionwise. Then, 4-fluoro-3-nitrobenzyl bromide (1.53 g, 1.2 eq) was added and the solution stirred at room temperature during one day. The reaction mixture was hydrolysed with 70 mL of water and extracted with 3*50 mL of CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and the solvent removed under vacuum. Crude product was purified by flash chromatography on silica gel with petroleum ether/ ethyl acetate (9/1) to afford the diester as yellow oil in 59 % yield (1.38 g). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.30 (t, $^3J_{HH}$ = 7.5Hz, 6H, $H^{2'}$), 1.48 (s, 9H, H^{14}), 3.68 (s, 2H, H^4), 4.17-4.37 (m, 4H, $H^{1'}$), 5.76 (br s, 1H, H^{11}), 7.20 (dd, $^3J_{HF}$ = 10.4 Hz, $^3J_{HH}$ = 8.6 Hz, 1H, H^9), 7.30-7.35 (m, 1H, H^6), 7.77 (dd, $^3J_{HH}$ = 7.3, $^4J_{HF}$ = 2.2 Hz, 1H, H^{10}). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.0 ($C^{2'}$), 28.1 (C^{14}), 37.2 (C^4), 62.9 ($C^{1'}$), 66.8 (C^2), 80.8 (C^{13}), 118.2 (d, $^2J_{CF}$ = 21.4 Hz, C^9), 127.3 (C^6), 132.6 (C^5), 136.8 (d, $^3J_{CF}$ = 7.7 Hz, C^{10}), 137.1 (d, $^2J_{CF}$ = 9.2 Hz, C^7), 154.0 (C^{12}), 154.8 (d, $^1_{CF}$ = 264,1 Hz, C^8), 167.1 (C^1+C^3). ^{19}F NMR ($CDCl_3$) δ -119.91. HRMS (ESI) calculated for $C_{19}H_{25}N_2O_8FNa$ [M+Na^+] 451.1493; found 451.1502. IR (cm^{-1}) ν 3436, 2981, 1730, 1713, 1538, 1157.

Ethyl 2-acetamido-3-(2-oxo-2H-chromen-7-yl)propanoate



To a solution of acetamidomalonate (1.09 g, 5.02 mmol, 1.2 eq) in freshly distilled DMF (20 mL) was added sodium hydride (60 % in oil, 0.200 g, 5.02 mmol, 1.2 eq) portionwise. The coumarine chloromethyl coumpound (1 g, 4.2 mmol, 1 eq) was added and the solution was stirred at room temperature for one day. The reaction mixture was hydrolysed with 70 mL of water and extracted with 3*30 mL of CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and the volatiles were removed under vacuum. Crude product was purified by flash chromatography on silica gel with petroleum ether/ ethyl acetate (6/4) to afford the diester as a white solid in 55 % yield (0.87 g). Mp 192 °C.^{1}H NMR (300 MHz, $CDCl_3$) δ 1.31 (t, $^3J_{HH}$ = 7.1 Hz, 6H, $H^{2'}$), 2.05 (s, 3H, H^{16}), 3.75 (s, 2H, H^4), 4.24-4.34 (m, 4H,$H^{1'}$), 6.40 (d, $^3J_{HH}$ = 9.5 Hz, 1H, H^9), 6.57 (br s, 1H, H^{14}), 6.93 (br d, $^3J_{HH}$ = 8 Hz, 1H, H^{13}), 6.95 (d, $^4J_{HH}$ = 2 Hz, 1H, H^6), 7.38 (d, $^3J_{HH}$ = 8 Hz, 1H, H^{12}), 7.67 (d, $^3J_{HH}$ = 9.5 Hz, 1H, H^{10}). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.0 ($C^{2'}$), 23.0 (C^{16}), 37.7 (C^4), 62.9 ($C^{1'}$), 67.0 (C^2), 116.5 (C^9), 117.9 (C^6+C^{11}), 126.3 (C^{13}), 127.6 (C^{12}), 140.2 (C^5), 143.0 (C^{10}), 153.9 (C^7), 160.6 (C^8), 167.1 (C^1+C^3), 169.3 (C^{15}). HRMS (ESI) calculated for $C_{19}H_{21}NO_7Na$ [M+Na^+] 398.1216; found 398.1208. IR (cm^{-1}) ν 3349, 1729, 1621, 1184.

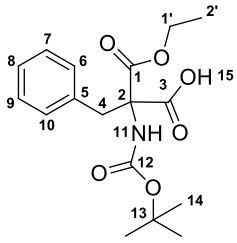
Ethyl 2-(*N*-(tert-butoxycarbonyl)amino)-3-(2-oxo-2H-chromen-7-yl)propanoate



To a solution of diethyl *N*-Boc-aminomalonate (1.38 g, 5.02 mmol, 1.2 eq) in freshly distilled DMF (20 mL) was added sodium hydride (60% in oil, 0.200 g, 1.2 eq) portionwise. Then, the coumarine chloromethyl coumpound (1 g, 4.18 mmol, 1 eq) was added and the solution was stirred at room temperature for one day. The reaction mixture was hydrolyzed with 70 mL of water and extracted with 3*50 mL of CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and the volatiles removed under vacuum. The crude product was purified by flash chromatography on silica gel with petroleum ether/ ethyl acetate (9/1) to afford the diester as a white solid in 56 % yield (1.00 g). Mp 117 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29 (t, $^3J_{HH}$ = 6.0 Hz, 6H, $H^{2'}$), 1.48 (s, 9H, H^{17}), 3.70 (s, 2H, H^4), 4.20-4.34 (m, 4H, $H^{1'}$), 5.76 (br s, 1H, H^{14}), 6.39 (d, $^3J_{HH}$ = 9.0 Hz, 1H, H^9), 6.97 (d, $^3J_{HH}$ = 7.8 Hz, 1H, H^{13}), 7.02 (s, 1H, H^6), 7.38 (d, $^3J_{HH}$ = 7.8 Hz, 1H, H^{12}), 7.67 (d, $^3J_{HH}$ = 9.0 Hz, 1H, H^{10}). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.0 ($C^{2'}$), 28.2 (C^{17}), 38.3 (C^4), 62.8 ($C^{1'}$), 66.9 (C^2), 80.6 (C^{16}), 116.3 (C^9), 117.7 (C^6), 118.1 (C^{11}), 126.3 (C^{13}), 127.5 (C^{12}), 140.3 (C^5), 143.1 (C^{10}), 153.8 (C^7), 153.9 (C^8), 160.7 (C^1+C^3), 167.3 (C^{15}). HRMS (ESI) calculated for $C_{22}H_{27}NO_8Na$ [M+Na^+] 456.1634; found 456.1635. IR (cm^{-1}) ν 3436, 2977, 1712, 1620, 1159.

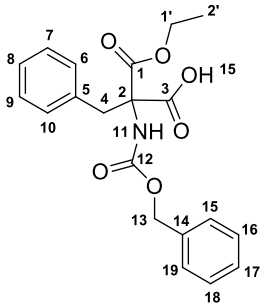
2) Synthesis of Malonic Acid Half Oxyesters (MAHOs)

2-(N-(tert-butoxycarbonyl)amino)-2-benzyl-propanedioic acid ethyl monoester (**2a**)



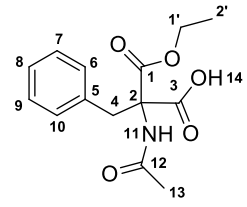
To a solution of KOH (0.384 g, 6.84 mmol, 5 eq) in 24 mL of water and ethanol (1:1) was added 2-(*N*-(tert-butoxycarbonyl)amino)-2-benzyl-propanedioic diethyl ester (0.5 g, 1.36 mmol, 1 eq). The reaction mixture was stirred during one day at room temperature. After concentration of 70 % of solvent at room temperature, and addition of 50 mL of water, the basic aqueous phase was extracted with diethyl ether (3*20 mL). The aqueous phase was then slowly acidified with a 1M HCl solution in an ice bath until pH = 2. The acidic aqueous phase was extracted with 3*30 mL of CH_2Cl_2 and the combined organic layers were dried over $MgSO_4$. Evaporation of volatile compounds under reduced pressure afforded the monoester as a white solid in 98 % yield (452 mg). Mp 65 °C. ^{1}H NMR (400 MHz, MeOD) δ 1.27 (t, $^3J_{HH}$ = 7.0 Hz, 3H, $H^{2'}$), 1.48 (s, 9H, H^{14}), 3.50-3.55 (m, 2H, H^4), 4.15-4.31 (m, 2H, $H^{1'}$), 7.06-7.08 (m, 2H, H^6+H^{10}), 7.19-7.24 (m, 3H, H^7+H^8+H^9). ^{13}C NMR (100 MHz, MeOD) δ 14.3 ($C^{2'}$), 28.7 (C^{14}), 39.1 (C^4), 63.3 ($C^{1'}$), 68.3 (C^2), 81.2 (C^{13}), 128.0 (C^8), 129.2 (C^7+C^9), 131.1 (C^6+C^{10}), 136.8 (C^5), 155.8 (C^{12}), 169.6 (C^1), 170.0 (C^3). HRMS (ESI) calculated for $C_{17}H_{24}NO_6$ MH^+ 338.1604; found 338.1602. IR (cm^{-1}) ν 2980, 1716, 1682, 1495, 1156, 700.

2-(*N*-(benzyloxycarbonyl)amino)-2-benzyl-propanedioic acid ethyl monoester (**2b**)



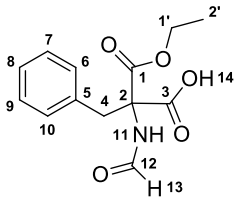
To a solution of KOH (0.702 g, 12.51 mmol, 5 eq) in 24 mL of water and ethanol (1:1) was added 2-(*N*-(benzyloxycarbonyl)amino)-2-benzyl-propanedioic diethyl ester (1.0 g, 2.50 mmol, 1 eq). The reaction mixture was stirred during one day at room temperature. After concentration of 70 % of solvent at room temperature, and addition of 50 mL of water, the basic aqueous phase was extracted with diethyl ether (3*20 mL). The aqueous phase was then slowly acidified with a 1M HCl solution in an ice bath until pH = 2. The acidic aqueous phase was extracted with 3*30 mL of CH_2Cl_2 and the combined organic layers were dried over $MgSO_4$. Evaporation of volatile compounds under reduced pressure afforded the monoester as a colorless oil in quantitative yield (927 mg). ^{1}H NMR (400 MHz, CD_3OD) δ 1.22 (t, $^3J_{HH}$ = 7.1 Hz, 3H, $H^{2'}$), 3.53-3.57 (m, 2H, H^4), 4.17-4.25 (m, 2H, $H^{1'}$), 5.13 (s, 2H, H^{13}), 6.95-6.98 (m, 2H, H^6+ H^{10}), 7.15-7.17 (m, 3H, H^7+H^8+H^9), 7.33-7.39 (m, 5H, H^{15}-H^{19}). ^{13}C NMR (100 MHz, CD_3OD) δ 14.2 ($C^{2'}$), 39.0 (C^4), 63.4 ($C^{1'}$), 67.7 (C^2), 68.7 (C^{13}), 128.0 (C^8), 129.1 (C^{15}+C^{19}), 129.2 (C^{16}+C^{17}+C^{18}), 129.5 (C^6+C^{10}), 131.1 (C^7-C^9), 136.6 (C^5), 138.2 (C^{14}), 156.4 (C^{12}), 169.4 (C^1), 169.8 (C^3). HRMS (ESI) calculated for $C_{21}H_{22}NO_6$ MH^+ 372.1447; found 372.1444. IR (cm^{-1}) ν 3417, 2980, 1723, 1263, 698.

2-(*N*-acetylamino)-2-benzyl-propanedioic acid ethyl monoester (**2c**)



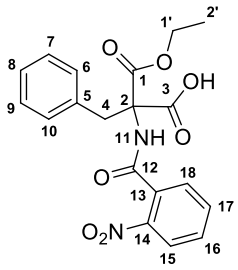
To a solution of KOH (0.91 g, 16.2 mmol, 5 eq) in 24 mL of water and ethanol (1:1) was added 2-(*N*-acetylamino)-2-benzyl-propanedioic diethyl ester (1.0 g, 3.25 mmol, 1 eq). The reaction mixture was stirred during one day at room temperature. After concentration of 70 % of solvent at room temperature, and addition of 50 mL of water, the basic aqueous phase was extracted with diethyl ether (3*20 mL). The aqueous phase was then slowly acidified with a 1M HCl solution in an ice bath until pH = 2. The acidic aqueous phase was extracted with 3*30 mL of CH_2Cl_2 and the combined organic layers were dried over $MgSO_4$. Evaporation of volatile compounds under reduced pressure afforded the monoester as a white solid in 95 % yield (863 mg). Mp 128 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 1.26 (t, $^3J_{HH}$ = 7.1 Hz, 3H, $H^{2'}$), 1.99 (s, 3H, H^{13}), 3.54 [A(AB), $^2J_{AB}$ = 13.8 Hz, 1H, H^4], 3.60 [B(AB), $^2J_{AB}$ = 13.8 Hz, 1H, H^4], 4.17-4.28 (m, 2H, $H^{1'}$), 7.04-7.06 (m, 2H, H^6+H^{10}), 7.18-7.27 (m, 3H, H^7+H^8+H^9). ^{13}C NMR (100 MHz, CD_3OD) δ 14.2 ($C^{2'}$), 22.4 (C^{13}), 38.7 (C^4), 63.3 ($C^{1'}$), 68.8 (C^2), 128.0 (C^8), 129.3 (C^7+C^9), 131.1 (C^6+C^{10}), 136.9 (C^5), 169.3 (C^{12}), 169.9 (C^1), 172.4 (C^3). HRMS (ESI) calculated for $C_{14}H_{18}NO_5$ MH^+ 280.1185; found 280.1189. IR (cm^{-1}) ν 3326, 1729, 1606, 1267, 701.

2-(*N*-formamido)-2-benzyl-propanedioic acid ethyl monoester (**2d**)



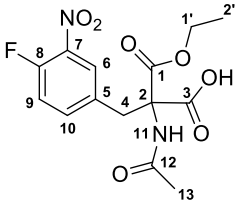
To a solution of KOH (0.151 g, 2.69 mmol, 1 eq) in 11 mL of water and ethanol (1:10) was added 2-(*N*-formamido)-2-benzyl-propanedioic diethyl ester (0.79 g, 2.69 mmol, 1 eq). The reaction mixture was stirred during one day at room temperature. After concentration of 70 % of solvent at room temperature and addition of 50 mL of water, the basic aqueous phase was extracted with diethyl ether (3*20 mL). The aqueous phase was then slowly acidified with a 1M HCl solution in an ice bath (pH = 2). The acidic aqueous phase was extracted with 3*30 mL of CH_2Cl_2 and the combined organic layers were dried over $MgSO_4$. Evaporation of volatile compounds under reduced pressure afforded the monoester as a white solid in 80 % yield (536 mg). Mp 120 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 1.16 (t, $^3J_{HH}$ = 7.1 Hz, 3H, $H^{2'}$), 3,42 [A(AB), $^2J_{AB}$ = 18.4 Hz, 1H, H^4], 3.46 [B(AB), $^2J_{AB}$ = 18.4 Hz, 1H, H^4], 4.12-4.18 (m, 2H, $H^{1'}$), 7.01-7.03 (m, 2H, H^6+H^{10}), 7.20-7.29 (m, 3H, H^7+H^8+H^9), 8.00 (d, $^3J_{HH}$ = 1,4 Hz, 1H, H^{13}), 8,33 (br s, 1H, H^{11}). ^{13}C NMR (100 MHz, CD_3OD) δ 13.8 ($C^{2'}$), 37.2 (C^4), 61.5 ($C^{1'}$), 66.1 (C^2), 126.8 (C^8), 128.0 (C^7+C^9), 129.8 (C^6+C^{10}), 135.3 (C^5), 160.7 (C^{12}), 167.3 (C^1), 168.0 (C^3). HRMS (ESI) calculated for $C_{13}H_{15}NO_5Na$ [M+Na^+] 288.0848; found 288.0841.

2-(*N*-(2-nitrobenzoyl)amino)-2-benzyl-propanedioic acid ethyl monoester (**2e**)



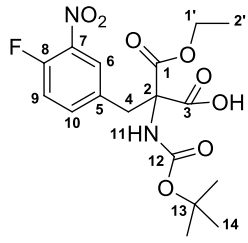
To a solution of KOH (0.677 g, 12.06 mmol, 5 eq) in 40 mL of water and ethanol (1:1) was added 2-(*N*-(2-nitrobenzoyl)amino)-2-benzyl-propanedioic diethyl ester (1.0 g, 2.41 mmol, 1 eq). The reaction mixture was stirred during one day at room temperature. After concentration of 70 % of solvent at room temperature, and addition of 50 mL of water, the basic aqueous phase was extracted with diethyl ether (3*20 mL). The aqueous phase was then slowly acidified with a 1M HCl solution in an ice bath until pH = 2. The acidic aqueous phase was extracted with 3*30 mL of CH_2Cl_2 and the combined organic layers were dried over $MgSO_4$. Evaporation of volatile compounds under reduced pressure afforded the monoester as a white solid in 98 % yield (914 mg). Mp 142 °C. ^{1}H NMR (400 MHz, MeOD) δ 1.31 (t, $^3J_{HH}$ = 7.1 Hz, 3H, $H^{2'}$), 3.68 [A(AB), $^2J_{AB}$ = 13.9 Hz, 1H, H^4], 3.75 [B(AB), $^2J_{AB}$ = 13.9 Hz, 1H, H^4], 4.27 (q, $^3J_{HH}$ = 7.1 Hz, 2H, $H^{1'}$), 7.23-7.31 (m, 5H, H^6-H^{10}), 7.46 (dd, $^3J_{HH}$ = 7.7 Hz, $^4J_{HH}$ = 1.5 Hz, 1H, H^{18}), 7.67 (td, $^3J_{HH}$ = 7.7 Hz, $^4J_{HH}$ = 1.6 Hz, 1H, H^{16}), 7.72 (td, $^3J_{HH}$ = 7.5 Hz, $^4J_{HH}$ = 1.4 Hz, 1H, H^{17}), 8.05 (dd, $^3J_{HH}$ = 7.7 Hz, $^4J_{HH}$ = 1.2 Hz,1H, H^{15}). ^{13}C NMR (125 MHz, MeOD) δ 12.8 ($C^{2'}$), 37.6 (C^4), 62.1 ($C^{1'}$), 67.9 (C^2), 124.2 (C^{15}), 126.8 (C^8), 127.9 (C^7+C^9), 128.8 (C^{18}), 130.0 (C^6+C^{10}), 130.9 (C^{16}), 131.3 (C^{13}), 133.1 (C^{17}), 135.3 (C^5), 147.2 (C^{14}), 166.3 (C^{12}), 167.6 (C^1) 168.2 (C^3). HRMS (ESI) calculated for $C_{19}H_{19}N_2O_7$ MH^+ 387.1192; found 387.1203. IR (cm^{-1}) ν 2970, 1738, 1672, 1531, 1349, 1203.

2-(*N*-acetylamino)-2-(4-fluoro-3-nitrobenzyl)propanedioic acid ethyl monoester (**7-Ac**)



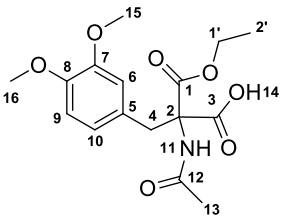
To a solution of KOH (0.045 g, 2 mmol, 1.5 eq) in 24 mL of water and ethanol (1:1) was added the diethyl ester (0.2 g, 1 eq). The reaction mixture was stirred during one day at room temperature. After concentration of 70 % of solvent at room temperature, the basic aqueous phase was extracted with diethyl ether (3*20 mL). The aqueous phase was then slowly acidified with a 1M HCl solution in an ice bath until pH = 2. The acidic aqueous phase was extracted with 3*30 mL of CH_2Cl_2 and the combined organic layers were dried over $MgSO_4$. The giving product was then obtained after removal of the solvent as a slightly yellow solid in 77 % yield (143 mg). Mp 117 °C. ^{1}H NMR (300 MHz, CD_3OD) δ 1.27 (t, $^3J_{HH}$ = 7.5 Hz, 3H, $H^{2'}$), 2.03 (s, 3H, H^{13}), 3.61 ([A(AB), $^2J_{AB}$ = 14.0 Hz, 1H, H^4]), 3.69 ([B(AB), $^2J_{AB}$ = 14.0 Hz, 1H, H^4]) 4.24 (q, $^3J_{HH}$ = 7.5 Hz, 2H, $H^{1'}$), 7.31-7.43 (m, 1H, H^9), 7.41-7.46 (m, 1H, H^6), 7.79 (dd, $^3J_{HH}$ = 7.1, $^4J_{HF}$ = 2.4 Hz, 1H, H^{10}). ^{13}C NMR (75.5 MHz, CD_3OD) δ 14.4 ($C^{2'}$), 22.5 (C^{13}), 38.0 (C^4), 63.7 ($C^{1'}$), 68.6 (C^2), 119.3 (d, $^2J_{CF}$ = 21.3 Hz, C^9), 128.4 (C^{10}), 134.6 (d, $^4J_{CF}$ = 3.5 Hz, C^5), 138.3 (d, $^3J_{CF}$ = 6.6 Hz, C^6), 138.7 (d, $^3J_{CF}$ = 9.1 Hz, C^7), 156.1(d, $^1J_{CF}$ = 262.4 Hz, C^8), 168.9 (C^1), 169.5 (C^{12}), 173.0 (C^3). ^{19}F NMR (CD_3OD) δ -122.67. HRMS (ESI) calculated for $C_{14}H_{15}N_2O_7FNa$ [M+Na^+] 365.0761; found 365.0750. IR (cm^{-1}) ν 3253, 1754, 1719, 1536, 1203.

2-(*N*-Bocamino)-2-(4-fluoro-3-nitrobenzyl)propanedioic acid ethyl monoester (**7-Boc**)



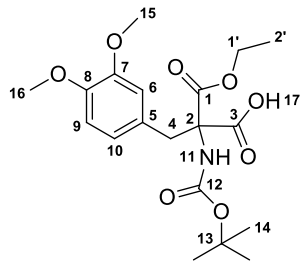
To a solution of KOH (98 mg, 1.75 mmol, 1.5 eq) in a mixture of 24 mL of water and ethanol (1:1) was added the diethyl ester (0.5 g, 1 eq) and the reaction mixture was stirred for one day at room temperature. After concentration of 70 % of solvent at room temperature, the basic aqueous phase was extracted with diethyl ether 3*20 mL. The aqueous phase was then slowly acidified with a 1M HCl solution in an ice bath (pH = 2-3). The acidic aqueous phase was extracted by 3*20 mL of CH_2Cl_2 and the combined organic layers were dried over $MgSO_4$. The giving product was then obtained after removal of the solvent as a white solid in 69 % yield (322 mg). Mp 75 °C. ^{1}H NMR (300 MHz, CD_3OD) δ 1.27 (t, $^3J_{HH}$ = 7.2 Hz, 3H, $H^{2'}$), 1.48 (s, 9H, H^{14}), 3.58-3.69 (m, 2H, H^4), 4.18-4.28 (m, 2H, $H^{1'}$), 7.33 (dd, $^3J_{HF}$ = 11.0 Hz, $^3J_{HH}$ = 8.6 Hz, 1H, H^9), 7.42-7.46 (m, 1H, H^6), 7.80 (dd, $^3J_{HH}$ = 6.7 Hz, $^4J_{HF}$= 1.3 Hz, 1H, H^{10}). ^{13}C NMR (75.5 MHz, CD_3OD) δ 14.3 ($C^{2'}$), 28.6 (C^{14}), 38.1 (C^4), 63.7 ($C^{1'}$), 68.2 (C^2), 81.4 (C^{13}), 119.1 (d, $^2J_{CF}$ = 15.6 Hz, C^9), 128.4 (d, $^3J_{CF}$ = 8.4 Hz, C^{10}), 134.6 (C^5), 138.5 (d, $^3J_{CF}$ = 6.4 Hz, C^6), 145.2 (d, $^2J_{CF}$ = 6.6 Hz, C^7), 154.2 (d, $^1J_{CF}$ = 257.3 Hz, C^8), 157.2 (C^{12}), 169.3 (C^1), 169.6 (C^3). ^{19}F NMR (CD_3OD) -123.09. HRMS (ESI) calculated for $C_{17}H_{21}N_2O_8FNa$ [M+Na^+] 423.1180; found 423.1162. IR (cm^{-1}) ν 2980, 1737, 1620, 1250.

2-(*N*-acetylamino)-2-(3,4-diméthoxybenzyl)-propanedioic acid ethyl monoester (**8-Ac**)



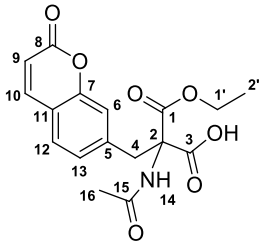
To a solution of KOH (0.381 g, 6.80 mmol, 5 eq) in 24 mL of water and ethanol (1:1) was added the diethyl ester (0.5 g, 1.36 mmol, 1 eq). The reaction mixture was stirred during one day at room temperature. After concentration of 70 % of solvent at room temperature, and addition of 50 mL of water, the basic aqueous phase was extracted with diethyl ether (3*20 mL). The aqueous phase was then slowly acidified with a 1M HCl solution in an ice bath (pH = 2). The acidic aqueous phase was extracted with 3*30 mL of CH_2Cl_2 and the combined organic layers were dried over $MgSO_4$. Evaporation of volatile compounds under reduced pressure afforded 2-(*N*-acetylamino)-2-(3,4-diméthylbenzyl)-propanedioic acid ethyl monoester as a white solid in 76 % yield (350 mg). Mp 148 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 1.28 (t, $^3J_{HH}$ = 7.1 Hz, 3H, $H^{2'}$), 2.02 (s, 3H, H^{13}), 3,50 [A(AB), $^2J_{AB}$ = 13.9 Hz, 1H, H^4], 3.56 [B(AB), $^2J_{AB}$ = 13.9 Hz, 1H, H^4], 3.80 (s, 6H, H^{15}+H^{16}), 4.20-4.30 (m, 2H, $H^{1'}$), 6.62-6.65 (m, 2H, H^6+H^{10}), 6.86 (d, $^3J_{HH}$ = 7.9 Hz, 1H, H^9). ^{13}C NMR (100 MHz, CD_3OD) δ 14.2 ($C^{2'}$), 22.4 (C^{13}), 38.7 (C^4), 56.4 (C^{15}+C^{16}), 63.2 ($C^{1'}$), 68.9 (C^2), 112.9 (C^9), 114.9 (C^6), 123.6 (C^{10}), 130.0 (C^5), 149.7 (C^8+C^7), 150.1 (C^1+C^3), 172.4 (C^{12}). HRMS (ESI) calculated for $C_{16}H_{22}NO_7$ MH^+ 340.1396; found 340.1399. IR (cm^{-1}) ν 3334, 2971, 1742, 1643, 1144.

2-(*N*-(tert-butoxycarbonyl)amino)-2-(3,4-diméthoxybenzyl)-propanedioic acid ethyl monoester (**8-Boc**)



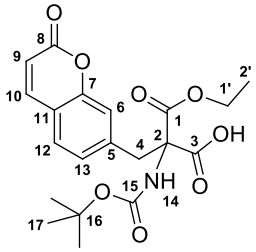
To a solution of KOH (0.329 g, 5.87 mmol, 5 eq) in 24 mL of water and ethanol (1:1) was added the diethyl ester (0.5 g, 1.17 mmol, 1 eq). The reaction mixture was stirred during one day at room temperature. After concentration of 70 % of solvent at room temperature, and addition of 50 mL of water, the basic aqueous phase was extracted with diethyl ether (3*20 mL). The aqueous phase was then acidified slowly with a 1M HCl solution in an ice bath (pH = 2). The acidic aqueous phase was extracted with 3*30 mL of CH_2Cl_2 and the combined organic layers were dried over $MgSO_4$. Evaporation of volatile compounds under reduced pressure afforded the monoester as colorless oil in 71 % yield (331 mg). ^{1}H NMR (400 MHz, MeOD) δ 1.27 (t, $^3J_{HH}$ = 7.1 Hz, 3H, $H^{2'}$), 1.44 (s, 9H, H^{14}), 3.53 (s, 2H, H^4), 3.80 (s, 3H, H^{15}), 3.82 (s, 3H, H^{16}), 4.18-4.32 (m, 2H, $H^{1'}$), 6.60 (s, 1H, H^6), 6.60 (d, $^3J_{HH}$ = 7.9 Hz, 1H, H^{10}), 6.73 (d, $^3J_{HH}$ = 7.9 Hz, 1H, H^9). ^{13}C NMR (100 MHz, MeOD) δ 13.9 ($C^{2'}$), 28.3 (C^{14}), 38.1 (C^4), 55.7 (C^{15}+C^{16}), 62.7 ($C^{1'}$), 67.9 (C^2), 80.5 (C^{13}), 111.0 (C^9), 113.4 (C^6), 122.1 (C^{10}), 127.4 (C^5), 148.2 (C^8), 148.5 (C^7), 154.3 (C^{12}), 168.0 (C^1), 170.3 (C^3). IR (cm^{-1}) ν 3431, 2977, 1738, 1714, 1157, 767.

2-(acetamido)-2-(2-oxo-2H-chromen-7-yl)-propanedioic acid ethyl monoester (**9-Ac**)



To a solution of KOH (0.149 g, 2.66 mmol, 5 eq) in a mixture of 12 mL of water and ethanol (1:1) was added the ethyl 2-acetamido-3-(2-oxo-2H-chromen-7-yl)propanoate (0.2 g, 1 eq) in one portion at room temperature. The reaction mixture was stirred overnight at room temperature. After concentration of 70 % of solvent at room temperature, the basic aqueous phase was extracted with 3*30 mL of diethyl ether. The aqueous phase was then slowly acidified with a 1M HCl solution in an ice bath (pH = 2-3). The acidic aqueous phase was extracted by 3*30 mL of CH_2Cl_2 and the combined organic layers were dried over $MgSO_4$. The title product was then obtained after removal of the solvent as a white solid in 56 % yield (104 mg). Mp 148 °C. ^{1}H NMR (500 MHz, DMSO) δ 1.16 (t, $^3J_{HH}$ = 7.0 Hz, 3H, $H^{2'}$), 1.94 (s, 3H, H^{16}), 3.50 [A(AB), $^2J_{AB}$ = 13.5 Hz, 1H, H^4], 3.55 [B(AB), $^2J_{AB}$ = 13.5 Hz, 1H, H^4], 4.13 (q, $^3J_{HH}$ = 7.0 Hz, 2H, $H^{1'}$), 6.47 (d, $^3J_{HH}$ = 9.5 Hz, 1H, H^9), 6.98 (s, 1H, H^6), 6.99-7.01 (m, 1H, H^{13}), 7.63 (d, $^3J_{HH}$ = 8.1 Hz , 1H, H^{12}), 7.96 (br s, 1H, H^{14}), 8.05 (d, $^3J_{HH}$ = 9.5 Hz, 1H, H^{10}). ^{13}C NMR (125 MHz, DMSO) δ 13.8 ($C^{2'}$), 22.2 (C^{16}), 37.4 (C^4), 60.5 ($C^{1'}$), 66.8 (C^2), 115.5 (C^9), 116.7 (C^6), 117.2 (C^{11}), 126.4 (C^{13}), 128.1 (C^{12}), 142.2 (C^5), 144.0 (C^{10}), 153.1 (C^7), 159.9 (C^8), 169.2 (C^1), 169.3 (C^3), 171.3 (C^{15}). HRMS (ESI) calculated for $C_{17}H_{17}NO_7Na$ [M+Na^+] 370.0903; found 370.0906. IR (cm^{-1}) ν 3351, 1729, 1600, 1202.

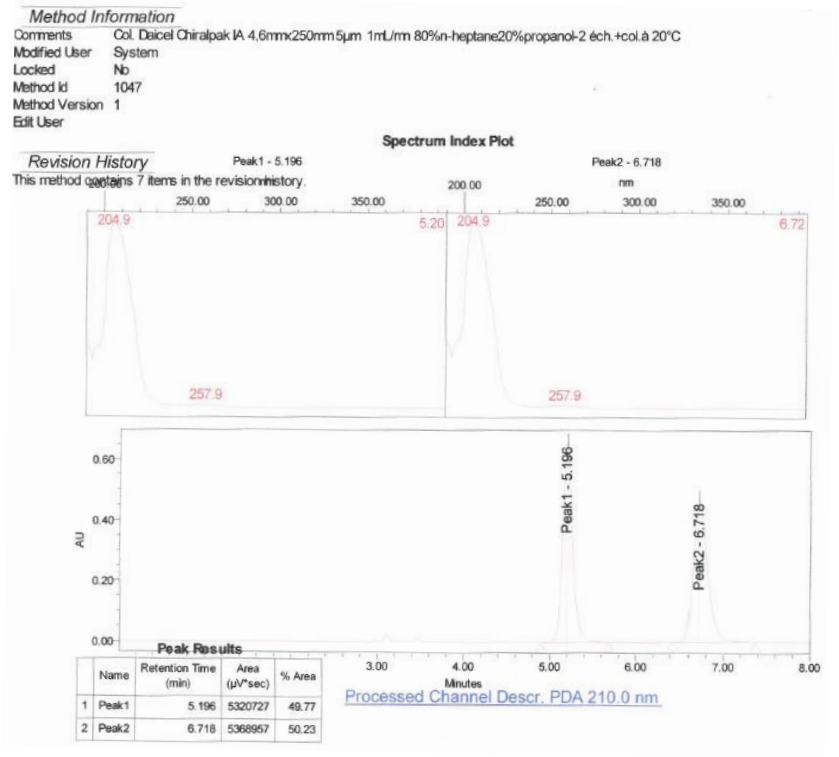
2-(*N*-(tert-butoxycarbonyl)amino)-2-(2-oxo-2H-chromen-7-yl)-propanedioic acid ethyl monoester (**9-Boc**)

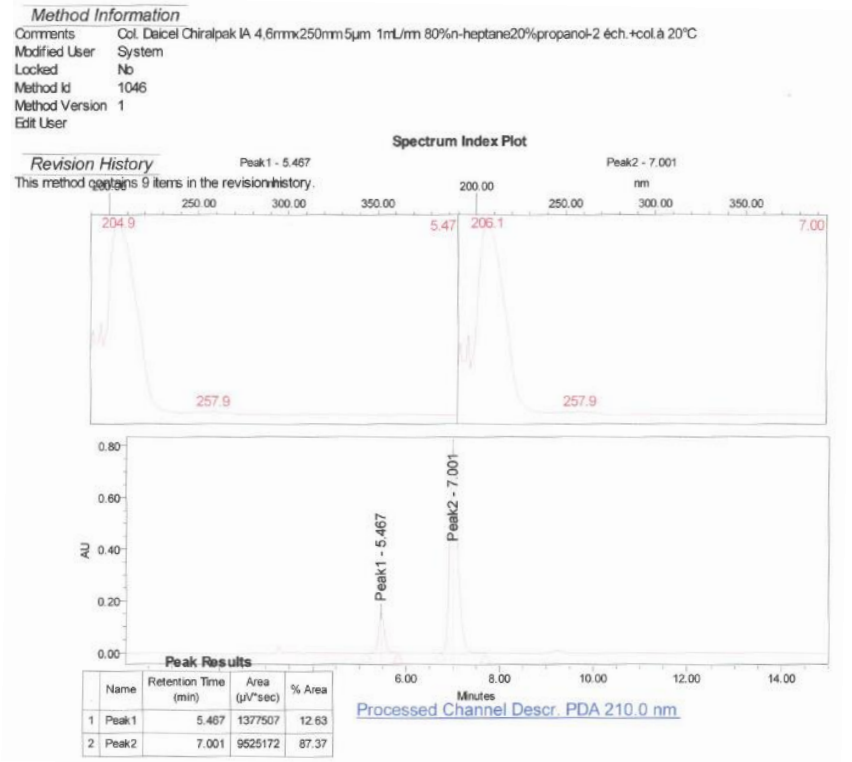


To a solution of KOH (0.325 g, 5.79 mmol, 5 eq) in a mixture of 12 mL of water and ethanol (1:1) was added the ethyl 2-*N*-(tert-butoxycarbonyl)amino-3-(2-oxo-2H-chromen-7-yl)propanoate (0.5 g, 1.15 mmol, 1 eq) in one portion at room temperature. The reaction mixture was stirred overnight at room temperature. After concentration of 70 % of solvent at room temperature, the basic aqueous phase was extracted with 3*30 mL of diethyl ether. The aqueous phase was then acidified slowly with a 1M HCl solution in an ice bath (pH = 2-3). The acidic aqueous phase was extracted by 3*30 mL of CH_2Cl_2 and the combined organic layers were dried over $MgSO_4$. The title product was then obtained after removal of the solvent as a white solid in quantitative yield (467 mg). Mp 129 °C. ^{1}H NMR (500 MHz, DMSO) δ 1.17 (t, $^3J_{HH}$ = 6.7 Hz, 3H, $H^{2'}$), 1.42 (s, 9H, H^{17}), 3.53 (s, 2H, H^4), 4.09-4.20 (m 2H, $H^{1'}$), 6.21 (s, 1H, H^{14}), 6.46 (d, $^3J_{HH}$ = 9.5 Hz, 1H, H^9), 6.99-7.01 (m, 2H, H^6+H^{13}), 7.62 (d, $^3J_{HH}$ = 8.0 Hz, 1H, H^{12}), 8.03 (d, $^3J_{HH}$ = 9.5 Hz, 1H, H^{10}). ^{13}C NMR (125 MHz, DMSO) δ 13.9 ($C^{2'}$), 27.9 (C^{17}), 37.6 (C^4), 61.2 ($C^{1'}$), 66.6 (C^2), 78.9 (C^{16}), 115.6 (C^9), 116.8 (C^6), 117.3 (C^{11}), 126.3 (C^{13}), 127.8 (C^{12}), 141.3 (C^5), 144.0 (C^{10}), 153.1 (C^7), 159.9 (C^8), 167.4 (C^{15}), 168.2 (C^1), 171.3 (C^3). HRMS (ESI) calculated for $C_{21}H_{25}NO_7Na$ [M+Na^+] 428.1321; found 428.1311. IR (cm^{-1}) ν 2982, 1736, 1621, 1159, 683.

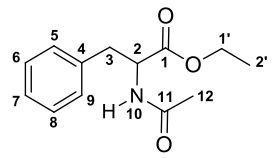
3) Procedure for the synthesis of amino acids

General procedure for asymmetric decarboxylation of hemimalonic ester by using a thiourea chiral base. Synthesis of amino acid **3c** (see table 2, entry 4): A solution of hemimalonic ester **2c** (25 mg, 0.09 mmol, 1 eq) and QD-thiourea **4a** (53.2 mg, 0.09 mmol, 1 eq) in 2 mL of dry THF was stirred at 30 °C. The reaction was monitored by TLC (cyclohexane/ethyl acetate: 6/4). After completion of the reaction, the solvent was removed under reduced pressure and the crude product was purified by flash chromatography (cyclohexane/ethyl acetate: 6/4 then 1/1). The ee was determined by chiral HPLC [Daicel Chiralpak IA, n-heptane: isopropanol = 80:20, 1.0 mL/min, λ = 204 nm. Racemic standard is Tr_1 = 5.2 min, Tr_2 = 6.7 min].



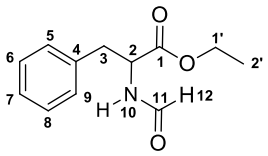


Ethyl 2-acetamido-3-phenylpropanoate (**3c**)



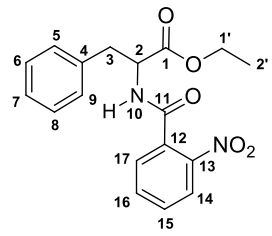
To a solution of 2-(*N*-acetylamino)-2-benzyl-propanoic acid ethyl monoester (0.5 g, 1.79 mmol, 1 eq) in dry THF was added triethylamine (0.362 g, 3.58 mmol, 2 eq). The reaction mixture was stirred at room temperature during 3 days. After removal of the solvent, purification of the crude product by flash chromatography on silica gel with cyclohexane/ethyl acetate (6/4) afforded the title compound as a white solid in 94% yield (397 mg). Mp 66 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25 (t, $^{3}J_{HH}$ = 7.2 Hz, 3H, $H^{2'}$), 1.99 (s, 3H, H^{12}), 3.09 [A(ABX), $^{2}J_{AB}$ = 13.8 Hz, $^{3}J_{AX}$ = 6.0 Hz 1H, H^{3}], 3.13 [B(ABX), $^{2}J_{AB}$ = 13.8 Hz, $^{3}J_{BX}$ = 6.0 Hz 1H, H^{3}], 4.17 (q, $^{3}J_{HH}$ = 7.3 Hz, 2H, $H^{1'}$), 4.87 [M(ABXM), $^{3}J_{MH10}$ = 7.6 Hz, $^{3}J_{AX}$ = 6.0 Hz, $^{3}J_{BX}$ = 6.0 Hz 1H, H^{2}], 5.98 (br s, 1H, H^{10}), 7.11 (d, $^{3}J_{HH}$ = 6.6 Hz, 2H, H^{5}+H^{9}), 7.22-7.31 (m, 3H, H^{6}+H^{7}+H^{8}). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0 ($C^{2'}$), 23.1 (C^{12}), 37.8 (C^{3}), 53.1 (C^{2}), 61.4 ($C^{1'}$), 127.0 (C^{7}), 128.4 (C^{6}+C^{8}), 129.3 (C^{5}+C^{9}), 135.8 (C^{4}), 169.5 (C^{11}), 171.6 (C^{1}). HRMS (ESI) calculated for $C_{13}H_{17}NO_3Na$ [M+Na^+] 258.1106; found 258.1113. IR (cm^{-1}) ν 3315, 1729, 1642, 1531, 1199, 696.

Ethyl 2-formamido-3-phenylpropanoate (**3d**)



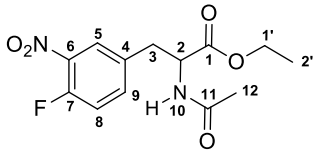
To a solution of 2-(*N*-formamido)-2-benzyl-propanoic acid ethyl monoester (25 mg, 0.10 mmol, 1 eq) in dry THF was added triethylamine (11.1 mg, 0.11 mmol, 1.1 eq). The reaction mixture was stirred at room temperature during 3 days. After removal of the solvent, purification of the crude product by flash chromatography on silica gel with cyclohexane/ethyl acetate (6/4) afforded the title compound as colorless oil in 97% yield (20 mg). The ee was determined by chiral HPLC [Daicel Chiralpak IA, n-heptane: isopropanol = 90:10, 1.0 mL/min, λ = 204 nm. Tr_1 = 10.2 min, Tr_2 = 13.1 min]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25 (t, $^{3}J_{HH}$ = 7.1 Hz, 3H, $H^{2'}$), 3.11 [A(ABX), $^{2}J_{AB}$ = 11.1 Hz, $^{3}J_{AX}$ = 4.7 Hz 1H, H^{3}], 3.15 [B(ABX), $^{2}J_{AB}$ = 11.1 Hz, $^{3}J_{BX}$ = 4.7 Hz, 1H, H^{3}], 4.17 (q, $^{3}J_{HH}$ = 7.1 Hz, 2H, $H^{1'}$), 4.91-4.95 (m, 1H, H^{2}), 5.98 (br d, $^{3}J_{HH}$ = 5.7 Hz, 1H, H^{10}), 7.11-7.14 (m, 2H, H^{5}+H^{9}), 7.22-7.32 (m, 3H, H^{6}+H^{7}+H^{8}), 8.12 (s, 1H, H^{12}). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0 ($C^{2'}$), 37.8 (C^{3}), 51.8 (C^{2}), 61.7 ($C^{1'}$), 127.1 (C^{7}), 128.5 (C^{6}+C^{8}), 129.3 (C^{5}+C^{9}), 135.6 (C^{4}), 160.7 (C^{11}), 171.2 (C^{1}). HRMS (ESI) calculated for $C_{12}H_{15}NO_3Na$ [M+Na^+] 244.0950; found 244.0948. IR (cm^{-1}) ν 3288, 1737, 1661, 1197, 699.

Ethyl 2-(*N*-(2-nitrobenzoyl)amino)-3-phenylpropanoate (**3e**)



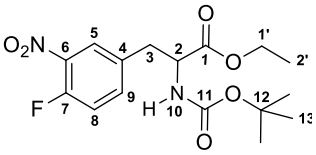
To a solution of 2-(*N*-(2-nitrobenzoyl)amino)-2-(benzyl)propanedioic acid ethyl monoester (0.200 g, 0.517 mmol, 1 eq) in dry tetrahydrofuran was added triethylamine (0.104 g, 1.03 mmol, 2 eq). The reaction mixture was stirred at room temperature during 3 days. After removal of the solvent, the crude product was purified by flash chromatography on silica gel with cyclohexane/ethyl acetate (8/2) to afford the title compound in quantitative yield (175 mg). Mp 102 °C. The ee was determined by chiral HPLC [Daicel Chiralpak IA, n-heptane: ethanol = 70:30, 1.0 mL/min, λ = 205 nm. Tr_1 = 7.5 min, Tr_2 = 9.3 min]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (t, $^{3}J_{HH}$ = 7.1 Hz, 3H, $H^{2'}$), 3.26 (d, $^{3}J_{HH}$ = 5.7 Hz, 2H, H^{3}), 4.16-4.21 (m, 2H, $H^{1'}$), 5.07 (dt, $^{3}J_{HH}$ = 7.7 Hz , $^{3}J_{HH}$ = 5.7 Hz, 1H, H^{2}), 6.40 (br d, $^{3}J_{HH}$ = 7.7 Hz, 1H, H^{10}), 7.17-7.29 (m, 5H, H^{5}-H^{9}), 7.39 (dd, $^{3}J_{HH}$ = 7.6 Hz, $^{4}J_{HH}$ = 1.3 Hz, 1H, H^{17}), 7.55 (td, $^{3}J_{HH}$ = 7.6 Hz, $^{4}J_{HH}$ = 1.2 Hz, 1H, H^{16}), 7.61 (td, $^{3}J_{HH}$ = 7.6 Hz, $^{4}J_{HH}$ = 1.3 Hz, 1H, H^{15}), (dd, $^{3}J_{HH}$ = 7.6 Hz, $^{4}J_{HH}$ = 1.2 Hz, 1H, H^{14}). ^{13}C NMR (100 MHz, $CDCl_3$) 14.1 ($C^{2'}$), 37.8 (C^{3}), 53.6 (C^{2}), 61.8 ($C^{1'}$), 124.6 (C^{14}), 127.2 (C^{7}), 128.61 (C^{6}+C^{8}), 126.65 (C^{17}), 129.5 (C^{5}+C^{9}), 130.7 (C^{15}), 132.3 (C^{13}), 133.6 (C^{16}), 135.7 (C^{4}), 146.7 (C^{12}), 165.7 (C^{11}), 171.1 (C^{1}). HRMS (ESI) calculated for $C_{18}H_{18}N_2O_5Na$ [M+Na^+] 365.1113; found 365.1113. IR (cm^{-1}) ν 2970, 1748, 1641, 1529, 1350, 1215.

Ethyl 2-(*N*-acetylamino)-2-(4-fluoro-3-nitrobenzyl)propanoate (**10-Ac**)



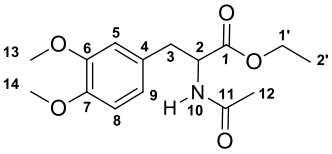
To a solution of ethyl monoester (0.100 g, 0.292 mmol, 1 eq) in dry THF was added triethylamine (0.886 g, 0.876 mmol, 3 eq). The reaction mixture was stirred at room temperature during 3 days. After removal of the solvent, the crude product was purified by flash chromatography on silica gel with cyclohexane/ethyl acetate (3/7) to afford the giving product in quantitative yield (87 mg). Mp 87 °C. The ee was determined by chiral HPLC [Daicel ADH, n-hexane: isopropanol = 85:15, 1.0 mL/min, λ = 205 nm. Tr_1 = 17.4 min, Tr_2 = 19.0 min]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.25 (t, $^3J_{HH}$ = 7.1 Hz, 3H, $H^{2'}$), 1.98 (s, 3H, H^{12}), 3.08 [A(ABX), $^2J_{AB}$ = 14.0 Hz, $^3J_{AX}$ = 5.9 Hz, 1H, H^3], 3.22 [B(ABX), $^2J_{AB}$ = 14.0 Hz, $^3J_{BX}$ = 5.9 Hz, 1H, H^3], 4.16 [A(ABX_3), $^2J_{AB}$ = 7.1 Hz, $^3J_{AX}$ = 1.5 Hz, 1H, $H^{1'}$], 4.19 [B(ABX_3), $^2J_{AB}$ = 7.1 Hz, $^3J_{BX}$ = 1.5 Hz, 1H, $H^{1'}$], 4.81 [M(ABXM), $^3J_{XH10}$ = 1.1 Hz, $^3J_{AX}$ = 5.9 Hz, $^3J_{BX}$ = 5.9 Hz 1H, H^2], 6.30 (br s, 1H, H^{10}), 7.20 (dd, $^3J_{HH}$ = 9.8, $^3J_{HF}$ = 10.1 Hz, 1H, H^8), 7.40-7.43 (m, 1H, H^9), 7.80 (dd, $^3J_{HH}$ = 7.0 Hz, $^4J_{HF}$ = 2.2 Hz, 1H, H^5). ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.5 ($C^{2'}$), 23.0 (C^{12}), 36.8 (C^3), 53.0 (C^2), 62.0 ($C^{1'}$), 118.4 (d, $^2J_{CF}$ = 21.2 Hz, C^8), 126.7 (d, $^3J_{CF}$ = 2.6 Hz, C^5), 133.5 (d, $^4J_{CF}$ = 3.8 Hz, C^4), 136.4 (d, $^3J_{CF}$ = 8.4 Hz, C^9), 136.9 (d, $^2J_{CF}$ = 7.3 Hz, C^6), 155.0 (d, $^1J_{CF}$ = 262.9 Hz, C^7), 169.9 (C^{11}), 171.0 (C^1). ^{19}F NMR ($CDCl_3$) δ -119.8. HRMS (ESI) calculated for $C_{13}H_{15}N_2O_5FNa$ [M+Na^+] 321.0863; found 321.0848. IR (cm^{-1}) ν 3223, 2944, 1732, 1644, 1620, 1246.

Ethyl 2-(*N*-Bocamino)-2-(4-fluoro-3-nitrobenzyl)propanoate (**10-Boc**)



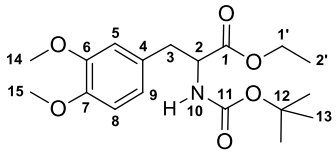
To a solution of ethyl monoester (50 mg, 0.124 mmol, 1 eq) in dry THF was added triethylamine (38 mg, 0.374 mmol, 3 eq). The reaction mixture was stirred at room temperature during 3 days. After removal of the solvent, purification of the crude product by flash chromatography on silica gel with cyclohexane/ethyl acetate (3/7) afforded the title compound as a white solid in 98% yield (43mg). Mp 99 °C. The ee was determined by chiral HPLC [Daicel Chiralpak IC, n-heptane: isopropanol = 80:20, 1.0 mL/min, λ = 204 nm. Tr_1 = 8.4 min, Tr_2 = 10.9 min]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.21 (t, $^3J_{HH}$ = 7.1 Hz, 3H, $H^{2'}$), 1.35 (s, 9H, H^{13}), 2.99 [A(ABX), $^2J_{AB}$ = 14.0 Hz, $^3J_{AX}$ = 5.4 Hz, 1H, H^3], 3.17 [B(ABX), $^2J_{AB}$ = 14.0 Hz, $^3J_{BX}$ = 6.2 Hz, 1H, H^3], 4.14 (q, $^3J_{HH}$ = 7.1 Hz, 2H, $H^{1'}$), 4.48 (br d, $^3J_{HH}$ = 6.4 Hz, 1H, H^2), 5.03 (br d, $^3J_{HH}$ = 6.4 Hz, 1H, H^{10}), 7.15 (dd, $^3J_{HF}$ = 10.5 Hz, $^3J_{HH}$ = 8.5 Hz, 1H, H^8), 7.34-7.38 (m, 1H, H^9), 7.77 (dd, $^3J_{HH}$ = 7.0 Hz, $^4J_{HF}$ = 2.1 Hz, 1H, H^5). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.1 ($C^{2'}$), 28.2 (C^{13}), 37.4 (C^3), 54.2 (C^2), 61.9 ($C^{1'}$), 80.3 (C^{12}), 118.4 (d, $^2J_{CF}$ = 15.7 Hz, C^8), 126.8 (d, $^3J_{CF}$ = 2.3 Hz C^5), 133.6 (C^4), 136.4 (d, $^3J_{CF}$ = 6.3 Hz, C^9), 137.1 (d, $^2J_{CF}$ = 6.7 Hz, C^6), 154.6 (d, $^1J_{CF}$ = 264.3 Hz, C^7), 154.9 (C^{11}), 171.0 (C^1). ^{19}F NMR ($CDCl_3$) δ -120.01. HRMS (ESI) calculated for $C_{16}H_{21}N_2O_6FNa$ [M+Na^+] 379.1265; found 379.1281. IR (cm^{-1}) ν 3350, 2929, 1745, 1682, 1537, 1158.

Ethyl 2-acetamido-3-(3,4-diméthoxyphenyl)propanoate (**11-Ac**)



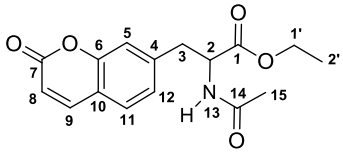
To a solution of ethyl monoester (100 mg, 0.29 mmol, 1 eq) in dry THF (5mL) was added triethylamine (0.89 mg, 0.88 mmol, 3 eq). The reaction mixture was stirred at room temperature during 3 days. After removal of the solvent, purification of the crude product by flash chromatography on silica gel with cyclohexane/ethyl acetate (6/4) afforded the title compound as a white solid in 98 % yield (85 mg). Mp 120 °C. The ee was determined by chiral HPLC [Daicel Chiralpak IC, n-heptane: isopropanol = 60:40, 1.0 mL/min, λ = 204 nm. Tr_1 = 13.9 min, Tr_2 = 16.4 min]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (t, $^3J_{HH}$ = 7.1 Hz, 3H, $H^{2'}$), 1.99 (s, 3H, H^{12}), 3.05 [A(ABX), $^2J_{AB}$ = 14.0 Hz, $^3J_{AX}$ = 6.0 Hz, 1H, H^3], 3.09 [B(ABX), $^2J_{AB}$ = 14.0 Hz, $^3J_{BX}$ = 6.0 Hz, 1H, H^3], 3.84 (s, 3H, H^{13}), 3.85 (s, 3H, H^{14}), 4.16 [A(ABX_3), $^2J_{AB}$ = 14.0Hz, $^3J_{AX}$ = 7.1 Hz, 1H, $H^{1'}$], 4.20 [B(ABX_3), $^2J_{AB}$ = 14.3 Hz, $^3J_{AX}$ = 7.1 Hz, 1H, $H^{1'}$], 4.80-4.85 (m, 1H, H^2), 5.93 (d, $^3J_{HH}$ = 7.3 Hz, 1H, H^{10}), 6,63 (s, 1H, H^5), 6.64 (d, $^3J_{HH}$ = 7.7 Hz, 1H, H^9), 5.93 (d, $^3J_{HH}$ = 7.7 Hz, 1H, H^8). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1 ($C^{2'}$), 23.2 (C^{12}), 37.5 (C^3), 53.2 (C^2), 55.8 (C^{13}+C^{14}), 61.5 ($C^{1'}$), 111.2 (C^8), 112.4 (C^5), 121.4 (C^9), 128.3 (C^4), 148.1 (C^7), 148.9 (C^6), 169.5 (C^1), 171.7 (C^{11}). HRMS (ESI) calculated for $C_{15}H_{21}NO_5Na$ [M+Na^+] 318.1317; found 318.1303. IR (cm^{-1}) ν 3284, 2923, 1738, 1639, 1217, 798.

Ethyl 2-(*N*-(tert-butoxycarbonyl)amino)-3-(3,4-diméthoxyphenyl)propanoate (**11-Boc**)



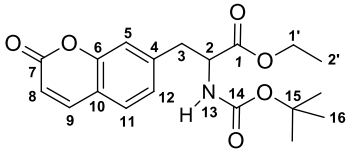
To a solution of ethyl monoester (100 mg, 0.25 mmol, 1 eq) in dry THF (5mL) was added triethylamine (76 mg, 0.75 mmol, 3 eq). The reaction mixture was stirred at room temperature during 3 days. After removal of the solvent, purification of the crude product by flash chromatography on silica gel with cyclohexane/ethyl acetate (8/2) afforded the title compound as a white solid in 95% yield (85 mg). Mp 95 °C. The ee was determined by chiral HPLC [Daicel Chiralpak IA, n-heptane: isopropanol = 80:20, 1.0 mL/min, λ = 204 nm. Tr_1 = 7.6 min, Tr_2 = 9.4 min]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.23 (t, $^3J_{HH}$ = 7.1 Hz, 3H, $H^{2'}$), 1.41 (s, 9H, H^{13}), 2.97-3.07 (m, 2H, H^3), 3.84 (s, 6H, H^{14}+H^{15}), 4.16 (q, $^3J_{HH}$ = 7.1 Hz, 2H, $H^{1'}$), 4.52 (m, 1H, H^2), 4.96 (d, $^3J_{HH}$ = 7.7 Hz, 1H, H^{10}), 6.64 (s, 1H, H^5), 6.66 (d, $^3J_{HH}$ = 8.1 Hz, 1H, H^9), 6.78 (d, $^3J_{HH}$ = 8.1 Hz, 1H, H^8). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2 ($C^{2'}$), 28.3 (C^{13}), 37.9 (C^3), 54.5 (C^2), 55.8 (C^{14}+C^{15}), 61.3 ($C^{1'}$), 79.8 (C^{12}), 111.2 (C^8), 112.5 (C^5), 121.4 (C^9), 128.5 (C^4), 148.1 (C^7), 148.8 (C^6), 155.1 (C^{11}), 171.9 (C^1). HRMS (ESI) calculated for $C_{18}H_{27}NO_6Na$ [M+Na^+] 376.1736; found 376.1731. IR (cm^{-1}) ν 3345, 2924, 1731, 1698, 1159.

Ethyl 2-(*N*-acetylamino)-2-(2-oxo-2H-chromen-7-yl)propanoate (**12-Ac**)



To a solution of ethyl monoester (50 mg, 0.143 mmol, 1 eq) in dry THF (5mL) was added triethylamine (44 mg, 0.431 mmol, 3 eq). The reaction mixture was stirred at room temperature during 3 days. After removal of the solvent, the crude product was purified by flash chromatography on silica gel with cyclohexane/ethyl acetate (6/4) to afford the giving product in 91 % yield (39 mg). Mp 145 °C. The ee was determined by chiral HPLC [Daicel ADH, n-hexane: isopropanol = 80:20, 1.0 mL/min, λ = 205 nm. Tr_1 = 18.7 min, Tr_2 = 20.1 min]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.27 (t, $^3J_{HH}$ = 7.1 Hz, 3H, $H^{2'}$), 2.00 (s, 3H, H^{15}), 3.15 [A(ABX), $^2J_{AB}$ = 13.5 Hz, $^3J_{AX}$ = 5.5 Hz, 1H, H^3], 3.27 [B(ABX), $^2J_{AB}$ = 13.5 Hz, $^3J_{BX}$ = 5.8 Hz, 1H, H^3], 4.19 [A(ABX_3), $^2J_{AB}$ = 1.9 Hz, $^3J_{AX}$ = 7.1 Hz, 1H, $H^{1'}$], 4.21 [B(ABX_3), $^2J_{AB}$ = 2.0 Hz, $^3J_{BX}$ = 7.1 Hz, 1H, $H^{1'}$], 4.89 (m, 1H, H^2], 6.04 (br d, $^3J_{HH}$ = 7.3 Hz, 1H, H^{13}), 6.39 (d, $^3J_{HH}$ = 9.5 Hz, 1H, H^8), 7.05 (d, $^3J_{HH}$ = 7.6 Hz, 1H, H^{12}), 7.06 (s, 1H, H^5), 7.40 (d, $^3J_{HH}$ = 7.6 Hz, 1H, H^{11}), 7.67 (d, $^3J_{HH}$ = 9.5 Hz, 1H, H^9). ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2 ($C^{2'}$), 23.2 (C^{15}), 37.9 (C^3), 52.9 (C^2), 61.9 ($C^{1'}$), 116.4 (C^8), 117.5 (C^5), 117.7 (C^{10}), 125.7 (C^{12}), 127.8 (C^{11}), 140.9 (C^4), 143.1 (C^9), 153.9 (C^6), 160.7 (C^7), 169.9 (C^{14}), 171.1 (C^1). HRMS (ESI) calculated for $C_{16}H_{17}NO_5Na$ [M+Na^+] 326.1004; found 326.1014. IR (cm^{-1}) ν 3287, 2924, 1724, 1619, 1181.

Ethyl 2-(*N*-(tert-butoxycarbonyl)amino)-2-(2-oxo-2H-chromen-7-yl)propanoate (**12-Boc**)



To a solution of ethyl monoester (50 mg, 0.123 mmol, 1 eq) in dry THF (5mL) was added triethylamine (37 mg, 0.370 mmol, 3 eq). The reaction mixture was stirred at room temperature during 3 days. After removal of the solvent, purification of the crude product by flash chromatography on silica gel with cyclohexane/ethyl acetate (6/4) afforded the title compound as a white solid in 93 % yield (41 mg). Mp 101 °C. The ee was determined by chiral HPLC [Daicel ADH, n-hexane: isopropanol = 80:20, 1.0 mL/min, λ = 204 nm. Tr_1 = 27.6 min, Tr_2 = 30.6 min]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25 (t, $^3J_{HH}$ = 7.1 Hz, 3H, $H^{2'}$), 1.40 (s, 9H, H^{16}), 3.11 ([A(ABX), $^2J_{AB}$ = 13.6 Hz, $^3J_{AX}$ = 5.8 Hz 1H, H^3]), 3.23 ([B(ABX), $^2J_{AB}$ = 13.6 Hz, $^3J_{BX}$ = 5.4 Hz 1H, H^3]), 4.18 (q, $^3J_{HH}$ = 7.1 Hz, 2H, $H^{1'}$), 4.57-4.59 (m, 1H, H^2), 5.06 (br d, $^3J_{HH}$ = 7.0 Hz, 1H, H^{13}), 6.38 (d, $^3J_{HH}$ = 9.5 Hz, 1H, H^8), 7.08 (d, $^3J_{HH}$ = 7.8 Hz, 1H, H^{12}), 7.10 (s, 1H, H^5), 7.39 (d, $^3J_{HH}$ = 7.8 Hz, 1H, H^{11}), 7.66 (d, $^3J_{HH}$ = 9.5 Hz, 1H, H^9). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.2 ($C^{2'}$), 28.2 (C^{16}), 38.5 (C^3), 54.2 (C^2), 61.7 ($C^{1'}$), 80.2 (C^{15}), 116.3 (C^8), 117.6 (C^5+C^{10}), 125.7 (C^{12}), 127.8 (C^{11}), 141.2 (C^4), 143.1 (C^9), 154.0 (C^6), 155.0 (C^{14}), 160.7 (C^7), 171.2 (C^1). HRMS (ESI) calculated for $C_{19}H_{23}NO_6Na$ [M+Na^+] 384.1423; found 384.1430. IR (cm^{-1}) ν 3329, 2925, 1735, 1727, 1699, 1223.