A Palladium Catalyzed Domino Reaction as Key Step for the Synthesis of Functionalized Aromatic Amino Acids

Supporting Information

Tina Stark, Marcel Suhartono, Michael W. Göbel, Mark Lautens

a Institute of Organic Chemistry and Chemical Biology, Goethe University, Max-von-Laue-Straße 7, 60438 Frankfurt am Main, Germany
b Davenport Research Laboratories, Department of Chemistry, University of Toronto, 80 St. George Street, Toronto, Ontario M5S 3H6, Canada

m.goebel@chemie.uni-frankfurt.de; mlautens@chem.utoronto.ca

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General Information:

NMR: Bruker DPX 250 (\textsuperscript{1}H: 250 MHz; \textsuperscript{13}C: 63 MHz), Bruker AM 300 (\textsuperscript{13}C: 75 MHz; \textsuperscript{19}F: 282 MHz) or Bruker Avance 400 (\textsuperscript{1}H: 400 MHz); \textsuperscript{1}H chemical shifts (\delta) are given in ppm relative to CDCl\textsubscript{3} (7.26 ppm) as internal standard; multiplicities are indicated as s for singlet, d-doublet, dd-doublet of doublets, t-triplet, q-quartet, m-multiplet, br s-broad singlet, * denotes rotamer signals; if necessary, \textsuperscript{1}H,\textsuperscript{1}H-COSY spectra were used for proton assignment; \textsuperscript{13}C chemical shifts (\delta) are reported with proton decoupling in ppm relative to CDCl\textsubscript{3} (77.0 ppm) as internal standard; \textsuperscript{19}F chemical shifts (\delta) are reported with decoupling in ppm. FT-IR: Perkin-Elmer 1600 series or Perkin-Elmer Spectrum Two; peaks are reported in cm\textsuperscript{-1}; intensities are classified as strong (s), medium (m) or weak (w). Melting points (uncorrected): Kofler hot-plate microscope. Optical rotation: Perkin-Elmer polarimeter 241 with thermostats Haake G and Haake D8; values are given as follows [\alpha]D\textsuperscript{T}°C (c = g/100 mL, solvent). Elementary analysis: Elementar vario micro cube; values are given in %. Mass spectrometry: Fisons VG Platform II (ESI); values are given as follows m/z ratio (intensity in %). High-resolution mass spectrometry (HRMS): MALDI Orbitrap XL (Thermo Fisher Scientific); values are given as m/z ratios. Enantiomeric excesses were determined by HPLC analysis using analytical chiral columns from Daice Chemical Industries Ltd (Chiralpak IA). Triphenylphosphine was recrystallized from EtOH. All other reagents were obtained from commercial suppliers and were used without further purification. 2,4,6-Triisopropylbenzenesulfonyl azide (tris-azide) was synthesized according to literature.\textsuperscript{[1]}

Experimental section:

1-Iodo-2-phenylbenzene (1e)\textsuperscript{[2]}

2-Aminobiphenyl (2.00 g; 11.8 mmol) was suspended in H\textsubscript{2}O (12 mL) at 0 °C and HCl (12 M; 2.4 mL) was added. After slow addition of a solution of NaNO\textsubscript{2} (978 mg; 14.2 mmol) in H\textsubscript{2}O (3 mL) the reaction mixture was stirred for 45 min at 0 °C. A solution of ice cooled KI (3.90 g; 23.5 mmol) in H\textsubscript{2}O (3 mL) was added and the reaction mixture was allowed to warm to room temperature overnight.

The reaction mixture was extracted with Et\textsubscript{2}O (4x) and the organic layers were washed with a HCl solution (3 M), saturated NaHCO\textsubscript{3}, saturated Na\textsubscript{2}S\textsubscript{2}O\textsubscript{5}, and brine. After drying over MgSO\textsubscript{4} and concentration in vacuo the crude product was purified by column chromatography (pure n-hexane). A colourless oil (3.07 g; 93%) was obtained.

\textsuperscript{1}H NMR (250 MHz, CDCl\textsubscript{3}): 7.96 (dd, J = 0.8 Hz, 8 Hz, 1H, aryl-H), 7.44 – 7.29 (m, 7H, aryl-H), 7.04 (m, 1H, aryl-H). \textsuperscript{13}C NMR (63 MHz, CDCl\textsubscript{3}): 146.7, 144.2, 139.5, 130.1, 129.3, 128.7, 128.1, 127.9, 127.6, 98.6. IR (neat): 3056 (m), 1578 (w), 1525 (m), 1460 (s), 1426 (m), 1351 (w), 1294 (w), 1251 (w), 1159 (w), 1114 (w), 1072 (m), 1017 (s), 1004 (s), 915 (w), 835 (m), 790 (w), 775 (m), 755 (w).
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858 (w), 746 (s), 699 (s), 648 (s). **Rf** (n-hexane/EtOAc, 25:1) = 0.75. **Elementary analysis:** calcd for C_{12}H_{9}I (280.10): C 51.46, H 3.24; found C 51.60, H 3.36.

**General procedure for the conversion of aryl bromides to aryl iodides (1f, 1h, 1i); GP1:**

Aryl bromide (10 mmol) was dissolved in dry THF (30 mL) and cooled to -78 °C under an argon atmosphere. n-Butyllithium (1.6 M in n-hexane; 7.5 mL; 12 mmol) was added dropwise. After 15 minutes a solution of I\(_2\) (3.81 g; 15 mmol) in dry THF (10 mL) was added and the reaction mixture was allowed to warm to room temperature overnight.

For workup the reaction mixture was concentrated in vacuo. H\(_2\)O was added to the residue and it was extracted with DCM (3x). The combined organic phases were washed with saturated Na\(_2\)S\(_2\)O\(_5\) solution and H\(_2\)O. After drying over MgSO\(_4\) and concentration under reduced pressure, the crude product was purified by column chromatography.

1-**Iodonaphthalene (1f)**

Eluent for column chromatography: n-hexane/EtOAc, 50:1.

Yield: 2.16 g (85%); colourless oil.

\(^1\)H **NMR** (250 MHz, CDCl\(_3\)): 8.11 - 8.08 (m, 2H, aryl-H), 7.86 – 7.76 (m, 2H, aryl-H), 7.62 – 7.49 (m, 2H, aryl-H), 7.19 (t, J = 8 Hz, 1H, aryl-H). \(^{13}\)C **NMR** (63 MHz, CDCl\(_3\)): 137.4, 134.4, 134.1, 132.1, 129.0, 128.5, 127.7, 126.8, 126.7, 99.5. **IR** (neat): 3052 (w), 2375 (w), 1555 (m), 1499 (s), 1374 (m), 1251 (m), 1200 (m), 1130 (w), 1022 (w), 944 (s), 788 (s), 763 (s). **Rf** (n-hexane/EtOAc, 25:1) = 0.75. **Elementary analysis:** calcd for C\(_{10}\)H\(_7\)I (254.07): C 47.27, H 2.78; found C 47.55, H 2.90.

9-**Iodophenanthrene (1h)**

Eluent for column chromatography: n-hexane/EtOAc, 50:1.

Yield: 2.59 g (85%); colourless solid after recrystallization from DCM/n-hexane.

\(^1\)H **NMR** (250 MHz, CDCl\(_3\)): 8.68 – 8.62 (m, 2H, aryl-H), 8.45 (s, 1H, aryl-H), 8.23 (m, 1H, aryl-H), 7.79 – 7.56 (m, 5H, aryl-H). \(^{13}\)C **NMR** (63 MHz, CDCl\(_3\)): 138.6, 133.3, 133.0, 132.1, 130.7, 130.4, 127.8, 127.6, 127.5, 127.3, 127.1, 122.81, 122.75, 98.7. **IR** (KBr): 1488 (w), 1445 (w), 1366 (w), 1186 (w), 952 (w), 901 (w), 879 (m), 845 (m), 744 (s), 719 (s), 616 (w). **mp:** 89 – 91 °C (lit: 91 – 92 °C \[^{[3]}\]). **Rf** (n-hexane/EtOAc, 25:1) = 0.70. **HRMS:** calcd for C\(_{14}\)H\(_9\)I [M]+ 303.9743; found 303.9744.

1-**Iodopyrene (1i)**

Eluent for column chromatography: n-hexane/EtOAc, 50:1.

Yield: 2.85 g (87%); light yellow solid after recrystallization from MeCN.
**Anthracen-1-yl trifluoromethanesulfonate (1g)**

1-Anthracenol (390 mg; 2.0 mmol) was dissolved in dry DCM (10 mL). After addition of pyridine (322 μL; 4.0 mmol) the brown solution was cooled to 0 °C and a solution of triflic anhydride (404 μL; 2.4 mmol) in dry DCM (4 mL) was added dropwise. The reaction mixture was stirred at room temperature for 1 h. Then, the reaction was quenched by addition of diluted HCl. After washing once with saturated NaHCO₃ solution and brine the organic phase was dried over MgSO₄ and purified by column chromatography (cyclohexane/EtOAc, 50:1). The product was directly used for the next step.

Yield: 587 mg (90%); yellow oil.

**3-Iodo-1-[(4-methylbenzene)sulfonyl]-1H-indole (1j)** [5]

Indole (4.0 g; 34.1 mmol) and KOH (4.78 g; 85.3 mmol) were dissolved in DMF (60 mL). After dropwise addition of a solution of I₂ (8.73 g; 34.4 mmol) in DMF (60 mL) the brown solution was stirred at room temperature for 30 min. KOH (4.78 g; 85.3 mmol) and tosylchloride (13.65 g; 71.6 mmol) were added and the stirring was continued overnight.

H₂O was added to the reaction mixture and it was extracted with Et₂O (3x). The combined organic layers were washed with H₂O and brine before drying over MgSO₄. After concentration to dryness the crude product was crystallized from n-hexane. A light yellow solid (8.07 g; 60%) was obtained.

**Elementary analysis**
General procedure for the Catellani reaction (2a-j); GP2:

Pd(OAc)$_2$ (45 mg; 0.2 mmol) and triphenylphosphine (115 mg; 0.44 mmol) were filled into an oven dried sealable tube and dissolved in dry MeCN (12 mL) under argon atmosphere. After 5 min Cs$_2$CO$_3$ (3.26 g; 10 mmol), the aryl iodide (2 mmol), 1,3-dibromopropane (20 mmol; for iodobenzene (1a): 2.24 mL; 22 mmol) and methylacrylate (906 μL; 10 mmol) were added. The reaction mixture was purged with argon for 5 min. After addition of norbornene (942 mg; 10 mmol) the tube was sealed and heated at 90 °C for 18 h.

For workup the cooled reaction mixture was filtered over Celite®, washed with DCM, concentrated in vacuo and purified by column chromatography.

Methyl (2E)-3-[2,6-bis(3-bromopropyl)phenyl]prop-2-enoate (2a)


Yield: 544 mg (67%); yellow oil.

$^1$H NMR (250 MHz, CDCl$_3$): 7.87 (d, $J = 16.3$ Hz, 1H, aryl-CH=CH), 7.21 (m, 1H, aryl-H), 7.12 (m, 2H, aryl-H), 6.03 (d, $J = 16.3$ Hz, 1H, aryl-CH=CH), 3.83 (s, 3H, COOCH$_3$), 3.38 (t, $J = 6.5$ Hz, 4H, CH$_2$-Br), 2.79 (t, $J = 7.3$ Hz, 4H, CH$_2$-CH$_2$-CH$_2$-Br), 2.07 (m, 2H, CH$_2$-Br).

$^{13}$C NMR (63 MHz, CDCl$_3$): 166.5, 143.2, 139.0, 134.2, 128.4, 127.7, 124.8, 51.8, 33.6, 33.0, 32.0. IR (neat): 2949 (m), 1722 (s), 1641 (m), 1576 (w), 1456 (m), 1434 (m), 1309 (m), 1272 (m), 1195 (m), 1169 (s), 1038 (w), 984 (m), 866 (w), 793 (w), 764 (m). $R_f$ (n-hexane/EtOAc, 3:1) = 0.70. HRMS: calcd for C$_{16}$H$_{21}$Br$_2$O$_2$ [M+H]$^+$ 402.9903: found 402.9900.

Methyl (2E)-3-[2-(3-bromopropyl)-6-methylphenyl]prop-2-enoate (2b)


Yield: 567 mg (95%); orange oil.

$^1$H NMR (250 MHz, CDCl$_3$): 7.86 (d, $J = 16.5$ Hz, 1H, aryl-CH=CH), 7.21 – 7.08 (m, 3H, aryl-H), 6.06 (d, $J = 16.5$ Hz, 1H, aryl-CH=CH), 3.83 (s, 3H, COOCH$_3$), 3.39 (t, $J = 6.5$ Hz, 2H, CH$_2$-Br), 2.82 (t, $J = 7.5$ Hz, 2H, CH$_2$-CH$_2$-CH$_2$-Br), 2.33 (s, 3H, CH$_3$), 2.08 (m, 2H, CH$_2$-CH$_2$-Br). $^{13}$C NMR (63 MHz, CDCl$_3$): 166.8, 143.3, 139.1, 136.5, 134.0, 128.7, 128.4, 127.3, 124.2, 51.7, 33.6, 33.0, 32.0, 21.1. IR (neat): 2950 (s), 1721 (s), 1639 (w), 1525 (w), 1436 (s), 1308 (s), 1267 (s), 1168 (s), 1038 (m), 987 (m), 865 (w), 766 (m). $R_f$ (n-hexane/EtOAc, 3:1) = 0.75. HRMS: calcd for C$_{14}$H$_{18}$Br$_2$O$_2$ [M+H]$^+$ 297.0485: found 297.0486.

Methyl (2E)-3-[2-(3-bromopropyl)-6-methoxyphenyl]prop-2-enoate (2c)


Yield: 430 mg (69%); colourless oil.

$^1$H NMR (250 MHz, CDCl$_3$): 7.86 (d, $J = 16.3$ Hz, 1H, aryl-CH=CH), 7.24 (m, 1H, aryl-H), 6.89 – 6.81 (m, 2H, aryl-H), 6.72 (d, $J = 16.3$ Hz, 1H, aryl-CH=CH), 3.87 (s, 3H, COOCH$_3$),
3.81 (s, 3H, OCH₃), 3.40 (t, J = 6.5 Hz, 2H, CH₂-Br), 2.93 (t, J = 7.3 Hz, 2H, CH₂CH₂CH₂-Br), 2.12 (m, 2H, CH₂CH₂Br). ¹³C NMR (63 MHz, CDCl₃): 168.3, 159.4, 142.3, 138.2, 130.2, 122.6, 122.5, 121.9, 109.3, 55.5, 51.6, 33.9, 32.9, 32.1. IR (neat): 2948 (m), 2839 (w), 1714 (s), 1627 (s), 1595 (s), 1573 (m), 1470 (s), 1436 (s), 1312 (s), 1266 (s), 1193 (s), 1167 (s), 1075 (s), 986 (m), 948 (w), 869 (w), 791 (m), 756 (m).

Rf (n-hexane/EtOAc, 3:1) = 0.60. HRMS: calcd for C₁₄H₁₈BrO₃ [M+H]+ 313.0434: found 313.0434.

Methyl (2E)-3-[2-(3-bromopropyl)-6-(trifluoromethyl)phenyl]prop-2-enoate (2d)


Yield: 310 mg (44%); colourless oil.

¹H NMR (250 MHz, CDCl₃): 7.88 (dd, J = 1.8 Hz, 16.3 Hz, 1H, aryl-CH=CH), 7.58 (d, J = 8 Hz, 1H, aryl-H), 7.47 – 7.35 (m, 2H, aryl-H), 6.05 (d, J = 16.3 Hz, 1H, aryl-CH=CH), 3.83 (s, 3H, COOCH₃), 3.38 (t, J = 6.5 Hz, 2H, CH₂-Br), 2.84 (t, J = 7.3 Hz, 2H, CH₂CH₂CH₂-Br), 2.08 (m, 2H, CH₂CH₂Br). ¹³C NMR (63 MHz, CDCl₃): 166.0, 140.6, 140.2, 132.96, 132.95, 128.2, 126.3, 126.2, 124.3, 124.2, 51.9, 33.3, 32.6, 31.6. ¹⁹F NMR (282 MHz, CDCl₃): - 58.2. IR (neat): 2953 (m), 1726 (s), 1652 (m), 1458 (m), 1437 (m), 1320 (s), 1280 (s), 1163 (s), 1125 (s), 1038 (m), 1010 (m), 981 (m), 865 (w), 804 (m), 764 (m), 719 (w). Rf (n-hexane/EtOAc, 3:1) = 0.65. HRMS: calcd for C₁₄H₁₃BrF₃O₂ [M+H]+ 351.0202: found 351.0201.

Methyl (2E)-3-[2-(3-bromopropyl)-6-phenylphenyl]prop-2-enoate (2e)


Yield: 379 mg (53%); yellow oil.

¹H NMR (250 MHz, CDCl₃): 7.76 (d, J = 16.5 Hz, 1H, aryl-CH=CH), 7.37 – 7.19 (m, 8H, aryl-H), 5.66 (d, J = 16.5 Hz, 1H, aryl-CH=CH), 3.69 (s, 3H, COOCH₃), 3.43 (t, J = 6.5 Hz, 2H, CH₂-Br), 2.93 (t, J = 7.5 Hz, 2H, CH₂CH₂CH₂-Br), 2.12 (m, 2H, CH₂CH₂Br). ¹³C NMR (63 MHz, CDCl₃): 166.7, 142.9, 142.4, 141.2, 139.7, 132.7, 129.7, 128.9, 128.5, 128.2, 127.2, 124.8, 51.6, 33.7, 33.0, 32.1. IR (neat): 3057 (m), 3023 (m), 2949 (m), 1572 (w), 1496 (w), 1458 (m), 1436 (s), 1309 (s), 1270 (s), 1234 (m), 1195 (s), 1170 (s), 1073 (w), 1037 (m), 983 (m), 865 (w), 801 (m), 763 (s), 702 (s). Rf (n-hexane/EtOAc, 3:1) = 0.70. HRMS: calcd for C₁₉H₂₀BrO₂ [M+H]+ 359.0641: found 359.0642.

Methyl (2E)-3-[2-(3-bromopropyl)naphthalen-1-yl]prop-2-enoate (2f)


Yield: 597 mg (90%); yellow oil.

¹H NMR (250 MHz, CDCl₃): 8.20 (d, J = 16.3 Hz, 1H, aryl-CH=CH), 8.03 (m, 1H, aryl-H), 7.85 – 7.77 (m, 2H, aryl-H), 7.53 – 7.43 (m, 2H, aryl-H), 7.38 (d, J = 8.5 Hz, 1H, aryl-H), 6.23 (d, J = 16.3 Hz, 1H, aryl-CH=CH), 3.88 (s, 3H, COOCH₃), 3.42 (t, J = 6.5 Hz, 2H, CH₂-Br),
2.99 (t, J = 7.8 Hz, 2H, CH₂-CH₂-CH₂-Br), 2.18 (m, 2H, CH₂-CH₂-Br). ¹³C NMR (63 MHz, CDCl₃): 166.7, 142.5, 136.4, 132.3, 131.3, 128.9, 128.2, 127.5, 126.6, 125.8, 125.5, 124.9, 51.8, 33.8, 32.9, 32.1. IR (neat): 3052 (m), 2950 (m), 1721 (s), 1641 (m), 1508 (w), 1435 (m), 1272 (s), 1171 (s), 1037 (m), 865 (m), 818 (w), 751 (m).  

Rₚ (n-hexane/EtOAc, 3:1) = 0.65. HRMS: calcd for C₁₇H₁₇BrO₂Na [M+Na]⁺ 355.0304: found 355.0307.

**Methyl (2E)-3-[2-(3-bromopropyl)anthracen-1-yl]prop-2-enoate (2g)**

Eluent for column chromatography: n-hexane/EtOAc, 50:1 → 25:1.

Yield: 585 mg (76%); yellow solid after recrystallization from MeCN.

¹ H NMR (250 MHz, CDCl₃): 8.54 (s, 1H, aryl-H), 8.40 (s, 1H, aryl-H), 8.32 (d, J = 16.3 Hz, 1H, aryl-CH=CH), 8.02 – 7.93 (m, 3H, aryl-H), 7.51 – 7.45 (m, 2H, aryl-H), 7.35 (d, J = 8.8 Hz, 1H, aryl-H), 6.35 (d, J = 16.5 Hz, 1H, aryl-CH=CH), 3.92 (s, 3H, COOCH₃), 3.45 (t, J = 6.5 Hz, 2H, CH₂-Br), 3.03 (t, J = 7.3 Hz, 2H, CH₂-CH₂-CH₂-Br), 2.22 (m, 2H, CH₂-CH₂-Br). ¹³C NMR (63 MHz, CDCl₃): 166.9, 142.6, 136.0, 132.1, 131.3, 130.7, 130.5, 129.7, 129.3, 128.5, 127.8, 127.4, 126.7, 125.75, 125.7, 123.8, 51.9, 33.9, 32.9, 32.3. IR (neat): 2945 (w), 1710 (s), 1634 (w), 1455 (m), 1437 (m), 1321 (w), 1264 (s), 1193 (m), 1166 (m), 1133 (w), 1038 (s), 981 (m), 877 (s), 858 (m), 803 (w), 739 (s), 715 (m), 653 (w), 619 (w), 554 (m). mp: 74 – 77 °C.  

Rₚ (n-hexane/EtOAc, 3:1) = 0.55. HRMS: calcd for C₂₁H₁₉BrO₂ [M⁺] 382.0563: found 382.0561.

**Methyl (2E)-3-[10-(3-bromopropyl)phenanthren-9-yl]prop-2-enoate (2h)**

Eluent for column chromatography: n-hexane/EtOAc 25:1, → 10:1.

Yield: 219 mg (29%); colourless solid after recrystallization from DCM/n-hexane.

¹ H NMR (250 MHz, CDCl₃): 8.76 – 8.69 (m, 2H, aryl-H), 8.26 (d, J = 16.3 Hz, 1H, aryl-CH=CH), 8.17 (m, 1H, aryl-H), 8.00 (m, 1H, aryl-H), 7.70 – 7.55 (m, 4H, aryl-H), 6.23 (d, J = 16.3 Hz, 1H, aryl-CH=CH), 3.90 (s, 3H, COOCH₃), 3.55 (t, J = 6.5 Hz, 2H, CH₂-Br), 3.34 (t, J = 8 Hz, 2H, CH₂-CH₂-CH₂-Br), 2.23 (m, 2H, CH₂-CH₂-Br). ¹³C NMR (63 MHz, CDCl₃): 166.6, 144.0, 133.1, 130.7, 130.6, 130.3, 130.0, 129.7, 127.2, 126.9, 126.5, 126.3, 126.1, 124.8, 123.2, 122.8, 110.0, 51.9, 33.5, 33.2, 28.8 ppm. IR (KBr): 3072 (w), 2951 (w), 1717 (s), 1639 (m), 1493 (w), 1432 (m), 1322 (m), 1270 (s), 1176 (s), 1035 (w), 1006 (w), 758 (s), 726 (m). mp: 93 – 96 °C.  

Rₚ (n-hexane/EtOAc, 3:1) = 0.65. HRMS: calcd for C₂₁H₁₉BrO₂ [M⁺] 382.0563: found 382.0569.

**Methyl (2E)-3-[2-(3-bromopropyl)pyren-1-yl]prop-2-enoate (2i)**

Eluent for column chromatography: n-hexane/EtOAc 25:1, → 10:1.

Yield: 562 mg (69%); yellow solid after recrystallization from MeCN.
$^1$H NMR (250 MHz, CDCl$_3$): 8.43 (d, J = 16.3 Hz, 1H, aryl-CH=CH), 8.33 (d, J = 9.5 Hz, 1H, aryl-H), 8.18 (d, J = 7.5 Hz, 2H, aryl-H), 8.10 – 7.97 (m, 5H, aryl-H), 6.38 (d, J = 16.3 Hz, 1H, aryl-CH=CH), 3.93 (s, 3H, COOCH$_3$), 3.48 (t, J = 6.5 Hz, 2H, CH$_2$Br), 3.25 (t, J = 7.3 Hz, 2H, CH$_2$CH$_2$CH$_2$Br), 2.31 (m, 2H, CH$_2$CH$_2$Br). $^{13}$C NMR (63 MHz, CDCl$_3$): 166.8, 142.8, 136.6, 131.4, 131.1, 129.5, 129.2, 128.3, 128.2, 127.0, 126.3, 126.0, 125.8, 125.6, 125.3, 124.6, 124.4, 123.7, 51.9, 34.0, 33.0, 32.6.

IR (KBr): 2927 (m), 2857 (w), 1721 (s), 1638 (m), 1596 (w), 1437 (m), 1285 (s), 1200 (m), 1171 (s), 988 (m), 884 (m), 842 (s), 763 (m), 713 (m), 671 (w), 604 (w).

mp: 121 – 124 °C. $R_f$ (n-hexane/EtOAc, 3:1) = 0.60.

Elementary analysis: calcd for C$_{23}$H$_{19}$BrO$_2$: C 67.82, H 4.70; found C 67.56, H 4.76.

Methyl (2E)-3-[2-(3-bromopropyl)-1-[(4-methylbenzene)sulfonyl]-1H-indol-3-yl]prop-2-enoate (2j)


Yield: 71 mg (7%) (calculated from the $^1$H NMR with mesitylene as standard); colourless solid after recrystallization from DCM/n-hexane.

$^1$H NMR (250 MHz, CDCl$_3$): 8.25 (m, 1H, aryl-H), 7.88 (d, J = 16.3 Hz, 1H, aryl-CH=CH), 7.78 (m, 1H, aryl-H), 7.62 (d, J = 8.3 Hz, 2H, aryl-H), 7.40 – 7.29 (m, 2H, aryl-H), 7.21 (d, J = 6.5 Hz, 2H, aryl-H), 6.54 (d, J = 16.3 Hz, 1H, aryl-CH=CH), 3.82 (s, 3H, COOCH$_3$), 3.48 (t, J = 7.3 Hz, 2H, CH$_2$CH$_2$CH$_2$Br), 3.33 (t, J = 7.3 Hz, 2H, CH$_3$), 2.35 (s, 3H, CH$_3$), 2.32 (m, 2H, CH$_2$CH$_2$Br). $^{13}$C NMR (63 MHz, CDCl$_3$): 167.6, 145.4, 142.4, 137.0, 135.3, 130.1, 127.4, 126.3, 125.2, 124.5, 120.1, 118.9, 117.1, 115.3, 105.0, 51.7, 33.7, 32.7, 25.4, 21.6. IR (KBr): 2951 (m), 2371 (w), 1715 (s), 1632 (s), 1447 (m), 1372 (s), 1279 (s), 1232 (m), 1175 (s), 1121 (m), 1088 (m), 1008 (m), 978 (m), 850 (w), 812 (w), 746 (m), 681 (m), 657 (w), 574 (s). mp: 104 – 106 °C. $R_f$ (n-hexane/EtOAc, 3:1) = 0.55. MS (ESI): calcd for C$_{22}$H$_{22}$BrNO$_4$S [M$^+$] 475.05, found 396.5 (100.00) [M-Br]$^+$, 476.4 (42.95) [M+H]$^+$, 498.4 (75.62) [M+Na]$^+$.

General procedure for the substitution reaction with HNBoc$_2$ (3a-i); GP3:

The alkyl bromide 2a-i (1 equiv), Cs$_2$CO$_3$ (2 equiv; for 2a 3 equiv) and HNBoc$_2$ (1.1 equiv; for 2a 2.1 equiv) were dissolved in dry DMF in a sealable tube and heated to 90 °C overnight.

For workup H$_2$O was added and the reaction mixture was extracted with EtOAc (3x). The combined organic layers were dried over MgSO$_4$, concentrated in vacuo and purified by column chromatography.

Methyl (2E)-3-[2,6-bis(3-{bis[(tert-butoxy)carbonyl]amino}propyl)phenyl]prop-2-enoate (3a)

Following GP3 using bromide 2a (904 mg; 2.24 mmol), Cs$_2$CO$_3$ (2.19 g; 6.72 mmol) and HNBoc$_2$ (1.02 g; 4.70 mmol) in dry DMF (10 mL).

Yield: 1.51 g (99%); colourless oil.

$^{1}$H NMR (250 MHz, CDCl₃): 7.84 (d, J = 16.5 Hz, 1H, aryl-CH=CH), 7.23 – 7.06 (m, 3H, aryl-H), 6.00 (d, J = 16.5 Hz, 1H, aryl-CH=CH), 3.80 (s, 3H, COOCH₃), 3.58 (t, J = 7.5 Hz, 4H, CH₂-CH₂-NBoc₂), 2.61 (t, J = 7.8 Hz, 4H, CH₂-CH₂-CH₂-CH₂-NBoc₂), 1.81 (m, 4H, CH₂-CH₂-CH₂-NBoc₂), 1.48 (s, 36H, t-Bu). $^{13}$C NMR (63 MHz, CDCl₃): 166.4, 152.5, 143.4, 139.8, 133.9, 128.3, 126.9, 124.5, 82.1, 51.6, 46.2, 30.9, 30.1, 28.1. IR (neat): 2979 (s), 1789 (m), 1726 (s), 1696 (s), 1642 (w), 1456 (m), 1393 (s), 1367 (s), 1303 (s), 1170 (s), 1138 (s), 1113 (s), 1041 (w), 983 (w), 888 (w), 855 (m), 763 (m).

Rf ($n$-hexane/EtOAc, 3:1) = 0.50. HRMS: calcd for C₃₆H₅₆N₂O₁₀Na [M+Na]+ 699.3827: found 699.3821.

Methyl (2E)-3-[2-(3-{bis[(tert-butoxy)carbonyl]amino}propyl]-6-methylphenyl]prop-2-enoate (3b)

Following GP3 using bromide 2b (300 mg; 1.01 mmol), Cs₂CO₃ (658 mg; 2.02 mmol) and HNBOc₂ (241 mg; 1.11 mmol) in dry DMF (5 mL).


Yield: 421 mg (96%); colourless oil.

$^{1}$H NMR (250 MHz, CDCl₃): 7.84 (d, J = 16.5 Hz, 1H, aryl-CH=CH), 7.16 (m, 1H, aryl-H), 7.13 – 7.05 (m, 2H, aryl-H), 6.04 (d, J = 16.5 Hz, 1H, aryl-CH=CH), 3.81 (s, 3H, COOCH₃), 3.59 (t, J = 7.5 Hz, 2H, CH₂-NBOc₂), 2.64 (t, J = 7.8 Hz, 2H, CH₂-CH₂-CH₂-NBOc₂), 2.32 (s, 3H, CH₃), 1.83 (m, 2H, CH₂-CH₂-NBOc₂), 1.48 (s, 18H, t-Bu). $^{13}$C NMR (63 MHz, CDCl₃): 166.8, 152.5, 143.5, 140.0, 136.3, 133.9, 128.4, 128.3, 126.8, 124.1, 82.1, 51.6, 46.2, 30.9, 30.1, 28.0, 21.1. IR (neat): 2979 (m), 1789 (w), 1724 (s), 1697 (s), 1640 (w), 1525 (w), 1458 (m), 1438 (m), 1393 (m), 1367 (s), 1270 (m), 1170 (s), 1137 (s), 1111 (s), 1039 (w), 986 (w), 856 (m), 763 (m). $R_f$ (n-hexane/EtOAc, 3:1) = 0.65. HRMS: calcd for C₂₄H₃₅NO₆Na [M+Na]+ 456.2357: found 456.2370.

Methyl (2E)-3-[2-(3-{bis[(tert-butoxy)carbonyl]amino}propyl]-6-methoxyphenyl]prop-2-enoate (3c)

Following GP3 using bromide 2c (566 mg; 1.81 mmol), Cs₂CO₃ (1.18 g; 3.62 mmol) and HNBOc₂ (432 mg; 1.99 mmol) in dry DMF (12 mL).


Yield: 697 mg (86%); colourless oil.

$^{1}$H NMR (250 MHz, CDCl₃): 7.85 (d, J = 16.3 Hz, 1H, aryl-CH=CH), 7.21 (m, 1H, aryl-H), 6.81 (m, 2H, aryl-H), 6.67 (d, J = 16.3 Hz, 1H, aryl-CH=CH), 3.85 (s, 3H, COOCH₃), 3.79 (s, 3H, OCH₃), 3.60 (t, J = 7.5 Hz, 2H, CH₂-NBOc₂), 2.75 (t, J = 7.8 Hz, 2H, CH₂-CH₂-CH₂-NBOc₂), 1.85 (m, 2H, CH₂-CH₂-CH₂-NBOc₂), 1.46 (s, 18H, t-Bu). $^{13}$C NMR (63 MHz, CDCl₃): 168.1, 159.2, 152.4, 143.2, 138.3, 130.1, 122.5, 122.1, 109.0, 82.1, 81.9, 55.4, 51.5, 46.1, 31.0, 30.3, 28.0. IR (neat): 2979 (m), 1791 (m), 1716 (s), 1628 (m), 1595 (m), 1574 (m), 1471 (m), 1393 (m), 1367 (s), 1310 (m), 1264 (s), 1168 (s), 1137 (s), 1112 (s), 1041 (w), 986 (w), 853 (m), 784
Methyl (2E)-3-[2-(3-{bis[(tert-butoxy)carbonyl]amino}propyl)-6-(trifluoromethyl)phenyl] prop-2-enoate (3d)

Following GP3 using bromide 2d (285 mg; 0.81 mmol), Cs₂CO₃ (528 mg; 1.62 mmol) and HNBoc₂ (193 mg; 0.89 mmol) in dry DMF (6 mL).

Eluent for column chromatography: n-hexane/EtOAc, 10:1.

Yield: 359 mg (91%); colourless oil.

\(^{1}H\) NMR (250 MHz, CDCl₃): 7.87 (dd, \(J = 1.5\) Hz, 16.3 Hz, 1H, aryl-CH=CH), 7.55 (d, \(J = 7.3\) Hz, 1H, aryl-H), 7.44 – 7.33 (m, 2H, aryl-H), 6.03 (d, \(J = 16.3\) Hz, 1H, aryl-CH=CH), 3.82 (s, 3H, COOCH₃), 3.59 (t, \(J = 7.3\) Hz, 2H, CH₂-NBoc₂), 2.65 (t, \(J = 7.8\) Hz, 2H, CH₂-CH₂-CH₂-NBoc₂), 1.83 (m, 2H, CH₂-CH₂-NBoc₂), 1.48 (s, 18H, t-Bu). \(^{13}C\) NMR (63 MHz, CDCl₃): 166.0, 152.5, 141.1, 140.8, 133.7, 132.5, 128.1, 126.10, 126.10, 123.94, 123.85, 82.3, 51.8, 46.0, 30.5, 29.8, 28.0. \(^{19}F\) NMR (282 MHz, CDCl₃): - 58.1. IR (neat): 2980 (m), 1795 (m), 1730 (s), 1654 (w), 1458 (m), 1394 (m), 1368 (s), 1319 (s), 1139 (s), 1041 (w), 981 (w), 853 (m), 806 (w), 764 (w). \(R_f\) (n-hexane/EtOAc, 3:1) = 0.60. HRMS: calcd for C₂₄H₃₅NO₇K [M+K]⁺ 488.2045: found 488.2032.

Methyl (2E)-3-[2-(3-{bis[(tert-butoxy)carbonyl]amino}propyl)-6-phenylphenyl] prop-2-enoate (3e)

Following GP3 using bromide 2e (367 mg; 1.02 mmol), Cs₂CO₃ (665 mg; 2.04 mmol) and HNBoc₂ (243 mg; 1.12 mmol) in dry DMF (7 mL).


Yield: 454 mg (90%); colourless oil.

\(^{1}H\) NMR (250 MHz, CDCl₃): 7.73 (d, \(J = 16.3\) Hz, 1H, aryl-CH=CH), 7.39 – 7.29 (m, 5H, aryl-H), 7.23 – 7.16 (m, 3H, aryl-H), 5.67 (d, \(J = 16.3\) Hz, 1H, aryl-CH=CH), 3.69 (s, 3H, COOCH₃), 3.63 (t, \(J = 7.5\) Hz, 2H, CH₂-NBoc₂), 2.75 (t, \(J = 8\) Hz, 2H, CH₂-CH₂-CH₂-NBoc₂), 1.89 (m, 2H, CH₂-CH₂-NBoc₂), 1.48 (s, 18H, t-Bu). \(^{13}C\) NMR (63 MHz, CDCl₃): 166.6, 152.5, 143.1, 142.3, 141.3, 140.6, 132.6, 129.7, 128.6, 128.49, 128.46, 128.1, 127.1, 124.6, 82.1, 51.5, 46.2, 31.1, 30.2, 28.1. IR (neat): 2979 (m), 1790 (m), 1723 (s), 1638 (m), 1458 (m), 1438 (m), 1393 (m), 1367 (s), 1306 (m), 1170 (s), 1138 (s), 1114 (s), 1040 (w), 983 (w), 854 (w), 763 (m), 702 (m). \(R_f\) (n-hexane/EtOAc, 3:1) = 0.55. HRMS: calcd for C₂₉H₃₂F₃NO₆Na [M+Na]+ 518.2513: found 518.2506.
Methyl (2E)-3-[2-(3-{bis[(tert-butoxy)carbonyl]amino}propyl)naphthalen-1-yl]prop-2-enoate (3f)

Following GP3 using bromide 2f (582 mg; 1.75 mmol), Cs$_2$CO$_3$ (1.14 g; 3.50 mmol) and HNBoc$_2$ (419 mg; 1.93 mmol) in dry DMF (8 mL).

Eluent for column chromatography: $n$-hexane/EtOAc, 25:1 $\rightarrow$ 10:1.

Yield: 747 mg (91%); light yellow oil.

$^1$H NMR (250 MHz, CDCl$_3$): 8.18 (d, $J = 16.3$ Hz, 1H, aryl-CH=CH), 8.01 (m, 1H, aryl-H), 7.83 – 7.76 (m, 2H, aryl-H), 7.51 – 7.42 (m, 2H, aryl-H), 7.36 (d, $J = 8.5$ Hz, 1H, aryl-H), 6.22 (d, $J = 16.3$ Hz, 1H, aryl-CH=CH), 3.87 (s, 3H, COOCH$_3$), 3.64 (t, $J = 7.5$ Hz, 2H, CH$_2$-NBoc$_2$), 2.82 (t, $J = 7.5$ Hz, 2H, CH$_2$-CH$_2$-CH$_2$-NBoc$_2$), 1.91 (m, 2H, CH$_2$-CH$_2$-CH$_2$-NBoc$_2$), 1.47 (s, 18H, t-Bu).

$^{13}$C NMR (63 MHz, CDCl$_3$): 166.7, 152.5, 142.6, 137.5, 132.2, 131.4, 131.0, 130.7, 128.8, 128.2, 127.4, 126.5, 125.7, 124.9, 82.1, 51.7, 46.2, 31.2, 30.4, 28.0. IR (neat): 2979 (s), 1791 (m), 1725 (s), 1642 (m), 1595 (w), 1509 (m), 1479 (m), 1436 (m), 1368 (s), 1299 (s), 1171 (s), 1134 (s), 1042 (m), 986 (m), 856 (m), 819 (m). R$_f$ ($n$-hexane/EtOAc, 3:1) = 0.60. HRMS: calcd for C$_{27}$H$_{35}$NO$_6$Na [M+Na]$^+$ 492.2357: found 492.2373.

Methyl (2E)-3-[2-(3-{bis[(tert-butoxy)carbonyl]amino}propyl)anthracen-1-yl]prop-2-enoate (3g)

Following GP3 using bromide 2g (627 mg; 1.64 mmol), Cs$_2$CO$_3$ (1.07 g; 3.28 mmol) and HNBoc$_2$ (391 mg; 1.80 mmol) in dry DMF (11 mL).

Eluent for column chromatography: $n$-hexane/EtOAc, 50:1 $\rightarrow$ 25:1 $\rightarrow$ 10:1.

Yield: 652 mg (77%); yellow solid after recrystallization from MeCN.

$^1$H NMR (250 MHz, CDCl$_3$): 8.52 (s, 1H, aryl-H), 8.39 (s, 1H, aryl-H), 8.30 (d, $J = 16.5$ Hz, 1H, aryl-CH=CH), 8.02 – 7.92 (m, 3H, aryl-H), 7.50 – 7.44 (m, 2H, aryl-H), 7.34 (d, $J = 8.8$ Hz, 1H, aryl-H), 6.33 (d, $J = 16.3$ Hz, 1H, aryl-CH=CH), 3.91 (s, 3H, COOCH$_3$), 3.66 (t, $J = 7.5$ Hz, 2H, CH$_2$-NBoc$_2$), 2.86 (t, $J = 8$ Hz, 2H, CH$_2$-CH$_2$-CH$_2$-NBoc$_2$), 1.95 (m, 2H, CH$_2$-CH$_2$-CH$_2$-NBoc$_2$), 1.48 (s, 18H, t-Bu). $^{13}$C NMR (63 MHz, CDCl$_3$): 166.8, 152.5, 142.8, 137.0, 132.0 131.2, 130.5, 130.2, 129.8, 129.2, 128.5, 127.8, 127.3, 126.6, 125.7, 125.61, 125.59, 123.7, 82.2, 51.8, 46.3, 31.3, 30.4, 28.1. IR (neat): 2987 (w), 1747 (m), 1712 (s), 1641 (w), 1462 (w), 1368 (m), 1292 (m), 1273 (m), 1164 (s), 1126 (s), 1106 (s), 983 (m), 885 (m), 861 (m), 806 (w), 780 (m), 745 (s), 714 (w), 622 (w). mp: 91 – 94 °C. R$_f$ ($n$-hexane/EtOAc, 3:1) = 0.65. HRMS: calcd for C$_{31}$H$_{37}$NO$_6$Na [M+Na]$^+$ 542.2513: found 542.2506.

Methyl (2E)-3-[10-(3-{bis[(tert-butoxy)carbonyl]amino}propyl)phenanthren-9-yl]prop-2-enoate (3h)

Following GP3 using bromide 2h (411 mg; 1.07 mmol), Cs$_2$CO$_3$ (697 mg; 2.14 mmol) and HNBoc$_2$ (256 mg; 1.18 mmol) in dry DMF (8 mL).

Eluent for column chromatography: $n$-hexane/EtOAc, 25:1 $\rightarrow$ 10:1.
Yield: 448 mg (81%); colourless solid after recrystallization from DCM/n-hexane.

$^1$H NMR (250 MHz, CDCl$_3$): 8.72 (m, 2H, aryl-H), 8.24 (d, $J = 16.5$ Hz, 1H, aryl-CH=CH), 8.11 (m, 1H, aryl-H), 7.99 (dd, $J = 1$ Hz, 7.8 Hz, 1H, aryl-H), 7.70 – 7.54 (m, 4H, aryl-H), 6.22 (d, $J = 16.5$ Hz, 1H, aryl-CH=CH), 3.89 (s, 3H, COOCH$_3$), 3.75 (t, $J = 7.3$ Hz, 2H, CH$_2$-NBOc$_2$), 3.16 (t, $J = 8.3$ Hz, 2H, CH$_2$-CH$_2$-CH$_2$-NBOc$_2$), 1.96 (m, 2H, CH$_2$-CH$_2$-NBOc$_2$), 1.49 (s, 18H, t-Bu).

$^{13}$C NMR (63 MHz, CDCl$_3$): 166.5, 152.5, 144.0, 133.9, 130.6, 130.3, 130.2, 130.1, 129.6, 127.0, 126.79, 126.76, 126.3, 126.2, 126.0, 124.9, 123.2, 122.7, 82.2, 46.4, 31.6, 30.5, 28.0.

IR (neat): 2977 (s), 1785 (m), 1725 (s), 1643 (m), 1525 (w), 1440 (m), 1364 (s), 1267 (s), 1138 (s), 1042 (m), 988 (w), 856 (m), 755 (s).

mp: 81 – 84 °C. $R_f$ (n-hexane/EtOAc, 3:1) = 0.55. HRMS: calcd for C$_{31}$H$_{37}$NO$_6$Na [M+Na]$^+$ 542.2513: found 542.2505.

Methyl (2E)-3-[2-(3-{bis[(tert-butoxy)carbonyl]amino}propyl)pyren-1-yl] prop-2-enoate (3i)

Following GP3 using bromide 2i (418 mg; 1.03 mmol), Cs$_2$CO$_3$ (671 mg; 2.06 mmol) and HNBoc$_2$ (246 mg; 1.13 mmol) in dry DMF (8 mL).


Yield: 553 mg (99%); yellow solid after recrystallization from DCM/n-hexane.

$^1$H NMR (250 MHz, CDCl$_3$): 8.42 (d, $J = 16.3$ Hz, 1H, aryl-CH=CH), 8.33 (d, $J = 9.3$ Hz, 1H, aryl-H), 8.18 (d, $J = 7.8$ Hz, 2H, aryl-H), 8.10 – 7.96 (m, 5H, aryl-H), 6.37 (d, $J = 16.3$ Hz, 1H, aryl-CH=CH), 3.91 (s, 3H, COOCH$_3$), 3.72 (t, $J = 7.5$ Hz, 2H, CH$_2$-NBOc$_2$), 3.09 (t, $J = 8$ Hz, 2H, CH$_2$-CH$_2$-CH$_2$-NBOc$_2$), 2.07 (m, 2H, CH$_2$-CH$_2$-NBOc$_2$), 1.47 (s, 18H, t-Bu).

$^{13}$C NMR (63 MHz, CDCl$_3$): 166.7, 152.6, 142.9, 137.6, 131.3, 131.0, 130.4, 129.4, 129.0, 128.1, 128.0, 127.0, 126.1, 125.9, 125.4, 125.2, 124.5, 124.431, 124.426, 123.5, 82.1, 51.8, 46.3, 31.6, 30.5, 28.0. IR (KBr): 2978 (m), 2869 (w), 1749 (s), 1712 (s), 1629 (w), 1598 (w), 1443 (m), 1364 (s), 1306 (s), 1264 (s), 1136 (s), 1033 (m), 987 (w), 887 (w), 855 (m), 777 (m), 717 (w), 688 (w). $R_f$: 0.10 – 0.13. HRMS: calcd for C$_{33}$H$_{37}$NO$_6$ [M]$^+$ 543.2615: found 543.2619.

General procedure for the conversion to the carboximides (5a-i); GP4:

The starting material was dissolved in MeOH (or in some cases in a mixture of MeOH and EtOAc). After addition of palladium on activated carbon (10% Pd basis, moistened with water; 20 wt-%) the reaction mixture was stirred under a H$_2$ atmosphere for 8 h. The catalyst was removed by filtration over Celite® and the solvent was removed under reduced pressure.

The crude product was dissolved in MeOH and an aq NaOH solution (8 M; 1:1, v/v) was added. The reaction mixture was stirred at room temperature overnight.

For workup the solution was acidified with HCl (4 M) under ice cooling and extracted with DCM (3x). After drying over MgSO$_4$ the solvent was removed under reduced pressure.
The crude carboxylic acid was dissolved in dry THF under an argon atmosphere and cooled to -78 °C. Pivaloylchloride (1.2 equiv) and NEt₃ (1.5 equiv) were added which led to the formation of a colourless precipitate. The mixture was stirred at -78 °C for 15 min and at 0 °C for 45 min.

In a second flask (R)-4-benzyl-2-oxazolidinone (2 equiv) was dissolved in THF under an argon atmosphere and cooled to -78 °C. After dropwise addition of n-butyllithium (1.6 M in hexane; 1.9 equiv), it was stirred at -78 °C for approximately 30 min.

After 45 min at 0 °C the activated carboxylic acid was again cooled to -78 °C and the lithiated oxazolidinone was added. The reaction mixture was then allowed to warm to room temperature overnight.

For workup diluted NaHCO₃ solution was added and it was extracted with DCM (3x). The combined organic phases were washed with diluted NaHCO₃-solution and with brine, dried over MgSO₄ and concentrated under reduced pressure. The product was purified by column chromatography.

tert-Butyl N-[3-(2{-[4R]-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl}-3-[(tert-butoxy)carbonyl]amino)propyl]phenyl]propyl carbamate (5a)

Following GP4 using methylester 3a (2.07 g; 3.06 mmol), Pd/C (414 mg), MeOH (30 mL); NaOH (8 M; 20 mL), MeOH (20 mL); Piv-Cl (452 μL; 3.67 mmol), NEt₃ (640 μL; 4.59 mmol), dry THF (34 mL), (R)-4-benzyl-2-oxazolidinone (1.08 g; 6.12 mmol), n-BuLi (1.6 M in n-hexane; 3.63 mL; 5.81 mmol), dry THF (17 mL).

Eluent for column chromatography: cyclohexane/EtOAc, 3:1 → 1:1.

Yield: 1.38 g (72% over 3 steps); colourless solid after recrystallization from DCM/n-hexane.

1H NMR (250 MHz, CDCl₃): 7.39 – 7.29 (m, 3H, aryl-H), 7.25 – 7.22 (m, 2H, aryl-H), 7.14 – 7.01 (m, 3H, aryl-H), 4.76 – 4.61 (m, 3H, CH + NH), 4.29 – 4.17 (m, 2H, CH₂-O), 3.37 (dd, J = 3.3 Hz, 13.3 Hz, CH-H-phenyl), 3.21 (m, 4H, C-H₂-NH-Boc), 3.13 – 2.97 (m, 4H, CH₂-C₂H₂-CH₂-NH-Boc), 2.81 (dd, J = 9.8 Hz, 13.3 Hz, 1H, CHH-phenyl), 2.69 (t, J = 7.8 Hz, 4H, C₂H₂-CH₂-CH₂-NH-Boc), 1.79 (m, 4H, CH₂-CH₂-CH₂-NH-Boc), 1.44 (s, 18H, t-Bu).

13C NMR (63 MHz, CDCl₃): 172.4, 156.0, 153.5, 140.3, 135.9, 135.3, 129.4, 129.0, 127.5, 127.4, 126.6, 79.1, 66.4, 55.3, 40.8, 38.0, 36.4, 31.9, 30.3, 28.4, 23.6. IR (neat): 3370 (m), 2972 (m), 1788 (s), 1702 (m), 1683 (s), 1519 (s), 1445 (w), 1395 (m), 1366 (s), 1294 (m), 1249 (m), 1216 (s), 1166 (s), 1119 (m), 1058 (m), 870 (w), 782 (w), 757 (w), 699 (m), 599 (m). mp: 126 – 128 °C. Rf (n-hexane/EtOAc, 2:1) = 0.25. [α]D20 = -55.5° (c = 0.94, MeOH).


tert-Butyl N-[3-{2-{[4R]-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl}-3-methyl phenyl]propyl]carbamate (5b)

Following GP4 using methylester 3b (362 mg; 0.83 mmol), Pd/C (72 mg), MeOH (8 mL); NaOH (8 M; 5 mL), MeOH (5 mL); Piv-Cl (123 μL; 1.00 mmol), NEt₃ (174 μL; 1.25 mmol), dry
THF (9 mL), (R)-4-benzyl-2-oxazolidinone (294 mg; 1.66 mmol), n-BuLi (1.6 M in n-hexane; 988 μL; 1.58 mmol), dry THF (4.5 mL).

Eluent for column chromatography: cyclohexane/EtOAc, 3:1 → 1:1.

Yield: 321 mg (80% over 3 steps); colourless solid after recrystallization from DCM/n-hexane.

**1H NMR** (250 MHz, CDCl₃): 7.39 – 7.29 (m, 3H, aryl-H), 7.25 – 7.22 (m, 2H, aryl-H), 7.11 – 7.00 (m, 3H, aryl-H), 4.76 – 4.64 (m, 2H, CH + NH), 4.28 – 4.16 (m, 2H, CH₂-O), 3.36 (dd, J = 3.3 Hz, 13.5 Hz, 1H, CHH-phenyl), 3.21 (t, J = 7 Hz, 2H, CH₂-NH-Boc), 3.14 – 2.98 (m, 4H, CH₂-CO + CH₂-CH₂-CO), 2.82 (dd, J = 9.5 Hz, 13.5 Hz, 1H, CHH-phenyl), 2.69 (t, J = 7.8 Hz, 2H, CH₂-CO₂-NH-Boc), 1.79 (m, 2H, CH₂-CH₂-NH-Boc), 1.45 (s, 9H, t-Bu).

**13C NMR** (63 MHz, CDCl₃): 172.6, 156.0, 153.4, 139.9, 136.7, 136.4, 135.3, 129.4, 129.0, 128.5, 127.4, 127.2, 126.4, 79.1, 66.3, 55.2, 40.7, 38.0, 35.4, 31.9, 30.2, 28.4, 24.0, 19.9.

**IR** (neat): 3374 (w), 2981 (m), 1788 (s), 1760 (m), 1706 (s), 1680 (s), 1513 (s), 1394 (m), 1365 (m), 1299 (m), 1274 (m), 1229 (m), 1186 (s), 1164 (s), 1120 (m), 1098 (m), 1049 (m), 978 (m), 866 (w), 780 (m), 761 (s), 735 (s), 701 (s), 676 (m), 593 (m), 511 (w).

**mp**: 55 – 57 °C. **Rf** (n-hexane/EtOAc, 2:1) = 0.40. **[α]D²⁰** = -63.2° (c = 1.09, MeOH).


**tert-Butyl N-[3-2-(3-[(4R)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl]-3-methoxyphenyl)propyl]carbamate (5c)**

Following GP4 using methylester 3c (1.11 g; 2.47 mmol), Pd/C (222 mg), MeOH/EtOAc (3:1; 29 mL); NaOH (8 M; 17 mL), MeOH (17 mL); Piv-Cl (365 μL; 2.96 mmol), NEt₃ (517 μL; 3.71 mmol), dry THF (29 mL), (R)-4-benzyl-2-oxazolidinone (875 mg; 4.94 mmol), n-BuLi (1.6 M in n-hexane; 2.93 mL; 4.69 mmol), dry THF (14.5 mL).

Eluent for column chromatography: cyclohexane/EtOAc, 3:1 → 1:1.

Yield: 948 mg (77% over 3 steps); colourless solid after recrystallization from DCM/n-hexane.

**1H NMR** (250 MHz, CDCl₃): 7.38 – 7.28 (m, 3H, aryl-H), 7.24 – 7.21 (m, 2H, aryl-H), 7.13 (t, J = 8 Hz, 1H, aryl-H), 6.77 (d, J = 7.8 Hz, 1H, aryl-H), 6.72 (d, J = 8.3 Hz, 1H, aryl-H), 4.73 – 4.64 (m, 2H, CH + NH), 4.24 – 4.14 (m, 2H, CH₂-O), 3.82 (s, 3H, OCH₃), 3.35 (dd, J = 3.3 Hz, 13.3 Hz, 1H, CHH-phenyl), 3.22 – 3.10 + 3.01 (m, 4H + m, 2H, CH₂-CO₂-NH-Boc + CH₂-CO₂-NH-Boc), 2.78 (dd, J = 9.8 Hz, 13.3 Hz, 1H, CHH-phenyl), 2.69 (t, J = 7.8 Hz, 2H, CH₂-CO₂-NH-Boc), 1.77 (m, 2H, CH₂-CO₂-NH-Boc), 1.44 (s, 9H, t-Bu). **13C NMR** (63 MHz, CDCl₃): 173.0, 157.9, 156.0, 153.4, 141.1, 135.4, 129.4, 129.0, 127.3, 127.0, 126.7, 121.7, 108.2, 79.1, 66.2, 55.4, 55.3, 40.7, 38.0, 35.3, 31.7, 30.2, 28.4, 21.0. **IR** (neat): 3369 (m), 2975 (w), 1791 (s), 1694 (s), 1684 (s), 1584 (m), 1530 (m), 1458 (m), 1394 (m), 1368 (m), 1305 (m), 1264 (s), 1216 (s), 1168 (s), 1121 (m), 1104 (m), 1027 (m), 1007 (m), 864 (w), 797 (w), 776 (m), 757 (m), 733 (m), 695 (m), 643 (m), 550 (w), 532 (m), 506 (w).

**mp**: 97 – 100 °C. **Rf** (n-hexane/EtOAc, 2:1) = 0.35. **[α]D²⁰** = -59.5° (c = 0.55, MeOH). **HRMS**: calcd for C₂₈H₃₆N₂O₆K [M+K]+ 535.2205: found 535.2205.
**tert-Butyl N-[3-(2-{3-[(4R)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl}-3-(trifluoromethyl)phenyl)propyl]carbamate (5d)**

Following GP4 using methylester 3d (1.43 g; 2.93 mmol), Pd/C (286 mg), MeOH (30 mL); NaOH (8 M; 19 mL), MeOH (19 mL); Piv-Cl (434 μL; 3.52 mmol), NEt₃ (613 μL; 4.40 mmol), dry THF (33 mL), (R)-4-benzyl-2-oxazolidinone (1.04 g; 5.86 mmol), n-BuLi (1.6 M in n-hexane; 3.48 mL; 5.57 mmol), dry THF (16.5 mL).

Eluent for column chromatography: cyclohexane/EtOAc, 3:1 → 1:1.

Yield: 1.06 g (68% over 3 steps); colourless solid after recrystallization from DCM/n-hexane.

**1H NMR** (250 MHz, CDCl₃): 7.53 (d, J = 7.8 Hz, 1H, aryl-H), 7.39 – 7.29 (m, 5H, aryl-H), 7.24 – 7.21 (m, 2H, aryl-H), 4.78 – 4.61 (m, 2H, CH + NH), 4.30 – 4.18 (m, 2H, CH₂-O), 3.36 (dd, J = 3.3 Hz, 13.3 Hz, 1H, C₆H₆-phenyl), 3.26 – 3.09 (m, 6H, CH₂-CO + C₆H₂-CH₂-CO + C₆H₂-NH-Boc), 2.84 (dd, J = 9.5 Hz, 13.3 Hz, 1H, CHH-phenyl), 2.71 (m, 2H, CH₂-CH₂-CH₂-NH-Boc), 1.81 (m, 2H, CH₂-CH₂-CH₂-NH-Boc), 1.44 (s, 9H, t-Bu).

**13C NMR** (63 MHz, CDCl₃): 171.9, 156.0, 153.5, 142.2, 136.8, 135.2, 133.1, 129.4, 129.0, 127.4, 126.6, 124.4, 124.3, 122.6, 79.3, 66.4, 55.2, 40.5, 37.9, 36.5, 31.8, 29.5, 28.4, 23.4. **19F NMR** (282 MHz, CDCl₃): -59.2. **IR** (neat): 3675 (w), 3373 (w), 2988 (m), 1785 (m), 1711 (s), 1682 (s), 1524 (m), 1456 (w), 1395 (m), 1373 (m), 1314 (m), 1298 (m), 1242 (m), 1210 (m), 1187 (m), 1151 (m), 1113 (s), 1049 (s), 977 (w), 879 (w), 797 (w), 735 (m), 700 (s), 590 (w), 508 (w). **mp**: 91 – 94 °C. **Rf** (n-hexane/EtOAc, 2:1) = 0.35. **[D]D₂₀ = -61.7° (c = 1.03, MeOH). HRMS: calcd for C₂₈H₃₃F₃N₂O₅K [M+K]+ 573.1973: found 573.1966.

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**tert-Butyl N-[3-(2-{3-[(4R)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl}-3-phenyl phenyl)propyl]carbamate (5e)**

Following GP4 using methylester 3e (1.03 g; 2.08 mmol), Pd/C (206 mg), MeOH (21 mL); NaOH (8 M; 15 mL), MeOH (15 mL); Piv-Cl (308 μL; 2.50 mmol), NEt₃ (435 μL; 3.12 mmol), dry THF (25 mL), (R)-4-benzyl-2-oxazolidinone (737 mg; 4.16 mmol), n-BuLi (1.6 M in n-hexane; 2.47 mL; 3.95 mmol), dry THF (12.5 mL).

Eluent for column chromatography: cyclohexane/EtOAc, 3:1 → 1:1.

Yield: 796 mg (71% over 3 steps); colourless oil.

**1H NMR** (250 MHz, CDCl₃): 7.45 – 7.36 (m, 3H, aryl-H), 7.34 – 7.26 (m, 5H, aryl-H), 7.24 – 7.11 (m, 4H, aryl-H), 7.04 (m, 1H, aryl-H), 4.68 (br s, 1H, NH), 4.58 (m, 1H, CH), 4.20 – 4.09 (m, 2H, CH₂-O), 3.28 – 3.17 (m, 3H, CH₂-NH-Boc + CHH-phenyl), 3.04 – 2.88 (m, 4H, CH₂-CH₂-CO + CH₂-CO), 2.76 – 2.67 (m, 3H, CH₂-CH₂-CH₂-NH-Boc + CHH-phenyl), 1.86 (m, 2H, CH₂-CH₂-CH₂-NH-Boc), 1.50 + 1.45 (s*, 9H, t-Bu). **13C NMR** (63 MHz, CDCl₃): 172.1, 156.0, 153.3, 142.3, 140.1, 135.8, 135.2, 129.1, 129.3, 129.4, 128.7, 128.4, 128.1, 127.3, 126.8, 126.1, 79.1, 66.2, 55.0, 40.6, 37.8, 36.2, 31.9, 30.3, 28.4, 28.0, 23.7. **IR** (neat): 3389 (m), 3060 (m), 3027 (m), 2976 (s), 2931 (s), 2869 (m), 1781 (s), 1698 (s), 1604 (w), 1583 (w), 1516 (s), 1454 (s), 1391 (s), 1366 (s), 1303 (s), 1249 (s), 1213 (s), 1169 (s), 1108 (s), 1074 (m), 1052 (m), 985 (m), 920 (w), 865 (w), 803 (w), 763 (s), 704 (s), 636 (w), 549 (w), 508 (w). **Rf** (n-hexane/EtOAc, 3:1 → 1:1). **[D]D₂₀ = -39.1° (c = 1.06, DCM). HRMS: calcd for C₃₃H₃₈N₂O₅K [M+K]+ 581.2412: found 581.2408. 15.
tert-Butyl N-[3-(1-[(4R)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl]naphthalen-2-yl)propyl]carbamate (5f)

Following GP4 using methylester 3f (889 mg; 1.89 mmol), Pd/C (178 mg), MeOH (19 mL); NaOH (8 M; 12 mL), MeOH (12 mL); Piv-Cl (280 μL; 2.27 mmol), NEt3 (396 μL; 2.84 mmol), dry THF (24 mL), (R)-4-benzyl-2-oxazolidinone (670 mg; 3.78 mmol), n-BuLi (1.6 M in n-hexane; 2.24 ml; 3.59 mmol), dry THF (12 mL).

Eluent for column chromatography: cyclohexane/EtOAc, 3:1 → 1:1.

Yield: 628 mg (64% over 3 steps); colourless solid after recrystallization from DCM/n-hexane.

1H NMR (250 MHz, CDCl3): 8.09 (d, J = 8.5 Hz, 1H, aryl-H), 7.81 (dd, J = 1 Hz, 8 Hz, 1H, aryl-H), 7.69 (d, J = 8.5 Hz, 1H, aryl-H), 7.53 (m, 1H, aryl-H), 7.45 (m, 1H, aryl-H), 7.40 – 7.29 (m, 4H, aryl-H), 7.25 – 7.23 (m, 2H, aryl-H), 4.77 – 4.68 (m, 2H, CH + NH), 4.25 – 4.17 (m, 2H, CH2-O), 3.50 (m, 2H, CH2-NH-Boc), 3.38 (dd, J = 3.3 Hz, 13.3 Hz, 1H, CH-phenyl), 3.29 – 3.23 (m, 4H, CH2-CH2-CO + CH2-CO), 2.92 – 2.78 (m, 3H, CH2-CH2-CH2-NH-Boc + CHH-phenyl), 1.87 (m, 2H, CH2-NH-Boc), 1.45 (s, 9H, t-Bu).

13C NMR (63 MHz, CDCl3): 172.6, 156.0, 153.4, 137.2, 135.3, 132.8, 132.6, 132.1, 129.4, 129.0, 128.7, 128.1, 127.4, 127.1, 126.3, 124.9, 123.5, 79.1, 66.3, 55.3, 40.8, 38.0, 36.4, 32.0, 30.8, 28.4, 23.2. IR (neat): 3355 (m), 2972 (w), 1784 (s), 1699 (s), 1679 (s), 1522 (s), 1474 (m), 1442 (w), 1378 (s), 1367 (s), 1347 (m), 1305 (m), 1268 (m), 1239 (m), 1208 (m), 1193 (s), 1171 (s), 1095 (m), 1030 (m), 1018 (w), 996 (s), 946 (w), 927 (w), 870 (w), 818 (m), 793 (w), 782 (w), 764 (m), 752 (m), 738 (s), 705 (s), 671 (w), 613 (m), 579 (m), 565 (m), 530 (m). mp: 105 – 108 °C. Rf (n-hexane/EtOAc, 2:1) = 0.35. [α]D20 = -58.8° (c = 0.50, MeOH). HRMS: calcd for C31H36N2O5K [M+K]+ 555.2256: found 555.2249.

tert-Butyl N-[3-(1-[(4R)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl]anthracen-2-yl)propyl]carbamate (5g)

Following GP4 using methylester 3g (294 mg; 0.57 mmol), Pd/C (59 mg), MeOH/EtOAc (2:1; 8 mL); NaOH (8 M; 4 mL), MeOH (4 mL); Piv-Cl (84 μL; 0.68 mmol), NEt3 (120 μL; 0.86 mmol), dry THF (7 mL), (R)-4-benzyl-2-oxazolidinone (202 mg; 1.14 mmol), n-BuLi (1.6 M in n-hexane; 675 μL; 1.08 mmol), dry THF (3.5 mL).

Eluent for column chromatography: cyclohexane/EtOAc, 3:1 → 1:1.

Yield: 114 mg (35% over 3 steps); yellow solid after recrystallization from DCM/n-hexane.

1H NMR (250 MHz, CDCl3): 8.65 (s, 1H, aryl-H), 8.39 (s, 1H, aryl-H), 8.07 (m, 1H, aryl-H), 7.98 (m, 1H, aryl-H), 7.86 (d, J = 8.8 Hz, 1H, aryl-H), 7.49 – 7.42 (m, 2H, aryl-H), 7.39 – 7.23 (m, 6H, aryl-H), 4.79 – 4.70 (m, 2H, CH + NH), 4.26 – 4.17 (m, 2H, CH2-O), 3.64 + 3.43 – 3.22 (m, 2H + m, 5H, CH2-NH-Boc + CHH-phenyl + CH2-CH2-CO + CH2-CO), 2.95 – 2.76 (m, 3H, CH2-CH2-CH2-NH-Boc + CHH-phenyl), 1.91 (m, 2H, CH2-CH2-CH2-NH-Boc), 1.45 (s, 9H, t-Bu). 13C NMR (63 MHz, CDCl3): 172.7, 156.1, 153.4, 136.5, 135.3, 132.1, 132.0, 131.1, 130.9, 130.6, 129.4, 129.0, 128.7, 128.0, 127.7, 127.5, 127.4, 126.9, 125.34, 125.28, 122.1, 79.1, 66.3, 55.3, 40.7, 38.0, 36.3, 31.8, 31.0, 28.4, 23.5. IR (neat): 3367 (w), 2966 (w), 1790 (s), 1698 (s), 1686 (s), 1537 (s), 1446 (w), 1394 (m), 1365 (m), 1292 (m), 1269 (m), 1250 (m), 1211 (s), 1172 (s), 1121 (m), 1068 (w), 1032 (w), 1000 (m), 879 (m), 818 (m), 793 (w), 782 (w), 764 (m), 752 (m), 738 (s), 705 (s), 671 (w), 613 (m), 579 (m), 565 (m), 530 (m).
tert-Butyl N-[3-{10-[(4R)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl} phenanthren-9-yl]propylcarbamate (5h)

Following GP4 using methylester 3h (1.38 g; 2.66 mmol), Pd/C (276 mg), MeOH/EtOAc (2:1; 26 mL); NaOH (8 M; 17 mL), MeOH (17 mL); Piv-Cl (393 μL; 3.19 mmol), NEt3 (556 μL; 3.99 mmol), dry THF (30 mL), (R)-4-benzyl-2-oxazolidinone (943 mg; 5.32 mmol), n-BuLi (1.6 M in n-hexane; 3.16 mL; 5.05 mmol), dry THF (15 mL).

Eluent for column chromatography: cyclohexane/EtOAc, 3:1 → 1:1.

Yield: 1.03 g (68% over 3 steps); colourless solid after recrystallization from DCM/n-hexane.

1H NMR (250 MHz, CDCl3): 8.75 – 8.70 (m, 2H, aryl-H), 8.18 (m, 1H, aryl-H), 8.10 (m, 1H, aryl-H), 7.70 – 7.60 (m, 4H, aryl-H), 7.40 – 7.25 (m, 5H, aryl-H), 4.87 (br s, 1H, NH), 4.77 (m, 1H, CH), 4.29 – 4.18 (m, 2H, CH2-O), 3.58 + 3.45 – 3.23 (m, 2H + m, 7H, C6H2-CH2-CO + C6H5-phenyl + CH2-CO + CH2-CH2-CH2-NH-Boc + C6H2-CH2-CH2-NH-Boc), 2.86 (dd, J = 9.8 Hz, 13.5 Hz, 1H, CHH-phenyl), 1.94 (m, 2H, C6H2-CH2-NH-Boc), 1.47 (s, 9H, t-Bu).

13C NMR (63 MHz, CDCl3): 172.6, 156.1, 153.5, 135.3, 134.0, 131.5, 130.9, 130.8, 130.2, 130.0, 129.4, 129.0, 127.4, 127.0, 126.8, 125.9, 125.8, 124.5, 124.2, 123.1, 123.0, 79.2, 66.4, 55.3, 41.2, 38.0, 36.1, 31.1, 28.4, 26.5, 24.3.

IR (neat): 3363 (w), 2977 (m), 1783 (s), 1760 (m), 1707 (s), 1677 (s), 1509 (s), 1445 (m), 1394 (s), 1365 (s), 1271 (m), 1238 (m), 1208 (m), 1186 (s), 1167 (s), 1120 (m), 1098 (m), 993 (m), 977 (m), 864 (w), 752 (s), 735 (m), 724 (s), 701 (m), 669 (w), 592 (m), 509 (w).

mp: 166 – 168 °C. Rf (n-hexane/EtOAc, 2:1) = 0.30. [α]D20 = -63.6° (c = 0.50, DCM). HRMS: calcd for C35H38N2O5K [M+K]+ 605.2412: found 605.2409.

tert-Butyl N-[3-{1-[3-[(4R)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl}pyren-2-yl]propyl]carbamate (5i)

Following GP4 using methylester 3i (1.54 g; 2.83 mmol), Pd/C (308 mg), MeOH/EtOAc (1:2; 29 mL); NaOH (8 M; 18 mL), MeOH (18 mL); Piv-Cl (419 μL; 3.40 mmol), NEt3 (592 μL; 4.25 mmol), dry THF (32 mL), (R)-4-benzyl-2-oxazolidinone (1.00 g; 5.66 mmol), n-BuLi (1.6 M in n-hexane; 3.36 mL; 5.38 mmol), dry THF (16 mL).

Eluent for column chromatography: cyclohexane/EtOAc, 3:1 → 1:1.

Yield: 1.30 g (78% over 3 steps); colourless solid after recrystallization from DCM/n-hexane.

1H NMR (250 MHz, CDCl3): 8.36 (d, J = 9.5 Hz, 1H, aryl-H), 8.18 – 8.12 (m, 3H, aryl-H), 8.04 – 7.94 (m, 4H, aryl-H), 7.39 – 7.23 (m, 5H, aryl-H), 4.86 – 4.71 (m, 2H, CH + NH), 4.26 – 4.17 (m, 2H, CH2-O), 3.76 3.43 – 3.30 (m, 2H + m, 5H, CH2-CH2-CO + CH3 phenyl + CH2-CO + CH2-CH2-NH-Boc), 3.18 (m, 2H, CH2-CH2-CH2-NH-Boc), 2.84 (dd, J = 9.8 Hz, 13.5 Hz, 1H, CHH-phenyl), 2.03 (m, 2H, CH2-CH2-NH-Boc), 1.46 + 1.43 (s*, 9H, t-Bu).

13C NMR (63 MHz, CDCl3): 172.5, 156.1, 153.4, 138.0, 135.2, 132.3, 131.1, 130.4, 130.1, 129.4,
General procedure for the conversion of carboximides 5a-i to the protected amino acids (7a-i); GP5:

Carboximide 5a-i was dissolved in dry THF and cooled to -78 °C under an argon atmosphere. In a second flask KHMDS (0.5 M in toluene; 2.5 equiv, for 5a 3.5 equiv) was diluted in dry THF and cooled to -78 °C under an argon atmosphere. The KHMDS solution was added to the carboximide and stirred at -78 °C for 30 min. Then a solution of tris-azide (1.5 equiv) in dry THF cooled to -78 °C was added. After 2 min at -78 °C the reaction was quenched by addition of HOAc (4.6 equiv) and it was warmed to 30 °C in a water bath. After 3 h at 30 °C it was stirred at room temperature overnight.

For workup DCM was added and the organic layer was washed with brine. It was extracted with DCM (3x) and washed with saturated NaHCO₃ solution. After drying over MgSO₄ the crude product was purified by column chromatography (pentane/Et₂O 1:1 → 1:3).

The azide was dissolved in a THF/H₂O solution and cooled to 0 °C. H₂O₂ (30%; 4 equiv) and freshly pestled LiOH (2 equiv) were added. After 2.5 h at 0 °C the reaction was quenched with an aq Na₂S₂O₅ solution (4.4 equiv). Then it was acidified with HCl (4 M) at 0 °C, extracted with EtOAc (3x), dried over Na₂SO₄ and concentrated under reduced pressure.

The intermediate was dissolved in MeOH and treated with Pd/C (10% Pd basis, moistened with water; 20 wt-%) under a H₂ atmosphere for 6 h. The catalyst was removed by filtration over Celite®.

After concentration under reduced pressure the amine was dissolved in a H₂O/dioxane solution (1:1, v/v) and cooled to 0 °C. NaHCO₃ (3 equiv) and a solution of Fmoc-OSu (1.1 equiv) in dioxane was added. Afterwards, the reaction mixture was stirred at room temperature overnight.

For workup it was acidified with HCl (1 M) under ice cooling and extracted with EtOAc (3x). After drying over MgSO₄ the protected amino acid was dissolved in dry DMF. NaHCO₃ (2 equiv) and benzyl bromide (3 equiv) were added and the reaction mixture was stirred at room temperature overnight.

H₂O was added and it was extracted with EtOAc (3x). The combined organic phases were washed with H₂O (2x), dried over MgSO₄ and purified by column chromatography.
Benzyl (2R)-3-[2,6-bis(3-[[{(tert-butoxy)carbonyl]amino}propyl]phenyl]-2-[[{9H-fluoren-9-ylmethoxy}carbonyl]amino]propanoate (7a)

Following GP5 using carboximide 5a (550 mg; 0.88 mmol), KHMDS (0.5 M in toluene; 6.16 mL; 3.08 mmol), tris-azide (408 mg; 1.32 mmol), HOAc (232 µL; 4.05 mmol), dry THF (3 x 6 mL); isolated azide 6a (401 mg; 0.60 mmol); H₂O₂ (30%; 245 µL; 2.40 mmol), LiOH (29 mg; 1.20 mmol), THF (9.2 mL), H₂O (2.7 mL), Na₂S₂O₅ (502 mg; 2.64 mmol; in 1.9 mL H₂O); Pd/C (80 mg), MeOH (7 mL); Fmoc-OSu (223 mg; 0.66 mmol), NaHCO₃ (151 mg, 1.80 mmol), BnBr (214 µL; 1.80 mmol), dry DMF (7 mL).

Eluent for column chromatography: cyclohexane/EtOAc, 10:1 → 5:1 → 3:1.

Yield: 281 mg (40% over 5 steps); colourless solid after recrystallization from DCM/n-hexane.

¹H NMR (400 MHz, CDCl₃): 7.77 (d, J = 7.2 Hz, 2H, aryl-H), 7.61 – 7.58 (m, 2H, aryl-H), 7.42 – 7.28 (m, 7H, aryl-H), 7.11 – 7.01 (m, 3H, aryl-H), 6.97 (d, J = 7.6 Hz, 2H, aryl-H), 5.55 (d, J = 5.6 Hz, 1H, NH-Fmoc), 5.04 (d, J = 12 Hz, 1H, COO-CH₃-phenyl), 4.97 (d, J = 12.4 Hz, 1H, COO-CH₃-phenyl), 4.73 (m, 2H, NH-Boc), 4.56 (q, J = 8 Hz, 1H, α-CH), 4.40 (m, 2H, CH₂-fluorenyl), 4.21 (m, 1H, CH-fluorenyl), 3.18 – 3.03 (m, 6H, D₃-CH₂-C₄H₂ + C₄H₂-NH-Boc), 2.70 – 2.55 (m, 4H, CH₂CH₂CH₂-NH-Boc), 1.71 (m, 4H, CH₂CH₂CH₂-NH-Boc), 1.44 + 1.42 (s*, 18H, t-Bu).

¹³C NMR (75 MHz, CDCl₃): 172.1, 156.0, 155.6, 143.8, 143.7, 141.3, 141.0, 134.7, 131.6, 128.6, 128.5, 128.3, 128.2, 127.7, 127.5, 127.2, 127.0, 125.1, 125.0, 120.0, 82.0, 79.0, 67.3, 66.9, 58.5, 54.7, 47.1, 40.4, 32.0, 31.8, 30.2, 28.4. IR (neat): 3356 (m), 2979 (w), 1736 (m), 1684 (s), 1520 (s), 1451 (m), 1391 (w), 1369 (s), 1273 (s), 1254 (s), 1239 (s), 1168 (s), 1106 (m), 1091 (m), 1033 (m), 997 (m), 872 (w), 782 (w), 757 (m), 739 (s), 695 (m), 621 (m), 543 (w). mp: 149 – 152 °C. [α]D²⁰ = -3.1° (c = 0.77, DCM). HRMS: calcd for C₄₇H₅₇N₃O₈Na [M+Na]⁺ 814.4038: found 814.4063.

Benzyl (2R)-3-[2-3-{{[(tert-butoxy)carbonyl]amino}propyl}-6-methylphenyl]-2-{{[(9H-fluoren-9-ylmethoxy)carbonyl]amino}propanoate (7b)

Following GP5 using carboximide 5b (231 mg; 0.48 mmol), KHMDS (0.5 M in toluene; 2.40 mL; 1.20 mmol), tris-azide (223 mg; 0.72 mmol), HOAc (126 µL; 2.21 mmol), dry THF (3 x 3 mL); isolated azide 6b (100 mg; 0.19 mmol); H₂O₂ (30%; 78 µL; 0.76 mmol), LiOH (9 mg; 0.38 mmol), THF (2.9 mL), H₂O (0.9 mL), Na₂S₂O₅ (160 mg; 0.84 mmol; in 0.6 mL H₂O); Pd/C (20 mg), MeOH (2 mL); Fmoc-OSu (71 mg; 0.21 mmol), NaHCO₃ (48 mg, 0.57 mmol), dioxane/H₂O (1:1; 1.3 mL), dioxane (0.7 mL); NaHCO₃ (32 mg; 0.38 mmol), BnBr (68 µL; 0.57 mmol), dry DMF (2 mL).

Eluent for column chromatography: cyclohexane/EtOAc, 10:1 → 5:1.

Yield: 56 mg (18% over 5 steps); colourless solid after recrystallization from DCM/n-hexane.

¹H NMR (400 MHz, CDCl₃): 7.76 (d, J = 7.6 Hz, 2H, aryl-H), 7.58 – 7.52 (m, 2H, aryl-H), 7.40 (t, J = 7.2 Hz, 2H, aryl-H), 7.33 – 7.26 (m, 5H, aryl-H), 7.08 – 7.05 (m, 3H, aryl-H), 6.99 – 6.96 (m, 2H, aryl-H), 5.47 (d, J = 7.6 Hz, 1H, NH-Fmoc), 5.07 (d, J = 12.4 Hz, 1H, COO-CH₃-phenyl), 5.00 (d, J = 12 Hz, 1H, COO-CH₃-phenyl), 4.80 (br s, 1H, NH-Boc), 4.61 (q,
J = 8 Hz, 1H, \( \alpha \)-CH), 4.36 (d, \( J = 6.8 \) Hz, 2H, CH\(_2\)-fluorenyl), 4.17 (t, \( J = 6.8 \) Hz, 1H, CH-fluorenyl), 3.21 – 3.07 (m, 4H, \( \alpha \)-CH-CH\(_2\) + CH\(_2\)-NH-Boc), 3.05 (s, 3H, CH\(_3\)), 1.72 (m, 2H, CH\(_2\)-CH\(_2\)-NH-Boc), 1.42 (s, 9H, t-Bu). \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): 172.2, 156.0, 155.6, 143.8, 143.7, 141.3, 140.7, 137.2, 134.8, 132.2, 128.6, 128.5, 128.3, 127.7, 127.4, 127.0, 125.1, 120.0, 79.0, 67.3, 67.1, 54.0, 47.1, 40.5, 32.9, 31.8, 30.1, 28.4, 26.9, 20.3. IR (neat): 3356 (w), 2979 (w), 1757 (m), 1701 (s), 1682 (s), 1528 (s), 1451 (m), 1390 (w), 1366 (m), 1263 (s), 1214 (m), 1168 (s), 1105 (m), 1089 (m), 1040 (m), 991 (m), 874 (w), 756 (m), 738 (s), 698 (m). mp: 94 – 96 °C. \( R_f \) (n-hexane/EtOAc, 2:1) = 0.40. \([\text{D}]_\text{D}^{20} = -6.8^\circ \) (c = 0.22, DCM). HRMS: calcd for C\(_{40}\)H\(_{44}\)N\(_2\)O\(_6\)Na [M+Na]+ 671.3092: found 671.3091.


Following GP5 using carboximide 5c (433 mg; 0.87 mmol), KHMDs (0.5 M in toluene; 4.36 mL; 2.18 mmol), tris-azide (405 mg; 1.31 mmol), HOAc (229 \( \mu \)L; 4.00 mmol), dry THF (3 x 6 mL); isolated azide 6c (273 mg; 0.51 mmol); H\(_2\)O\(_2\) (30%; 208 \( \mu \)L; 2.04 mmol), LiOH (24 mg; 1.02 mmol), THF (7.8 mL), H\(_2\)O (2.3 mL), Na\(_2\)S\(_2\)O\(_5\) (426 mg; 2.24 mmol; in 1.6 mL H\(_2\)O); Pd/C (55 mg), MeOH (6 mL); Fmoc-OSu (189 mg; 0.56 mmol), NaHCO\(_3\) (129 mg, 1.53 mmol), dioxane/H\(_2\)O (1:1; 4 mL), dioxane (2 mL); NaHCO\(_3\) (86 mg; 1.02 mmol), BnBr (182 \( \mu \)L; 1.53 mmol), dry DMF (6 mL).

Eluent for column chromatography: cyclohexane/EtOAc, 10:1 \( \rightarrow \) 5:1.

Yield: 83 mg (14% over 5 steps); colourless solid after recrystallization from DCM/n-hexane. \(^1\)H NMR (400 MHz, CDCl\(_3\)): 7.75 (d, \( J = 7.6 \) Hz, 2H, aryl-H), 7.55 – 7.50 (m, 2H, aryl-H), 7.39 (t, \( J = 7.6 \) Hz, 2H, aryl-H), 7.34 – 7.25 (m, 7H, aryl-H), 7.16 (t, \( J = 8 \) Hz, 1H, aryl-H), 6.81 (d, \( J = 7.6 \) Hz, 1H, aryl-H), 6.71 (d, \( J = 8.4 \) Hz, 1H, aryl-H), 5.79 (d, \( J = 7.2 \) Hz, 1H, NH-Fmoc), 5.15 (s, 2H, COO-CH\(_2\)-phenyl), 4.67 (br s, 1H, NH-Boc), 4.49 (m, 1H, \( \alpha \)-CH), 4.31 (m, 2H, CH\(_2\)-fluorenyl), 4.16 (m, 1H, CH-fluorenyl), 3.78 (s, 3H, OCH\(_3\)), 3.20 – 3.07 (m, 4H, \( \alpha \)-CH-CH\(_2\) + CH\(_2\)-NH-Boc), 2.65 (m, 2H, CH\(_2\)-CH\(_2\)-CH\(_2\)-NH-Boc), 1.73 (m, 2H, CH\(_2\)-CH\(_2\)-NH-Boc), 1.43 (s, 9H, t-Bu). \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): 172.1, 157.8, 156.0, 155.8, 144.0, 143.8, 142.0, 141.3, 135.4, 128.5, 128.2, 128.0, 127.8, 127.0, 125.1, 122.9, 122.2, 119.9, 108.2, 79.1, 67.0, 66.9, 55.4, 54.8, 47.1, 40.5, 31.5, 29.8, 28.4. IR (neat): 3367 (w), 2962 (w), 1750 (m), 1700 (m), 1677 (s), 1584 (w), 1519 (s), 1470 (m), 1448 (m), 1392 (w), 1363 (w), 1269 (s), 1221 (m), 1163 (s), 1108 (m), 1097 (m), 1044 (m), 994 (w), 956 (m), 868 (w), 783 (m), 752 (m), 740 (s), 697 (m), 621 (m), 536 (m). mp: 143 – 146 °C. \( R_f \) (n-hexane/EtOAc, 2:1) = 0.35. \([\text{D}]_\text{D}^{20} = -4.4^\circ \) (c = 0.46, DCM). HRMS: calcd for C\(_{40}\)H\(_{44}\)N\(_2\)O\(_7\)Na [M+Na]+ 687.3041: found 687.3041.


Following GP5 using carboximide 5d (380 mg; 0.71 mmol), KHMDs (0.5 M in toluene; 3.56 mL; 1.78 mmol), tris-azide (331 mg; 1.07 mmol), HOAc (187 \( \mu \)L; 3.27 mmol), dry THF (3 x 5 mL); isolated azide 6d (280 mg; 0.49 mmol); H\(_2\)O\(_2\) (30%; 200 \( \mu \)L; 1.96 mmol), LiOH
(23 mg; 0.98 mmol), THF (7.5 mL), H₂O (2.2 mL), Na₂S₂O₅ (411 mg; 2.16 mmol; in 1.5 mL H₂O); Pd/C (56 mg), MeOH (6 mL); Fmoc-OSu (182 mg; 0.54 mmol), NaHCO₃ (123 mg, 1.47 mmol), dioxane/H₂O (1:1; 4 mL), dioxane (2 mL); NaHCO₃ (82 mg; 0.98 mmol), BnBr (175 μL; 1.47 mmol), dry DMF (6 mL).

Eluent for column chromatography: cyclohexane/EtOAc, 10:1 → 5:1.

Yield: 232 mg (46% over 5 steps); colourless solid after recrystallization from DCM/n-hexane.

**¹H NMR** (400 MHz, CDCl₃): 7.76 (d, J = 7.2 Hz, 2H, aryl-H), 7.55 (t, J = 8.4 Hz, 2H, aryl-H), 7.42 – 7.28 (m, 9H, aryl-H), 7.22 (t, J = 8 Hz, 1H, aryl-H), 7.07 (m, 2H, aryl-H), 5.63 (d, J = 8 Hz, 1H, NH-Fmoc), 5.19 – 4.98 (m, 3H, COO-CH₂-phenyl + NH-Boc), 4.69 (q, J = 8 Hz, 1H, D-CH), 4.33 (m, 2H, CH₂-fluorenyl), 4.15 (t, J = 6.8 Hz, 1H, CH-fluorenyl), 3.36 – 3.20 (m, 4H, D-CH-C₂H₂ + C₂H₂-NH-Boc), 2.88 (m, 2H, C₂H₂-CH₂-CH₂-NH-Boc), 1.79 (m, 2H, C₂H₂-CH₂-NH-Boc), 1.43 + 1.39 (s*, 9H, t-Bu).

**¹³C NMR** (75 MHz, CDCl₃): 170.9, 156.1, 155.6, 143.8, 143.6, 143.2, 141.3, 134.7, 133.3, 132.5, 128.4, 128.3, 128.0, 127.7, 127.1, 127.0, 126.4, 125.1, 124.2, 120.0, 79.0, 67.3, 67.2, 54.1, 47.0, 40.4, 32.7, 31.7, 29.6, 28.4, 26.9. **¹⁹F NMR** (282 MHz, CDCl₃): - 57.7. **IR** (neat): 3348 (m), 2973 (w), 1744 (m), 1681 (s), 1529 (s), 1451 (m), 1367 (w), 1253 (m), 1166 (s), 1115 (s), 1092 (m), 1045 (m), 1007 (m), 869 (w), 782 (w), 756 (m), 739 (s), 696 (m), 621 (m), 542 (w). **mp**: 87 – 89 °C. **Rf** (n-hexane/EtOAc, 2:1) = 0.45. **[α]D²⁰** = -1.9° (c = 0.37, DCM). **HRMS**: calcd for C₄₀H₄₁F₃N₂O₆Na [M+Na]⁺ 725.2809: found 725.2830.

**Benzyl (2R)-3-[(tert-butoxy)carbonyl]amino)propyl]-6-phenylphenyl-2-[(9H-fluoren-9-ylmethoxy)carbonyl][amino]propanoate (7e)**

Following GP5 using carboximide 5e (500 mg; 0.92 mmol), KHMDS (0.5 M in toluene; 4.60 mL; 2.30 mmol), tris-azide (427 mg; 1.38 mmol), HOAc (242 μL; 4.23 mmol), dry THF (3 x 6 mL); isolated azide 6e (306 mg; 0.52 mmol); H₂O₂ (30%; 212 μL; 2.08 mmol), LiOH (25 mg; 1.04 mmol), THF (8.0 mL), H₂O (2.3 mL), Na₂S₂O₅ (435 mg; 2.29 mmol; in 1.6 mL H₂O); Pd/C (61 mg), MeOH (6 mL); Fmoc-OSu (192 mg; 0.57 mmol), NaHCO₃ (131 mg, 1.56 mmol), dioxane/H₂O (1:1; 4 mL), dioxane (2 mL); NaHCO₃ (87 mg; 1.04 mmol), BnBr (186 μL; 1.56 mmol), dry DMF (6 mL).

Eluent for column chromatography: cyclohexane/EtOAc, 10:1 → 5:1.

Yield: 183 mg (28% over 5 steps); colourless solid after recrystallization from DCM/n-hexane.

**¹H NMR** (400 MHz, CDCl₃): 7.77 – 7.76 (m, 2H, aryl-H), 7.53 – 7.49 (m, 2H, aryl-H), 7.43 – 7.29 (m, 10H, aryl-H), 7.24 – 7.17 (m, 6H, aryl-H), 7.00 (d, J = 6.8 Hz, 1H, aryl-H), 5.03 (m, 2H, COO-CH₂-phenyl), 4.80 (d, J = 8.4 Hz, 1H, NH-Fmoc), 4.68 (br s, 1H, NH-Boc), 4.35 – 4.28 (m, 3H, α-CH + CH₂-fluorenyl), 4.12 (t, J = 6.8 Hz, 1H, CH-fluorenyl), 3.21 – 3.13 (m, 3H, α-CH-CHH + CH₂-NH-Boc), 3.05 (m, 1H, CH₂-CHH), 2.76 (m, 2H, CH₂-CH₂-CH₂-NH-Boc), 1.82 (m, 2H, CH₂-CH₂-NH-Boc), 1.44 (s, 9H, t-Bu). **¹³C NMR** (75 MHz, CDCl₃): 171.6, 156.0, 155.6, 143.9, 143.7, 143.6, 142.0, 141.3, 140.8, 135.1, 131.6, 129.5, 128.9, 128.5, 128.4, 128.3, 128.0, 127.68, 127.66, 127.1, 127.03, 127.00, 126.9, 125.00, 124.98, 119.9, 79.1, 67.0, 66.7, 54.9, 47.1, 40.5, 31.61, 31.57, 30.1, 28.4. **IR** (neat): 3355 (w), 2931 (w), 1709 (s), 1506 (m), 1450 (m), 1391 (w), 1365 (m), 1336 (w), 1247 (m), 1166 (s), 1105 (w), 1046 (m), 758 (s), 739 (s), 703 (m), 621 (w), 539 (w). **mp**: 55 – 57 °C. **Rf** (n-hexane/EtOAc,

Following GP5 using carboximide 5f (450 mg; 0.87 mmol), KHMDS (0.5 M in toluene; 4.36 mL; 2.18 mmol), tris-azide (405 mg; 1.31 mmol), HOAc (229 μL; 4.00 mmol), dry THF (3 x 6 mL); isolated azide 6f (235 mg; 0.42 mmol); H₂O₂ (30%; 172 μL; 1.68 mmol), LiOH (20 mg; 0.84 mmol), THF (6.4 mL), Na₂S₂O₅ (352 mg; 1.85 mmol; in 1.3 mL H₂O); Pd/C (47 mg), MeOH (5 mL); Fmoc-OSu (155 mg; 0.46 mmol), NaHCO₃ (106 mg, 1.26 mmol), dioxane/H₂O (1:1; 3.3 mL), dioxane (1.7 mL); NaHCO₃ (71 mg; 0.84 mmol), BnBr (150 μL; 1.26 mmol), dry DMF (5 mL).

Eluent for column chromatography: cyclohexane/EtOAc, 10:1 → 5:1.

Yield: 112 mg (19% over 5 steps); colourless solid after recrystallization from DCM/η-hexane.

¹H NMR (400 MHz, CDCl₃): 8.09 (d, J = 8.8 Hz, 1H, aryl-H), 7.80 – 7.76 (m, 3H, aryl-H), 7.68 (d, J = 8.4 Hz, 1H, aryl-H), 7.63 – 7.50 (m, 3H, aryl-H), 7.43 – 7.39 (m, 3H, aryl-H), 7.35 – 7.29 (m, 3H, aryl-H), 7.24 – 7.19 (m, 3H, aryl-H), 6.83 (d, J = 6.8 Hz, 2H, aryl-H), 5.59 (d, J = 7.6 Hz, 1H, NH-Fmoc), 4.95 (d, J = 12 Hz, 1H, COO-CH₃-phenyl), 4.86 (br s, 1H, NH-Boc), 4.72 (q, J = 7.6 Hz, 1H, α-CH), 4.64 (d, J = 12 Hz, 1H, COO-CH₃-phenyl), 4.38 (d, J = 7.2 Hz, 2H, CH₂-fluorenyl), 4.17 (t, J = 7.2 Hz, 1H, CH-fluorenyl), 3.66 – 3.52 (m, 2H, CH₂-fluorenyl), 3.19 (m, 2H, C₆H₄-NH-Boc), 2.82 (m, 2H, CH₂-CH₂-CH₂-NH-Boc), 1.79 (m, 2H, CH₂-CH₂-NH-Boc), 1.41 (s, 9H, t-Bu).

¹³C NMR (75 MHz, CDCl₃): 172.1, 156.1, 155.6, 143.8, 143.7, 141.3, 138.5, 134.5, 132.8, 132.5, 128.7, 128.3, 128.2, 128.02, 127.97, 127.8, 127.7, 127.0, 126.5, 125.1, 125.0, 123.3, 119.9, 79.1, 67.4, 67.1, 54.7, 47.1, 40.5, 31.83, 31.78, 30.6, 28.4, 26.9. IR (neat): 3353 (m), 2972 (w), 1734 (m), 1683 (s), 1519 (s), 1451 (m), 1391 (w), 1366 (m), 1273 (s), 1238 (s), 1168 (s), 1106 (m), 1090 (m), 1032 (m), 999 (m), 871 (w), 816 (w), 782 (w), 756 (m), 738 (s), 695 (m), 621 (m), 541 (w). mp: 121 - 124 °C. Rₚ (n-hexane/EtOAc, 2:1) = 0.35. [α]₀²⁰ = -8.6° (c = 0.30, DCM). HRMS: calcd for C₄₃H₄₄N₂O₆Na [M+Na]⁺ 707.3092: found 707.3113.

Benzyl (2R)-3-[10-(3-[(tert-butoxy)carbonyl]amino)phenanthren-9-yl]-2-[[9H-fluoren-9-ylmethoxy]carbonyl]amino)propanoate (7h)

Following GP5 using carboximide 5h (600 mg; 1.06 mmol), KHMDS (0.5 M in toluene; 5.30 mL; 2.65 mmol), tris-azide (492 mg; 1.59 mmol), HOAc (279 μL; 4.88 mmol), dry THF (3 x 7 mL); isolated azide 6h (414 mg; 0.68 mmol); H₂O₂ (30%; 278 μL; 2.72 mmol), LiOH (33 mg; 1.36 mmol), THF (10.4 mL), H₂O (3.1 mL), Na₂S₂O₅ (568 mg; 2.99 mmol; in 2.1 mL H₂O); Pd/C (83 mg), MeOH (8 mL); Fmoc-OSu (253 mg; 0.75 mmol), NaHCO₃ (171 mg, 2.04 mmol), dioxane/H₂O (1:1; 5.3 mL), dioxane (2.7 mL); NaHCO₃ (114 mg; 1.36 mmol), BnBr (243 μL; 2.04 mmol), dry DMF (8 mL).

Eluent for column chromatography: cyclohexane/EtOAc, 10:1 → 5:1.

Yield: 174 mg (22% over 5 steps); colourless solid after recrystallization from DCM/n-hexane.
1H NMR (400 MHz, CDCl3): 8.73 – 8.69 (m, 2H, aryl-H), 8.19 (m, 1H, aryl-H), 8.03 (d, J = 6.8 Hz, 1H, aryl-H), 7.77 (d, J = 7.2 Hz, 2H, aryl-H), 7.66 – 7.57 (m, 6H, aryl-H), 7.42 – 7.39 (m, 2H, aryl-H), 7.30 (t, J = 7.2 Hz, 2H, aryl-H), 7.12 (t, J = 7.6 Hz, 2H, aryl-H), 6.68 (d, J = 7.6 Hz, 2H, aryl-H), 5.70 (d, J = 5.2 Hz, 1H, NH-Fmoc), 5.02 (br s, 1H, NH-Boc), 4.85 + 4.58 (m, 2H + m, 1H, COO-CH2-phenyl + α-CH), 4.42 (m, 2H, CH2-fluorenyl), 4.19 (t, J = 6.8 Hz, 1H, CH-fluorenyl), 3.78 – 3.60 (m, 2H, D-CH-C6H2), 3.40 – 3.10 (m, 4H, C6H2-NH-Boc + C6H2-CH2-CH2-NH-Boc), 1.86 (m, 2H, C6H2-CH2-NH-Boc), 1.47 + 1.43 (s*, 9H, t-Bu).

13C NMR (75 MHz, CDCl3): 172.1, 156.1, 155.7, 143.8, 143.7, 141.3, 135.4, 134.2, 131.2, 130.7, 130.4, 129.1, 128.3, 128.1, 127.9, 127.7, 127.6, 127.0, 126.8, 126.2, 125.9, 125.1, 124.8, 124.1, 123.1, 123.0, 120.0, 81.4, 79.1, 67.4, 67.2, 58.6, 54.6, 47.1, 40.8, 32.7, 30.8, 28.4, 26.5. IR (neat): 3346 (w), 2980 (w), 1733 (m), 1688 (s), 1515 (s), 1447 (m), 1366 (w), 1343 (w), 1275 (s), 1169 (s), 1085 (m), 1031 (m), 1001 (m), 869 (w), 755 (s), 737 (s), 726 (m), 621 (m), 541 (w). mp: 147 – 150 °C. Rf (n-hexane/EtOAc, 2:1) = 0.35. [α]20D = -3.8° (c = 0.42, DCM). HRMS: calcld for C47H46N2O6Na [M+Na]+ 757.3248: found 757.3269.

Benzyl (2R)-3-{2-(3-[(tert-butoxy)carbonyl]amino)propyl}pyren-1-yl)-2-{{[9H-fluoren-9-ylmethoxy]carbonyl}amino}propionate (7i)

Following GP5 using carboximide 5i (520 mg; 0.88 mmol), KHMD (0.5 M in toluene; 4.40 mL; 2.20 mmol), tris-azide (408 mg; 1.32 mmol), HOAc (232 μL; 4.05 mmol), dry THF (3 x 6 mL); isolated azide 6i (373 mg; 0.59 mmol); H2O2 (30%; 241 μL; 2.36 mmol), LiOH (28 mg; 1.18 mmol), THF (9.0 mL), H2O (2.7 mL), Na2S2O5 (494 mg; 2.60 mmol; in 1.8 mL H2O); Pd/C (75 mg), MeOH (7 mL). Eluent for column chromatography: cyclohexane/EtOAc, 10:1 → 5:1.

Yield: 112 mg (17% over 5 steps); colourless solid after recrystallization from DCM/n-hexane.

1H NMR (400 MHz, CDCl3): 8.70 (m, 1H, aryl-H), 8.33 (m, 1H, aryl-H), 8.20 – 8.10 (m, 2H, aryl-H), 8.03 (m, 1H, aryl-H), 7.97 – 7.94 (m, 2H, aryl-H), 7.78 – 7.74 (m, 2H, aryl-H), 7.66 – 7.54 (m, 3H, aryl-H), 7.40 – 7.37 (m, 2H, aryl-H), 7.32 – 7.22 (m, 2H, aryl-H), 7.14 – 6.98 (m, 2H, aryl-H), 6.86 (m, 1H, aryl-H), 6.68 (d, J = 7.6 Hz, 1H, aryl-H), 6.53 (m, 1H, aryl-H), 5.69 (m, 1H, NH-Fmoc), 4.97 – 4.80 + 4.67 (m, 3H + m, 1H, NH-Boc + COO-CH2-phenyl + α-CH), 4.42 (m, 2H, CH2-fluorenyl), 4.18 (m, 1H, CH-fluorenyl), 3.95 – 3.60 (m, 2H, α-CH-CH2), 3.27 – 3.09 (m, 4H, CH2-NH-Boc + CH2-CH2-CH2-NH-Boc), 1.89 (m, 2H, CH2-CH2-NH-Boc), 1.43 (s, 9H, t-Bu). 13C NMR (75 MHz, CDCl3): 172.0, 156.1, 155.6, 143.82, 143.78, 143.7, 143.1, 138.8, 131.1, 130.45, 130.39, 130.3, 129.9, 128.2, 128.0, 127.95, 127.86, 127.7, 127.3, 127.2, 127.0, 126.8, 126.3, 126.2, 125.9, 125.7, 125.2, 125.1, 124.9, 124.7, 123.7, 123.1, 123.0, 120.0, 79.1, 67.4, 67.1, 55.2, 54.6, 47.1, 40.6, 32.4, 31.0, 28.4, 26.9. IR (neat): 3344 (w), 2980 (w), 1733 (w), 1688 (s), 1515 (s), 1447 (m), 1366 (w), 1343 (s), 1275 (s), 1238 (s), 1169 (s), 1085 (m), 1031 (m), 1001 (m), 869 (w), 755 (s), 737 (s), 726 (s), 696 (m), 621 (m), 541 (w). mp: 147 – 150 °C. Rf (n-hexane/EtOAc, 2:1) = 0.35. [α]20D = +4.5° (c = 0.31, DCM). HRMS: calcld for C49H46N2O10Na [M+Na]+ 781.3248: found 781.3244.
NMR spectra

1-iodo-2-phenylbenzene (1e)
1-iodonaphthalene (1f)
Anthracen-1-yl trifluoromethanesulfonate (1g)
9-iodophenanthrene (1h)
1-Iodopyrene (1i)
3-Iodo-1-[(4-methylbenzene)sulfonyl]-1H-indole (1j)
Methyl (2E)-3-[2,6-bis(3-bromopropyl)phenyl]prop-2-enoate (2a)
Methyl (2E)-3-[2-(3-bromopropyl)-6-methylphenyl]prop-2-enoate (2b)
Methyl (2E)-3-[2-(3-bromopropyl)-6-methoxyphenyl]prop-2-enoate (2c)
Methyl (2E)-3-{2-(3-bromopropyl)-6-(trifluoromethyl)phenyl}prop-2-enoate (2d)
Methyl (2E)-3-[2-(3-bromopropyl)-6-phenylphenyl]prop-2-enoate (2e)
Methyl (2E)-3-[2-(3-bromopropyl)naphthalen-1-yl]prop-2-enoate (2f)
Methyl (2E)-3-[2-{3-bromopropyl}anthracen-1-yl]prop-2-enoate (2g)
Methyl (2E)-3-[10-(3-bromopropyl)phenanthren-9-yl]prop-2-enoate (2h)
Methyl (2E)-3-[2-(3-bromopropyl)pyren-1-yl]prop-2-enoate (2i)
Methyl (2E)-3-[2-(3-bromopropyl)-1-[(4-methylbenzene)sulfonyl]-1H-indol-3-yl]prop-2-enoate (2j)
Methyl (2E)-3-[2,6-bis(3-[bis[(tert-butoxy)carbonyl]amino]propyl)phenyl]prop-2-enoate (3a)
Methyl (2E)-3-[2-[(tert-butoxy)carbonyl]amino]propyl]-6-methylphenyl]prop-2-enoate (3b)
Methyl (2E)-3-[2-(3-bis[(tert-butoxy)carbonyl]amino)propyl]-6-methoxyphenyl]prop-2-enoate (3c)
Methyl (2E)-3-[2-{3-[bis[(tert-butoxy)carbonyl]amino}propyl]-6-(trifluoromethyl)phenyl]prop-2-enoate (3d)
Methyl (2E)-3-[2-(bis[tert-butoxy]carbonyl)amino]propyl)naphthalen-1-yl]prop-2-enoate (3f)
Methyl (2E)-3-[2-{3-[bis[(tert-butoxy)carbonyl]amino]propyl}anthracen-1-yl]prop-2-enoate (3g)
Methyl (2E)-3-{10-[(3-{bis[(tert-butoxy)carbonyl]amino}propyl)phenanthren-9-yl]prop-2-enoyl} (3h)
Methyl (2E)-3-[2-((tert-butoxy)carbonyl)amino)propyl]pyren-1-yl] prop-2-enoate (3i)
tert-Butyl N-[3-{(2-[[4R]-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl]-3-[[tert-butoxy]carbonyl]amino}propyl]phenylpropyl]carbamate (5a)
tert-Butyl N-[3-{2-[(4R)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl}-3-methylphenyl]propyl]carbamate (5b)
**tert-Butyl N-[3-{2-[3-[(4R)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl}-3-methoxyphenyl]propyl]carbamate (5c)**
tert-Butyl \(N\)-[3-\{2-\{3-\{\{4R\}\}4\}-benzyl-2-oxo-1,3-oxazolidin-3-yl\}-3-oxopropyl\}-3-(trifluoromethyl)phenylpropyl\}carbamate (5d)
**tert-Butyl N-[3-(2-{3-[(4R)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl}-3-phenylphenyl)propyl]carbamate (5e)**

![NMR Spectra](image)
tert-Butyl N-[3-{1-[3-([(4R)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl]naphthalen-2-yl]propyl}carbamate (5f)
**tert-Butyl N-[3-{1-[3-[[4R]-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl] anthracen-2-yl]propyl}carbamate (5g)**
tert-Butyl N-[3-(10-[(4R)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl]phenanthren-9-yl]propyl]carbamate (5h)
tert-Butyl N-[3-\{1-\{3-\{4R\}-4-benzyl-2-oxo-1,3-oxazolidin-3-yl\}-3-oxopropyl\}pyren-2-yl\}propyl\]carbamate (SI)
Benzyl (2R)-3-[2-((tert-butoxy)carbonyl)amino]propyl]-6-methylphenyl]-2-[(9H-fluoren-9-ylmethoxy)carbonyl]amino]propanoate (7b)
Benzyl (2R)-3-[2-[(tert-butoxy)carbonyl]amino]propyl]-6-methoxyphenyl]-2-[(9H-fluoren-9-ylmethoxy)carbonyl]amino]propanoate (7c)
Benzyl (2R)-3-[2-(3-[(tert-butoxy)carbonyl]amino)propyl]pyren-1-yl]-2-{[(9H-fluoren-9-ylmethoxy)carbonyl]amino}propanoate (7i)
**ee-Determination**

**Racemisation:** [6]

Amino acid 7c (33 mg; 50 μmol) was dissolved in a piperidine-DMF solution (25%; 0.4 mL) and stirred for 1.5 h at room temperature. Afterwards, H₂O and EtOAc were added and the layers were separated. The aq phase was extracted with EtOAc (2x) and the combined organic phases were washed with H₂O. After drying over MgSO₄ the crude reaction mixture was splitted into two parts and the solvent was evaporated. For racemisation the first half was dissolved in HOAc (0.2 mL) in a sealable tube and salicylaldehyde (1.3 μL; 12.5 μmol) was added. The mixture was heated to 100 °C for 1 h. After cooling, MeOH was added and the solvent was evaporated. Having treated the sample this way a second time, it was analyzed by HPLC (rac-8c). The second half was dissolved in a TFA/DCM mixture (1:1, v/v; 0.2 mL) and stirred for 2 h at room temperature. DCM was added; the sample was concentrated in vacuo and treated this way a second time. Afterwards, the sample was analyzed by HPLC (8c).

**HPLC trace for rac-8c:**

![HPLC trace](image)

<table>
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<th>Ret.time [min]</th>
<th>Start [min]</th>
<th>End [min]</th>
<th>Height [mVolt]</th>
<th>Area [mV•min]</th>
<th>% Area</th>
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</table>
HPLC trace for enantiomerically enriched 8c:

HPLC System Agilent 1100 Series
Column: Chiralpak IA
Eluent: n-hexane/propan-2-ol, 10:1
Flow: 0.8 mL/min
Detector freq.: 254 nm
References


