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

Supporting Information

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General Information:

NMR: Bruker DPX 250 (^{1}H: 250 MHz; ^{13}C: 63 MHz), Bruker AM 300 (^{13}C: 75 MHz; ^{19}F: 282 MHz) or Bruker Avance 400 (^{1}H: 400 MHz); ^{1}H chemical shifts (δ) are given in ppm relative to $CDCl_3$ (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, ^{1}H,^{1}H-COSY spectra were used for proton assignment; ^{13}C chemical shifts (δ) are reported with proton decoupling in ppm relative to $CDCl_3$ (77.0 ppm) as internal standard; ^{19}F chemical shifts (δ) are reported with decoupling in ppm. FT-IR: Perkin-Elmer 1600 series or Perkin-Elmer Spectrum Two; peaks are reported in cm^{-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 $[\alpha]_D^{T\ °C}$ (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. Analytical thin layer chromatography (TLC): alumina plates precoated with silica gel 60 F_{254} indicator (EMD); spots were visualized by UV light (254 nm). Flash column chromatography: Silica gel 60 (0.04 – 0.063 mm; Macherey-Nagel). Enantiomeric excesses were determined by HPLC analysis using analytical chiral columns from Daicel 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.[1]

Experimental section:

1-Iodo-2-phenylbenzene (1e) [2]

2-Aminobiphenyl (2.00 g; 11.8 mmol) was suspended in H_2O (12 mL) at 0 °C and HCl (12 M; 2.4 mL) was added. After slow addition of a solution of $NaNO_2$ (978 mg; 14.2 mmol) in H_2O (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_2O (3 mL) was added and the reaction mixture was allowed to warm to room temperature overnight.

The reaction mixture was extracted with Et_2O (4x) and the organic layers were washed with a HCl solution (3 M), saturated $NaHCO_3$, saturated $Na_2S_2O_5$, and brine. After drying over $MgSO_4$ and concentration in vacuo the crude product was purified by column chromatography (pure *n*-hexane). A colourless oil (3.07 g; 93%) was obtained.

^{1}H NMR (250 MHz, $CDCl_3$): 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). **^{13}C NMR** (63 MHz, $CDCl_3$): 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),

858 (w), 746 (s), 699 (s), 648 (s). R_f (*n*-hexane/EtOAc, 25:1) = 0.75. **Elementary analysis**: calcd for $C_{12}H_9I$ (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_2O was added to the residue and it was extracted with DCM (3x). The combined organic phases were washed with saturated $Na_2S_2O_5$ solution and H_2O. 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). R_f (*n*-hexane/EtOAc, 25:1) = 0.75. **Elementary analysis**: calcd for $C_{10}H_7I$ (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]). R_f (*n*-hexane/EtOAc, 25:1) = 0.70. **HRMS**: calcd for $C_{14}H_9I$ $[M]^+$ 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.

^{1}H NMR (250 MHz, $CDCl_3$): 8.50 (m, 1H, aryl-H), 8.32 – 8.00 (m, 7H, aryl-H), 7.88 (m, 1H, aryl-H). **^{13}C NMR** (63 MHz, $CDCl_3$): 136.8, 132.6, 131.4, 131.07, 131.05, 131.0, 129.4, 128.0, 127.1, 126.5, 126.0, 125.8, 125.6, 125.5, 124.0, 96.2. **IR** (KBr): 3029 (w), 1584 (m), 1480 (w), 1451 (w), 1425 (m), 1310 (w), 1240 (w), 1200 (w), 1176 (w), 1077 (w), 1006 (m), 963 (m), 835 (s), 812 (m), 750 (m), 705 (s), 671 (m). **mp**: 85 – 87 °C (lit: 85 – 87 °C [4]). R_f (*n*-hexane/EtOAc, 25:1) = 0.65. **HRMS**: calcd for $C_{16}H_9I$ $[M]^+$ 327.9743: found 327.9741.

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 $NaHCO_3$ solution and brine the organic phase was dried over $MgSO_4$ and purified by column chromatography (cyclohexane/EtOAc, 50:1). The product was directly used for the next step.

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

^{1}H NMR (250 MHz, $CDCl_3$): 8.65 (m, 1H, aryl-H), 8.48 (m, 1H, aryl-H), 8.13 – 7.98 (m, 3H, aryl-H), 7.63 – 7.52 (m, 2H, aryl-H), 7.50 – 7.38 (m, 2H, aryl-H). **^{13}C NMR** (63 MHz, $CDCl_3$): 145.9, 132.5, 132.4, 132.3, 128.9, 128.7, 128.0, 127.0, 126.7, 124.7, 123.7, 122.1, 121.8, 121.4, 120.0, 116.8. **^{19}F NMR** (282 MHz, $CDCl_3$): - 73.3.

3-Iodo-1-[(4-methylbenzene)sulfonyl]-1*H*-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 I_2 (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.

H_2O was added to the reaction mixture and it was extracted with Et_2O (3x). The combined organic layers were washed with H_2O and brine before drying over $MgSO_4$. After concentration to dryness the crude product was crystallized from *n*-hexane. A light yellow solid (8.07 g; 60%) was obtained.

^{1}H NMR (250 MHz, $CDCl_3$): 7.96 (m, 1H, aryl-H), 7.78 (d, *J* = 8.5 Hz, 2H, aryl-H), 7.70 (s, 1H, aryl-H), 7.40 – 7.30 (m, 3H, aryl-H), 7.26 – 7.22 (m, 2H, aryl-H), 2.35 (s, 3H, CH_3). **^{13}C NMR** (63 MHz, $CDCl_3$): 145.3, 135.0, 134.4, 132.4, 130.0, 129.8, 126.9, 125.6, 123.9, 122.0, 113.4, 66.8, 21.6. **IR** (KBr): 3119 (m), 1592 (m), 1438 (m), 1370 (s), 1267 (m), 1171 (s), 1125 (s), 1086 (s), 1017 (s), 920 (m), 803 (m), 753 (m), 688 (s), 653 (s), 574 (s), 532 (s). **mp**: 131 – 133 °C (lit: 131- 133 °C [5]). R_f (*n*-hexane/EtOAc, 25:1) = 0.30. **Elementary analysis**: calcd for $C_{15}H_{12}INO_2S$ (397.23): C 45.35, H 3.04, N 3.53, S 8.07; found: C 45.32, H 3.09, N 3.44, S 7.80.

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_2CO_3 (3.26 g; 10 mmol), the aryl iodide (2 mmol), 1,3-dibromopropane (2.04 mL; 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 (2*E*)-3-[2,6-bis(3-bromopropyl)phenyl]prop-2-enoate (2a)

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

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

^{1}H NMR (250 MHz, $CDCl_3$): 7.87 (d, *J* = 16.3 Hz, 1H, aryl-C*H*=CH), 7.21 (m, 1H, aryl-H), 7.12 (m, 2H, aryl-H), 6.03 (d, *J* = 16.3 Hz, 1H, aryl-CH=C*H*), 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, 4H, CH_2-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 $C_{16}H_{21}Br_2O_2$ $[M+H]^+$ 402.9903: found 402.9900.

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

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

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

^{1}H NMR (250 MHz, $CDCl_3$): 7.86 (d, *J* = 16.5 Hz, 1H, aryl-C*H*=CH), 7.21 – 7.08 (m, 3H, aryl-H), 6.06 (d, *J* = 16.5 Hz, 1H, aryl-CH=C*H*), 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 (s), 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 $C_{14}H_{18}BrO_2$ $[M+H]^+$ 297.0485: found 297.0486.

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

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

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

^{1}H NMR (250 MHz, $CDCl_3$): 7.86 (d, *J* = 16.3 Hz, 1H, aryl-C*H*=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=C*H*), 3.87 (s, 3H, $COOCH_3$),

3.81 (s, 3H, OCH_3), 3.40 (t, *J* = 6.5 Hz, 2H, CH_2-Br), 2.93 (t, *J* = 7.3 Hz, 2H, C*H*$_2$-CH_2-CH_2-Br), 2.12 (m, 2H, C*H*$_2$-CH_2-Br). **^{13}C NMR** (63 MHz, $CDCl_3$): 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). ***R*$_f$** (*n*-hexane/EtOAc, 3:1) = 0.60. **HRMS**: calcd for $C_{14}H_{18}BrO_3$ $[M+H]^+$ 313.0434: found 313.0434.

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

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

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

^{1}H NMR (250 MHz, $CDCl_3$): 7.88 (dd, *J* = 1.8 Hz, 16.3 Hz, 1H, aryl-C*H*=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=C*H*), 3.83 (s, 3H, $COOCH_3$), 3.38 (t, *J* = 6.5 Hz, 2H, CH_2-Br), 2.84 (t, *J* = 7.3 Hz, 2H, C*H*$_2$-CH_2-CH_2-Br), 2.08 (m, 2H, C*H*$_2$-CH_2-Br). **^{13}C NMR** (63 MHz, $CDCl_3$): 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. **^{19}F NMR** (282 MHz, $CDCl_3$): - 58.2. **IR** (neat): 2953 (m), 1726 (s), 1652 (m), 1600 (w), 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). ***R*$_f$** (*n*-hexane/EtOAc, 3:1) = 0.65. **HRMS**: calcd for $C_{14}H_{15}BrF_3O_2$ $[M+H]^+$ 351.0202: found 351.0201.

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

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

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

^{1}H NMR (250 MHz, $CDCl_3$): 7.76 (d, *J* = 16.5 Hz, 1H, aryl-C*H*=CH), 7.37 – 7.19 (m, 8H, aryl-H), 5.66 (d, *J* = 16.5 Hz, 1H, aryl-CH=C*H*), 3.69 (s, 3H, $COOCH_3$), 3.43 (t, *J* = 6.5 Hz, 2H, CH_2-Br), 2.93 (t, *J* = 7.5 Hz, 2H, C*H*$_2$-CH_2-CH_2-Br), 2.12 (m, 2H, C*H*$_2$-CH_2-Br). **^{13}C NMR** (63 MHz, $CDCl_3$): 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), 1719 (s), 1637 (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). ***R*$_f$** (*n*-hexane/EtOAc, 3:1) = 0.70. **HRMS**: calcd for $C_{19}H_{20}BrO_2$ $[M+H]^+$ 359.0641: found 359.0642.

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

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

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

^{1}H NMR (250 MHz, $CDCl_3$): 8.20 (d, *J* = 16.3 Hz, 1H, aryl-C*H*=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=C*H*), 3.88 (s, 3H, $COOCH_3$), 3.42 (t, *J* = 6.5 Hz, 2H, CH_2-Br),

2.99 (t, *J* = 7.8 Hz, 2H, C*H*$_2$-CH$_2$-CH$_2$-Br), 2.18 (m, 2H, C*H*$_2$-CH$_2$-Br). **^{13}C NMR** (63 MHz, $CDCl_3$): 166.7, 142.5, 136.4, 132.3, 131.3, 131.1, 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), 986 (m), 865 (w), 818 (m), 751 (m). ***R*$_f$** (*n*-hexane/EtOAc, 3:1) = 0.65. **HRMS**: calcd for $C_{17}H_{17}BrO_2Na$ $[M+Na]^+$ 355.0304: found 355.0307.

Methyl (2*E*)-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, $CDCl_3$): 8.54 (s, 1H, aryl-H), 8.40 (s, 1H, aryl-H), 8.32 (d, *J* = 16.3 Hz, 1H, aryl-C*H*=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=C*H*), 3.92 (s, 3H, $COOCH_3$), 3.45 (t, *J* = 6.5 Hz, 2H, CH_2-Br), 3.03 (t, *J* = 7.3 Hz, 2H, C*H*$_2$-CH$_2$-CH$_2$-Br), 2.22 (m, 2H, C*H*$_2$-CH$_2$-Br). **^{13}C NMR** (63 MHz, $CDCl_3$): 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, 125.76, 125.75, 125.7, 123.8, 51.9, 33.9, 32.9, 32.3. **IR** (neat): 2945 (w), 1710 (s), 1634 (w), 1455 (w), 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. ***R*$_f$** (*n*-hexane/EtOAc, 3:1) = 0.55. **HRMS**: calcd for $C_{21}H_{19}BrO_2$ $[M]^+$ 382.0563: found 382.0561.

Methyl (2*E*)-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, $CDCl_3$): 8.76 – 8.69 (m, 2H, aryl-H), 8.26 (d, *J* = 16.3 Hz, 1H, aryl-C*H*=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=C*H*), 3.90 (s, 3H, $COOCH_3$), 3.55 (t, *J* = 6.5 Hz, 2H, CH_2-Br), 3.34 (t, *J* = 8 Hz, 2H, C*H*$_2$-CH$_2$-CH$_2$-Br), 2.23 (m, 2H, C*H*$_2$-CH$_2$-Br). **^{13}C NMR** (63 MHz, $CDCl_3$): 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. ***R*$_f$** (*n*-hexane/EtOAc, 3:1) = 0.65. **HRMS**: calcd for $C_{21}H_{19}BrO_2$ $[M]^+$ 382.0563: found 382.0569.

Methyl (2*E*)-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-C*H*=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=C*H*), 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, C*H*$_2$-CH_2-CH_2-Br), 2.31 (m, 2H, C*H*$_2$-CH_2-Br). **^{13}C NMR** (63 MHz, $CDCl_3$): 166.8, 142.8, 136.6, 131.4, 131.1, 130.5, 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 $C_{23}H_{19}BrO_2$ (407.30): C 67.82, H 4.70; found C 67.56, H 4.76.

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

Eluent for column chromatography: *n*-hexane/EtOAc, 25:1 → 10:1 → 5:1.

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-C*H*=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* = 8 Hz, 2H, aryl-H), 6.54 (d, *J* = 16.3 Hz, 1H, aryl-CH=C*H*), 3.82 (s, 3H, $COOCH_3$), 3.48 (t, *J* = 6.5 Hz, 2H, CH_2-Br), 3.33 (t, *J* = 7.3 Hz, 2H, C*H*$_2$-CH_2-CH_2-Br), 2.35 (s, 3H, CH_3), 2.32 (m, 2H, C*H*$_2$-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 $C_{22}H_{22}BrNO_4S$ $[M]^+$ 475.05, found 396.5 (100.00) $[M\text{-}Br]^+$, 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_2CO_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_2O 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 (2*E*)-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_2CO_3 (2.19 g; 6.72 mmol) and $HNBoc_2$ (1.02 g; 4.70 mmol) in dry DMF (10 mL).

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

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

^{1}H NMR (250 MHz, $CDCl_3$): 7.84 (d, *J* = 16.5 Hz, 1H, aryl-C*H*=CH), 7.23 – 7.06 (m, 3H, aryl-H), 6.00 (d, *J* = 16.5 Hz, 1H, aryl-CH=C*H*), 3.80 (s, 3H, $COOCH_3$), 3.58 (t, *J* = 7.5 Hz, 4H, CH_2-$NBoc_2$), 2.61 (t, *J* = 7.8 Hz, 4H, C*H*$_2$-CH_2-CH_2-$NBoc_2$), 1.81 (m, 4H, C*H*$_2$-CH_2-$NBoc_2$), 1.48 (s, 36H, *t*-Bu). **^{13}C NMR** (63 MHz, $CDCl_3$): 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). R_f (*n*-hexane/EtOAc, 3:1) = 0.50. **HRMS**: calcd for $C_{36}H_{56}N_2O_{10}Na$ $[M+Na]^+$ 699.3827: found 699.3821.

Methyl (2*E*)-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), Cs_2CO_3 (658 mg; 2.02 mmol) and $HNBoc_2$ (241 mg; 1.11 mmol) in dry DMF (5 mL).

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

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

^{1}H NMR (250 MHz, $CDCl_3$): 7.84 (d, *J* = 16.5 Hz, 1H, aryl-C*H*=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=C*H*), 3.81 (s, 3H, $COOCH_3$), 3.59 (t, *J* = 7.5 Hz, 2H, CH_2-$NBoc_2$), 2.64 (t, *J* = 7.8 Hz, 2H, C*H*$_2$-CH_2-CH_2-$NBoc_2$), 2.32 (s, 3H, CH_3), 1.83 (m, 2H, C*H*$_2$-CH_2-$NBoc_2$), 1.48 (s, 18H, *t*-Bu). **^{13}C NMR** (63 MHz, $CDCl_3$): 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), 1306 (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 $C_{24}H_{35}NO_6Na$ $[M+Na]^+$ 456.2357: found 456.2370.

Methyl (2*E*)-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), Cs_2CO_3 (1.18 g; 3.62 mmol) and $HNBoc_2$ (432 mg; 1.99 mmol) in dry DMF (12 mL).

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

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

^{1}H NMR (250 MHz, $CDCl_3$): 7.85 (d, *J* = 16.3 Hz, 1H, aryl-C*H*=CH), 7.21 (m, 1H, aryl-H), 6.81 (m, 2H, aryl-H), 6.67 (d, *J* = 16.3 Hz, 1H, aryl-CH=C*H*), 3.85 (s, 3H, $COOCH_3$), 3.79 (s, 3H, OCH_3), 3.60 (t, *J* = 7.5 Hz, 2H, CH_2-$NBoc_2$), 2.75 (t, *J* = 7.8 Hz, 2H, C*H*$_2$-CH_2-CH_2-$NBoc_2$), 1.85 (m, 2H, C*H*$_2$-CH_2-$NBoc_2$), 1.46 (s, 18H, *t*-Bu). **^{13}C NMR** (63 MHz, $CDCl_3$): 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

(m), 757 (m). R_f (*n*-hexane/EtOAc, 3:1) = 0.50. **HRMS**: calcd for $C_{24}H_{35}NO_7K$ $[M+K]^+$ 488.2045: found 488.2032.

Methyl (2*E*)-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), Cs_2CO_3 (528 mg; 1.62 mmol) and $HNBoc_2$ (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, $CDCl_3$): 7.87 (dd, *J* = 1.5 Hz, 16.3 Hz, 1H, aryl-C*H*=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=C*H*), 3.82 (s, 3H, $COOCH_3$), 3.59 (t, *J* = 7.3 Hz, 2H, CH_2-$NBoc_2$), 2.65 (t, *J* = 7.8 Hz, 2H, CH_2-CH_2-CH_2-$NBoc_2$), 1.83 (m, 2H, CH_2-CH_2-$NBoc_2$), 1.48 (s, 18H, *t*-Bu). **^{13}C NMR** (63 MHz, $CDCl_3$): 166.0, 152.5, 141.1, 140.8, 133.7, 132.5, 128.1, 126.10, 126.07, 123.94, 123.85, 82.3, 51.8, 46.0, 30.5, 29.8, 28.0. **^{19}F NMR** (282 MHz, $CDCl_3$): - 58.1. **IR** (neat): 2980 (m), 1795 (m), 1730 (s), 1654 (s), 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 $C_{24}H_{32}F_3NO_6Na$ $[M+Na]^+$ 510.2074: found 510.2066.

Methyl (2*E*)-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), Cs_2CO_3 (665 mg; 2.04 mmol) and $HNBoc_2$ (243 mg; 1.12 mmol) in dry DMF (7 mL).

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

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

^{1}H NMR (250 MHz, $CDCl_3$): 7.73 (d, *J* = 16.3 Hz, 1H, aryl-C*H*=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=C*H*), 3.69 (s, 3H, $COOCH_3$), 3.63 (t, *J* = 7.5 Hz, 2H, CH_2-$NBoc_2$), 2.75 (t, *J* = 8 Hz, 2H, CH_2-CH_2-CH_2-$NBoc_2$), 1.89 (m, 2H, CH_2-CH_2-$NBoc_2$), 1.48 (s, 18H, *t*-Bu). **^{13}C NMR** (63 MHz, $CDCl_3$): 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 $C_{29}H_{37}NO_6Na$ $[M+Na]^+$ 518.2513: found 518.2506.

Methyl (2*E*)-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_2CO_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 → 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-C*H*=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=C*H*), 3.87 (s, 3H, $COOCH_3$), 3.64 (t, *J* = 7.5 Hz, 2H, CH_2-$NBoc_2$), 2.82 (t, *J* = 7.8 Hz, 2H, CH_2-CH_2-CH_2-$NBoc_2$), 1.91 (m, 2H, 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, 130.7, 128.8, 128.2, 127.4, 126.5, 125.7, 125.4, 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), 754 (m). R_f (*n*-hexane/EtOAc, 3:1) = 0.60. **HRMS**: calcd for $C_{27}H_{35}NO_6Na$ $[M+Na]^+$ 492.2357: found 492.2373.

Methyl (2*E*)-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_2CO_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 → 25:1 → 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-C*H*=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=C*H*), 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-$NBoc_2$), 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 $C_{31}H_{37}NO_6Na$ $[M+Na]^+$ 542.2513: found 542.2506.

Methyl (2*E*)-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_2CO_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 → 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-C*H*=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=C*H*), 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, 51.8, 46.4, 30.0, 28.0, 27.5. **IR** (neat): 2977 (s), 1785 (m), 1725 (s), 1643 (m), 1525 (w), 1440 (m), 1364 (s), 1267 (s), 1170 (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 $C_{31}H_{37}NO_6Na$ $[M+Na]^+$ 542.2513: found 542.2505.

Methyl (2*E*)-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_2CO_3 (671 mg; 2.06 mmol) and $HNBoc_2$ (246 mg; 1.13 mmol) in dry DMF (8 mL).

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

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-C*H*=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=C*H*), 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). **mp**: 130 – 132 °C. R_f (*n*-hexane/EtOAc, 3:1) = 0.50. **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 NEt_3 (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 $NaHCO_3$ solution was added and it was extracted with DCM (3x). The combined organic phases were washed with diluted $NaHCO_3$-solution and with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The product was purified by column chromatography.

tert-Butyl _N_-[3-(2-{3-[(4_R_)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl}-3-(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), NEt_3 (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.

^{1}H NMR (250 MHz, $CDCl_3$): 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, CH_2-O), 3.37 (dd, *J* = 3.3 Hz, 13.3 Hz, 1H, C*H*H-phenyl), 3.21 (m, 4H, CH_2-NH-Boc), 3.13 – 2.97 (m, 4H, CH_2-CO + CH_2-CH_2-CO), 2.81 (dd, *J* = 9.8 Hz, 13.3 Hz, 1H, CH*H*-phenyl), 2.69 (t, *J* = 7.8 Hz, 4H, CH_2-CH_2-CH_2-NH-Boc), 1.79 (m, 4H, CH_2-CH_2-NH-Boc), 1.44 (s, 18H, *t*-Bu). **^{13}C NMR** (63 MHz, $CDCl_3$): 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), 733 (w), 699 (m), 599 (m). **mp**: 126 – 128 °C. R_f (*n*-hexane/EtOAc, 2:1) = 0.25. **$[\alpha]_D^{20}$** = -55.5° (c = 0.94, MeOH). **HRMS**: calcd for $C_{35}H_{49}N_3O_7K$ $[M+K]^+$ 662.3202: found 662.3198.

tert-Butyl _N_-[3-(2-{3-[(4_R_)-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), NEt_3 (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.

^{1}H NMR (250 MHz, $CDCl_3$): 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, CH_2-O), 3.36 (dd, *J* = 3.3 Hz, 13.5 Hz, 1H, C*H*H-phenyl), 3.21 (t, *J* = 7 Hz, 2H, C*H*$_2$-NH-Boc), 3.14 – 2.98 (m, 4H, CH_2-CO + C*H*$_2$-CH_2-CO), 2.82 (dd, *J* = 9.5 Hz, 13.5 Hz, 1H, CH*H*-phenyl), 2.69 (t, *J* = 7.8 Hz, 2H, C*H*$_2$-CH_2-CH_2-NH-Boc), 2.37 (s, 3H, CH_3), 1.79 (m, 2H, C*H*$_2$-CH_2-NH-Boc), 1.45 (s, 9H, *t*-Bu). **^{13}C NMR** (63 MHz, $CDCl_3$): 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), 1209 (m), 1186 (s), 1164 (s), 1120 (m), 1098 (m), 1049 (m), 991 (m), 978 (m), 866 (w), 780 (m), 761 (s), 735 (s), 701 (s), 676 (m), 593 (m), 511 (w). **mp**: 55 – 57 °C. R_f (*n*-hexane/EtOAc, 2:1) = 0.40. $[\alpha]_D^{20}$ = -63.2° (c = 1.09, MeOH). **HRMS**: calcd for $C_{28}H_{36}N_2O_5K$ $[M+K]^+$ 519.2256: found 519.2245.

tert-Butyl *N*-[3-(2-{3-[(4*R*)-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), NEt_3 (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.

^{1}H NMR (250 MHz, $CDCl_3$): 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, CH_2-O), 3.82 (s, 3H, OCH_3), 3.35 (dd, *J* = 3.3 Hz, 13.3 Hz, 1H, C*H*H-phenyl), 3.22 – 3.10 + 3.01 (m, 4H + m, 2H, C*H*$_2$-CH_2-CO + C*H*$_2$-NH-Boc + CH_2-CO), 2.78 (dd, *J* = 9.8 Hz, 13.3 Hz, 1H, CH*H*-phenyl), 2.69 (t, *J* = 7.8 Hz, 2H, C*H*$_2$-CH_2-CH_2-NH-Boc), 1.77 (m, 2H, C*H*$_2$-CH_2-NH-Boc), 1.44 (s, 9H, *t*-Bu). **^{13}C NMR** (63 MHz, $CDCl_3$): 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. R_f (*n*-hexane/EtOAc, 2:1) = 0.35. $[\alpha]_D^{20}$ = -59.5° (c = 0.55, MeOH). **HRMS**: calcd for $C_{28}H_{36}N_2O_6K$ $[M+K]^+$ 535.2205: found 535.2197.

***tert*-Butyl *N*-[3-(2-{3-[(4*R*)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl}-3-(trifluoro methyl)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), NEt_3 (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.

^{1}H NMR (250 MHz, $CDCl_3$): 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, CH_2-O), 3.36 (dd, *J* = 3.3 Hz, 13.3 Hz, 1H, C*H*H-phenyl), 3.26 – 3.09 (m, 6H, CH_2-CO + CH_2-CH_2-CO + CH_2-NH-Boc), 2.84 (dd, *J* = 9.5 Hz, 13.3 Hz, 1H, CH*H*-phenyl), 2.71 (m, 2H, CH_2-CH_2-CH_2-NH-Boc), 1.81 (m, 2H, CH_2-CH_2-NH-Boc), 1.44 (s, 9H, *t*-Bu). **^{13}C NMR** (63 MHz, $CDCl_3$): 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. **^{19}F NMR** (282 MHz, $CDCl_3$): -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), 1009 (m), 977 (w), 879 (w), 797 (w), 763 (m), 735 (m), 700 (s), 590 (w), 508 (w). **mp**: 91 – 94 °C. R_f (*n*-hexane/EtOAc, 2:1) = 0.35. $[\alpha]_D^{20}$ = -61.7° (c = 1.03, MeOH). **HRMS**: calcd for $C_{28}H_{33}F_3N_2O_5K$ $[M+K]^+$ 573.1973: found 573.1966.

***tert*-Butyl *N*-[3-(2-{3-[(4*R*)-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), NEt_3 (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.

^{1}H NMR (250 MHz, $CDCl_3$): 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, CH_2-O), 3.28 – 3.17 (m, 3H, CH_2-NH-Boc + C*H*H-phenyl), 3.04 – 2.88 (m, 4H, CH_2-CH_2-CO + CH_2-CO), 2.76 – 2.67 (m, 3H, CH_2-CH_2-CH_2-NH-Boc + CH*H*-phenyl), 1.86 (m, 2H, CH_2-CH_2-NH-Boc), 1.50 + 1.45 (s*, 9H, *t*-Bu). **^{13}C NMR** (63 MHz, $CDCl_3$): 172.1, 156.0, 153.3, 143.1, 142.3, 140.1, 135.8, 135.2, 129.3, 129.1, 128.9, 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), 505 (w). R_f (*n*-hexane/EtOAc, 2:1) = 0.40. $[\alpha]_D^{20}$ = -39.1° (c = 1.06, DCM). **HRMS**: calcd for $C_{33}H_{38}N_2O_5K$ $[M+K]^+$ 581.2412: found 581.2408.

***tert*-Butyl *N*-[3-(1-{3-[(4*R*)-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), NEt_3 (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.

^{1}H NMR (250 MHz, $CDCl_3$): 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, CH_2-O), 3.50 (m, 2H, C*H*$_2$-NH-Boc), 3.38 (dd, *J* = 3.3 Hz, 13.3 Hz, 1H, C*H*H-phenyl), 3.29 – 3.23 (m, 4H, C*H*$_2$-CH_2-CO + CH_2-CO), 2.92 – 2.78 (m, 3H, C*H*$_2$-CH_2-CH_2-NH-Boc + CH*H*-phenyl), 1.87 (m, 2H, C*H*$_2$-CH_2-NH-Boc), 1.45 (s, 9H, *t*-Bu). **^{13}C NMR** (63 MHz, $CDCl_3$) : 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), 1006 (s), 979 (m), 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), 503 (m). **mp**: 105 – 108 °C. R_f (*n*-hexane/EtOAc, 2:1) = 0.35. $[\alpha]_D^{20}$ = -58.8° (c = 0.50, MeOH). **HRMS**: calcd for $C_{31}H_{36}N_2O_5K$ $[M+K]^+$ 555.2256: found 555.2249.

***tert*-Butyl *N*-[3-(1-{3-[(4*R*)-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), NEt_3 (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.

^{1}H NMR (250 MHz, $CDCl_3$): 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, CH_2-O), 3.64 + 3.43 – 3.22 (m, 2H + m, 5H, C*H*$_2$-NH-Boc + C*H*H-phenyl + C*H*$_2$-CH_2-CO + CH_2-CO), 2.95 – 2.76 (m, 3H, C*H*$_2$-CH_2-CH_2-NH-Boc + CH*H*-phenyl), 1.91 (m, 2H, C*H*$_2$-CH_2-NH-Boc), 1.45 (s, 9H, *t*-Bu). **^{13}C NMR** (63 MHz, $CDCl_3$): 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),

760 (m), 737 (s), 724 (m), 701 (m), 643 (m). **mp**: 165 – 167 °C. R_f (*n*-hexane/EtOAc, 2:1) = 0.35. $[\alpha]_D^{20}$ = -50.0° (c = 0.21, DCM). **HRMS**: calcd for $C_{35}H_{38}N_2O_5Na$ $[M+Na]^+$ 589.2673: found 589.2674.

tert-Butyl *N*-[3-(10-{3-[(4*R*)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl} phenanthren-9-yl)propyl]carbamate (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), NEt_3 (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.

^{1}H NMR (250 MHz, $CDCl_3$): 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, CH_2-O), 3.58 + 3.45 – 3.23 (m, 2H + m, 7H, CH_2-CH_2-CO + C*H*H-phenyl + CH_2-CO + CH_2-NH-Boc + CH_2-CH_2-CH_2-NH-Boc), 2.86 (dd, *J* = 9.8 Hz, 13.5 Hz, 1H, CH*H*-phenyl), 1.94 (m, 2H, CH_2-CH_2-NH-Boc), 1.47 (s, 9H, *t*-Bu). **^{13}C NMR** (63 MHz, $CDCl_3$): 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), 1047 (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. R_f (*n*-hexane/EtOAc, 2:1) = 0.30. $[\alpha]_D^{20}$ = -63.6° (c = 0.50, DCM). **HRMS**: calcd for $C_{35}H_{38}N_2O_5K$ $[M+K]^+$ 605.2412: found 605.2409.

tert-Butyl *N*-[3-(1-{3-[(4*R*)-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), NEt_3 (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.

^{1}H NMR (250 MHz, $CDCl_3$): 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, CH_2-O), 3.76 3.43 – 3.30 (m, 2H + m, 5H, CH_2-CH_2-CO + C*H*H-phenyl + CH_2-CO + CH_2-NH-Boc), 3.18 (m, 2H, CH_2-CH_2-CH_2-NH-Boc), 2.84 (dd, *J* = 9.8 Hz, 13.5 Hz, 1H, CH*H*-phenyl), 2.03 (m, 2H, CH_2-CH_2-NH-Boc), 1.46 + 1.43 (s*, 9H, *t*-Bu). **^{13}C NMR** (63 MHz, $CDCl_3$): 172.5, 156.1, 153.4, 138.0, 135.2, 132.3, 131.1, 130.4, 130.1, 129.4,

129.3, 129.0, 127.9, 127.4, 127.2, 127.0, 126.2, 125.6, 125.0, 124.814, 124.805, 123.9, 123.2, 79.1, 66.4, 55.3, 40.8, 38.0, 37.0, 32.4, 31.3, 28.4, 26.9, 23.8. **IR** (neat): 3367 (w), 2929 (w), 1793 (s), 1705 (s), 1677 (s), 1514 (s), 1394 (m), 1364 (m), 1296 (m), 1236 (m), 1208 (m), 1189 (s), 1099 (m), 1044 (m), 1009 (m), 978 (m), 867 (w), 840 (m), 826 (m), 760 (m), 749 (m), 736 (m), 701 (m), 683 (m), 592 (m), 506 (w). **mp**: 157 – 159 °C. $\boldsymbol{R_f}$ (*n*-hexane/EtOAc, 2:1) = 0.30. $\boldsymbol{[\alpha]_D^{20}}$ = -54.2° (c = 0.20, DCM). **HRMS**: calcd for $C_{37}H_{38}N_2O_5$ $[M]^+$ 590.2775: found 590.2764.

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 $NaHCO_3$ solution. After drying over $MgSO_4$ the crude product was purified by column chromatography (pentane/Et_2O 1:1 → 1:3).

The azide was dissolved in a THF/H_2O solution and cooled to 0 °C. H_2O_2 (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 $Na_2S_2O_5$ solution (4.4 equiv). Then it was acidified with HCl (4 M) at 0 °C, extracted with EtOAc (3x), dried over Na_2SO_4 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 H_2 atmosphere for 6 h. The catalyst was removed by filtration over Celite®.

After concentration under reduced pressure the amine was dissolved in a H_2O/dioxane solution (1:1, v/v) and cooled to 0 °C. $NaHCO_3$ (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 $MgSO_4$ the protected amino acid was dissolved in dry DMF. $NaHCO_3$ (2 equiv) and benzyl bromide (3 equiv) were added and the reaction mixture was stirred at room temperature overnight.

H_2O was added and it was extracted with EtOAc (3x). The combined organic phases were washed with H_2O (2x), dried over $MgSO_4$ and purified by column chromatography.

Benzyl (2*R*)-3-[2,6-bis(3-{[(*tert*-butoxy)carbonyl]amino}propyl)phenyl]-2-{[(9*H*-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); H_2O_2 (30%; 245 µL; 2.40 mmol), LiOH (29 mg; 1.20 mmol), THF (9.2 mL), H_2O (2.7 mL), $Na_2S_2O_5$ (502 mg; 2.64 mmol; in 1.9 mL H_2O); Pd/C (80 mg), MeOH (7 mL); Fmoc-OSu (223 mg; 0.66 mmol), $NaHCO_3$ (151 mg, 1.80 mmol), dioxane/H_2O (1:1; 4.7 mL), dioxane (2.3 mL); $NaHCO_3$ (101 mg; 1.20 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.

^{1}H NMR (400 MHz, $CDCl_3$): 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-C*H*H-phenyl), 4.97 (d, *J* = 12.4 Hz, 1H, COO-CH*H*-phenyl) 4.73 (m, 2H, NH-Boc), 4.56 (q, *J* = 8 Hz, 1H, α-CH), 4.40 (m, 2H, CH_2-fluorenyl), 4.21 (m, 1H, CH-fluorenyl), 3.18 – 3.03 (m, 6H, α-CH-CH_2 + CH_2-NH-Boc), 2.70 – 2.55 (m, 4H, CH_2-CH_2-CH_2-NH-Boc), 1.71 (m, 4H, CH_2-CH_2-NH-Boc), 1.44 + 1.42 (s*, 18H, *t*-Bu). **^{13}C NMR** (75 MHz, $CDCl_3$): 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, 32.4, 31.8, 30.2, 28.4. **IR** (neat): 3356 (m), 2979 (w), 1736 (m), 1684 (s), 1520 (s), 1451 (m), 1391 (w), 1366 (m), 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. R_f (*n*-hexane/EtOAc, 2:1) = 0.35. **$[\alpha]_D^{20}$** = -3.1° (c = 0.77, DCM). **HRMS**: calcd for $C_{47}H_{57}N_3O_8Na$ $[M+Na]^+$ 814.4038: found 814.4063.

Benzyl (2*R*)-3-[2-(3-{[(*tert*-butoxy)carbonyl]amino}propyl)-6-methylphenyl]-2-{[(9*H*-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); H_2O_2 (30%; 78 µL; 0.76 mmol), LiOH (9 mg; 0.38 mmol), THF (2.9 mL), H_2O (0.9 mL), $Na_2S_2O_5$ (160 mg; 0.84 mmol; in 0.6 mL H_2O); Pd/C (20 mg), MeOH (2 mL); Fmoc-OSu (71 mg; 0.21 mmol), $NaHCO_3$ (48 mg, 0.57 mmol), dioxane/H_2O (1:1; 1.3 mL), dioxane (0.7 mL); $NaHCO_3$ (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.

^{1}H NMR (400 MHz, $CDCl_3$): 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-C*H*H-phenyl), 5.00 (d, *J* = 12 Hz, 1H, COO-CH*H*-phenyl), 4.80 (br s, 1H, NH-Boc), 4.61 (q,

J = 8 Hz, 1H, α-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, α-CH-C*H*$_2$ + C*H*$_2$-NH-Boc), 2.65 (m, 2H, C*H*$_2$-CH_2-CH_2-NH-Boc), 2.30 (s, 3H, CH_3), 1.72 (m, 2H, C*H*$_2$-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, 128.1, 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), 621 (m), 541 (w). **mp**: 94 – 96 °C. ***R*$_f$** (*n*-hexane/EtOAc, 2:1) = 0.40. **$[\alpha]_D^{20}$** = -6.8° (c = 0.22, DCM). **HRMS**: calcd for $C_{40}H_{44}N_2O_6Na$ $[M+Na]^+$ 671.3092: found 671.3091.

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

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 µL; 4.00 mmol), dry THF (3 x 6 mL); isolated azide **6c** (273 mg; 0.51 mmol); H_2O_2 (30%; 208 µL; 2.04 mmol), LiOH (24 mg; 1.02 mmol), THF (7.8 mL), H_2O (2.3 mL), $Na_2S_2O_5$ (426 mg; 2.24 mmol; in 1.6 mL H_2O); Pd/C (55 mg), MeOH (6 mL); Fmoc-OSu (189 mg; 0.56 mmol), $NaHCO_3$ (129 mg, 1.53 mmol), dioxane/H_2O (1:1; 4 mL), dioxane (2 mL); $NaHCO_3$ (86 mg; 1.02 mmol), BnBr (182 µL; 1.53 mmol), dry DMF (6 mL).

Eluent for column chromatography: cyclohexane/EtOAc, 10:1 → 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, α-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, α-CH-C*H*$_2$ + C*H*$_2$-NH-Boc), 2.65 (m, 2H, C*H*$_2$-CH_2-CH_2-NH-Boc), 1.73 (m, 2H, C*H*$_2$-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, 127.6, 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. **$[\alpha]_D^{20}$** = -4.4° (c = 0.46, DCM). **HRMS**: calcd for $C_{40}H_{44}N_2O_7Na$ $[M+Na]^+$ 687.3041: found 687.3061.

Benzyl (2*R*)-3-[2-(3-{[(*tert*-butoxy)carbonyl]amino}propyl)-6-(trifluoromethyl)phenyl]-2-{[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino}propanoate (7d)

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 µL; 3.27 mmol), dry THF (3 x 5 mL); isolated azide **6d** (280 mg; 0.49 mmol); H_2O_2 (30%; 200 µL; 1.96 mmol), LiOH

(23 mg; 0.98 mmol), THF (7.5 mL), H_2O (2.2 mL), $Na_2S_2O_5$ (411 mg; 2.16 mmol; in 1.5 mL H_2O); Pd/C (56 mg), MeOH (6 mL); Fmoc-OSu (182 mg; 0.54 mmol), $NaHCO_3$ (123 mg, 1.47 mmol), dioxane/H_2O (1:1; 4 mL), dioxane (2 mL); $NaHCO_3$ (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.

^{1}H NMR (400 MHz, $CDCl_3$): 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-CH_2-phenyl + NH-Boc), 4.69 (q, *J* = 8 Hz, 1H, α-CH), 4.33 (m, 2H, CH_2-fluorenyl), 4.15 (t, *J* = 6.8 Hz, 1H, CH-fluorenyl), 3.36 – 3.20 (m, 4H, α-CH-C*H*$_2$ + C*H*$_2$-NH-Boc), 2.88 (m, 2H, C*H*$_2$-CH_2-CH_2-NH-Boc), 1.79 (m, 2H, C*H*$_2$-CH_2-NH-Boc), 1.43 + 1.39 (s*, 9H, *t*-Bu). **^{13}C NMR** (75 MHz, $CDCl_3$): 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. **^{19}F NMR** (282 MHz, $CDCl_3$): - 57.7. **IR** (neat): 3348 (m), 2973 (w), 1744 (m), 1681 (s), 1529 (s), 1451 (m), 1367 (w), 1313 (m), 1253 (s), 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. ***R*$_f$** (*n*-hexane/EtOAc, 2:1) = 0.45. **[α]$_D^{20}$** = -1.9° (c = 0.37, DCM). **HRMS**: calcd for $C_{40}H_{41}F_3N_2O_6Na$ $[M+Na]^+$ 725.2809: found 725.2830.

Benzyl (2*R*)-3-[2-(3-{[(*tert*-butoxy)carbonyl]amino}propyl)-6-phenylphenyl]-2-{[(9*H*-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); H_2O_2 (30%; 212 µL; 2.08 mmol), LiOH (25 mg; 1.04 mmol), THF (8.0 mL), H_2O (2.3 mL), $Na_2S_2O_5$ (435 mg; 2.29 mmol; in 1.6 mL H_2O); Pd/C (61 mg), MeOH (6 mL); Fmoc-OSu (192 mg; 0.57 mmol), $NaHCO_3$ (131 mg, 1.56 mmol), dioxane/H_2O (1:1; 4 mL), dioxane (2 mL); $NaHCO_3$ (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.

^{1}H NMR (400 MHz, $CDCl_3$): 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-CH_2-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 + CH_2-fluorenyl), 4.12 (t, *J* = 6.8 Hz, 1H, CH-fluorenyl), 3.21 – 3.13 (m, 3H, α-CH-C*H*H + C*H*$_2$-NH-Boc), 3.05 (m, 1H, α-CH-C*H*H), 2.76 (m, 2H, C*H*$_2$-CH_2-CH_2-NH-Boc), 1.82 (m, 2H, C*H*$_2$-CH_2-NH-Boc), 1.44 (s, 9H, *t*-Bu). **^{13}C NMR** (75 MHz, $CDCl_3$): 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. ***R*$_f$** (*n*-hexane/EtOAc,

2:1) = 0.45. $[\alpha]_D^{20}$ = -2.1° (c = 0.28, DCM). **HRMS**: calcd for $C_{45}H_{46}N_2O_6Na$ $[M+Na]^+$ 733.3248: found 733.3247.

Benzyl (2*R*)-3-[2-(3-{[(*tert*-butoxy)carbonyl]amino}propyl)naphthalen-1-yl]-2-{[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino}propanoate (7f)

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); H_2O_2 (30%; 172 µL; 1.68 mmol), LiOH (20 mg; 0.84 mmol), THF (6.4 mL), H_2O (1.9 mL), $Na_2S_2O_5$ (352 mg; 1.85 mmol; in 1.3 mL H_2O); Pd/C (47 mg), MeOH (5 mL); Fmoc-OSu (155 mg; 0.46 mmol), $NaHCO_3$ (106 mg, 1.26 mmol), dioxane/H_2O (1:1; 3.3 mL), dioxane (1.7 mL); $NaHCO_3$ (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/*n*-hexane.

^{1}H NMR (400 MHz, $CDCl_3$): 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-C*H*H-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-CH*H*-phenyl), 4.38 (d, *J* = 7.2 Hz, 2H, CH_2-fluorenyl), 4.17 (t, *J* = 7.2 Hz, 1H, CH-fluorenyl), 3.66 – 3.52 (m, 2H, α-CH-C*H*$_2$), 3.19 (m, 2H, C*H*$_2$-NH-Boc), 2.82 (m, 2H, C*H*$_2$-CH_2-CH_2-NH-Boc), 1.79 (m, 2H, C*H*$_2$-CH_2-NH-Boc), 1.41 (s, 9H, *t*-Bu). **^{13}C NMR** (75 MHz, $CDCl_3$): 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. R_f (*n*-hexane/EtOAc, 2:1) = 0.35. $[\alpha]_D^{20}$ = -8.6° (c = 0.30, DCM). **HRMS**: calcd for $C_{43}H_{44}N_2O_6Na$ $[M+Na]^+$ 707.3092: found 707.3113.

Benzyl (2*R*)-3-[10-(3-{[(*tert*-butoxy)carbonyl]amino}propyl)phenanthren-9-yl]-2-{[(9*H*-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); H_2O_2 (30%; 278 µL; 2.72 mmol), LiOH (33 mg; 1.36 mmol), THF (10.4 mL), H_2O (3.1 mL), $Na_2S_2O_5$ (568 mg; 2.99 mmol; in 2.1 mL H_2O); Pd/C (83 mg), MeOH (8 mL); Fmoc-OSu (253 mg; 0.75 mmol), $NaHCO_3$ (171 mg, 2.04 mmol), dioxane/H_2O (1:1; 5.3 mL), dioxane (2.7 mL); $NaHCO_3$ (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.

^{1}H NMR (400 MHz, $CDCl_3$): 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* = 7.2 Hz, 1H, aryl-H), 7.00 (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-CH_2-phenyl + α-CH), 4.42 (m, 2H, CH_2-fluorenyl), 4.19 (t, *J* = 6.8 Hz, 1H, CH-fluorenyl), 3.78 – 3.60 (m, 2H, α-CH-C*H*$_2$), 3.40 – 3.10 (m, 4H, C*H*$_2$-NH-Boc + C*H*$_2$-CH_2-CH_2-NH-Boc), 1.86 (m, 2H, C*H*$_2$-CH_2-NH-Boc), 1.47 + 1.43 (s*, 9H, *t*-Bu). **^{13}C NMR** (75 MHz, $CDCl_3$): 172.1, 156.1, 155.7, 143.8, 143.7, 141.3, 135.4, 134.2, 131.2, 130.7, 130.4, 129.9, 128.5, 128.2, 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), 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**: 184 – 186 °C. ***R*$_f$** (*n*-hexane/EtOAc, 2:1) = 0.35. **$[\alpha]_D^{20}$** = -3.8° (c = 0.42, DCM). **HRMS**: calcd for $C_{47}H_{46}N_2O_6Na$ $[M+Na]^+$ 757.3248: found 757.3269.

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

Following GP5 using carboximide **5i** (520 mg; 0.88 mmol), KHMDS (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); H_2O_2 (30%; 241 µL; 2.36 mmol), LiOH (28 mg; 1.18 mmol), THF (9.0 mL), H_2O (2.7 mL), $Na_2S_2O_5$ (494 mg; 2.60 mmol; in 1.8 mL H_2O); Pd/C (75 mg), MeOH (7 mL); Fmoc-OSu (219 mg; 0.65 mmol), $NaHCO_3$ (149 mg, 1.77 mmol), dioxane/H_2O (1:1; 4.7 mL), dioxane (2.3 mL); $NaHCO_3$ (99 mg; 1.18 mmol), BnBr (211 µL; 1.77 mmol), dry DMF (7 mL).

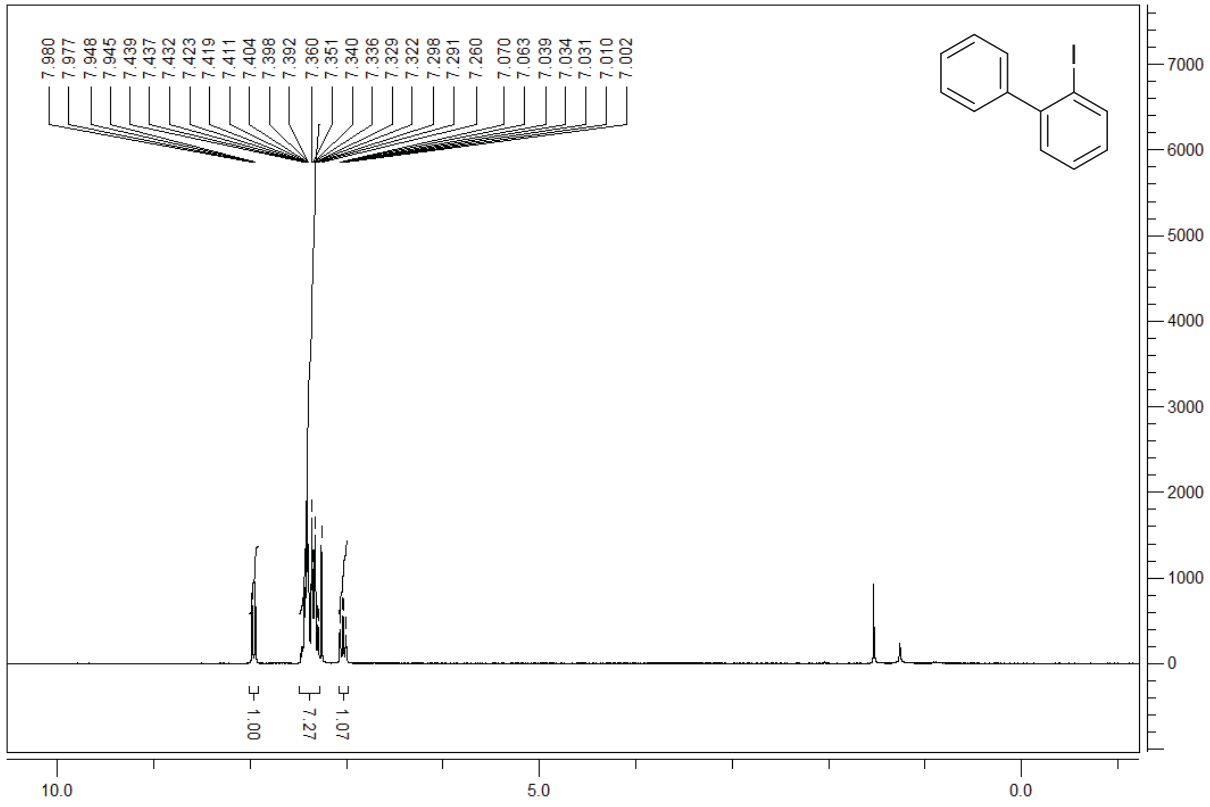
Eluent for column chromatography: cyclohexane/EtOAc, 10:1 → 5:1.

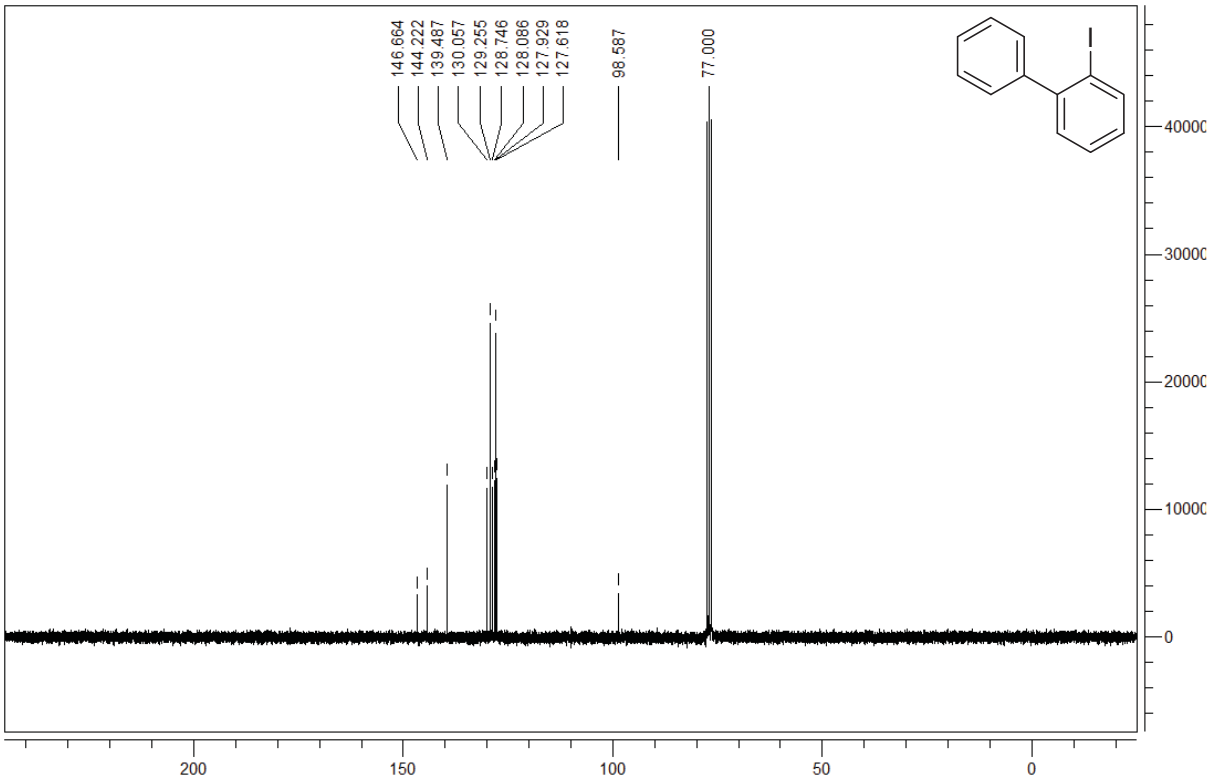
Yield: 112 mg (17% over 5 steps); colourless solid after recrystallization from DCM/*n*-hexane.

^{1}H NMR (400 MHz, $CDCl_3$): 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-CH_2-phenyl + α-CH), 4.42 (m, 2H, CH_2-fluorenyl), 4.18 (m, 1H, CH-fluorenyl), 3.95 – 3.60 (m, 2H, α-CH-C*H*$_2$), 3.27 – 3.09 (m, 4H, C*H*$_2$-NH-Boc + C*H*$_2$-CH_2-CH_2-NH-Boc), 1.89 (m, 2H, C*H*$_2$-CH_2-NH-Boc), 1.43 (s, 9H, *t*-Bu). **^{13}C NMR** (75 MHz, $CDCl_3$): 172.0, 156.1, 155.6, 143.82, 143.78, 143.7, 141.3, 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), 1690 (s), 1517 (s), 1450 (m), 1366 (w), 1344 (w), 1267 (s), 1169 (s), 1087 (m), 1032 (m), 871 (w), 841 (w), 827 (w), 755 (s), 738 (s), 696 (m), 621 (m), 541 (w). **mp**: 147 – 150 °C. ***R*$_f$** (*n*-hexane/EtOAc, 2:1) = 0.35. **$[\alpha]_D^{20}$** = +4.5° (c = 0.31, DCM). **HRMS**: calcd for $C_{49}H_{46}N_2O_6Na$ $[M+Na]^+$ 781.3248: found 781.3244.

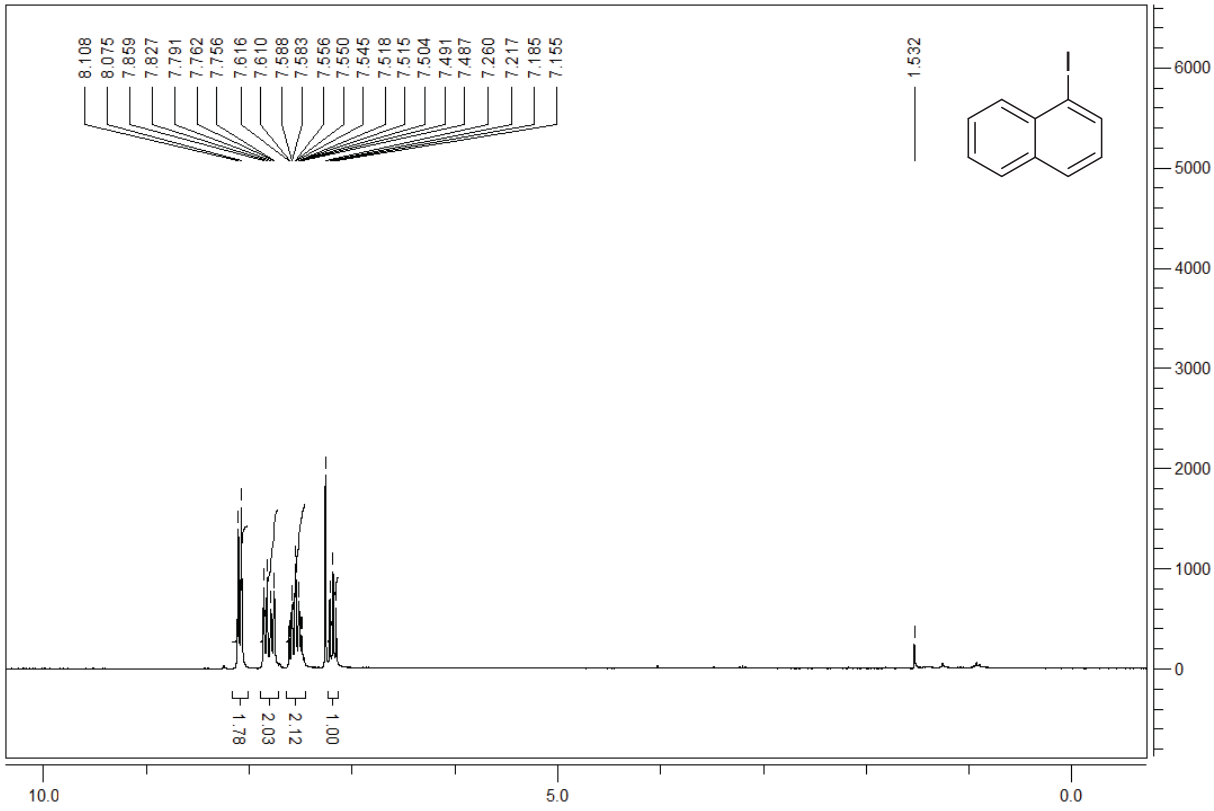
NMR spectra

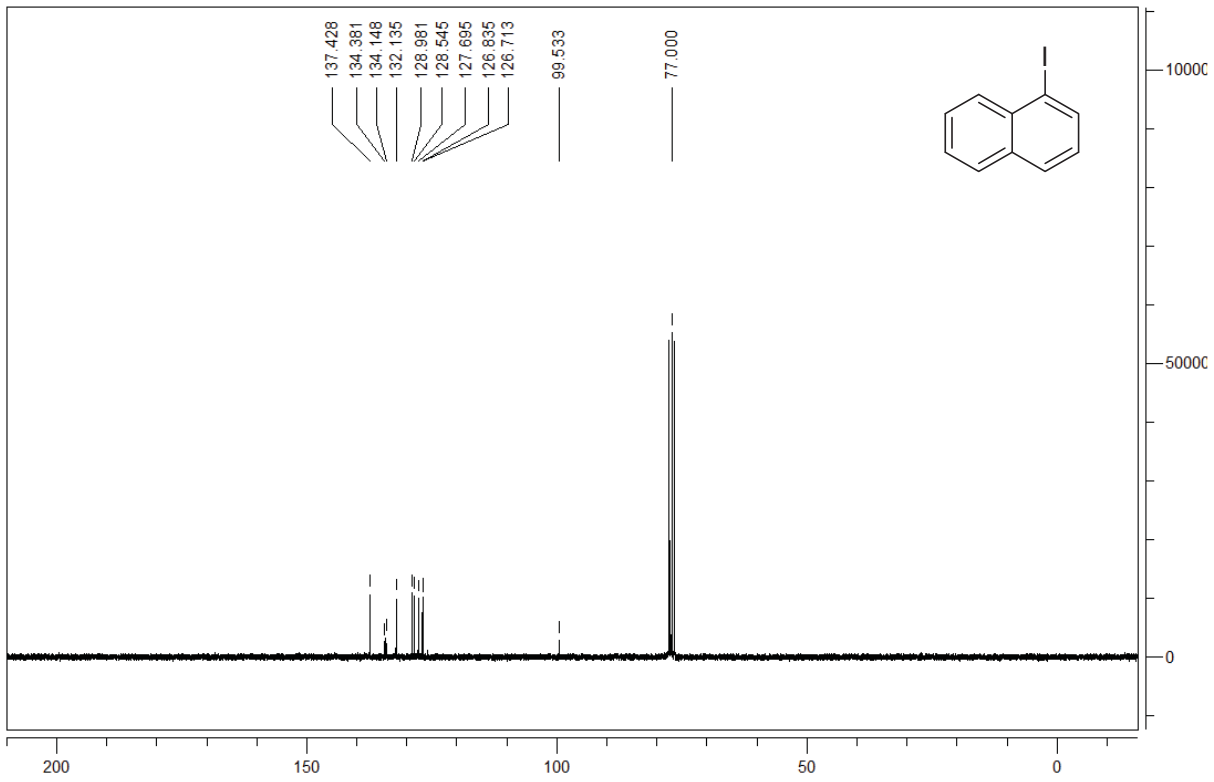
1-Iodo-2-phenylbenzene (**1e**)



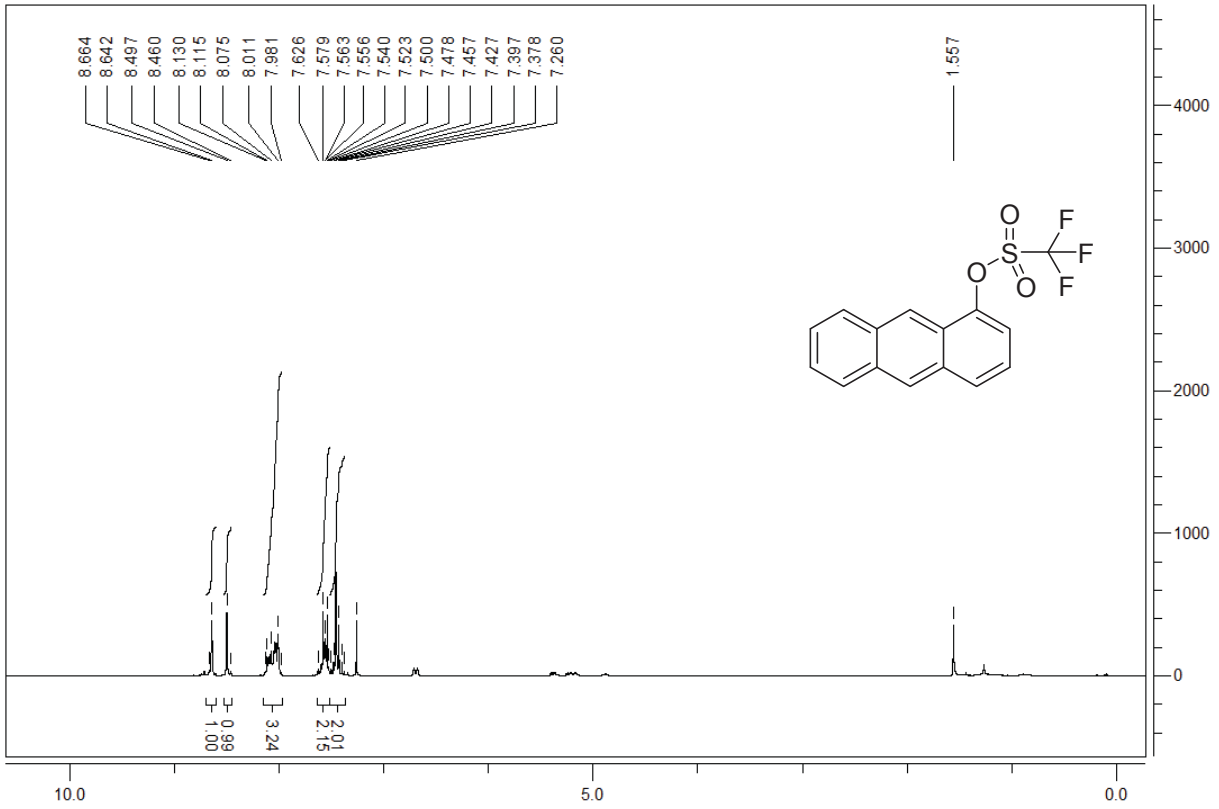


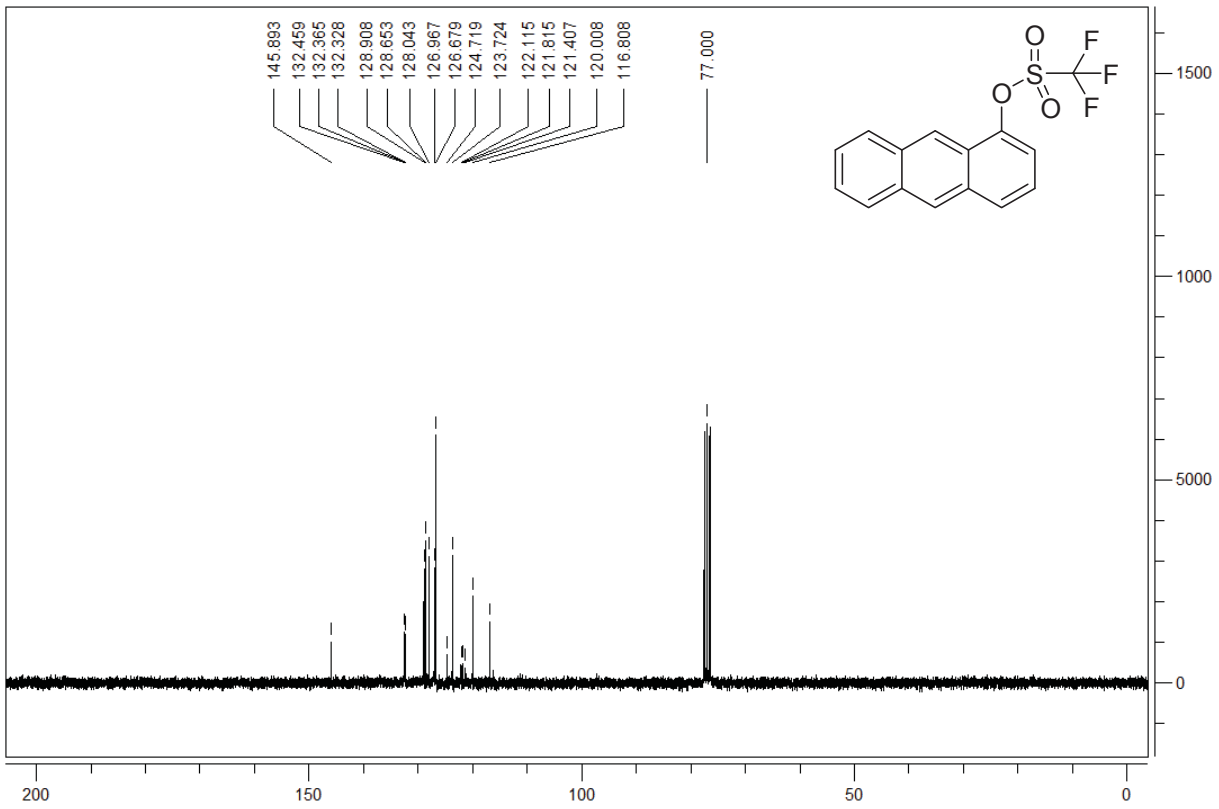
1-Iodonaphthalene (**1f**)



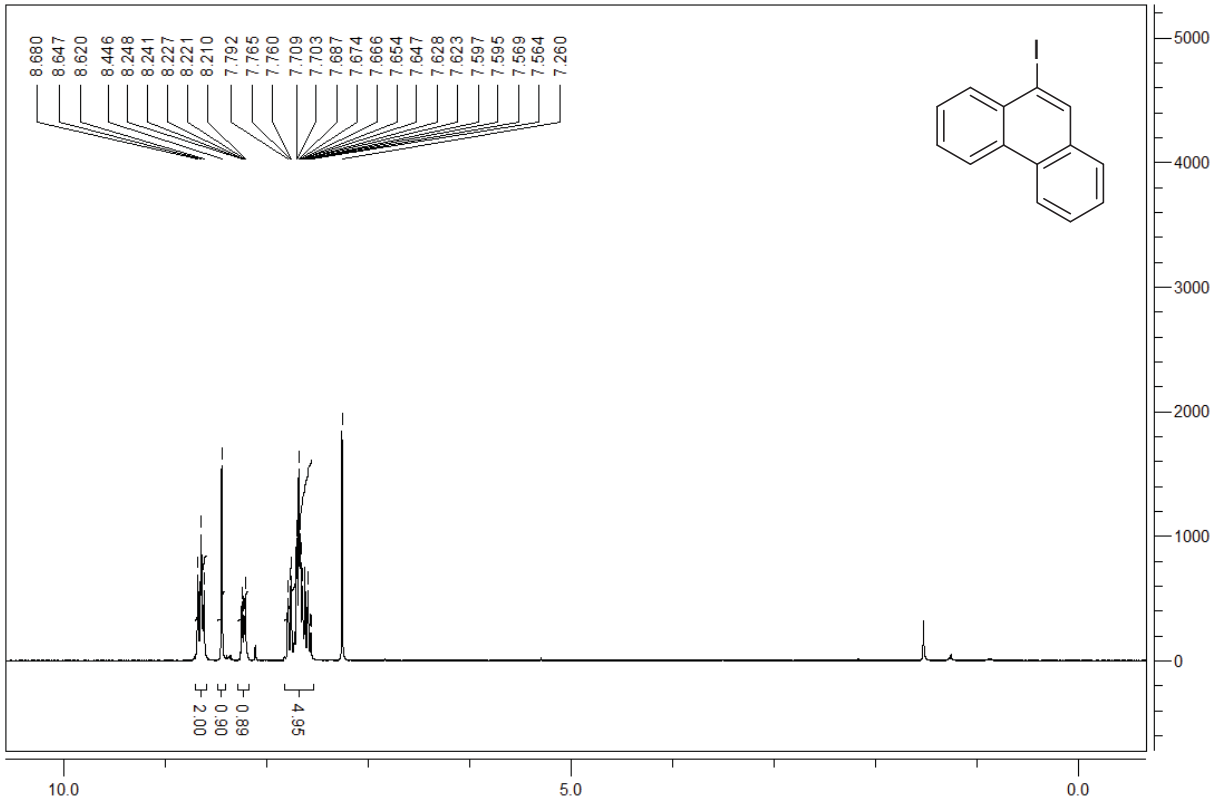


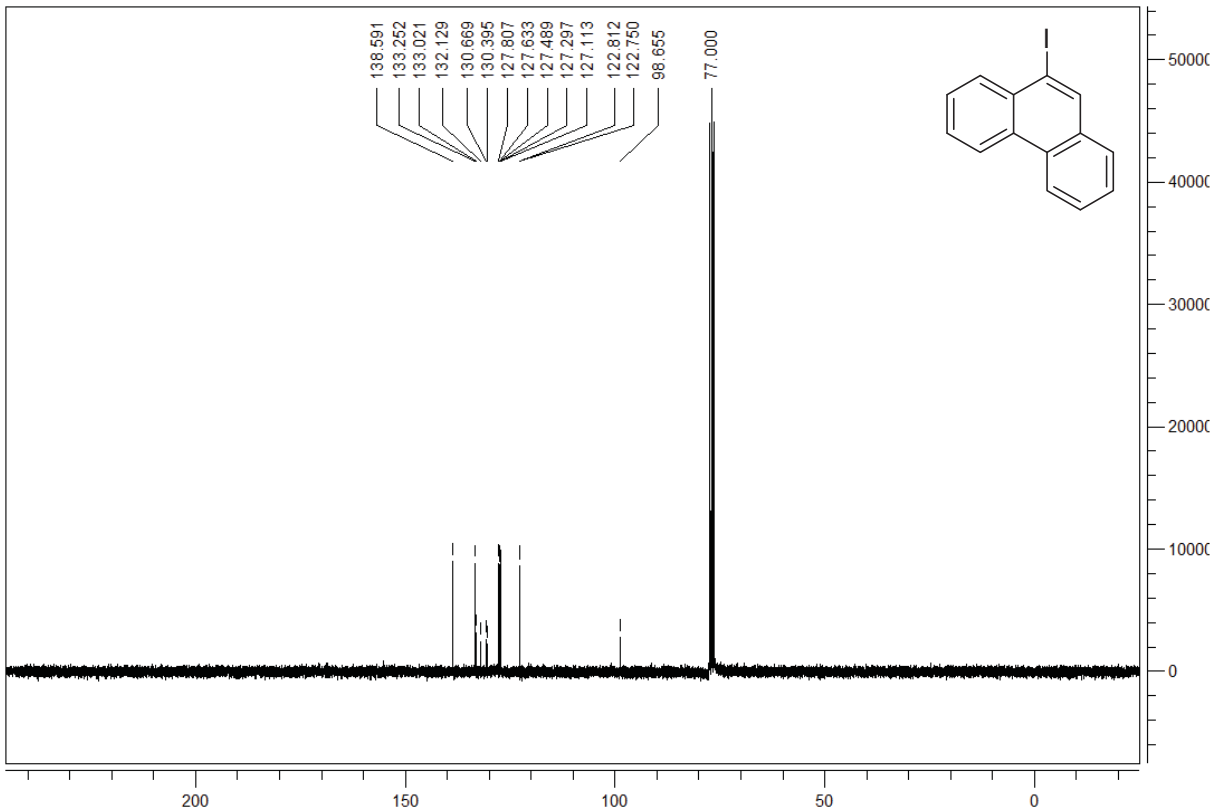
Anthracen-1-yl trifluoromethanesulfonate (**1g**)



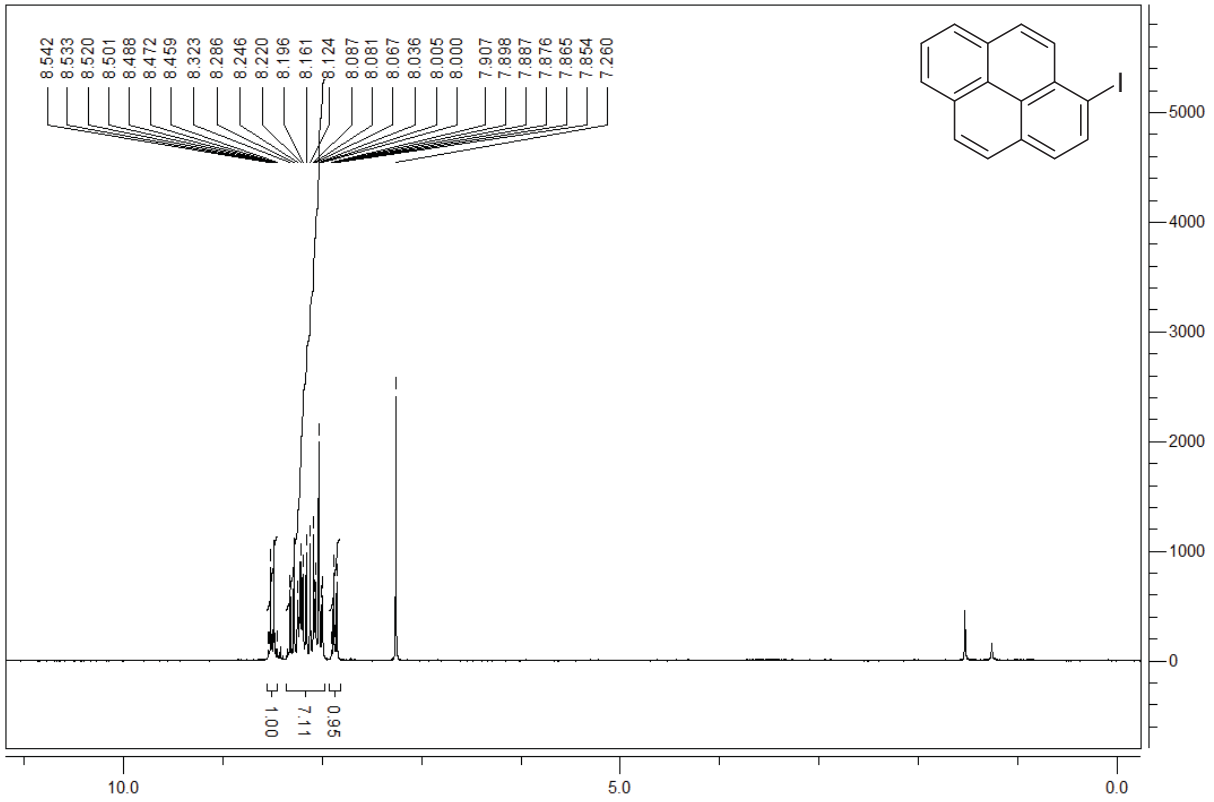


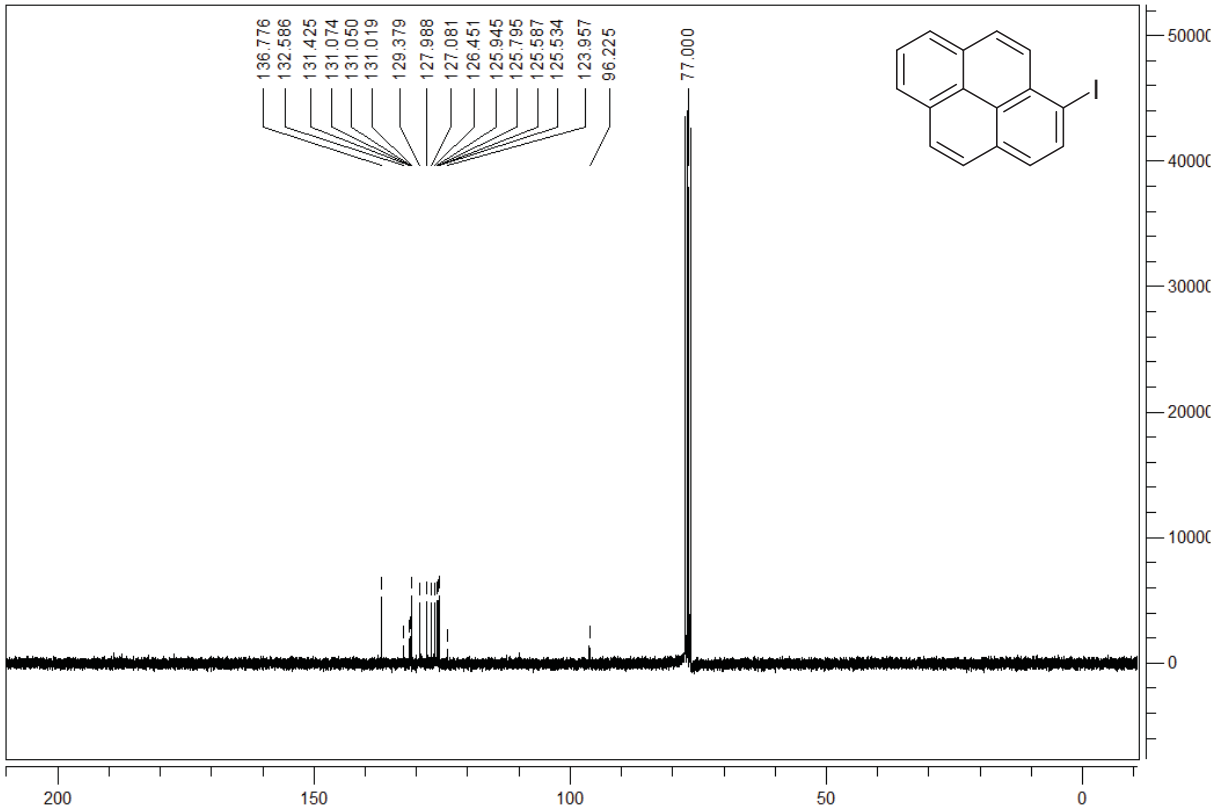
9-Iodophenanthrene (**1h**)



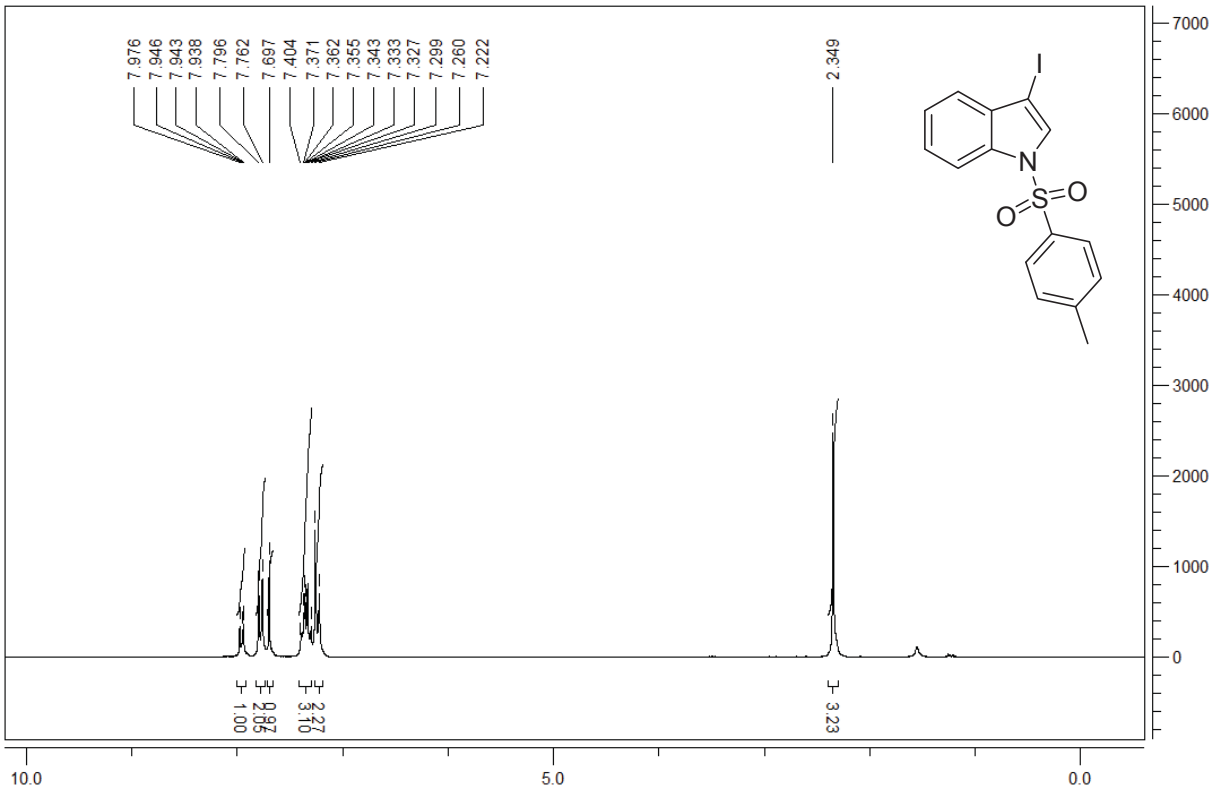


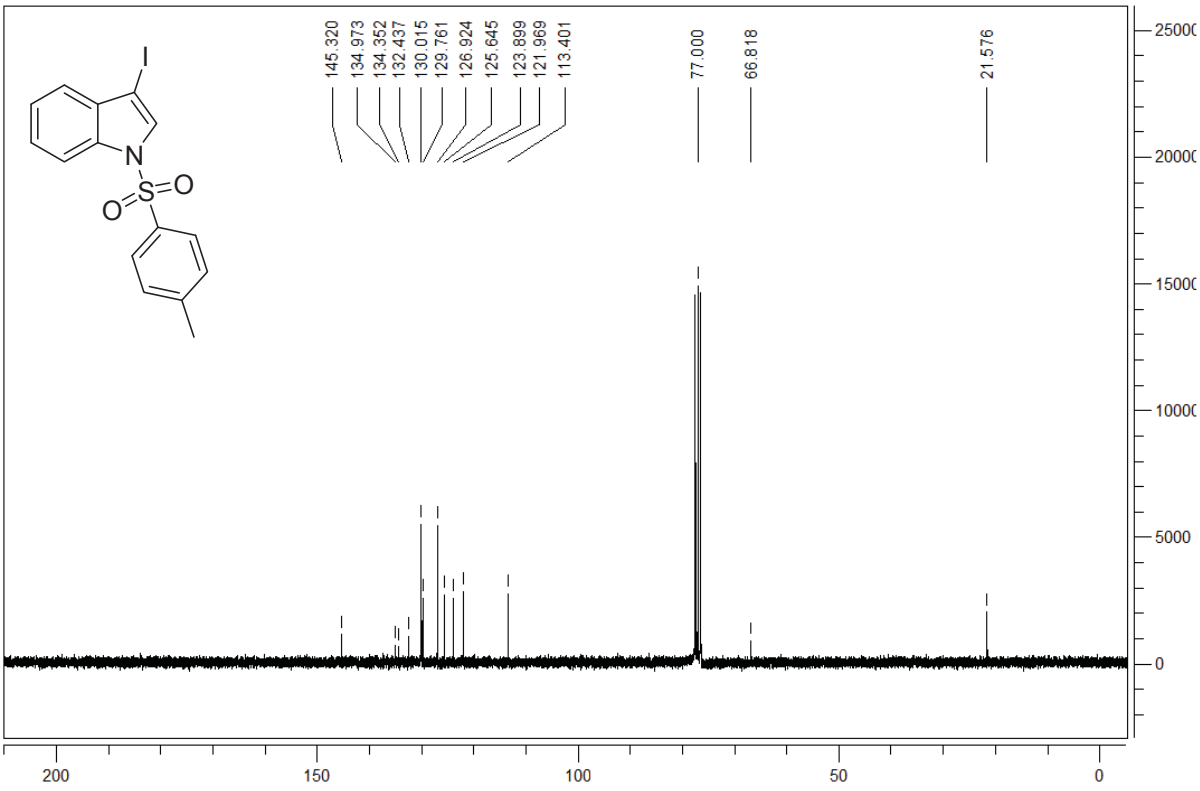
1-Iodopyrene (**1i**)



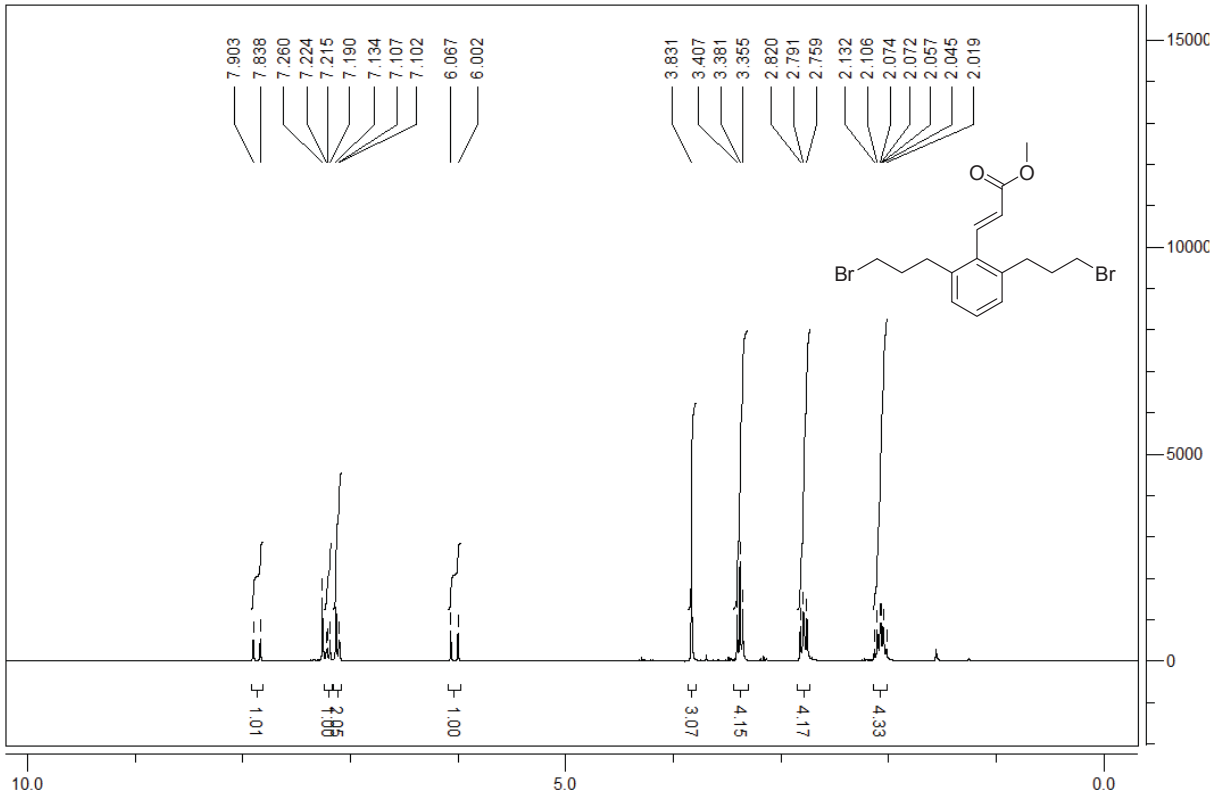


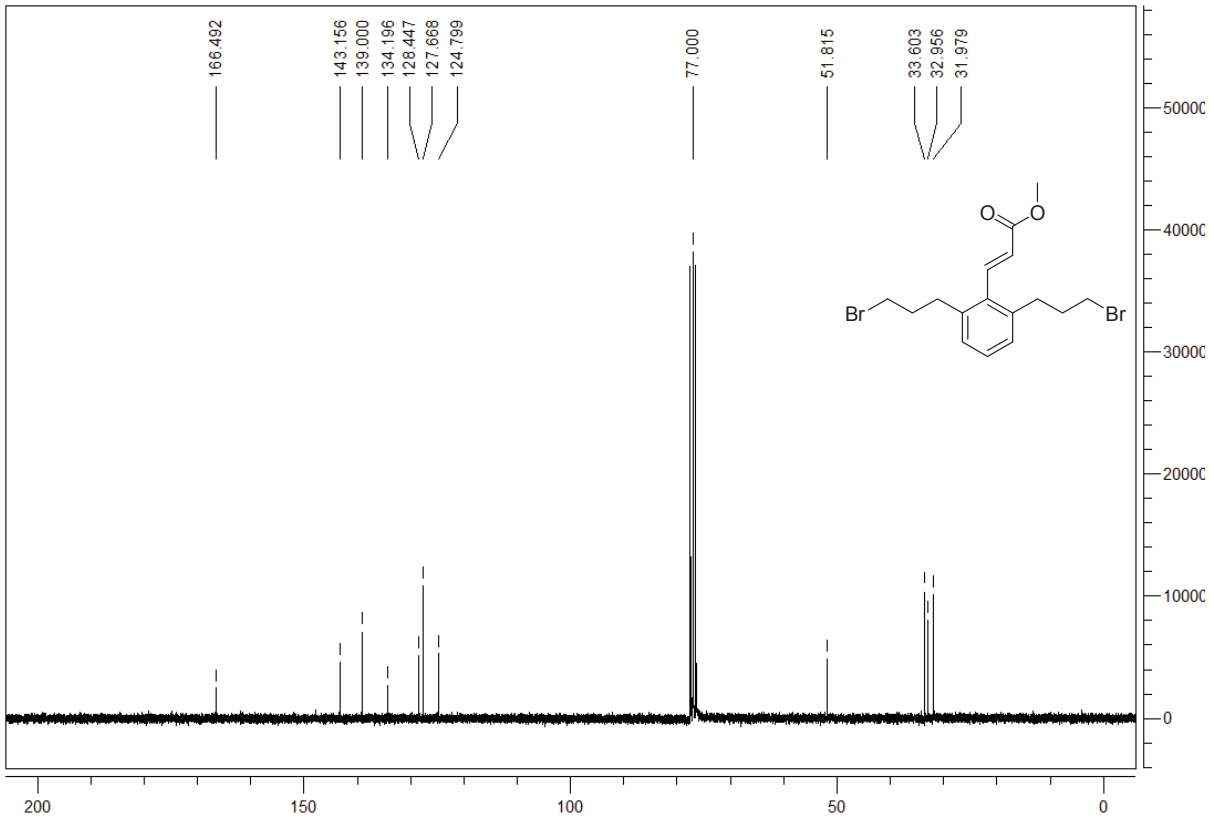
3-Iodo-1-[(4-methylbenzene)sulfonyl]-1*H*-indole (**1j**)



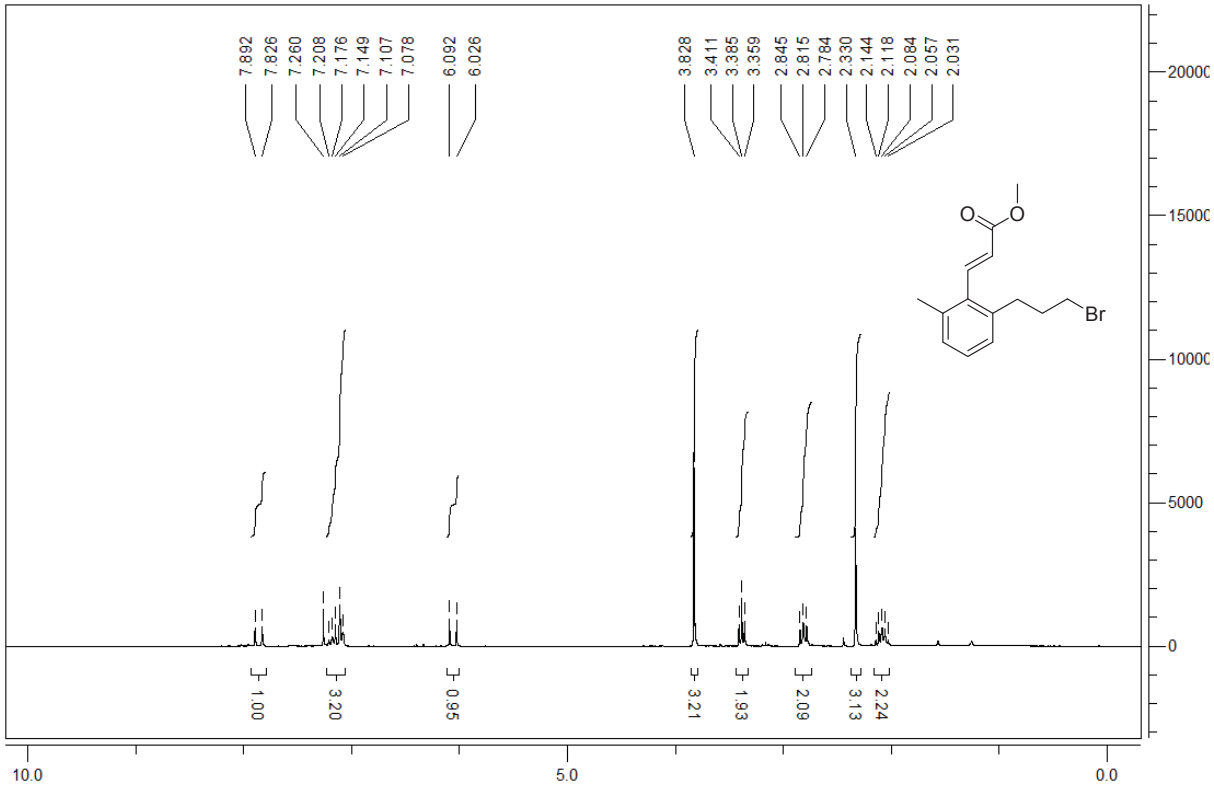


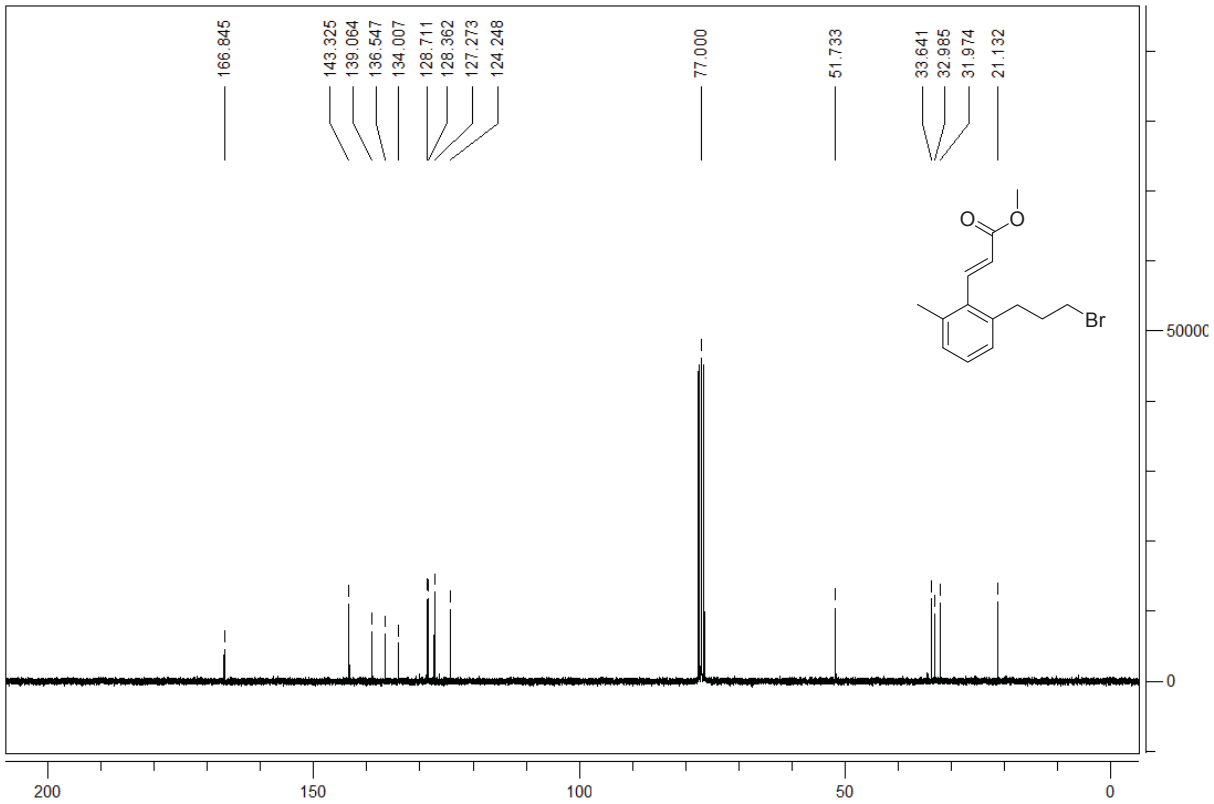
Methyl (2E)-3-[2,6-*bis*(3-bromopropyl)phenyl]prop-2-enoate (**2a**)



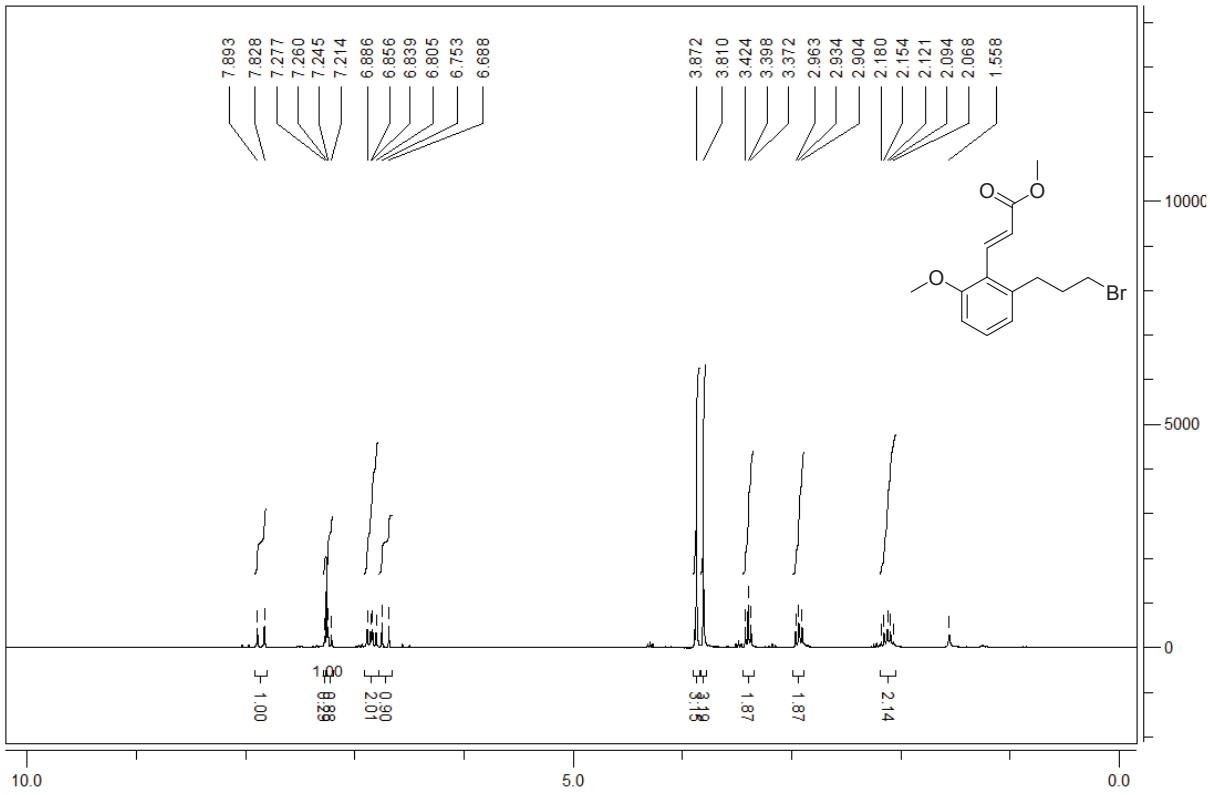


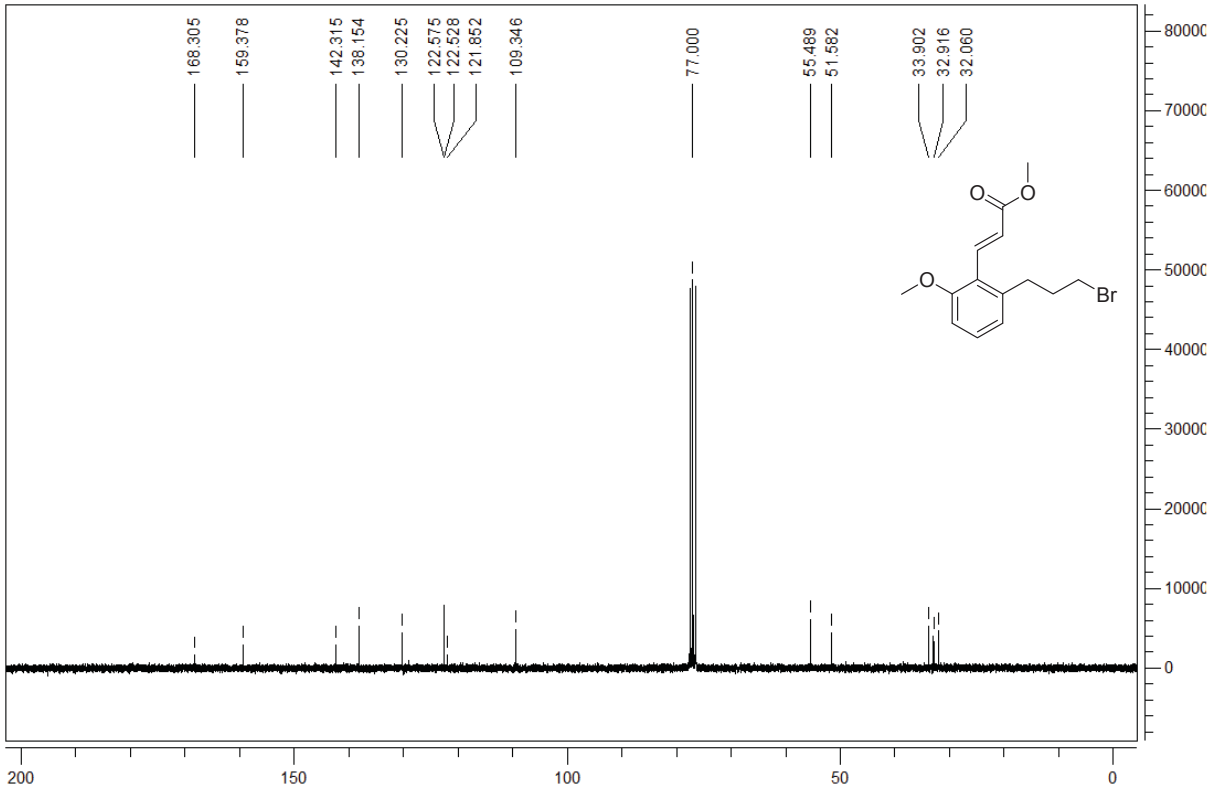
Methyl (2E)-3-[2-(3-bromopropyl)-6-methylphenyl]prop-2-enoate (**2b**)



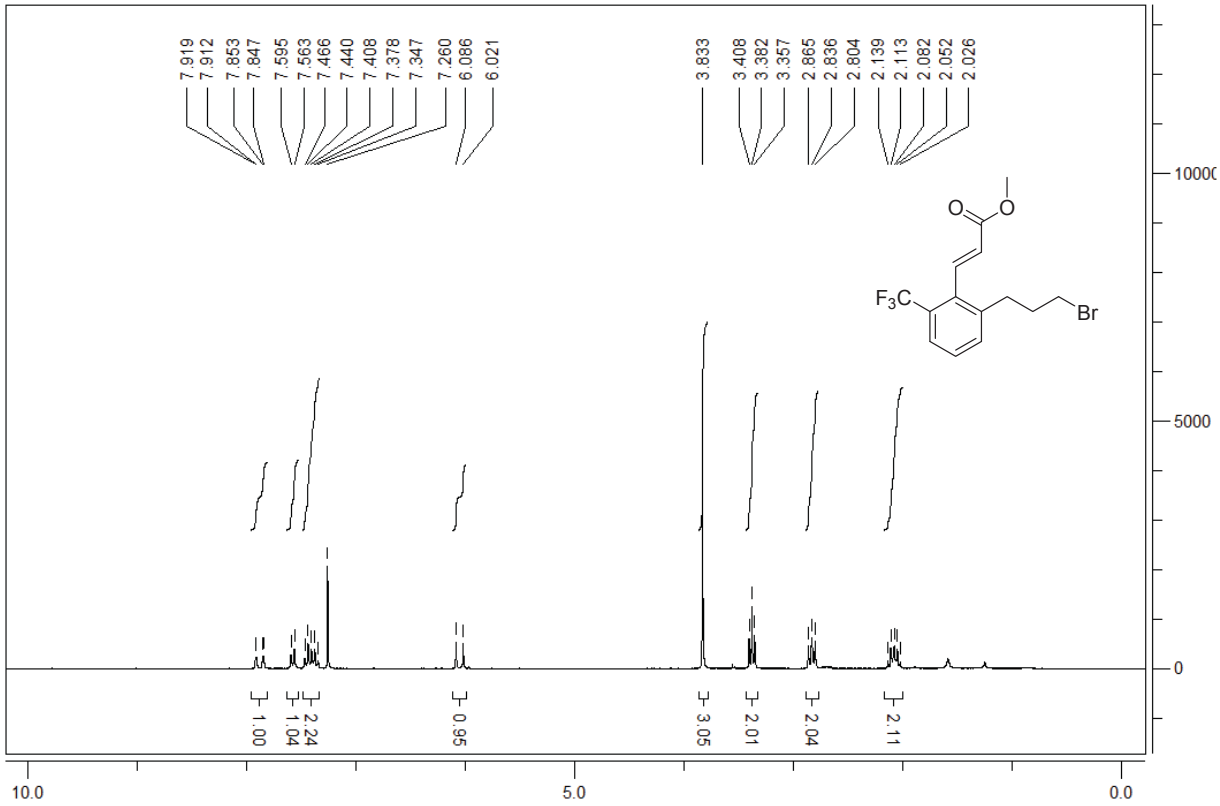


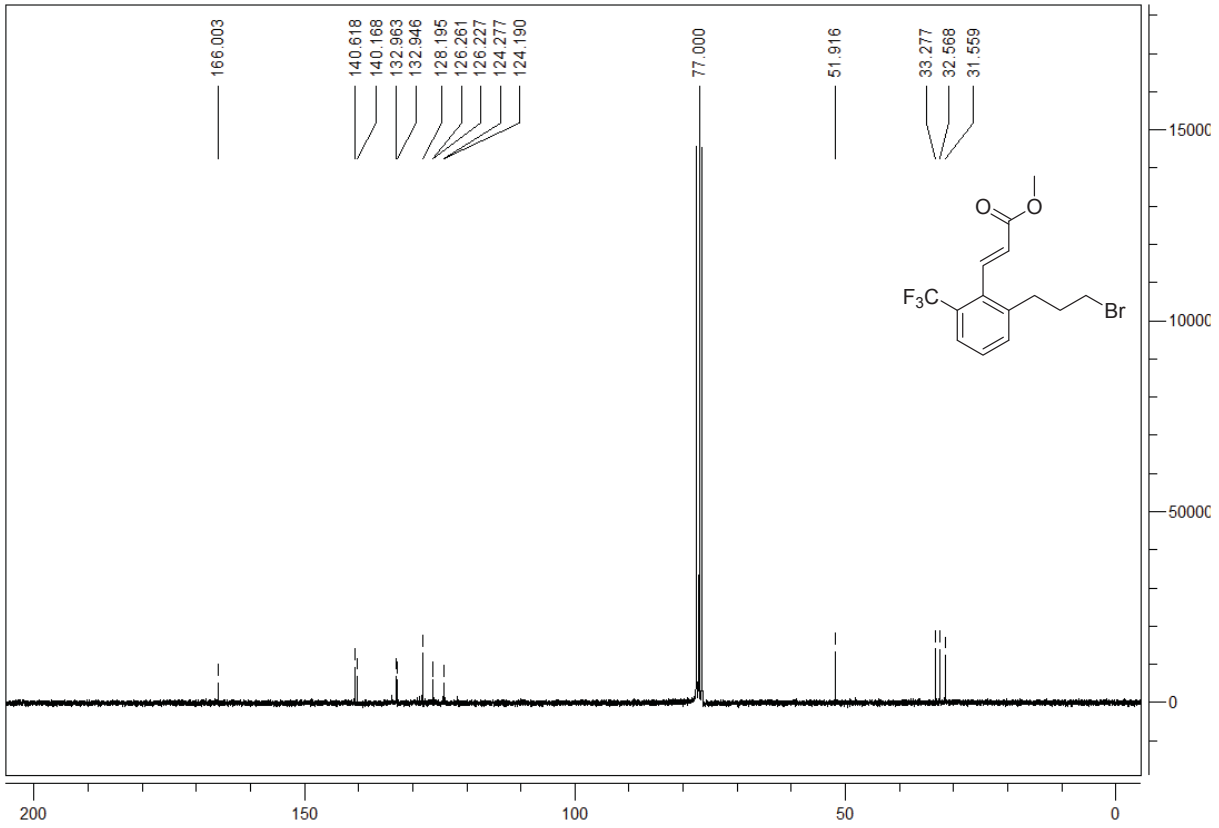
Methyl (2E)-3-[2-(3-bromopropyl)-6-methoxyphenyl]prop-2-enoate (**2c**)



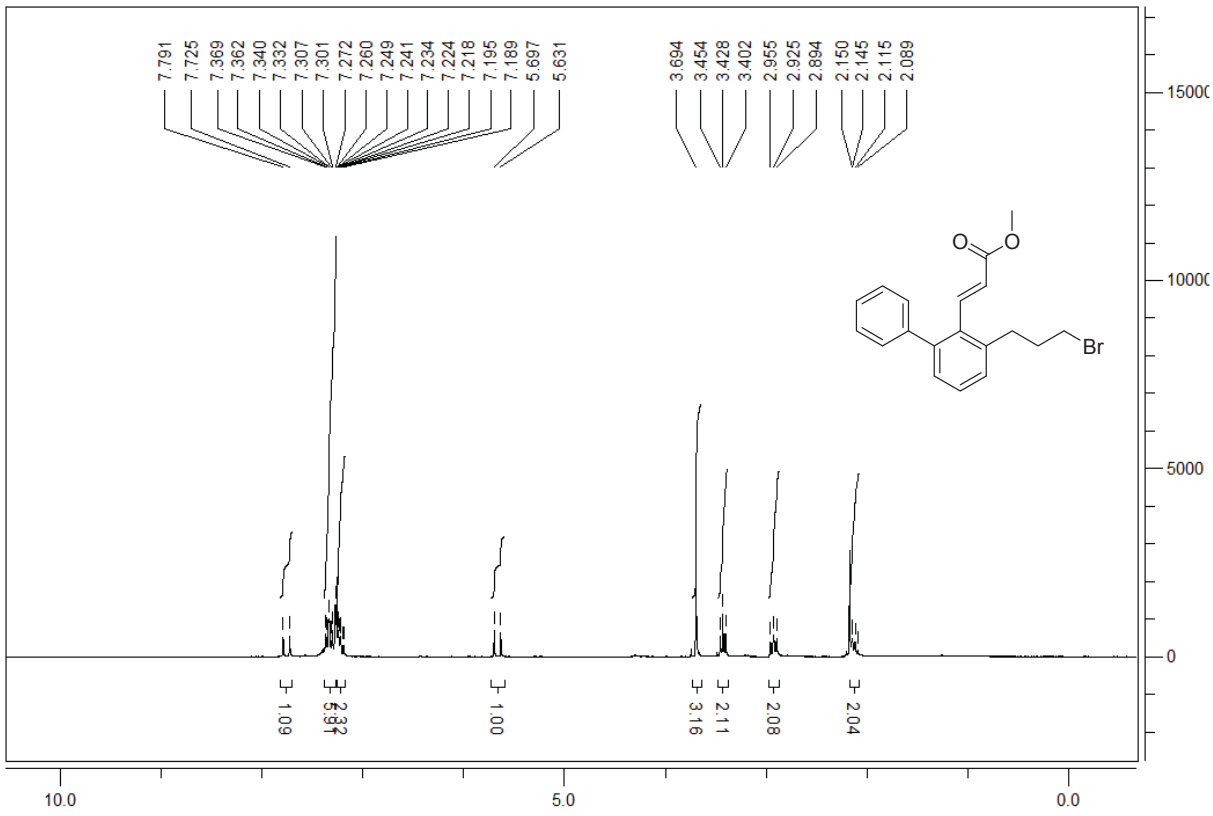


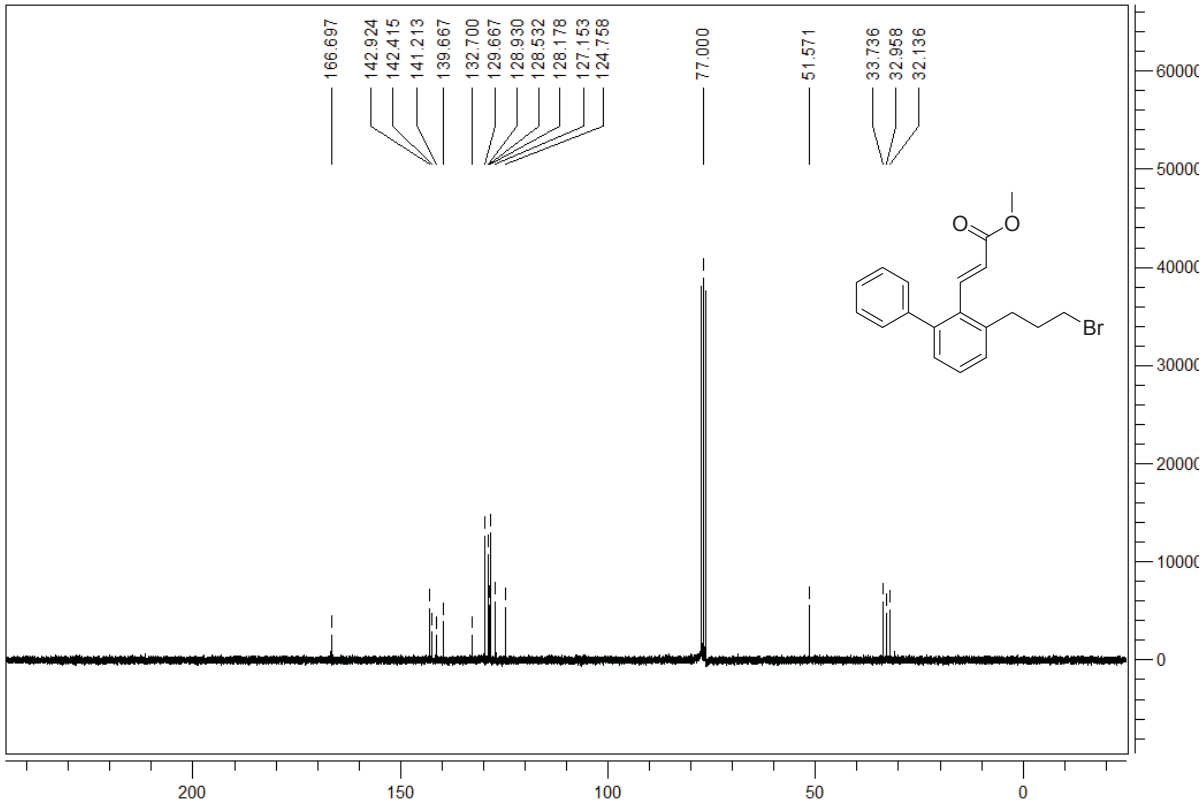
Methyl (2E)-3-[2-(3-bromopropyl)-6-(trifluoromethyl)phenyl]prop-2-enoate (**2d**)



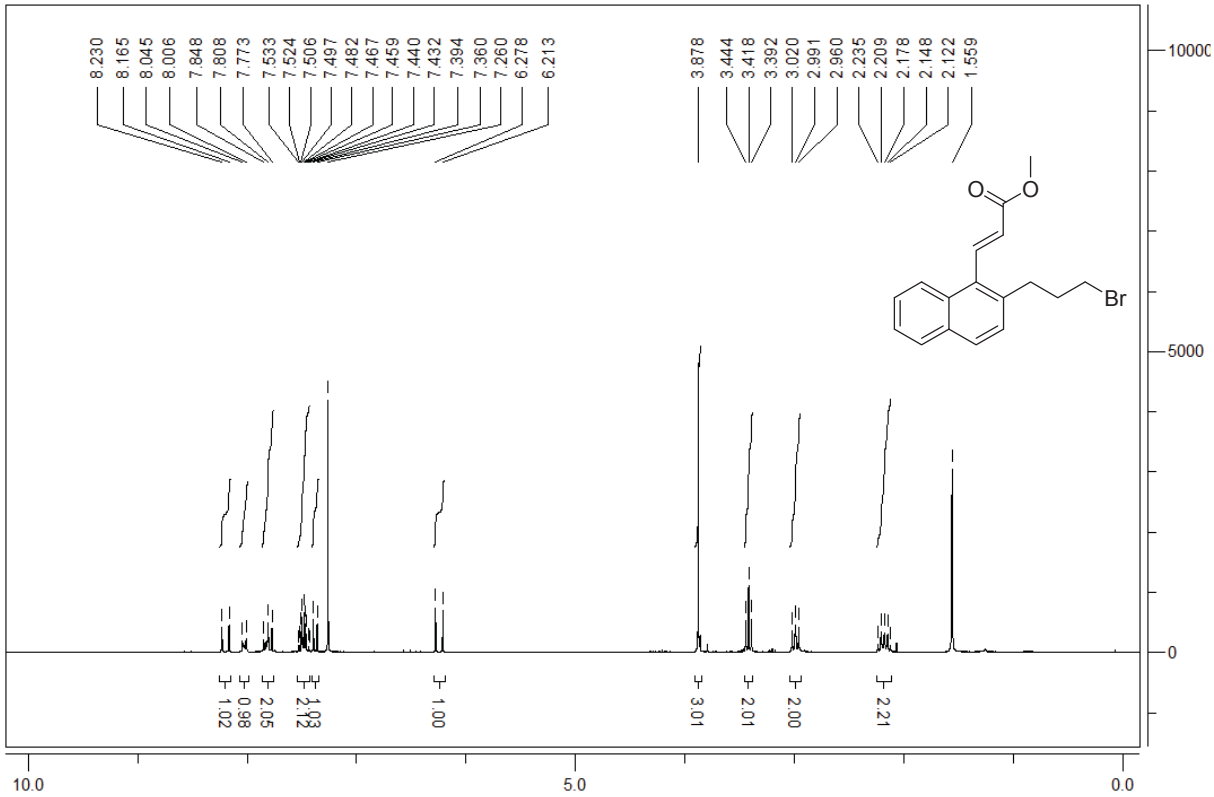


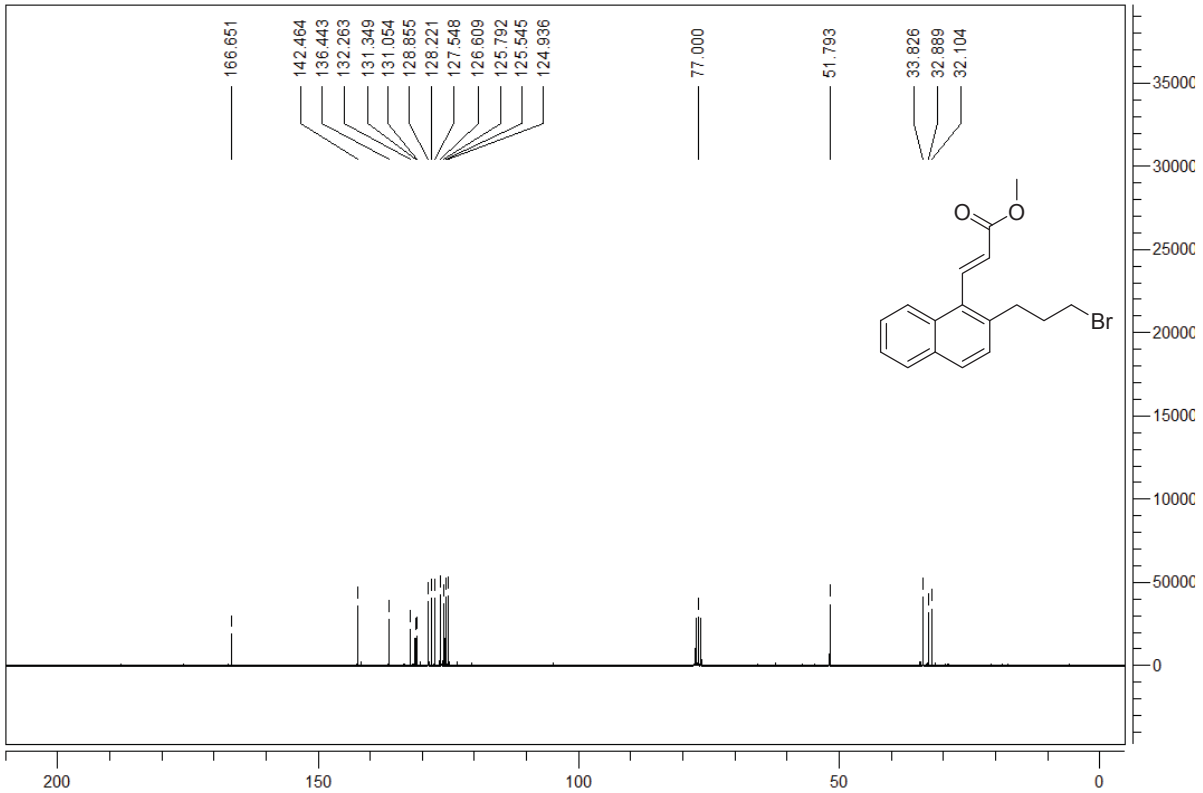
Methyl (2E)-3-[2-(3-bromopropyl)-6-phenylphenyl]prop-2-enoate (**2e**)



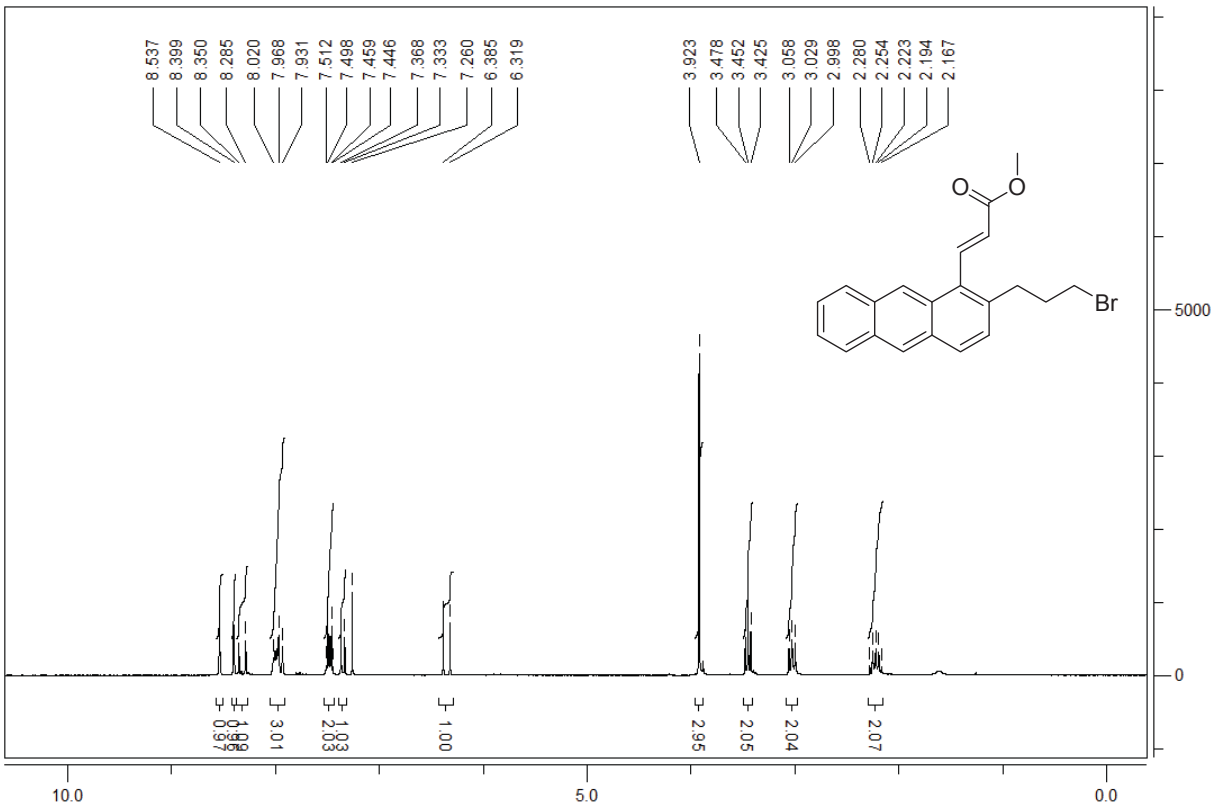


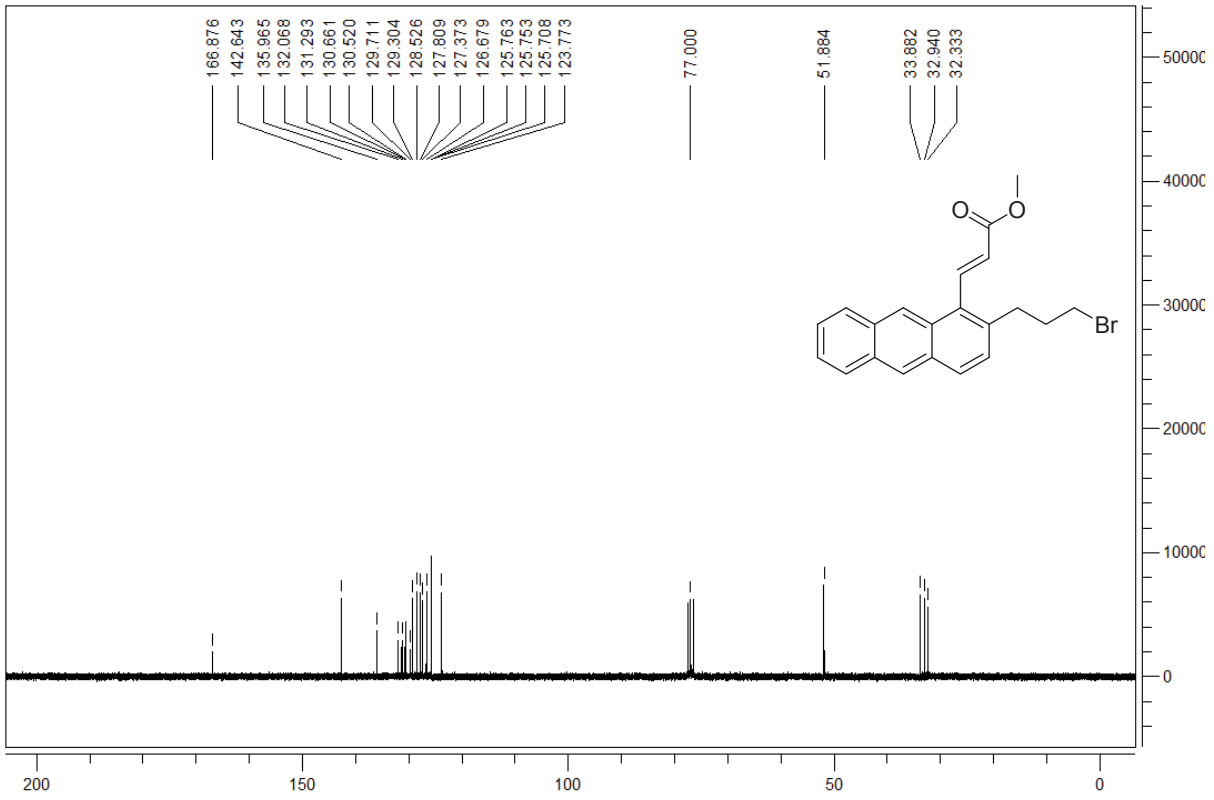
Methyl (2E)-3-[2-(3-bromopropyl)naphthalen-1-yl]prop-2-enoate (**2f**)



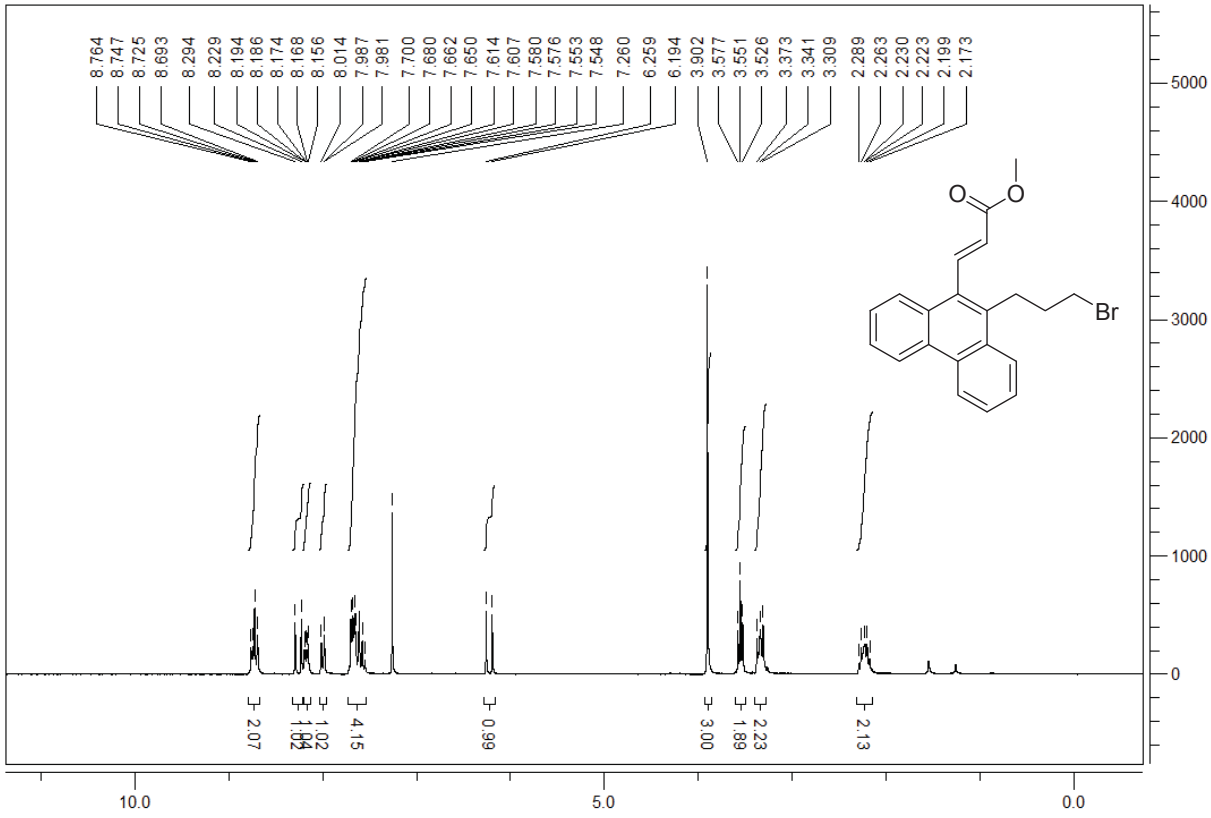


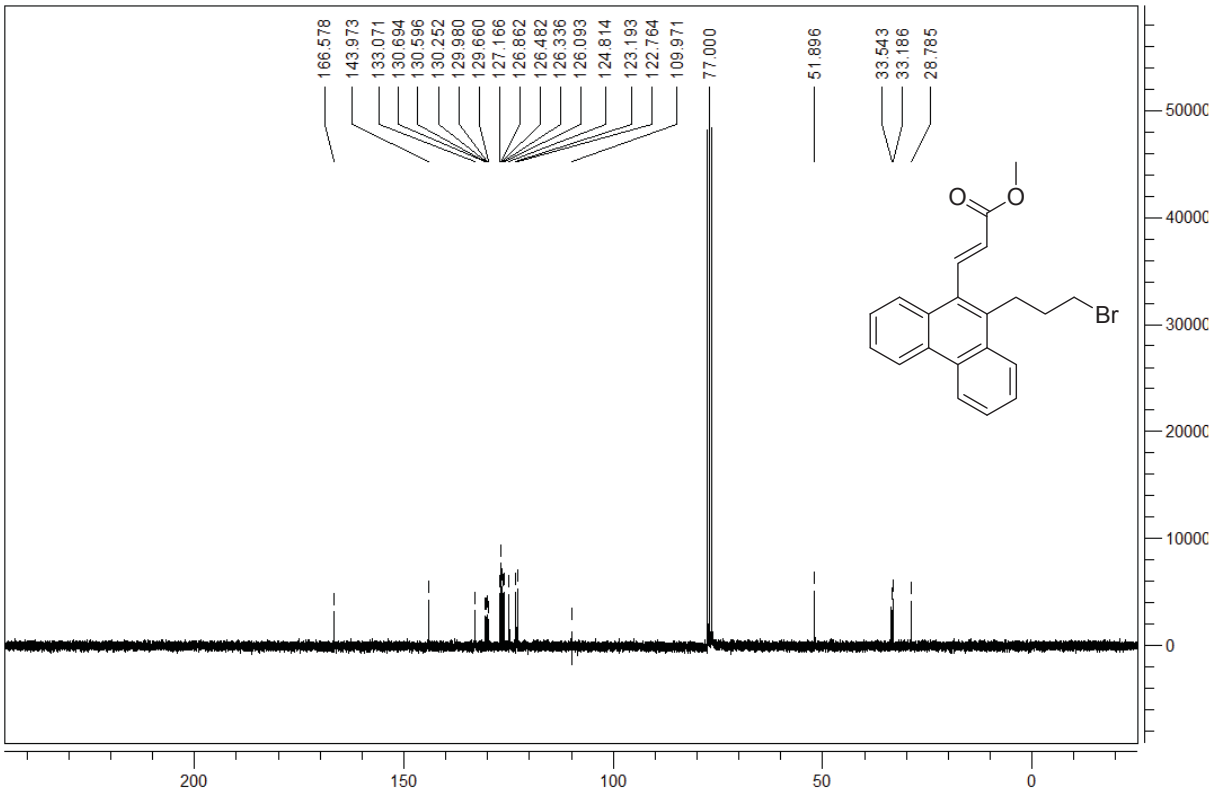
Methyl (2E)-3-[2-(3-bromopropyl)anthracen-1-yl]prop-2-enoate (**2g**)



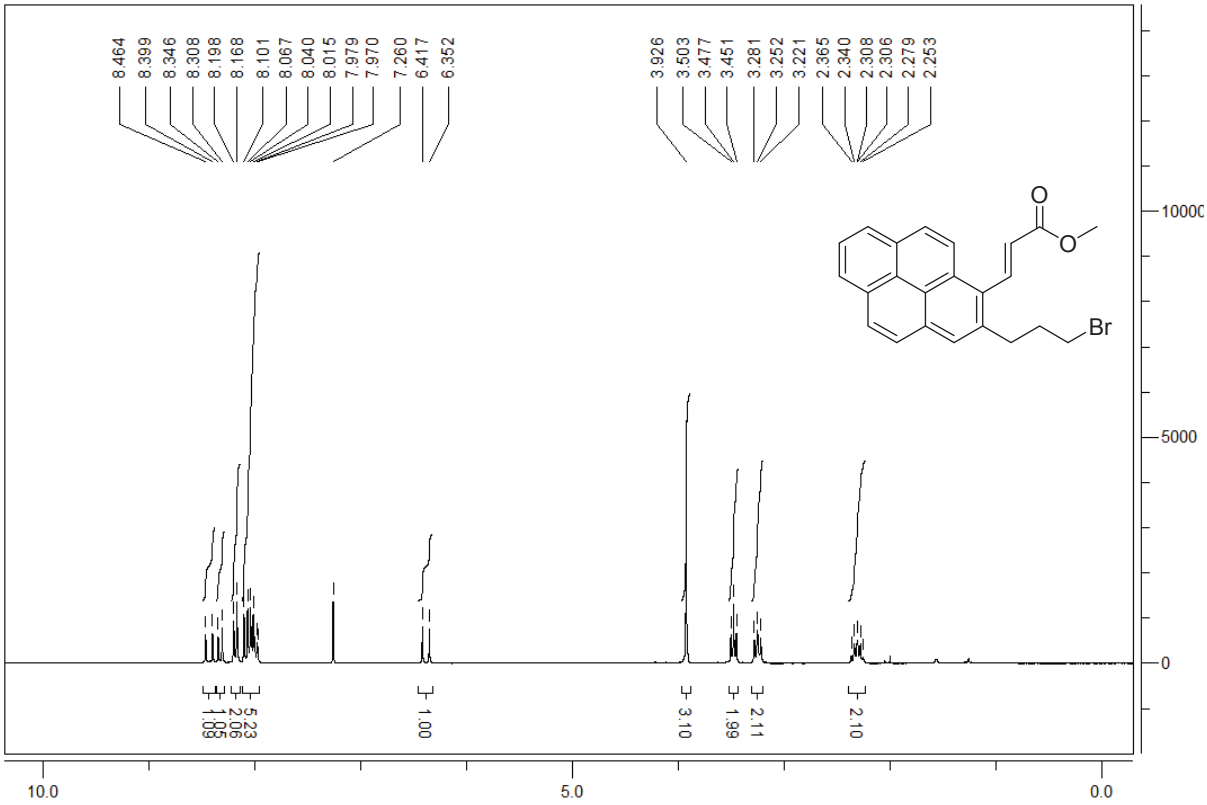


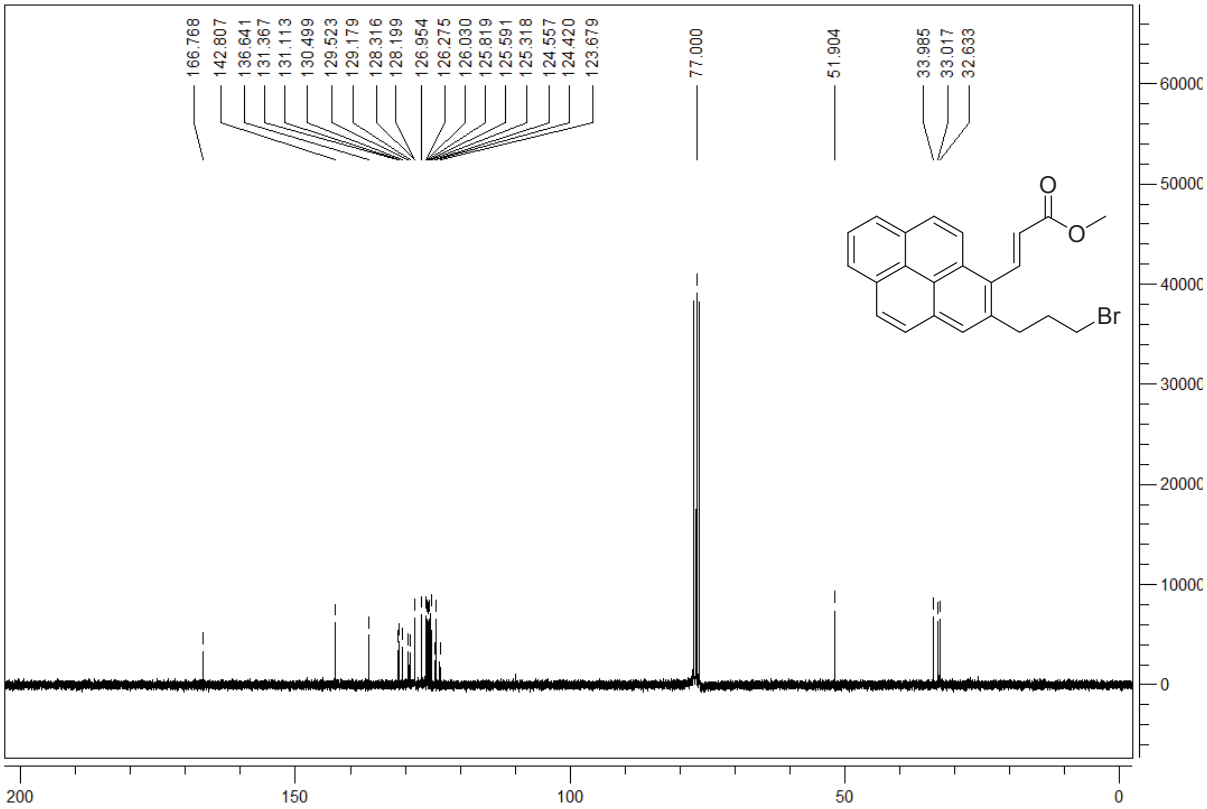
Methyl (2E)-3-[10-(3-bromopropyl)phenanthren-9-yl]prop-2-enoate (**2h**)



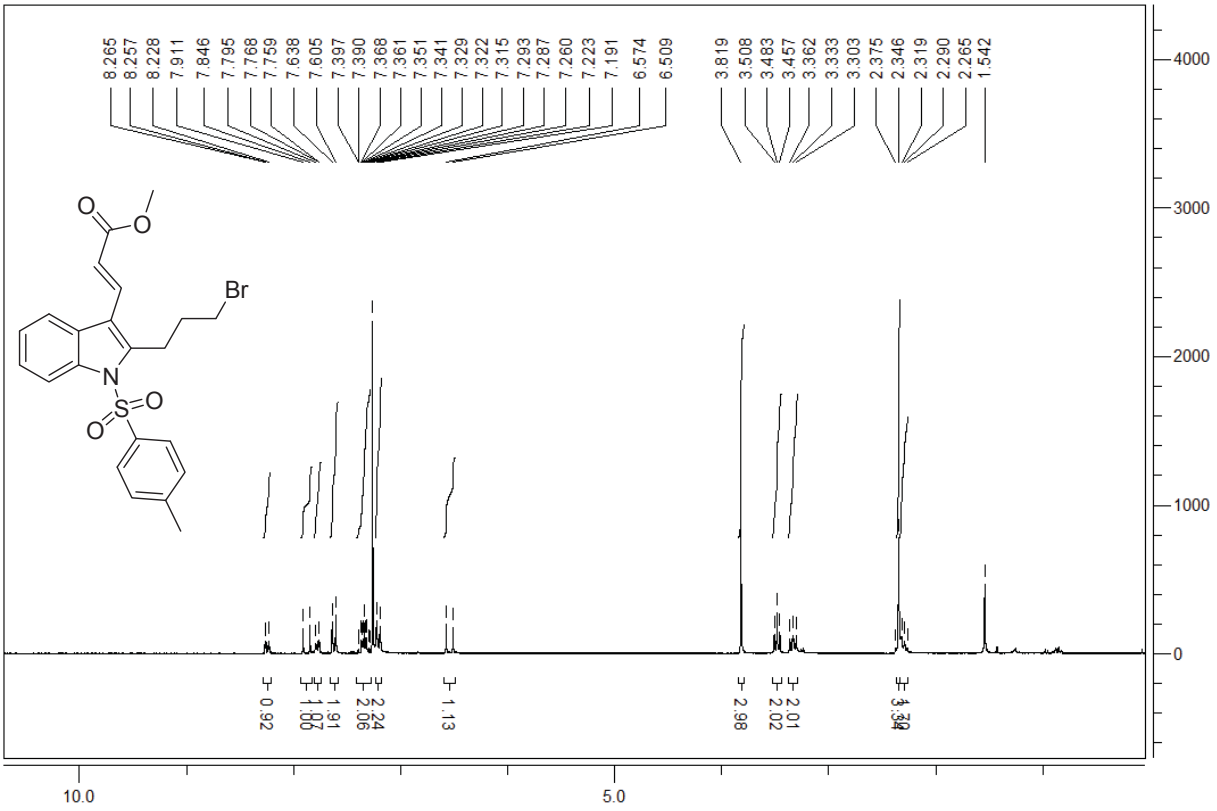


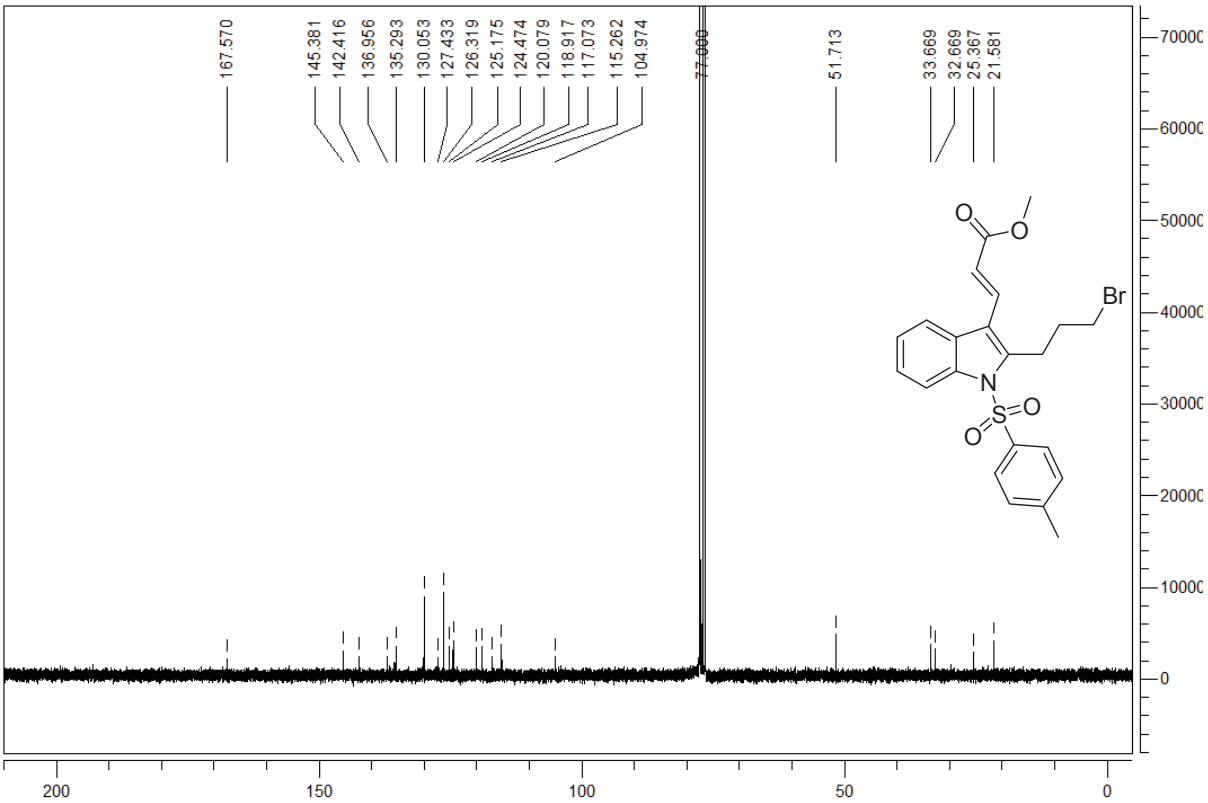
Methyl (2E)-3-[2-(3-bromopropyl)pyren-1-yl]prop-2-enoate (**2i**)



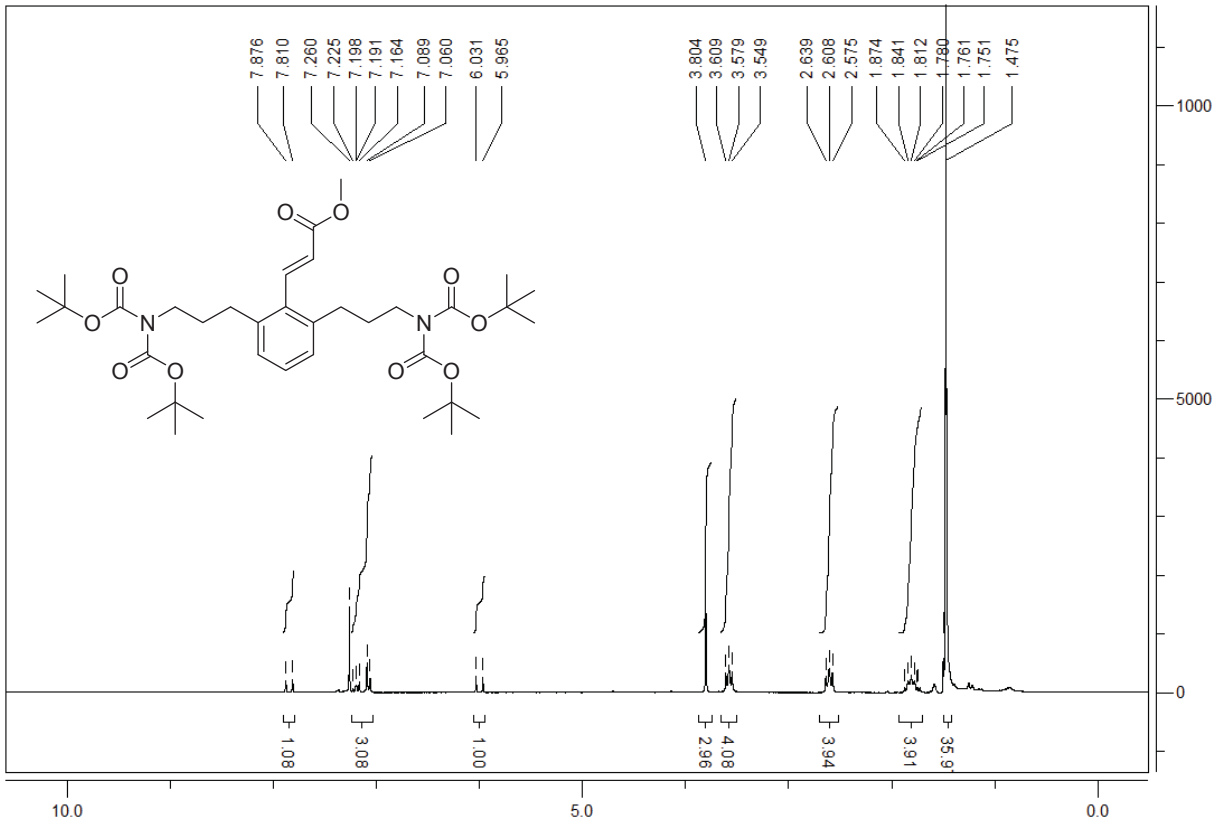


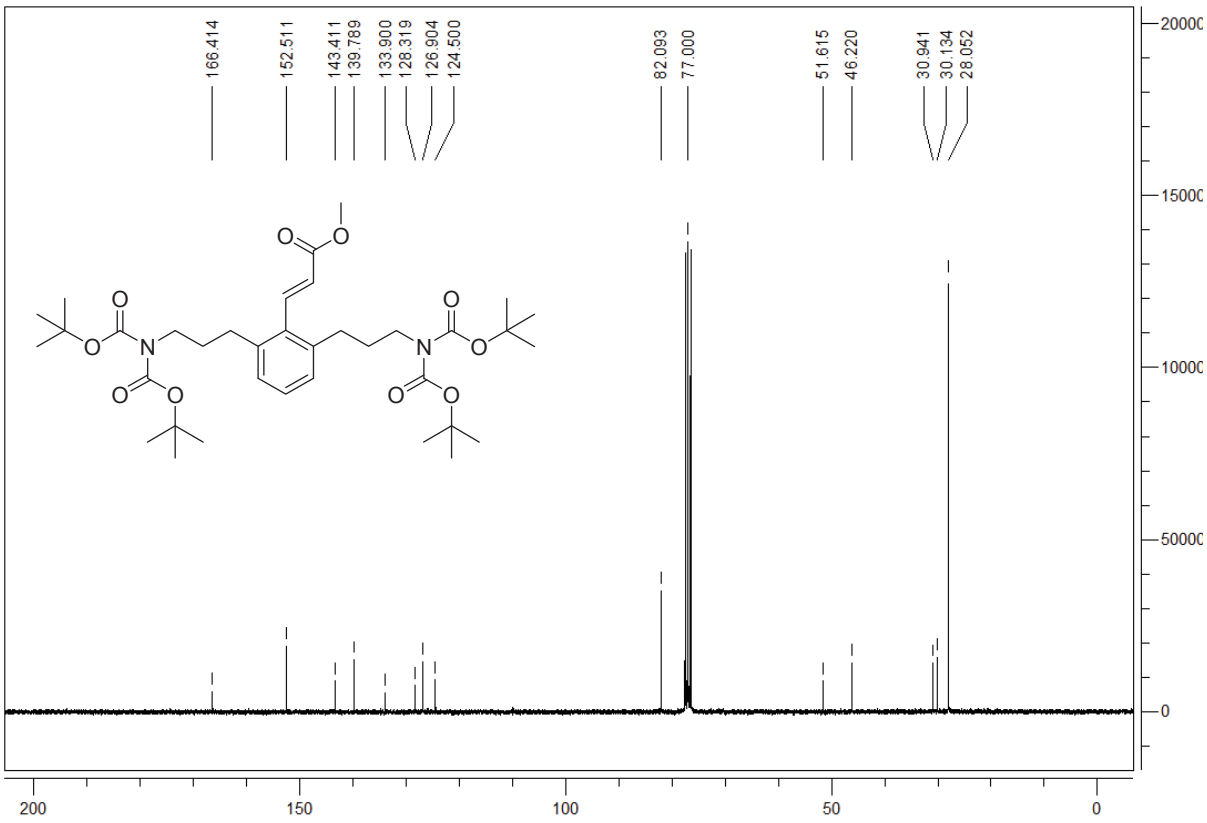
Methyl (2E)-3-[2-(3-bromopropyl)-1-[(4-methylbenzene)sulfonyl]-1H-indol-3-yl]prop-2-enoate (**2j**)



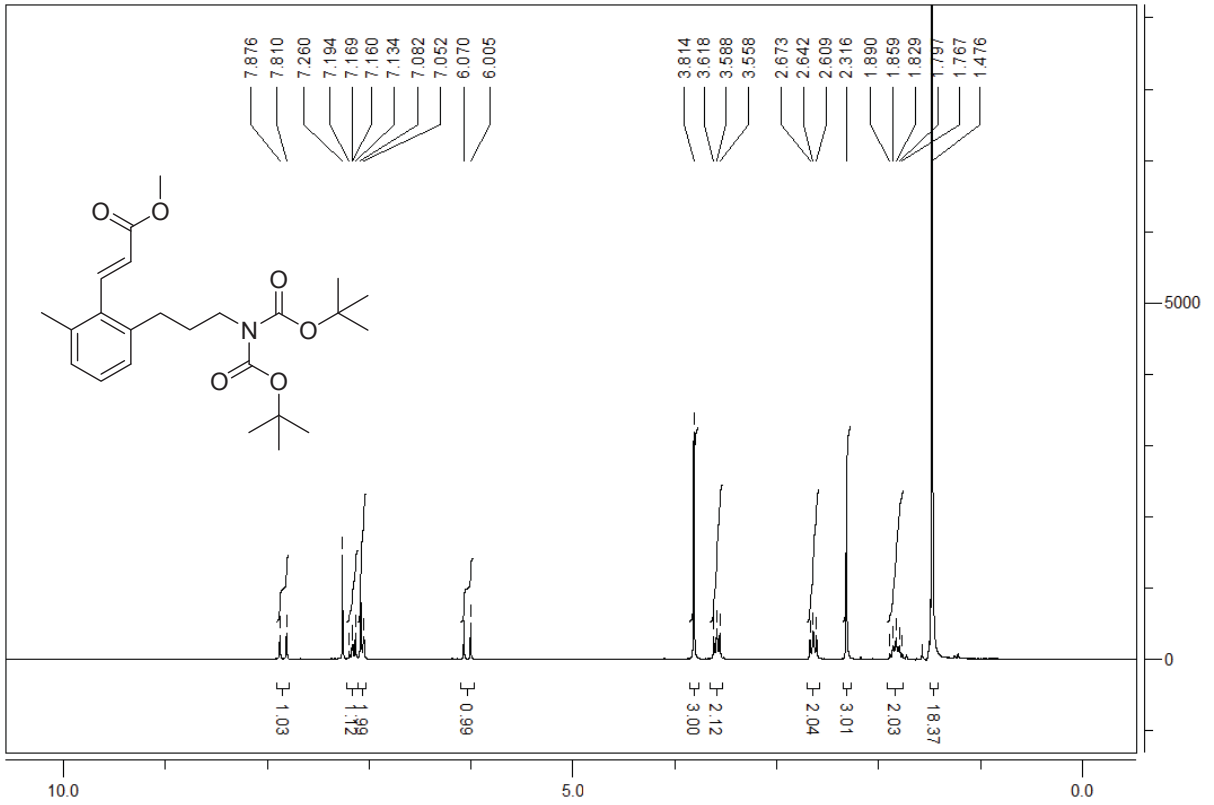


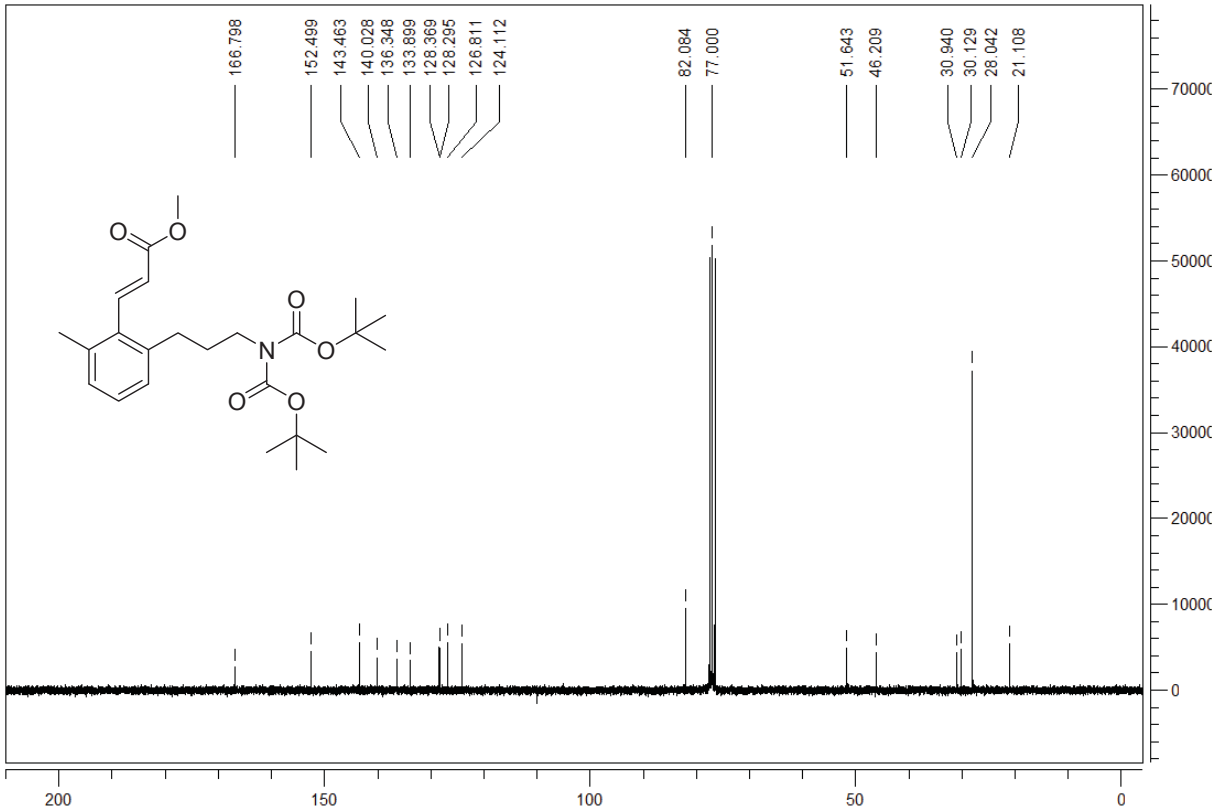
Methyl (2E)-3-[2,6-*bis*(3-{*bis*[(*tert*-butoxy)carbonyl]amino}propyl)phenyl]prop-2-enoate (**3a**)



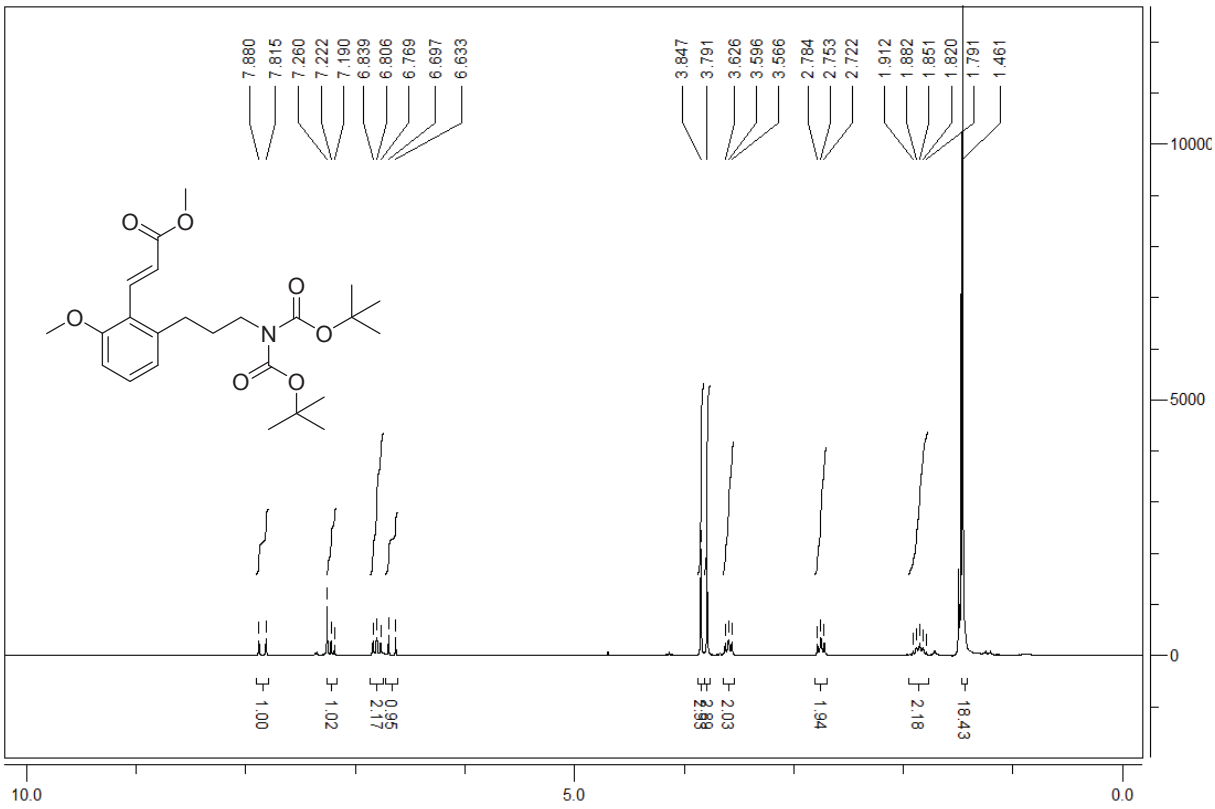


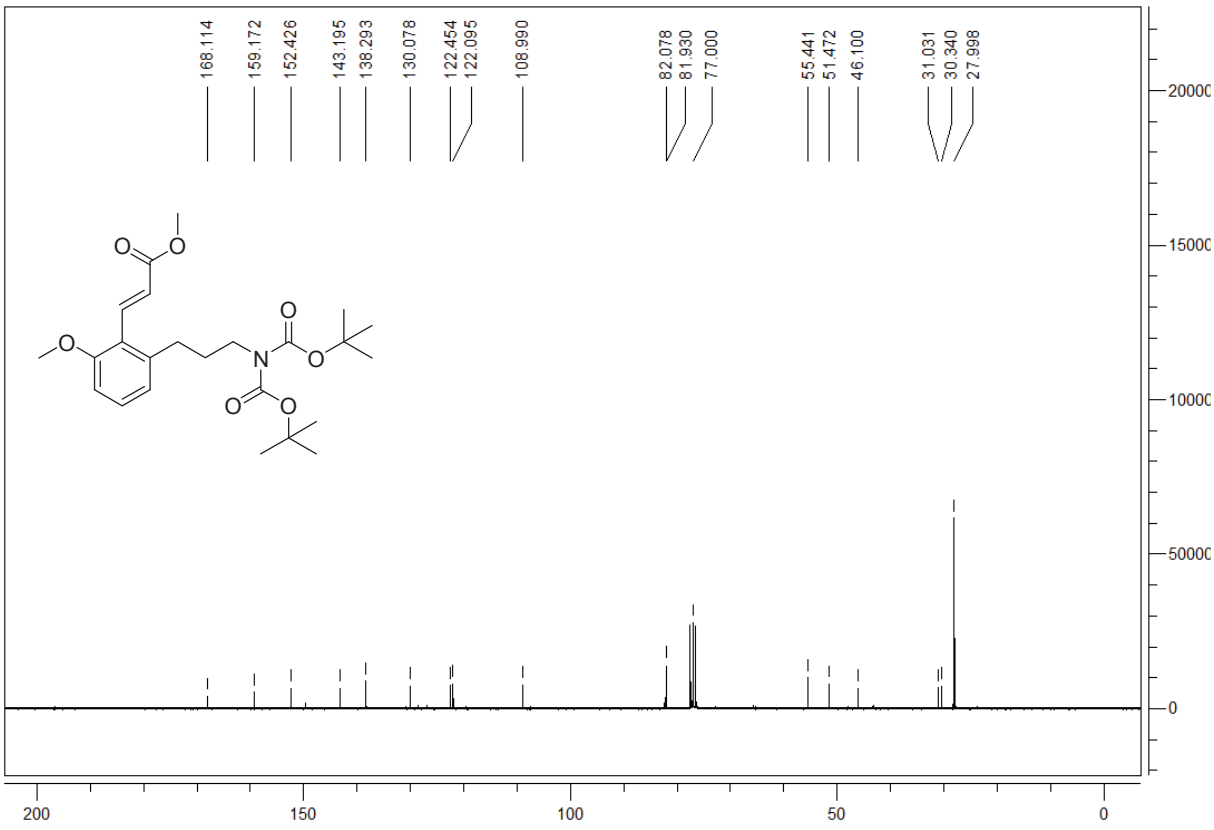
Methyl (2E)-3-[2-(3-{*bis*[(*tert*-butoxy)carbonyl]amino}propyl)-6-methylphenyl]prop-2-enoate (**3b**)



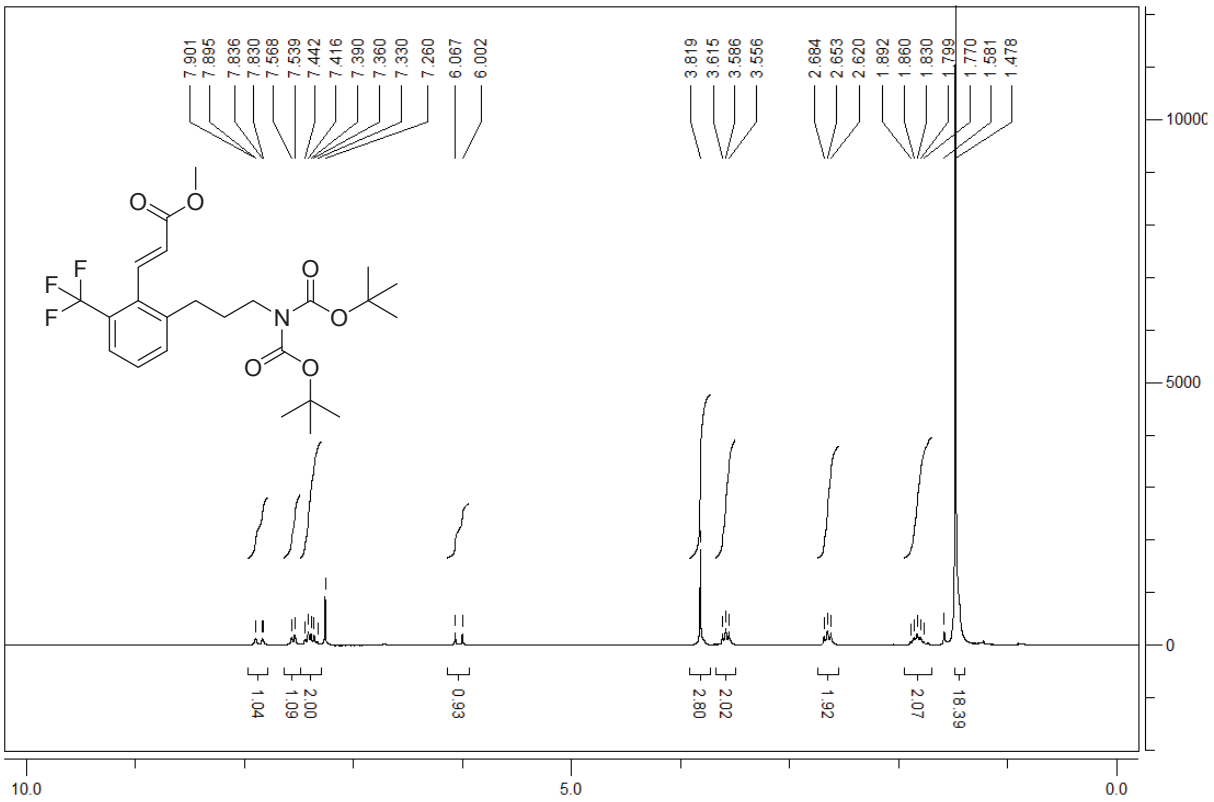


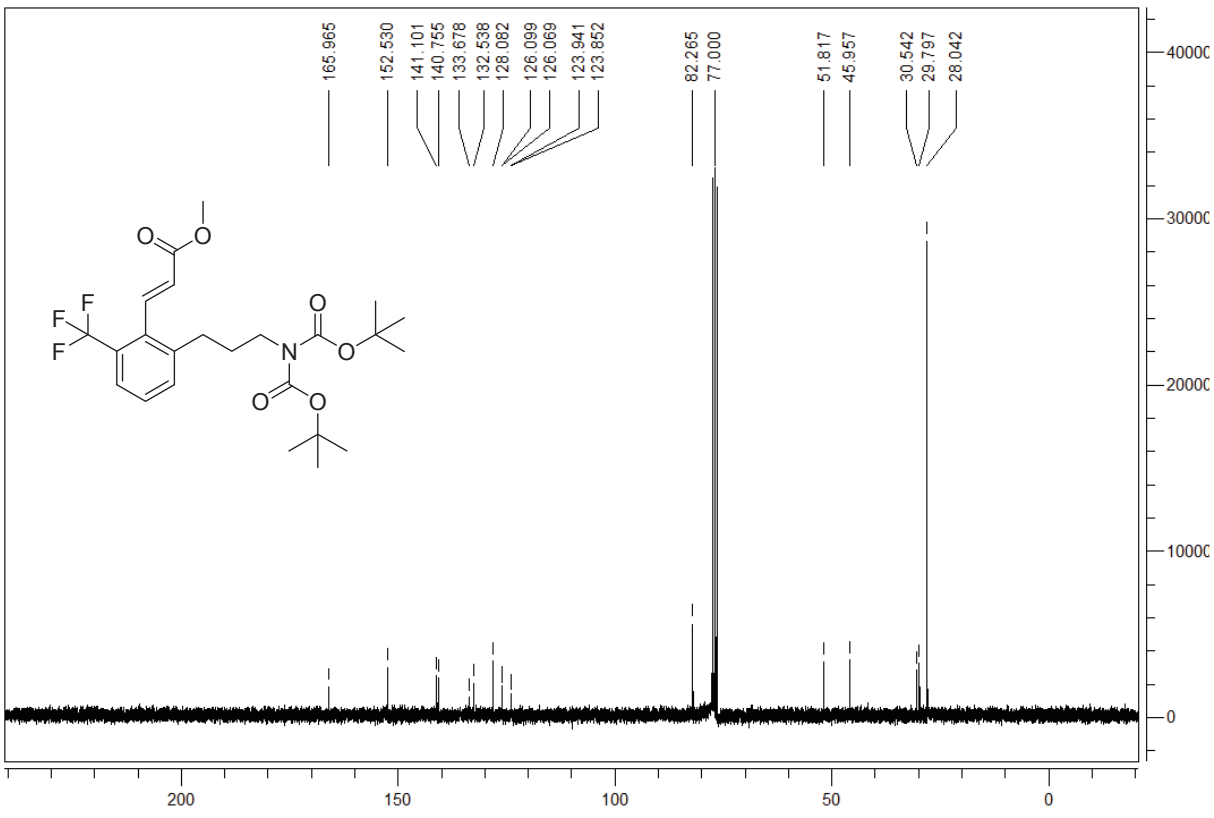
Methyl (2E)-3-[2-(3-{*bis*[(*tert*-butoxy)carbonyl]amino}propyl)-6-methoxyphenyl]prop-2-enoate (**3c**)



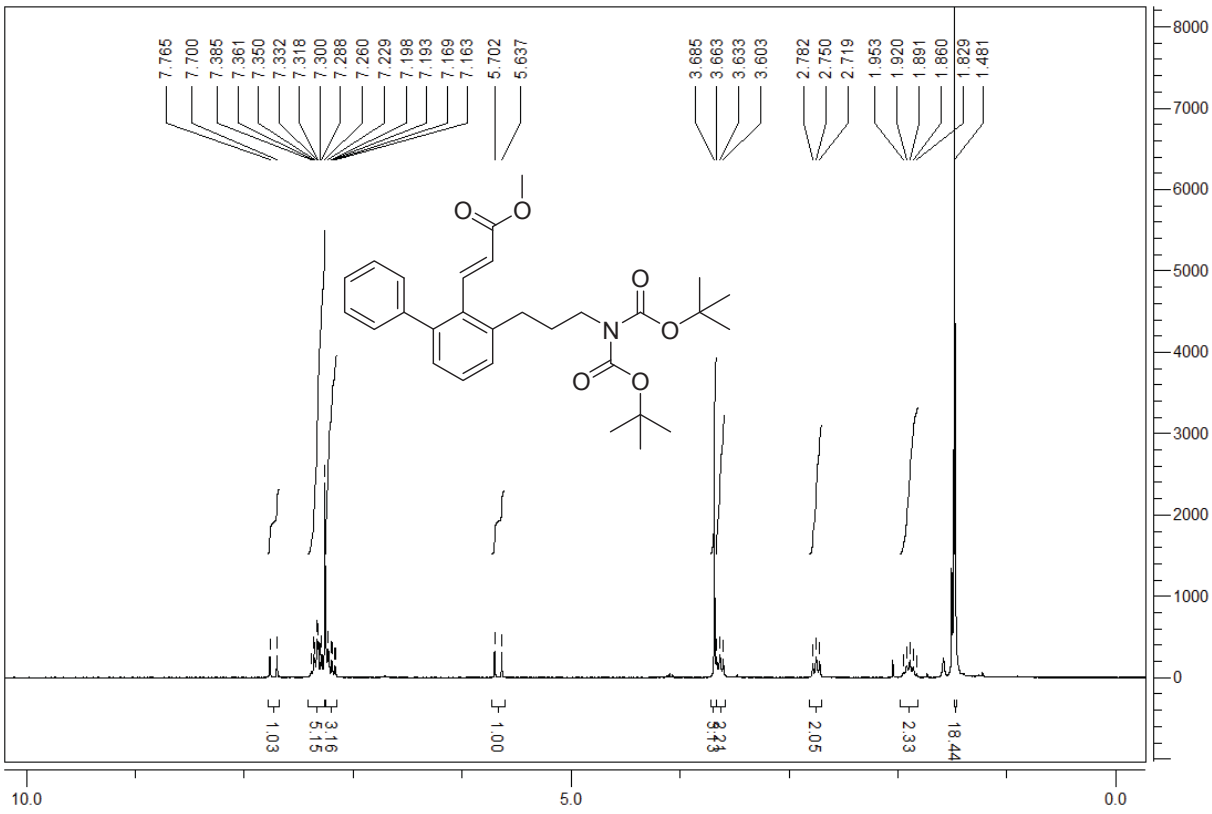


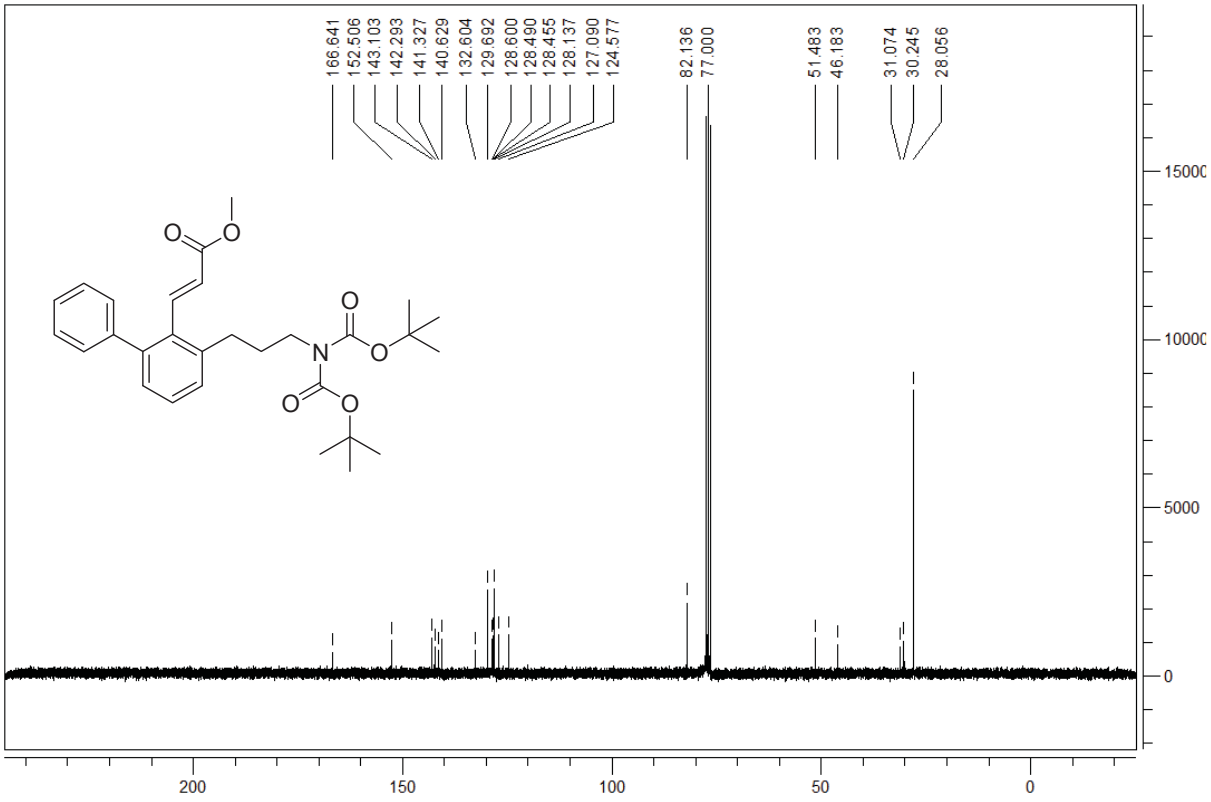
Methyl (2E)-3-[2-(3-{*bis*[(*tert*-butoxy)carbonyl]amino}propyl)-6-(trifluoromethyl)phenyl]prop-2-enoate (**3d**)



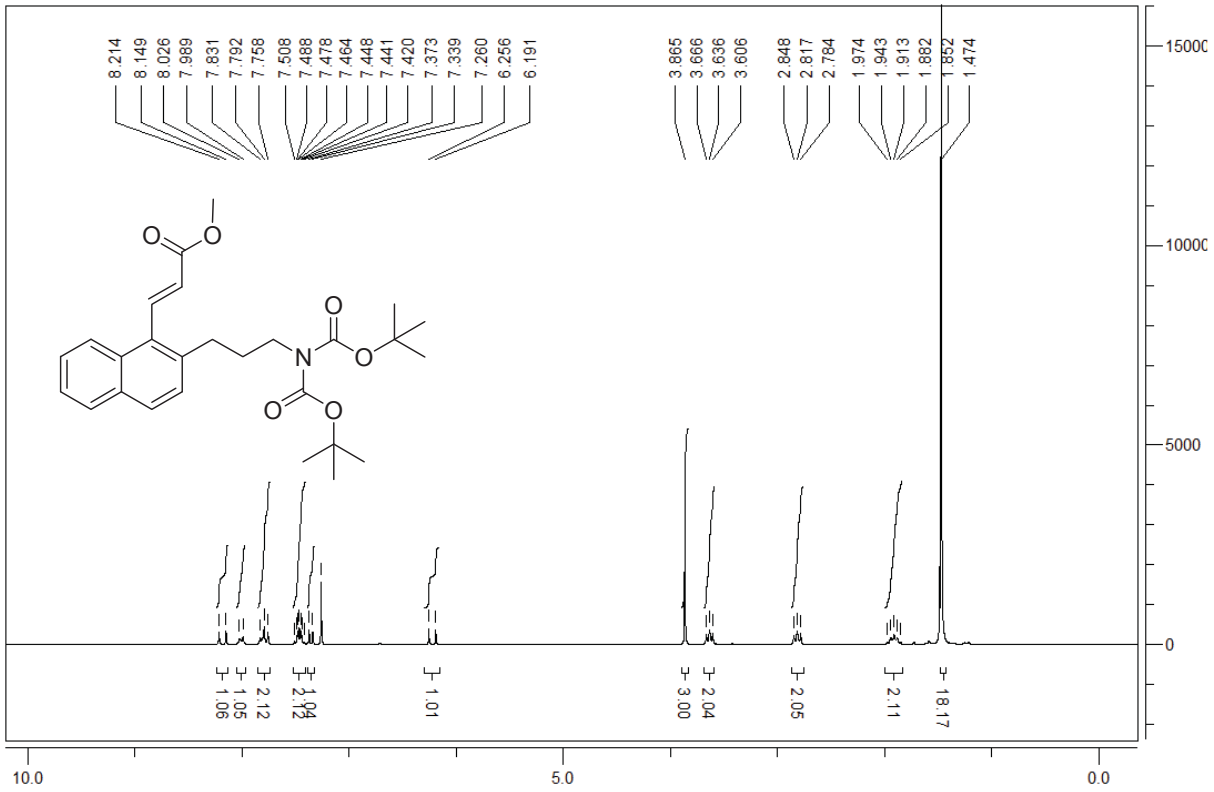


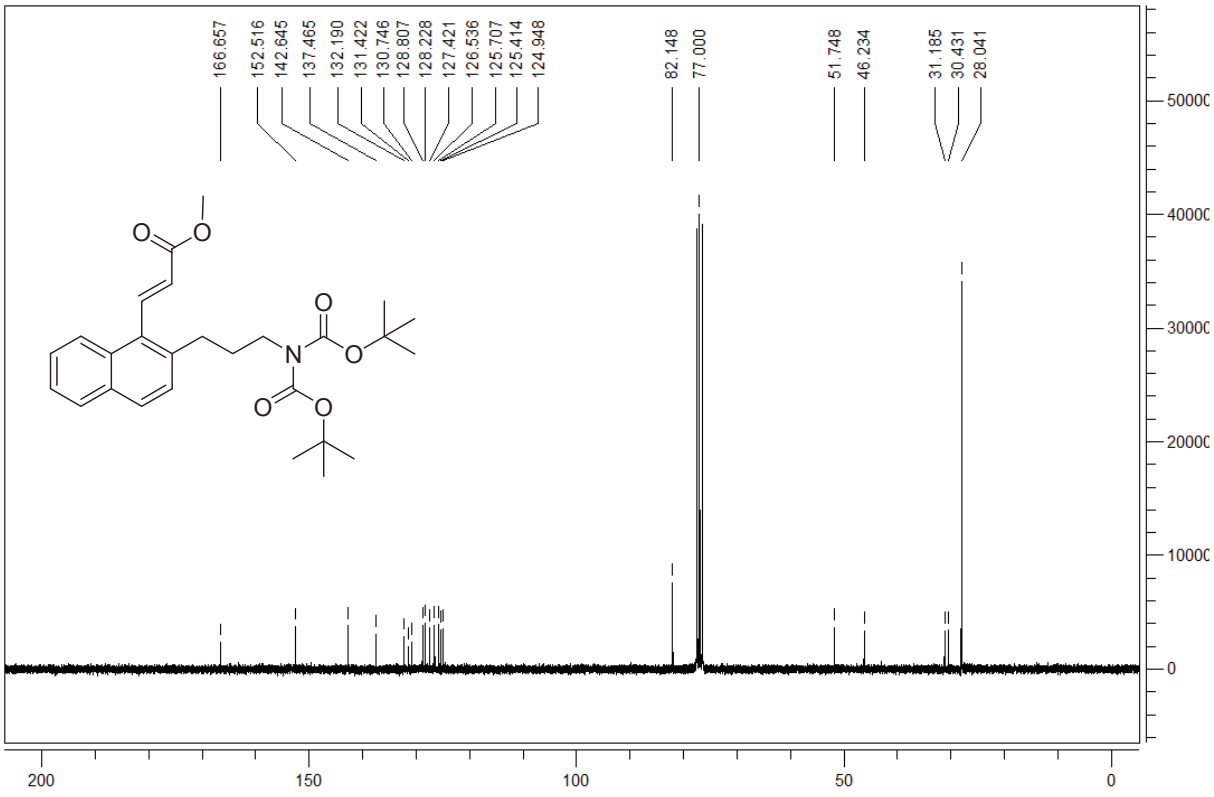
Methyl (2E)-3-[2-(3-{*bis*[(*tert*-butoxy)carbonyl]amino}propyl)-6-phenylphenyl]prop-2-enoate (**3e**)



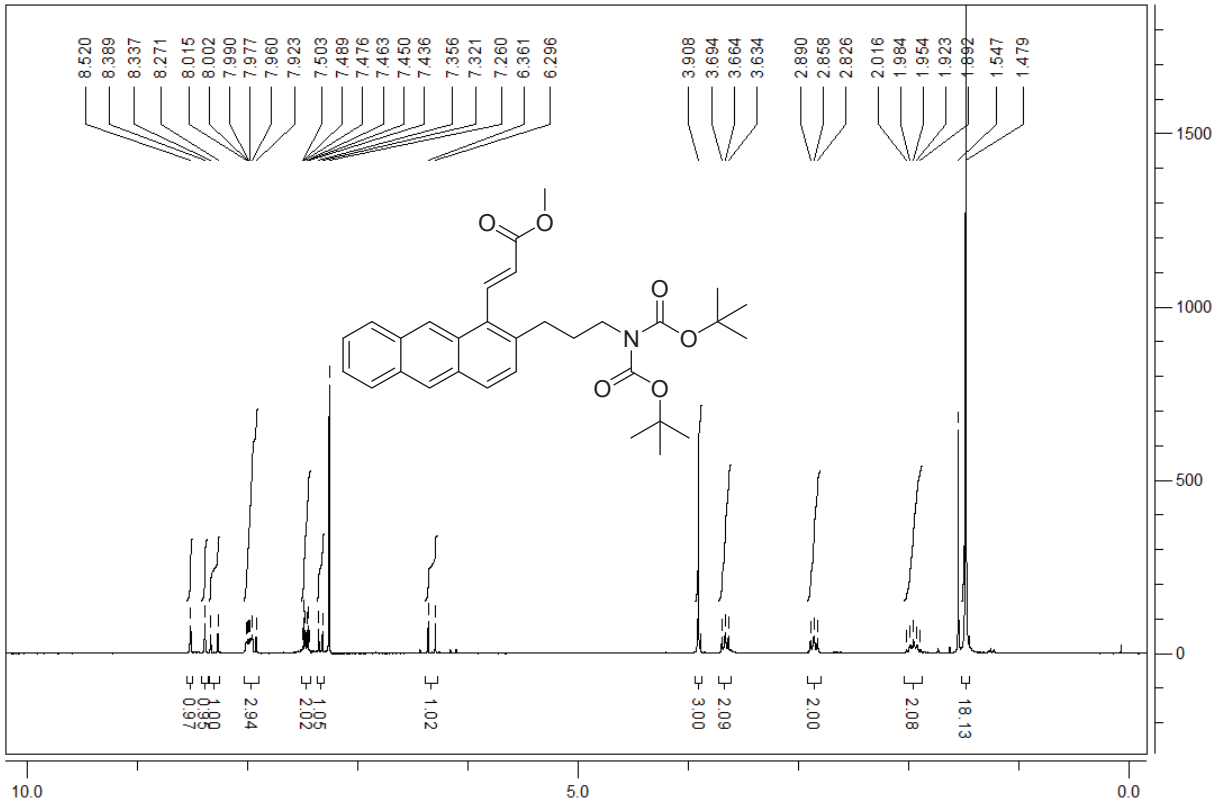


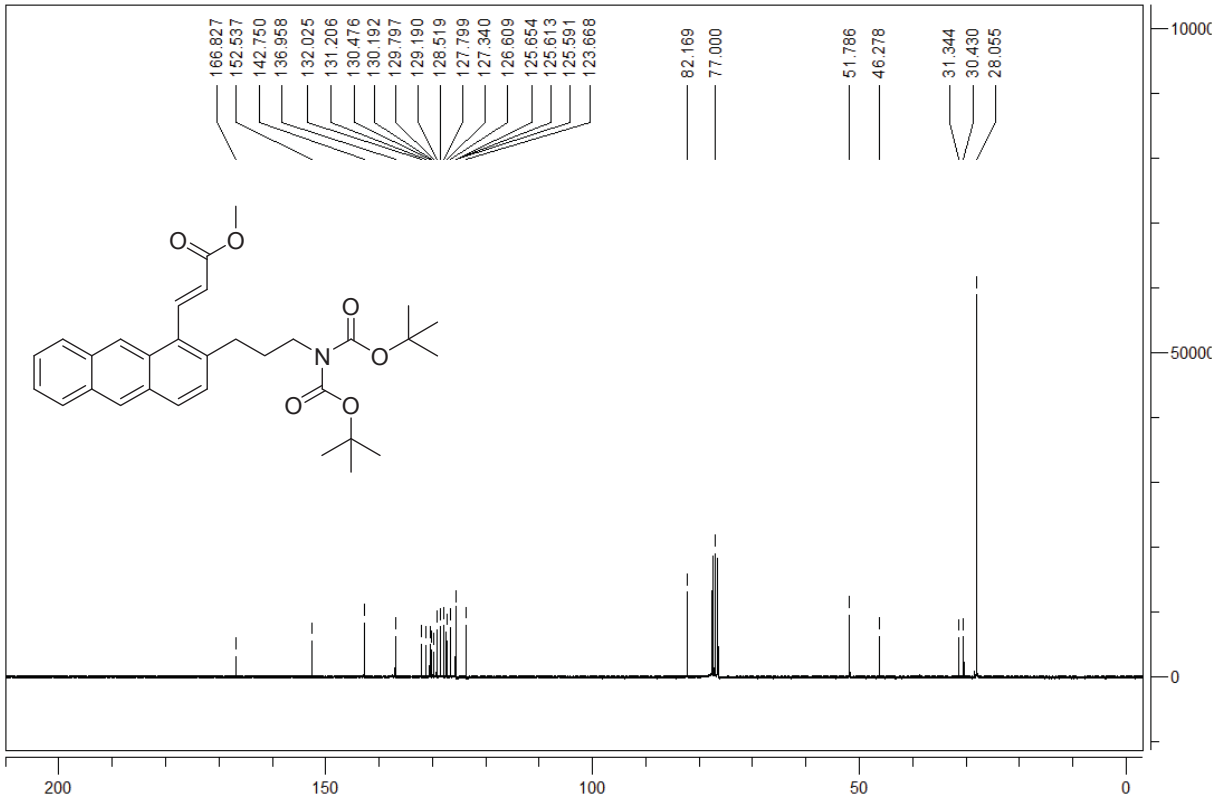
Methyl (2E)-3-[2-(3-{*bis*[(*tert*-butoxy)carbonyl]amino}propyl)naphthalen-1-yl]prop-2-enoate (**3f**)



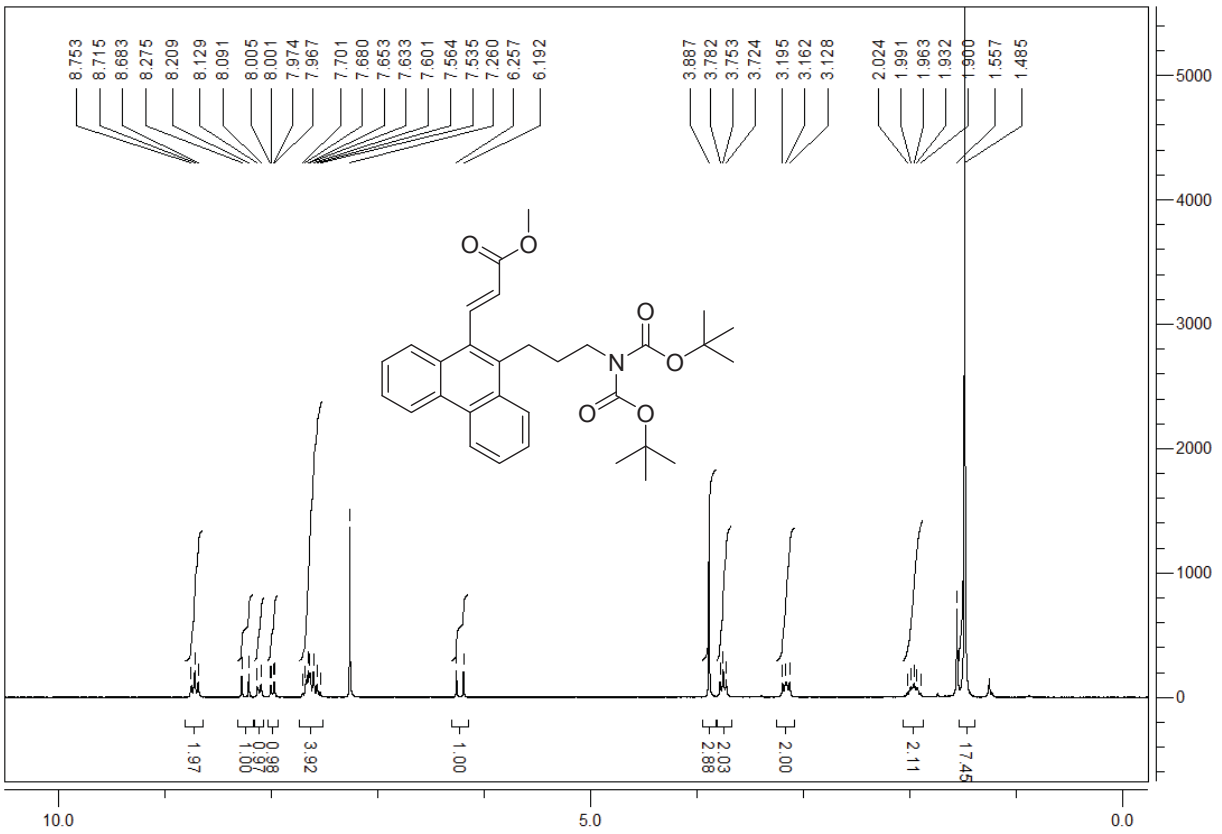


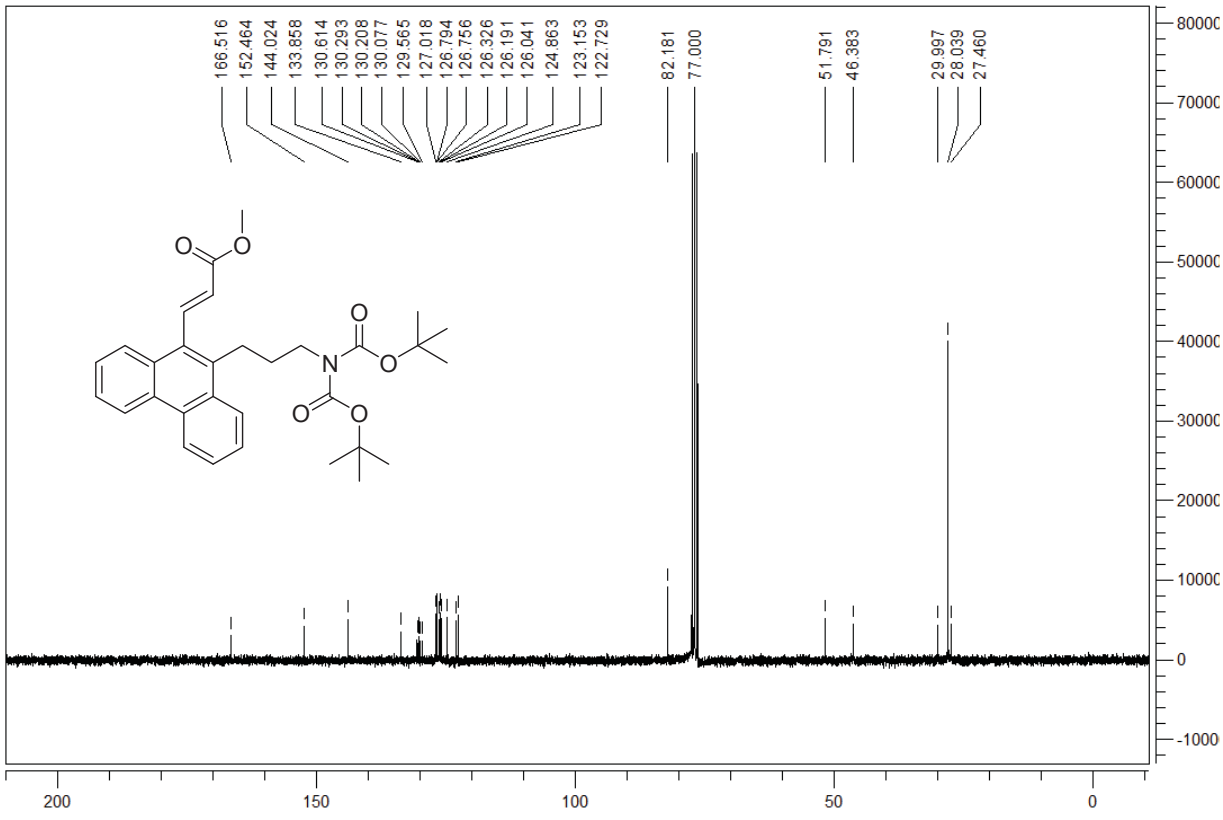
Methyl (2E)-3-[2-(3-{*bis*[(*tert*-butoxy)carbonyl]amino}propyl)anthracen-1-yl]prop-2-enoate (**3g**)



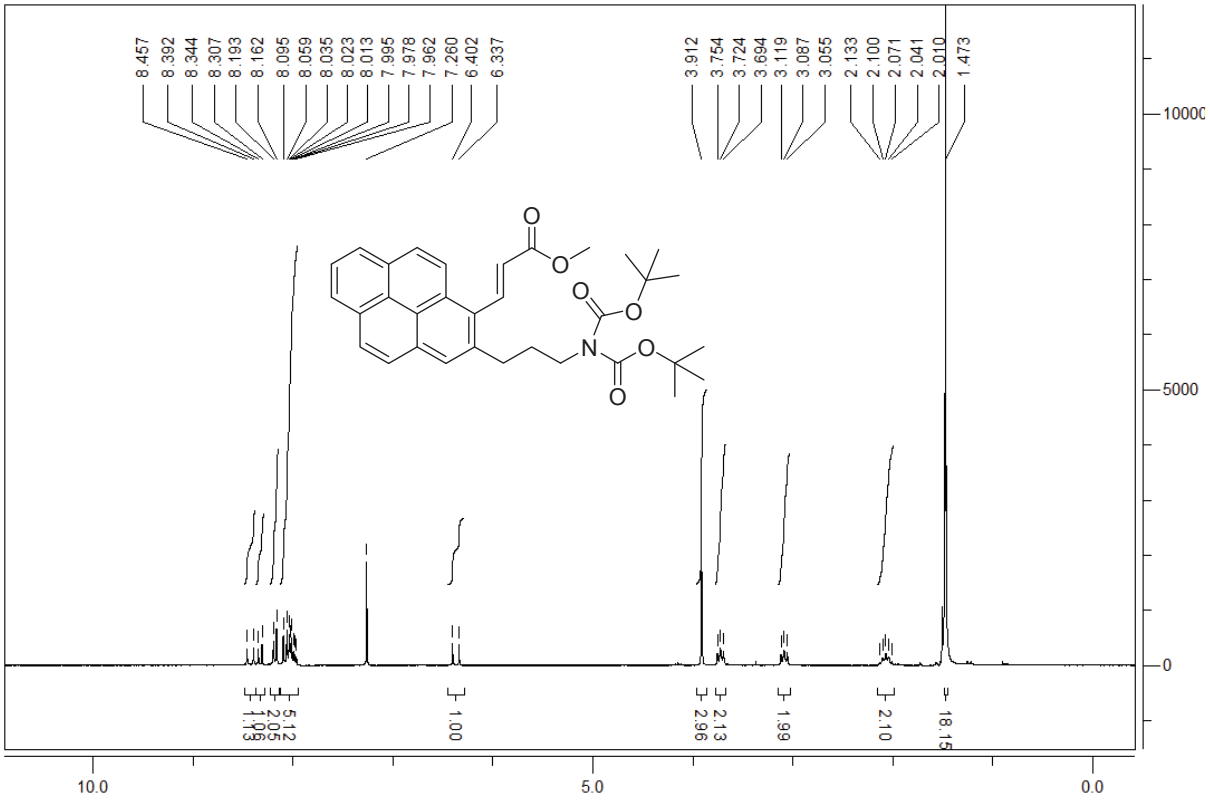


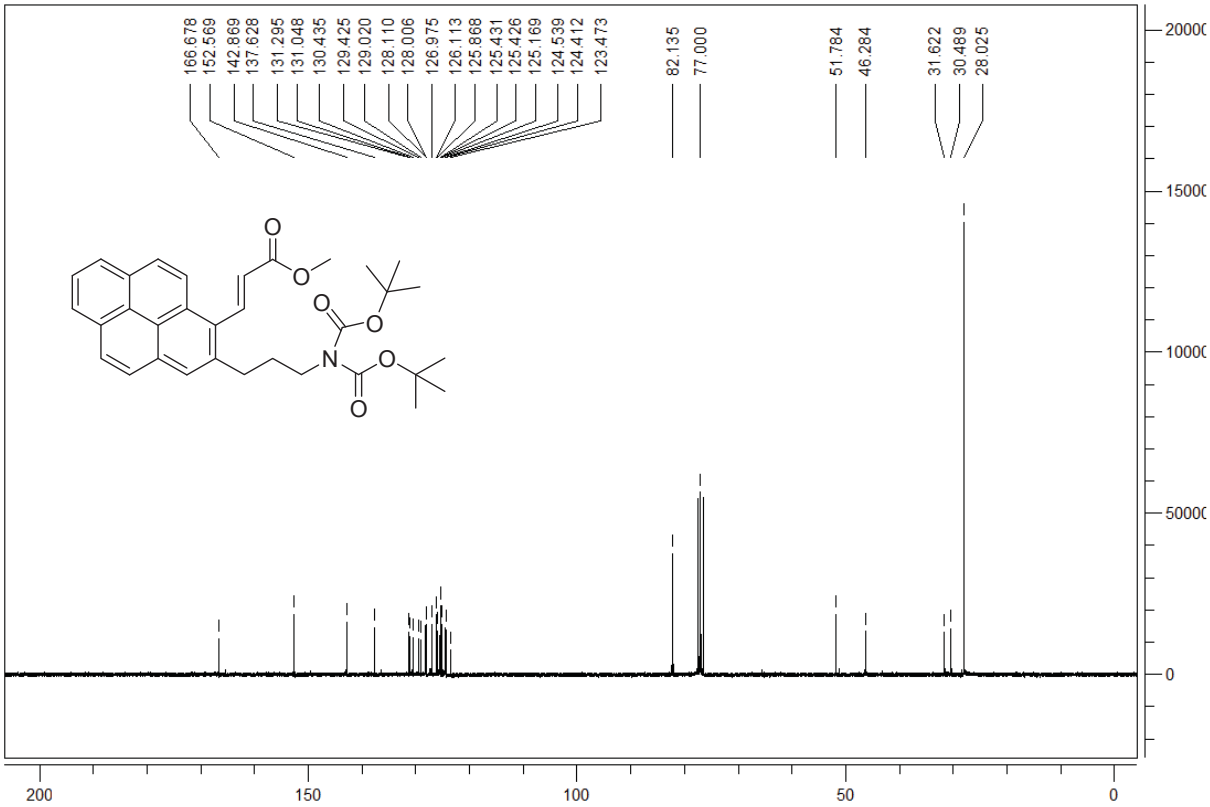
Methyl (2E)-3-[10-(3-{*bis*[(*tert*-butoxy)carbonyl]amino}propyl) phenanthren-9-yl]prop-2-enoate (**3h**)



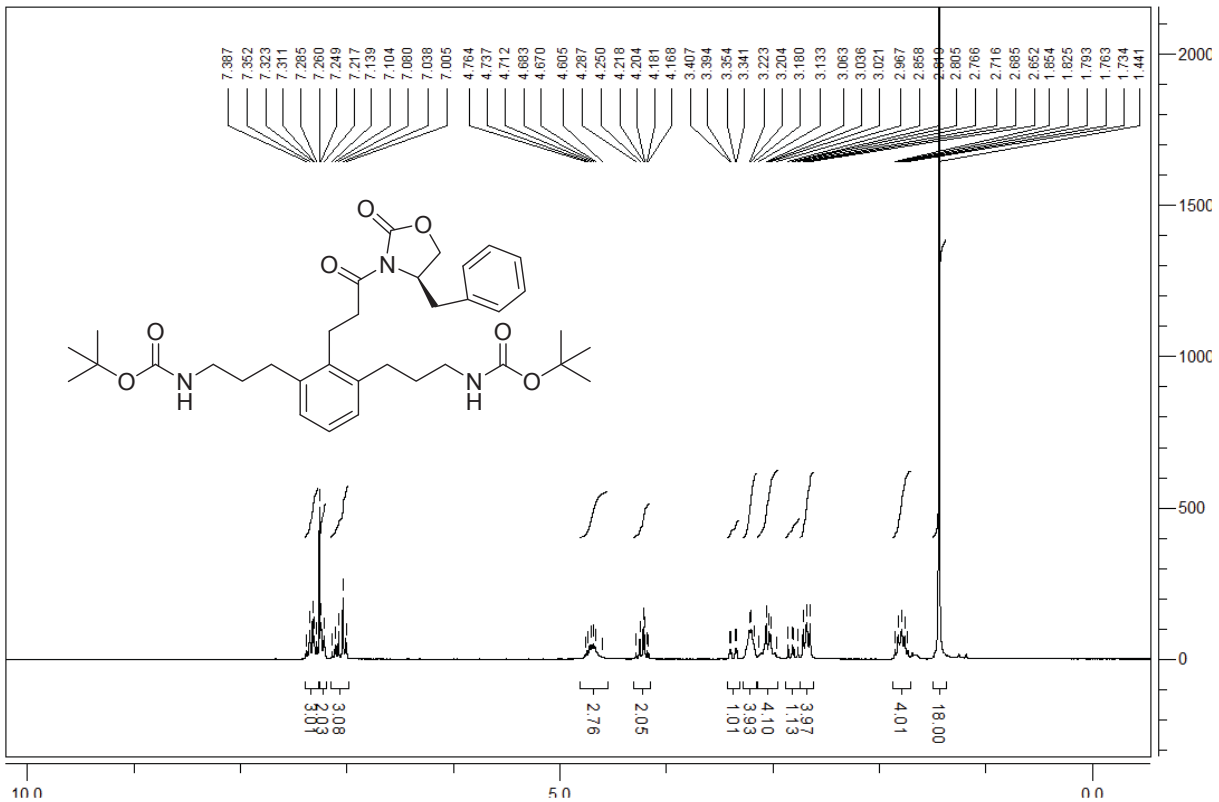


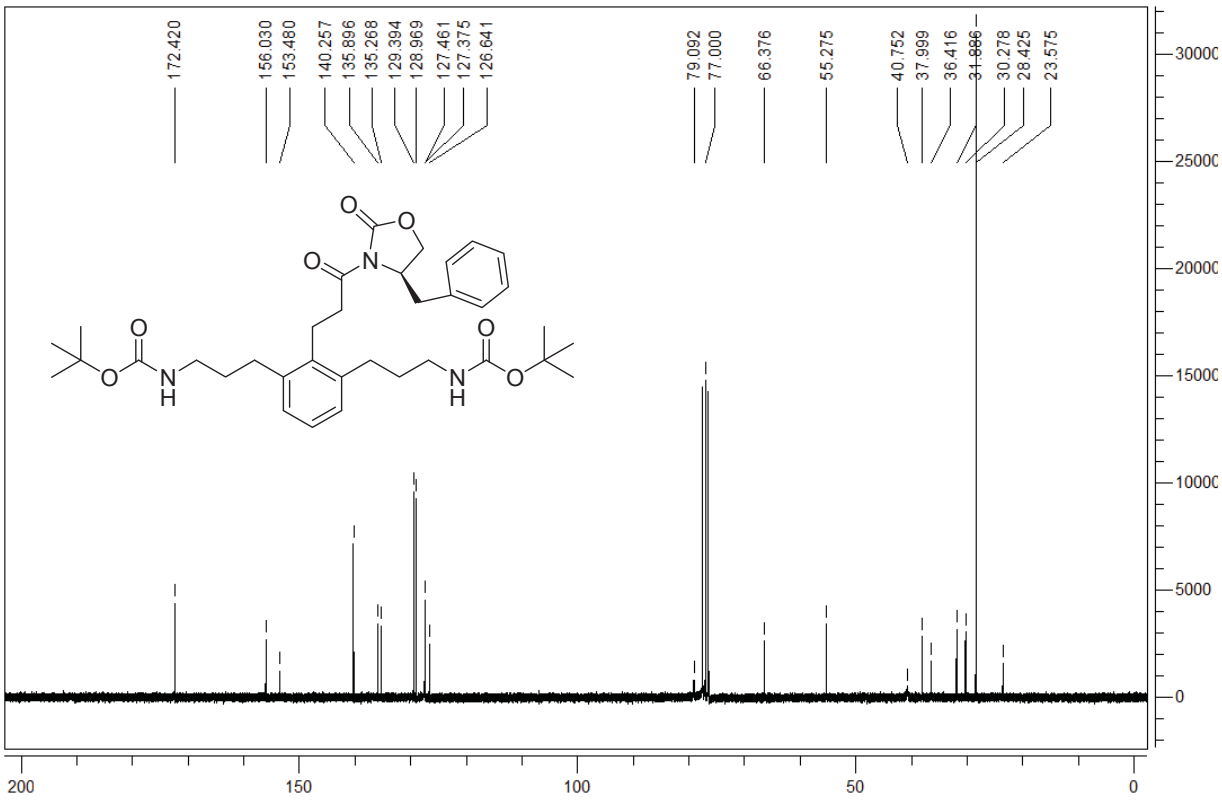
Methyl (2E)-3-[2-(3-{*bis*[(*tert*-butoxy)carbonyl]amino}propyl)pyren-1-yl] prop-2-enoate (**3i**)



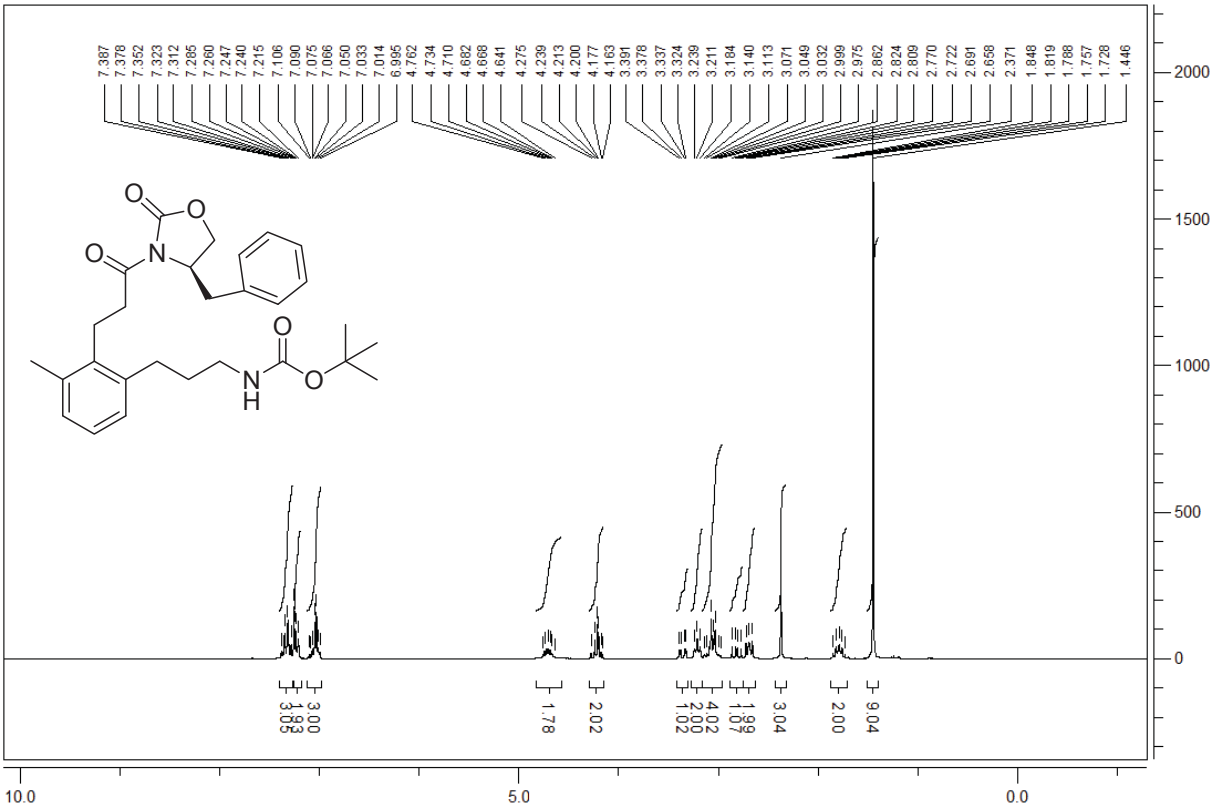


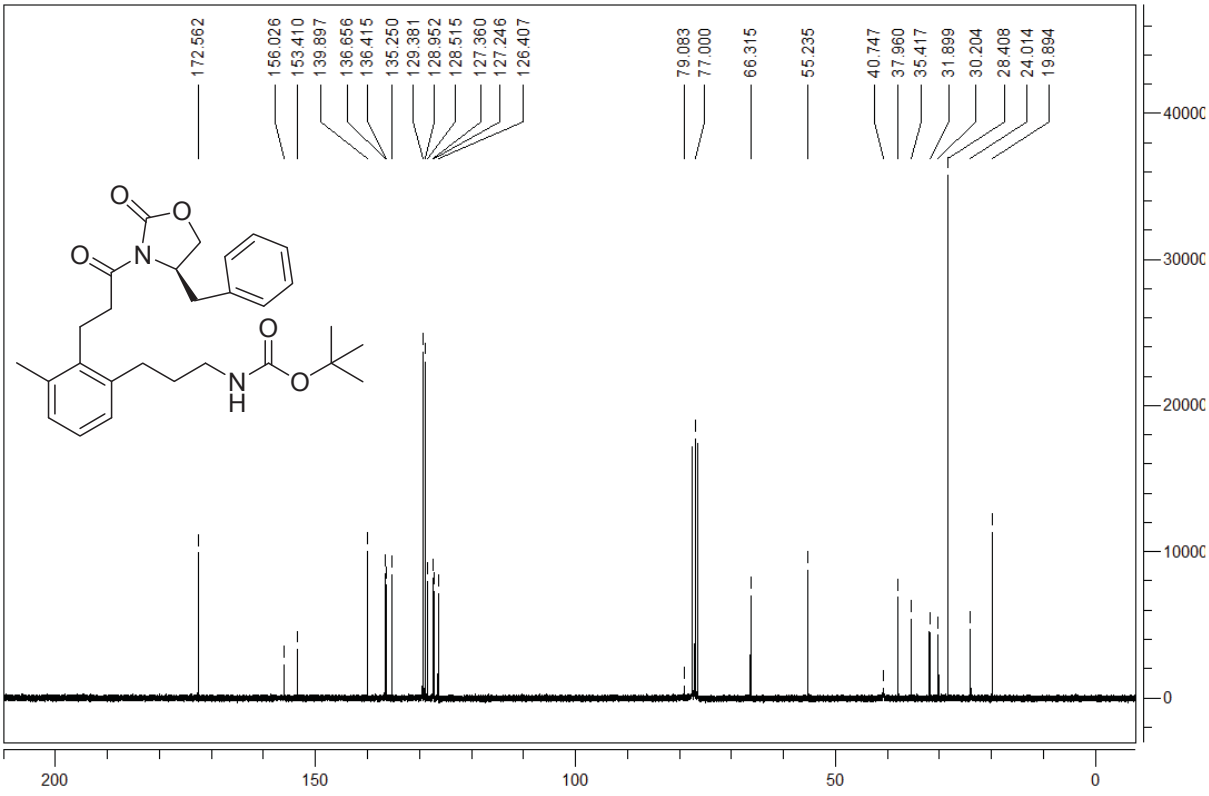
tert-Butyl *N*-[3-(2-{3-[(4R)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl}-3-(3-{[(*tert*-butoxy)carbonyl]amino}propyl)phenyl)propyl]carbamate (**5a**)



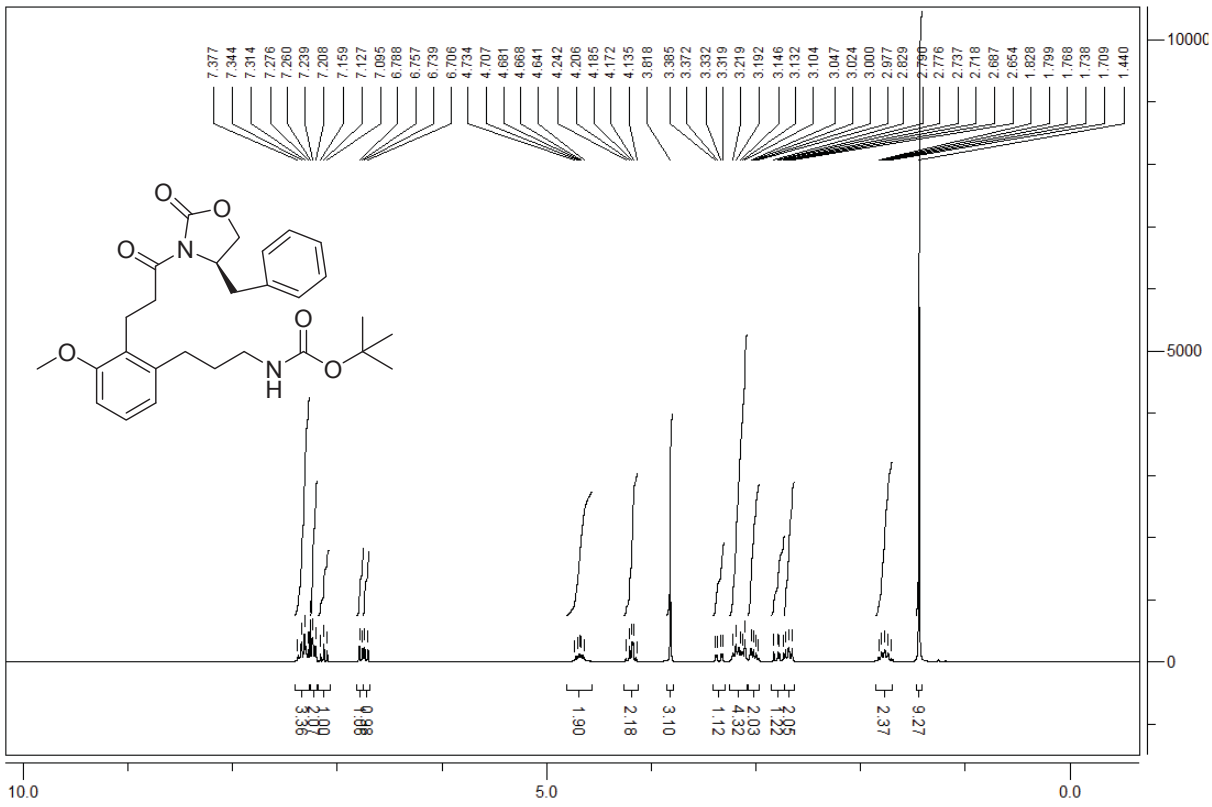


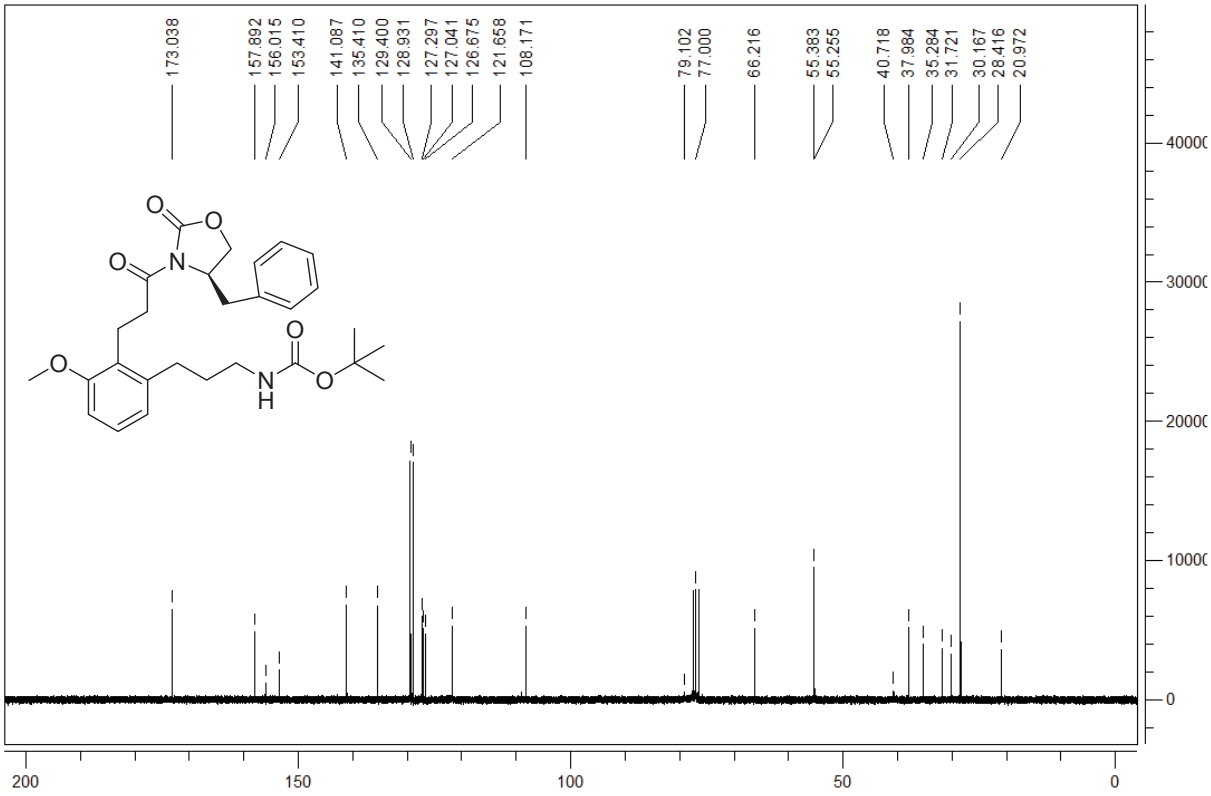
tert-Butyl *N*-[3-(2-{3-[(4R)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl}-3-methylphenyl)propyl]carbamate (**5b**)



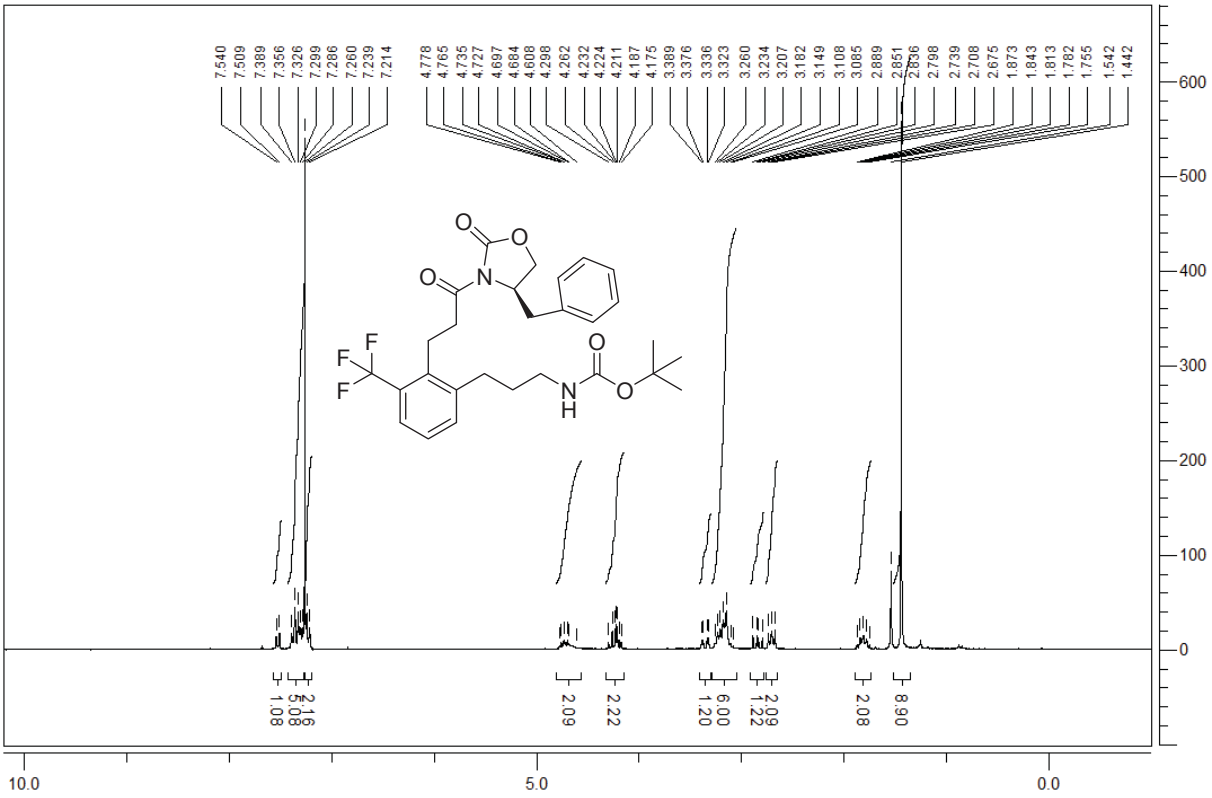


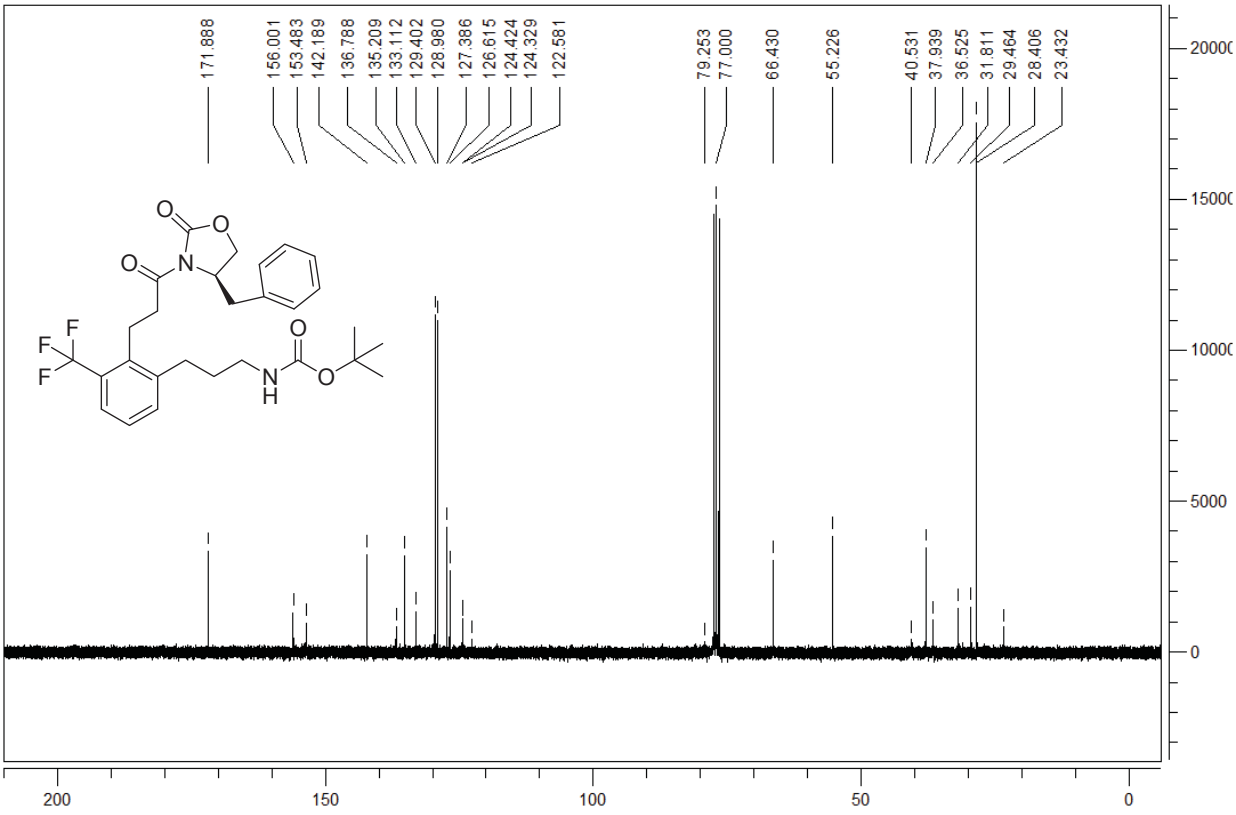
tert-Butyl *N*-[3-(2-{3-[(4R)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl}-3-methoxyphenyl)propyl]carbamate (**5c**)



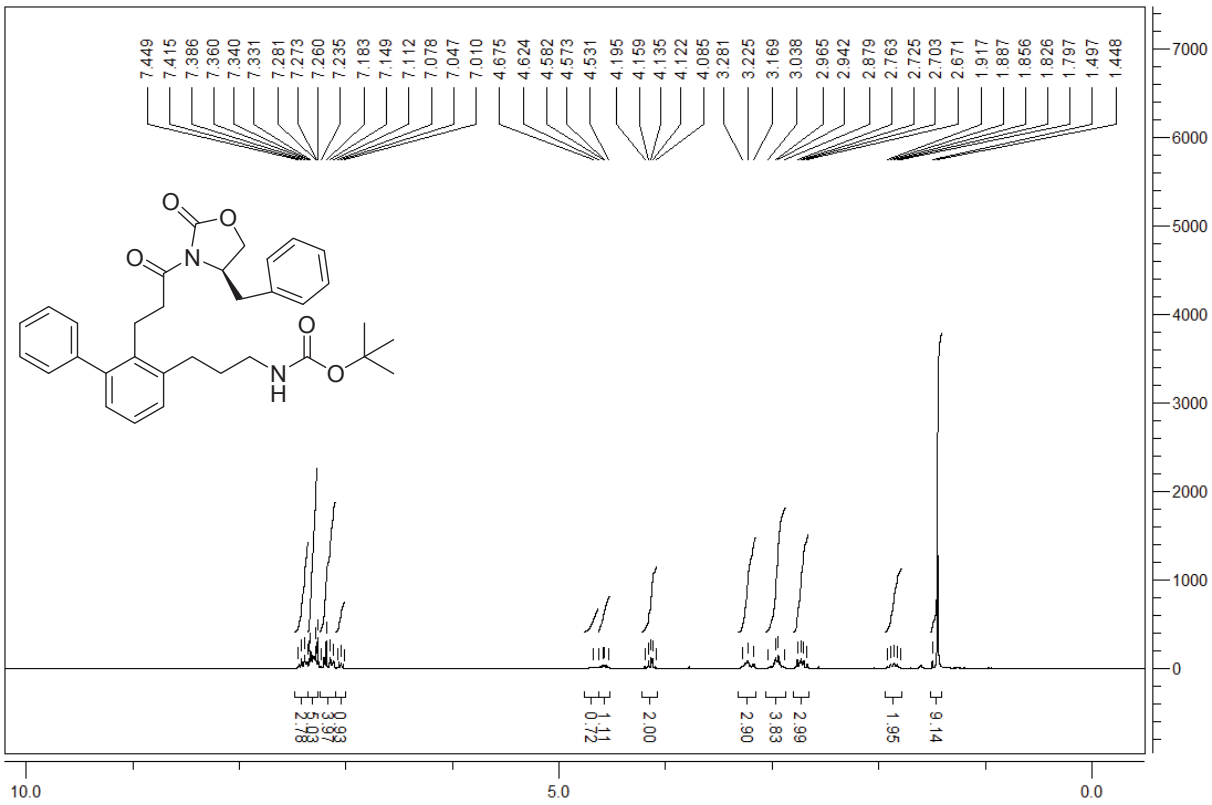


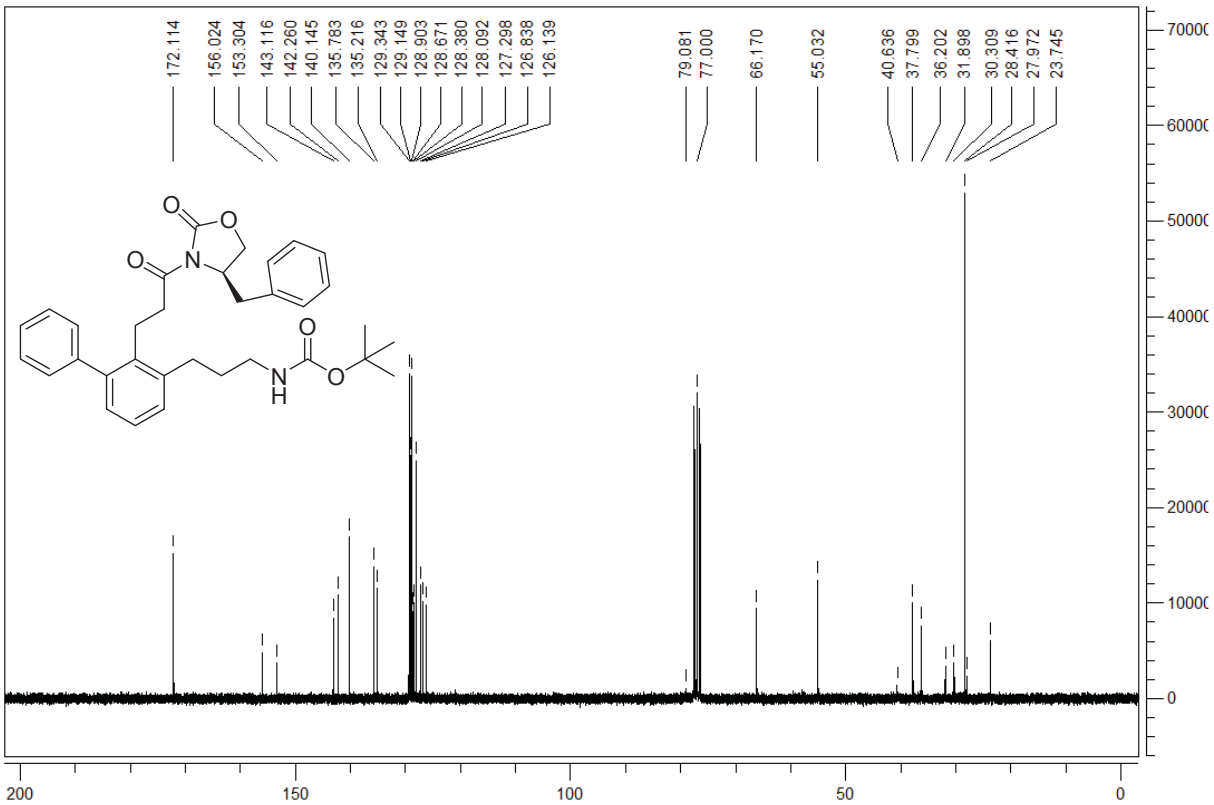
tert-Butyl *N*-[3-(2-{3-[(4R)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl}-3-(trifluoromethyl)phenyl)propyl]carbamate (**5d**)



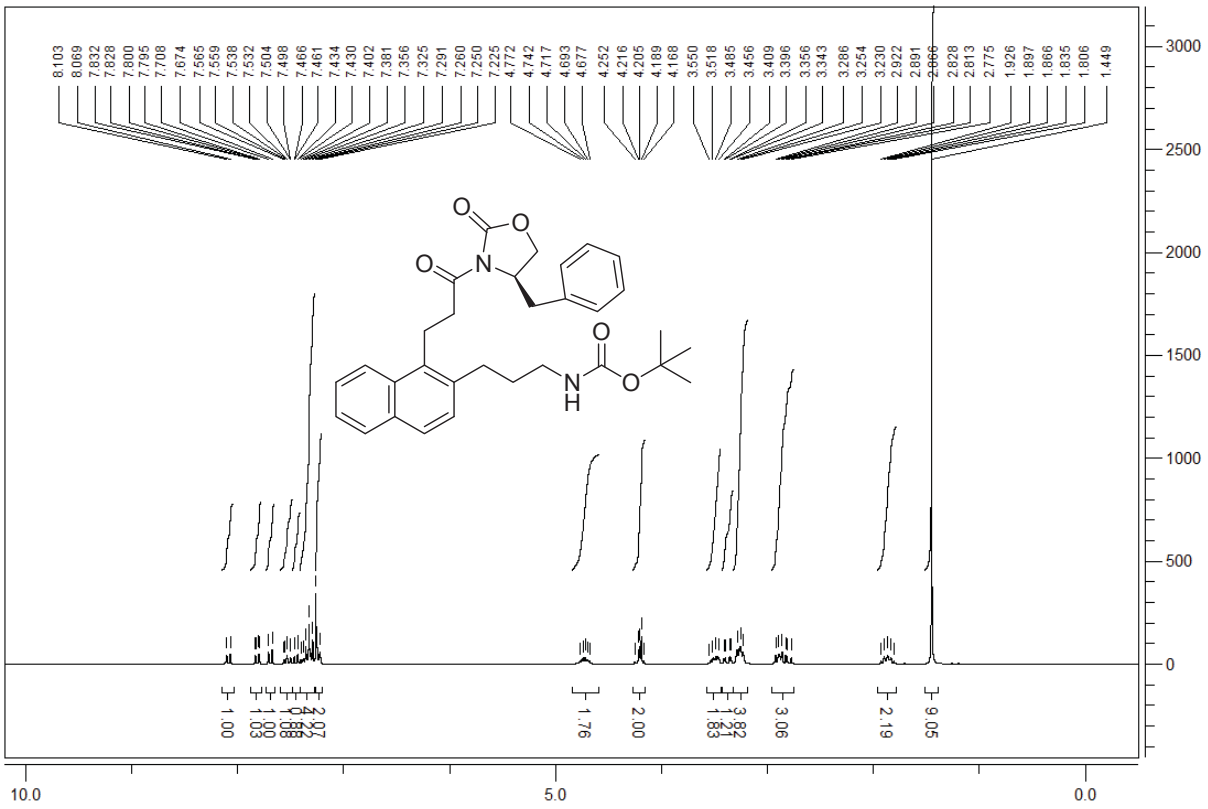


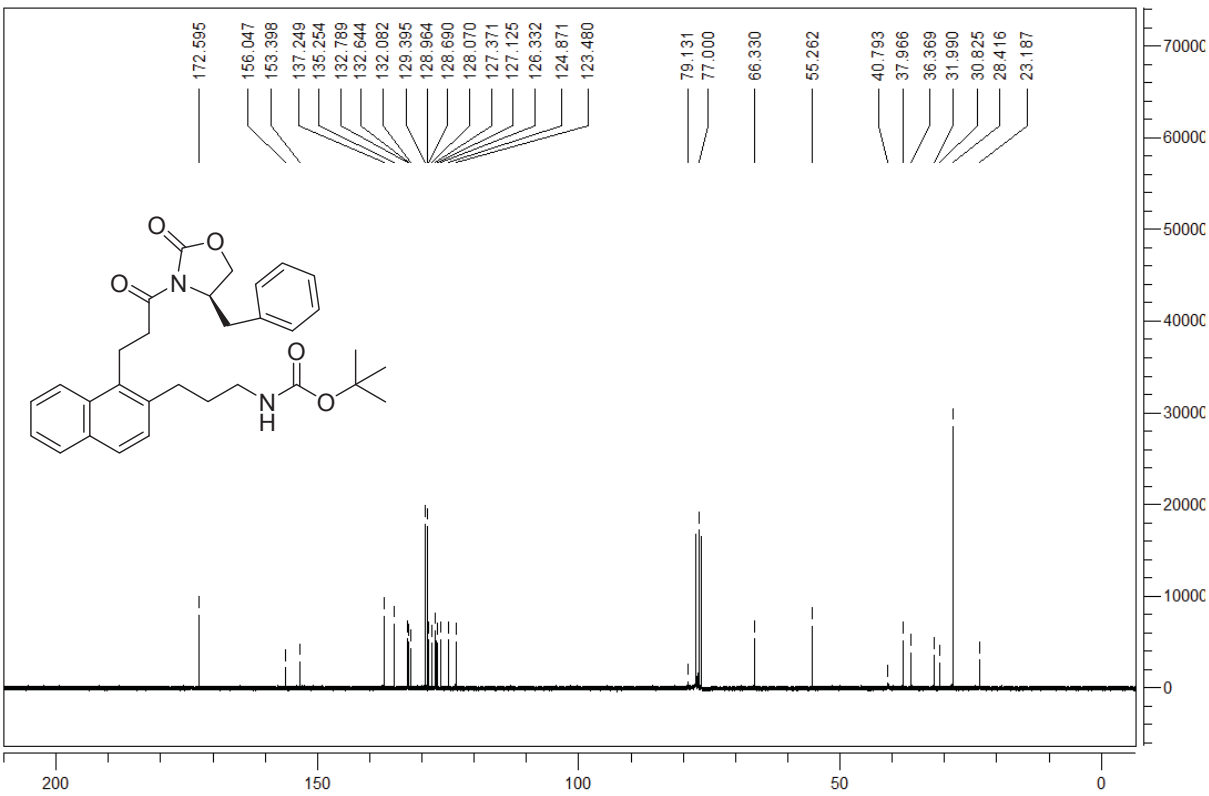
tert-Butyl *N*-[3-(2-{3-[(4R)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl}-3-phenylphenyl)propyl]carbamate (**5e**)



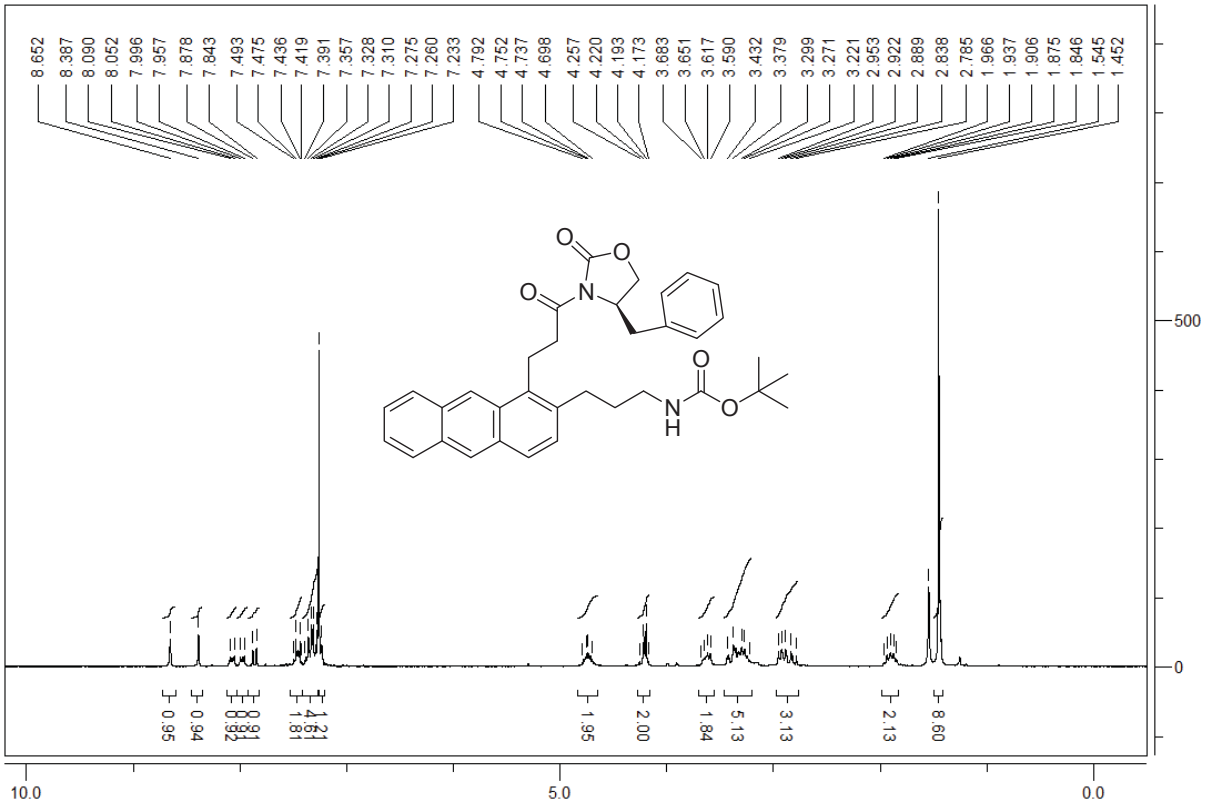


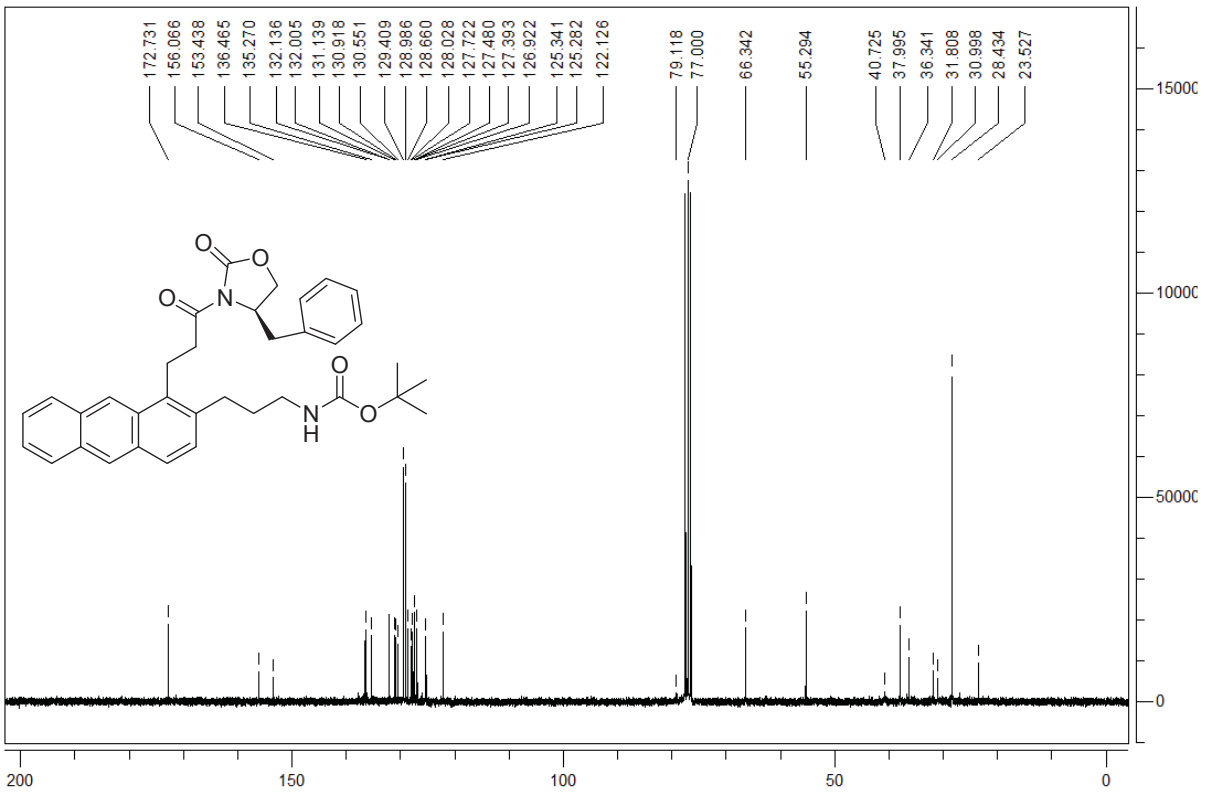
tert-Butyl *N*-[3-(1-{3-[(4R)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl}naphthalen-2-yl)propyl]carbamate (**5f**)



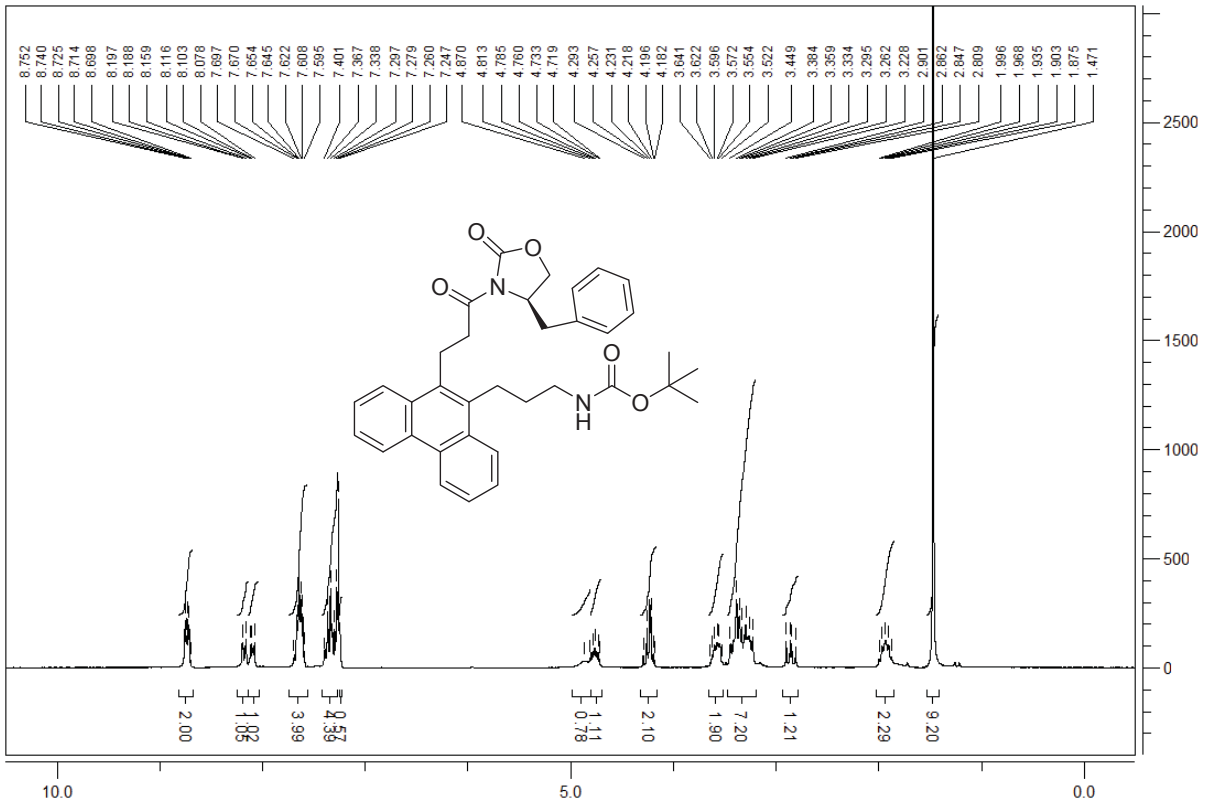


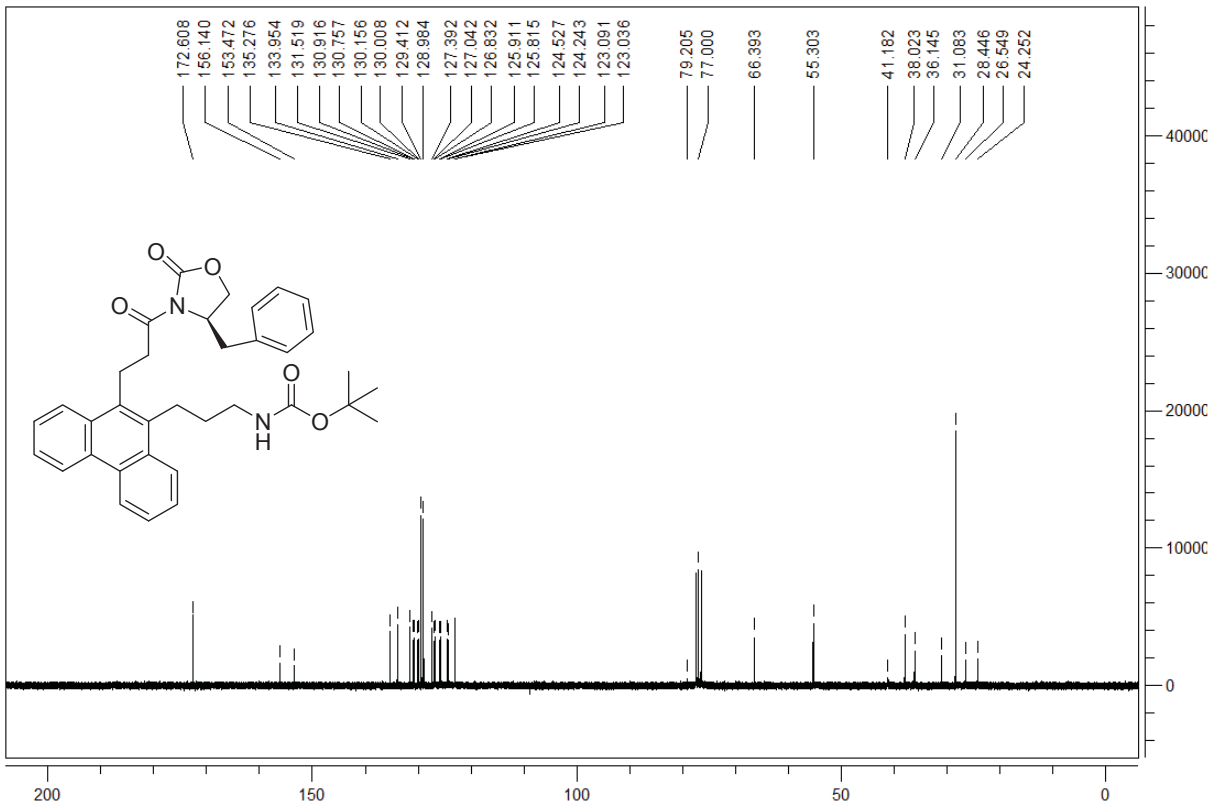
tert-Butyl *N*-[3-(1-{3-[(4R)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl} anthracen-2-yl)propyl]carbamate (**5g**)



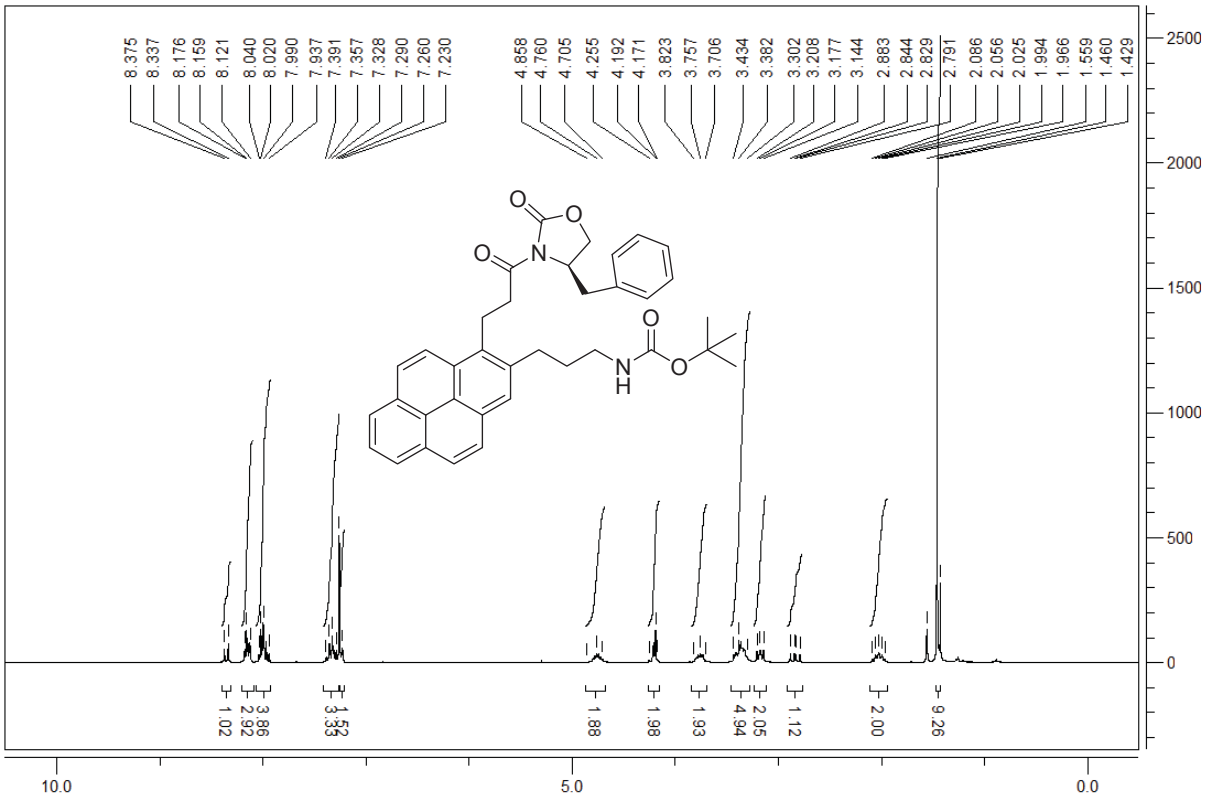


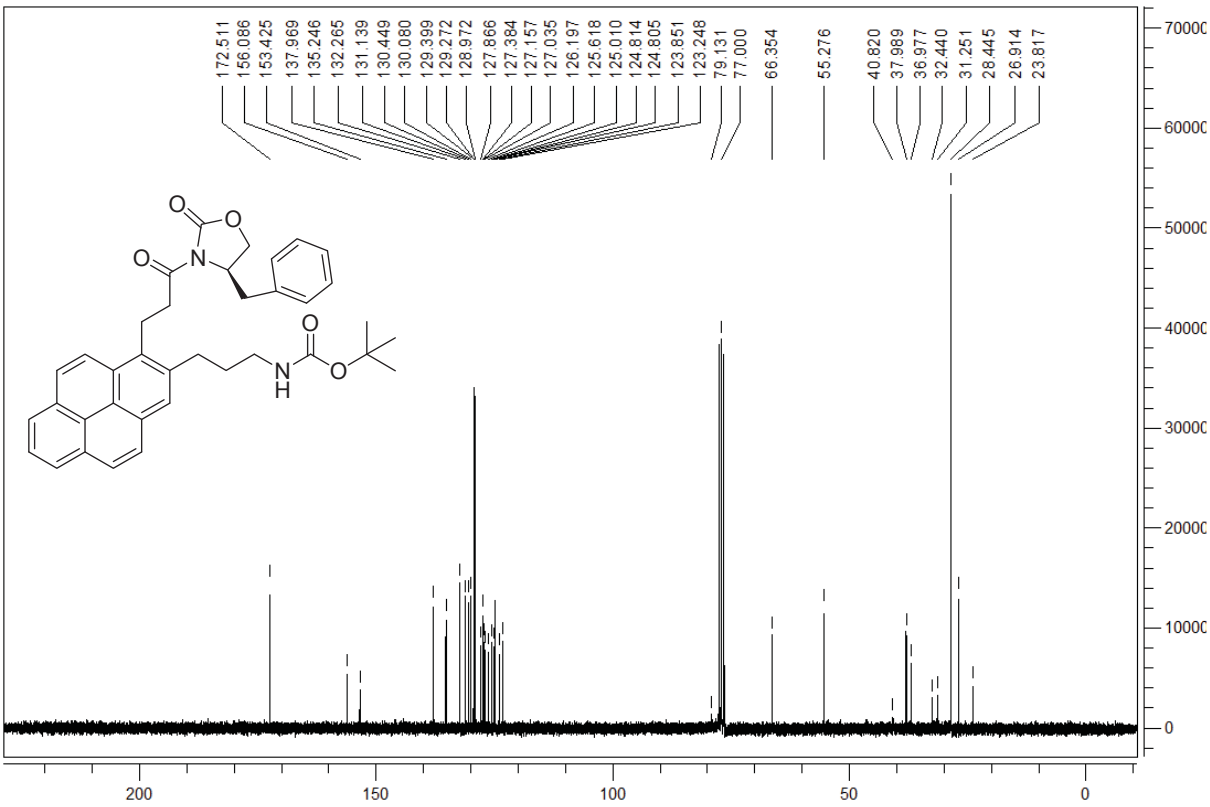
tert-Butyl *N*-[3-(10-{3-[(4R)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl}phenanthren-9-yl)propyl]carbamate (**5h**)



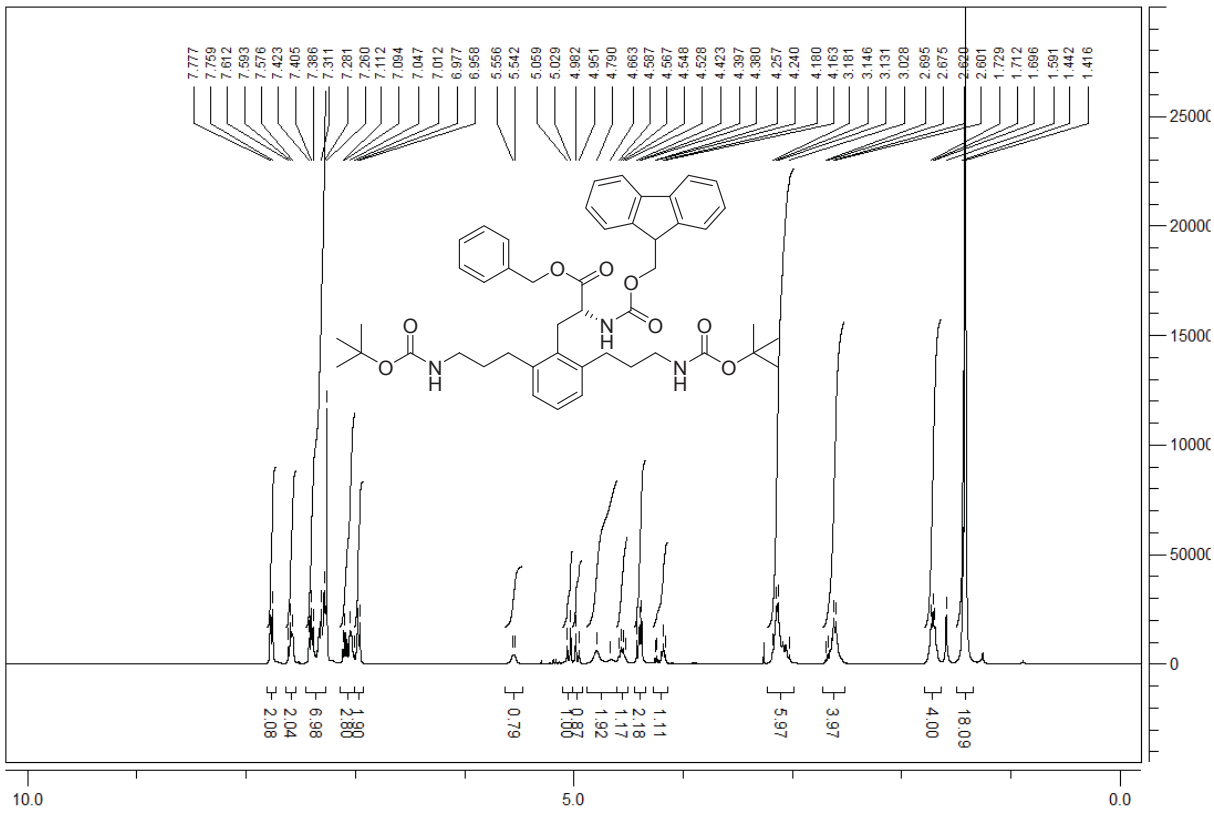


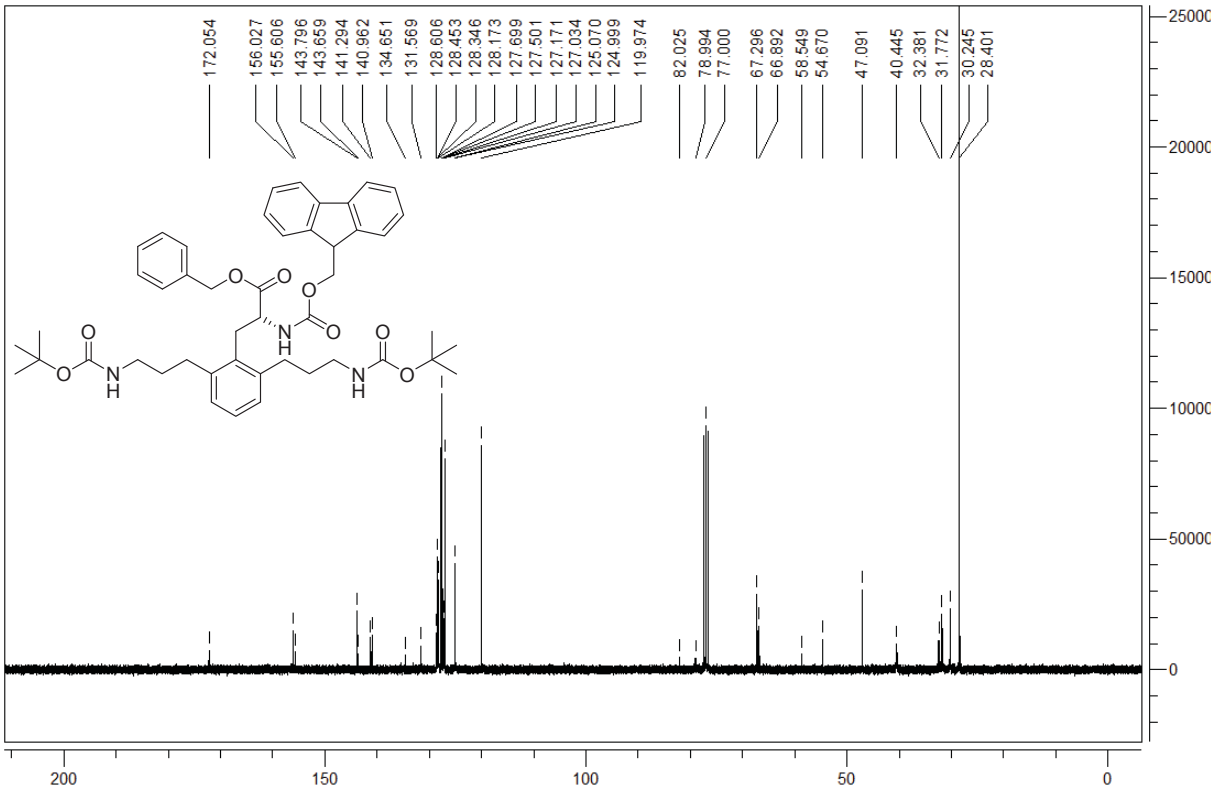
tert-Butyl *N*-[3-(1-{3-[(4R)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl}pyren-2-yl)propyl]carbamate (**5i**)



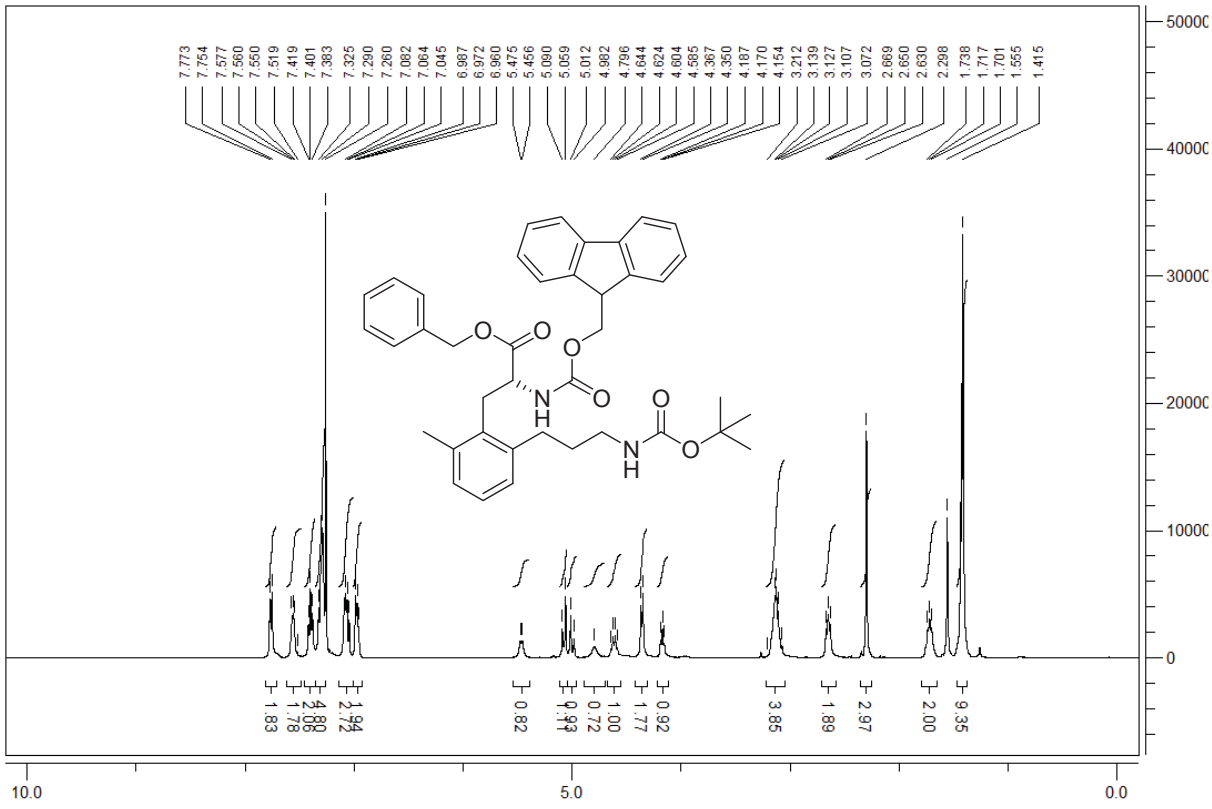


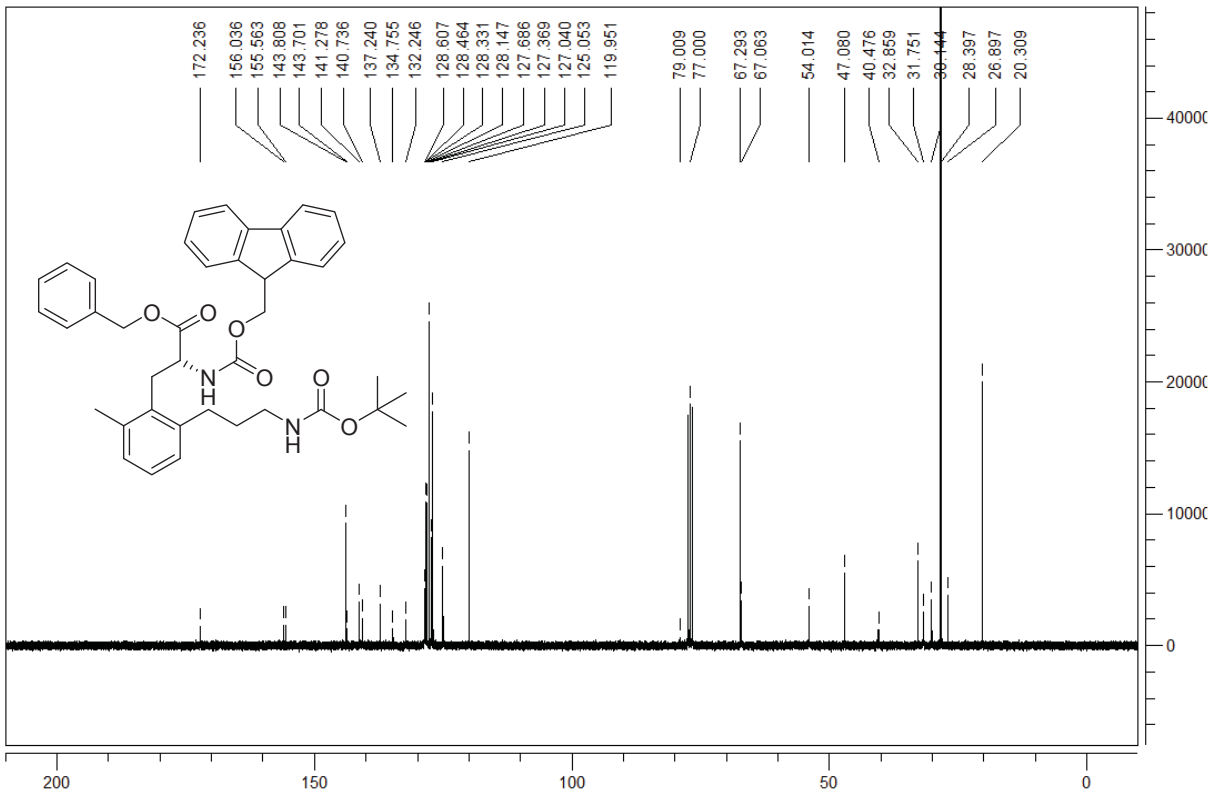
Benzyl (2R)-3-[2,6-*bis*(3-{[(*tert*-butoxy)carbonyl]amino}propyl)phenyl]-2-{[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino}propanoate (**7a**)



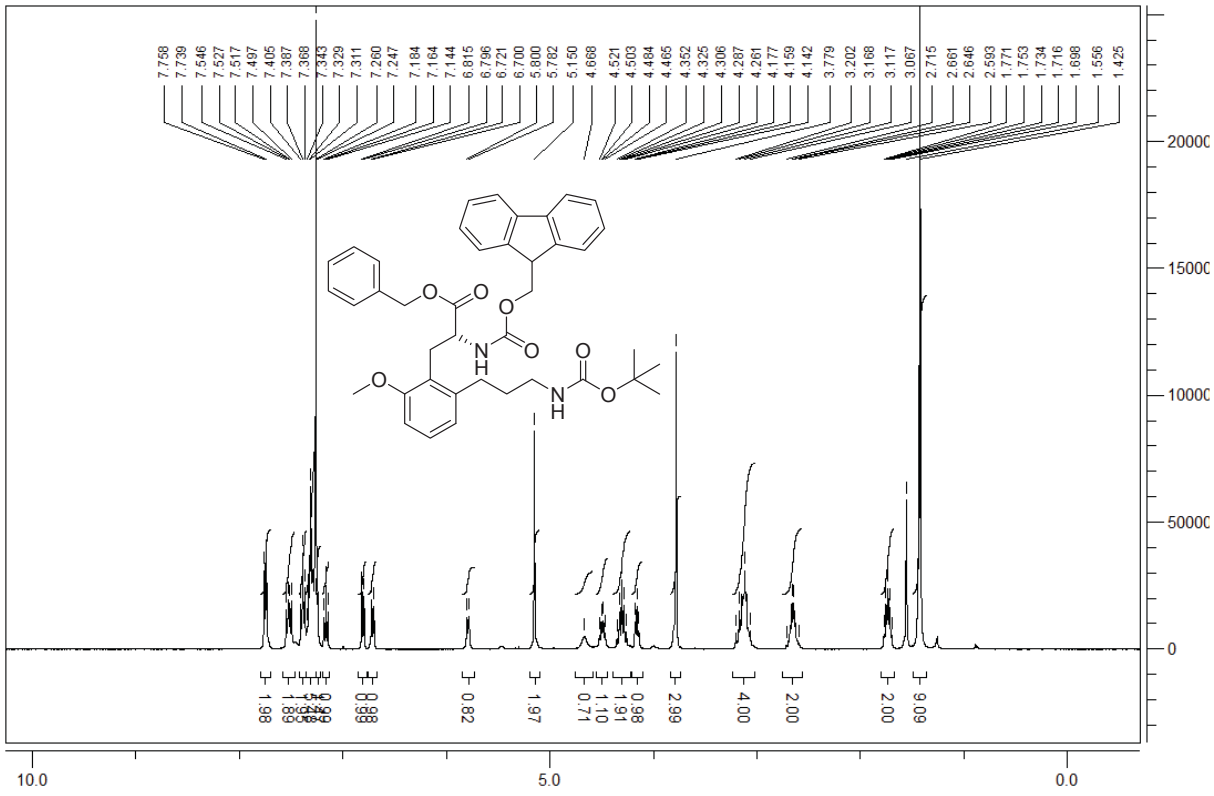


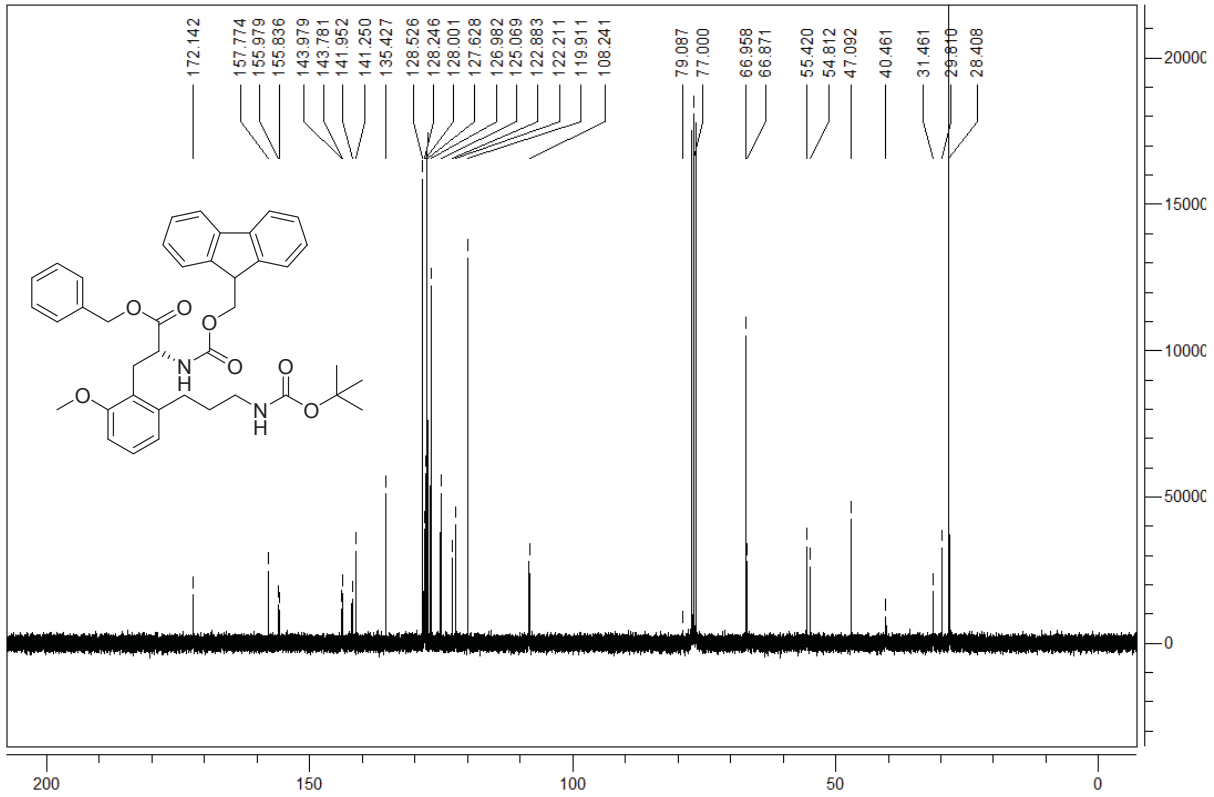
Benzyl (2R)-3-[2-(3-{[(*tert*-butoxy)carbonyl]amino}propyl)-6-methylphenyl]-2-{[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino}propanoate (**7b**)



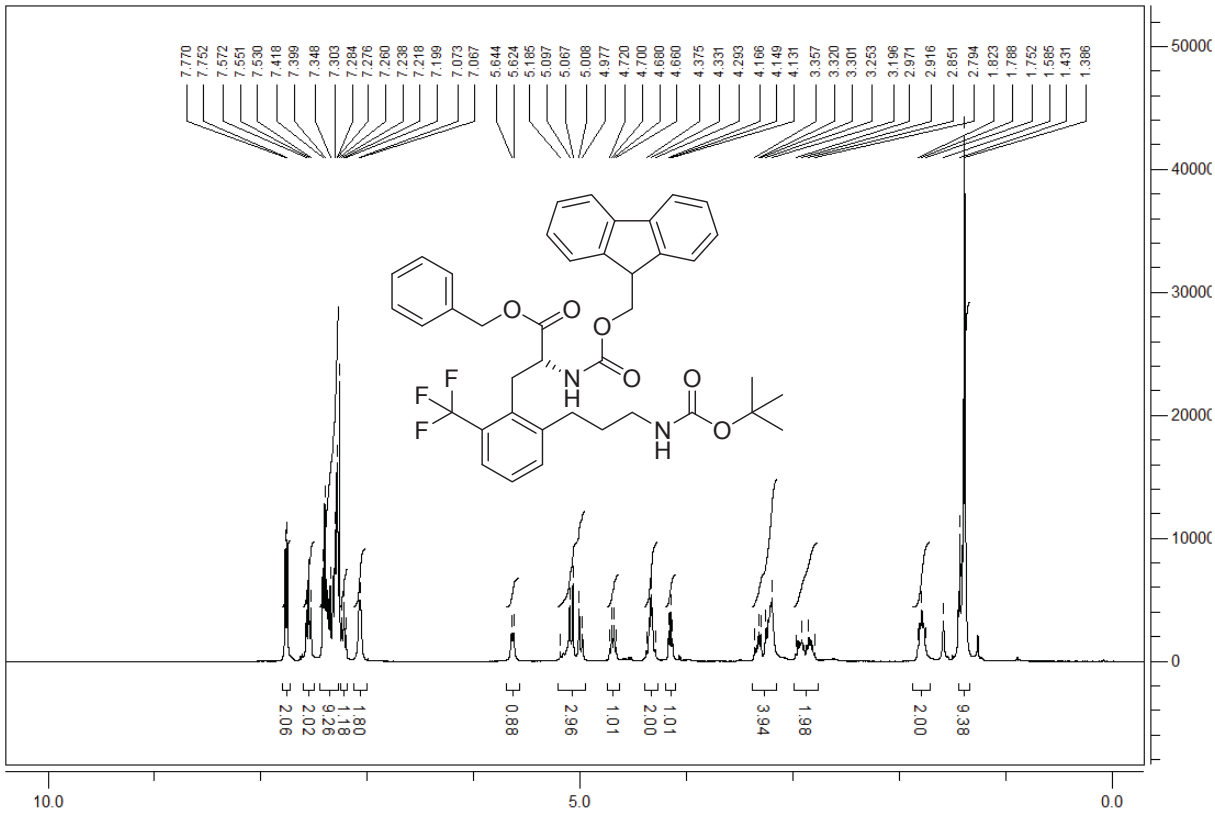


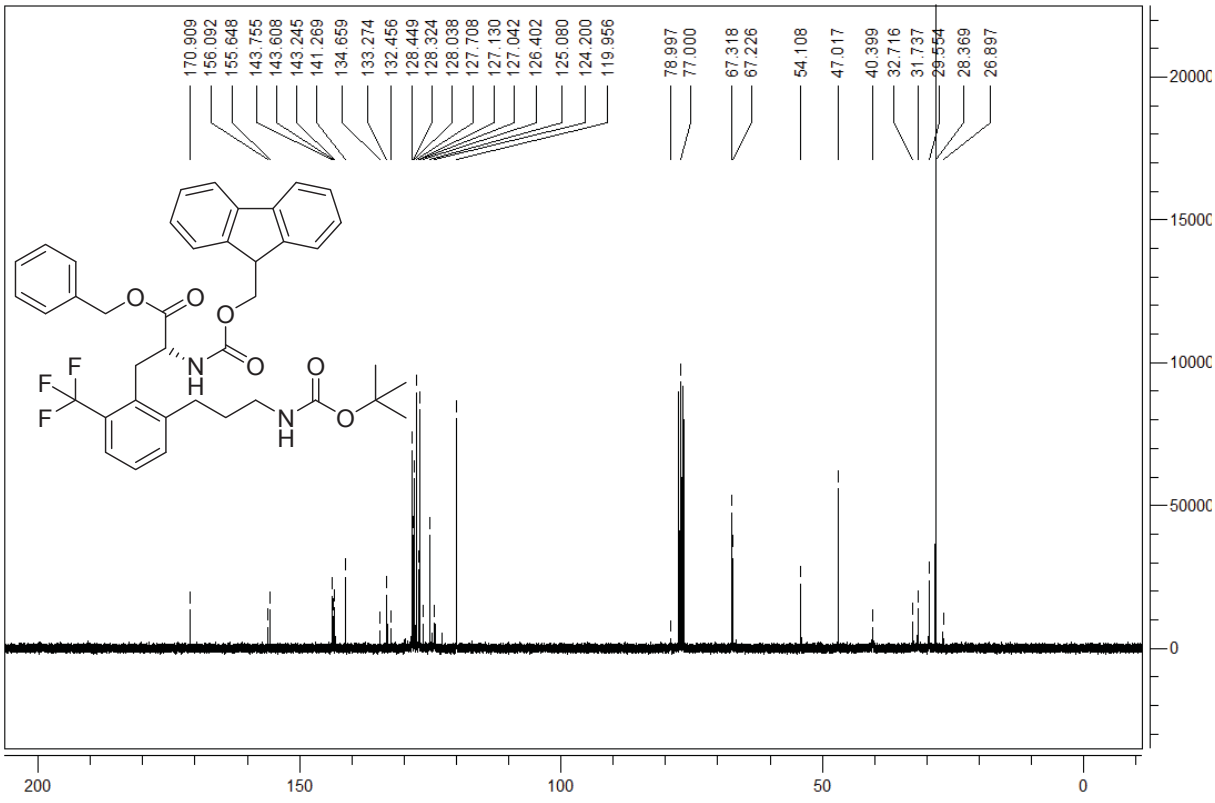
Benzyl (2R)-3-[2-(3-{[(*tert*-butoxy)carbonyl]amino}propyl)-6-methoxyphenyl]-2-{[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino}propanoate (**7c**)



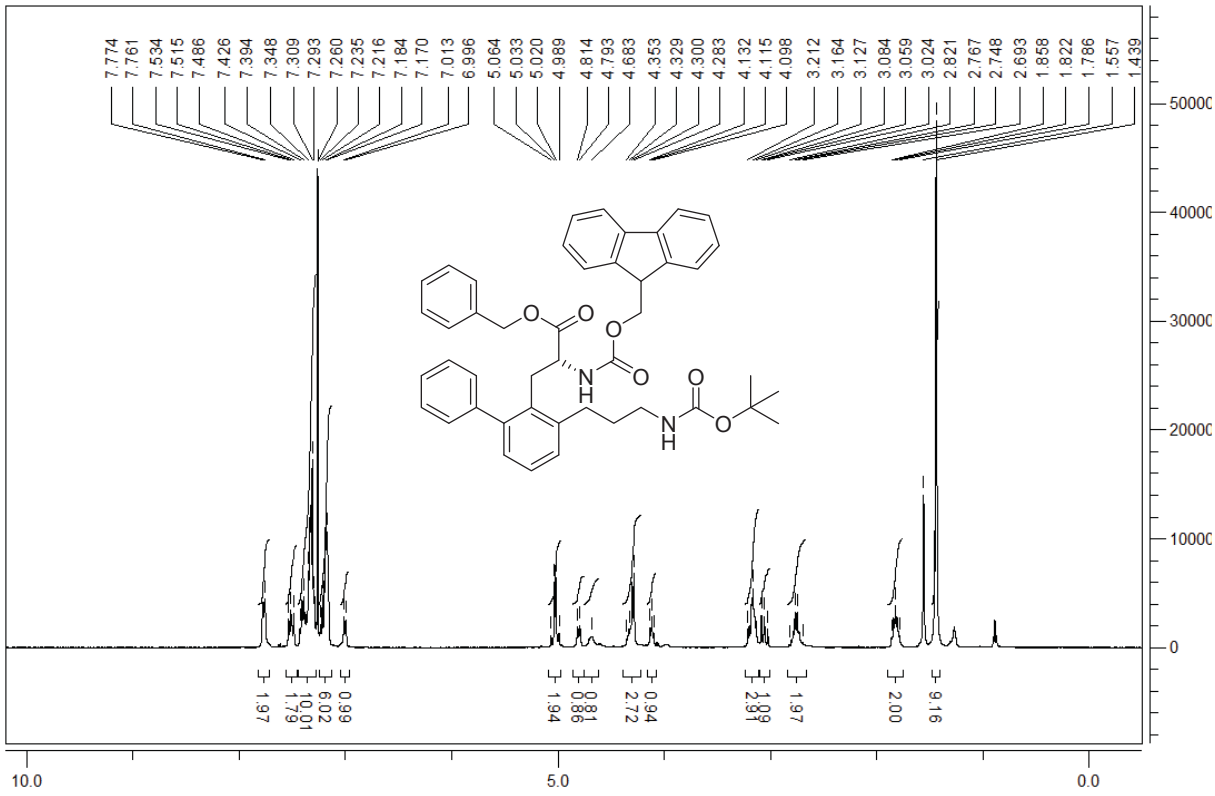


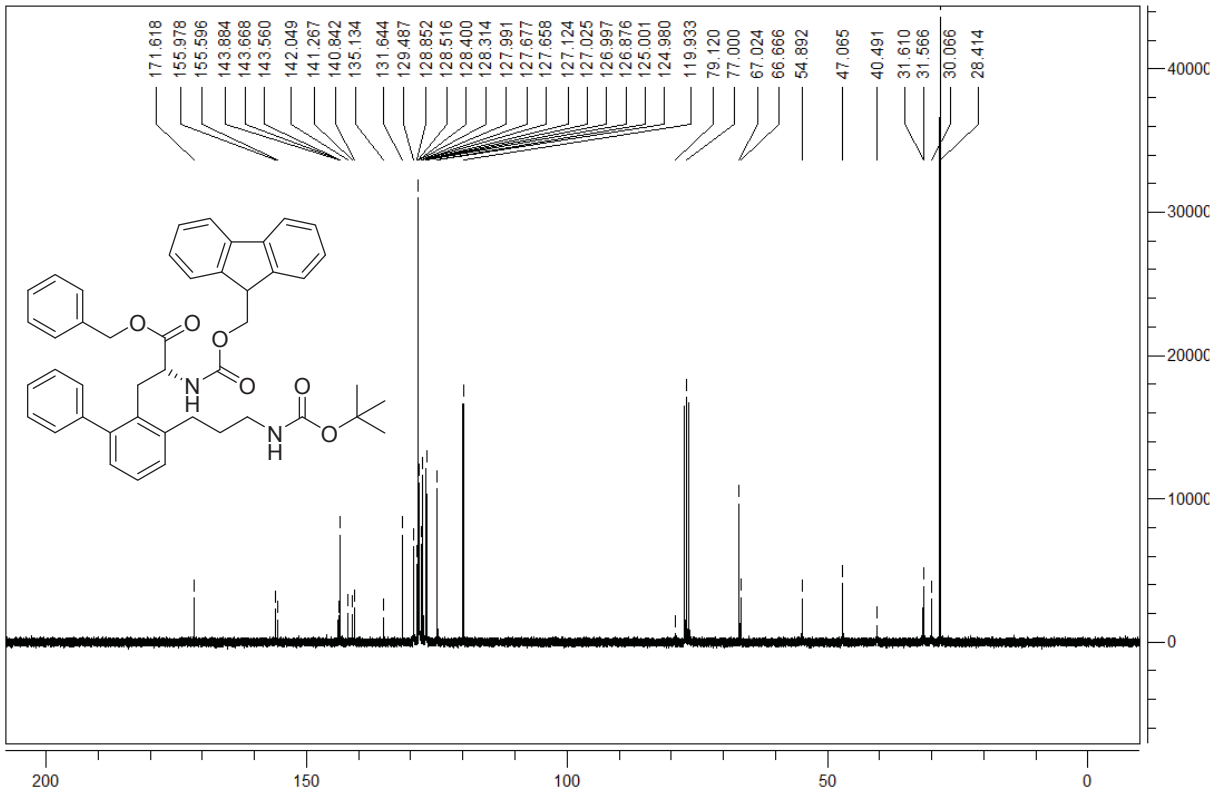
Benzyl (2R)-3-[2-(3-{[(*tert*-butoxy)carbonyl]amino}propyl)-6-(trifluoro methyl)phenyl]-2-{[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino}propanoate (**7d**)



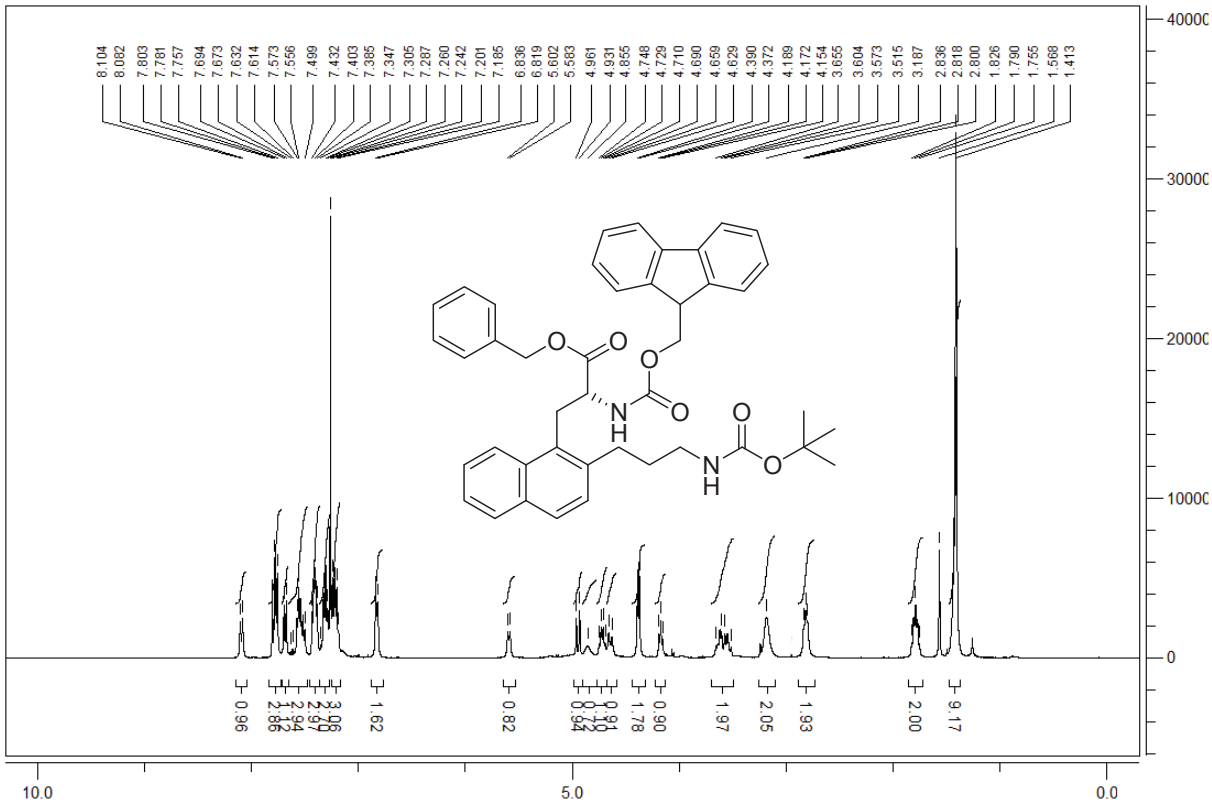


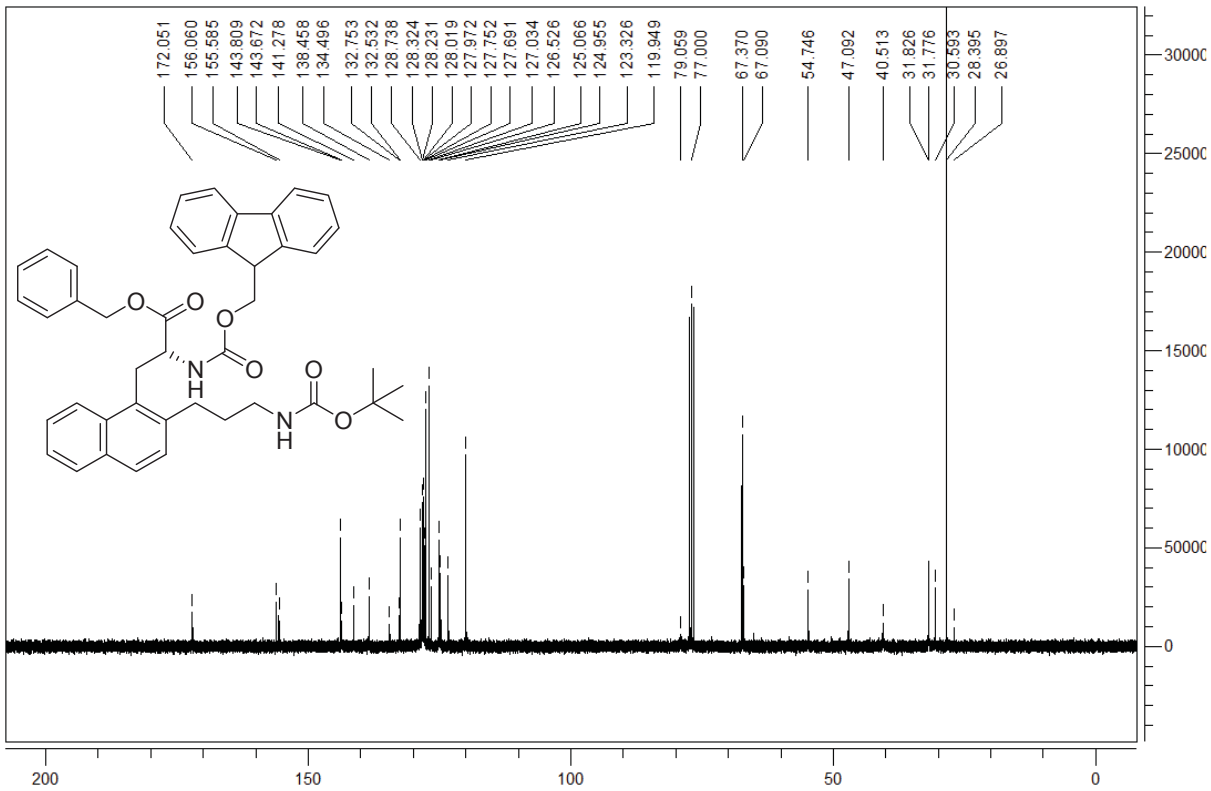
Benzyl (2R)-3-[2-(3-{[(*tert*-butoxy)carbonyl]amino}propyl)-6-phenylphenyl]-2-{[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino}propanoate (**7e**)



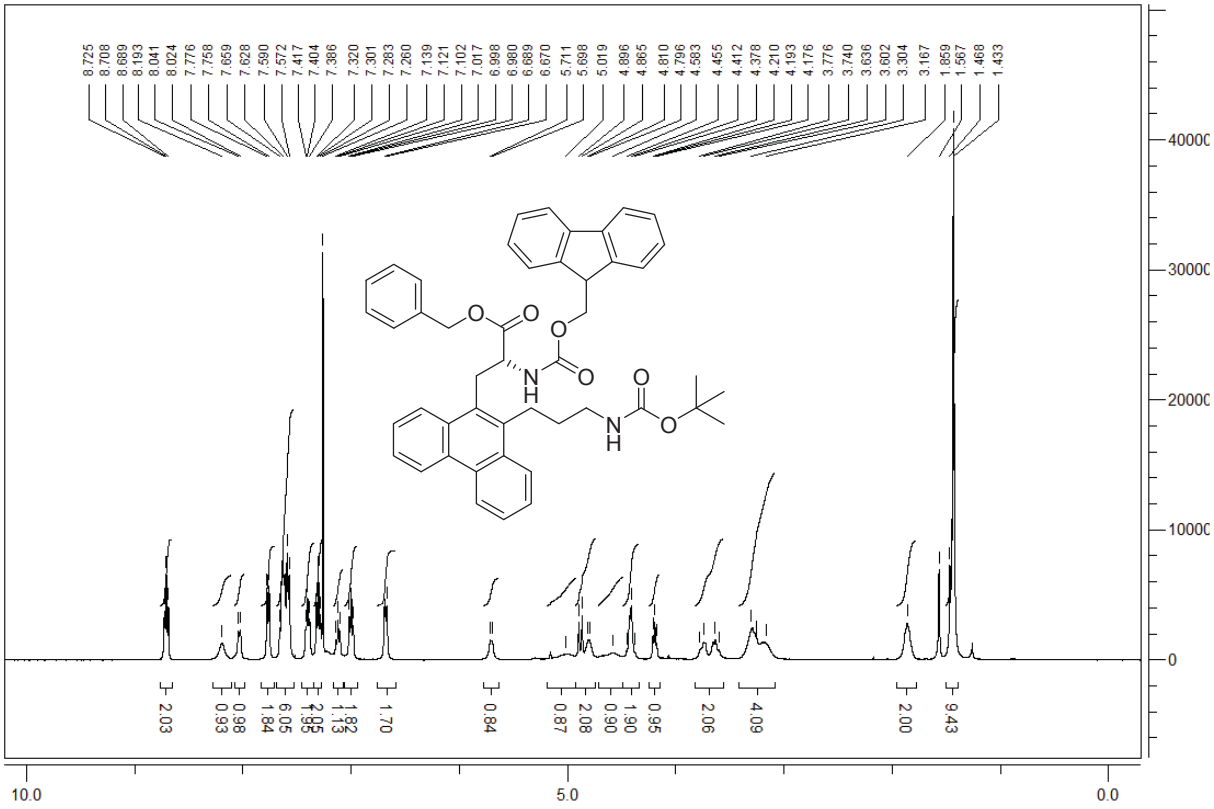


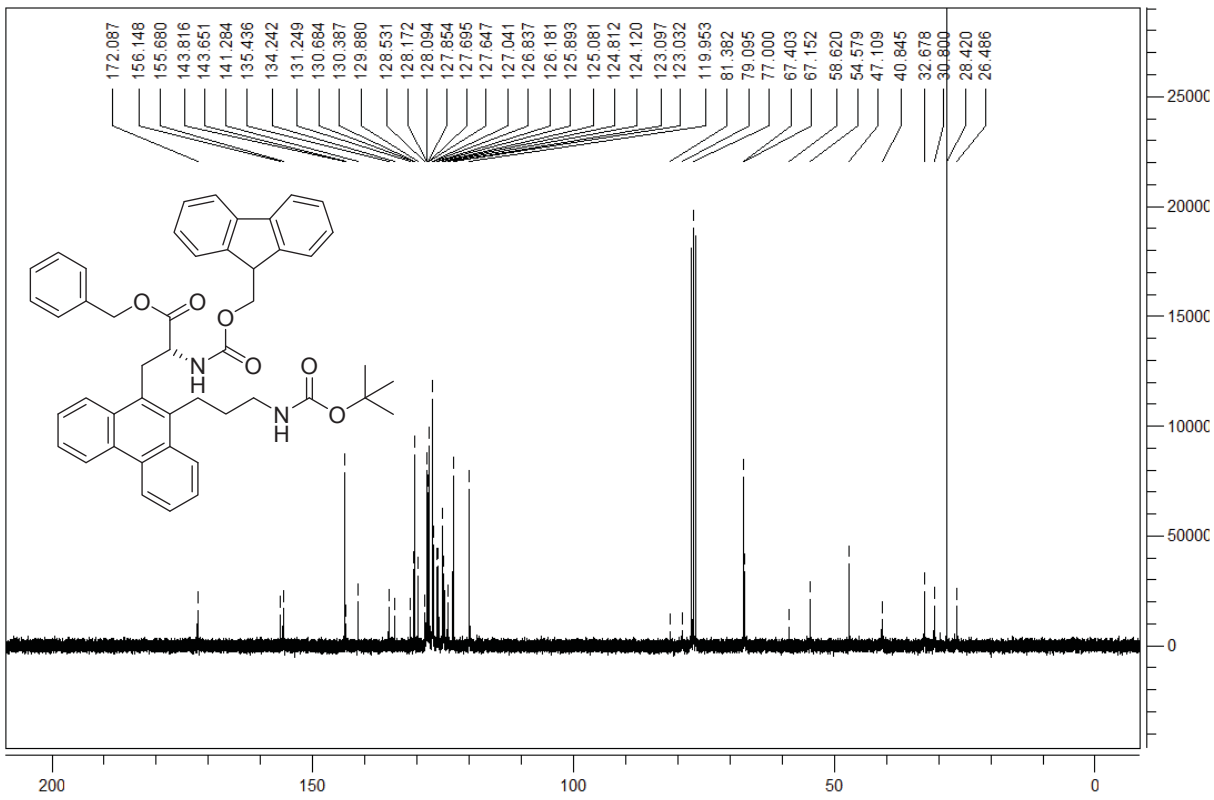
Benzyl (2R)-3-[2-(3-{[(*tert*-butoxy)carbonyl]amino}propyl)naphthalen-1-yl]-2-{[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino}propanoate (**7f**)



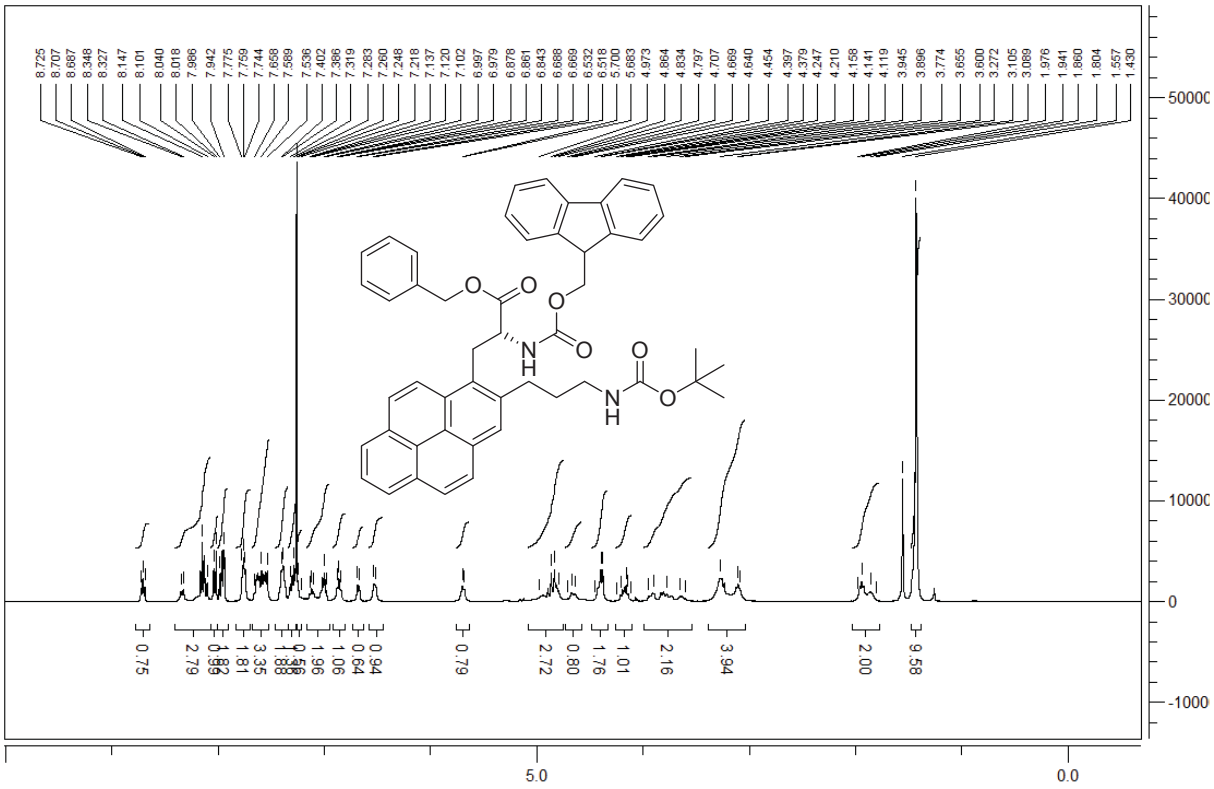


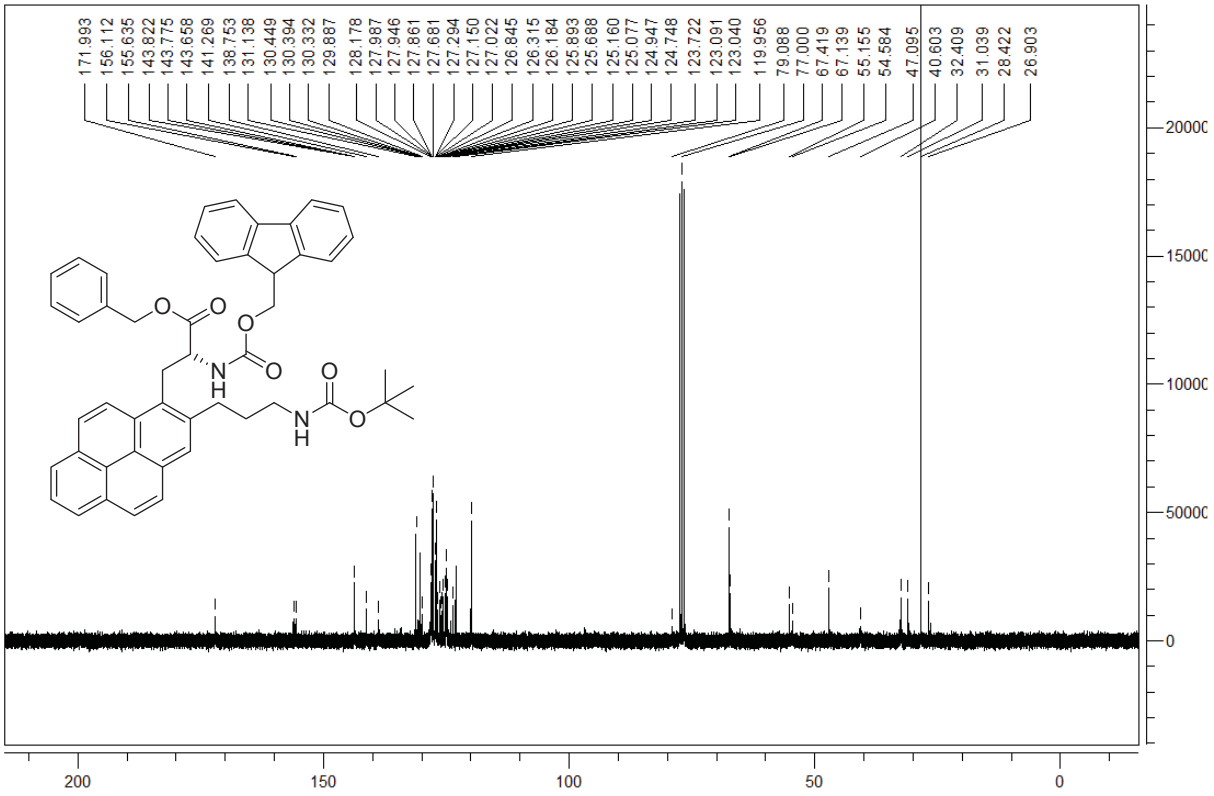
Benzyl (2R)-3-[10-(3-{[(*tert*-butoxy)carbonyl]amino}propyl)phenanthren-9-yl]-2-{[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino}propanoate (**7h**)





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



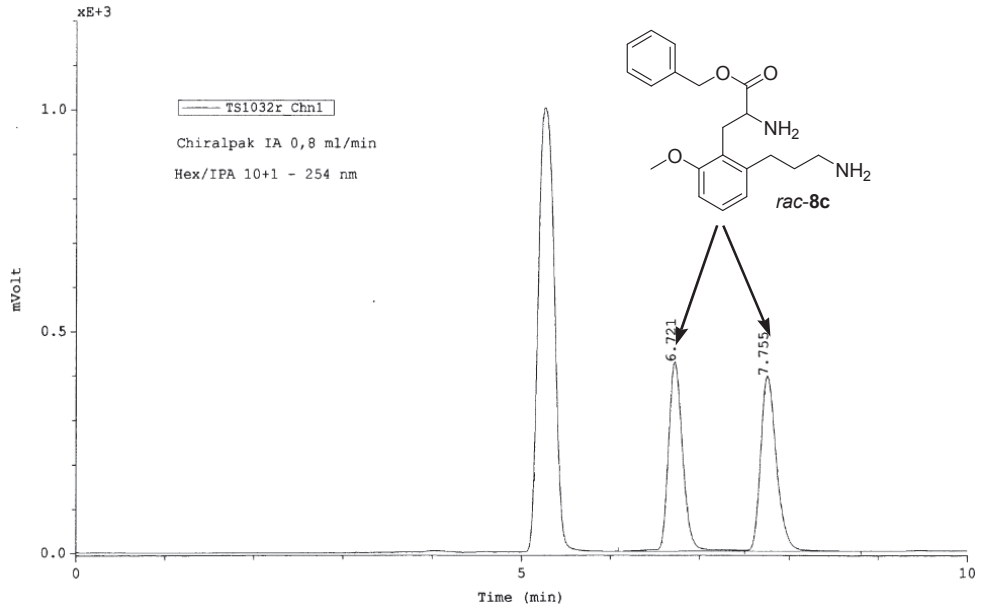


ee-Determination

Racemisation: [6]

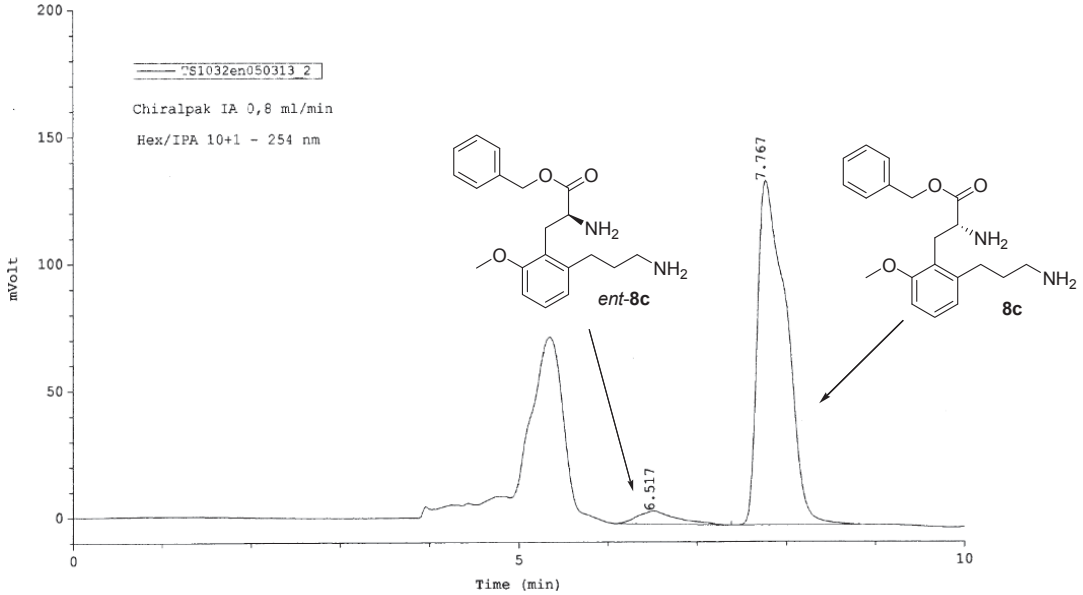
Amino acid **7c** (33 mg; 50 µmol) was dissolved in a piperidine-DMF solution (25%; 0.4 mL) and stirred for 1.5 h at room temperature. Afterwards, H_2O and EtOAc were added and the layers were separated. The aq phase was extracted with EtOAc (2x) and the combined organic phases were washed with H_2O. After drying over $MgSO_4$ 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**:



	Ret.time [min]	Start [min]	End [min]	Height [mVolt]	Area [mV*min]	% Area
1	6.721	6.09	7.51	428.04	80.1804	49.6446
2	7.755	7.51	8.81	397.328	81.3283	50.3554

HPLC trace for enantiomerically enriched **8c**:



	Ret.time [min]	Start [min]	End [min]	Height [mVolt]	Area [mV*min]	% Area
1	6.517	6.10	7.31	5.21249	2.62358	4.9290
2	7.767	7.38	8.88	135.909	50.6043	95.0710

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

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