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Supporting Information

69451 Weinheim, Germany

Microreactor Synthesis of β-Peptides

Oliver Flögel,[‡] Jeroen D. C. Codée,[‡] Dieter Seebach, Peter H. Seeberger[*]

Laboratory for Organic Chemistry
Swiss Federal Institute of Technology (ETH) Zürich
Wolfgang-Pauli-Strasse 10
CH-8093 Zürich
Switzerland

LCMS analysis:

LCMS analysis was performed using a Waters Symmetry® C18 5µm column (3.9 x 150 mm) or a Waters Sunfire® C8 5µm column (4.6 x 150 mm), using solvent systems A (20% isopropanol and 0.1% TFA in H_2O) and B (20% isopropanol and 0.1% TFA in acetonitrile), at a flowrate of 1 mL/min.

Micro reactor experiments:

In all experiments a Harvard Scientific PHD 2000 syringe pump was used to simultaneously advance the syringes.

Heating of the reactor was accomplished by submerging the complete reactor in an oil bath, which was heated using a thermo-couple.

General procedure for reaction scanning using the micro reactor:

The micro reactor was equipped with the following syringes:

Inlet A: 2.5 mL syringe, containing a solution of the amino acid-TFA salt (0.24 M) in DMF

Inlet B: 2.5 mL syringe, containing a solution of the acid fluoride (0.48 M) in DMF

Inlet C: 1.0 mL syringe, containing a solution of NMM (2.4 M) in DMF

Inlet D: 5.0 mL syringe, containing a solution of TFA (0.72 M) and reference substance (0.024 M or 0.012 M) in DMF

Before running the reactor it was rinsed with a copious amount of DMF. Before the first run the system was rinsed with 250 µL (pre-quench volume) of reaction mixture. Before every new run at a given temperature the system was equilibrated with 100 µL pre-quench reaction mixture, pumped through the reactor at the appropriate speed. Next, 3 aliquots of 25 µL (pre-quench volume) reaction mixture were collected, which were diluted with CH_2Cl_2 (1 mL) and analyzed by LCMS. The LCMS traces were integrated and the product peaks were normalized *vs* the internal standard. This way a data-set of *relative* conversions was obtained.

General procedure for a large scale reaction in the micro reactor:

The micro reactor was equipped with the following syringes:

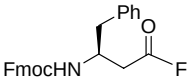
Inlet A: 2.5 mL syringe, containing a solution of the amino acid-TFA salt (0.24 M) in DMF

Inlet B: 2.5 mL syringe, containing a solution of the acid fluoride (0.48 M) in DMF

Inlet C: 1.0 mL syringe, containing a solution of NMM (2.4 M) in DMF
Inlet D: 5.0 mL syringe, containing a solution of TFA (0.72 M) in DMF

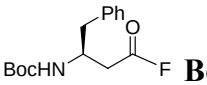
Before running the reactor it was rinsed with a copious amount of DMF at the reaction temperature. Next the system was equilibrated by rinsing the reactor with 250 μL pre-quench reaction volume at the appropriate speed. The reactor was run until the syringes were empty. The reaction mixture was collected, diluted with CH_2Cl_2, washed with aqueous KH_2PO_4 (1 M) and aqueous K_2HPO_4 (1 M), dried ($NaSO_4$) and concentrated. To purify the crude fluorous products the mixture was taken up in DMF and loaded onto a fluorous silica column (Fluorochrom silicagel), which was first eluted with MeOH/H_2O (80/20) followed by MeOH and MeOH/CH_2Cl_2 (1/1). The MeOH and MeOH/DCM fractions were collected and concentrated to provide the pure target compound. The non-fluorous products were purified using silica gel column chromatography.

General procedure for the synthesis of the acid fluorides from the parent amino acids:
The appropriate protected amino acid (1 equiv.) in CH_2Cl_2 (8 mL/1 mmol) was treated with pyridine (1 equiv.) and cyanuric fluoride (0.5 equiv.). After stirring for 3 h at r.t. the mixture was diluted with CH_2Cl_2 and washed twice with a small amount of ice water. The organic phase was dried (Na_2SO_4) and the solvent was removed under reduced pressure. The so obtained acid fluoride was used for the reaction without further purification.



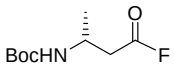
Fmoc-β^3-homophenylalanine fluoride (purity > 90%)

^{1}H-NMR (300 MHz, $CDCl_3$): 2.63 – 2.81 (*m*, 2 H); 2.83 – 3.09 (*m*, 2 H); 4.16 – 4.27 (*m*, 2 H); 4.41 (*d*, *J* = 6.3 Hz, 2 H); 5.06 (br.*d*, *J* = 7.5 Hz, NH), 7.16 (*d*, *J* = 6.6 Hz, 2 H), 7.24 – 7.45 (*m*, 5 H), 7.54 (*d*, *J* = 7.8 Hz, 2 H), 7.77 (*d*, *J* = 7.5 Hz, 2 H).
^{13}C-NMR (100 MHz, $CDCl_3$): 35.8 (*d*, *J* = 47.4 Hz), 39.4 (CH_2), 47.2, 48.6 (2 x CH), 66.7 (CH_2), 120.0, 125.0, 127.1, 127.1, 127.7, 128.9, 129.1 (7 x CH), 136.6, 141.3, 143.7, 155.5 (4 x C). Carbonyl-C-atom could not be detected due to low intensity.



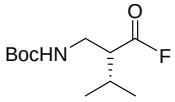
Boc-β^3-homophenylalanine fluoride (purity > 90%)

^{1}H-NMR (300 MHz, $CDCl_3$): 1.42 (*s*, 9 H); 2.55 – 3.05 (*m*, 4 H); 4.18 (br.*s*, 1 H); 4.81 (br.*s*, NH); 7.16 – 7.36 (*m*, 5 H).



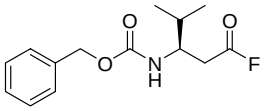
Boc-β^3-homoalanine fluoride (purity > 90%)

^{1}H-NMR (300 MHz, $CDCl_3$): 1.29 (*d*, *J* = 6.6 Hz, 3 H); 1.44 (*s*, 9 H); 2.62 – 2.83 (*m*, 2 H); 3.98 – 4.15 (*m*, 1 H); 4.70 (br.*s*, NH).



Boc-β^2-homovaline fluoride (purity > 90%)

^{1}H-NMR (300 MHz, $CDCl_3$): 1.04 (*d*, *J* = 6.6 Hz, 6 H); 1.44 (*s*, 9 H); 1.99 – 2.15 (*m*, 1 H); 2.75 (br.*s*, 1 H), 3.13 – 3.32 (*m*, 1 H); 3.42 – 3.60 (*m*, 1 H); 4.81 (br.*s*, NH).



Z-β^3-homovaline fluoride (purity > 90%)

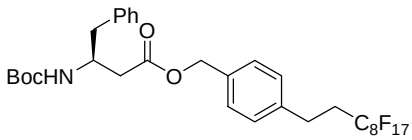
^{1}H-NMR (300 MHz, $CDCl_3$): 0.93 – 1.02 (*m*, 6 H); 1.82 – 2.02 (*m*, 1 H); 2.66 – 2.87 (*m*, 2 H), 3.78 – 3.93 (*m*, 1 H); 4.95 (br.*s*, NH); 5.09 (br.*s*, 2 H); 7.33 – 7.40 (*m*, 5 H).

General procedure for the deprotection of the Boc-protected peptides:

The Boc-protected amino acid was dissolved in TFA (5mL/1 mmol) at 0°C. Stirring for 0.5 h at 0°C and for 1.5 h at r.t., concentration under reduced pressure, coevaporation with toluene (2 x) and drying under high vacuum yielded the crude TFA salt which was used without further purification.

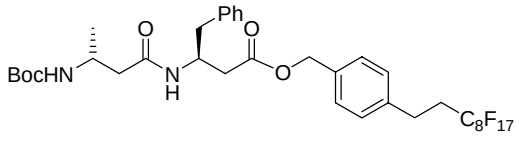
General procedure for hydrogenation of the protected tetrapeptides:

The tetrapeptide (1 mg/mL) was dissolved in EtOAc/*t*BuOH/H_2O (2:2:1) and treated with 1.5 weight equivalents Pd/C (10% Pd). H_2-gas was bubbled through the solution for 1 minute after which the mixture was stirred under a hydrogen atmosphere for 2.5 hours. The Pd/C was filtered off and the solvents were evaporated.



(*S*)-3-*tert*-Butoxycarbonylamino-4-phenyl-butyric acid 4-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-decyl)-benzyl ester 10b: To a solution of Boc-*β*^{3}hPhe-OH (1.45 g, 5.19 mmol) in CH_2Cl_2 (80 mL) and trifluorobenzene (40 mL) were added DMAP (98 mg, 0.80 mmol), 4-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)benzylalcohol

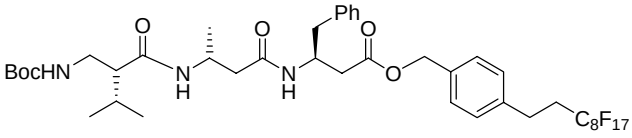
(2.22 g, 4.01 mmol) and diisopropylcarbodiimide (0.93 mL, 6.00 mmol). After stirring overnight at r.t. the reaction mixture was diluted with CH_2Cl_2 (300 mL) and washed with aq. KH_2PO_4-soln. (1 M, 75 mL), aq. K_2HPO_4-soln. (1 M, 75 mL), and brine (75 mL). The organic phase was dried ($NaSO_4$) and the solvent was removed under reduced pressure. After column chromatography on silica gel (dry loading) (CH_2Cl_2/acetone = 30:1 to 20:1) **10b** (2.83 g, 87 %) was isolated. Colorless solid. M.p. 92 – 93°C. R_f 0.47 (CH_2Cl_2/aceton = 40:1). $[\alpha]_D^{r.t.}$ = -1.8 (*c* = 0.6, EtOAc). IR ($CHCl_3$): 2980*w*, 1710*s*, 1500*s*, 1455*m*, 1370*m*, 1150*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.41 (*s*, 9 H); 2.26 – 2.46 (*m*, 2 H); 2.48, 2.56 (ABX-system, *J* = 5.8 Hz, 16.2 Hz, 1 H each); 2.80 (*dd*, *J* = 7.7 Hz, 13.7 Hz, 1 H); 2.88 – 2.97 (*m*, 1 H); 4.18 (br. *d*, *J* = 6.3 Hz, 1 H); 5.03 (*d*, *J* = 8.1 Hz, NH); 5.09 – 5.13 (AB-system, *J* = 12.2 Hz, 1 H each); 7.11 – 7.36 (*m*, 9 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 26.2 (CH_2), 28.3 (C*Me*$_3$), 32.9 (*t*, *J* = 22 Hz, CH_2), 37.7, 40.3 (2 x CH_2), 48.8 (CH), 66.1 (CH_2), 79.4 (C), 126.6, 128.5, 128.6, 128.9, 129.4 (5 x CH), 134.2, 137.6, 139.4, 155.1, 171.5 (5 x C). MALDI-MS: 854 (18, $[M + K]^+$), 830 (91, $[M + Na]^+$), 816 (1, $[M + H]^+$), 716 (100, $[M - C_5H_8O_2]^+$). MALDI-HRMS: 838.1809 $(M + Na)^+$, calc. for $C_{32}H_{30}F_{17}NO_4Na^+$: 838.1796. Anal. calc. for $C_{32}H_{30}NO_4F_{17}$ (815.57): C 47.13, H 3.71, N 1.72; found: C 46.86, H 3.65, N 1.75.



Fluorous dipeptide 12b: Dipeptide **12b** was synthesized using the general large scale protocol described above on 0.6 mmol scale. The microreactor was operated at 90°C at a pre-quench flow rate of 26.1 µL/min (residence time of 3 minutes). LCMS-analysis of the crude reaction mixture showed complete conversion of the amine and the formation of one single product. After work-up the crude product was crystallized form warm methanol (40 mL) to give 378 mg of the target compound as a white solid. The motherliquor was concentrated to give 150 mg of crude dipeptide, which was taken up in 2 mL of DMF and purified using FSPE (20 g Fluorchrom silicagel) to give another 94 mg of pure product (total yield: 91%). Colorless solid. LC-MS analysis (C18-column, 10% B in A: 2 min.; linear gradient to 100% in 9 min.; 100% B: 2 min), t_R 12.3 min. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.07 (*d*, *J* = 6.6 Hz, 3 H), 1.43 (*s*, 9 H), 2.20 – 2.60 (*m*, 6 H), 2.77 – 2.95 (*m*, 4 H), 3.86 (*m*, 1 H), 4.51 (*m*, 1 H), 5.05 – 5.16 (AB-system, *J* = 12.2 Hz, 1 H each), 5.25 (*br. s*, 1 H), 6.22 (*br. d*, *J* = 8.4 Hz, 1 H), 7.12 – 7.34 (*m*, 9 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 20.3, 26.2, 32.9 (*t*, *J* = 22 Hz, CH_2), 37.4, 40.0, 42.7, 44.1, 47.3, 66.2, 79.2, 126.6, 128.5, 128.8, 129.1, 134.0, 137.2, 139.3, 155.1, 170.0, 171.3. MALDI-MS: 939 ($[M + K]^+$), 923 ([M +

Na]$^+$), 901 ([M + H]$^+$), 801 ([M – $C_5H_8O_2$]$^+$). MALDI-HRMS: 923.2341 (M + Na)$^+$, calc. for $C_{36}H_{37}F_{17}N_2O_5Na^+$: 923.2323.

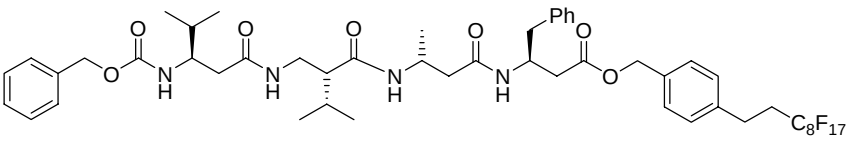
Dipeptide **12b** was deprotected as described above.



Fluorous tripeptide 14b: The condensation of the dipeptide and acid fluoride **13b** was scanned following the general protocol at 90°C and 120°C, and 0.5, 1.0, 2.0, 3.0 and 5.0 minutes reaction time.

Tripeptide **14b** was synthesized using the general large scale protocol described above on 0.4 mmol scale. The microreactor was operated at 120°C at a pre-quench flow rate of 15.66 µL/min (residence time of 5 minutes). LCMS-analysis of the crude reaction mixture showed complete conversion of the amine and the formation of the reaction product. After work-up the crude product was purified in three batches using FSPE (20 g Fluorchrom silicagel) to give the pure tripeptide (93%). Colorless solid. LCMS analysis (C18-column, 10% B in A: 2 min.; linear gradient to 100% in 9 min.; 100% B: 3 min), t_R 12.6 min. Major diastereomer: ^{1}H-NMR (300 MHz, $CDCl_3$): 0.83 – 0.96 (*m*, 7 H), 1.07 (*d*, *J* = 6.6 Hz, 3 H), 1.41 (*s*, 9 H), 1.91 – 2.05 (*m*, 2 H), 2.16 (*dd*, *J* = 5.1 Hz, 14.4 Hz, 1 H), 2.27 – 2.65 (*m*, 4 H), 2.78 – 2.95 (*m*, 4 H), 3.25 (*m*, 1 H), 3.40 (*m*, 1 H), 4.25 (*m*, 1 H), 4.56 (*m*, 1 H), 5.04 – 5.16 (AB-system, *J* = 12.2 Hz, 1 H each), 6.62 (*m*, 2 H), 7.14 – 7.35 (*m*, 9 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 19.6, 19.9, 20.9, 26.1, 28.3, 32.7 (*t*, *J* = 22, CH_2), 37.7, 40.0, 40.3, 41.7, 42.3, 47.4, 53.5, 66.3, 79.0, 126.7, 128.5, 128.9, 129.1, 133.9, 137.3, 139.4, 156.2, 170.2, 171.8, 173.1. MALDI-MS: 1052 ([M + K]$^+$), 1036 ([M + Na]$^+$), 1014 ([M + H]$^+$), 914 ([M – $C_5H_8O_2$]$^+$). MALDI-HRMS: 1036.315 (M + Na)$^+$, calc. for $C_{42}H_{48}F_{17}N_3O_6Na^+$: 1036.316.

Tripeptide **14b** was deprotected as described above.



Fluorous tetrapeptide 16b: The condensation of tripeptide and acid fluoride **15b** was scanned

following the general protocol at 120°C at 0.5, 1.0, 2.0, and 3.0 minutes reaction time using the following solutions:

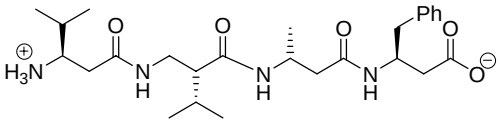
Inlet A: 2.5 mL syringe, containing a solution of the amino acid-TFA salt (0.18 M) in DMF

Inlet B: 1.0 mL syringe, containing as solution of the acid fluoride (0.9 M) in DMF

Inlet C: 1.0 mL syringe, containing a solution of NMM (1.8 M) in DMF

Inlet D: 5.0 mL syringe, containing a solution of TFA (0.54 M) and reference substance (0.018 M) in DMF

Tetrapeptide **16b** was synthesized using the large scale protocol (concentrations as mentioned above) on 0.2 mmol scale. The microreactor was operated at 120°C at a pre-quench flow rate of 52.2 μL/min (residence time of 1.5 minutes). LCMS-analysis of the crude reaction mixture showed complete conversion of the amine and the formation of the reaction product. After work-up the crude product was purified using FSPE (20 g Fluorchrom silicagel) to give the pure tetrapeptide (81% yield). ^{1}H-NMR analysis showed the presence of two rotamers, which prohibited detailed analysis. Purity of the compound was ascertained by LCMS analysis (C18-column, 10% B in A: 2 min.; linear gradient to 100% in 9 min.; 100% B: 2 min), t_R (major diastereomer): 12.8, t_R (minor diastereomer): 12.4; major:minor diastereomer = 11:1. MALDI-MS: 1199 ([M + K]$^+$), 1183 ([M + Na]$^+$), 1161 ([M + H]$^+$), 914 ([M – $C_5H_8O_2$]$^+$). MALDI-HRMS: 1183.383 (M + Na)$^+$, calc. for $C_{51}H_{57}F_{17}N_4O_7Na^+$: 1183.385.



***H*-β³hVal-β²h(*R*)Val-β³h(*R*)*Ala*-β³hPhe-OH (17)**: Tetrapeptide **16** was deprotected as described in the general hydrogenation protocol. 4-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-decyl)-toluene was removed by FSPE. The water/MeOH fraction was collected, evaporated, taken up in water and lyophilized. Fluffy white solid. LCMS analysis (C8-column, 5% B in A: 2 min.; linear gradient to 50% in 9 min.), t_R (major diastereomer): 7.7 min, t_R (minor diastereomer): 6.1 min.; major:minor diastereomer = 11:1. Purity >96%. ^{1}H-NMR (300 MHz, CD_3OD): 0.89 (*d*, *J* = 6.6, 3 H), 0.95 – 1.21 (*m*, 12 H), 1.71 – 1.86 (*m*, 1 H), 1.90 – 2.02 (*m*, 1 H), 2.10 – 2.23 (*m*, 2 H), 2.31 – 2.43 (*m*, 3 H), 2.49 (*dd*, *J* = 8.7 Hz, 15.6, 1 H), 2.66 (*dd*, *J* = 5.4 Hz, 16.2 Hz, 1 H), 2.72 (*dd*, *J* = 8.7 Hz, 13.5 Hz, 1 H), 2.89 (*dd*, *J* = 6.0 Hz, 13.7 Hz, 1 H), 3.34 – 3.42 (*m*, 1 H), 3.56 (*dd*, *J* = 3.5 Hz, 13.4 Hz, 1 H), 4.11 – 4.20 (*m*, 1 H), 4.38 – 4.48 (*m*, 1 H), 7.11 – 7.54 (*m*, 5 H). ESI-MS: 491.2 ([M + H]$^+$). MALDI-HRMS: 491.3221 (M +H)$^+$, calc. for $C_{26}H_{24}N_4O_5H^+$: 491.3228.

General procedure for the solution phase couplings:

General procedure for acid fluoride coupling.

To the appropriate *N*-deprotected amino acid (1 equiv.) dissolved in DMF (20 mL/1 mmol) was added NMM (4 equiv.) and the *N*-protected acid fluoride (2 equiv.). Reaction progress was followed by MS. When *N*-deprotected amino could not be observed anymore, the mixture was diluted with CH_2Cl_2 and washed with aq. KH_2PO_4-soln. (1 M), aq. K_2HPO_4-soln. (1 M), and brine. The organic phase was dried ($NaSO_4$) and the solvent was removed under reduced pressure. The crude peptide was purified by fluorous solid phase extraction (FSPE).

General procedure for peptide coupling using HATU.

The appropriate *N*-deprotected amino acid (1 equiv.) was dissolved in DMF (20 mL/1 mmol) and cooled in an ice-bath. To the mixture was successively added NMM (4 equiv.) and the *N*-protected amino acid (2 equiv.). To this solution HATU (1.8 equiv.) was added and the mixture was allowed to warm up to r.t. overnight. The mixture was then diluted with CH_2Cl_2 and washed with aq. KH_2PO_4-soln. (1 M), aq. K_2HPO_4-soln. (1 M), and brine. The organic phase was dried ($NaSO_4$) and the solvent was removed under reduced pressure. The crude peptide was purified by FC**.**

General procedure for the solid phase assembly of the tetrapeptide:

Procedure for anchoring N-Fmoc-protected amino acids on Wang resin; determination of loading.

Esterification of the Fmoc-protected amino acid with *Wang* resin was performed according to [1], by the MSNT/MeIm method. The resin was placed into a dried manual SPS reactor, swelled in CH_2Cl_2 (20 mL/g resin) for 1 h and washed with CH_2Cl_2. In a separate dry round-bottomed flask equipped with magnetic stirrer, the Fmoc-protected amino acid (5 equiv.) was dissolved in dry CH_2Cl_2 (5 mL/mmol), then MeIm (3.75 equiv.) and MSNT (5 equiv.) were added under Ar. Stirring was continued until the MSNT was dissolved. Thereafter, the solution was transferred using a syringe to the reaction vessel containing the resin and mixed by N_2 bubbling for 2 h. Subsequently, the resin was filtered, washed with DMF (5 mL, 5 × 1 min) 1 min) and CH_2Cl_2 (5 mL, 5 × 1 min), and dried under h. v. overnight. The resin

substitution was determined by measuring the absorbance of the dibenzofulvene-piperidine adduct: two aliquots of the Fmoc-amino acid resin were weighed exactly (m_1(resin) and m_2(resin)) and suspended in piperidine (20%) in DMF, in volumetric flasks (V_1 = V_2 = 10 mL). After 30–40 min the mixtures were transferred to a UV cell and piperidine (20%) to another UV cell (blank), and the absorbance (A) was measured at 290 nm. The concentrations (c_1 and c_2, [mM]) of the benzofulvene-piperidine adduct in soln. were determined using a calibration curve [1]. The loading (Subst.) was then calculated according to equation (1):

$$Subst_n \text{ [mmol/g resin]} = c_n \cdot V_n/\{m_n(\text{resin}) - [c_n \cdot V_n \cdot (MW - 18)/1000]\} \quad (1)$$

(MW = molecular weight of the Fmoc-protected amino acid)

The yield for the attachment to the resin (loading yield) was determined by equation (2):

$$\text{Loading yield} = [(Subst_1 + Subst_2)/2]/Subst_{theor.} \quad (2)$$

General procedure for capping.

Unreacted OH groups were capped by treating the peptide-resin with 50 mg DMAP in 5 mL DMF and 1 mL Ac_2O for 1 h under N_2-bubbling. The resin was then washed with DMF (5 mL, 5 × 1 min).

General procedure for Fmoc-deprotection.

The Fmoc-group was removed by treating the resin with 20% piperidine in DMF (4 mL, 4 × 10 min) under Ar bubbling. After filtration, the resin was washed with DMF (5 mL, 4 × 1 min).

General procedure for coupling of thę amino acids on Wang resin.

The Fmoc-deprotection was carried out according to *general procedure for Fmoc-deprotection*. Solid phase synthesis was continued by sequential incorporation of Fmoc-protected amino acids. For each coupling step, the resin was treated with a soln. of the Fmoc-protected amino acid (3 equiv.), HATU (2.8 equiv.) both in the minimal amount of DMF and *Hünig* base (6 equiv.) in DMF (20 mL/g resin) for 60 min. Monitoring of the coupling reaction was performed with the TNBS test [2]. In the case of a positive TNBS test (indicating incomplete coupling), the suspension was allowed to react further for 0.5 h. The resin was then filtered and washed with DMF (20 mL/g resin, 5 × 1 min) prior to the following

deprotection step. After the last coupling, the Fmoc group of the last amino acid was removed as previously described (*General procedure for Fmoc-deprotection*), and the resin was washed with DMF (20 mL/g resin, 5 × 1 min) and with CH_2Cl_2 (20 mL/g resin, 5 × 1 min), and dried under h. v. overnight.

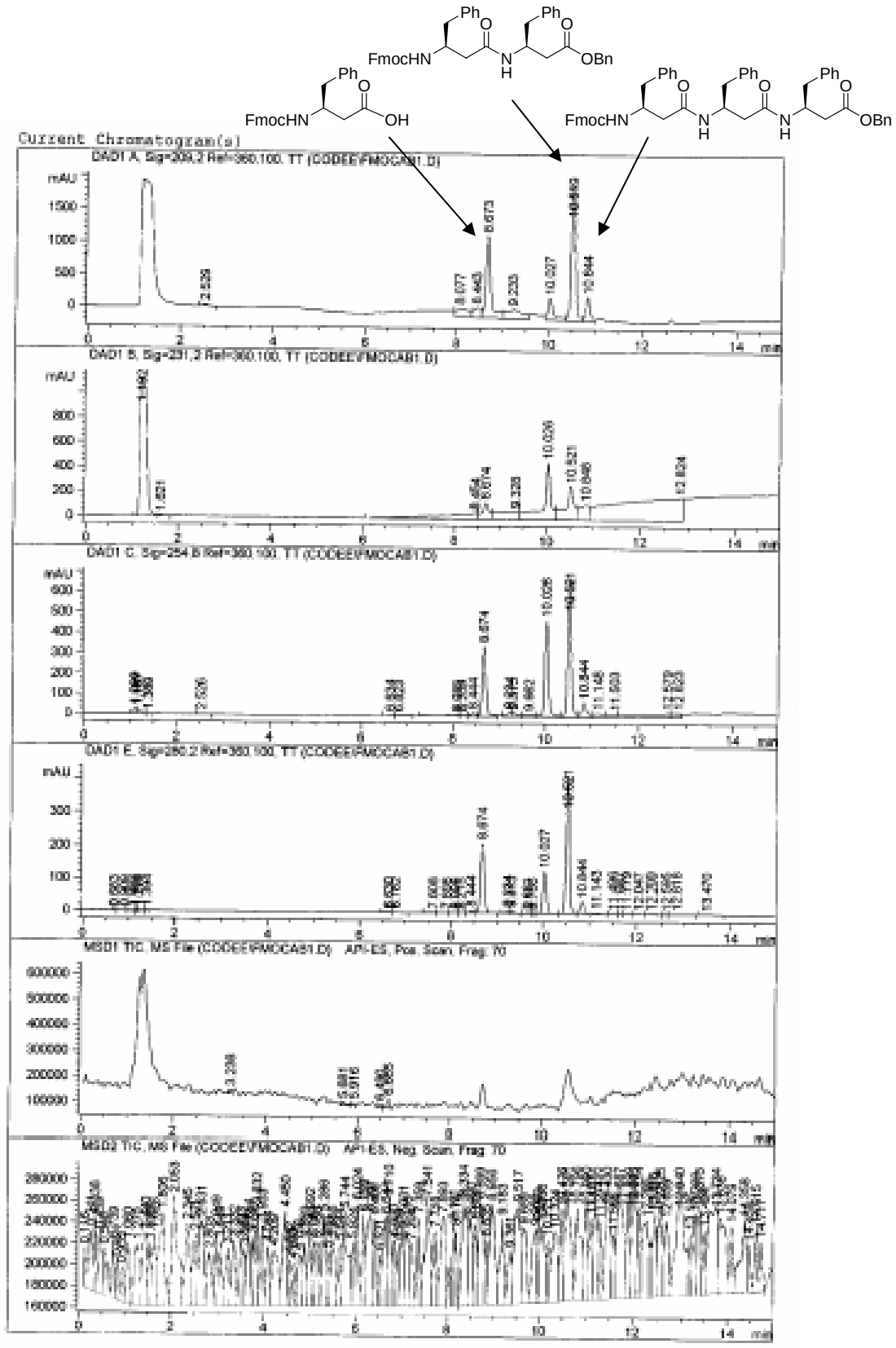
General procedure for cleavage from the Wang resin and final deprotection.

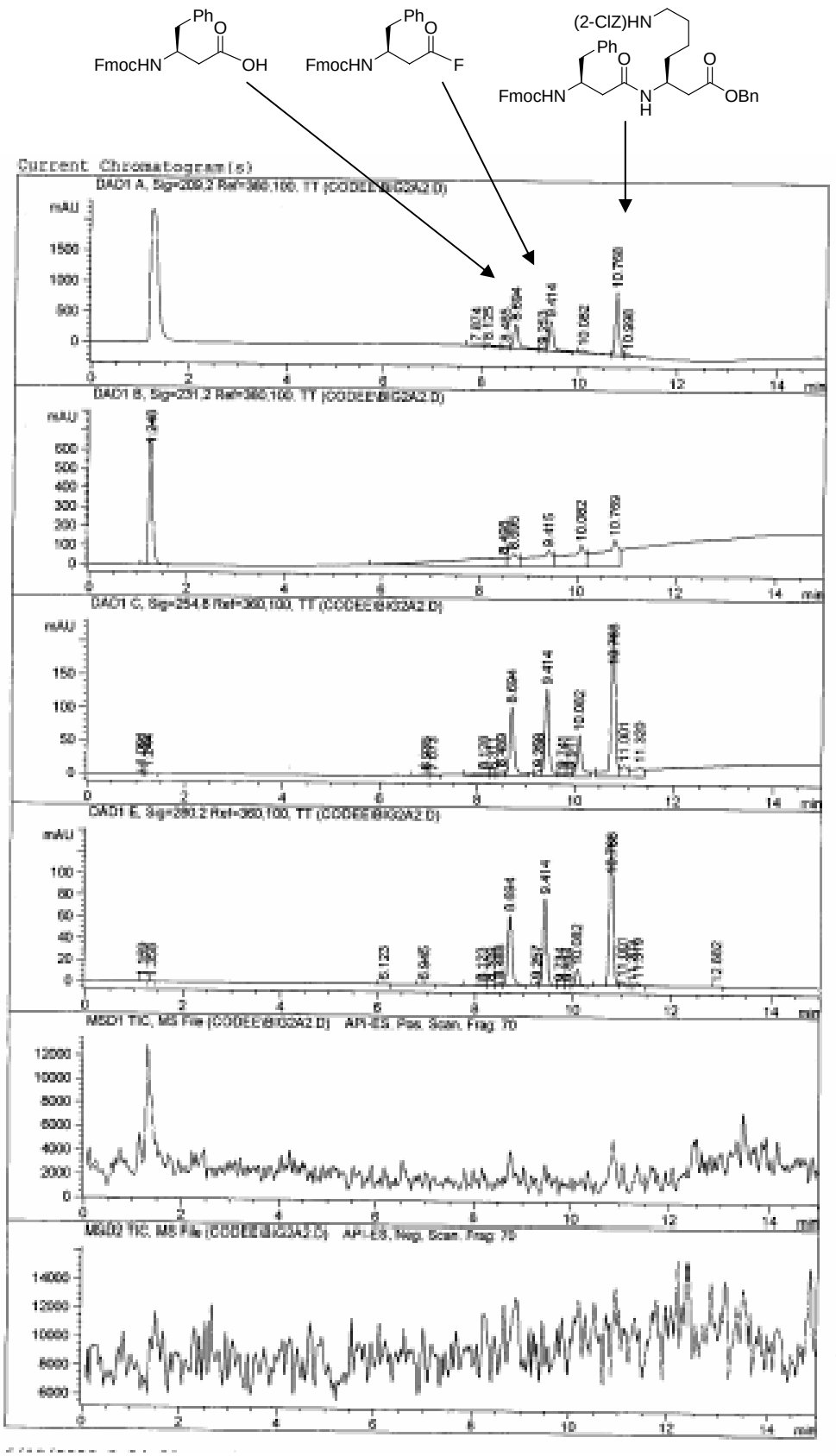
The cleavage from the resin and the peptide deprotection were performed according to [3]. The dry peptide-resin was suspended in a soln. of TFA/H_2O/TIS 95:2.5:2.5 (10 mL) for 2 h. The resin was removed by filtration, washed with TFA (2 ×), and the org. phase concentrated under reduced pressure. The resulting oily residue was treated with cold Et_2O, and the formed precipitate was separated. The crude peptide was dried under h. v. and stored at –20° before purification.

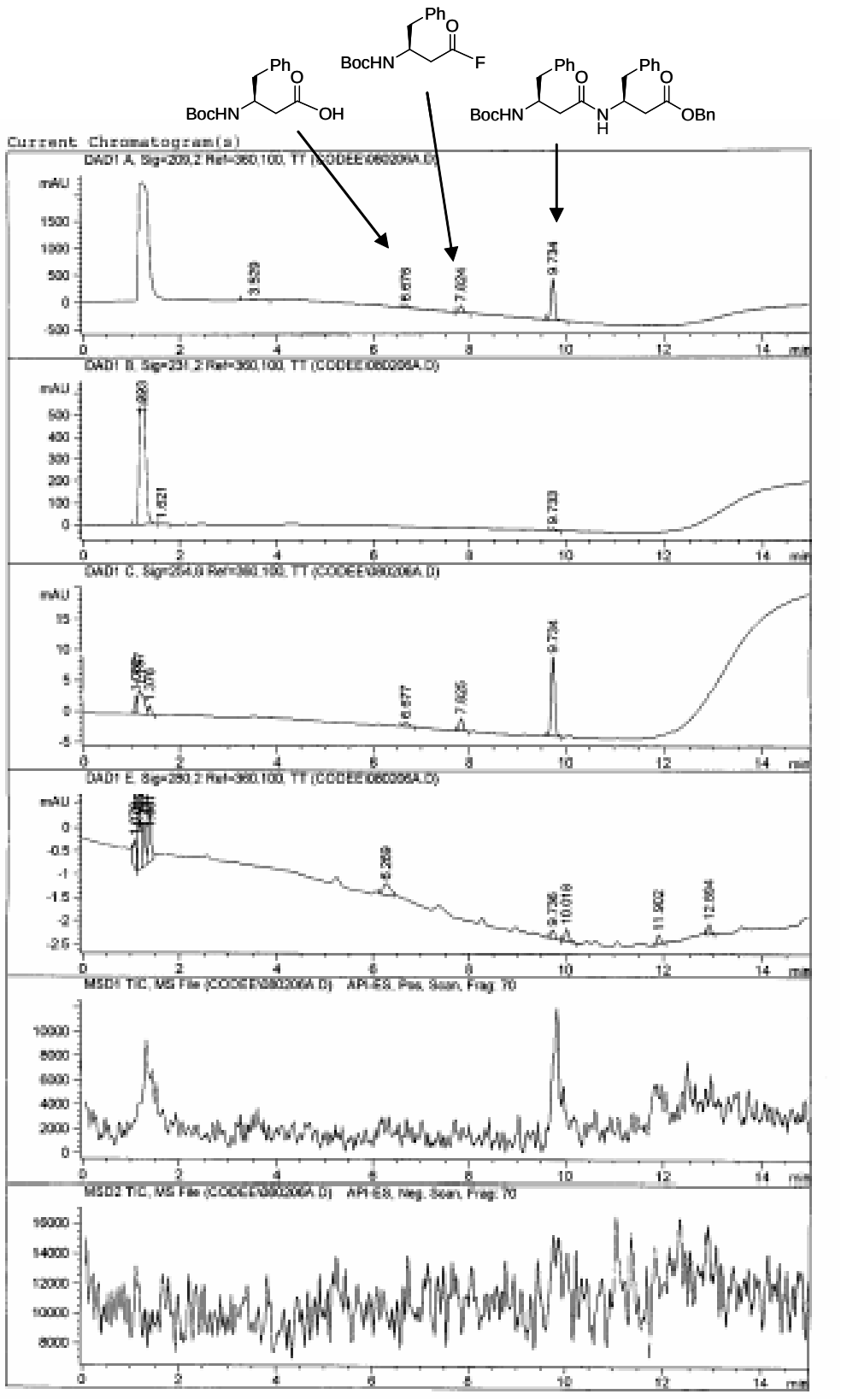
General procedure for HPLC analysis and purification of the peptides.

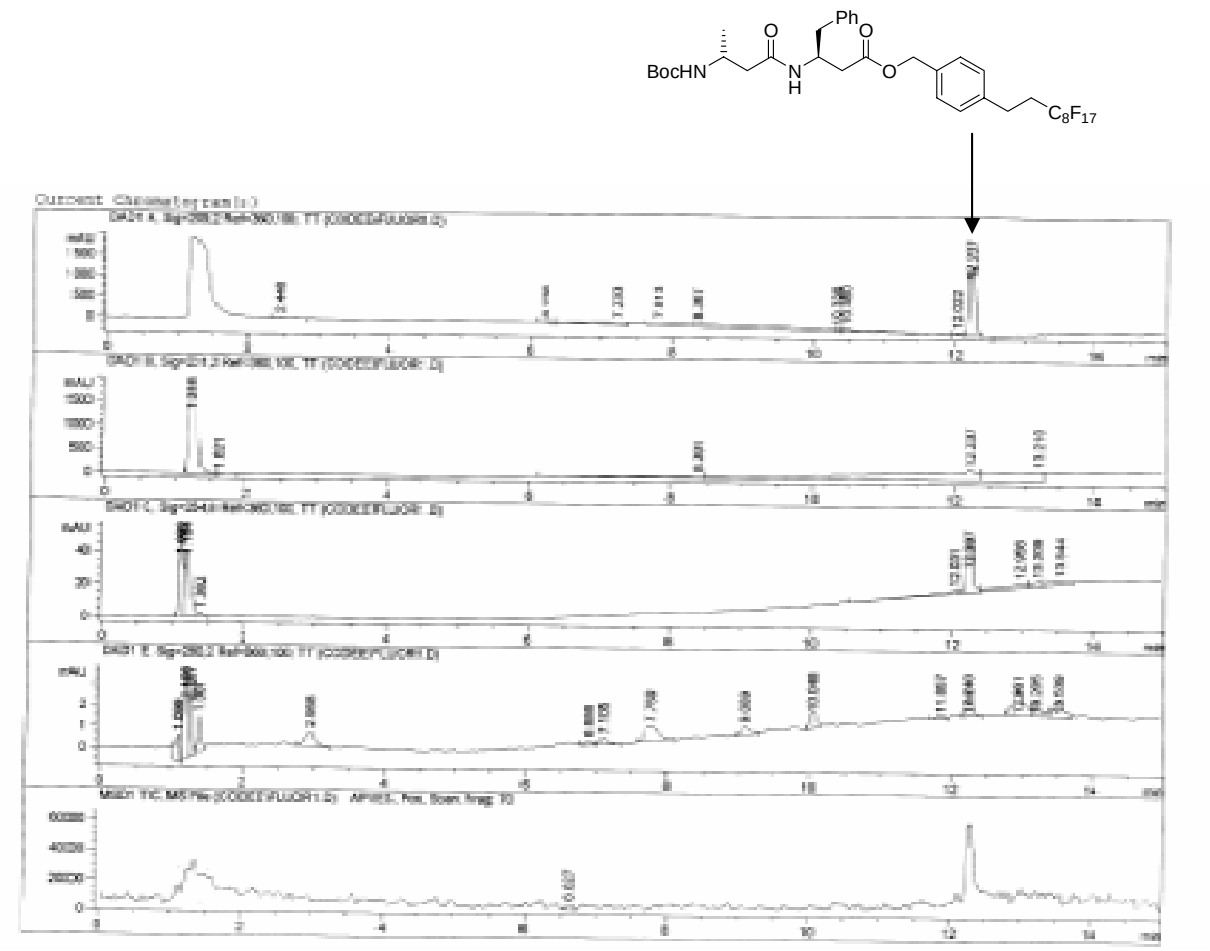
Macherey-Nagel C_8 column (*Nucleosil 100-5* C_8 (250 × 4 mm)) or *Macherey-Nagel* C_{18} column (*Nucleosil 100-5* C_{18} (250 × 4 mm)) by using a linear gradient of *A*: 0.1% TFA in H_2O and *B*: MeCN at a flow rate of 1 mL/min. Crude products were purified by prep. RP-HPLC on a *Macherey-Nagel* C_8 column (*Nucleosil 100-7* C_8 (250 × 21 mm) using gradient of *A* and *B* at a flow rate of 18 mL/min and then lyophilized.

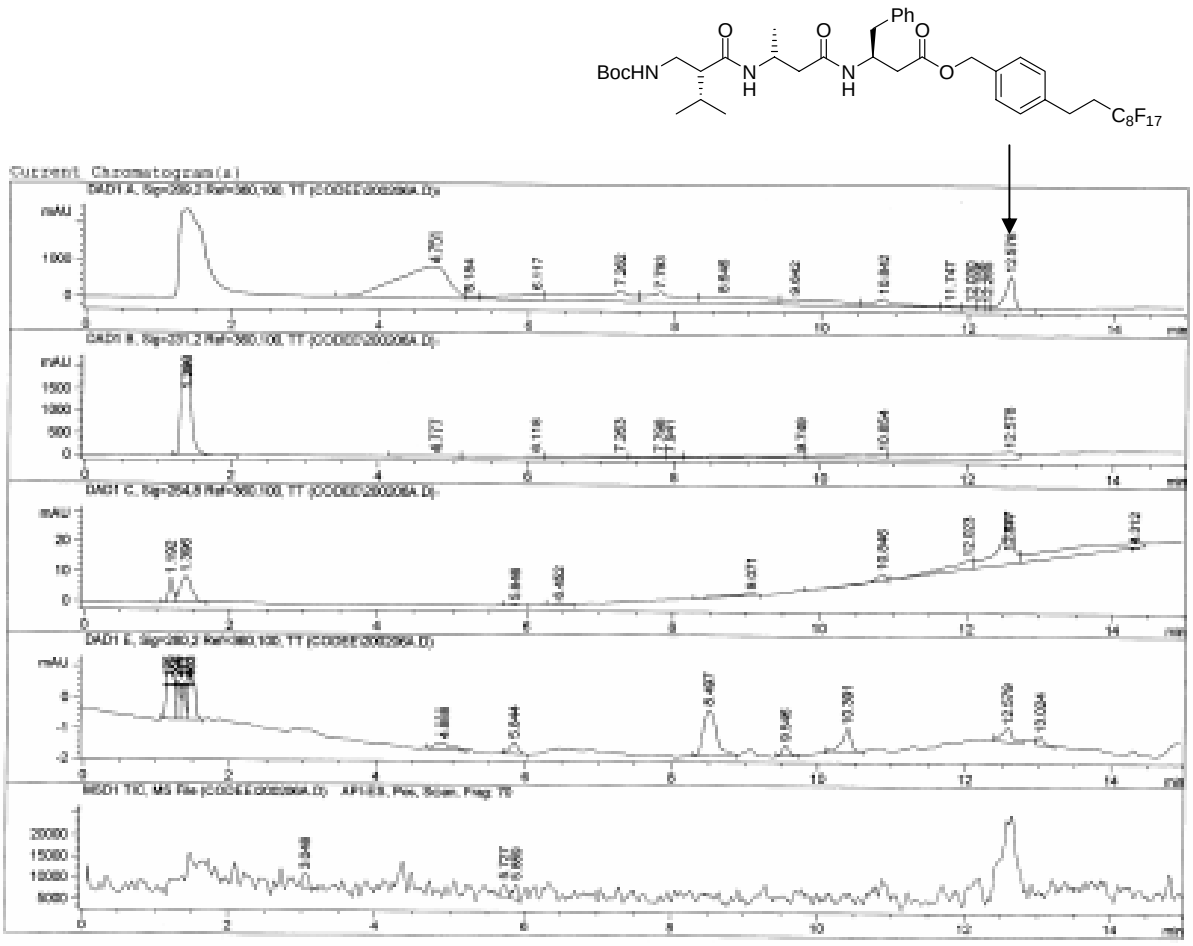
LCMS of the crude peptides:

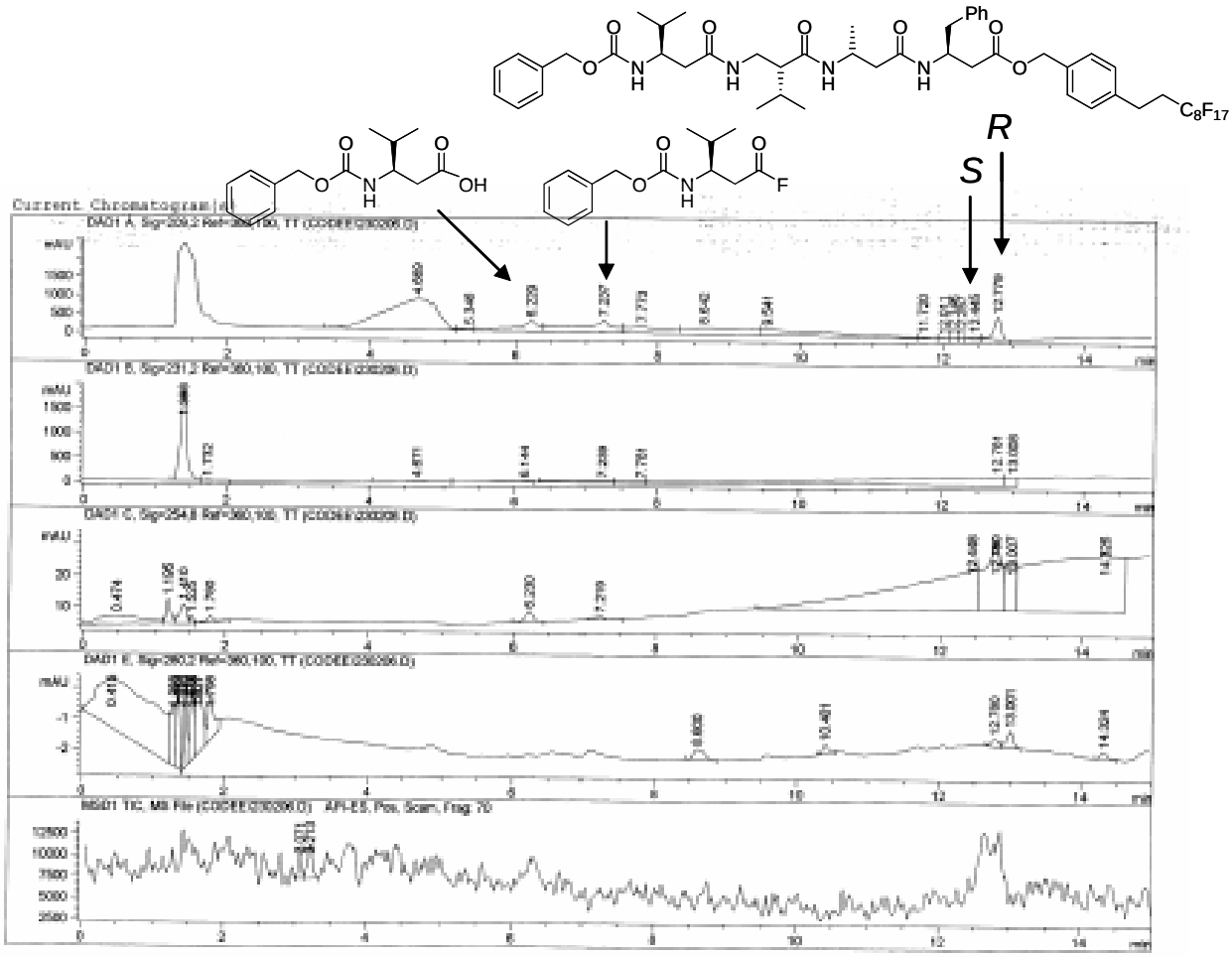



FmocHN
OH
Ph
O
FmocHN
F
Ph
O
(2-ClZ)HN
Ph
O
FmocHN
N
H
O
OBn
Current Chromatogram(s)
DAD1 A, Sig=220,2 Ref=360,100, TT (CCDEEB\G2A2.D)
DAD1 B, Sig=231,2 Ref=360,100, TT (CCDEEB\G2A2.D)
DAD1 C, Sig=254,8 Ref=360,100, TT (CCDEEB\G2A2.D)
DAD1 E, Sig=280,2 Ref=360,100, TT (CCDEEB\G2A2.D)
MSD1 TIC, MS File (CCDEEB\G2A2.D) API-ES, Pos, Scan, Frag: 70
MSD2 TIC, MS File (CCDEEB\G2A2.D) API-ES, Neg, Scan, Frag: 70

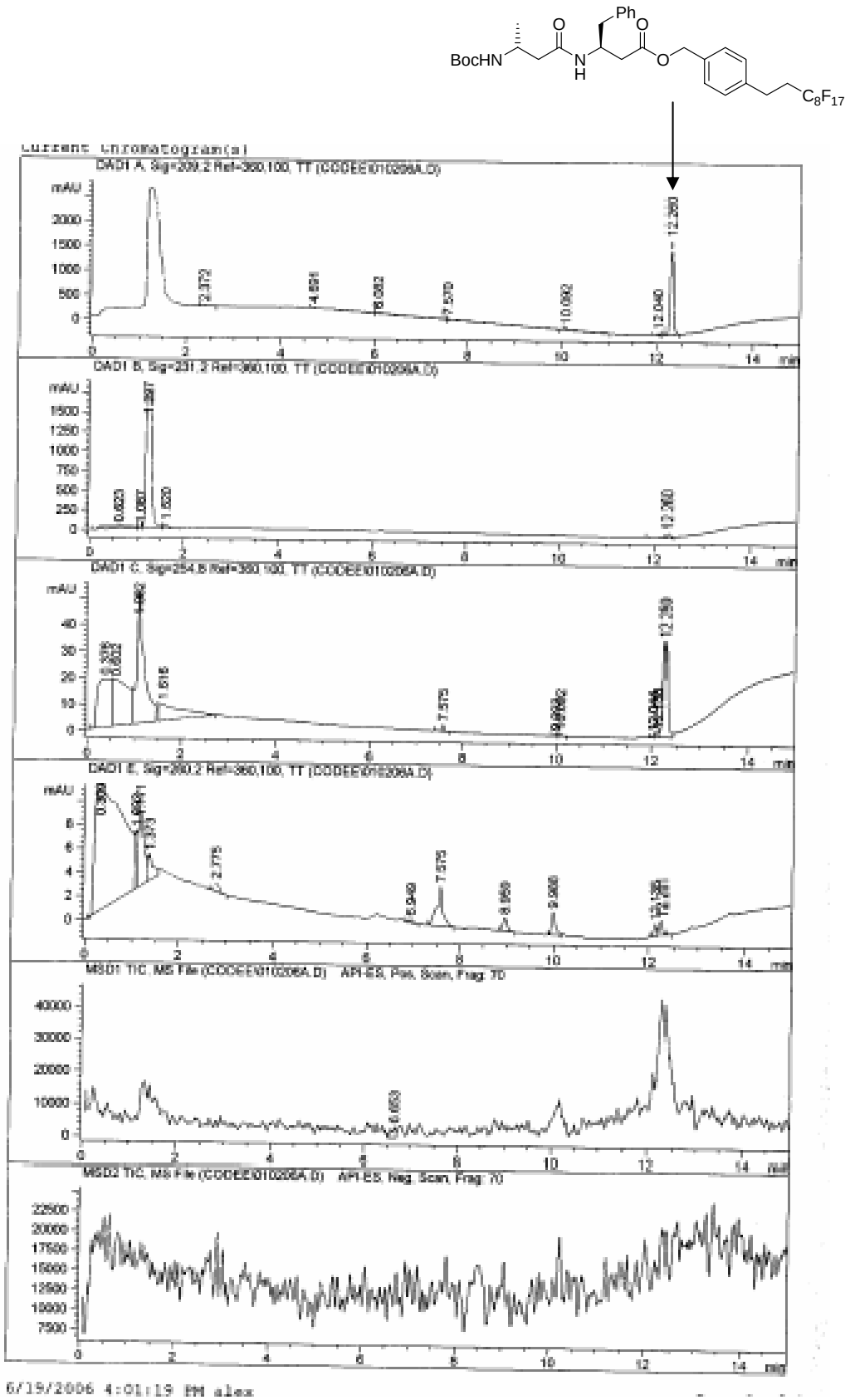

Ph
O
BocHN
F
Ph
O
BocHN
OH
Ph
O
Ph
O
BocHN
N
H
OBn
Current Chromatogram(s)
DAD1 A, Sig=220,2 Ref=360,100, TT (CODEE080206A.D)
mAU
3.529
6.676
7.624
9.734
min
DAD1 B, Sig=231,2 Ref=360,100, TT (CODEE080206A.D)
mAU
1.621
9.733
min
DAD1 C, Sig=254,0 Ref=360,100, TT (CODEE080206A.D)
mAU
6.677
7.625
9.734
min
DAD1 E, Sig=280,2 Ref=360,100, TT (CODEE080206A.D)
mAU
5.259
9.736
10.016
11.902
12.864
min
MSD1 TIC, MS File (CODEE080206A.D) API-ES, Pos, Scan, Frag: 70
min
MSD2 TIC, MS File (CODEE080206A.D) API-ES, Neg, Scan, Frag: 70
min

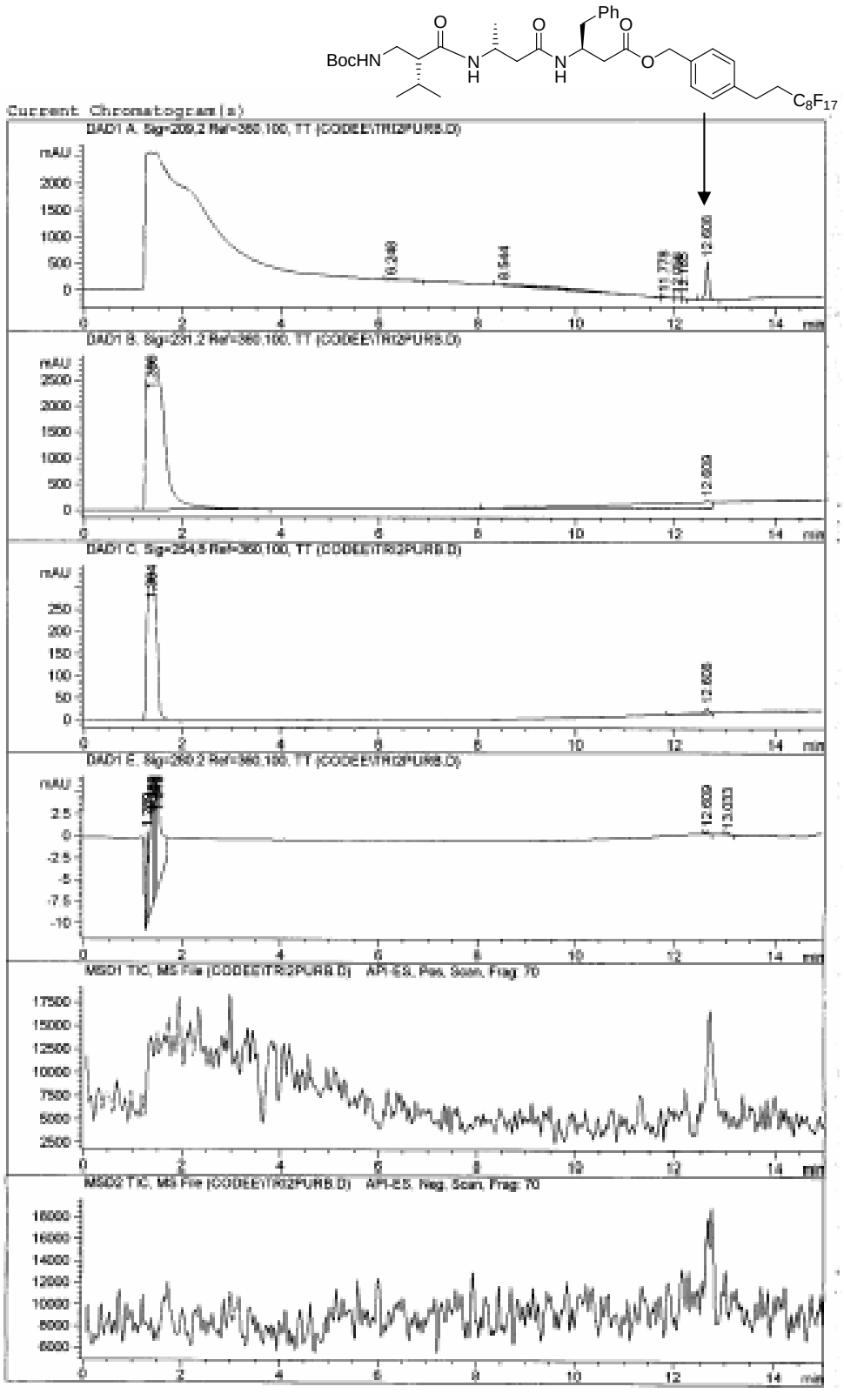

Ph
O
BocHN
N
H
O
O
C_8F_{17}

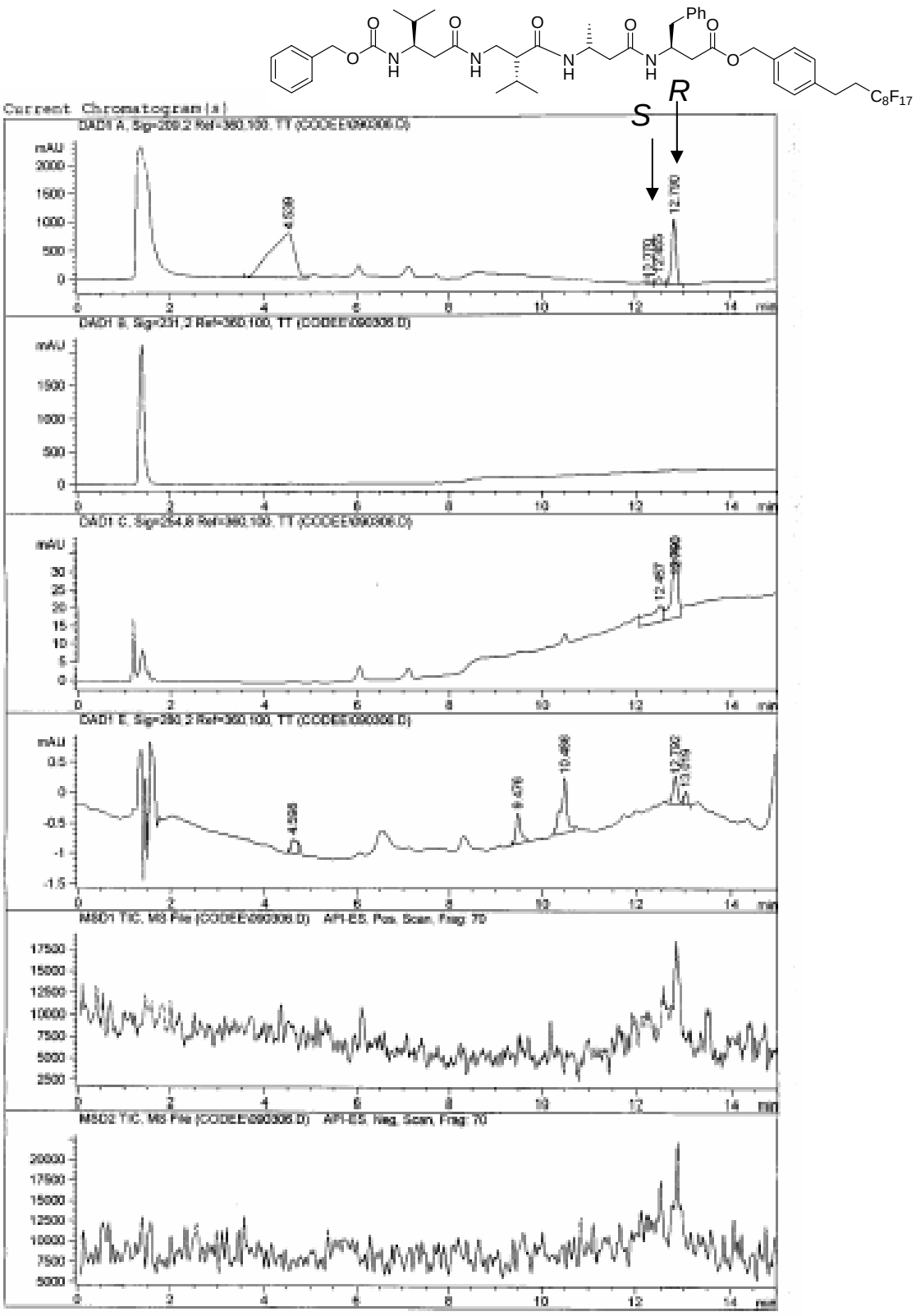

BocHN
O
N
H
O
N
H
Ph
O
O
C_8F_{17}
Current Chromatogram(s)

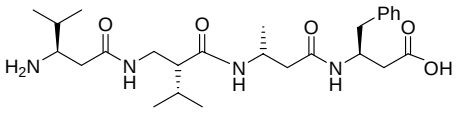

Ph
C_8F_{17}
OH
F
S
R

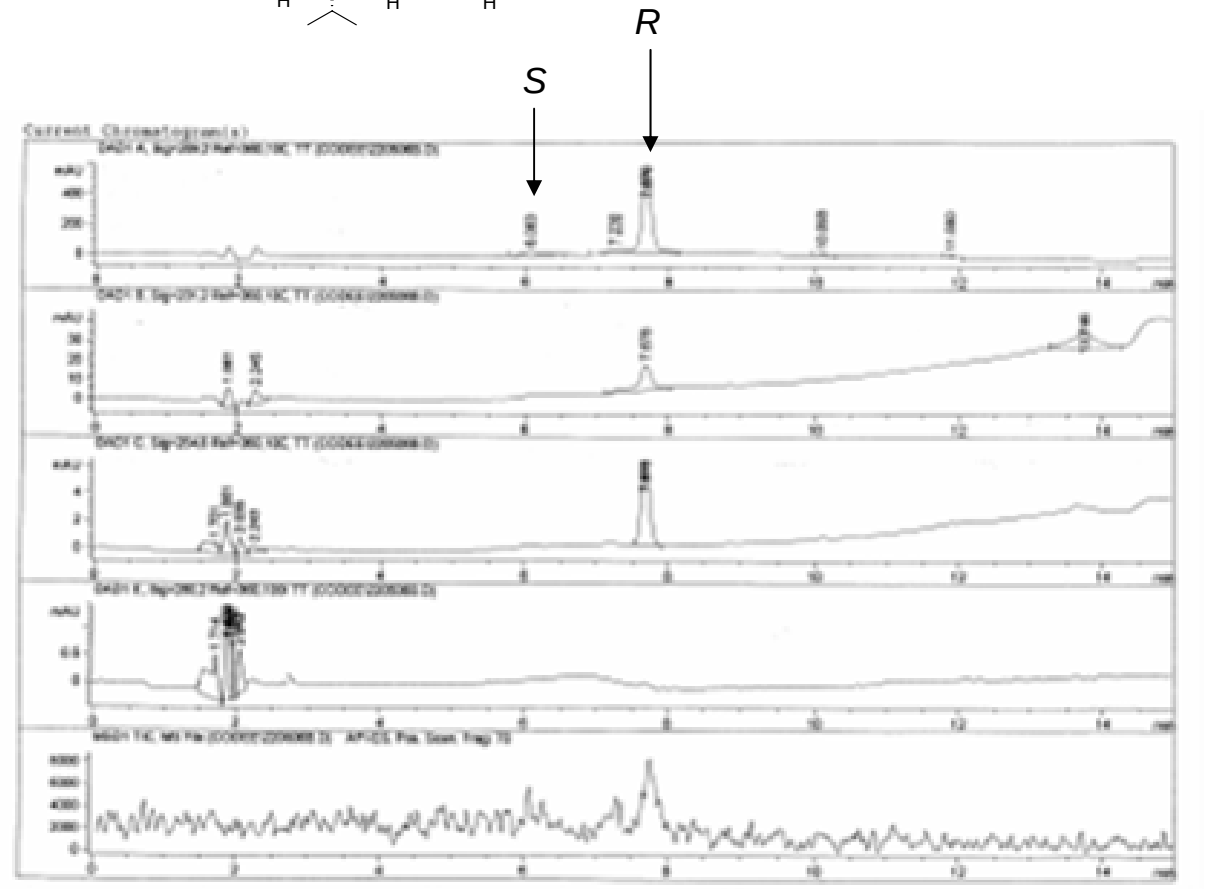
LCMS of the fluorous peptides after FSPE:




BocHN
O
N
H
O
N
H
Ph
O
O
C_8F_{17}
Current Chromatogram(s)
DAD1 A, Sig=209,2 Ref=360,100, TT (CODEE\TRI2PURB.D)
DAD1 B, Sig=231,2 Ref=360,100, TT (CODEE\TRI2PURB.D)
DAD1 C, Sig=254,8 Ref=360,100, TT (CODEE\TRI2PURB.D)
DAD1 E, Sig=280,2 Ref=360,100, TT (CODEE\TRI2PURB.D)
MSD1 TIC, MS File (CODEE\TRI2PURB.D) API-ES, Pos, Scan, Frag: 70
MSD2 TIC, MS File (CODEE\TRI2PURB.D) API-ES, Neg, Scan, Frag: 70
mAU
min


Ph
C_8F_{17}
S
R
Current Chromatogram(s)
DAD1 A, Sig=220,2 Ref=360,100, TT (CODEE\090306.D)
mAU
4.539
12.457
12.780
DAD1 B, Sig=231,2 Ref=360,100, TT (CODEE\090306.D)
mAU
DAD1 C, Sig=254,8 Ref=360,100, TT (CODEE\090306.D)
mAU
12.457
12.780
DAD1 E, Sig=280,2 Ref=360,100, TT (CODEE\090306.D)
mAU
4.558
9.476
10.466
12.790
13.169
MSD1 TIC, MS File (CODEE\090306.D) API-ES, Pos, Scan, Frag: 70
MSD2 TIC, MS File (CODEE\090306.D) API-ES, Neg, Scan, Frag: 70
min


H2N
O
N
H
O
N
H
O
N
H
Ph
O
OH


R
S

References

[1] W. C. Chan, P. D. White (Eds.), 'Fmoc Solid Phase Peptide Synthesis: A Practical Approach', *Vol. 222*, Oxford University Press, Oxford, **2000**.

[2] W. S. Hancock, J. E. Battersby, *Anal. Biochem.* **1976**, *71*, 260.

[3] Novabiochem 2002/3 catalogue: The Fine Art of Solid Phase Synthesis.