Supporting Information

Copper-catalyzed -Arylation of Semicarbazones for the Synthesis of Aryl-Azaglycine Containing Azapeptides

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Experimental section

General Methods.

Polystyrene Rink Amide resin (0.64 mmol/g, 75-100 mesh) was purchased from Advanced Chemtech™. Loading of the resin was determined by elemental analysis and standard Fmoc loading test[1]. Solid phase chemistry was performed in filtration tubes equipped with caps and stopcocks purchased from SUPELCO. 3-Iodoanisole, 4-iodoanisole, 4-iodotoluene, 1-iodo-4-fluorobenzene, and iodobenzene were purchased from Aldrich and filtered through a small plug of silica prior to use. Copper iodide was purchased from Aldrich and purified by dissolving it in a boiling saturated solution of aqueous NaI, followed by dilution with water, filtering and washing.[2] Ethylene diamine and 1,4-dioxane were freshly distilled over NaOH, followed by distillation over sodium, and stored under argon. Potassium *tert*-butoxide, *N*-methylmorpholine, and isobutyl chloroformate were purchased from Aldrich and used as received. The amino acids, Fmoc-His(Trt), Fmoc-D-Trp(Boc), Fmoc-Ala, Fmoc-Trp(Boc), Fmoc-D-Phe, FmocLys(Boc), and H-Phe-OtBu, and coupling reagents such as HBTU and diisopropylcarbodiimide (DIC) were purchased from GL Biochem™ and used as received. All solvents were obtained from VWR international. Anhydrous solvents [*N,N*-dimethylformamide (DMF), tetrahydrofuran (THF), dichloromethane (DCM)] were obtained by passage through a solvent filtration system (Glass-Contour, Irvine, CA). Analytical LCMS and HPLC analyses were performed on either a 5 µM, 150 or 50 mm x 4.6 mm C18 Phenomenex Gemini column™ with a flow rate of 0.5 mL/min using respectively a 0-80% or 0-40% gradient from pure water [0.1% formic acid (FA)] to mixtures with CH_3CN (0.1% FA) or MeOH (0.1% FA). Aza-peptides were purified on a semi-preparative column (5 µM, 250 mm x 21.2 mm, C18 Gemini column™) using respectively a 2-40% or 2-80% gradient from pure water (0.1% FA) to mixtures with MeOH (0.1% FA) at a flow rate of 10.6 mL/min. Thin-layer chromatography was performed on silica gel 60 F254 plates from Merck™.

Fmoc-based SPPS: Fmoc deprotection and HBTU couplings.

Peptide syntheses were performed under standard conditions on an automated shaker using polystyrene Rink amide resin (0.64 mmol/g, 75-100 mesh). Couplings of amino acids (3 equiv)

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[1] Novabiochem catalog, *3 : Peptide synthesis protocols*, EMD Biosciences, 2006-2007, p.3.4

[2] Armarego, W. L. F.; Perrin, D. D.; *Purification of Laboratory Chemicals*, Butterworth-Heinemann, 1996, p.381.

were performed in DMF using HBTU (3 equiv) as coupling reagent and DIEA (6 equiv). Fmoc deprotections were performed by treating the resin 2 x with 20% piperidine in DMF for 30 min. Resin was washed after each coupling and deprotection step sequentially with DMF (3 x 10 mL), MeOH (3 x 10 mL), and DCM (3 x 10 mL). The purity of peptide fragments was ascertained by LCMS analysis after cleavage and deprotection of a small aliquot of resin.

Procedure for the *N*-arylation of semicarbazone on solid support

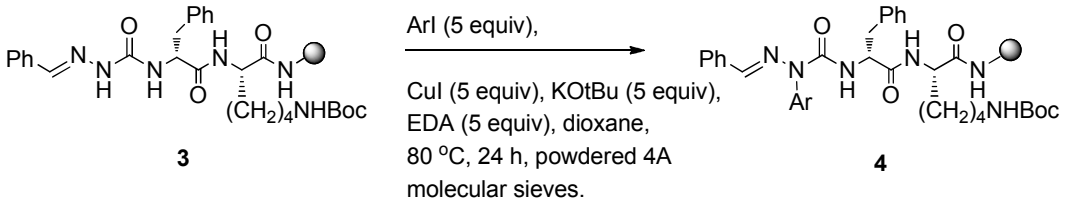
Table 1. Optimization of the N-Arylation conditions of resin bound semicarbazone **3**.

Entry	Solvent	Base	Additive	LCMS conversion (214nm) (%)
1	DMSO	Cs_2CO_3	N/A	20
2	DMSO	K_3PO_4	N/A	34
3	DMSO	K_2CO_3	N/A	34
4	DMSO	Cs_2CO_3	4-hydroxy-L-proline	49
5	DMF	Cs_2CO_3	N/A	51
6	DMF	Cs_2CO_3	Ethylene diamine[a]	49[b]
7	Dioxane	*t*BuOK	Ethylene diamine, powdered MS 4Å	75

a- Other ligands tried : L-Glycine, L-Sarcosine, L-Proline, 4-Hydroxy-L-Proline, L-Cysteine, N,N'-dimethylethylene diamine, (+/-)-trans-1,2-diaminocyclohexane.

b- Complete disappearance of starting material accompanied by formation of an unknown side product.

Representative protocol for *N*-arylation of semicarbazone on solid support



The swollen semicarbazone peptide bound resin **3** (300 mg, 0.192 mmoles) in freshly distilled dioxane was treated sequentially with the aryliodide (5 equiv, 0.96 mmoles), CuI (190 mg, 0.96 mmoles, 5 equiv), KOtBu (108 mg, 0.96 mmoles, 5 equiv), ethylene diamine (64 µL, 0.96

mmoles, 5 equiv) and powdered 4Å molecular sieves. The resin was kept under argon atmosphere throughout manipulations. The 6.0 mL SUPELCO filtration tubes were capped, sealed with parafilm, and heated in a water bath with sonication at 80 °C for 24 hours. The resin was filtered and washed under vacuum with DMF (3 x 10 mL), DMF/0.1N HCl (3:1) (3 x 10 mL), H_2O (3 x 10 mL), MeOH (3 x 10 mL), THF (3 x 10 mL), and DCM (3 x 10 mL). The extent of reaction conversion was monitored on an aliquot of resin which was subjected to TFA/TES/H_2O (95:2.5:2.5, v/v/v) for resin cleavage and the crude filtered solution was analyzed by LCMS.

Benzaldehyde semicarbazone-(benzene)-D-Phe-Lys-NH_2 (4a). LCMS (0-80% MeOH, 35 min) R.T. = 19.42 min; LCMS (ESI) calcd for $C_{29}H_{35}N_6O_3$ $[M+H]^+$, 515.2 found *m/z* 515.2. **Benzaldehyde semicarbazone-(3-anisole)-D-Phe-Lys-NH_2 (4b).** LCMS (0-80% MeOH, 35 min) R.T. = 18.91 min; LCMS (ESI) calcd for $C_{30}H_{37}N_6O_4$ $[M+H]^+$, 545.2 found *m/z* 545.2. **Benzaldehyde semicarbazone-(4-anisole)-D-Phe-Lys-NH_2 (4c).** LCMS (0-80% MeOH, 35 min) R.T. = 18.99 min; LCMS (ESI) calcd for $C_{30}H_{37}N_6O_4$ $[M+H]^+$, 545.2 found *m/z* 545.2. **Benzaldehyde semicarbazone-(4-toluene)-D-Phe-Lys-NH_2 (4d).** LCMS (0-80% MeOH, 35 min) R.T. = 19.47 min; LCMS (ESI) calcd for $C_{30}H_{37}N_6O_3$ $[M+H]^+$, 529.2 found *m/z* 529.2.
Benzaldehyde semicarbazone-(4-fluorobenzene)-D-Phe-Lys-NH_2 (4e). LCMS (0-80% MeOH, 35 min) R.T. = 18.74 min; LCMS (ESI) calcd for $C_{29}H_{34}N_6O_3F$ $[M+H]^+$, 533.2 found *m/z*533.2. **Benzaldehyde semicarbazone-(3-indole)-D-Phe-Lys-NH_2 (4f).** LCMS (0-80% MeOH, 35 min) R.T. = 19.91 min; LCMS (ESI) calcd for $C_{31}H_{36}N_7O_3$ $[M+H]^+$, 554.2 found *m/z* 554.2.
Benzaldehyde semicarbazone-(5-imidazole)-D-Phe-Lys-NH_2 (4g). LCMS (0-80% MeOH, 35 min) R.T. = 16.41 min; LCMS (ESI) calcd for $C_{36}H_{33}N_8O_3$ $[M+H]^+$, 439.2 found *m/z* 439.2. **Benzaldehyde semicarbazone-(benzene)-Ala-Trp-D-Phe-Lys-NH_2 (9a).** LCMS (0-80% MeOH, 35 min) R.T. = 19.10 min; LCMS (ESI) calcd for $C_{43}H_{50}N_9O_5$ $[M+H]^+$, 772.4 found *m/e* 772.4.**Benzaldehyde semicarbazone-(3-anisole)-Ala-Trp-D-Phe-Lys-NH_2 (9b).** LCMS (0-80% MeOH, 35 min) R.T. = 19.51 min; LCMS (ESI) calcd for $C_{44}H_{52}N_9O_6$ $[M+H]^+$, 802.4 found *m/e* 802.4. **Benzaldehyde semicarbazone-(4-anisole)-Ala-Trp-D-Phe-Lys-NH_2 (9c).** LCMS (0-80% MeOH, 35 min) R.T. = 19.45 min; LCMS (ESI) calcd for $C_{44}H_{52}N_9O_6$ $[M+H]^+$, 802.4 found *m/e* 802.4. **Benzaldehyde semicarbazone-(4-toluene)-Ala-Trp-D-Phe-Lys-NH_2 (9d).**

LCMS (0-80% MeOH, 35 min) R.T. = 19.91 min; LCMS (ESI) calcd for $C_{44}H_{52}N_9O_5$ $[M+H]^+$, 786.4 found *m/e* 786.4. **Benzaldehyde semicarbazone-(4-fluorobenzene)-Ala-Trp-D-Phe-Lys-NH_2 (9e).** LCMS (0-80% MeOH, 35 min) R.T. = 19.27 min; LCMS (ESI) calcd for $C_{43}H_{49}N_9O_5F$ $[M+H]^+$, 790.3 found *m/e* 790.4. **Benzaldehyde semicarbazone-(3-indole)-Ala-Trp-D-Phe-Lys-NH_2 (9f).** LCMS (0-80% MeOH, 35 min) R.T. = 19.46 min; LCMS (ESI) calcd for $C_{45}H_{51}N_{10}O_5$ $[M+H]^+$, 811.4 found *m/e* 811.4.

Representative protocol for deprotection of semicarbazone on solid support

Resin-bound semicarbazone **4** (300 mg, 0.192 mmoles) was treated with a solution of 1.5 M $NH_2OH{\cdot}HCl$ in pyridine (5 mL) and heated with sonication at 60°C for 12 h. The resin was filtered and washed under vacuum with 10% DIEA:DMF (3 x 10 mL), DMF (3 x 10 mL), MeOH (3 x 10 mL), THF (3 x 10 mL), and DCM (3 x 10 mL). The extent of reaction conversion was monitored on an aliquot (3 mg) of resin which was subjected to 1 mL of TFA/TES/H_2O (95:2.5:2.5, v/v/v) for resin cleavage and the crude was analyzed by LCMS. The procedure was repeated twice in cases where LCMS analysis revealed incomplete deprotection.

Characterization of [aza-arylgly] GHRP-6 aza-peptides (6a-g, 10a-f, R=H)

His-D-Trp-Ala-aza(phenylglycine)-D-Phe-Lys-NH_2 (6a). LCMS (0-80% MeOH, 35 min) R.T. = 9.53 min; (0-80% MeCN, 20 min) R.T. = 8.4 min; HRMS Calcd *m/z* for $C_{42}H_{53}N_{12}O_6$ $[M+H]^+$ 821.4205, found 821.4217. **His-D-Trp-Ala-aza(*o*-anisole)-D-Phe-Lys-NH_2 (6b).** LCMS (0-80% MeOH, 35 min) R.T. = 10.35 min; (0-40% MeCN, 35 min) R.T. = 14.17 min; HRMS Calcd *m/z* for $C_{43}H_{55}N_{12}O_7$ $[M+H]^+$ 851.4311, found 851.4293. **His-D-Trp-Ala-aza(*p*-anisole)-D-Phe-Lys-NH_2 (6c).** LCMS (0-80% MeOH, 35 min) R.T. = 10.21 min; (0-80% MeCN, 35 min) R.T. = 8.41 min; HRMS Calcd *m/z* for $C_{43}H_{55}N_{12}O_7$ $[M+H]^+$ 851.4311, found 851.4307. **His-D-Trp-Ala-aza(*p*-toluene)-D-Phe-Lys-NH_2 (6d).** LCMS (0-80% MeOH, 35 min) R.T. = 10.34 min; (0-40% MeCN, 35 min) R.T. = 14.53 min; HRMS Calcd *m/z* for $C_{43}H_{55}N_{12}O_6$ $[M+H]^+$ 835.4362, found 835.4352. **His-D-Trp-Ala-aza(*p*-fluoro benzene)-D-Phe-Lys-NH_2 (6e).** LCMS (0-80% MeOH, 35 min) R.T. = 9.77 min; (0-40% MeCN, 35 min) R.T. = 13.79 min; HRMS Calcd *m/z* for $C_{42}H_{52}FN_{12}O_6$ $[M+H]^+$ 839.4111, found 839.4107. **His-D-Trp-Ala-aza(indoyl)-D-Phe-Lys-NH_2 (6f).** LCMS (0-80% MeOH, 35 min) R.T. = 10.50 min; (0-80% MeCN, 35 min) R.T. = 8.62 min; HRMS Calcd *m/z* for $C_{44}H_{53}N_{13}O_6$ $[M+H]^+$ 860.4314, found 860.4321. **His-D-Trp-Ala-**

aza(imidazoyl)-D-Phe-Lys-NH_2 (6g). LCMS (0-80% MeOH, 35 min) R.T. = 7.84 min; (0-80% MeCN, 35 min) R.T. = 7.31 min; HRMS Calcd *m/z* for $C_{39}H_{51}N_{14}O_6$ $[M+H]^+$ 811.4111, found 811.4081. **His-Aza(phenylglycine)-Ala-Trp-D-Phe-Lys-NH_2 (10a).** LCMS (0-80% MeOH, 35 min) R.T. = 8.51 min; (0-40% MeCN, 35 min) R.T. = 11.50 min; HRMS Calcd *m/z* for $C_{42}H_{53}N_{12}O_6$ $[M+H]^+$ 821.4206, found 821.4204. **His-Aza(*o*-anisole)-Ala-Trp-D-Phe-Lys-NH_2 (10b).** LCMS (0-80% MeOH, 35 min) R.T. = 10.18 min; (0-40% MeCN, 35 min) R.T. = 12.90 min; HRMS Calcd *m/z* for $C_{43}H_{55}N_{12}O_7$ $[M+H]^+$ 851.4311, found 851.4296. **His-Aza(*p*-anisole)-Ala-Trp-D-Phe-Lys-NH_2 (10c).** LCMS (0-80% MeOH, 35 min) R.T. = 10.10 min; (0-80% MeCN, 35 min) R.T. = 7.39 min; HRMS Calcd *m/z* for $C_{43}H_{55}N_{12}O_7$ $[M+H]^+$ 851.4311, found 851.4301. **His-Aza(*p*-toluene)-Ala-Trp-D-Phe-Lys-NH_2 (10d).** LCMS (0-80% MeOH, 35 min) R.T. = 9.39 min; (0-80% MeCN, 35 min) R.T. = 7.61 min; HRMS Calcd *m/z* for $C_{43}H_{55}N_{12}O_6$ $[M+H]^+$ 835.4362, found 835.4359. **His-Aza(*p*-fluoro benzene)-Ala-Trp-D-Phe-Lys-NH_2 (10e).** LCMS (0-80% MeOH, 35 min) R.T. = 8.83 min; (0-80% MeCN, 35 min) R.T. = 7.43 min; HRMS Calcd *m/z* for $C_{42}H_{52}FN_{12}O_6$ $[M+H]^+$ 839.4111, found 839.4105. **His-Aza(indoyl)-Ala-Trp-D-Phe-Lys-NH_2 (10f).** LCMS (20-80% MeOH, 35 min) R.T. = 12.96 min; (0-80% MeCN, 35 min) R.T. = 11.65 min; HRMS Calcd *m/z* for $C_{44}H_{53}N_{13}O_6Na$ $[M+Na]^+$ 882.4134, found 882.4121.

CD Spectroscopy

All CD spectra were recorded on a Chirascan CD Spectrometer (Applied Photophysics, Leatherhead, United Kingdom) using a 1.0 cm path-length quartz cell containing 20 μM of peptide dissolved in Milli-Q water. The experimental settings were: 1 nm, bandwidth; 0.5 nm, step size; 3 sec, sampling time.

Benzylidene aza-glycinyl-phenylalaninyl *tert*-butyl ester

A solution of *p*-nitrophenylchloroformate (2.37 g, 10 mmol) in 100 mL of dry dichloromethane at 0 ^oC was treated dropwise with a solution of benzaldehyde hydrazone (1.2 g, 10 mmol) in 100 mL of dry dichloromethane. The ice bath was removed and the reactive mixture was allowed to warm to room temperature. After one hour, the solution was cooled back to 0 ^oC prior to addition of a premixed solution of phenylalanine *tert*-butyl ester hydrochloride (2.84 g, 10 mmol) and DIEA (1.9 mL, 20 mmol) in dry dichloromethane (30 mL). After stirring overnight, the crude

reactive mixture was concentrated under vacuum and purified using a gradient of 10% to 50% Et_2O in petroleum ether to give a yellow oil (1.68 g, 46%): R_f 1.75 (1:1 Et_2O : petroleum ether); $[\alpha]_D^{20}$ 61.25 (c 2.40, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46 (9H, s), 3.14-3.19 (2H, m), 4.56-4.62 (1H, m), 5.68 (1H, d, *J* = 6.2 Hz), 7.21-7.37 (7H, m), 8.21-8.26 (2H, m).^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 156.6, 153.3, 136.5, 130.3, 129.4, 128.1, 125.9, 122.8, 83.8, 56.1, 39.1, 28.8. HRMS *m/z* 368.19762, $(M+H)^+$ calcd for $[C_{21}H_{26}N_3O_3]^+$: 368.19687.

Benzylidene aza-glycinyl-phenylalanine

Benzylidene aza-glycinyl-phenylalaninyl *tert*-butyl ester (1.3 g, 3.54 mmol) was dissolved in 20 mL of a 1:1 mixture of dichloromethane and TFA and stirred at room temperature for 30 min, when complete disappearance of starting material was observed by TLC. Evaporation of the volatiles yielded a light brown solid that was used without further purification (935mg, 86%): R_f 0.11 (8 : 2 hexanes: EtOAc); $[\alpha]_D^{20}$ 86.7 (c 0.83, $CHCl_3$); mp 133.0 – 135.3 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.22 (1H, q, *J* = 6.4, 14.0 Hz), 3.34 (1H, q, *J* = 5.3, 14.1 Hz), 4.79 (1H, q, *J* = 6.4, 13.7 Hz), 5.57 (1H, d, *J* = 8.2 Hz), 7.09-7.41 (8H, m), 8.22-8.27 (2H, m).^{13}C NMR (100 MHz, $CDCl_3$) δ 175.4, 155.0, 152.3, 144.6, 134.5, 128.9, 128.6, 127.2, 124.8, 121.6, 54.3, 37.2.

Benzylidene aza-glycinyl-phenylalaninyl isopropylamide

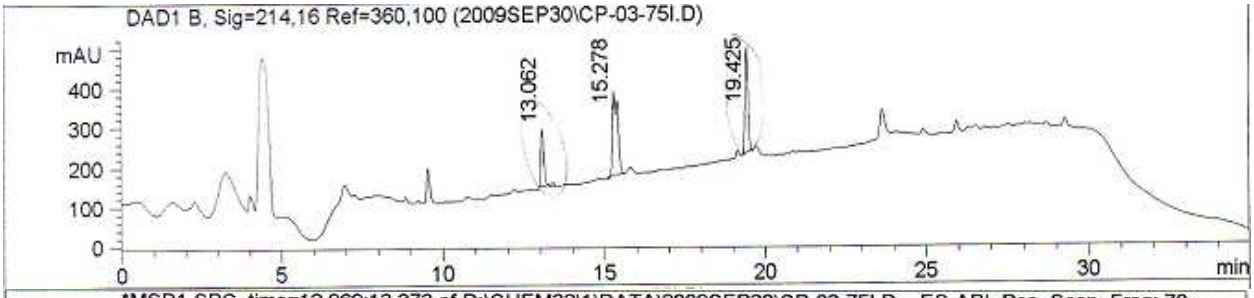
Benzylidene aza-glycinyl-phenylalanine (724 mg, 2.33 mmol) was dissolved in 30 mL of dry THF, cooled to -15 ^{o}C, and treated sequentially with isobutyl chloroformate (0.35 mL, 2.67 mmol) and *N*-methylmorpholine (0.26 mL, 2.33 mmol). The reaction was monitored by TLC. After 20 min, complete disappearance of the starting material and appearance of the activated intermediate was observed by TLC, R_f 0.97 (10% MeOH in DCM). Isopropyl amine was added in one portion to the reaction, which was stirred for an additional hour. The volatiles were removed under vacuum, and the residue was redissolved in EtOAc and extracted three times each with 5% $NaHCO_3$ and 5% citric acid. The organic layer was dried over $MgSO_4$, filtered and concentrated to a residue that was purified on a column of silica gel using a gradient of 10 to 35% EtOAc in hexanes to give benzylidine aza-glycinyl-phenylalaninyl isopropyalmide as a white solid (682 mg, 83%) : R_f 0.50 (1 : 1 hexanes: EtOAc); $[\alpha]_D^{20}$ 4.41 (c 0.77, MeOH); mp 150.2 – 153.6 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.94 (3H, d, *J* = 6.5 Hz), 1.05 (3H, d, *J* = 6.5 Hz), 3.04 (1H, q, *J* = 8.8, 13.4 Hz), 3.21 (1H, q, *J* = 5.8, 13.4 Hz), 3.95-3.97 (1H, m), 4.01-4.39

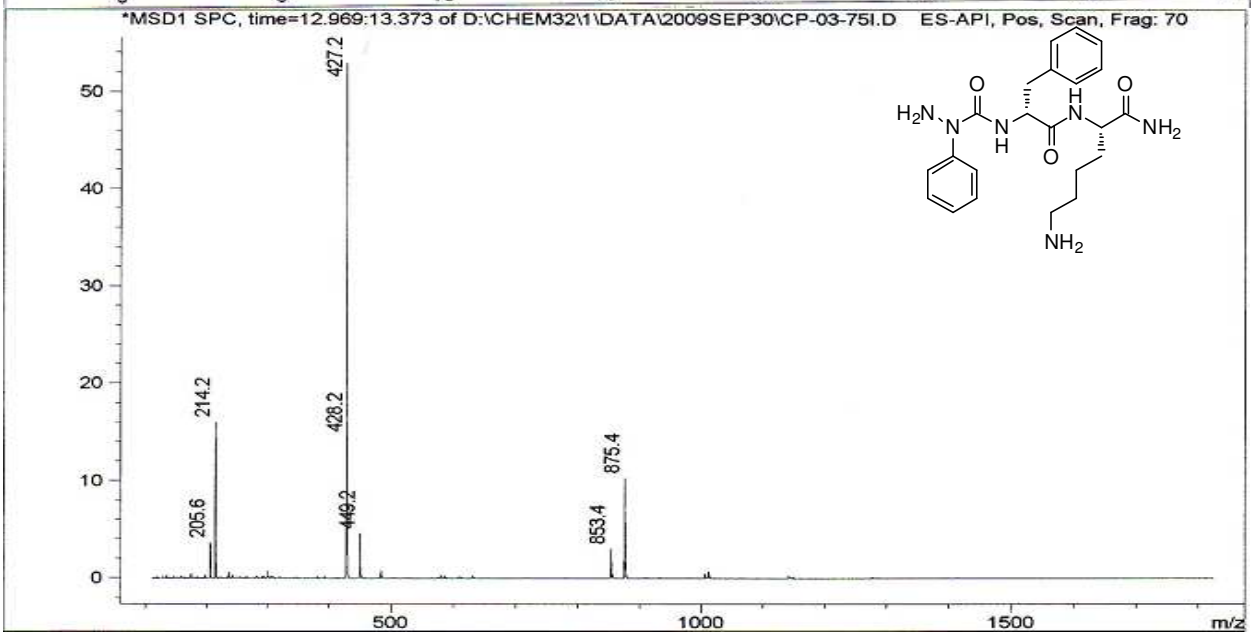
(1H, m), 5.36 (1H, d, J = 7.6), 6.26 (1H, d, J = 8.0), 7.22-7.37 (7H, m), 8.22-8.25 (2H, m) .^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 155.3, 152.2, 144.5, 135.8, 129.0, 128.5, 126.9, 125.8, 124.7, 121.6, 115.2, 56.4, 41.4, 39.2, 22.1, 21.9. HRMS *m/z* 353.1977, $(M+H)^+$ calcd for $[C_{20}H_{25}N_4O_2]^+$: 353.1972.

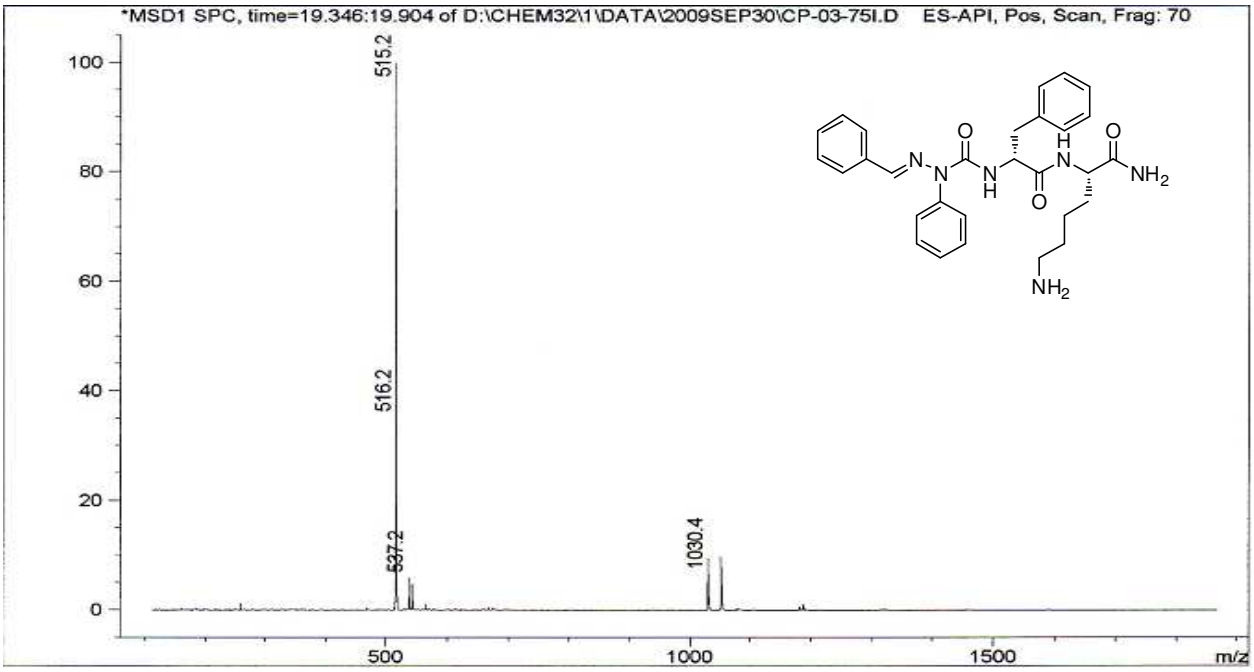
Aza-toluylglycine-phenylalaninyl isopropyl amide

Benzylidine aza-glycinyl-phenylalaninyl isopropylamide (200 mg, 0.57 mmol) was dissolved in 5 mL of freshly distilled dioxane in a flame-dried 10 mL round bottom flask. Potassium *tert*-butoxide (127 mg, 1.14 mmol), copper iodide (108 mg, 0.57 mmol), ethylene diamine (76 µL, 1.14 mmol), and 4-iodotoluene (149 mg, 0.68 mmol) were added to the flask in succession and the mixture was heated at reflux at 80 ^{o}C. After 12 h, the reactive mixture was cooled to room temperature and filtered through a pad of silica. The filtrate was evaporated under reduced pressure and the resulting oil was chromatographed on silica gel using 10% EtOAc in hexanes. Evaporation of the collected fractions gave aza-toluylglycine-phenylalaninyl isopropyl amide as a white solid (40 mg, 20%): R_f 0.79 (1 : 1 hexanes: EtOAc); $[\alpha]_D^{20}$ 93.8 (c 0.58, $CHCl_3$); mp 109.2 – 112.9 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.13-1.17 (6H, m), 2.39 (3H, s), 3.13-3.27 (2H, m), 4.09-4.18 (1H, m), 4.77 (1H, t, J = 4.17 Hz), 6.91-6.96 (2H, m), 7.17-7.27 (5H, m), 7.35-7.38 (2H, m) .^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 154.7, 135.4, 134.1, 130.8, 130.7, 129.0, 128.1, 121.9, 60.3, 44.5, 34.7, 21.7, 20.0, 19.9.

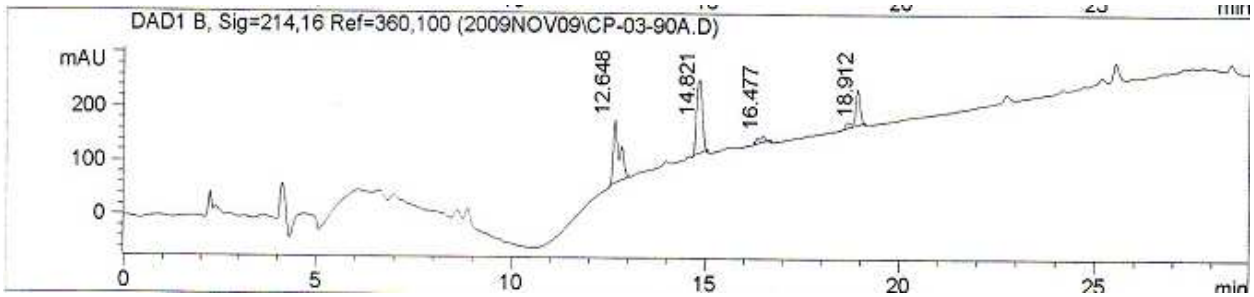
Benzaldehyde semicarbazone-(benzene)-D-Phe-Lys-NH_2 (4a):

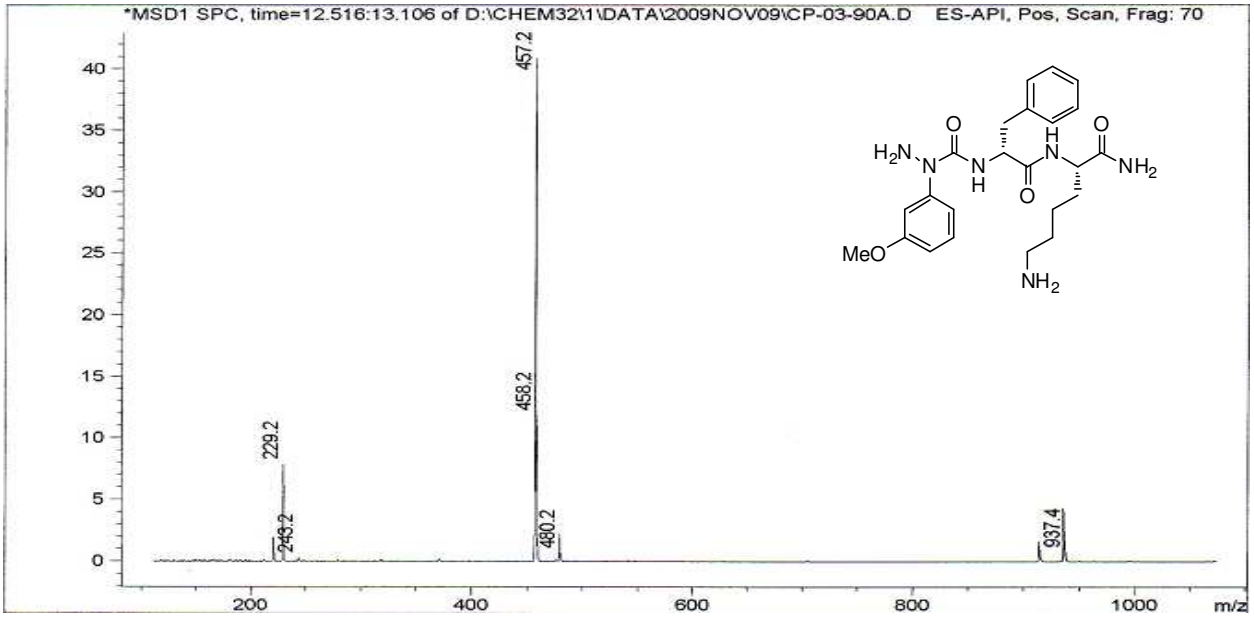


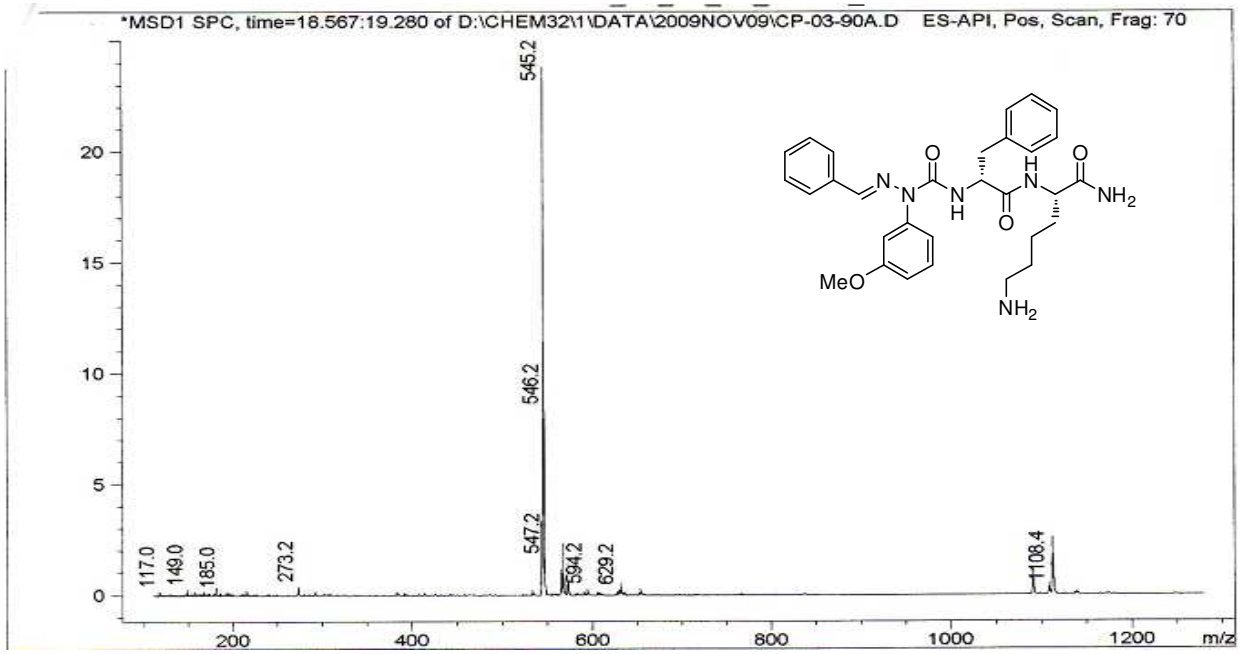




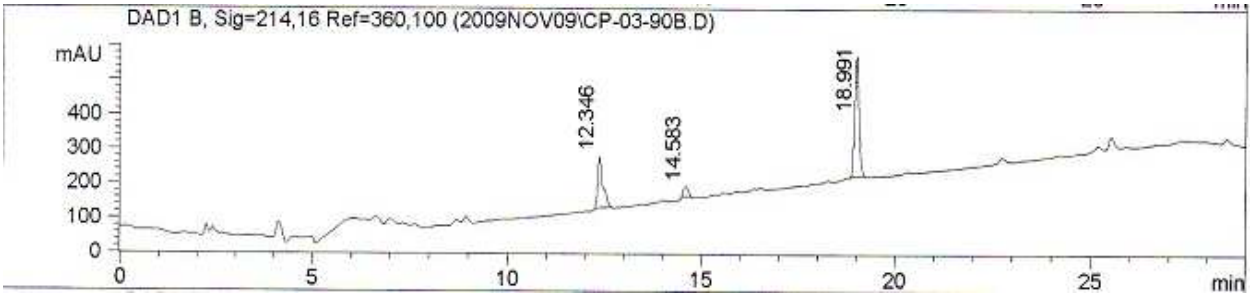
Benzaldehyde semicarbazone-(3-anisole)-D-Phe-Lys-NH_2 (4b)

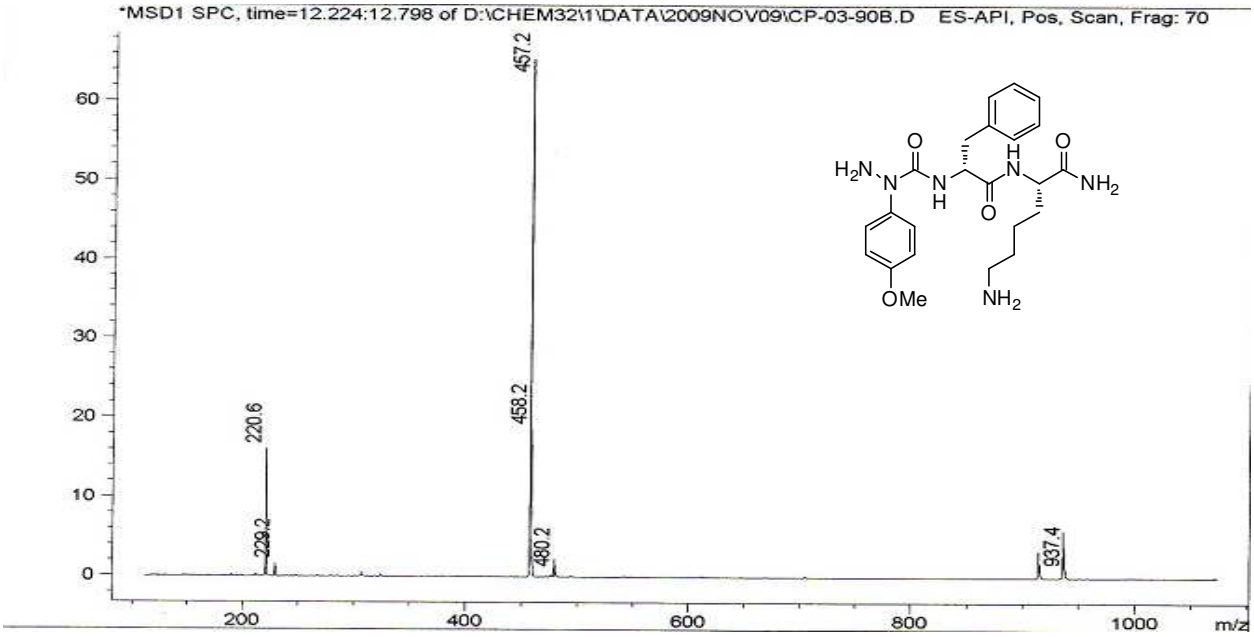


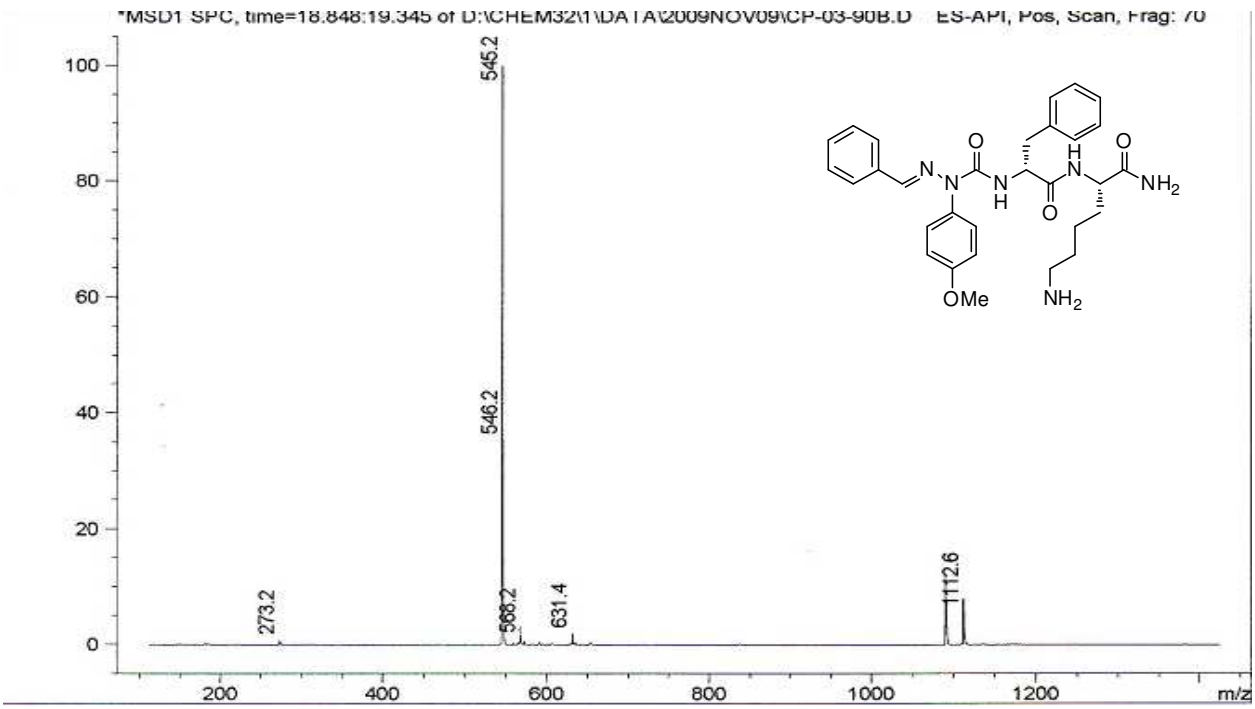




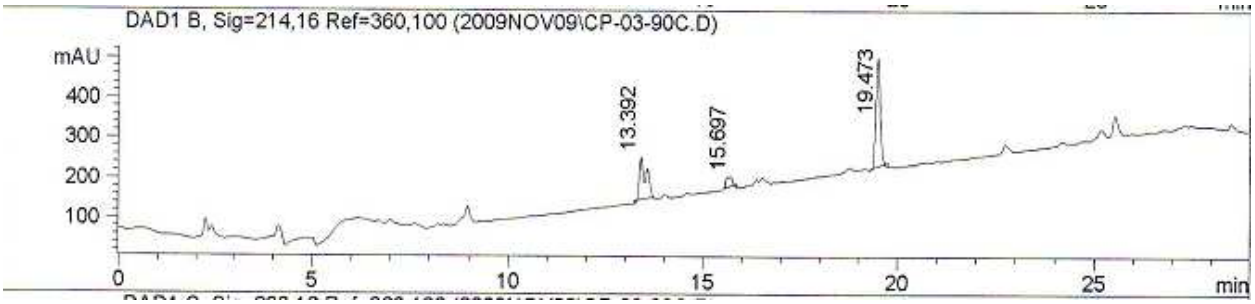
Benzaldehyde semicarbazone-(4-anisole)-D-Phe-Lys-NH_2 (4c)

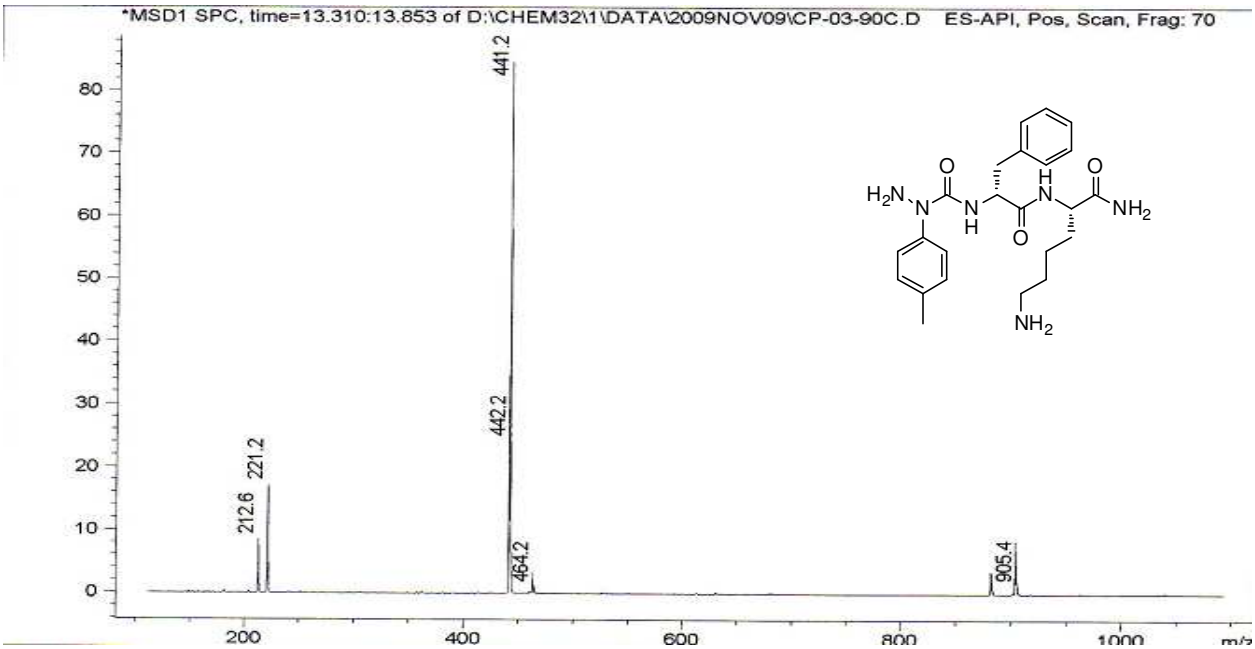


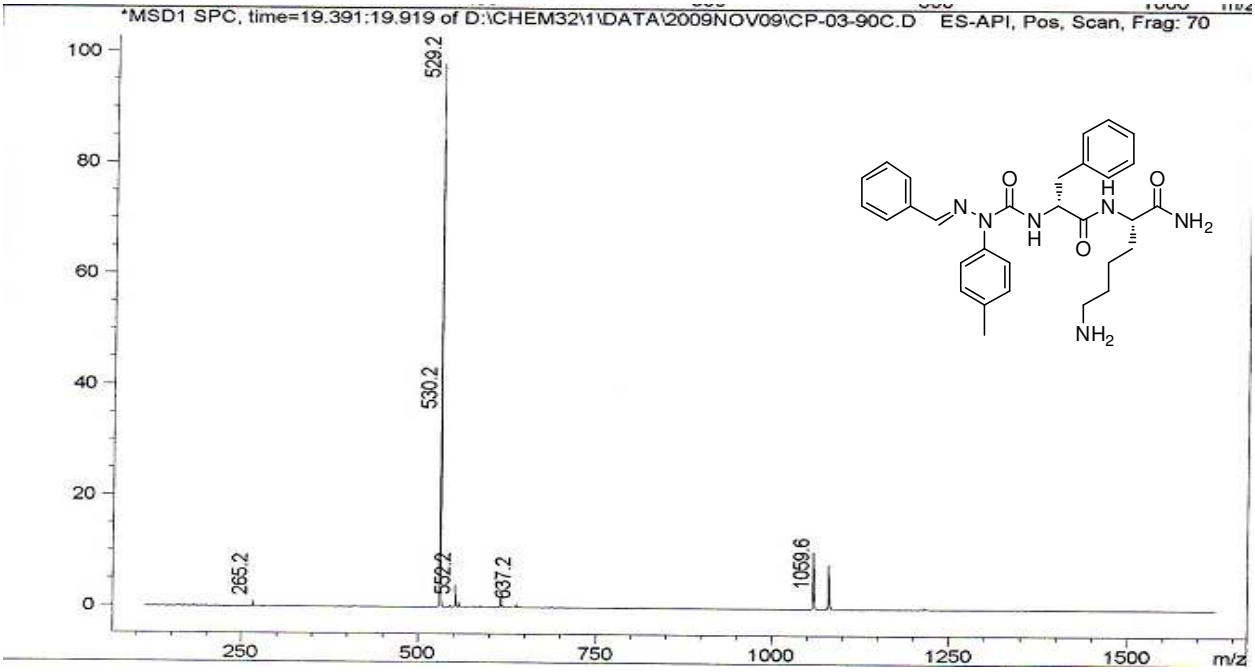




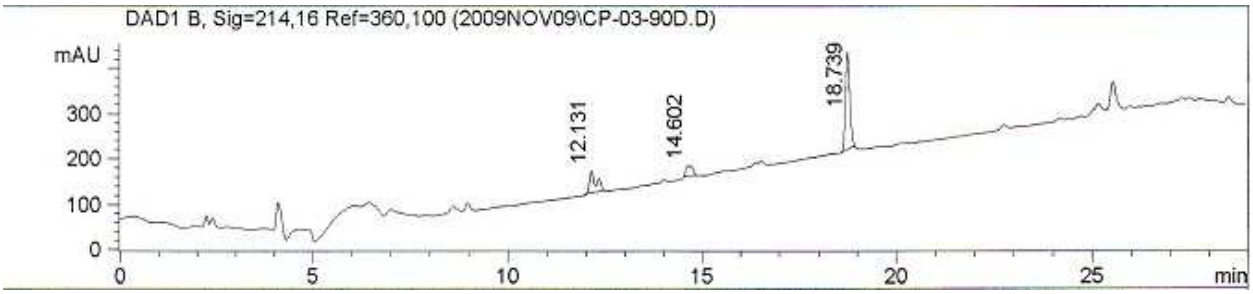
Benzaldehyde semicarbazone-(4-toluene)-D-Phe-Lys-NH_2 (4d)

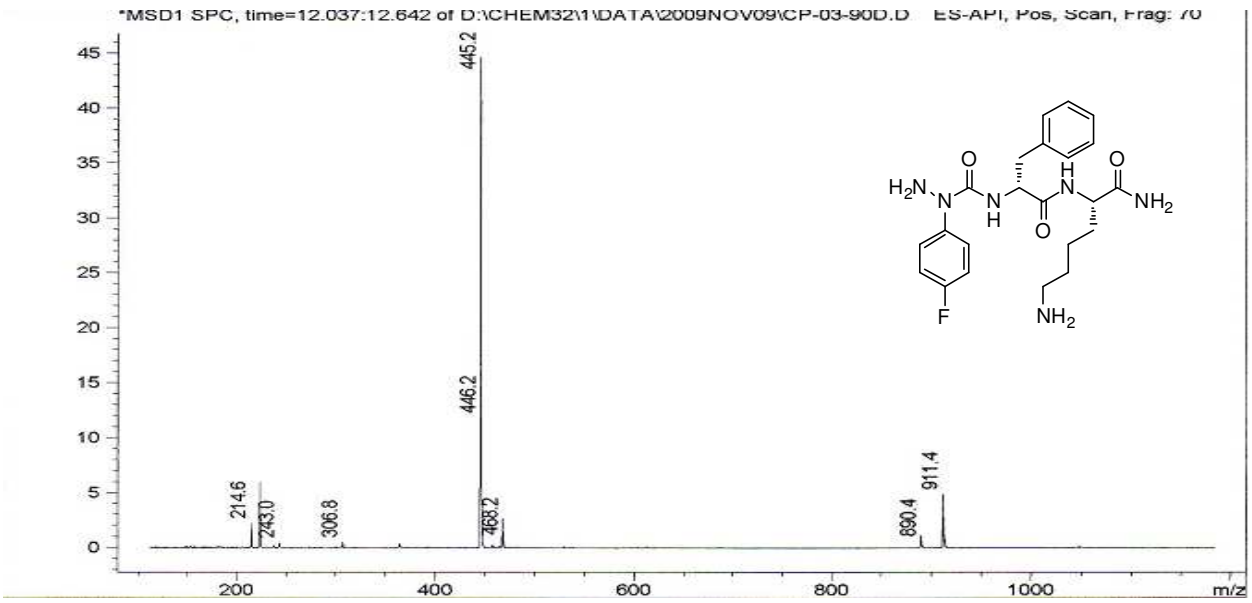


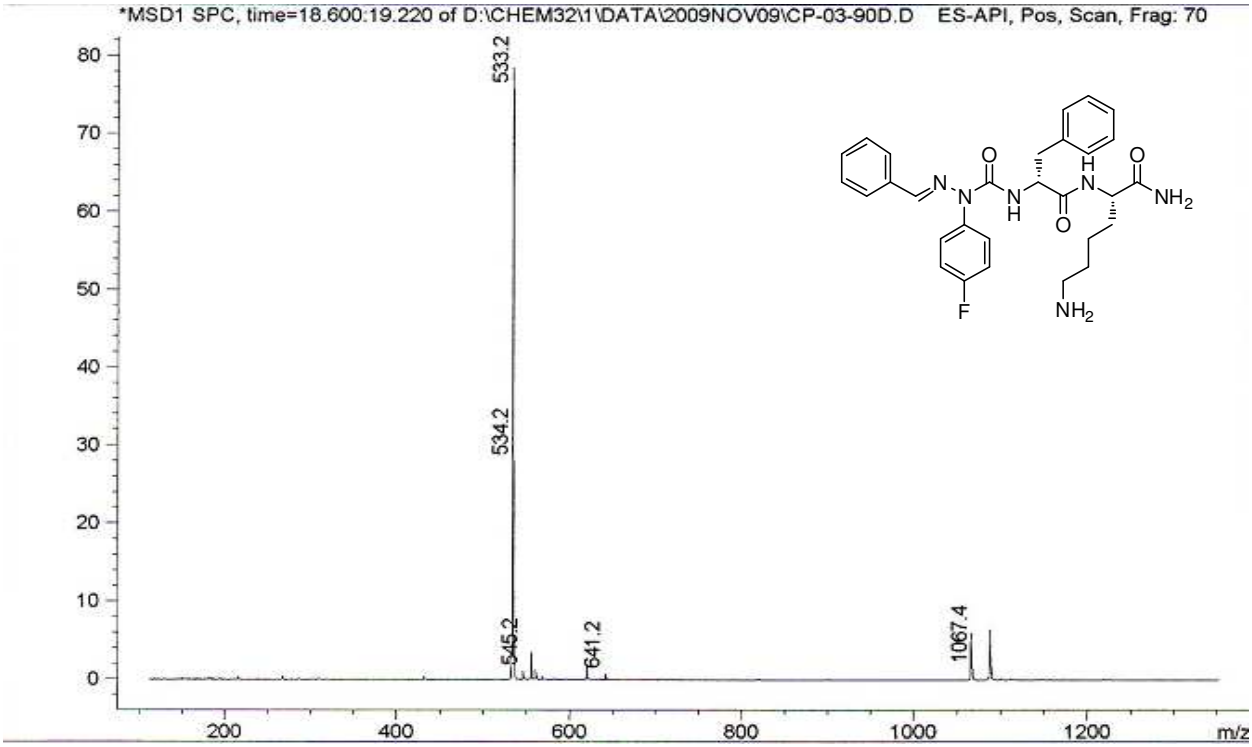




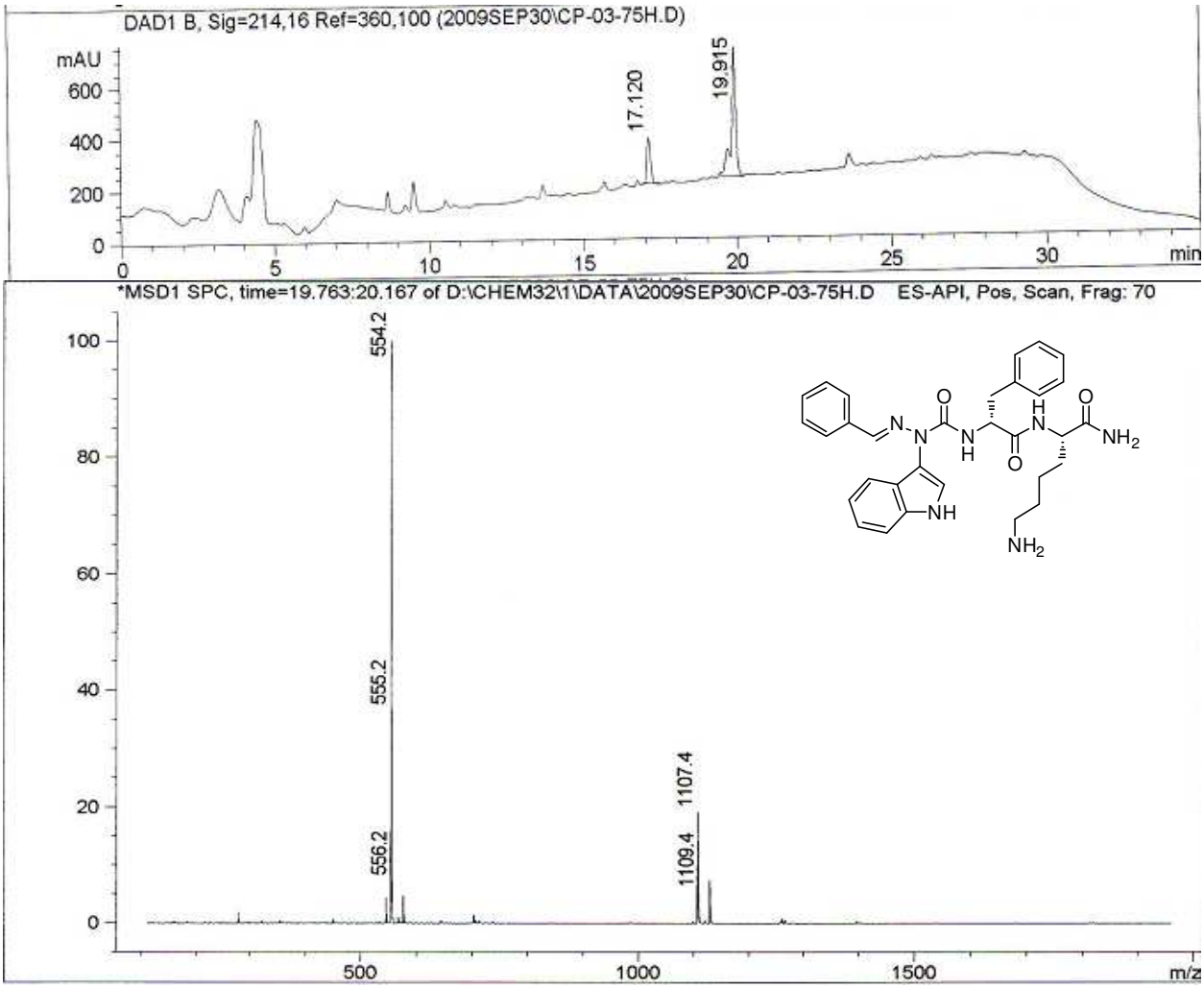
Benzaldehyde semicarbazone-(4-fluorobenzene)-D-Phe-Lys-NH_2 (4e)



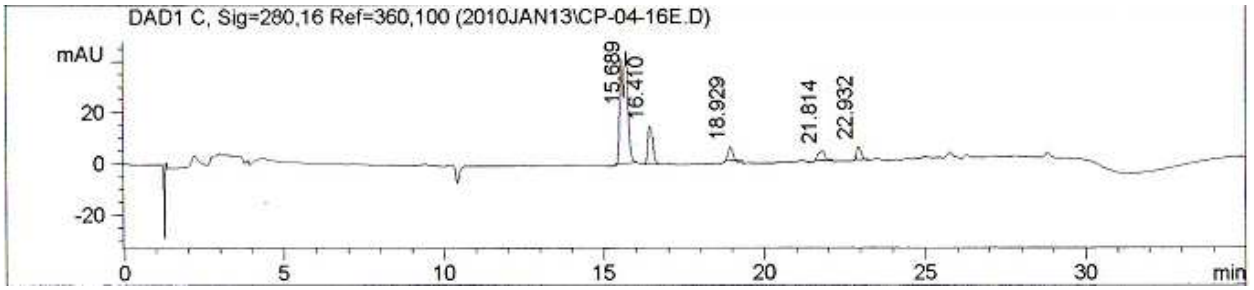


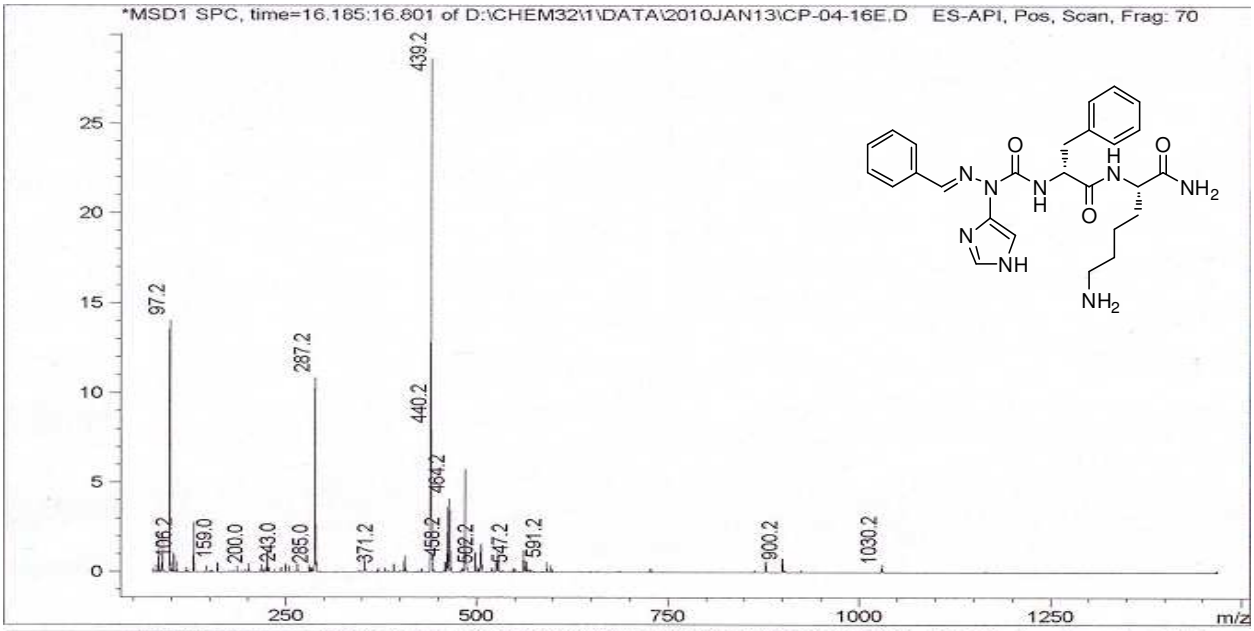


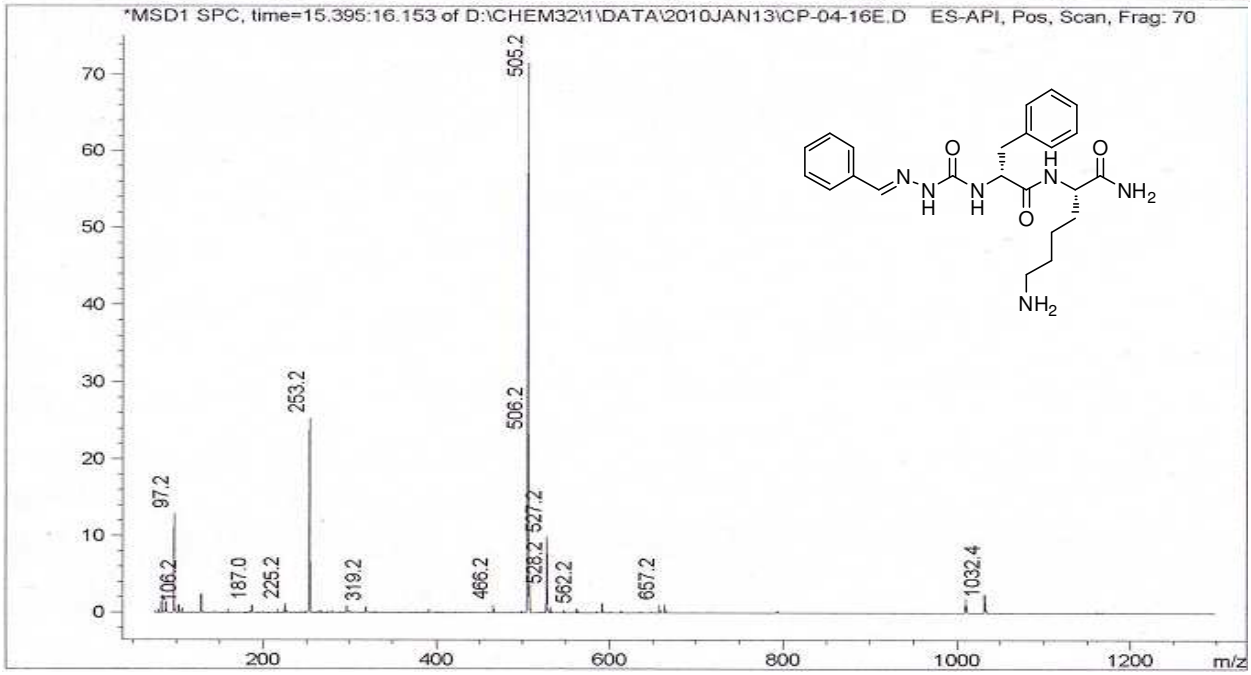
Benzaldehyde semicarbazone-(3-indole)-D-Phe-Lys-NH_2 (4f)



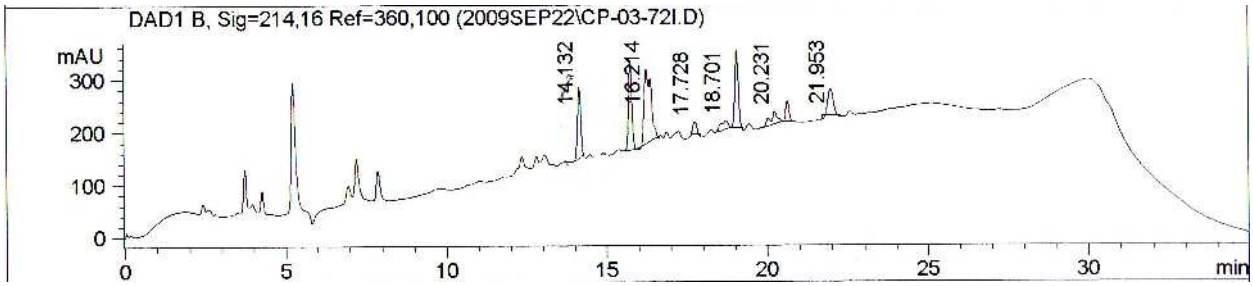
Benzaldehyde semicarbazone-(5-imidazole)-D-Phe-Lys-NH_2 (4g)

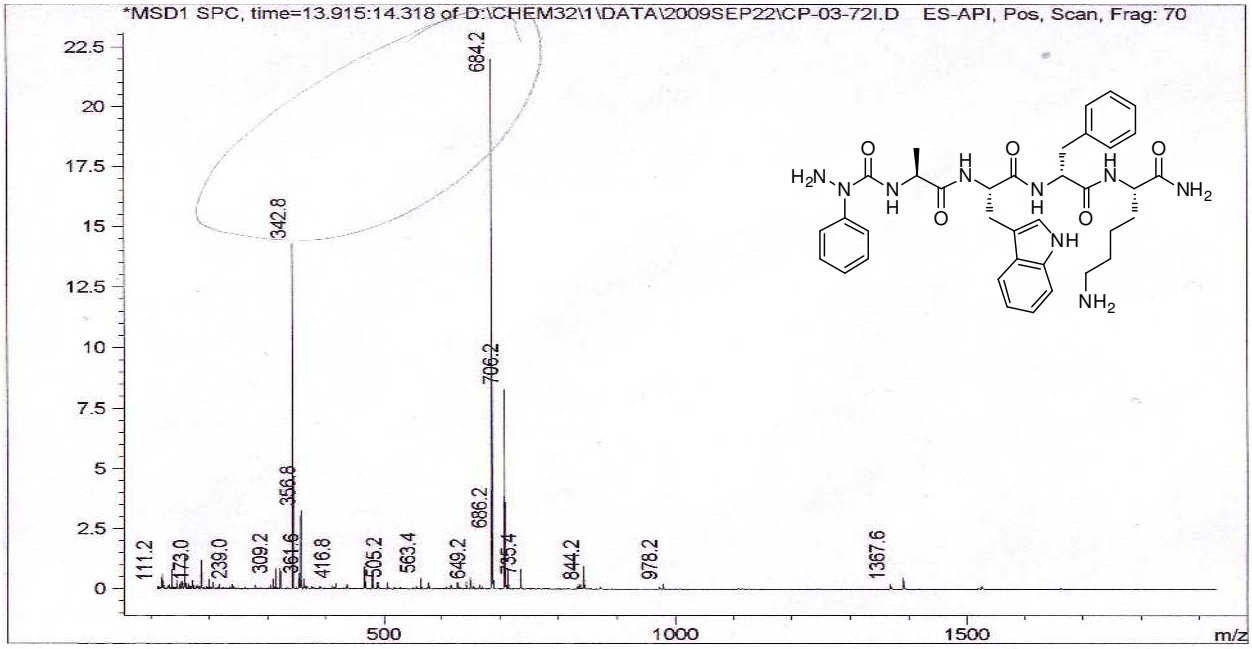


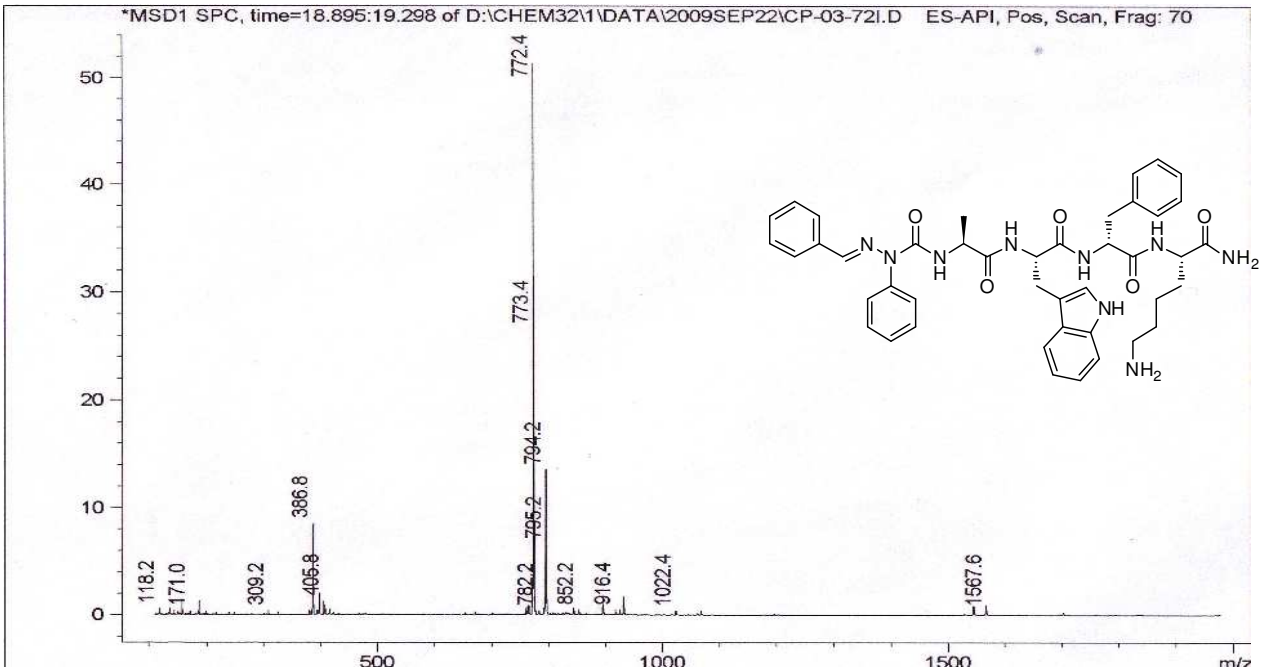




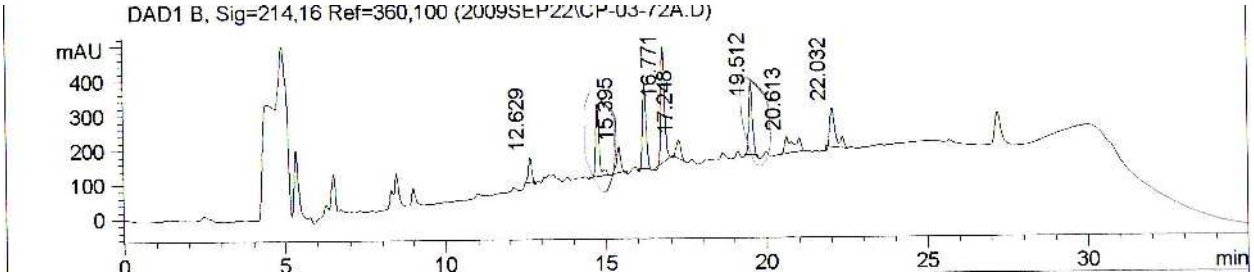
Benzaldehyde semicarbazone-(benzene)-Ala-Trp-D-Phe-Lys-NH_2 (9a)

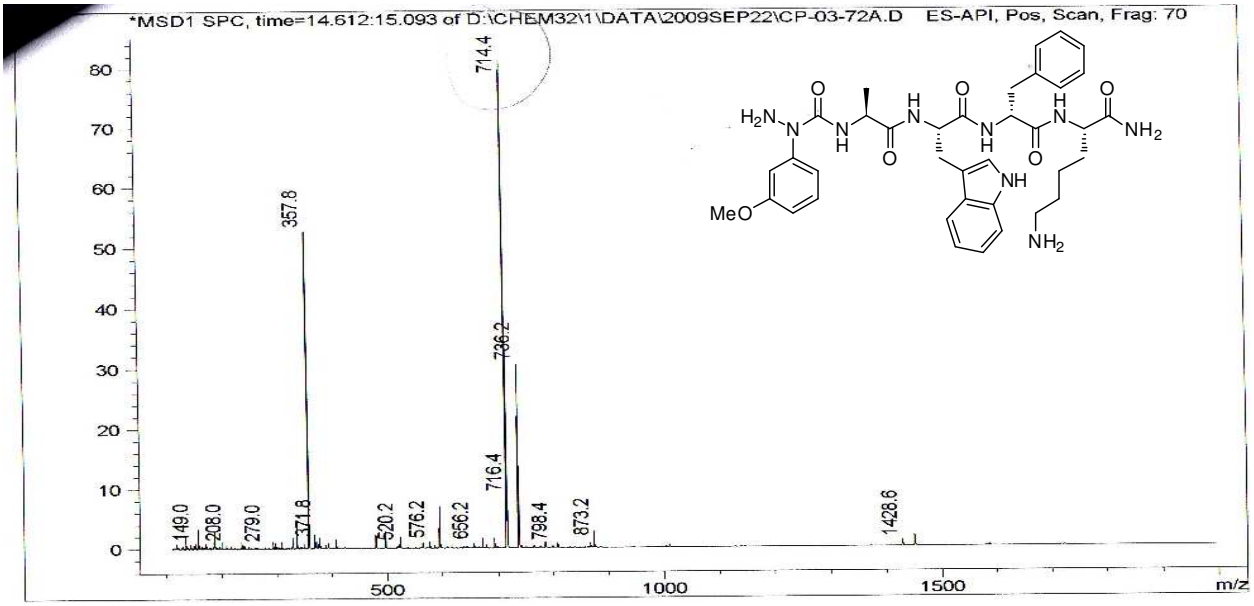


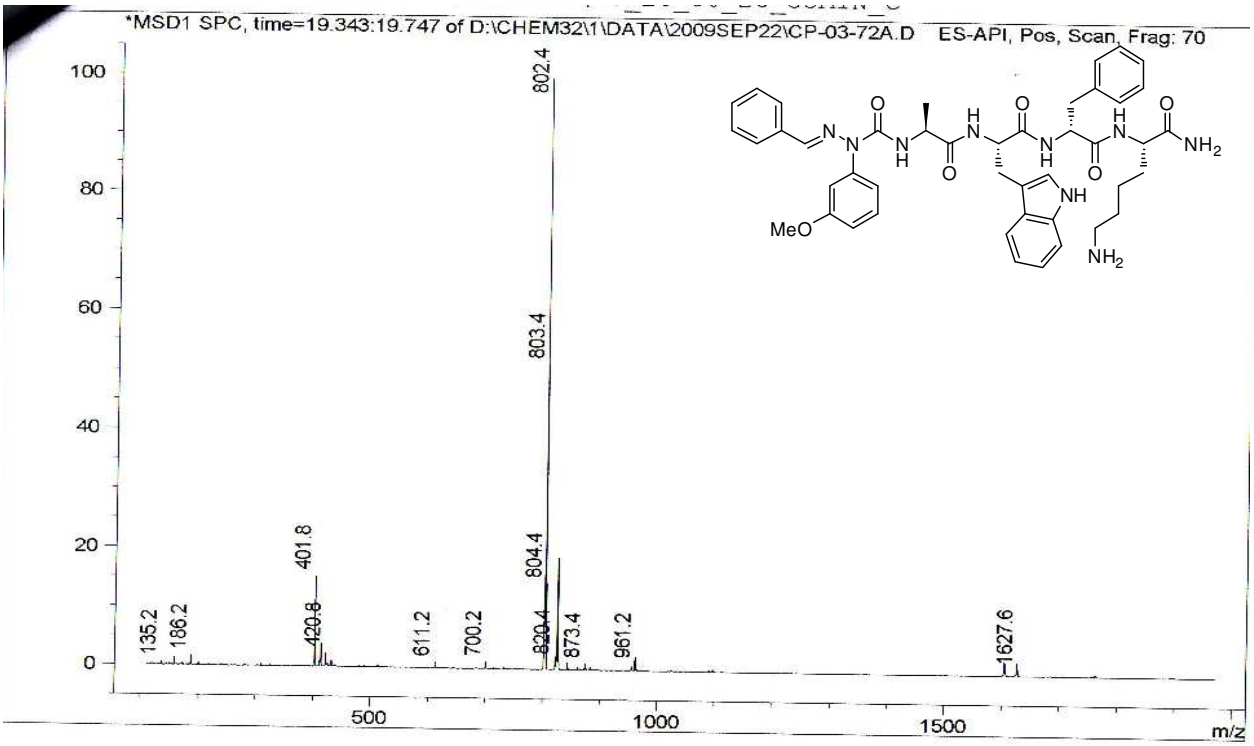




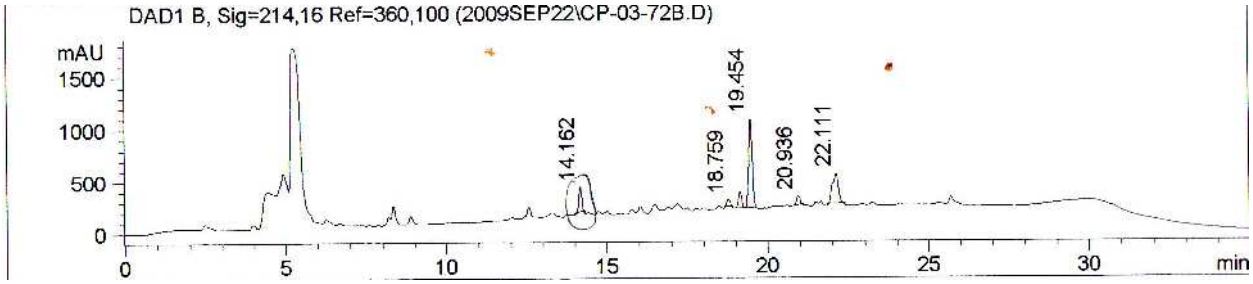
Benzaldehyde semicarbazone-(3-anisole)-Ala-Trp-D-Phe-Lys-NH_2 (9b)

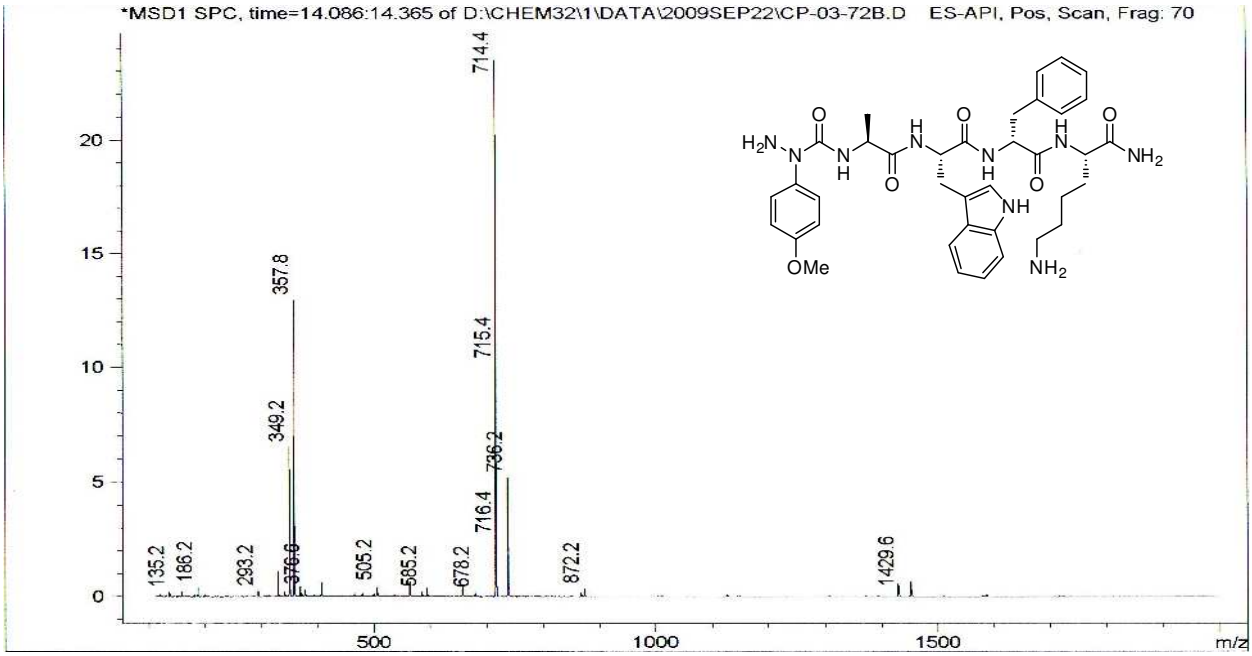


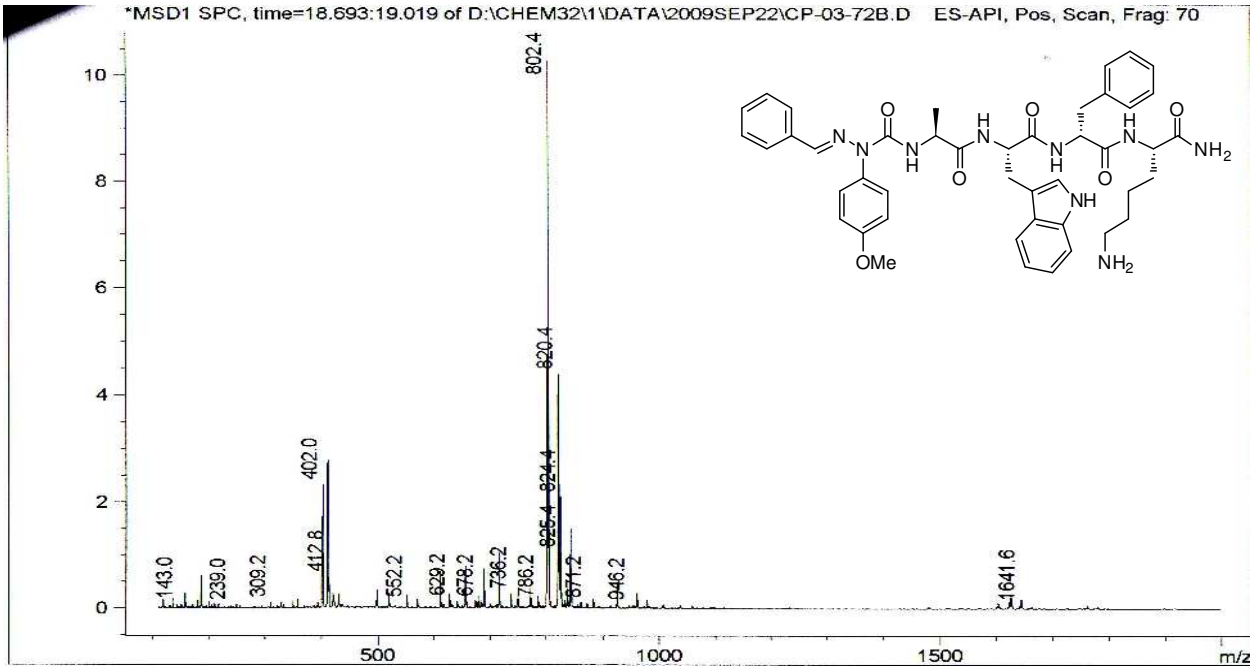




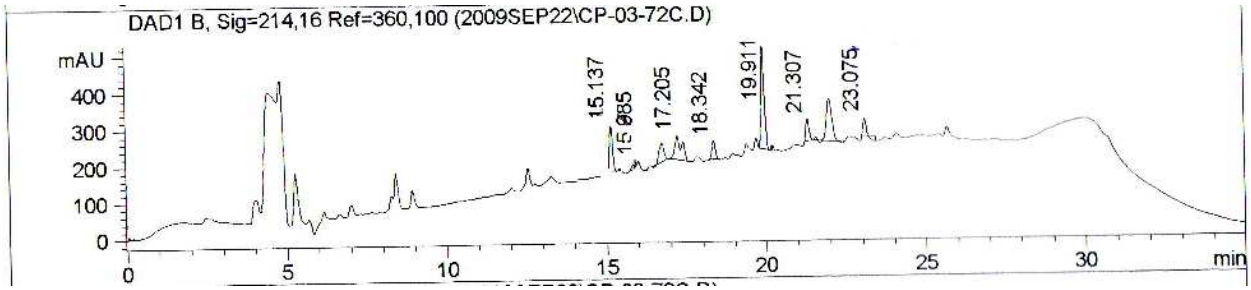
Benzaldehyde semicarbazone-(4-anisole)-Ala-Trp-D-Phe-Lys-NH_2 (9c)

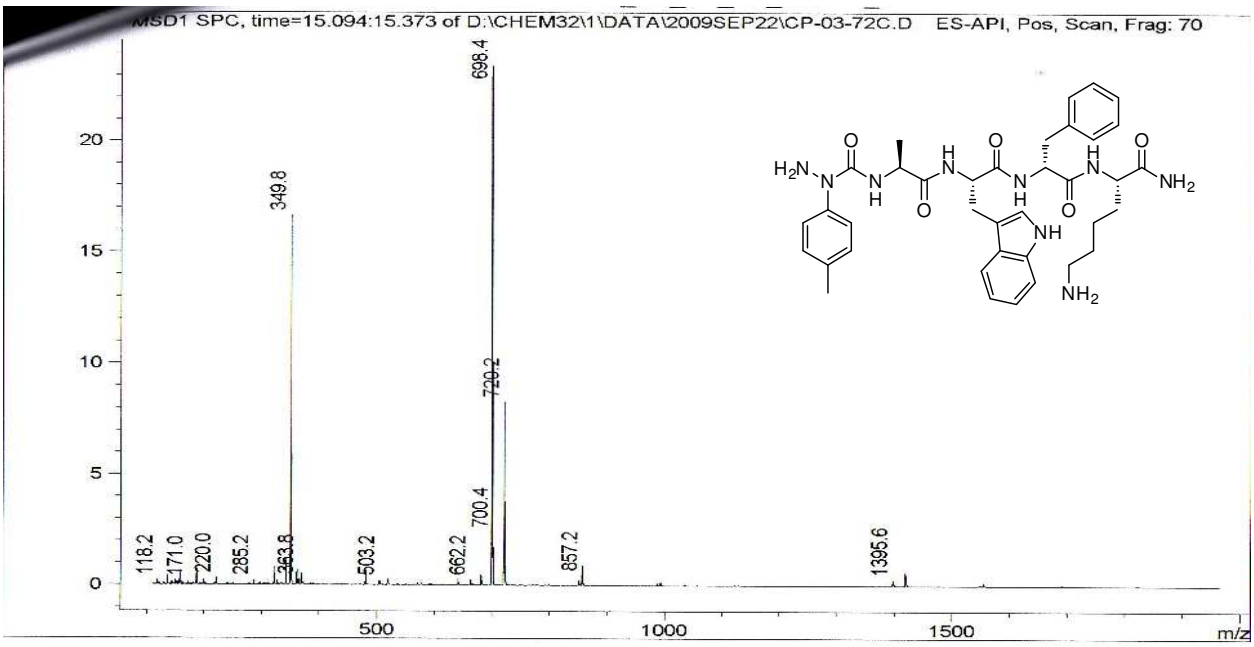


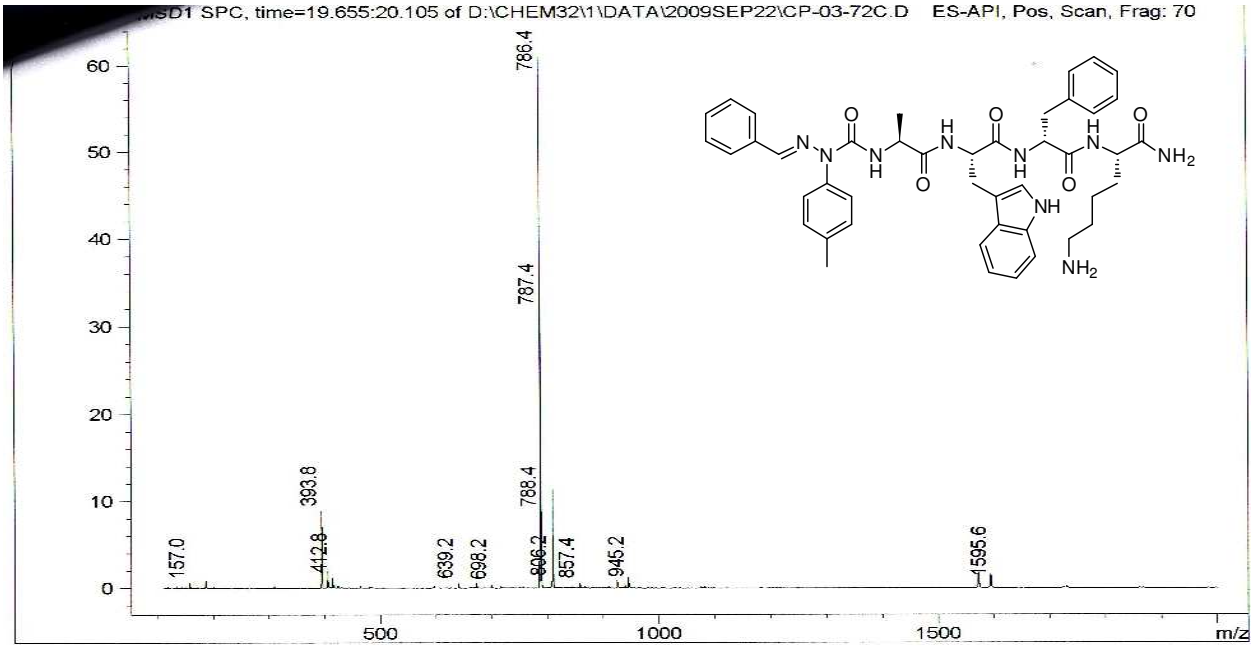




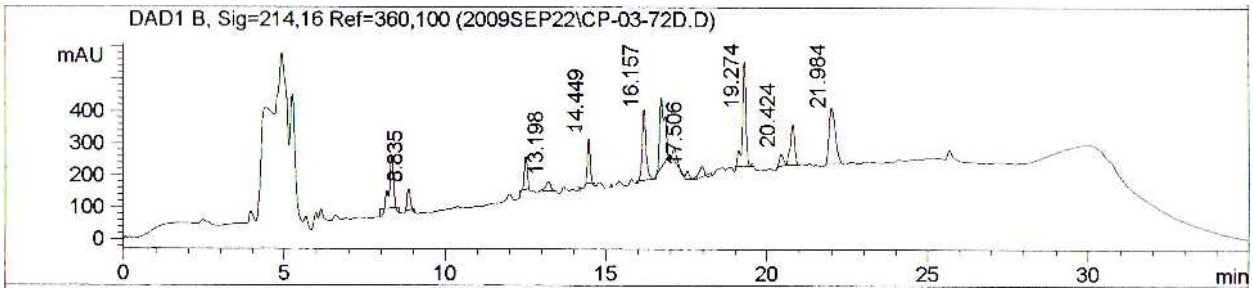
Benzaldehyde semicarbazone-(4-toluene)-Ala-Trp-D-Phe-Lys-NH_2 (9d)

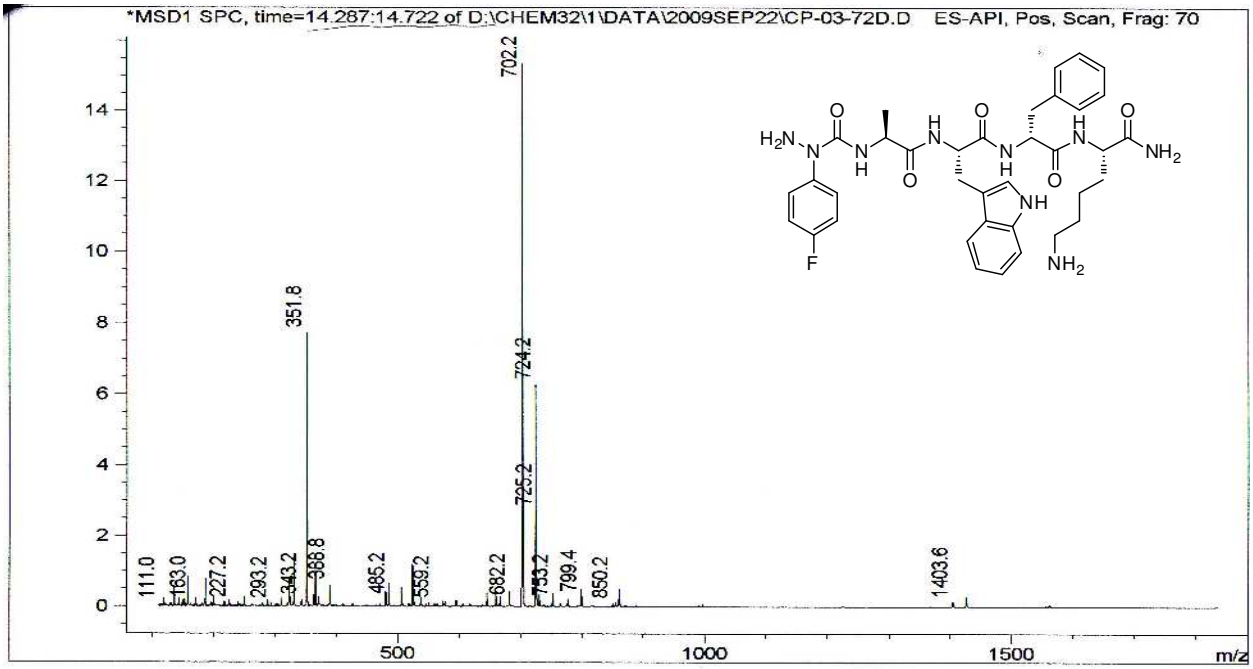


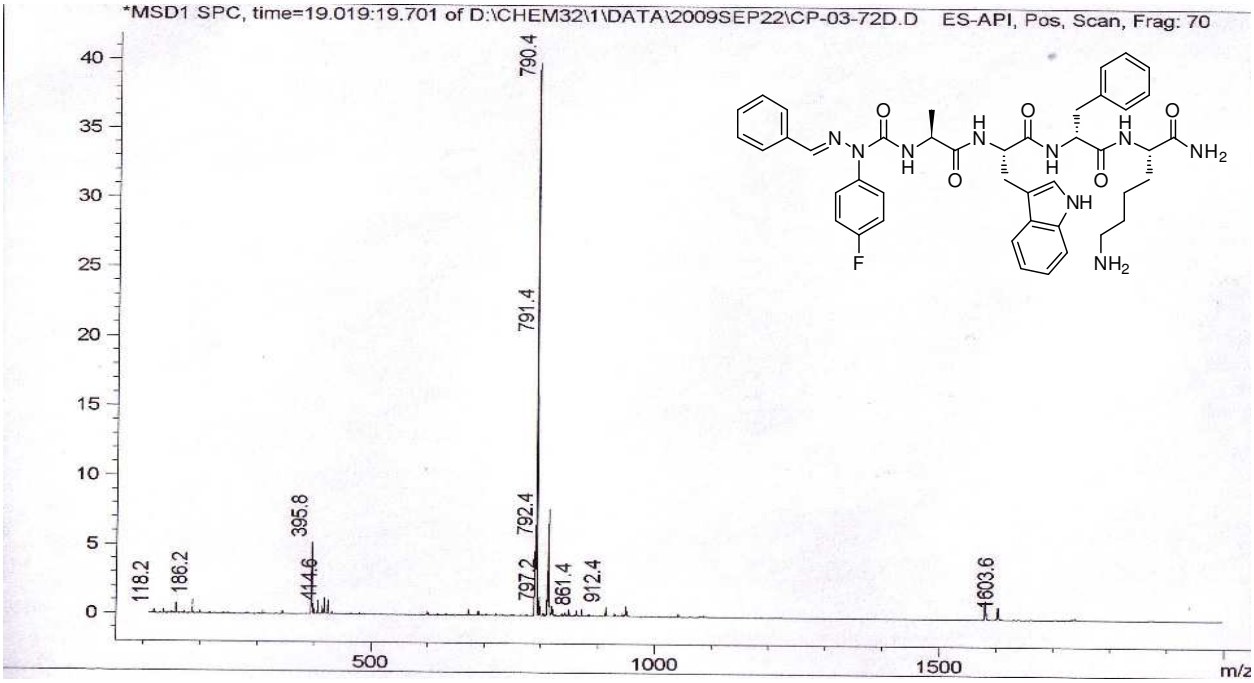




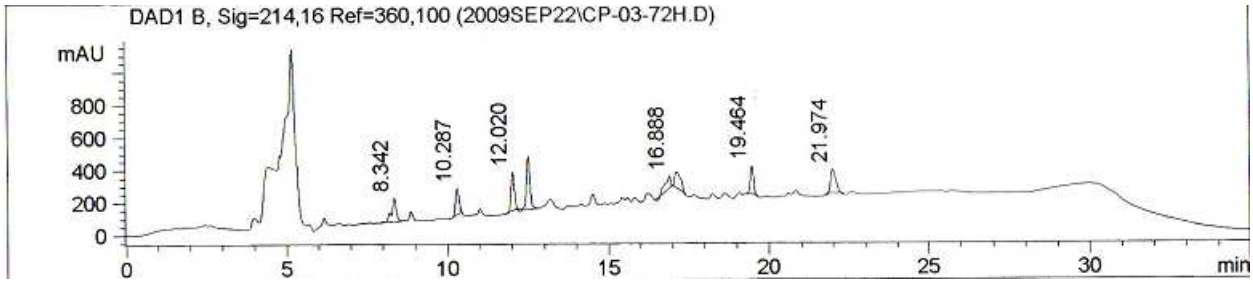
Benzaldehyde semicarbazone-(4-fluorobenzene)-Ala-Trp-D-Phe-Lys-NH_2 (9e)

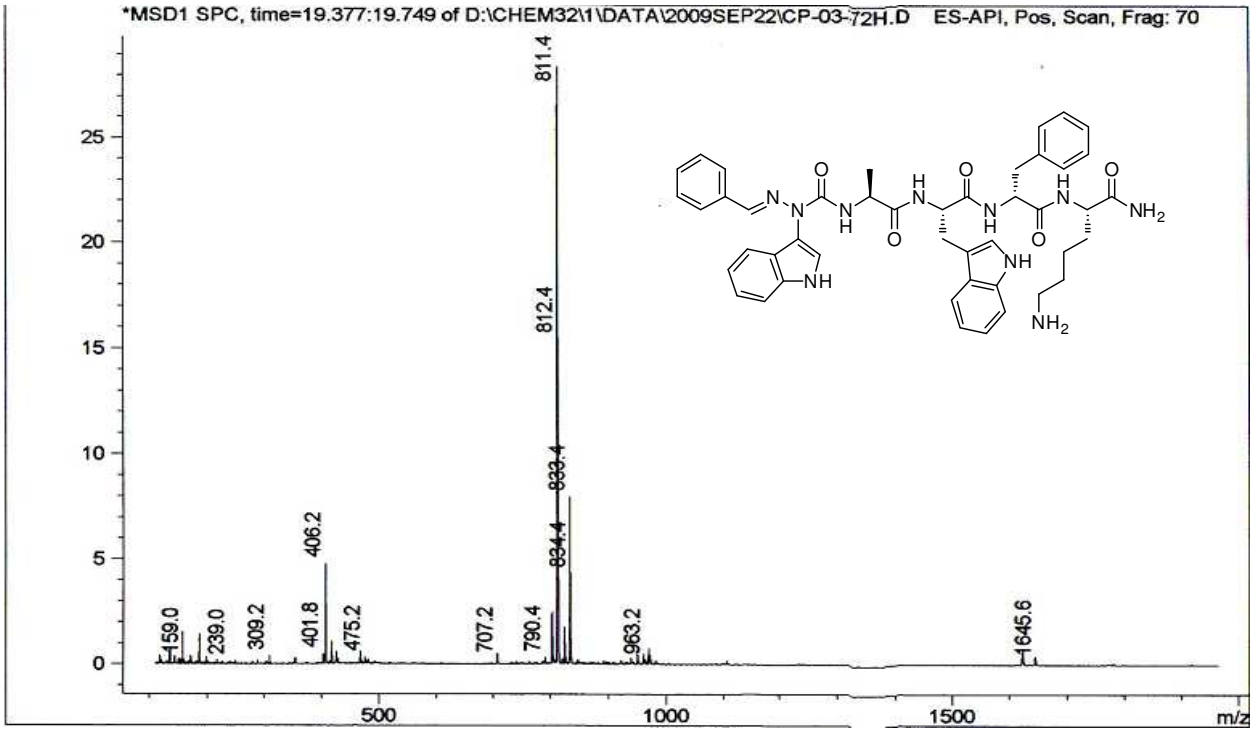




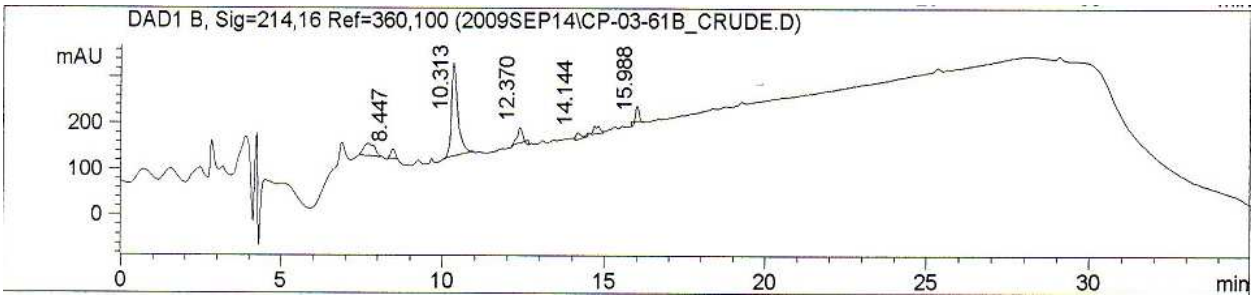


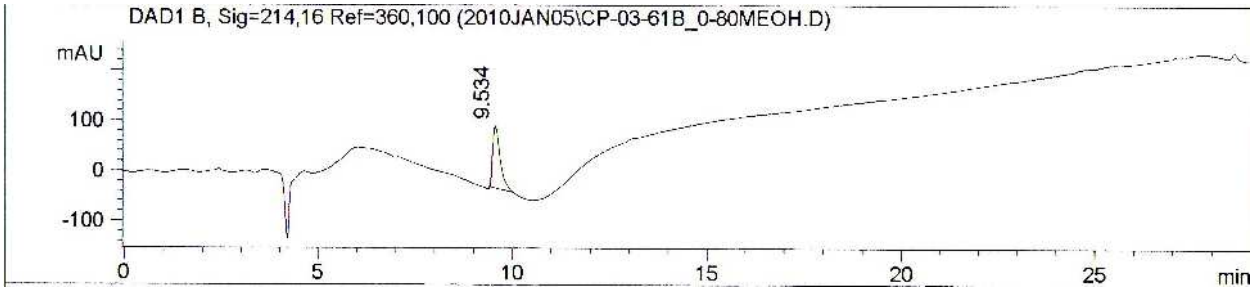
Benzaldehyde semicarbazone-(3-indole)-Ala-Trp-D-Phe-Lys-NH_2 (9f)

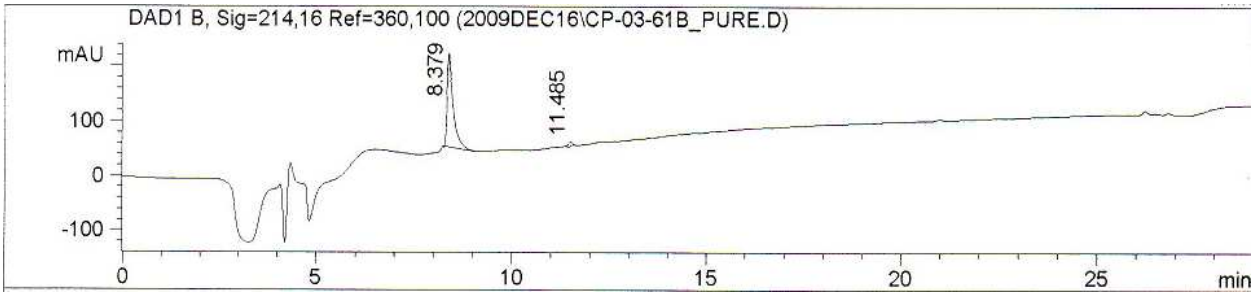


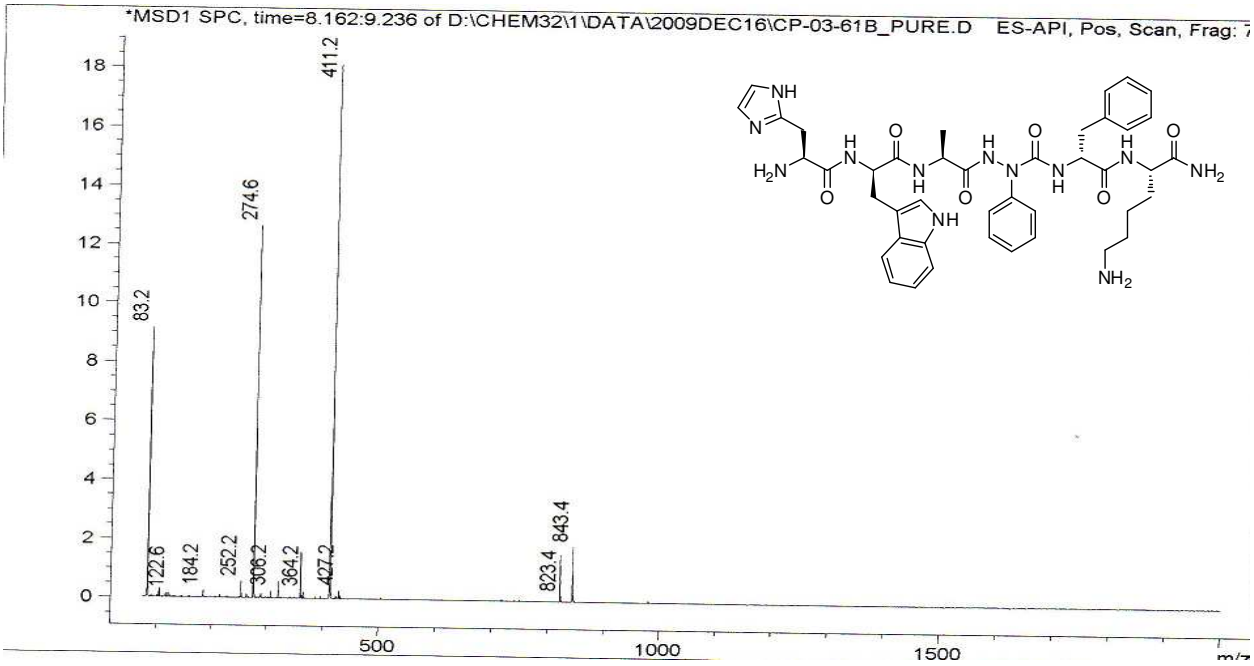


His-D-Trp-Ala-aza(phenylglycine)-D-Phe-Lys-NH_2 (6a)

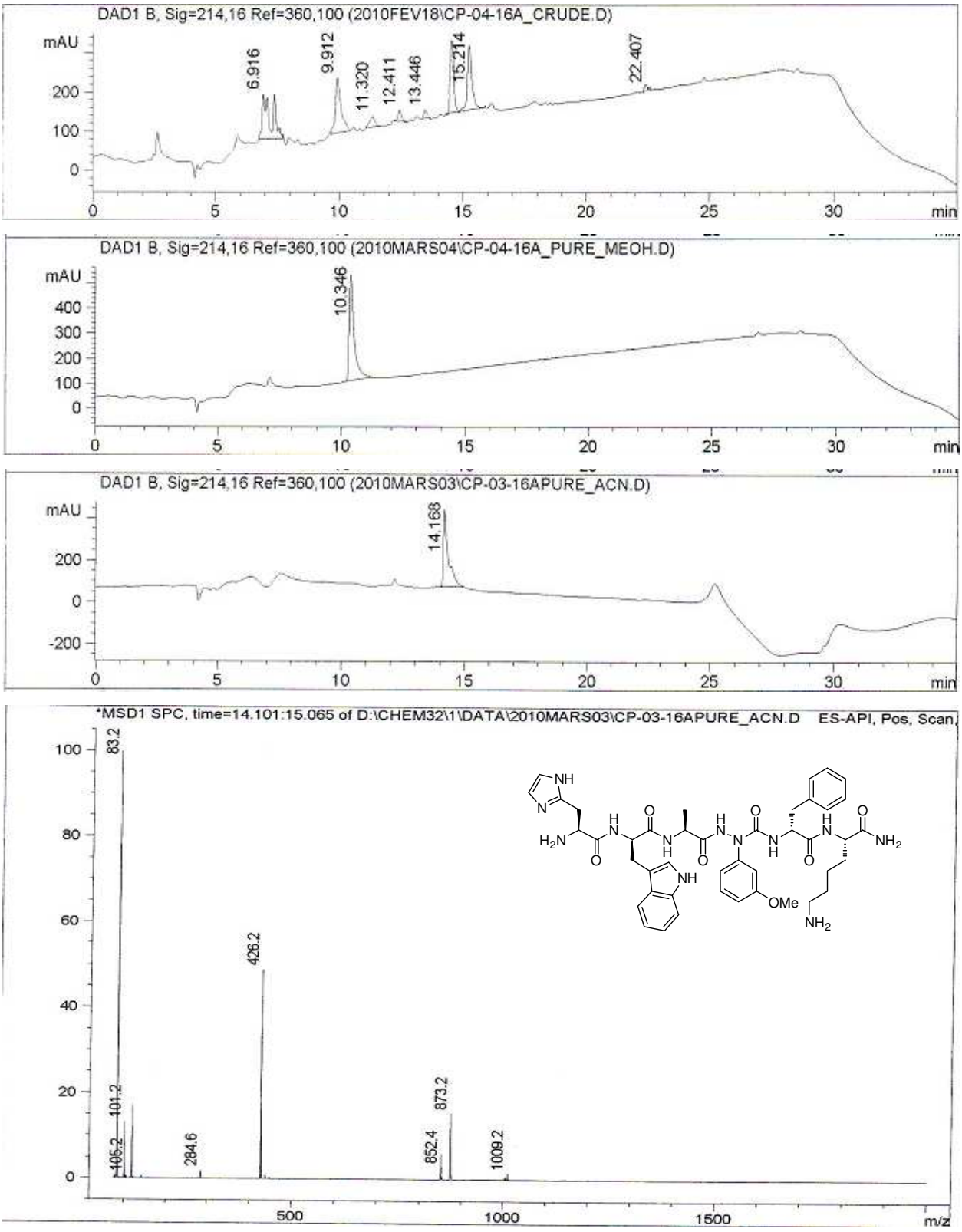




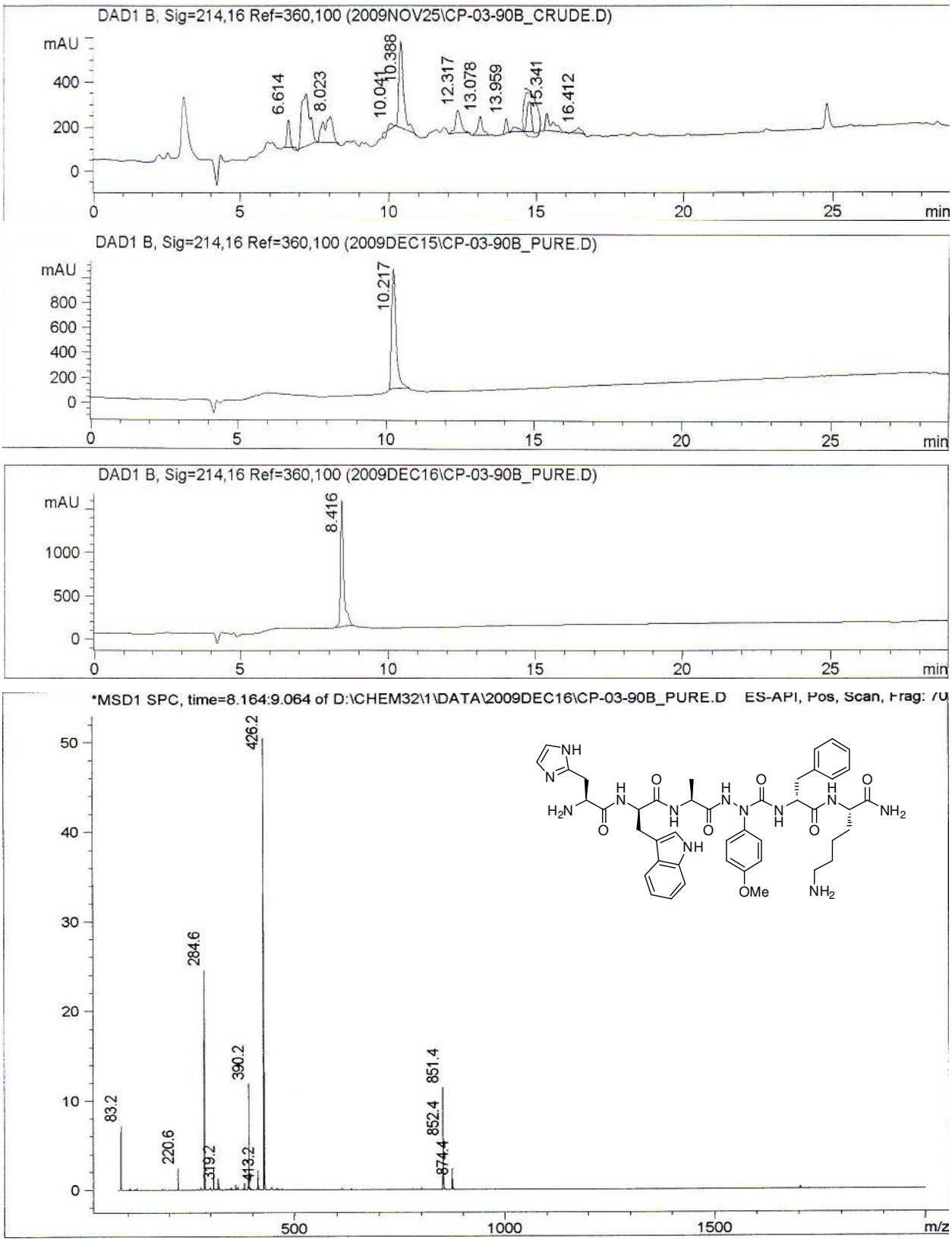




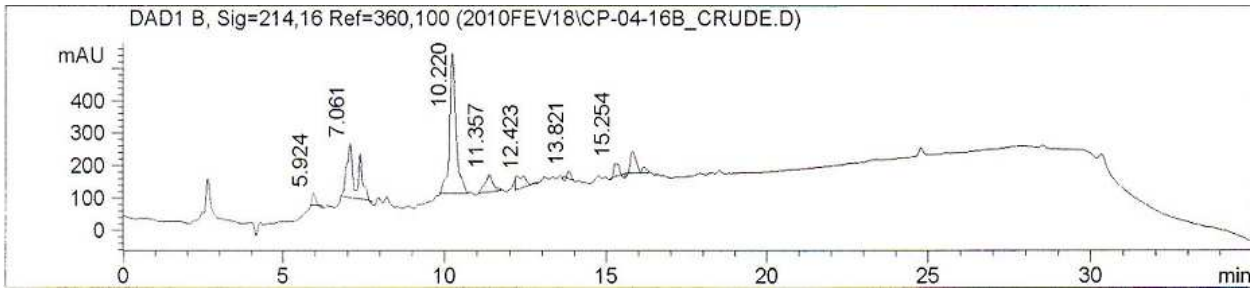
His-D-Trp-Ala-aza(*o*-anisole)-D-Phe-Lys-NH_2 (6b)

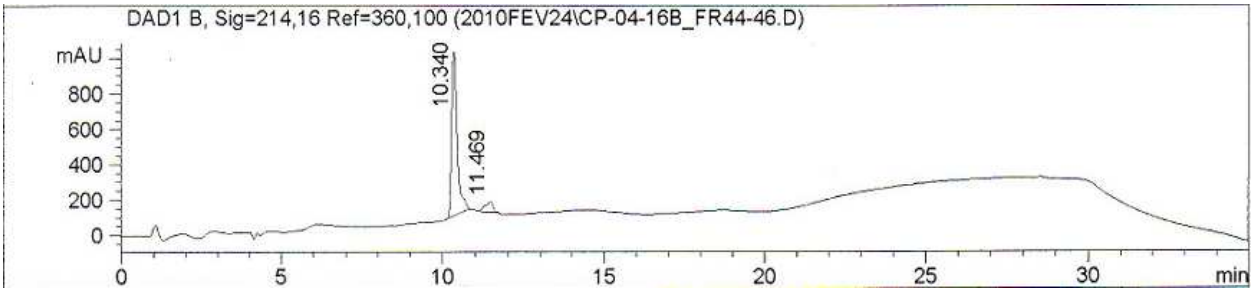


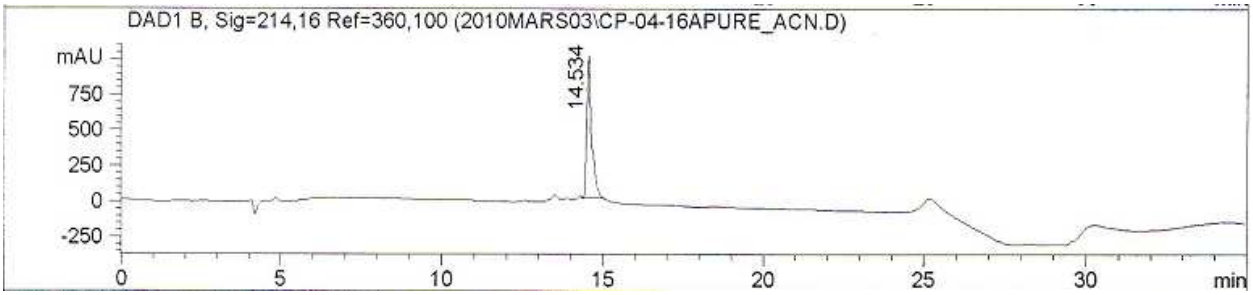
His-D-Trp-Ala-aza(*p*-anisole)-D-Phe-Lys-NH_2 (6c)

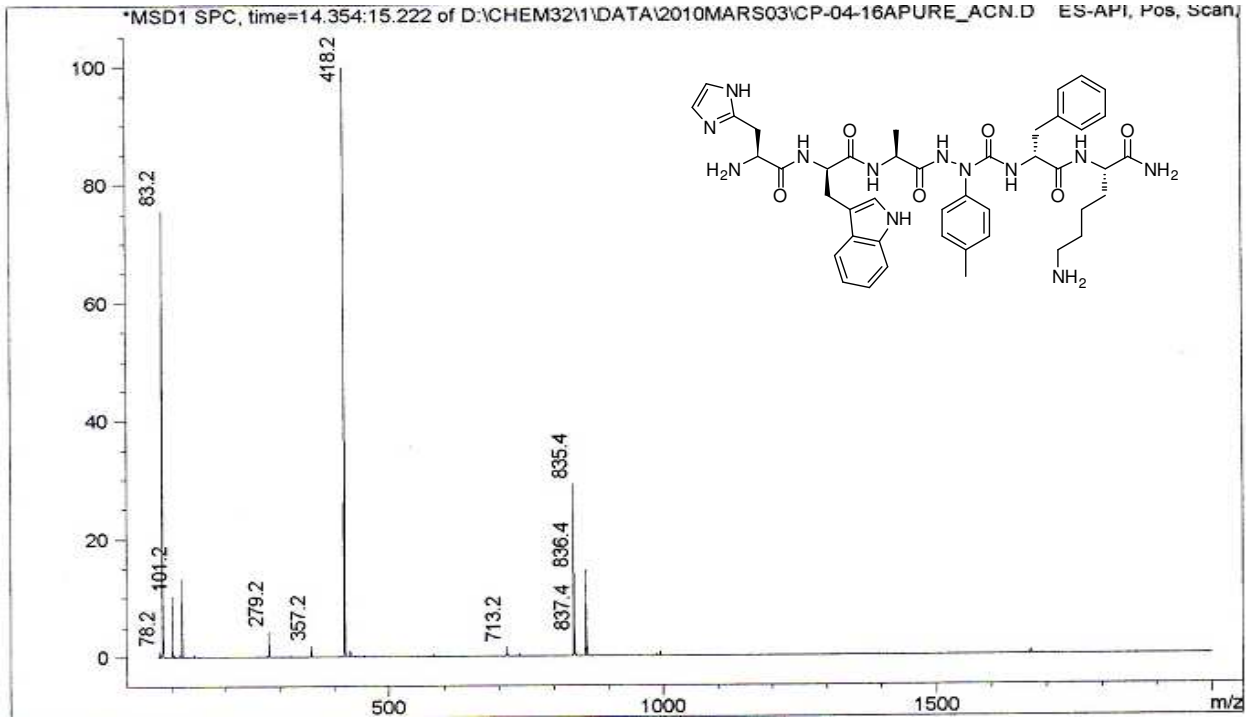


His-D-Trp-Ala-aza(*p*-toluene)-D-Phe-Lys-NH_2 (6d)

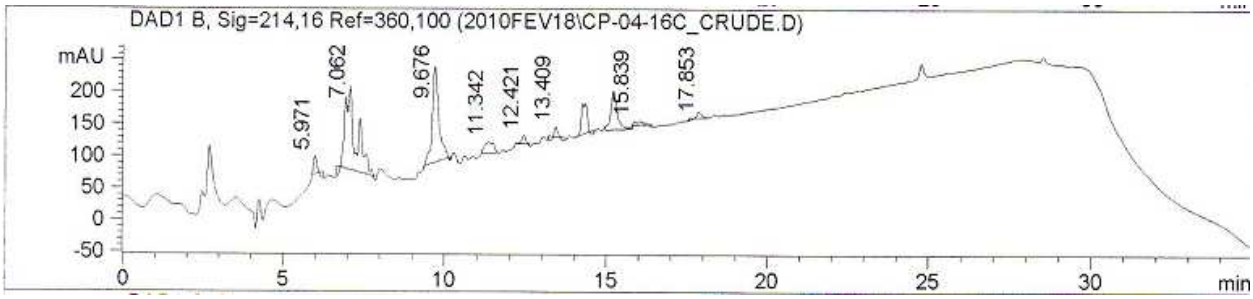


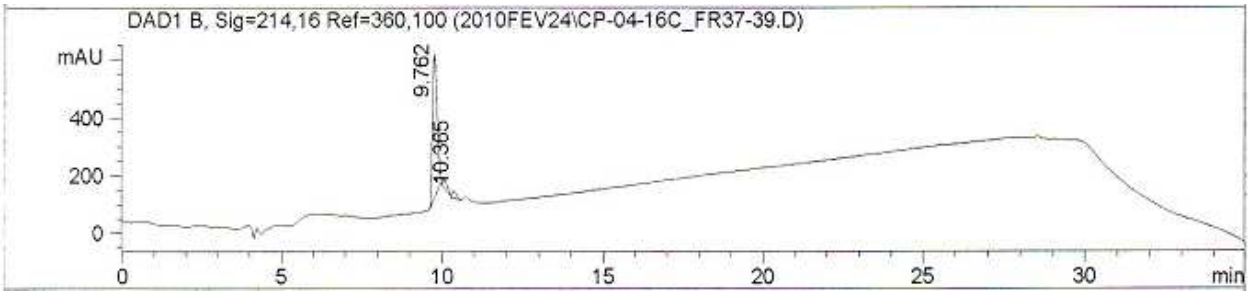


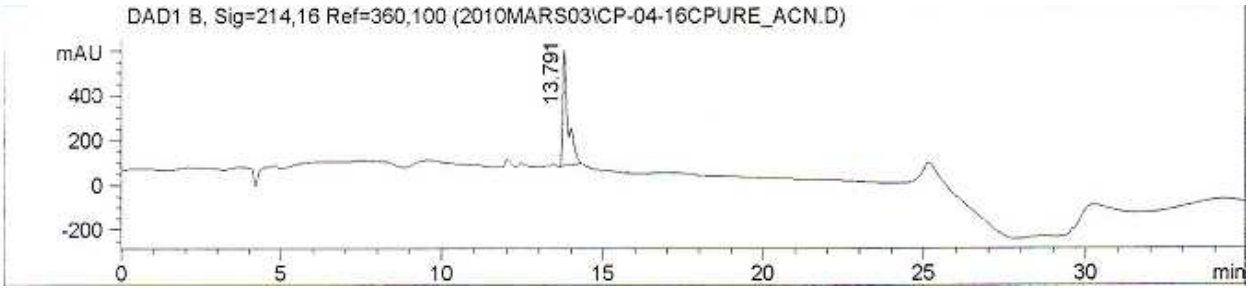


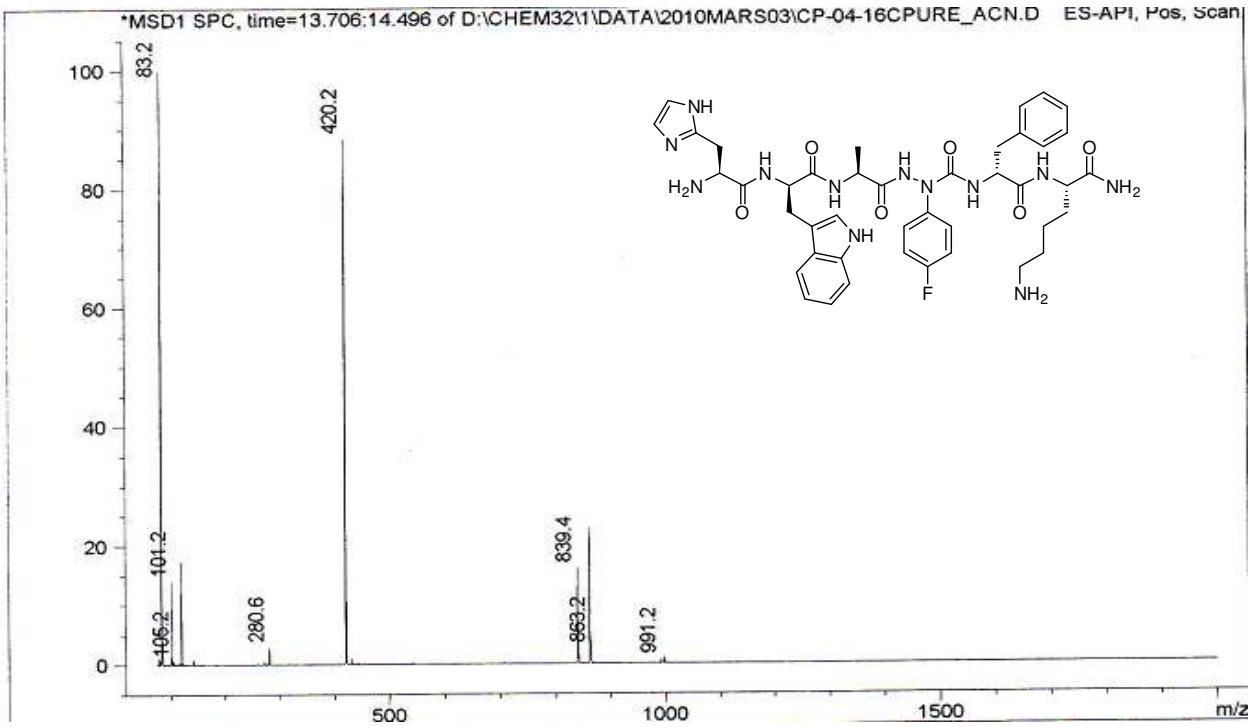


His-D-Trp-Ala-aza(*p*-fluoro benzene)-D-Phe-Lys-NH_2 (6e)

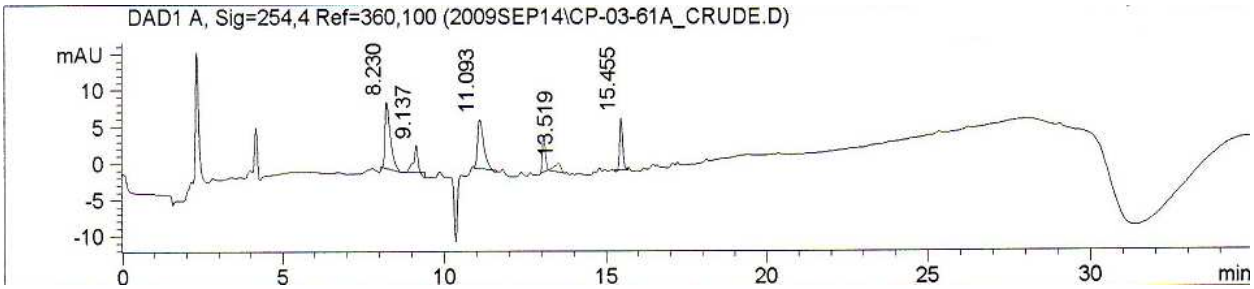


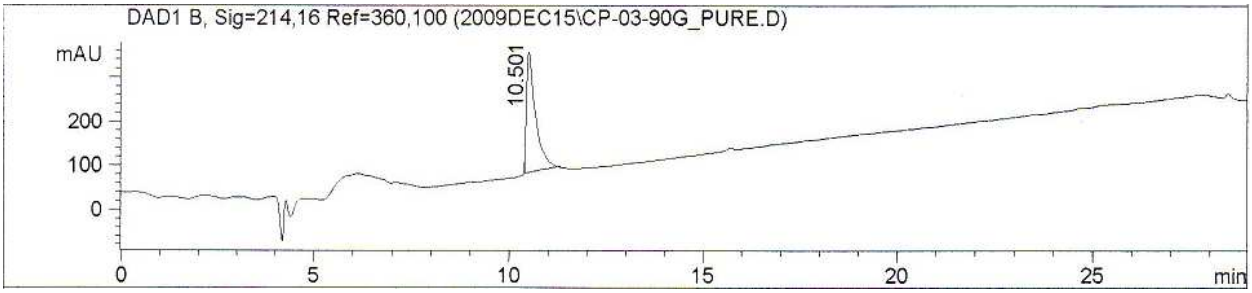


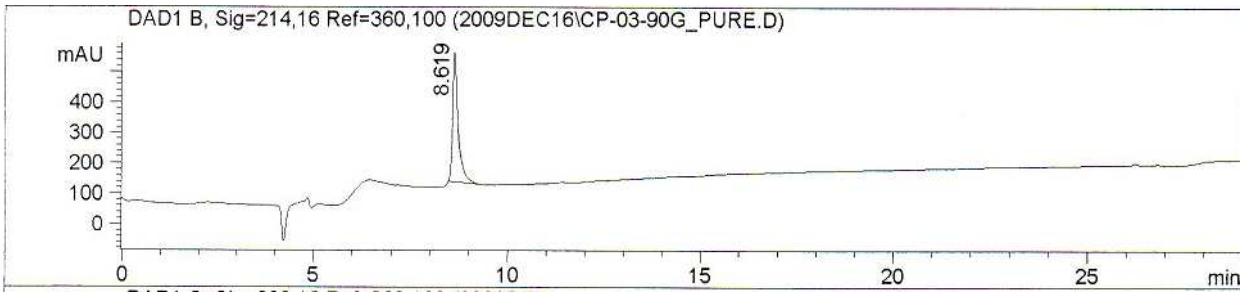


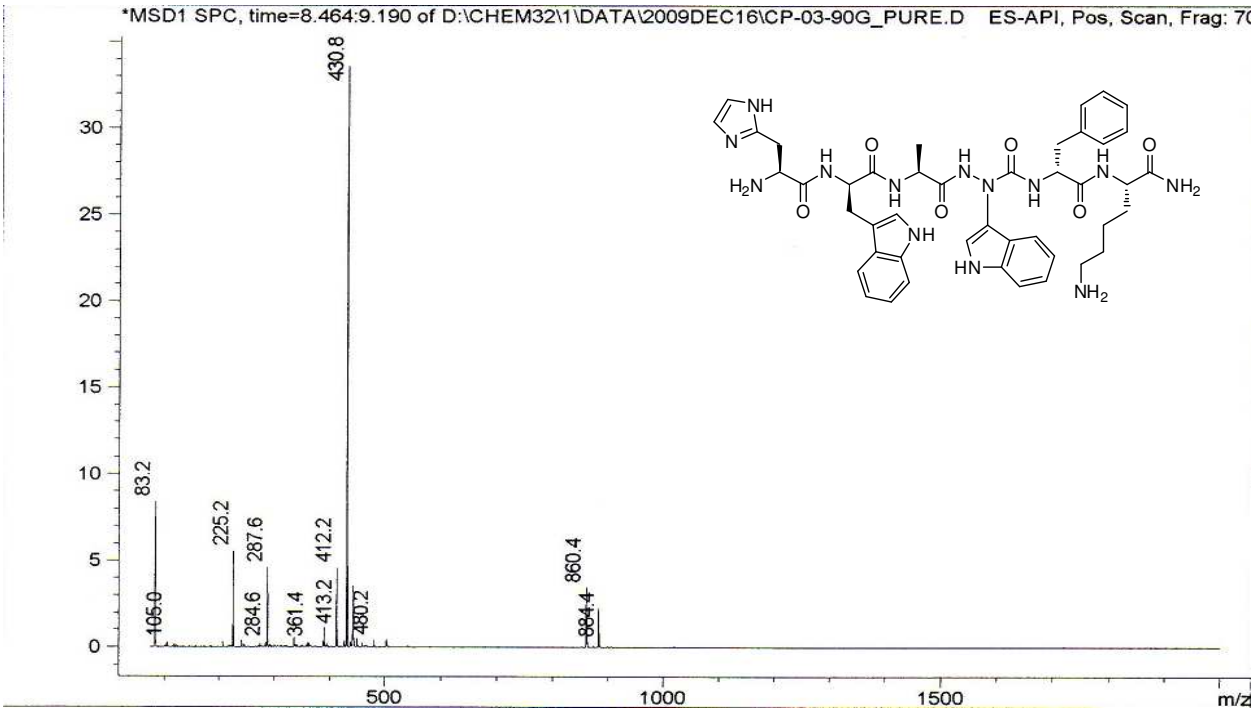


His-D-Trp-Ala-aza(indoyl)-D-Phe-Lys-NH_2 (6f)

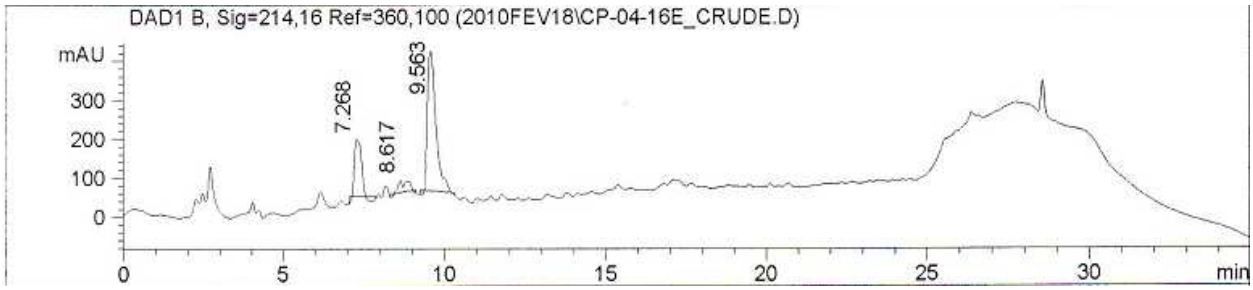


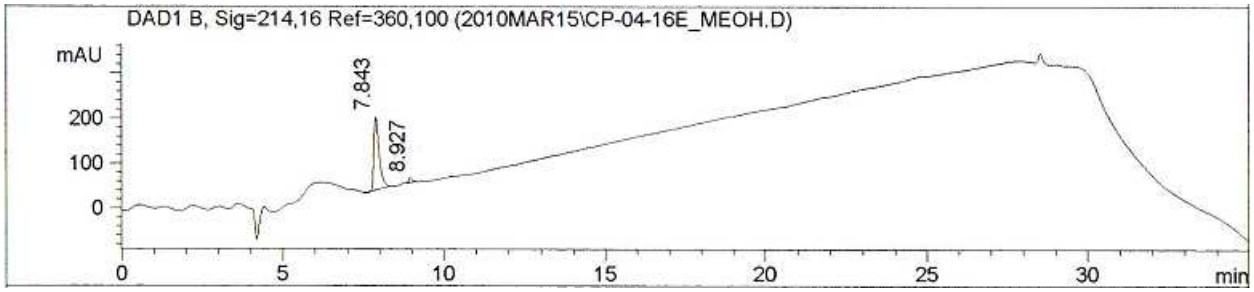


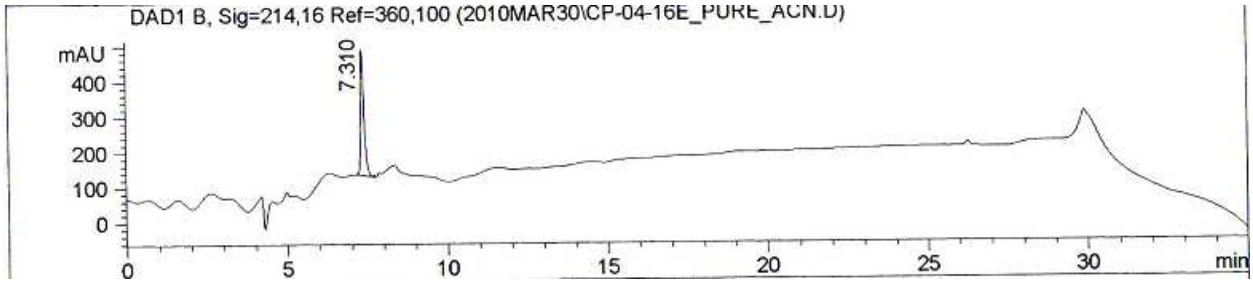


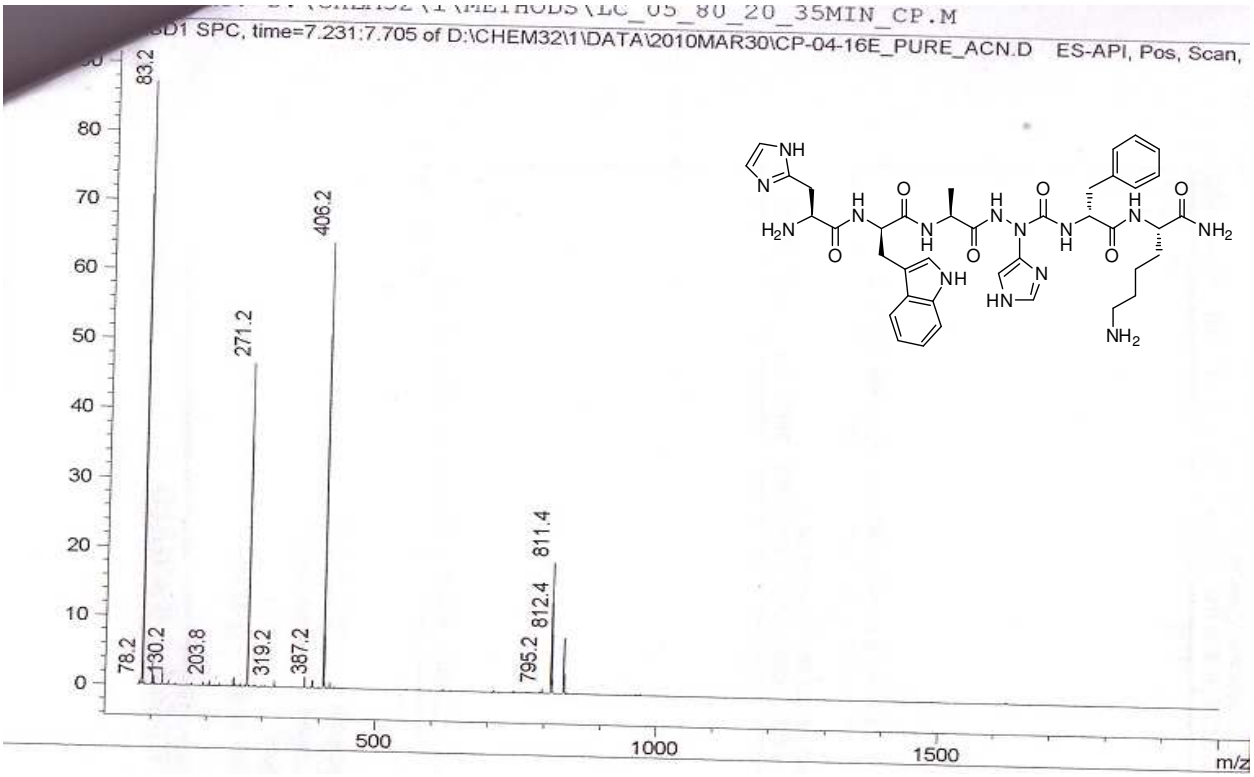


His-D-Trp-Ala-aza(imidazoyl)-D-Phe-Lys-NH_2 (6g)

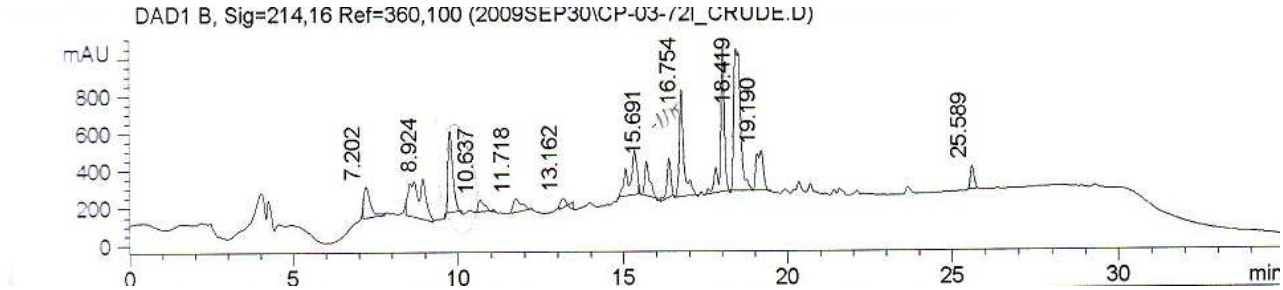


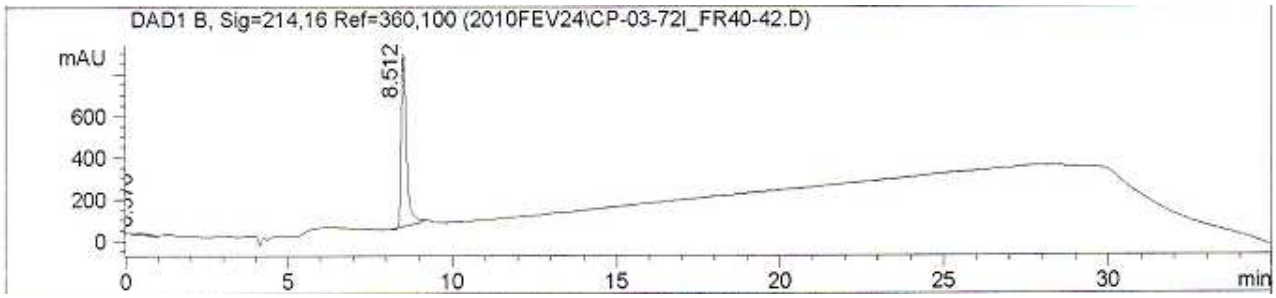


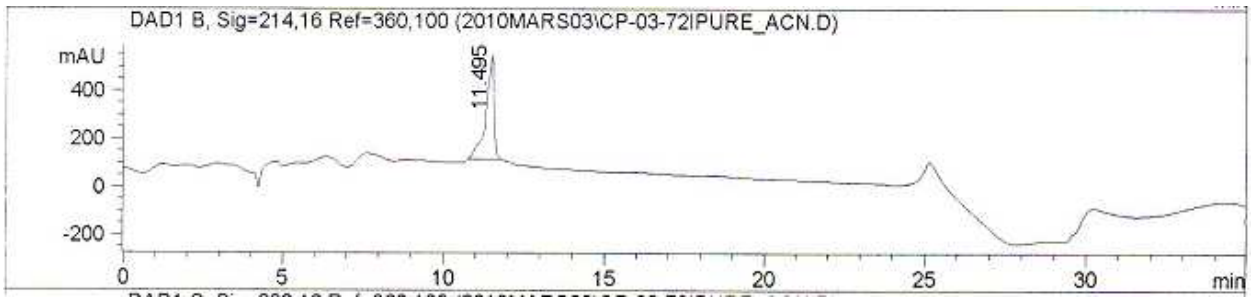


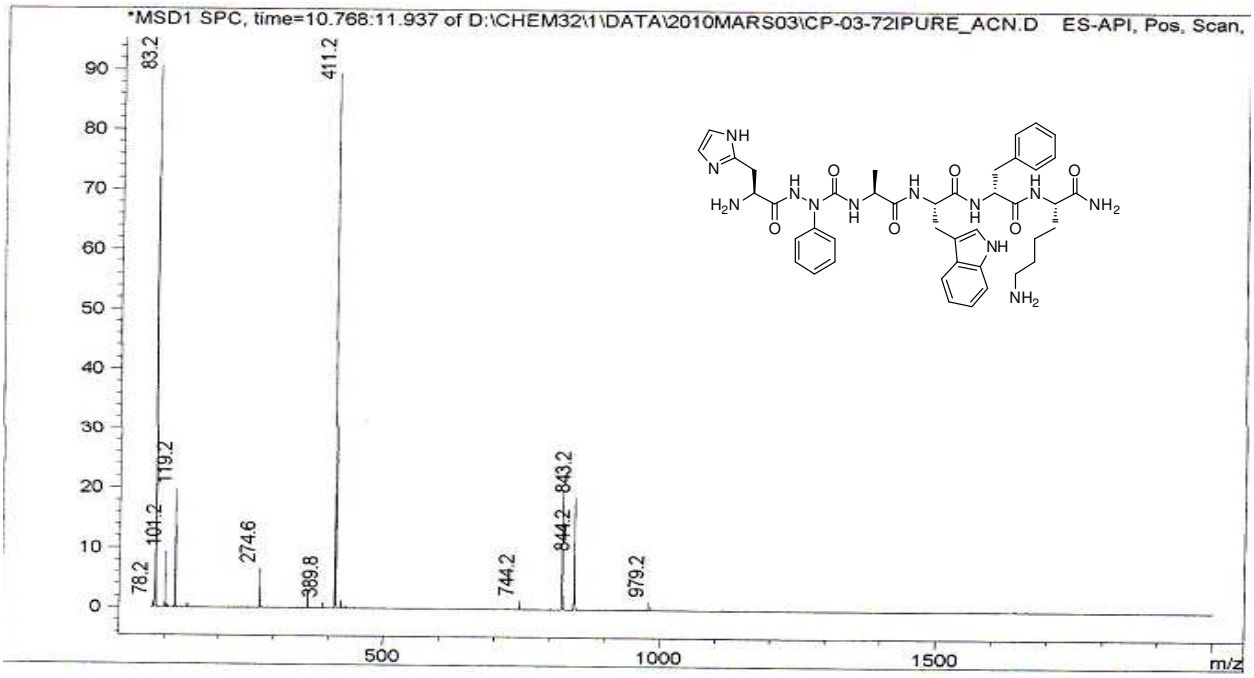


His-Aza(phenylglycine)-Ala-Trp-D-Phe-Lys-NH_2 (10a)

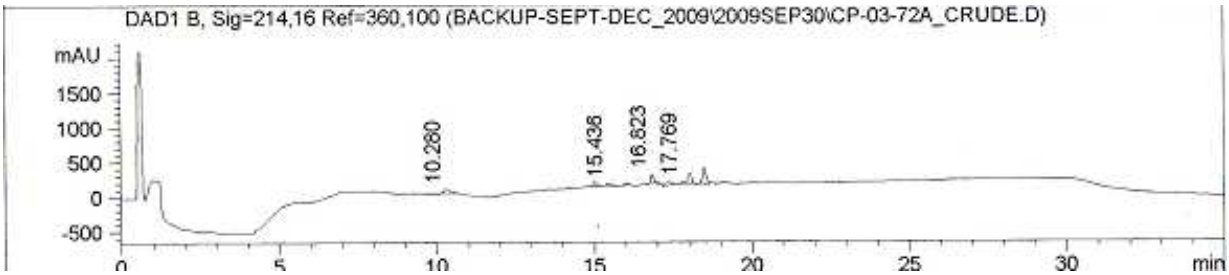


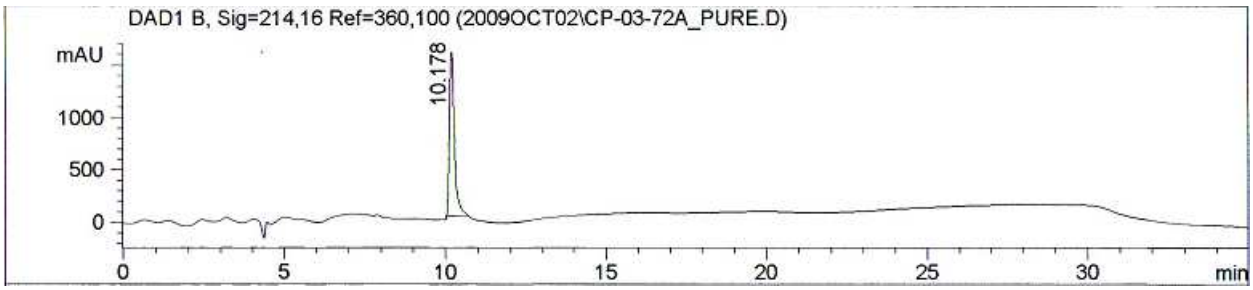


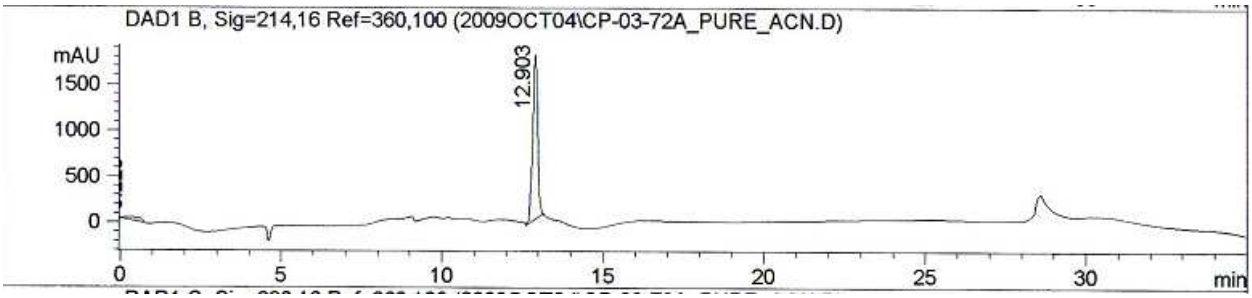


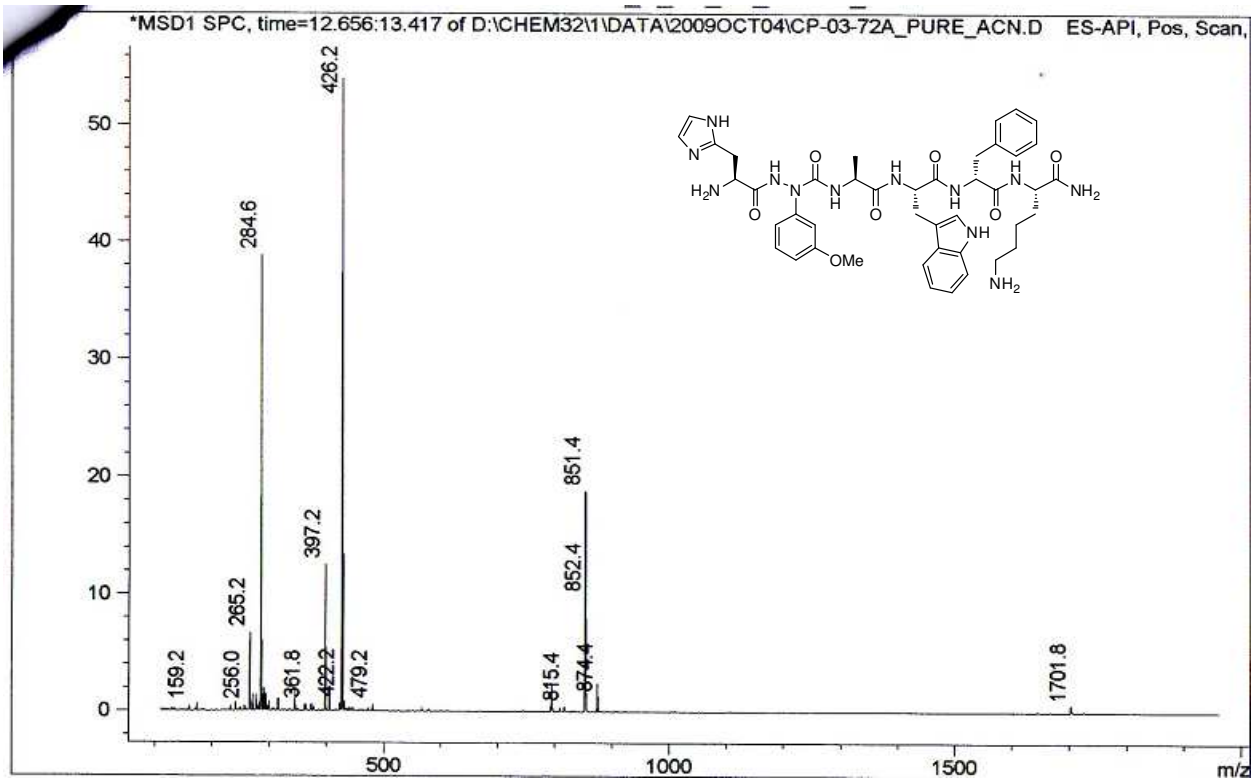


His-Aza(*o*-anisole)-Ala-Trp-D-Phe-Lys-NH_2 (10b)

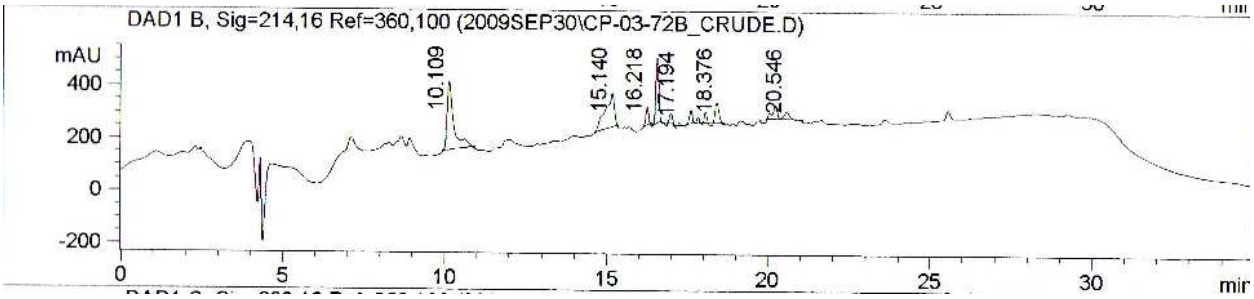


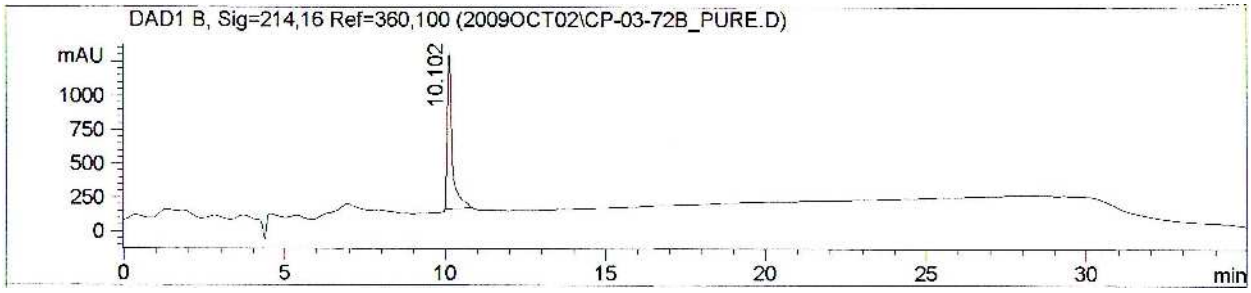


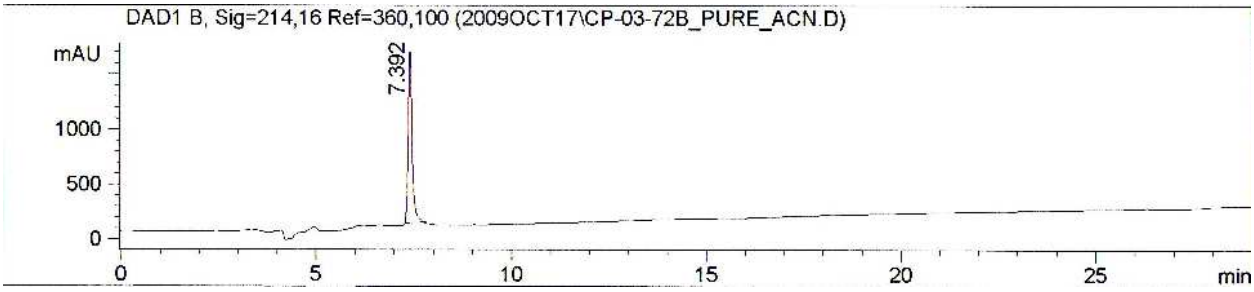


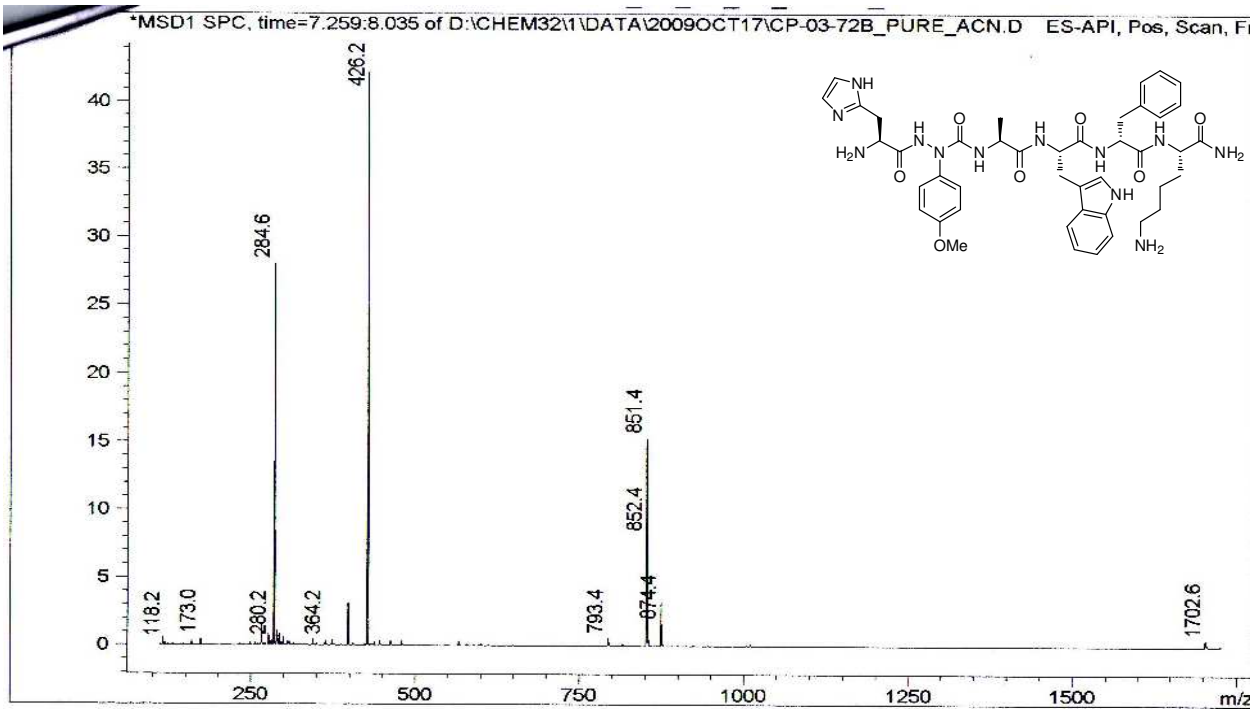


His-Aza(*p*-anisole)-Ala-Trp-D-Phe-Lys-NH_2 (10c)

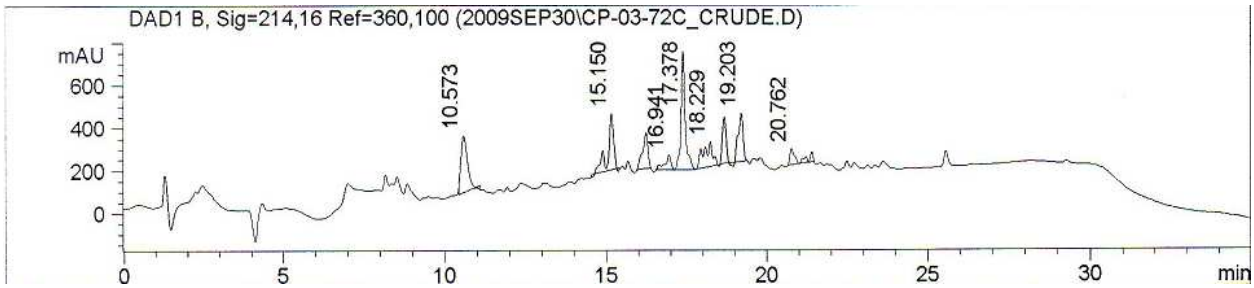


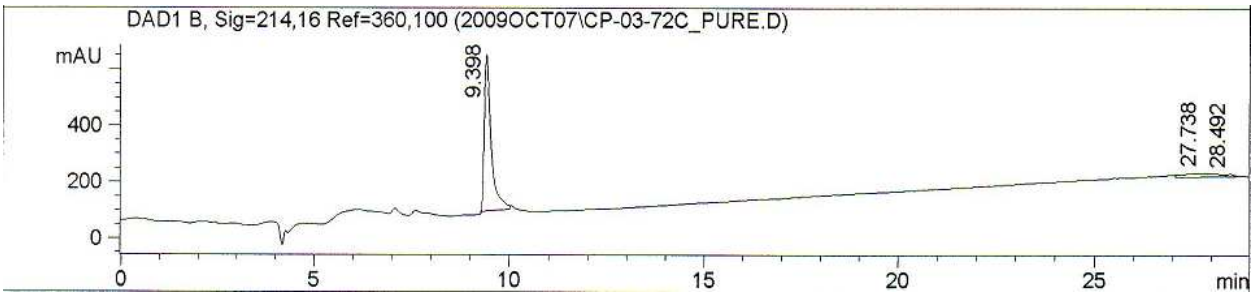


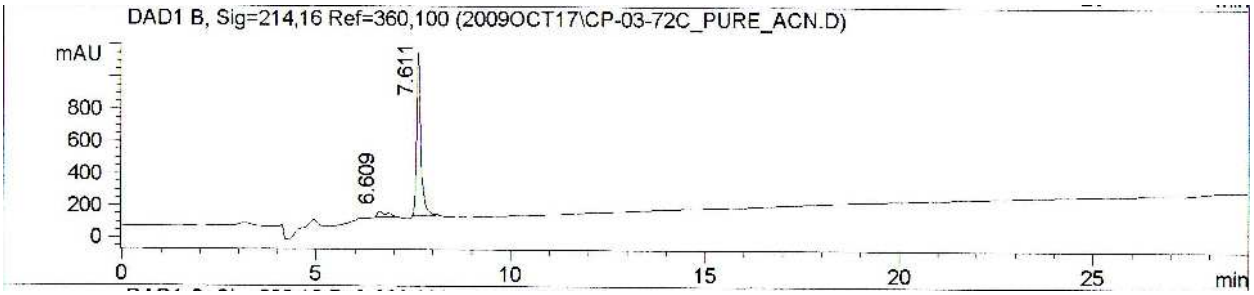


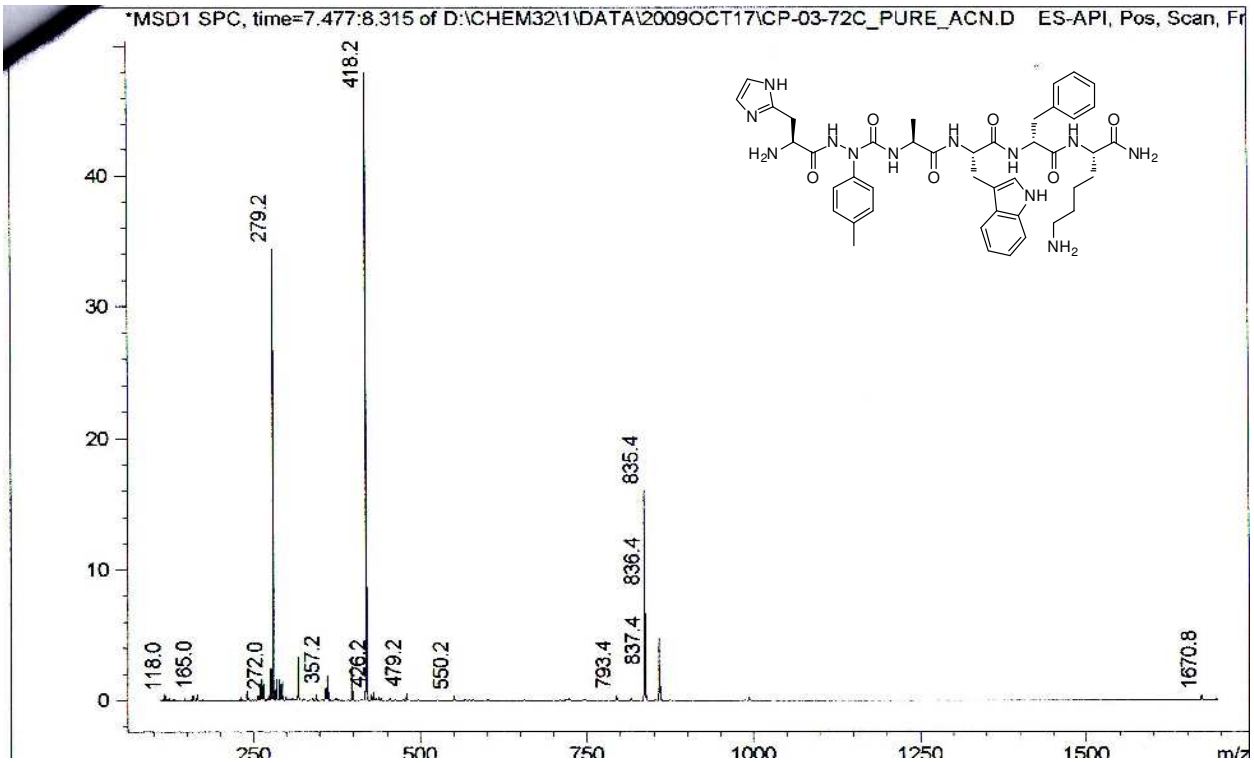


His-Aza(*p*-toluene)-Ala-Trp-D-Phe-Lys-NH_2 (10d)

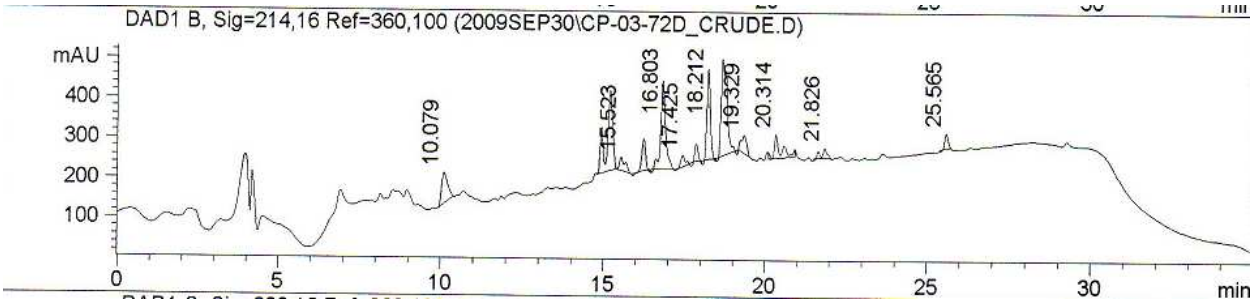


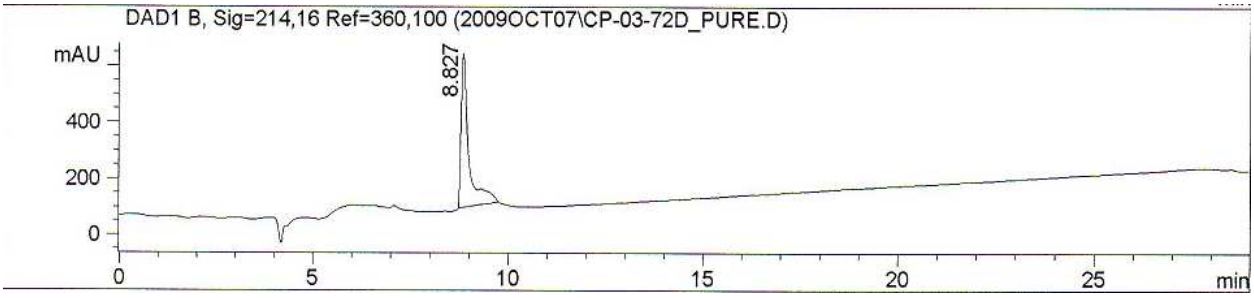


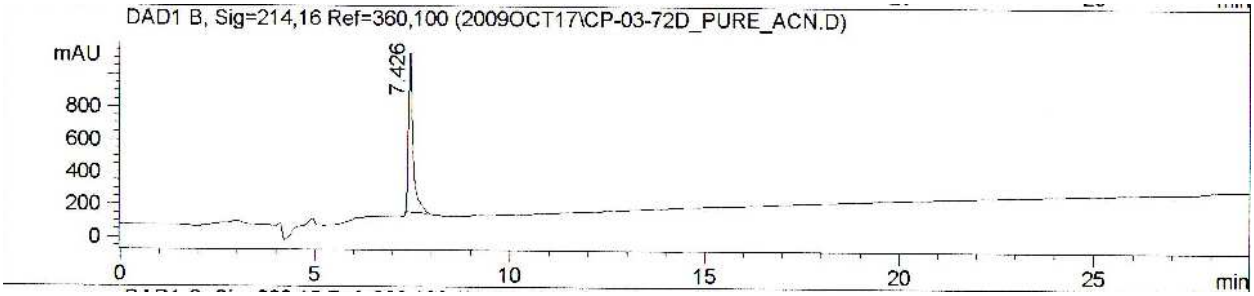


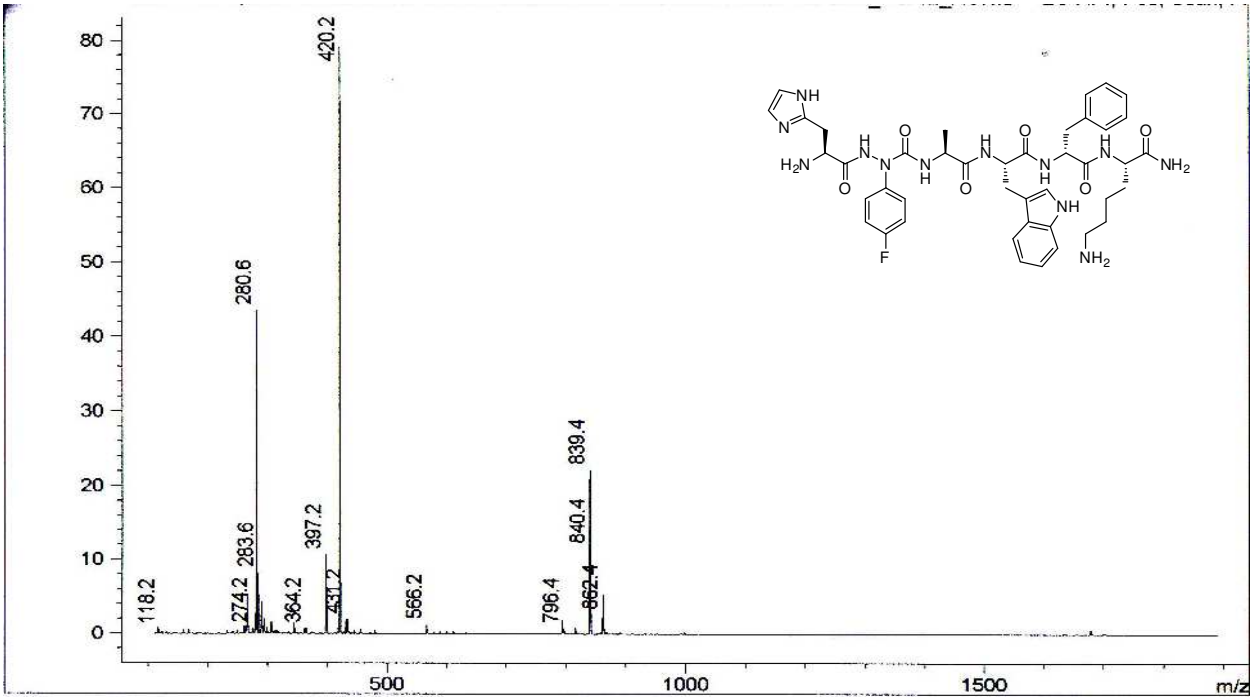


His-Aza(*p*-fluoro benzene)-Ala-Trp-D-Phe-Lys-NH_2 (10e)

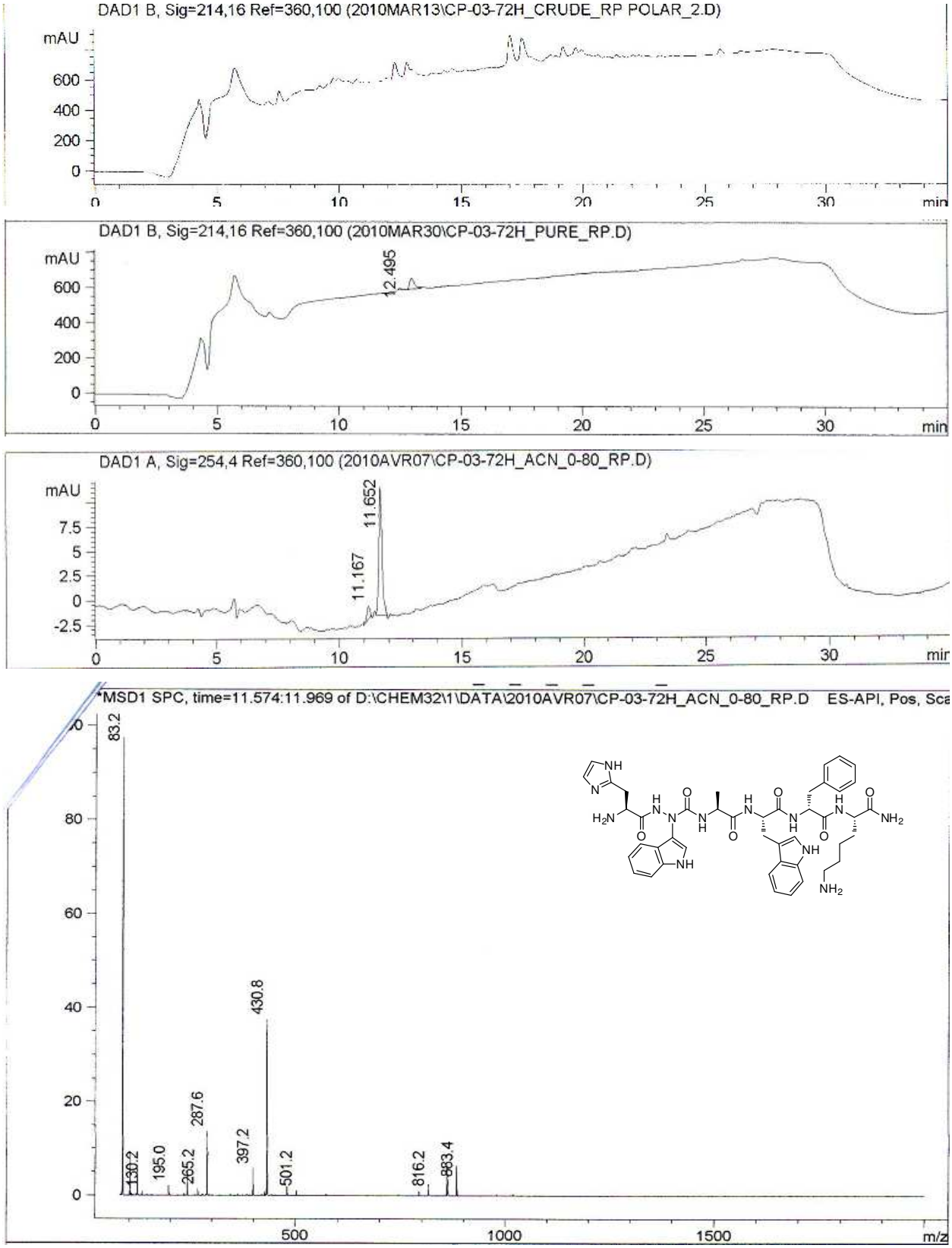


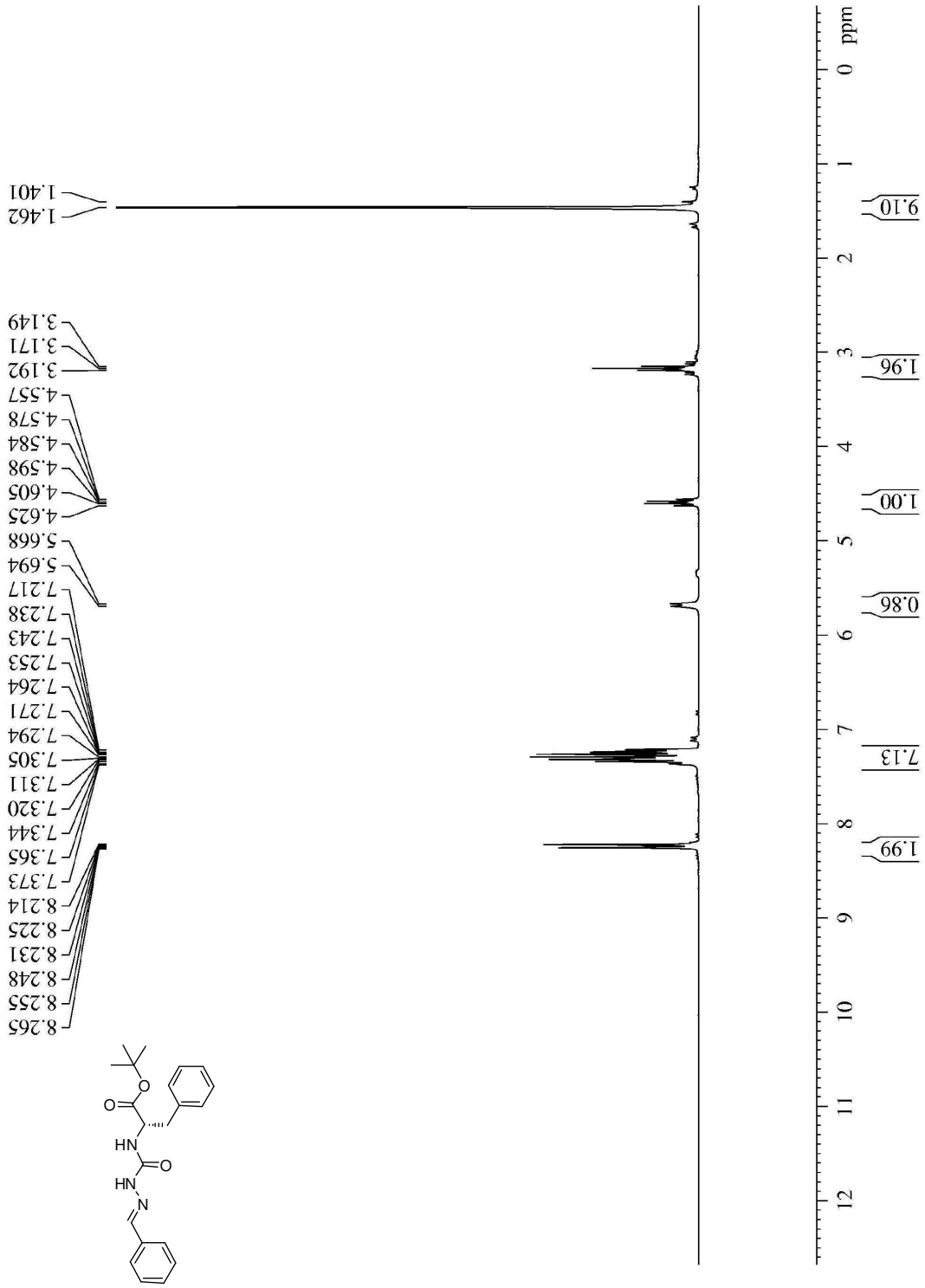






His-Aza(indoyl)-Ala-Trp-D-Phe-Lys-NH_2 (10f)

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8.231
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7.365
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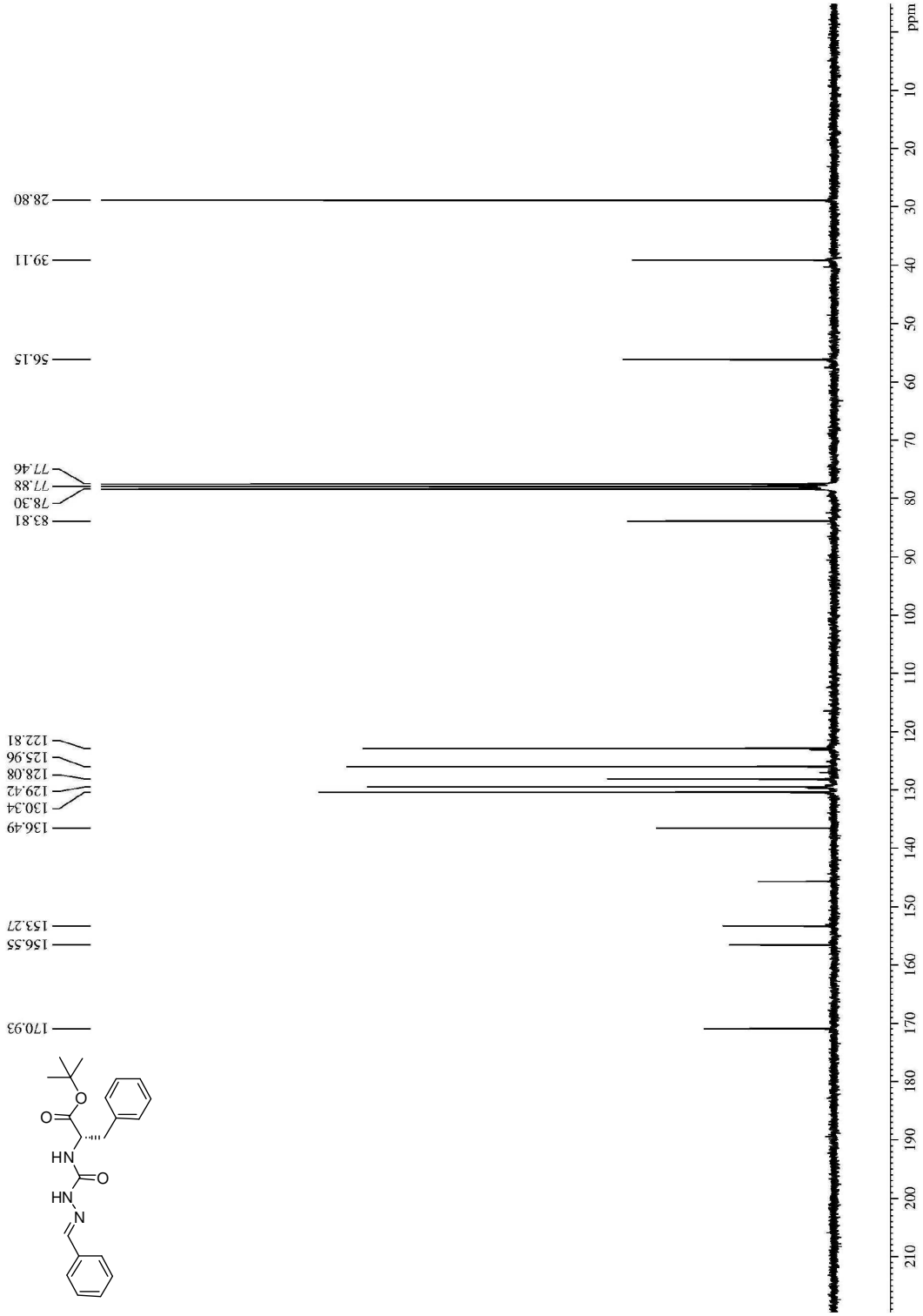
7.320
7.311
7.305
7.294
7.271
7.264
7.253
7.243
7.238
7.217
5.694
5.668
4.625
4.605
4.598
4.584
4.578
4.557
3.192
3.171
3.149
1.462
1.401
HN
HN
N
O
O
O
O
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
1.99
7.13
0.86
1.00
1.96
9.10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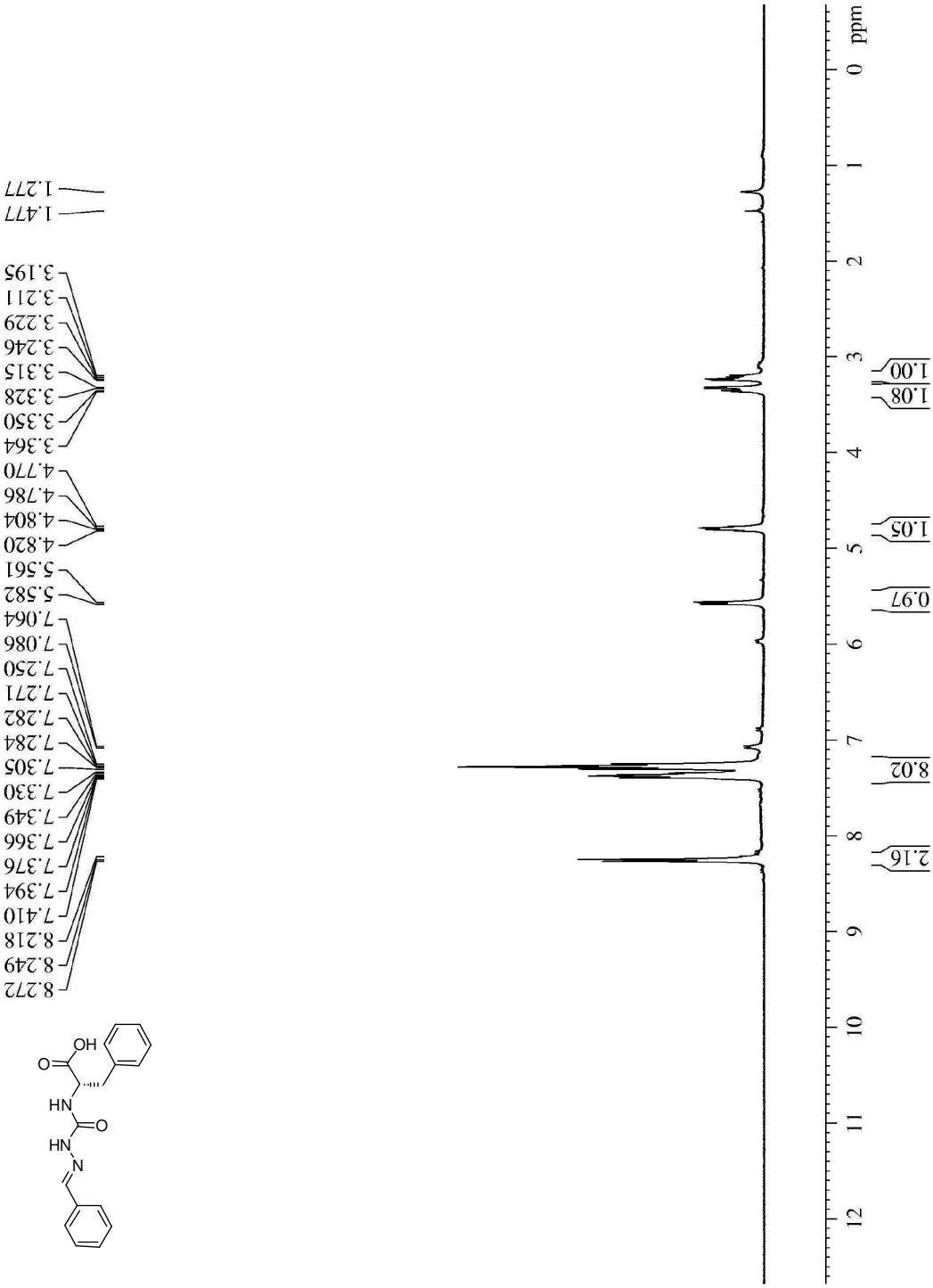
153.27
136.49
130.34
129.42
128.08
125.96
122.81
83.81
78.30
77.88
77.46
56.15
39.11
28.80
ppm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8.218
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7.349
7.330
7.305
7.284
7.282
7.271
7.250
7.086
7.064
5.582
5.561
4.820
4.804
4.786
4.770
3.364
3.350
3.328
3.315
3.246
3.229
3.211
3.195
1.477
1.277
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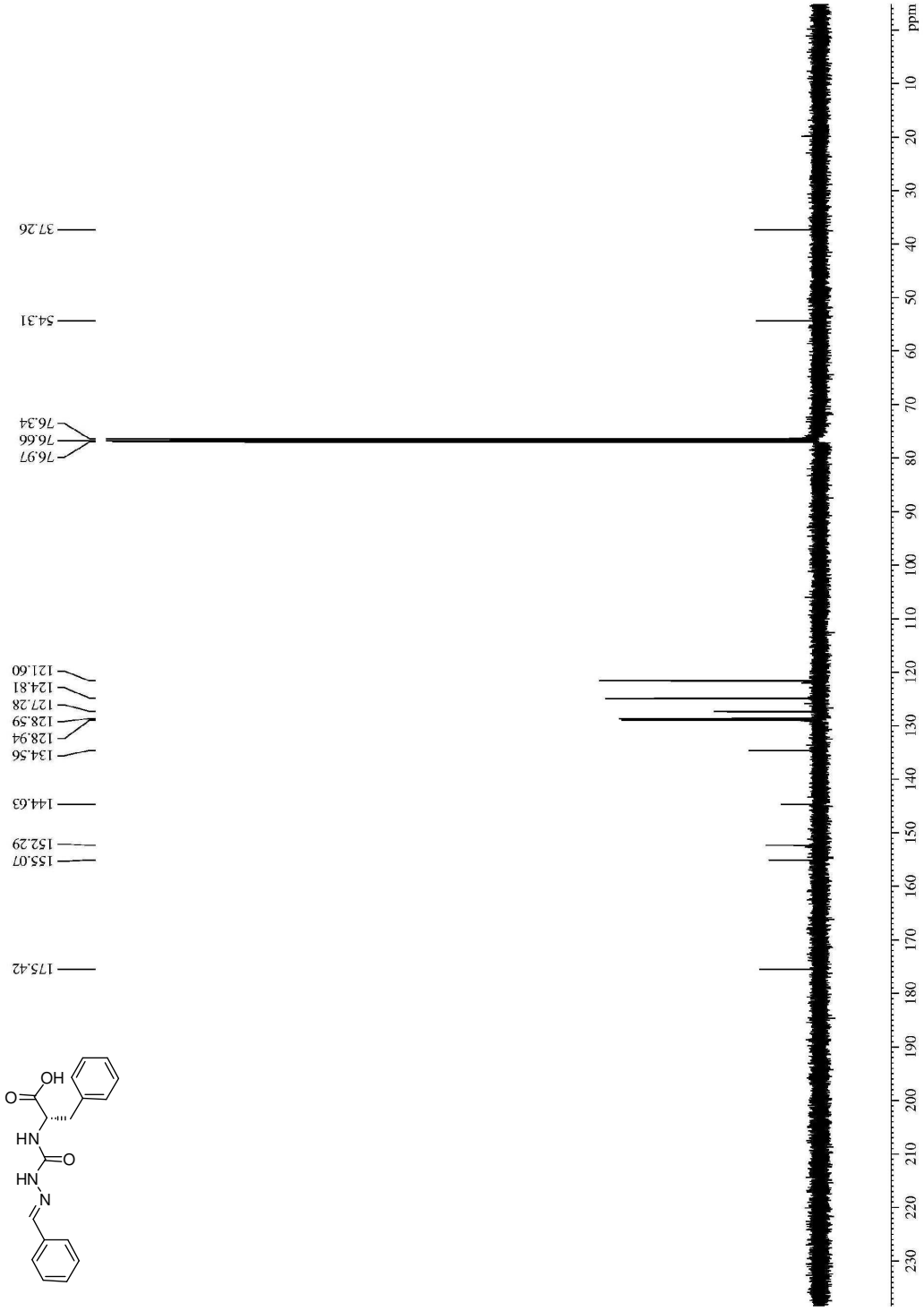
O
O
OH
O
2.16
8.02
0.97
1.05
1.08
1.00
ppm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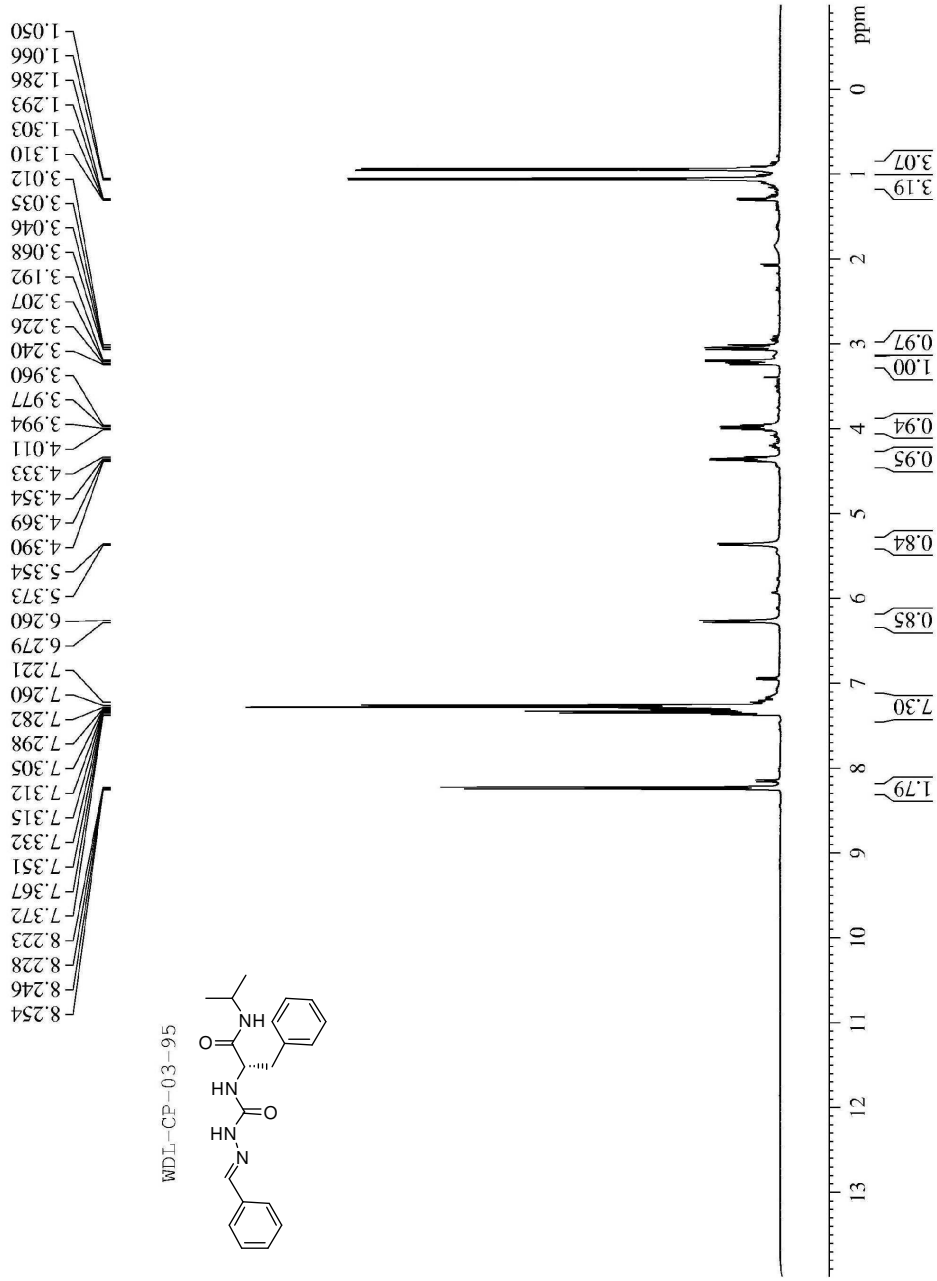
155.07
152.29
144.63
134.56
128.94
128.59
127.28
124.81
121.60
76.97
76.66
76.34
54.31
37.26
ppm


WDI-CP-03-95
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8.228
8.223
7.372
7.367
7.351
7.332
7.315
7.312
7.305
7.298
7.282
7.260
7.221
6.279
6.260
5.373
5.354
4.390
4.369
4.354
4.333
4.011
3.994
3.977
3.960
3.240
3.226
3.207
3.192
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3.046
3.035
3.012
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1.303
1.293
1.286
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0.84
0.95
0.94
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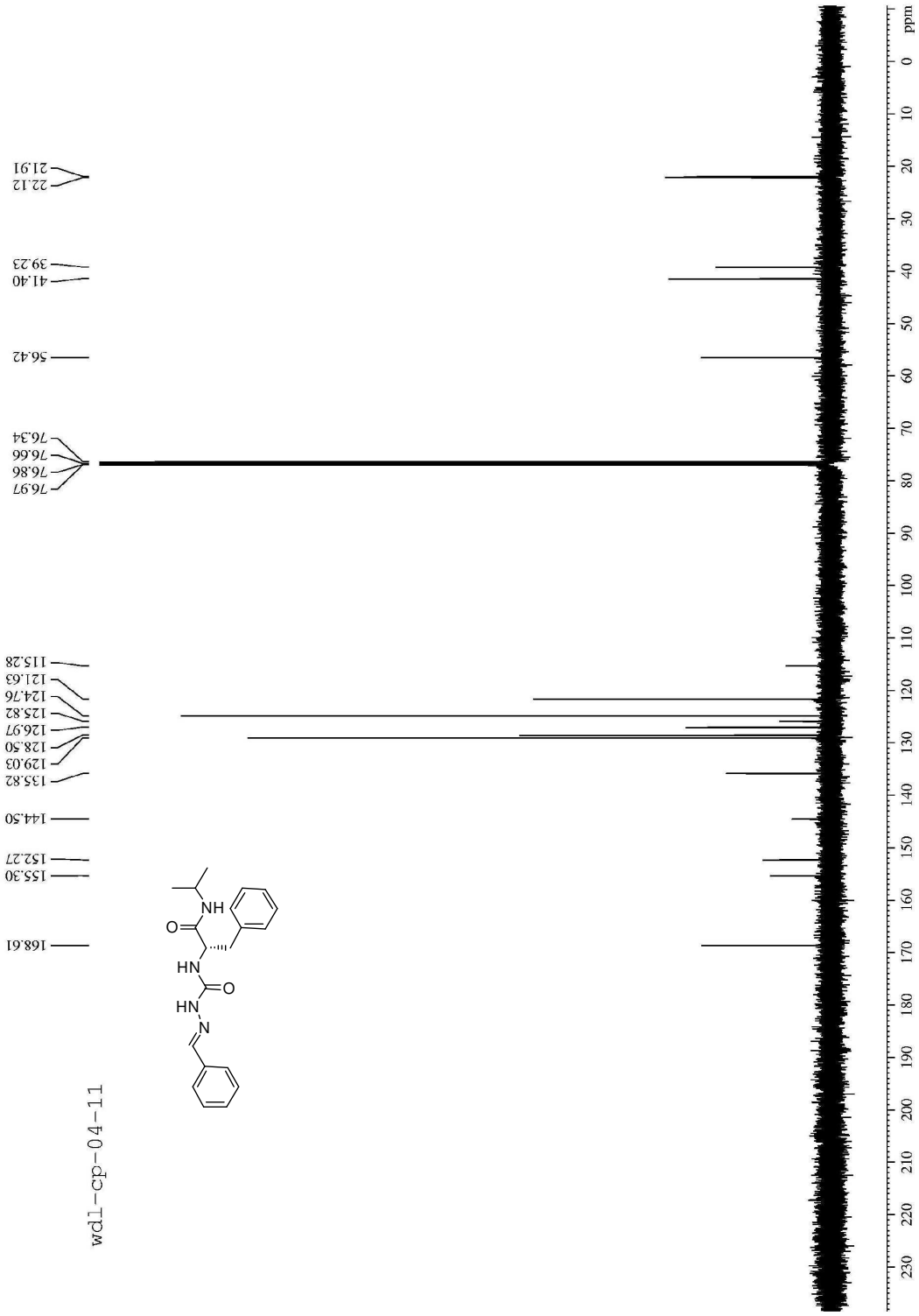
0.97
3.19
3.07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129.03
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125.82
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76.66
76.34
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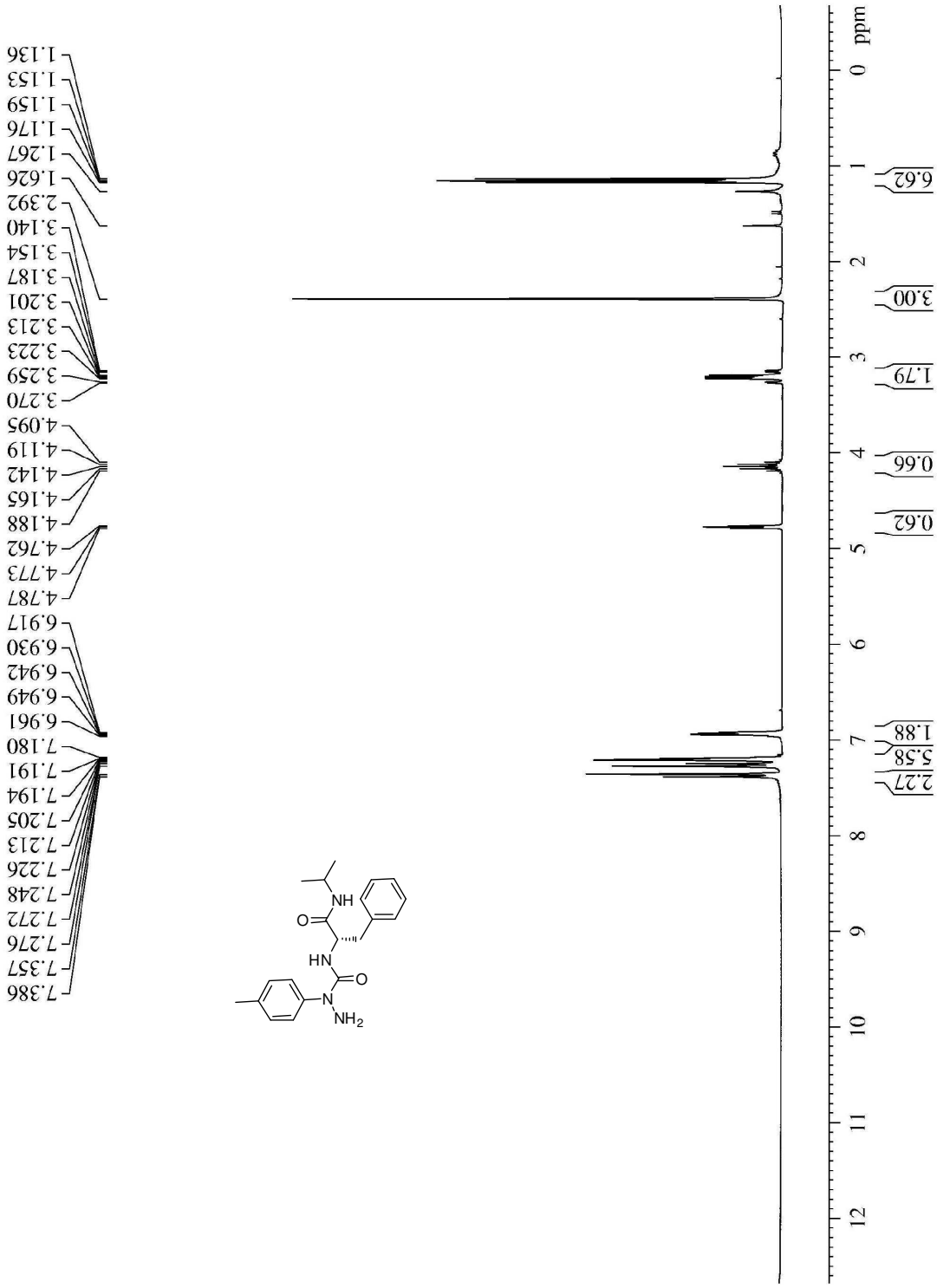
ppm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7.226
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7.205
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7.191
7.180
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6.949
6.942
6.930
6.917
4.787
4.773
4.762
4.188
4.165
4.142
4.119
4.095
3.270
3.259
3.223
3.213
3.201
3.187
3.154
3.140
2.392
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1.267
1.176
1.159
1.153
1.136
NH
O
HN
O
N
NH2
ppm
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2
3
4
5
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11
12
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3.00
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0.66
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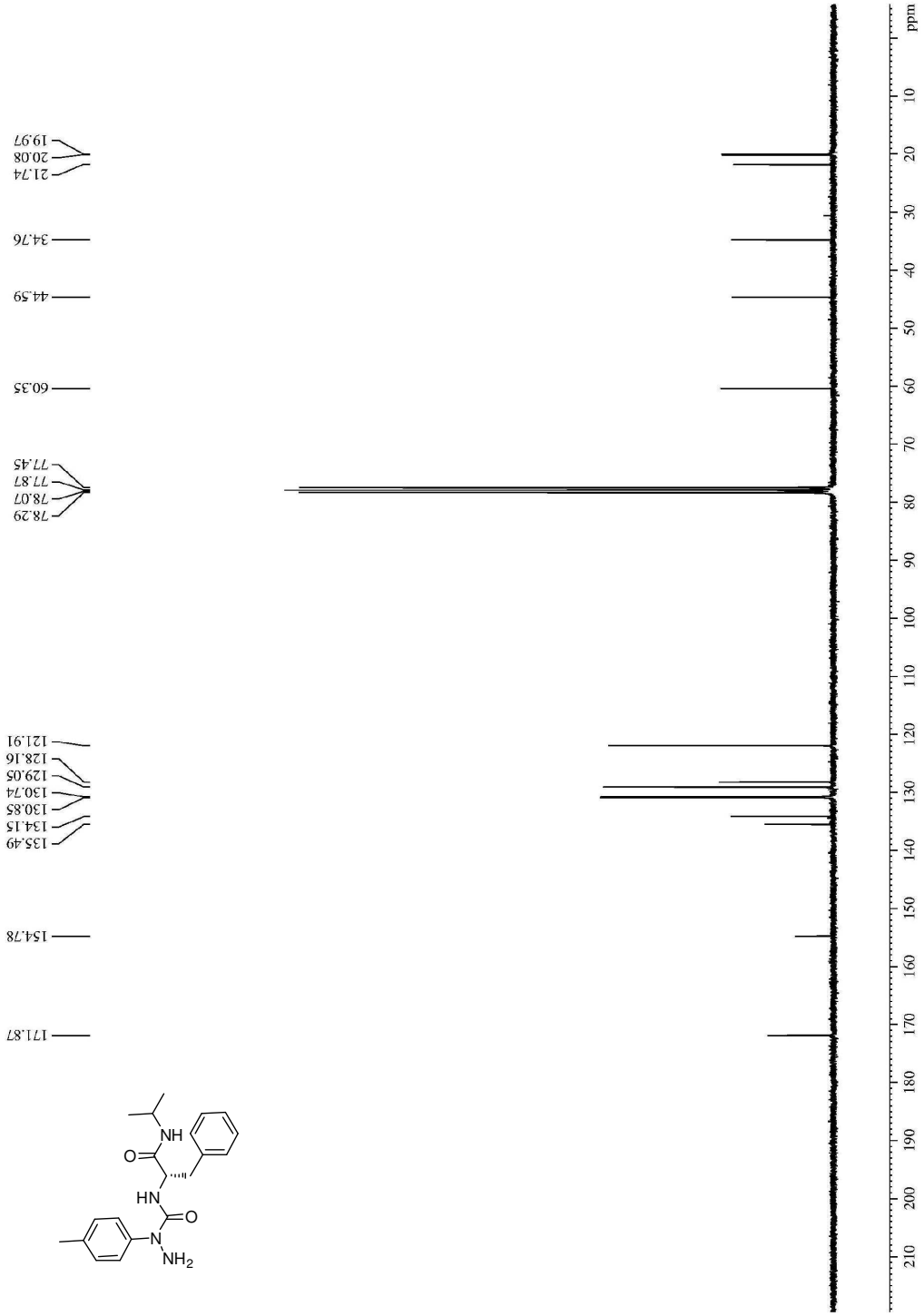
2.27
5.58
1.88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70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
NH
O
HN
O
N
NH2