

Supporting Information

Covered by Neuroligin-2 derived peptide polyamidoamine-based (PAMAM) dendrimers enhance pancreatic β -cells proliferation and functions

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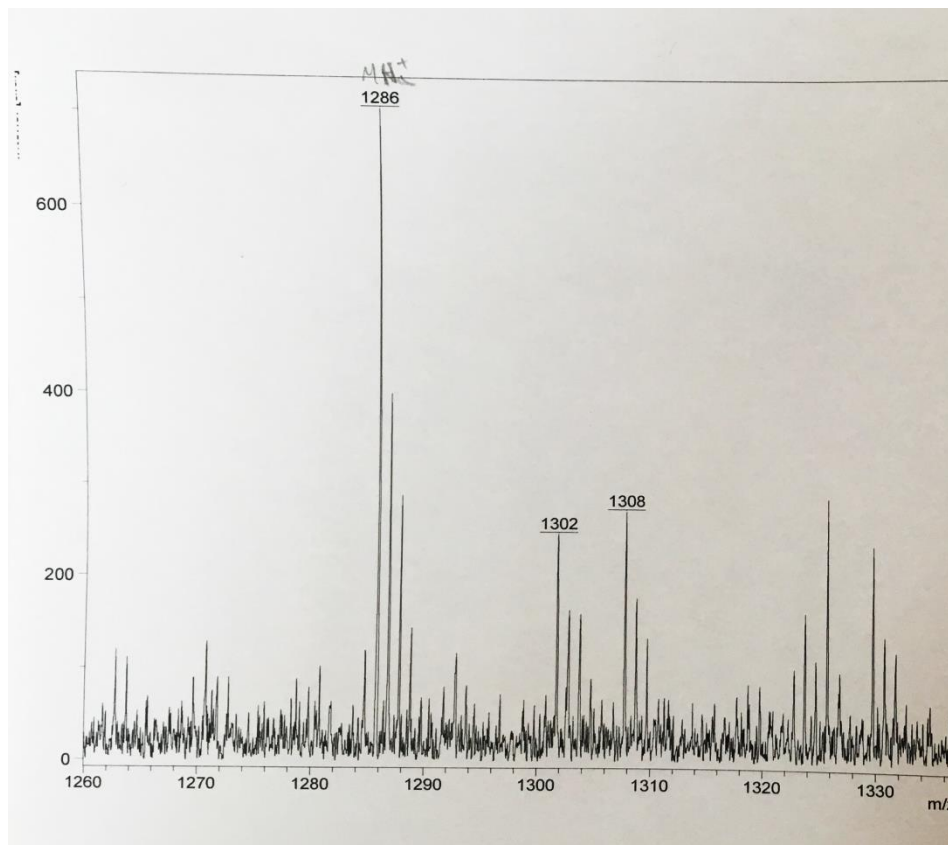
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1. Materials

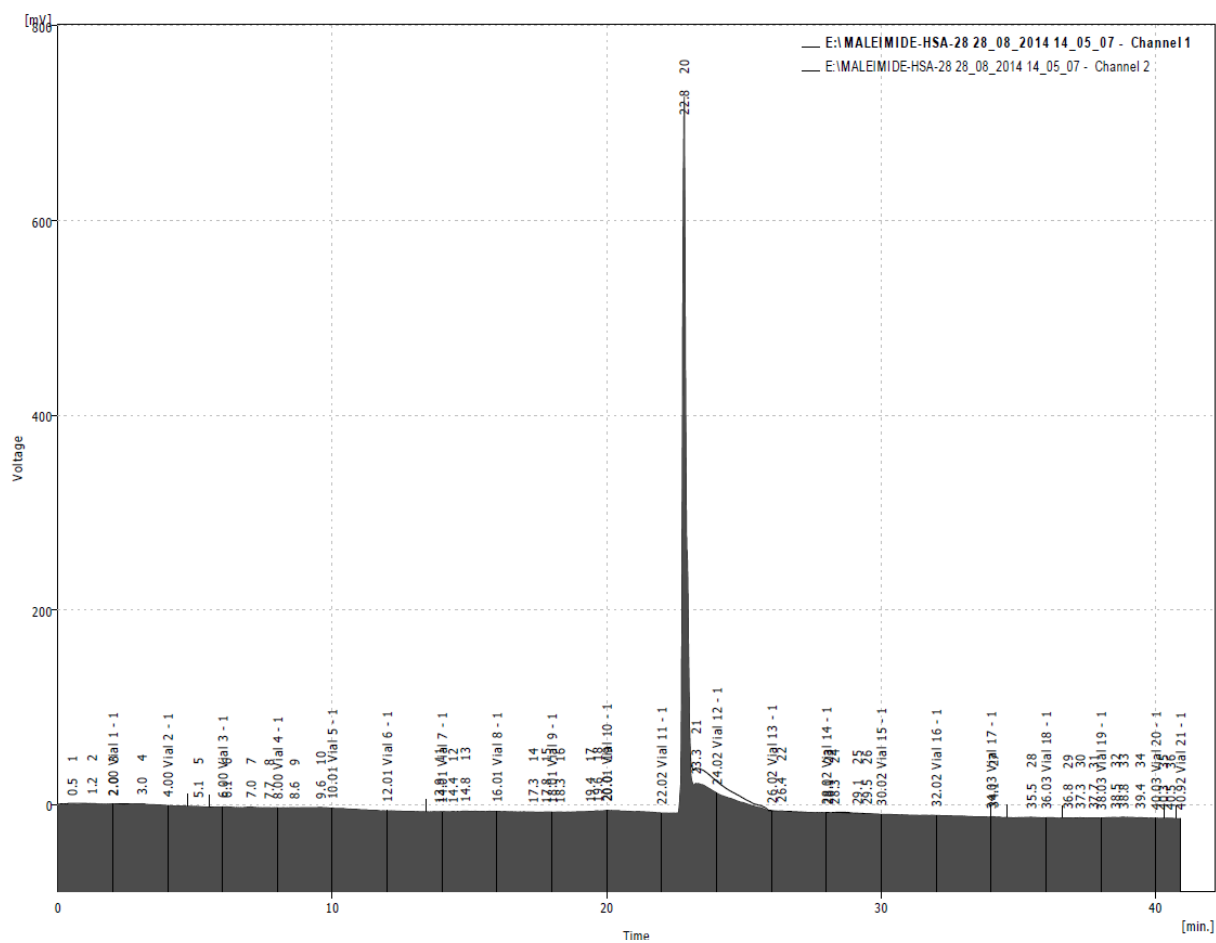
PAMAM dendrimer (ethylenediamine core, fifth generation), bovine serum albumin (BSA), glucose oxidase (GO), thapsigargin (Tg), protease inhibitor cocktail, radioimmunoprecipitation assay buffer (RIPA), rink amide resin, 2,2-diphenylethylamine, benzhydrylamine, phenethylamine, benzylamine, glycineamide hydrochloride, α - and β -naphthaldehyde, 1,2,3,4-tetraisoquinoline, n-bromoethylphthalimide, potassium carbonate, potassium iodide, tert-butyl acrylate, isobutylamine, triethylamine, 2-iminothiolane, 3-maleimidopropionic acid were purchased from Sigma-Aldrich (Merk), (Rehovot, Israel). Fetal calf serum (FCS), phosphate buffered saline (PBS), L-glutamine, Trypan blue, Roswell Park Memorial Institute medium (RPMI-1640), and antibiotics were purchased from Biological Industries (Beth-Haemek, Israel). Formaldehyde (4% in PBS) was purchased from Bio-Lab (Jerusalem, Israel). Rink amide resin, DIEA, protected amino acids were obtained from Chem Impex (Wood Dale, IL, USA). β -Mercaptoethanol was purchased from Bio-Rad (Hercules, CA, USA). Alfa Aesar (Ward Hill, MA, USA) supplied t-isopropanol-silane. Alexa Fluor 633 Phalloidin was purchased from Life Technologies (Carlsbad, CA, USA). Anti-glucagon, anti-C-peptide and anti-Pdx1 antibodies were supplied by Abcam (Cambridge, MA, USA). Mercodia Insulin ELISA kit was purchased from Mercodia (Uppsala, Sweden). All organic solvents were purchased from Carlo Erba Reagents (Val De Reuil, France).

2. Characterization data of modified HSA-28 peptide

a. Mass spectroscopy analytical data

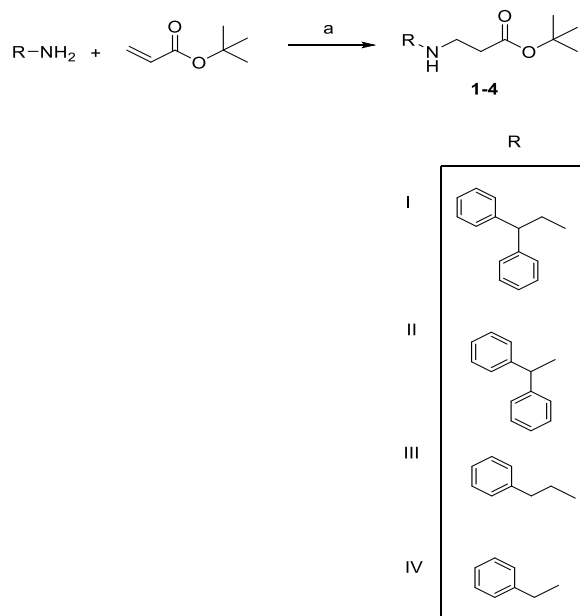


b. HPLC analytical data



3. Synthetic procedures

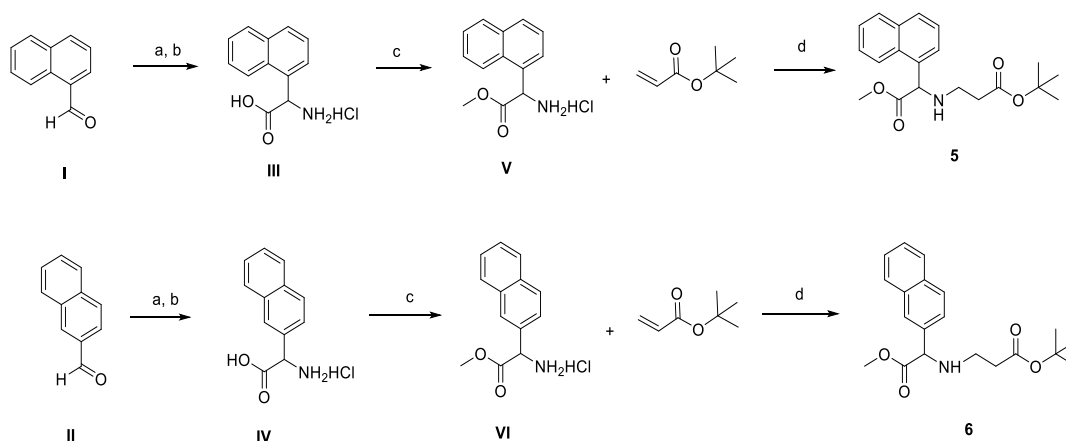
General procedure for the synthesis of tert-butylaminopropanoates (**1-4**).



Scheme 1. Synthesis of compounds **1-4**. Reagents and conditions. (a) EtOH, rt, overnight.

Tert-butyl acrylate (10 mmol) was added dropwise to the appropriate aromatic amines (**I**, 2,2-diphenylethylamine; **II**, benzhydrylamine; **III**, phenethylamine, **IV**, benzylamine, 10 mmol in EtOH, 5 ml). Stirring at rt was continued overnight. The reaction progress was followed by TLC (DCM/EtOAc 1:1, 1% TEA). After completion of the reaction, EtOH was evaporated under reduced pressure to yield colorless to yellow oil. The compounds were purified by column chromatography using the same conditions as in TLC monitoring.

General procedure for the synthesis tert-butyl 3-((2-methoxy-1-(naphthalen-1-yl)-2-oxoethyl)amino)propanoate (**5**) and tert-butyl 3-((2-methoxy-1-(naphthalen-2-yl)-2-oxoethyl)amino)propanoate (**6**)

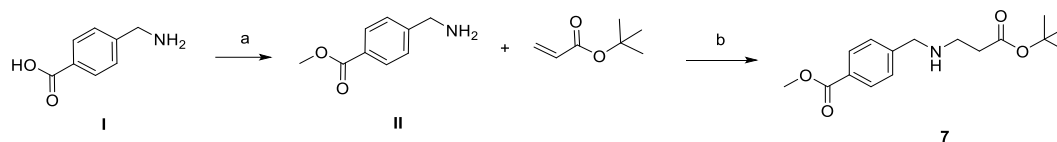


Scheme 2. Synthesis of compounds **5**, **6**. Reagents and conditions. (a) KCN, NH₄Cl, NH₄OH (30%), rt, overnight. (b) HCl, reflux, 2h. (c) SOCl₂, MeOH, reflux, 6h. (d) TEA, MeOH, rt, 48h.

Potassium cyanide (28 mmol) and ammonium chloride (28 mmol) were dissolved in 100 ml of aqueous solution of ammonia (30%). The solution was cooled on ice bath to 5 °C. Commercially available α - or β -naphthaldehyde (**I** and **II**, respectively, 12 mmol) were then added in three portions with 5 min intervals. The obtained mixture was stirred overnight at rt. Then, the mixture was diluted with 100 ml of water and extracted twice with 100 ml of toluene. The toluene fraction was extracted twice with 60 ml 6N HCl. The aqueous acidic layer was refluxed for 2h, then cooled to 0 °C, affording white to cream crystals that were collected by suction filtration. α - Naphthylphenyl glycine hydrochloride (**III**) and β -naphthylphenyl glycine hydrochloride (**IV**), respectively, were taken to the next step without any purification. Next, α - naphthylphenyl glycine hydrochloride or β - naphthylphenyl glycine hydrochloride (**III**, **IV**, respectively, 10 mmol) was dissolved in thionyl chloride

(0.05 mol) and the solution was stirred for 1 h at rt. After the indicated time, the solution was cooled on ice bath and 100 ml of MeOH and an additional amount of thionyl chloride (0.05 mol) was added. The obtained solution was refluxed for 6 h, cooled, and the solvent was evaporated under reduced pressure. The product was precipitated from a minimum amount of MeOH by the addition of diethyl ether. Methyl 2-amino-2-(naphthalen-1-yl)acetate (**V**) or methyl 2-amino-2-(naphthalen-2-yl)acetate (**VI**) were taken to the next step without any purification. Finally, compounds **V** or **VI** from the previous step (0.5 mmol) were dissolved in 25 ml of MeOH followed by the addition of an equivalent amount of TEA. Tert-butyl acrylate (0.5 mmol) was dissolved in 10 ml of MeOH and the mixture was added dropwise to solutions of compounds **V** or **VI**. The mixture was stirred at rt for 48 h. The monitoring of the reaction was performed through TLC (hexane/EtOAc 6:4, 2% TEA). After the indicated time, the solvent was evaporated under reduced pressure and compounds were purified by column chromatography using hexane/EtOAc 6:4, 2% TEA as an eluent to obtain compounds **5** or **6**, respectively, as light brown oil.

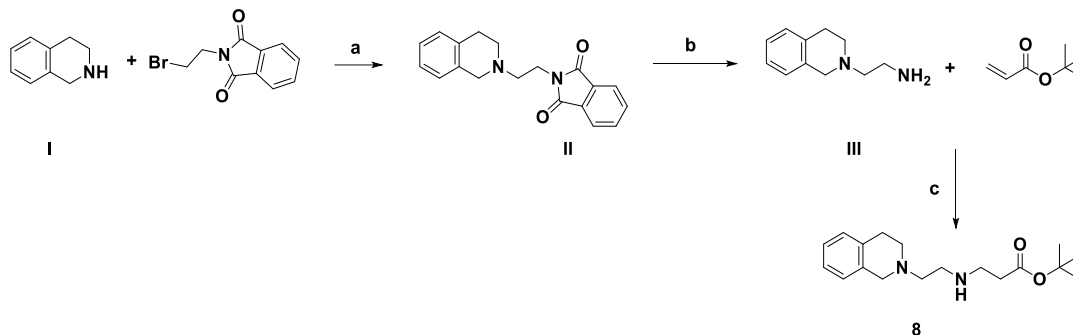
General procedure for the synthesis methyl 4-(((3-(tert-butoxy)-3-oxopropyl)amino)methyl)benzoate (**7**)



Scheme 3. *Synthesis of compound 7.* Reagents and conditions. (a) SOCl₂, MeOH, reflux, 6h. (b) TEA, MeOH, rt, overnight.

Commercially available 4-aminomethylbenzoate (**I**, 0.02 mol) was refluxed in MeOH (50 ml) for 6h in the presence of thionyl chloride (0.04 mol). After the indicated time, the mixture was cooled on the ice bath and the white precipitate was filtered, affording pure methyl 4-(aminomethyl)benzoate (**II**). In the next step, the obtained compound was reacted with tert-butyl acrylate by a method that was described above, yielding compound **7**. Monitoring of the reaction was performed using a mixture of hexane/EtOAc (6:4) in the presence of 1% TEA. The purification of **7** was performed by column chromatography using the same eluent.

General procedure for the synthesis tert-butyl 3-((2-(3,4-dihydroisoquinolin-2(1H)-yl)ethyl)amino)propanoate (**8**)

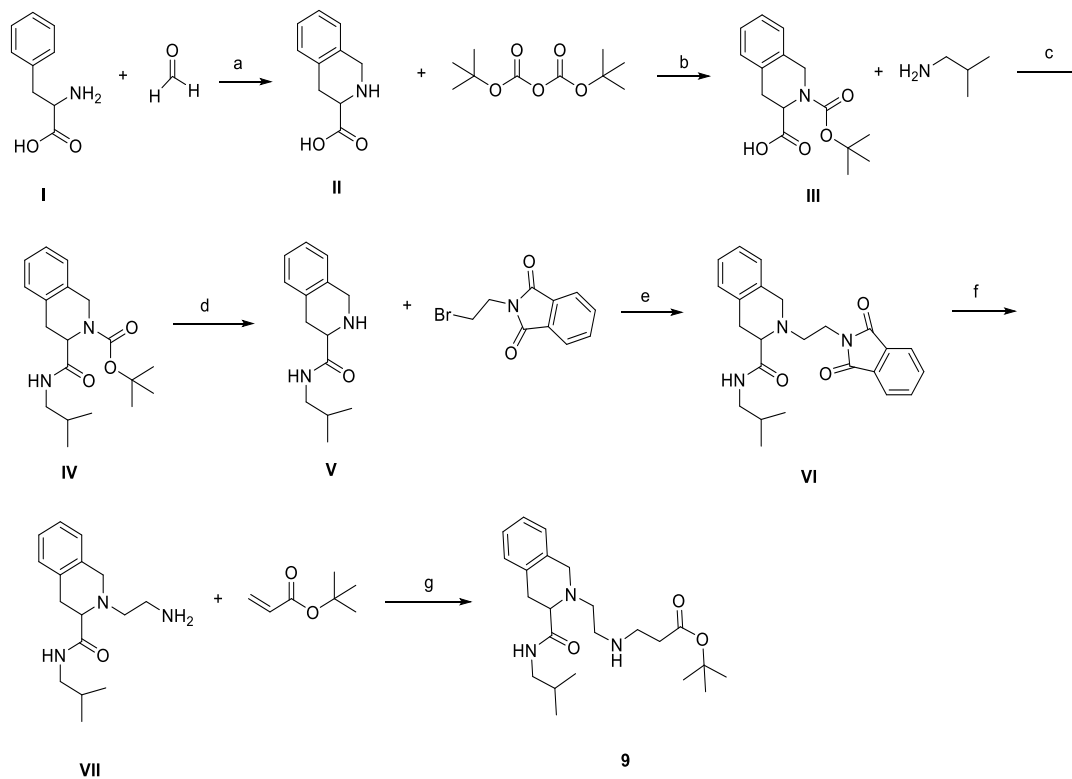


Scheme 4. *Synthesis of compound 8.* Reagents and conditions. (a) K_2CO_3 , KI, MeCN, reflux, 4h. (b) hydrazine hydrate, EtOH, reflux, 2h. (c) EtOH, rt, overnight

Commercially available 1,2,3,4-tetrahydroisoquinoline (**I**) (10 mmol) was dissolved in MeCN and treated with n-bromoethylphthalimide (12.5 mmol), potassium carbonate (30 mmol), and potassium iodide (12.5 mmol). The mixture was refluxed for 4h. After the indicated time, the reaction solution was filtered and the filtrate was evaporated under reduced pressure. The residue was dissolved in EtOAc and the solution was acidified with 2N of HCl followed by extraction with water. The pH of the aqueous phase was adjusted to pH 12 with 4N NaOH and extracted with DCM. Evaporation of the organic solvent afforded 2-(2-(3,4-dihydroisoquinolin-2(1H)-yl)ethyl)isoindoline-1,3-dione (**II**), which was taken to the next step without any purification. In the next step, the latter compound was dissolved in 40 ml of EtOH and 19 mmol of hydrazine hydrate was added to the solution. The reaction was refluxed for 2h and cooled to rt. The precipitation was gravitationally filtered and the filtrate was concentrated under vacuum. The residue was dissolved in 40

ml EtOAc, filtered, and evaporated again, affording 2-(3,4-dihydroisoquinolin-2(1H)-yl)ethan-1-amine (**III**), which was taken to the next step without purification. Finally, **III** was reacted with tert-butyl acrylate by a method described before, affording compound **8**. The monitoring of the reaction and the purification by column chromatography were performed under the same conditions mentioned above.

General procedure for the synthesis tert-butyl 3-((2-(3-(isobutylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl) ethyl) amino) propanoate (**9**)



Scheme 5. Synthesis of compound **9**. Reagents and conditions. (a) 32% HCl, H_2SO_4 , reflux, 48h. (b) NaOH, THF, H_2O , rt, 48h. (c) DCC, HOSu, TEA, DCM, rt, overnight. (d) DCM/TFA (1:1), rt, 1h. (e) K_2CO_3 , KI, MeCN, reflux, overnight. (f) hydrazine hydrate, EtOH, reflux, 2h. (g) EtOH, rt, overnight.

Cyclization of commercially available L-phenylalanine (**I**) (0.015 mmol) was performed by reaction with an excess of paraformaldehyde (2 gr) in the presence of concentrated sulfuric for the corresponding 1, 2, 3, 4-tetrahydroisoquinoline-3-carboxylic acid (**II**). Briefly, the amino acid was dissolved in 32% hydrochloric acid (50 ml), followed by the

addition of 0.5 ml of sulfuric acid. The solution was refluxed for 48h, cooled, and filtered. The resulting solid was dissolved in a hot mixture of H₂O/EtOH (1:1, 25 ml) and basified with ammonium hydroxide (30%) until pH 7.0. The obtained crystals were collected by filtration, washed with two portions of EtOH, affording **II**, which was taken to the next step without any purification.

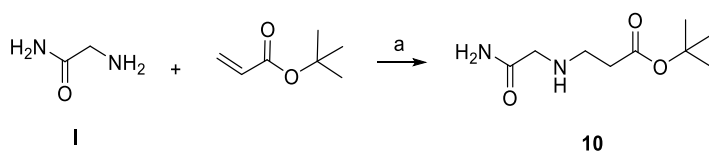
In the next step, the secondary amine of **II** was protected by Boc protecting group to afford 2-(tert-butoxycarbonyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid **III**. Briefly, 1, 2, 3, 4-tetrahydroisoquinoline-3-carboxylic acid (0.01 mol) and sodium hydroxide (0.015 mol) were dissolved in water and a solution of di-tert-butyl dicarbonate (0.016 mol) in THF (10 ml) was added dropwise. After having been stirred for 48h at rt, the solvent was evaporated, the residue was dissolved in EtOAc (25 ml), and washed with 5% KHSO₄ and brine. The organic solvent was dried over sodium sulphate, and evaporated, leading to 2-(tert-butoxycarbonyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (**III**).

In the next step, commercially available isobutylamine was coupled to a carboxylic moiety of **III** by DCC coupling reagent and HOSu to obtain tert-butyl 3-(isobutylcarbamoyl)-3,4-dihydroisoquinoline-2(1H)-carboxylate **IV**, followed by removal of Boc protecting group by TFA, leading to N-isobutyl-1,2,3,4-tetrahydroisoquinoline-3-carboxamide **V**. Isobutylamine (0.006 mol) was dissolved in DCM (50 ml). DCC (0.006 mol), HOSu (0.006 mol), and TEA (0.006 mol) were added to the solution followed by the addition of **III** (0.006 mol). After having been stirred overnight at rt, the mixture was cooled and filtered, and the filtrate was washed with 2% KHSO₄ and 5% NaHCO₃, dried over magnesium sulphate, filtered, and evaporated, affording **IV** tert-butyl 3-(isobutylcarbamoyl)-3,4-dihydroisoquinoline-2(1H)-carboxylate. The compound was

dissolved in a mixture of DCM/TFA 1:1 (20 ml) and the mixture was stirred for 1h, followed by evaporation of solvent, leading to 3-(isobutylcarbamoyl)-3,4-dihydroisoquinoline-2(1H)-carboxylate, **V**.

In the next step, a secondary amine of **V** was alkylated with bromoethylphthalimide (**VI**), followed by the removal of the phthalimide moiety by hydrazine hydrate (**VII**) and finally, 2-(2-aminoethyl)-N-isobutyl-1,2,3,4-tetrahydroisoquinoline-3-carboxamide (**VII**) was reacted with tert-butyl acrylate by the same method described before, affording **9**. The purification of **9** was performed through column chromatography using a mixture of hexane/EtOAc (8:2) as an eluent.

General procedure for the synthesis tert-butyl 3-((2-amino-2-oxoethyl)amino)propanoate (**10**)



Scheme 6. Synthesis of compound **10**. Reagents and conditions. (a) EtOH, TEA, 40 °C, 48h.

Glycinamide hydrochloride (**I**, 10 mmol) and TEA (10 mmol) were added to 70 ml of EtOH. The mixture was heated to 40 °C and stirred until all solids were completely dissolved. Then, 10 mmol of tert-butyl acrylate was mixed with 5 ml of EtOH and the mixture was added dropwise to the solution of glycinamide. Stirring at 40 °C was continued for 48h. The reaction progress was followed by TLC (hexane/EtOAc 8:2, 1% TEA) and

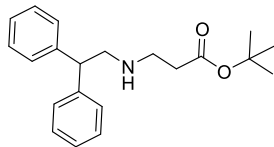
visualized in the iodide atmosphere. After completion of the reaction, EtOH was evaporated under reduced pressure to yield a colorless syrup. Compound 10 was purified by column chromatography using the same conditions as those used in TLC monitoring.

Coupling of compounds (**1-10**) to 3-maleimidopropionic acid followed by removal of t-butoxyl protecting group

3-maleimidopropionic acid was conjugated to compounds **1-10** (as described before) followed by deprotection of the t-butoxyl protecting group by neat TFA. All compounds purified by HPLC (gradient water/MeCN from 100% of water in 80 min, flow = 2 ml/min, $\lambda = 210$, $\lambda = 254$ nm).

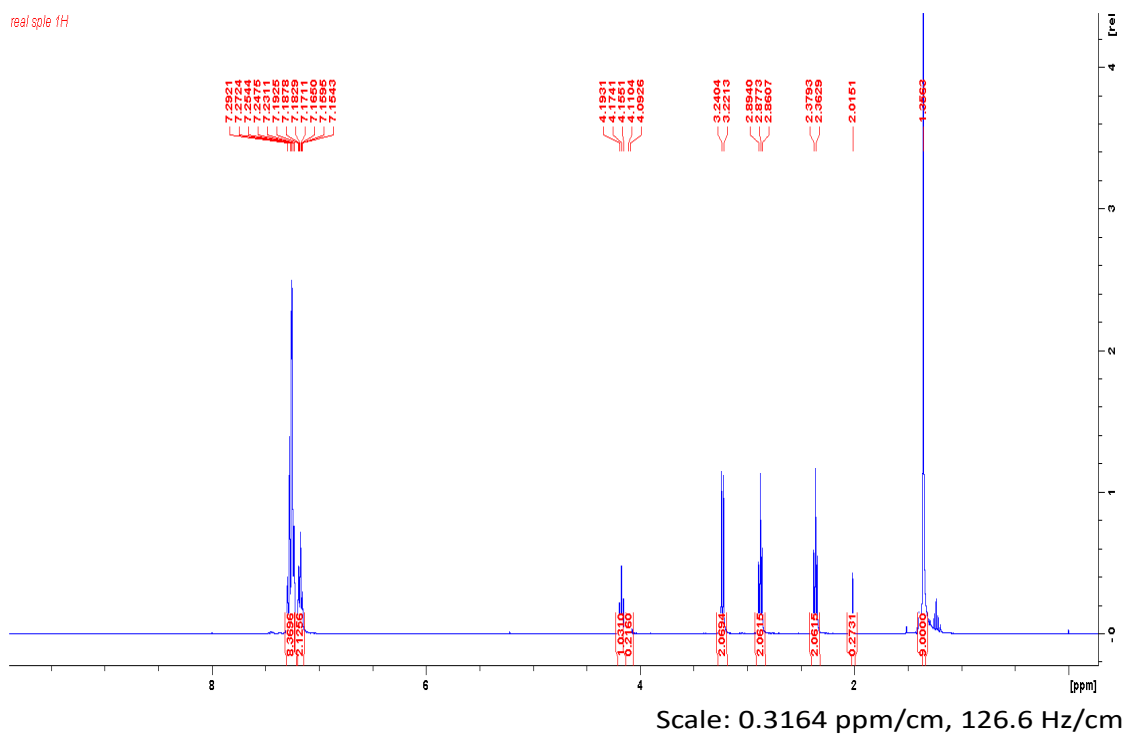
4. NMR spectra images

tert-butyl 3-((2,2-diphenylethyl)amino)propanoate (**1**)

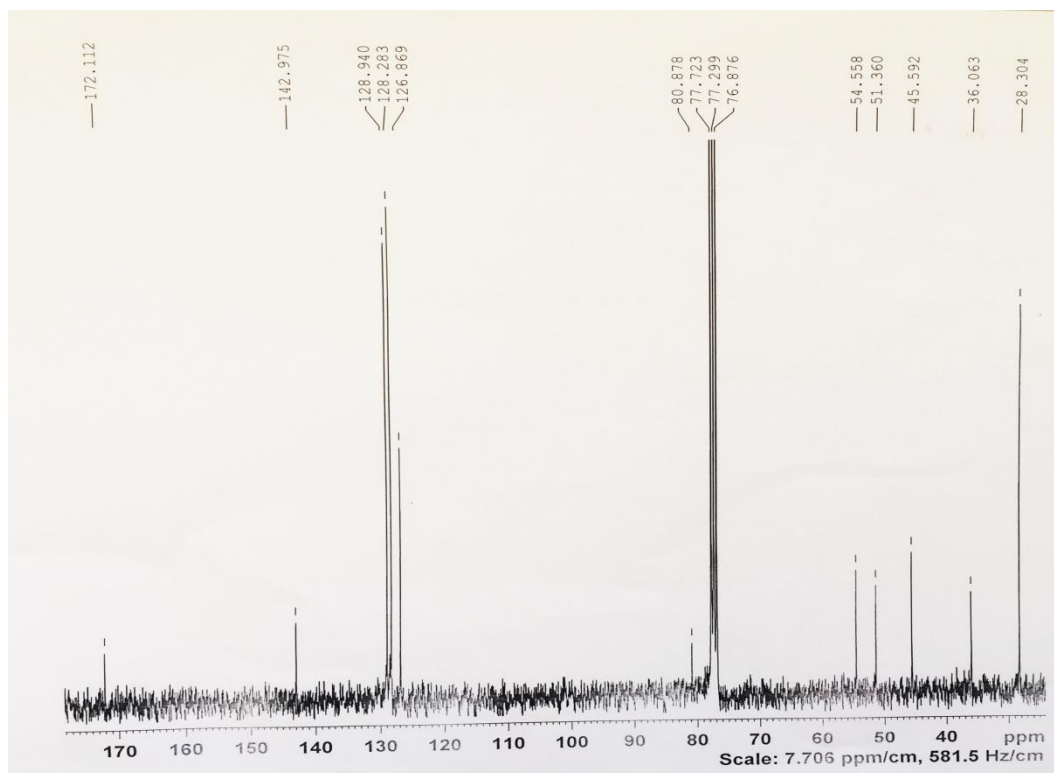


Yield 79%, pale yellow oil. ^1H NMR (CDCl_3 , 400 MHz): δ 1.356 (s, 9H), δ 2.362 (t, 2H, $J = 6.57$ Hz), δ 2.877 (t, 2H, $J = 6.68$ Hz), δ 3.230 (d, 2H, $J = 7.66$ Hz), δ 4.174 (t, 1H, $J = 7.63$ Hz), δ 7.146 – 7.298 (m, 10H). ^{13}C NMR (CDCl_3 , 75 MHz): δ 28.304, 30.063, 45.592, 51.360, 54.558, 80.878, 128.869, 128.283, 128.940, 142.975, 172.112 ppm.

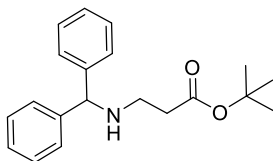
^1H NMR (CDCl_3 , 400 MHz)



^{13}C NMR (CDCl_3 , 75MHz)

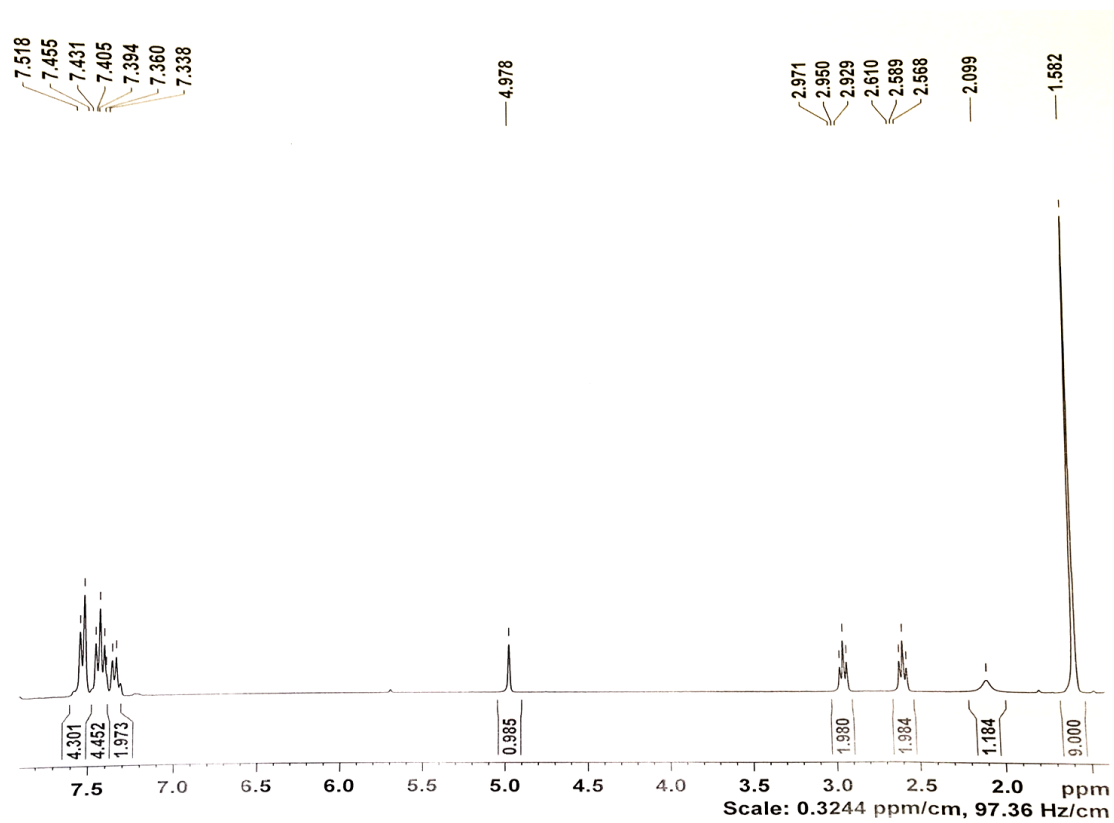


tert-butyl 3-(benzhydrylamino)propanoate (**2**)

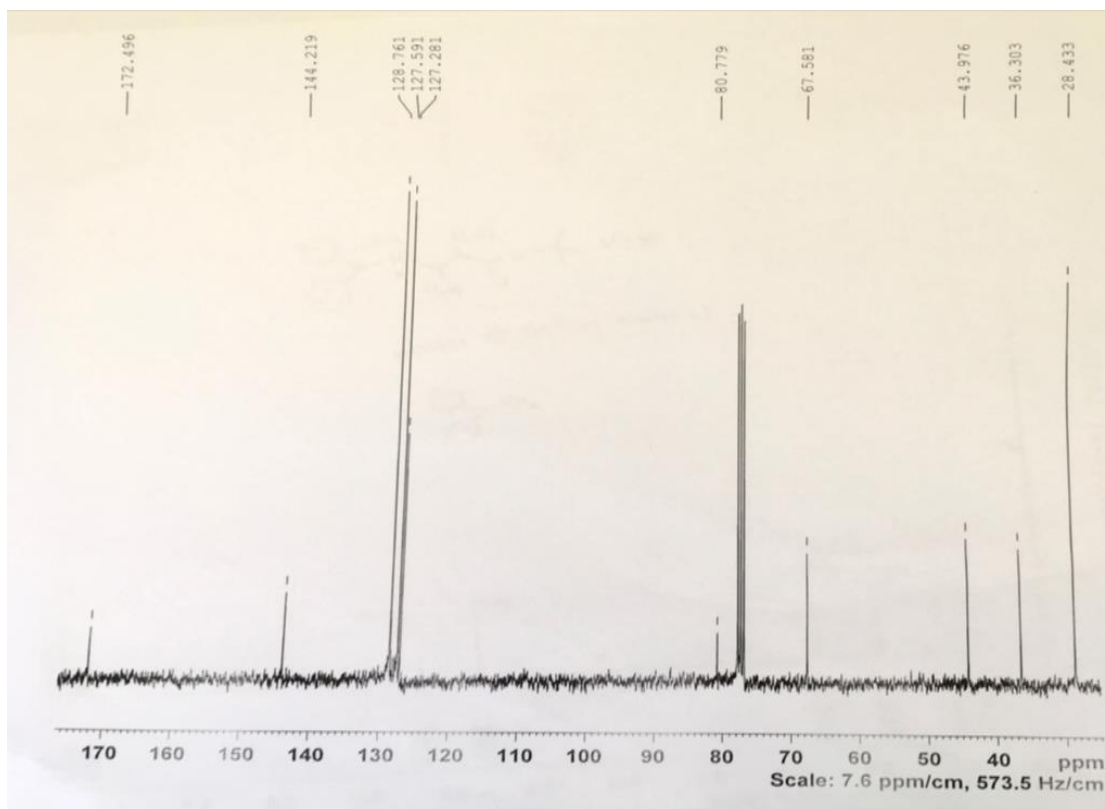


Yield 71%, pale yellow oil. ^1H NMR (CDCl_3 , 400 MHz): δ 1.582 (s, 9H), δ 2.099 (sbr, 1H), δ 2.589 (t, 2H, $J = 6.34$ Hz), δ 2.950 (t, 2H, $J = 6.39$ Hz), δ 4.978 (s, 1H), δ 7.338 – 7.518 (m, 10H). ^{13}C NMR (CDCl_3 , 75 MHz): 28.443, 36.303, 43.976, 67.581, 80.779, 127.281, 127.591, 128.761, 144.219, 172.496 ppm

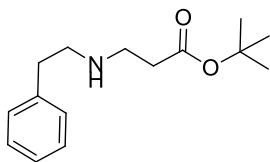
^1H NMR (CDCl_3 , 400 MHz)



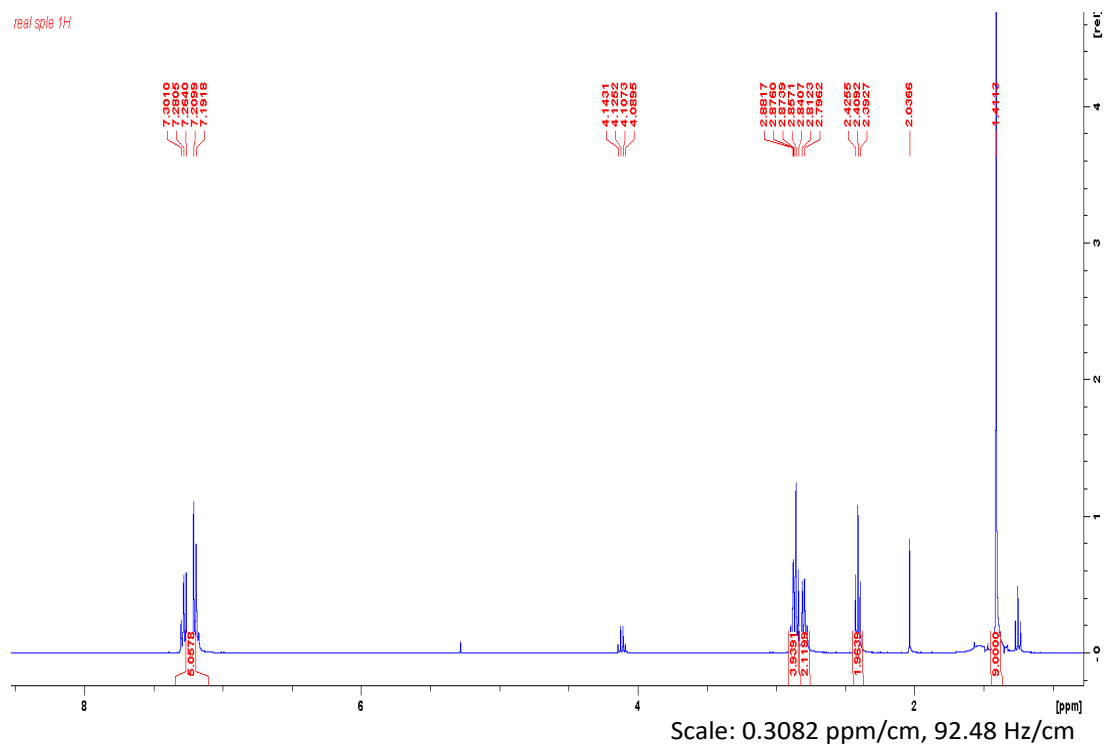
^{13}C NMR (CDCl_3 , 75MHz)



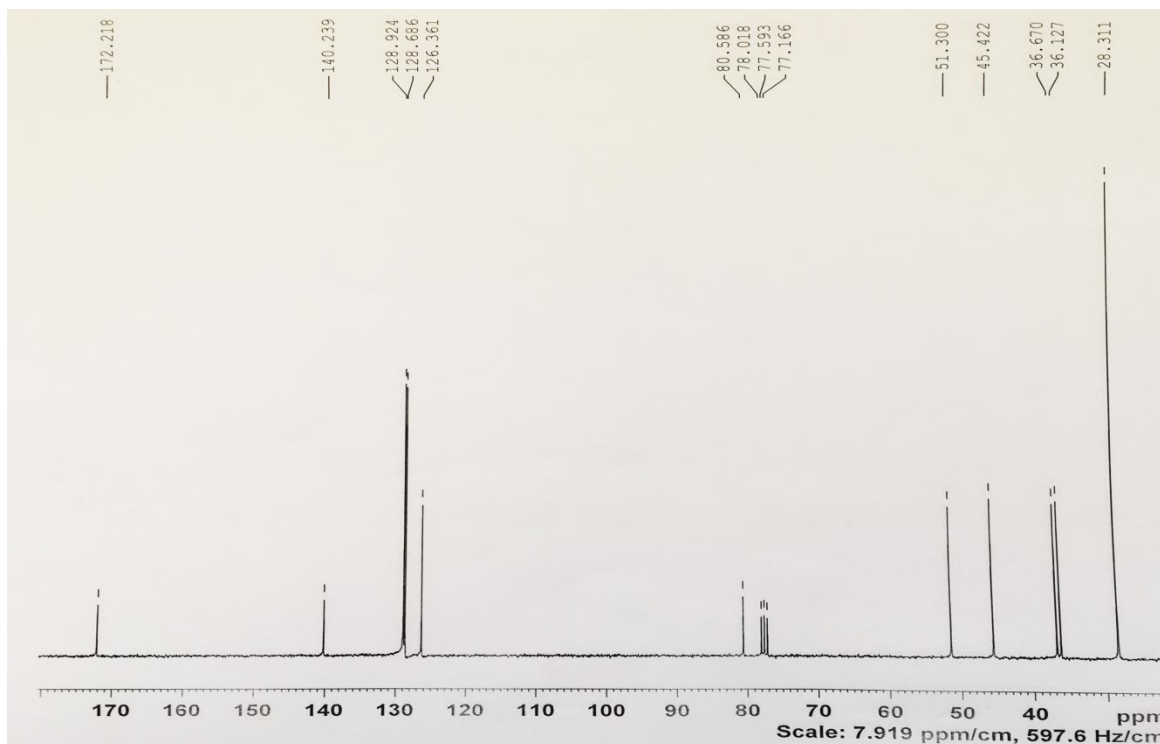
tert-butyl 3-(phenethylamino)propanoate (**3**)



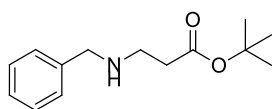
Yield 78%, colorless oil. ^1H NMR (CDCl_3 , 400 MHz): δ 1.411 (s, 9H), δ 2.409 (t, 2H, J = 7.45 Hz), δ 2.75 - 2.912 (m, 6H), δ 7.150 - 7.319 (m, 5H). ^{13}C NMR (CDCl_3 , 400 MHz): 28.311, 36.127, 36.670, 45.422, 51.300, 80.586, 126.361, 128.686, 128.924, 140.239, 172.218 ppm

¹H NMR (CDCl₃, 400 MHz)

^{13}C NMR (CDCl_3 , 75MHz)

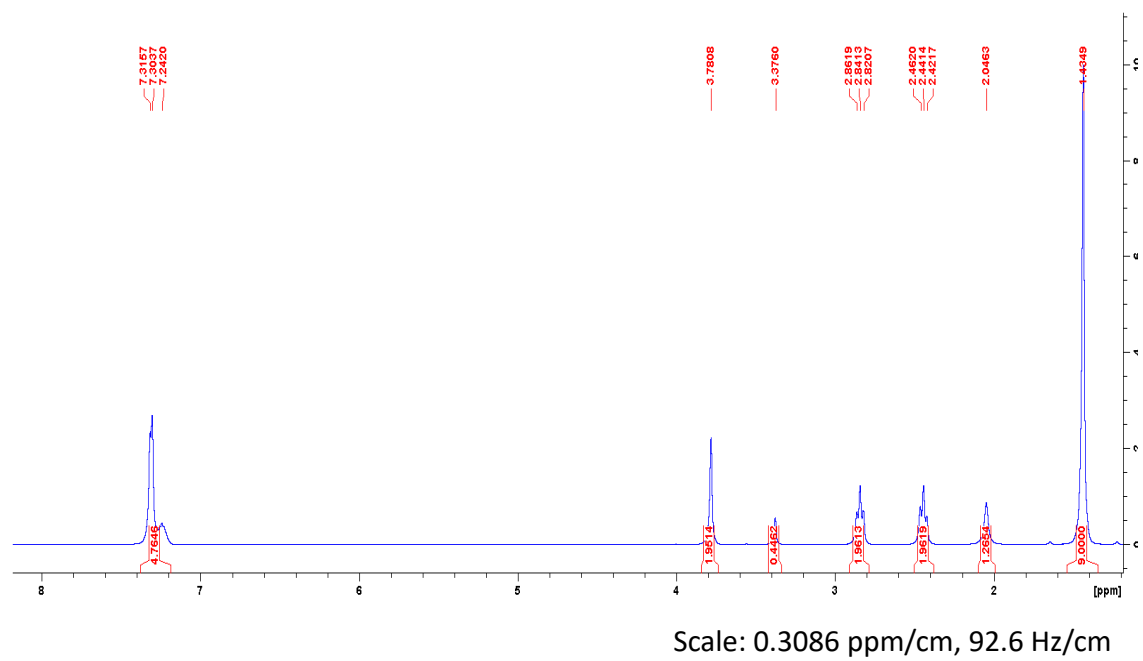


tert-butyl 3-(benzylamino)propanoate (**4**)

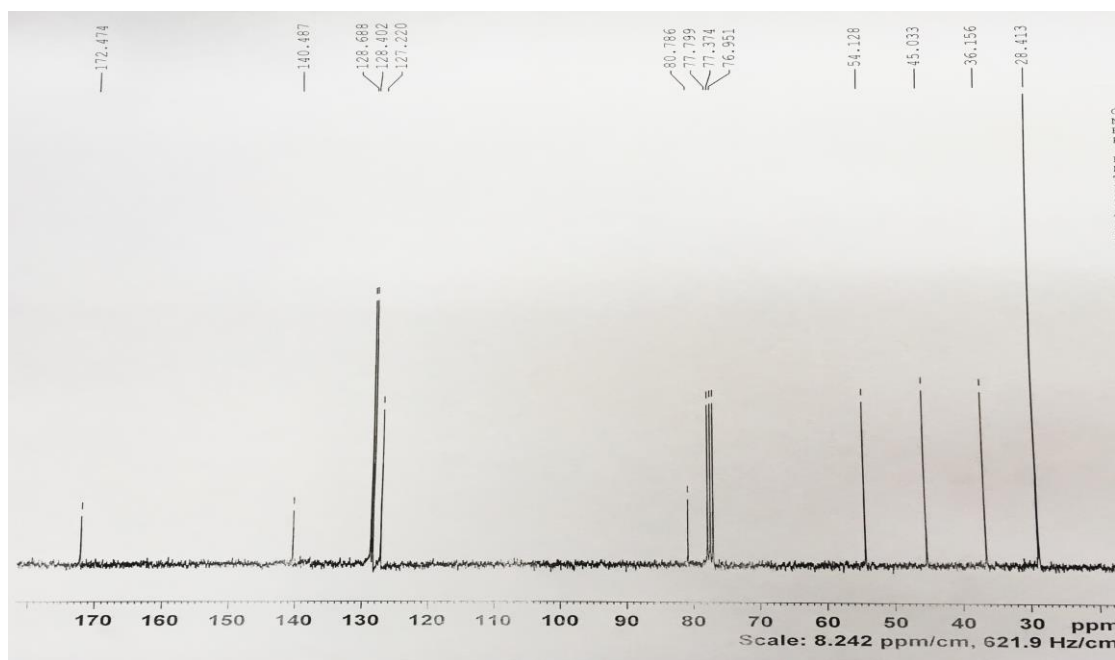


Yield 73%, colorless oil. ^1H NMR (CDCl_3 , 300 MHz): δ 1.434 (s, 9H), δ 2.441, (t, 2H, J = 6.18 Hz), δ 2.841 (t, 2H, J = 6.18 Hz), δ 3.780 (s, 2H), δ 7.175 -7.4 (m, 5H). ^{13}C NMR (CDCl_3 , 400 MHz): 28.413, 36.156, 45.033, 54.128, 80.786, 127.220, 128.402, 128.668, 140.487, 172.474 ppm.

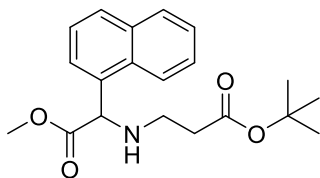
^1H NMR (CDCl_3 , 300 MHz)



^{13}C NMR (CDCl_3 , 75MHz)



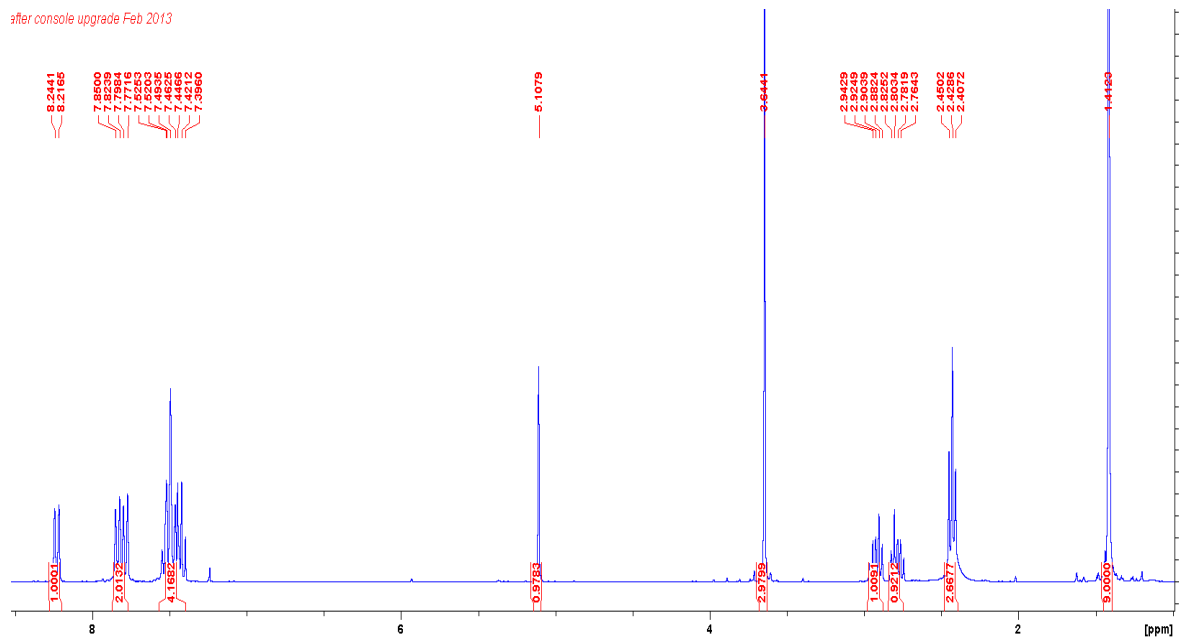
tert-butyl 3-((2-methoxy-1-(naphthalen-1-yl)-2-oxoethyl)amino)propanoate (**5**)



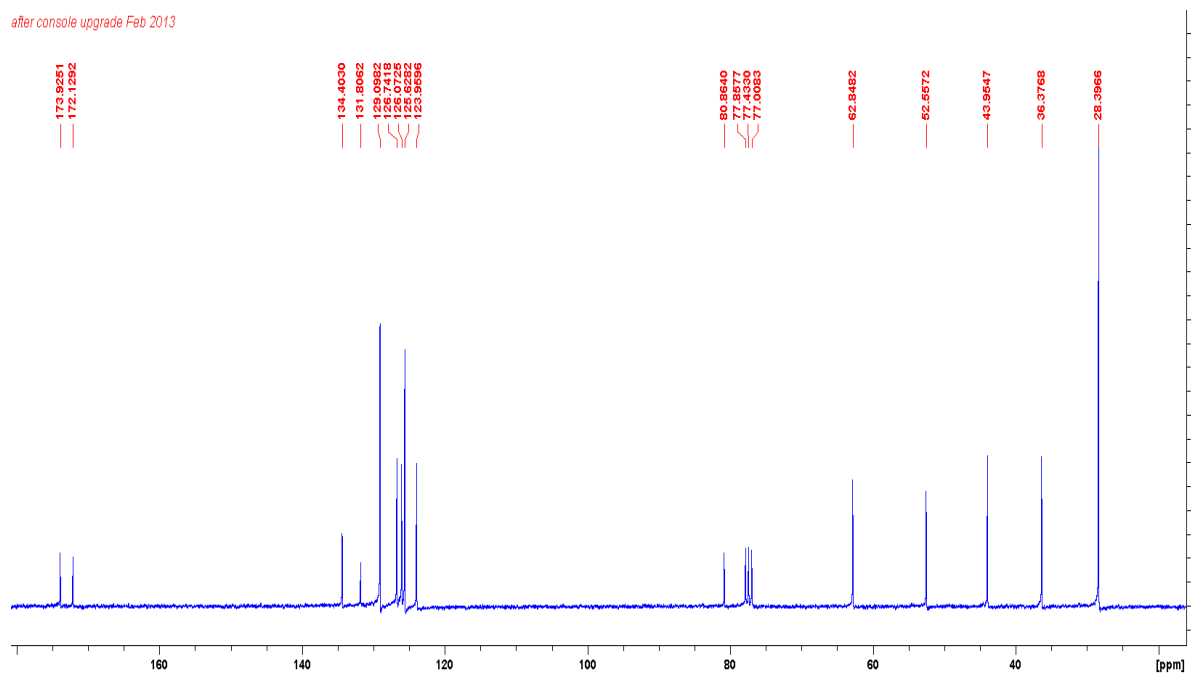
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Yield 21%, yellow oil. ^1H NMR (CDCl_3 , 300 MHz): δ 1.412 (s, 9H), δ 2.428 (t, 2H, $J = 6.43$ Hz), δ 2.729-2.980 (m, 2H), δ 3.644 (s, 3H), δ 5.107 (s, 1H), δ 7.374- 7.600 (m, 4H), δ 7.786 (d_{br}, 1H, $J = 8.08$ Hz), δ 7.837 (d_{br}, 1H, $J = 8.08$ Hz), δ 8.213 (d_{br}, 1H, $J = 8.08$ Hz). ^{13}C NMR (CDCl_3 , 75 MHz): δ 28.396, 36.376, 43.954, 52.557, 62.848, 80.864, δ 123.959, 125.628, 126.741, 129.098, 131.806, 134.403, 172.219, 173.925 ppm.

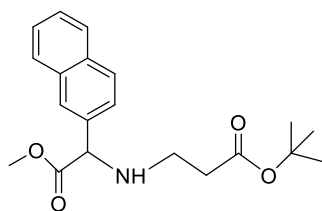
^1H NMR (CDCl_3 , 300 MHz)



^{13}C NMR (CDCl_3 , 75MHz)

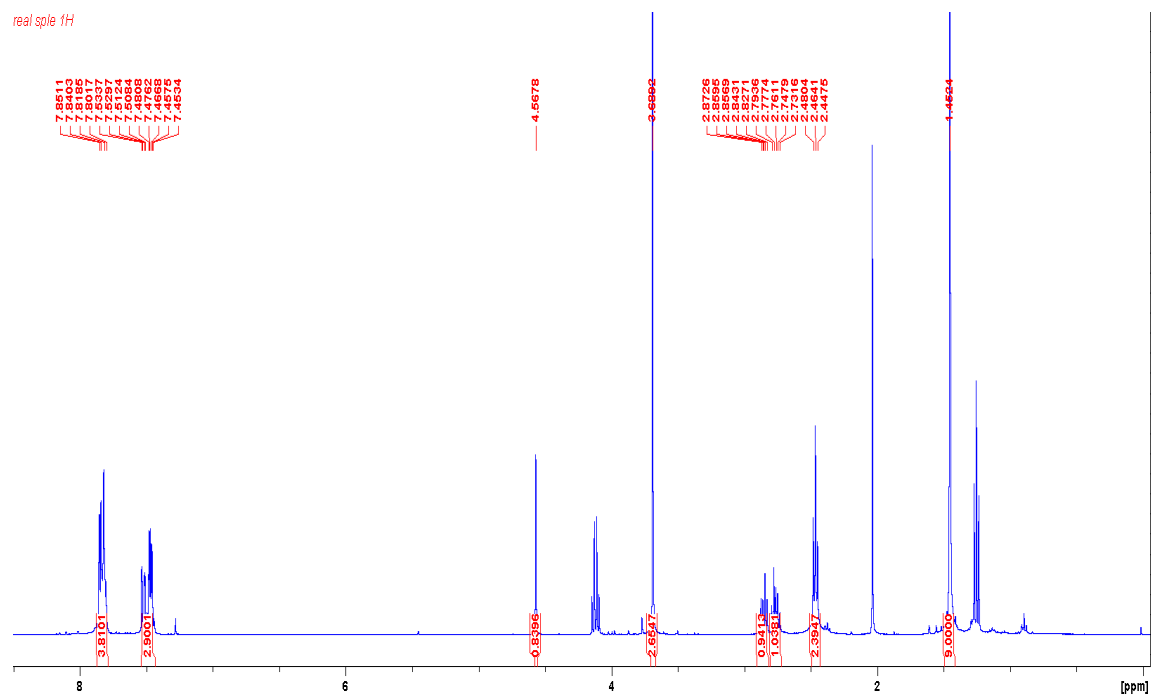


tert-butyl 3-((2-methoxy-1-(naphthalen-2-yl)-2-oxoethyl)amino)propanoate (**6**)



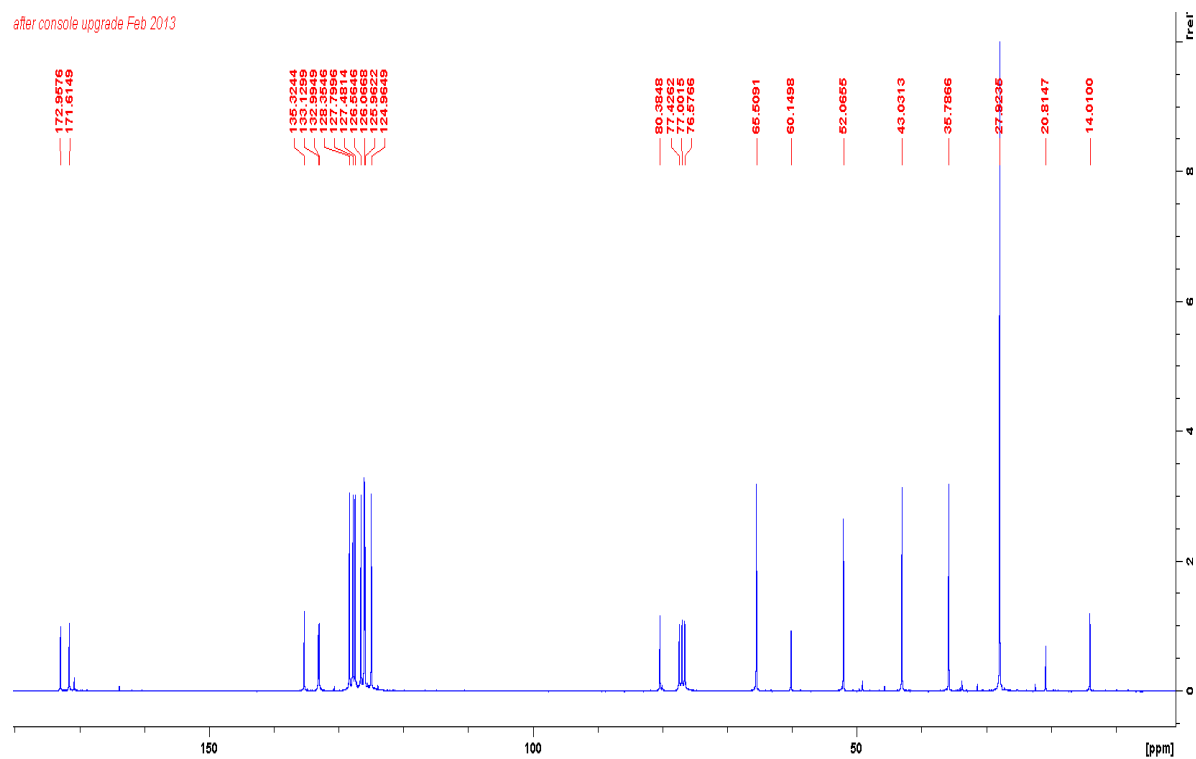
Yield 29%, brown oil. ^1H NMR (CDCl_3 , 300 MHz): δ 1.452 (s, 9H), δ 2.464 (t, 2H, J = 6.52 Hz), δ 2.710-2.900 (m, 2H), δ 3.689 (s, 3H), δ 4.567 (s, 1H), δ 7.423 - 7.550 (m, 3H), δ 7.773 - 7.900 (m, 4H). ^{13}C NMR (CDCl_3 , 75 MHz): δ 27.923, 35.786, 43.031, 52.065, 65.509, 80.384, 123.959, 124.964, 125.962, 126.066, 126.564, 127.481, 127.799, 128.354, 132.994, 133.129, 135.124, 171.614, 172.957 ppm.

^1H NMR (CDCl_3 , 300 MHz)

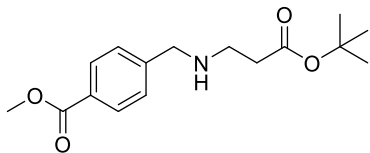


^{13}C NMR (CDCl_3 , 75MHz)

after console upgrade Feb 2013

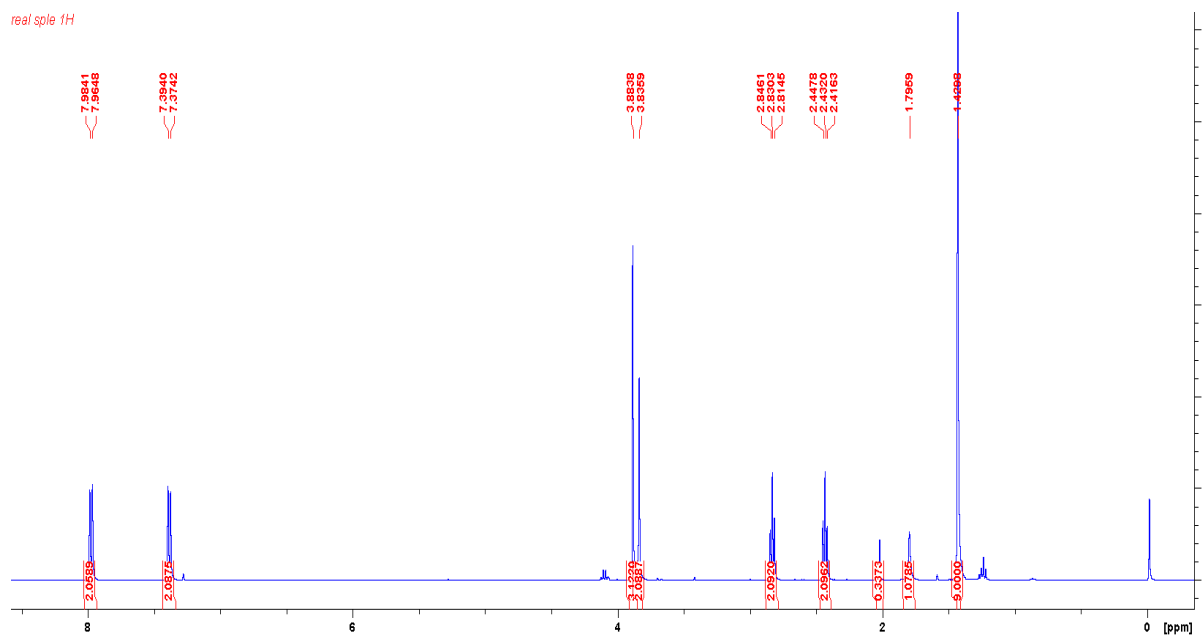


methyl 4-(((3-(tert-butoxy)-3-oxopropyl)amino)methyl)benzoate (**7**)

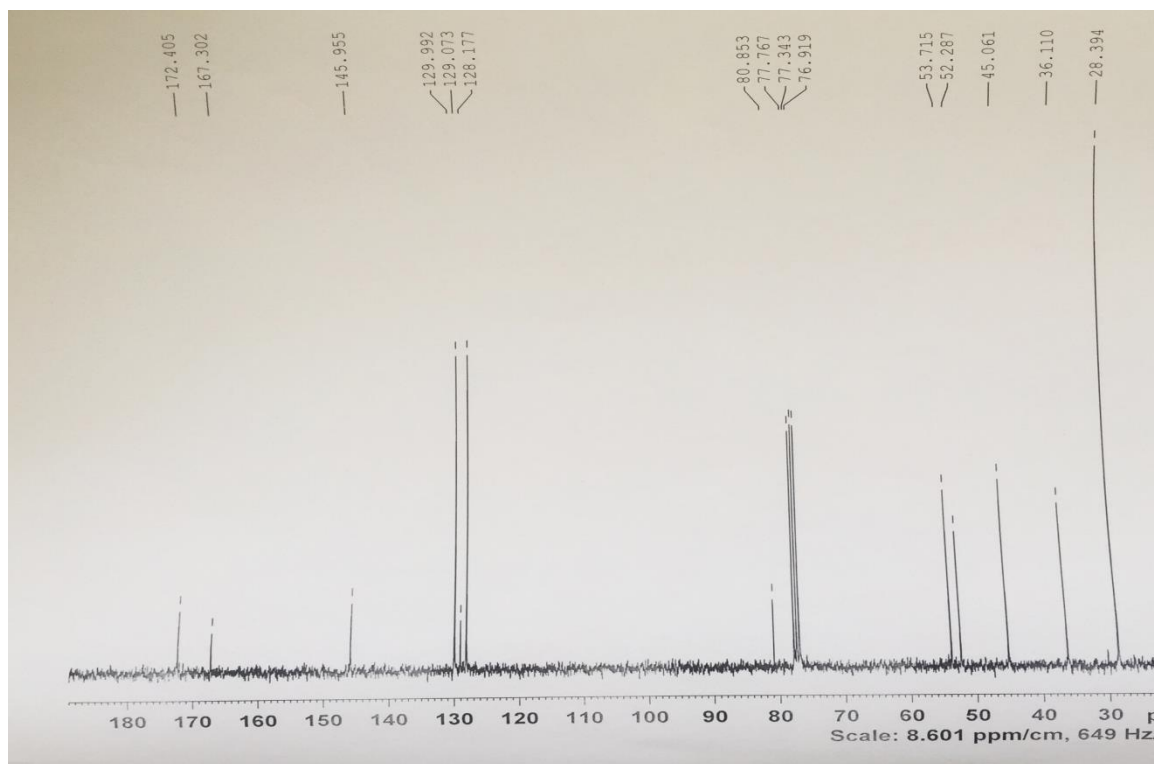


Yield 57%, colorless syrup. ^1H NMR (CDCl_3 , 300 MHz): δ 1.429 (s, 9H), δ 2.432 (t, 2H, $J = 6.25$ Hz), δ (t, 2H, $J = 6.25$ Hz), δ 3.835 (s, 2H), δ 3.883 (s, 3H), δ 7.384 (d_{br}, 2H, $J = 7.84$ Hz), δ 7.974 (d_{br}, 2H, $J = 7.84$ Hz). ^{13}C NMR (CDCl_3 , 75 MHz): 28.394, 36.110, 45.061, 52.287, 53.715, 80.853, 128.177, 129.073, 129.992, 145.995, 167.302, 172.405 ppm.

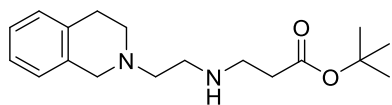
^1H NMR (CDCl_3 , 300 MHz)



^{13}C NMR (CDCl_3 , 75MHz)

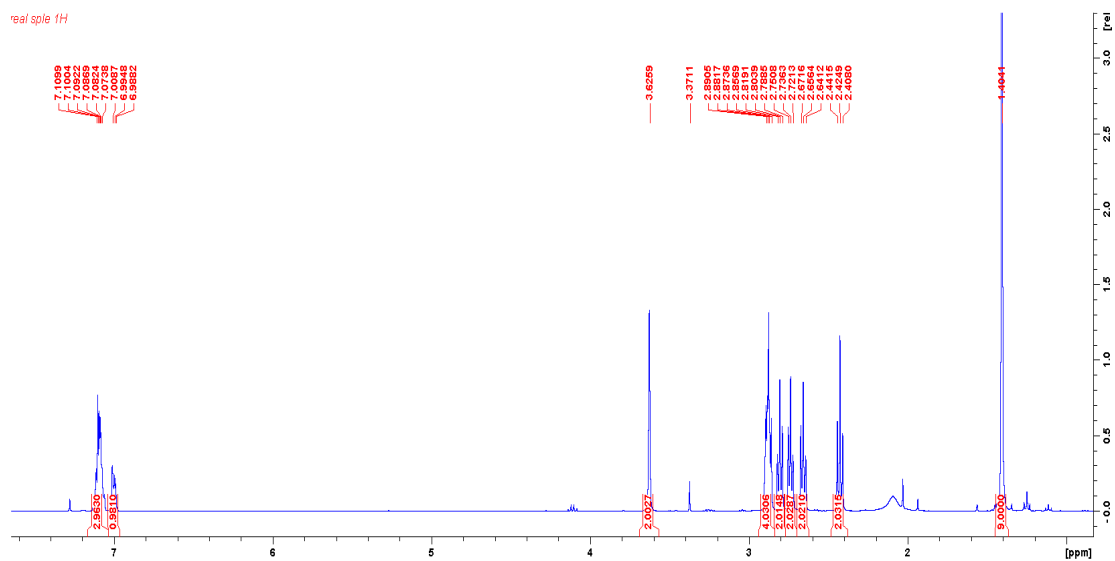


tert-butyl 3-((2-(3,4-dihydroisoquinolin-2(1H)-yl)ethyl)amino)propanoate (**8**)

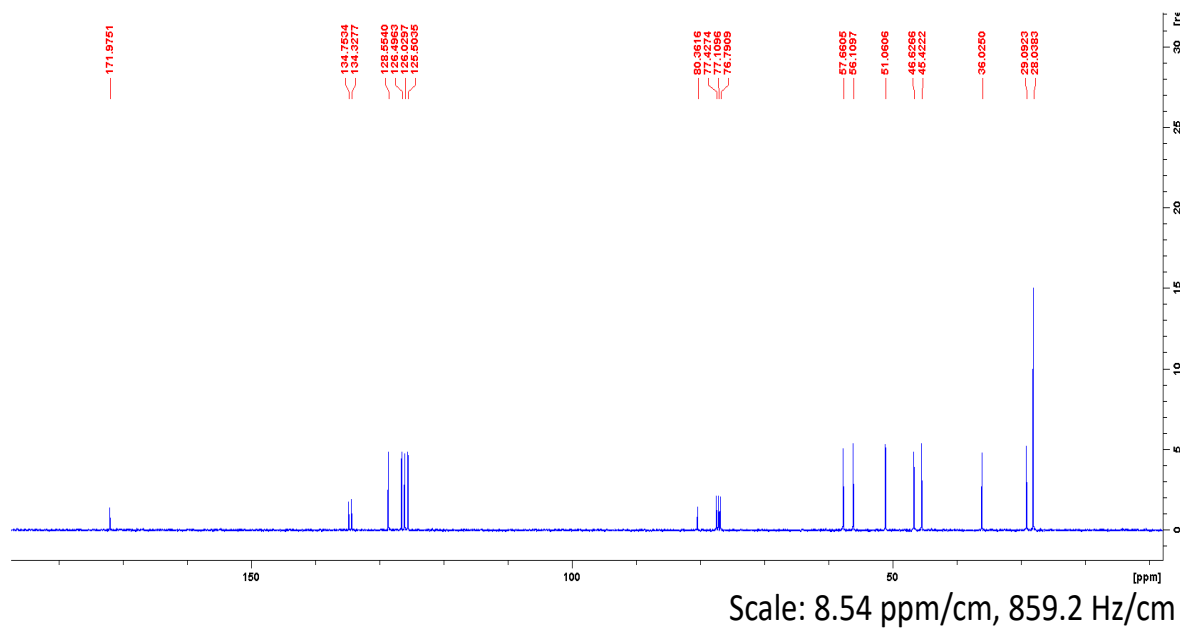


Yield 35%, pale yellow oil. ^1H NMR (CDCl_3 , 400 MHz): δ 1.404 (s, 9H), δ 2.424 (t, 2H, J = 6.62 Hz), δ 2.656 (t, 2H, J = 6.05 Hz), δ 2.736 (t, 2H, J = 5.81 Hz), δ 2.803 (t, 2H, J = 6.05 Hz), δ 2.837 – 2.920 (m, 4H), δ 3.629 (s, 2H), δ 6.966 – 7.035 (m, 1H), δ 7.042 – 7.150 (m, 3H). ^{13}C NMR (CDCl_3 , 100 MHz): δ 28.038, 29.092, 36.025, 45.422, 46.626, 51.060, 56.109, 57.660, 80.361, 125.503, 126.029, 126.496, 128.554, 134.327, 134.753, 171.975 ppm.

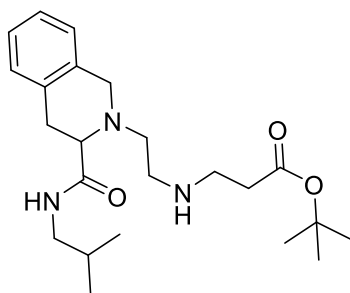
^1H NMR (CDCl_3 , 400 MHz)



^{13}C NMR (CDCl_3 , 100MHz)



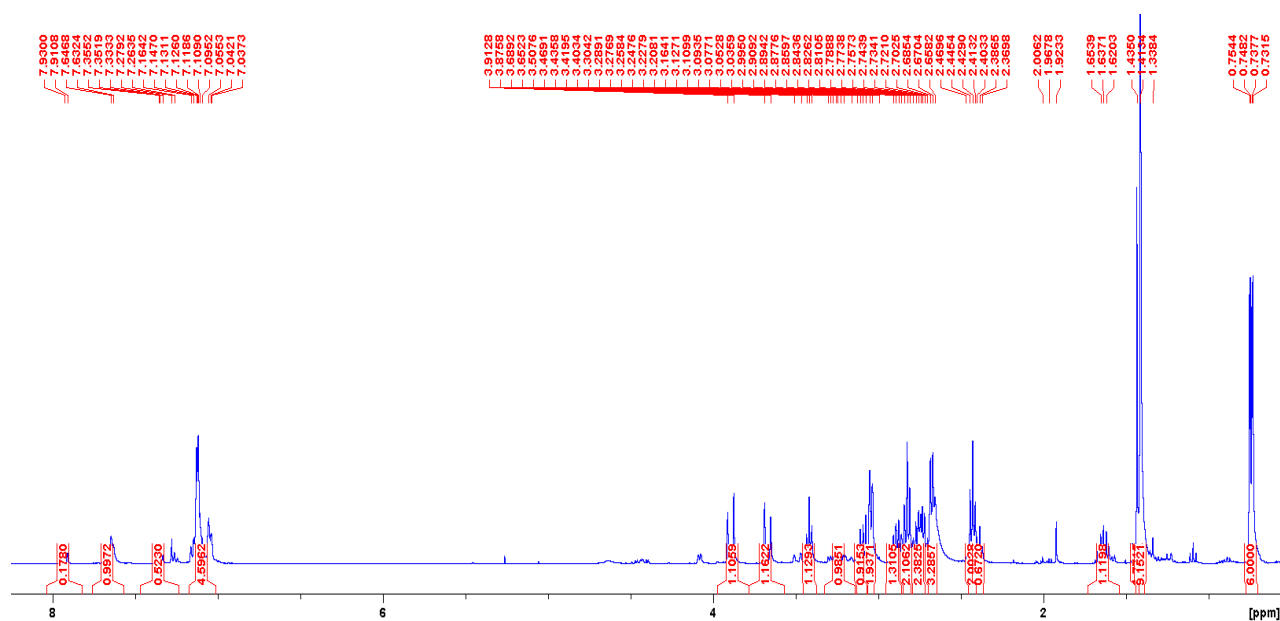
tert-butyl 3-((2-(3-(isobutylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl) ethyl) amino) propanoate (**9**)



Yield 24%, pale yellow oil. ^1H NMR (CDCl_3 , 400 MHz): δ 0.742 (dd, $J = 3.59$ Hz, $J = 2.44$ Hz, 6H), δ 1.413 (s, 9H), δ 1.435 (s, 2H), δ 2.330-2.501 (m, 3H), δ 2.565 - 2.712 (m, 3H),

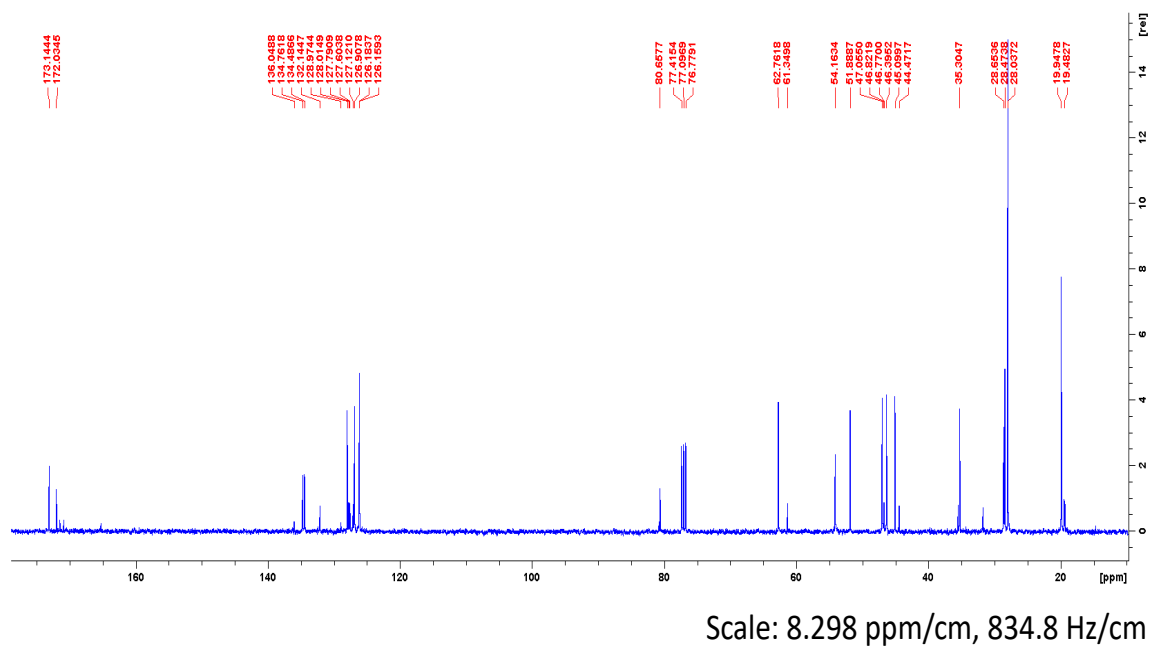
δ 2.710 – 2.799 (m, 2H), δ 2.826 (t, J = 6.19 Hz, 2H), δ 2.854 – 2.953 (m, 1H), δ 3.045 (d, J = 6.60 Hz, 2Hz), δ 3.420 (t, 1H, J = 6.93 Hz), δ 3.672 (d, J = 14.89 Hz, 1H), δ 3.894 (d, J = 14.89Hz, 1H), δ 7.00 – 7.180 (m, 4H). ^{13}C NMR (CDCl_3 , 75 MHz): δ 19.947, 28.0372, 28.473, 28.653, 35.304, 45.099, 46.395, 47.055, 51.888, 54.163, 62.761, 80.657, 126.159, 126.183, 126.907, 128.0149, 172.034, 173.144 ppm.

^1H NMR (CDCl_3 , 400 MHz)

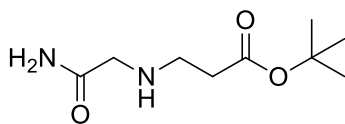


Scale: 0.4177 ppm/cm, 167.1 Hz/cm

^{13}C NMR (CDCl_3 , 100MHz)



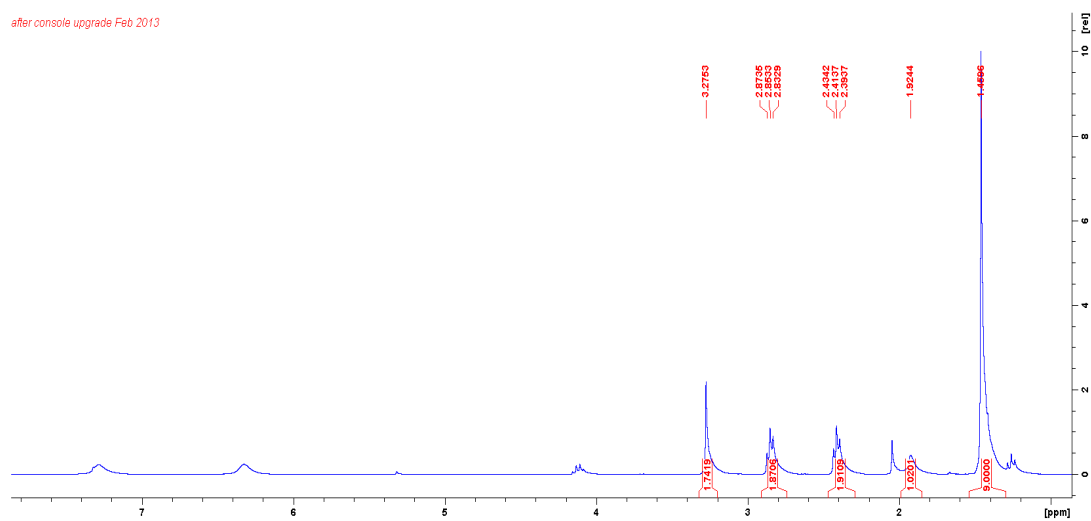
tert-butyl 3-((2-amino-2-oxoethyl)amino)propanoate (**10**)



Yield 44%, colorless syrup. ^1H NMR (CDCl_3 , 300 MHz): δ 1.459 (s, 9H), δ 1.924 (Sbr, 1H), δ 2.413 (t, J = 6.22 Hz, 2H), δ 2.853 (t, J = 6.06 Hz, 2H), δ 3.275 (s, 2H), δ 6.325 (Sbr, 1H), δ 7.279 (Sbr, 1H). ^{13}C NMR (CDCl_3 , 75 MHz): δ 28.226, 35.543, 45.354, 52.094, 81.189, 172.102, 174.397 ppm.

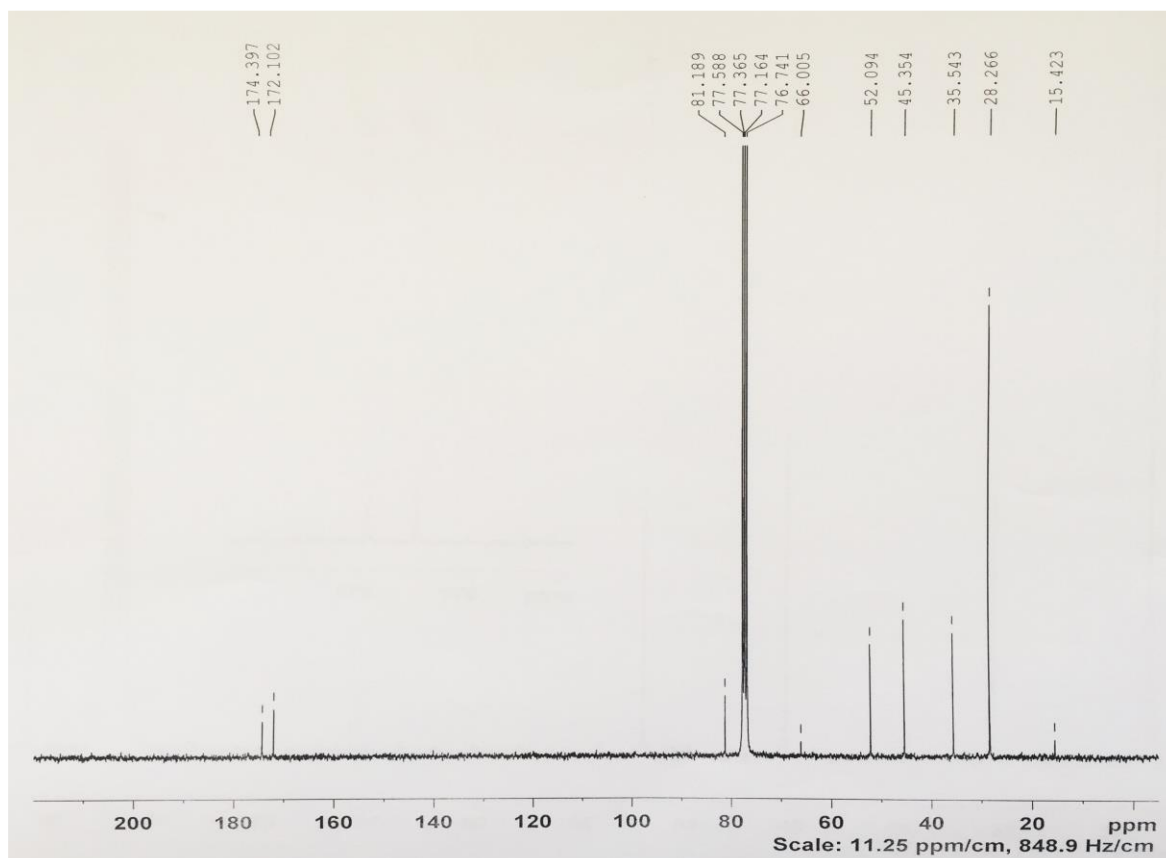
^1H NMR (CDCl_3 , 300 MHz)

after console upgrade Feb 2013



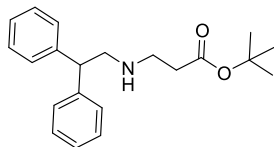
Scale: 0.314 ppm/cm, 94.24 Hz/cm

^{13}C NMR (CDCl_3 , 75 MHz)

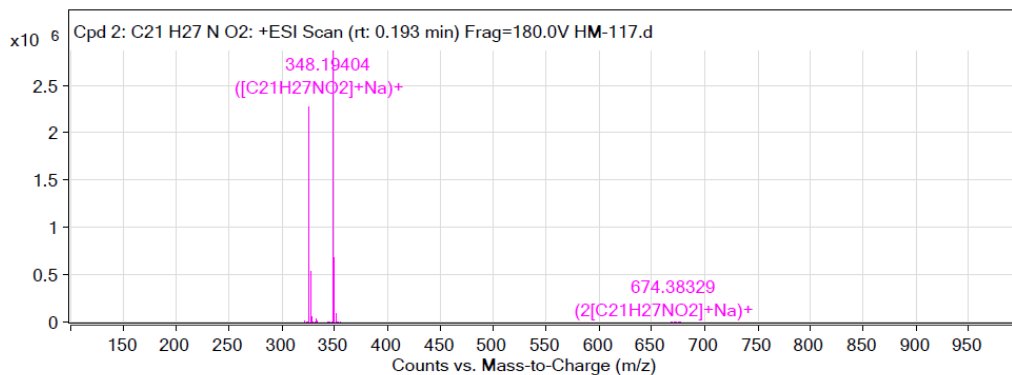


5. Mass spectroscopy analytical data

tert-butyl 3-((2,2-diphenylethyl)amino)propanoate (**1**)



MS Spectrum

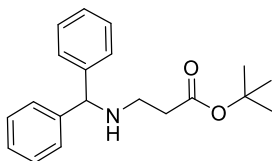


MS Spectrum Peak List

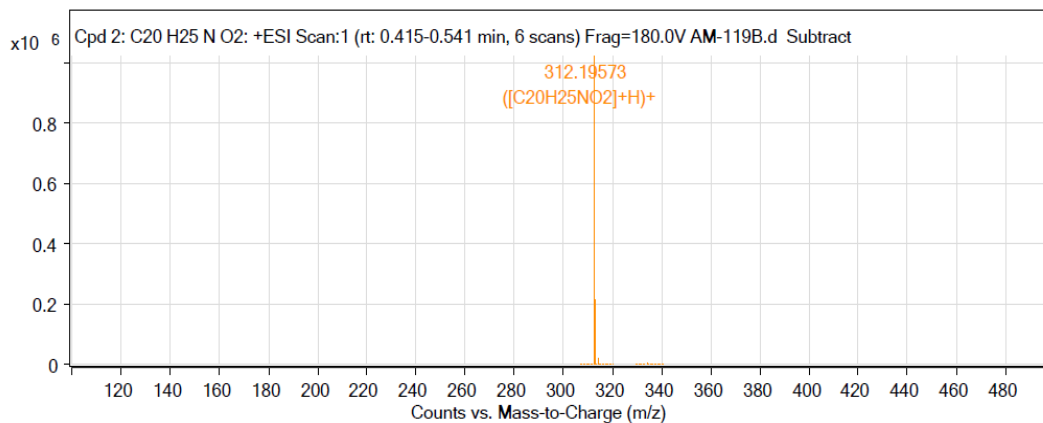
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
326.21179	326.21146	-1.04	1	2274720.75	C ₂₁ H ₂₇ NO ₂	(M+H) ⁺
327.21462	327.21475	0.43	1	535768.69	C ₂₁ H ₂₇ NO ₂	(M+H) ⁺
328.21675	328.21773	3	1	66081.25	C ₂₁ H ₂₇ NO ₂	(M+H) ⁺
329.21726	329.22055	10	1	6351.83	C ₂₁ H ₂₇ NO ₂	(M+H) ⁺
348.19404	348.1934	-1.84	1	2862664.5	C ₂₁ H ₂₇ NO ₂	(M+Na) ⁺
349.1966	349.1967	0.27	1	679667.38	C ₂₁ H ₂₇ NO ₂	(M+Na) ⁺
350.19953	350.19968	0.43	1	83553.23	C ₂₁ H ₂₇ NO ₂	(M+Na) ⁺
351.20156	351.20249	2.65	1	7812.88	C ₂₁ H ₂₇ NO ₂	(M+Na) ⁺
673.38927	673.39758	12.34	1	544.67	C ₂₁ H ₂₇ NO ₂	(2M+Na) ⁺
674.38329	674.40088	26.07	1	668.83	C ₂₁ H ₂₇ NO ₂	(2M+Na) ⁺

--- End Of Report ---

tert-butyl 3-(benzhydrylamino)propanoate (**2**)



MS Spectrum

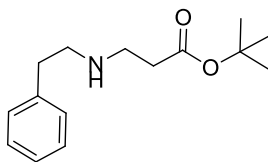


MS Spectrum Peak List

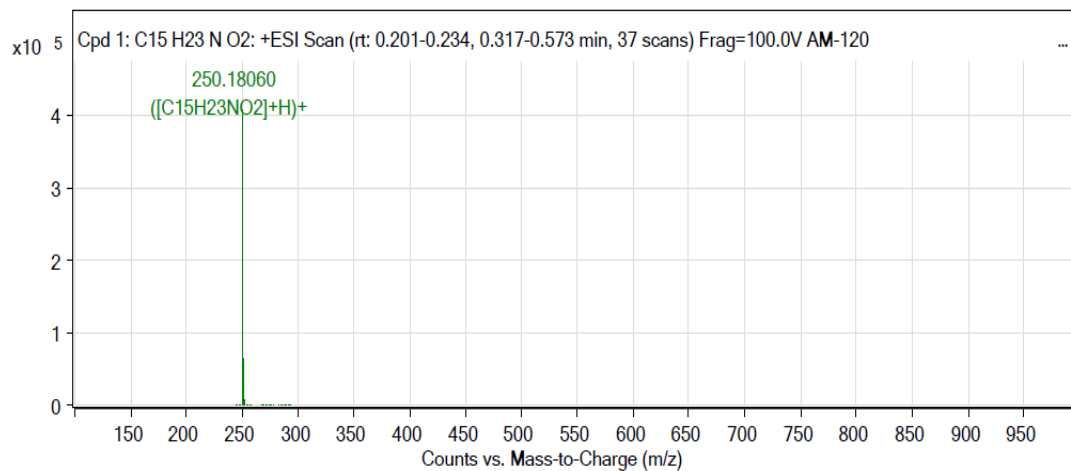
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
312.19573	312.19581	0.25	1	1019690.69	C ₂₀ H ₂₅ NO ₂	(M+H) ⁺
313.19901	313.1991	0.29	1	215669.58	C ₂₀ H ₂₅ NO ₂	(M+H) ⁺
314.20241	314.20205	-1.16	1	23741.54	C ₂₀ H ₂₅ NO ₂	(M+H) ⁺
315.20288	315.20483	6.18	1	2830.65	C ₂₀ H ₂₅ NO ₂	(M+H) ⁺
334.17729	334.17775	1.39	1	5208.8	C ₂₀ H ₂₅ NO ₂	(M+Na) ⁺
335.17764	335.18104	10.14	1	1009.97	C ₂₀ H ₂₅ NO ₂	(M+Na) ⁺
336.18043	336.18399	10.59	1	101.27	C ₂₀ H ₂₅ NO ₂	(M+Na) ⁺

--- End Of Report ---

tert-butyl 3-(phenethylamino)propanoate (**3**)



MS Spectrum

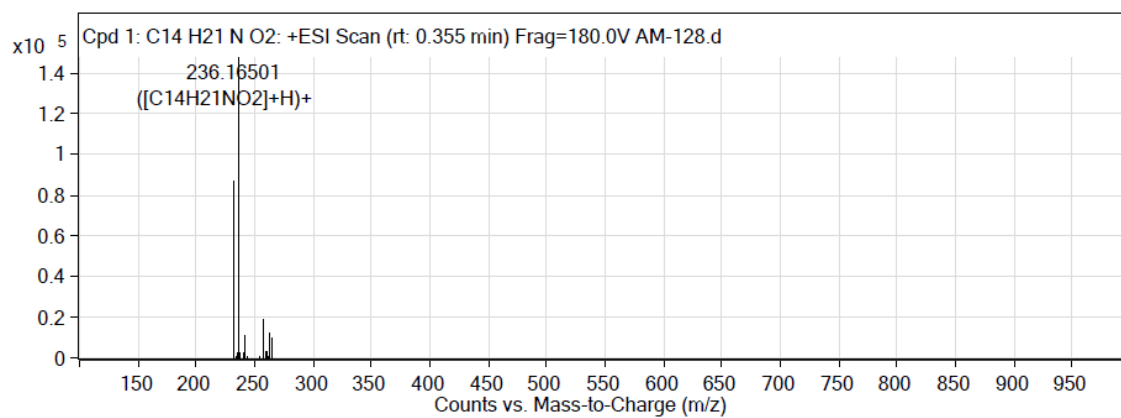
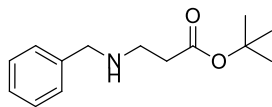


MS Spectrum Peak List

m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
250.1806	250.18016	-1.76	1	406925.44	C ₁₅ H ₂₃ NO ₂	(M+H) ⁺
251.18407	251.18343	-2.55	1	64045.84	C ₁₅ H ₂₃ NO ₂	(M+H) ⁺
252.18656	252.18616	-1.59	1	6789	C ₁₅ H ₂₃ NO ₂	(M+H) ⁺
253.18855	253.18879	0.92	1	442.21	C ₁₅ H ₂₃ NO ₂	(M+H) ⁺
272.16262	272.1621	-1.9	1	1341.53	C ₁₅ H ₂₃ NO ₂	(M+Na) ⁺
273.167	273.16537	-5.97	1	196.25	C ₁₅ H ₂₃ NO ₂	(M+Na) ⁺
288.13703	288.13604	-3.46	1	77.1	C ₁₅ H ₂₃ NO ₂	(M+K) ⁺

--- End Of Report ---

tert-butyl 3-(benzylamino)propanoate (**4**)

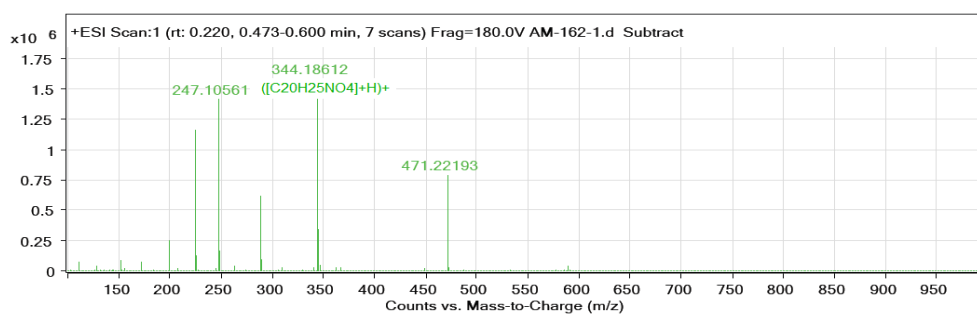
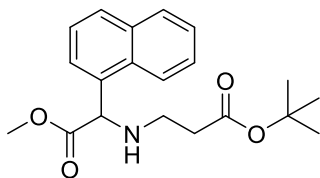


Peak List

m/z	z	Abund	Formula	Ion
236.16501	1	147437.94	C14H21NO2	(M+H)+
237.16827	1	24516.88	C14H21NO2	(M+H)+
238.17096	1	2485.19	C14H21NO2	(M+H)+
258.14657	1	19372.66	C14H21NO2	(M+Na)+
259.14904	1	3161.06	C14H21NO2	(M+Na)+
260.15368	1	667.34	C14H21NO2	(M+Na)+

--- End Of Report ---

tert-butyl 3-((2-methoxy-1-(naphthalen-1-yl)-2-oxoethyl)amino)propanoate (**5**)

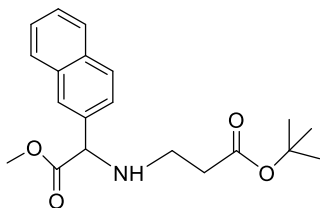


Peak List

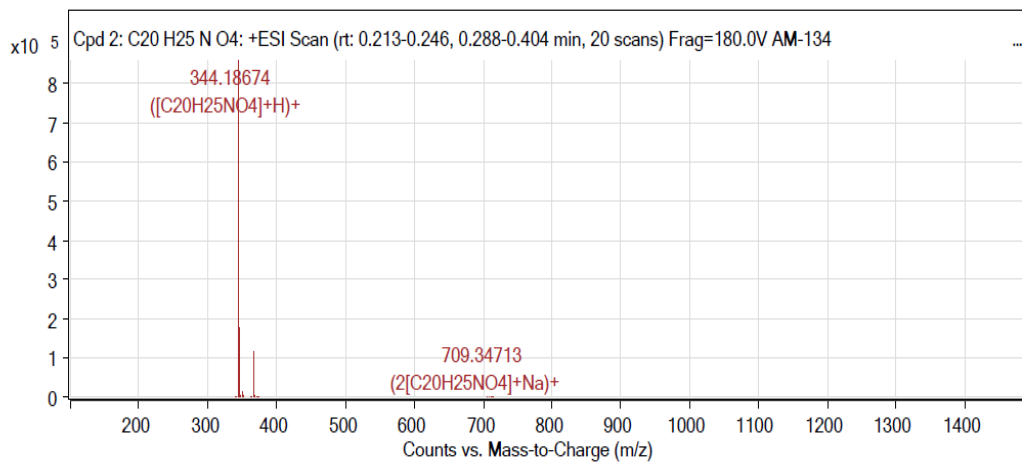
m/z	z	Abund
152.03445		90285.15
199.07523		251249.97
225.12364	1	1158127.5
225.19621		620029.81
226.12695	1	128014.73
247.10561	1	1411574.63
248.10883	1	164898.75
288.12293	1	613925
289.12658	1	94706.72
344.18612	1	1585702.75
345.18895	1	343424.69
471.22193	1	785861.56
472.22503	1	192275.16

--- End Of Report ---

tert-butyl 3-((2-methoxy-1-(naphthalen-2-yl)-2-oxoethyl)amino)propanoate (**6**)



MS Spectrum

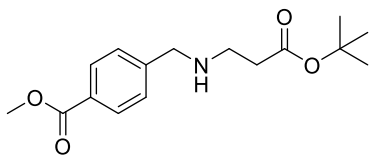


MS Spectrum Peak List

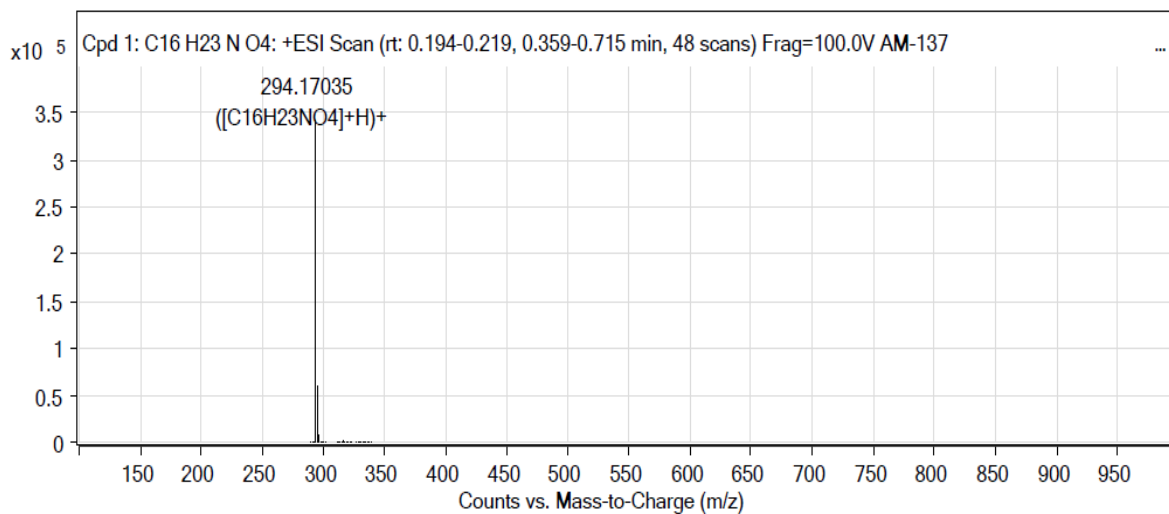
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
344.18674	344.18563	-3.2	1	857495.13	C ₂₀ H ₂₅ NO ₄	(M+H) ⁺
345.19019	345.18893	-3.66	1	175699.27	C ₂₀ H ₂₅ NO ₄	(M+H) ⁺
346.19246	346.19163	-2.4	1	22872.15	C ₂₀ H ₂₅ NO ₄	(M+H) ⁺
347.19519	347.19428	-2.64	1	2677.89	C ₂₀ H ₂₅ NO ₄	(M+H) ⁺
366.16852	366.16758	-2.57	1	116307.22	C ₂₀ H ₂₅ NO ₄	(M+Na) ⁺
367.17164	367.17087	-2.07	1	23618.03	C ₂₀ H ₂₅ NO ₄	(M+Na) ⁺
368.17429	368.17357	-1.96	1	3297.91	C ₂₀ H ₂₅ NO ₄	(M+Na) ⁺
369.17861	369.17622	-6.48	1	422.59	C ₂₀ H ₂₅ NO ₄	(M+Na) ⁺
709.34713	709.34594	-1.68	1	472.02	C ₂₀ H ₂₅ NO ₄	(2M+Na) ⁺
710.34953	710.34923	-0.42	1	76.82	C ₂₀ H ₂₅ NO ₄	(2M+Na) ⁺

--- End Of Report ---

methyl 4-(((3-(tert-butoxy)-3-oxopropyl)amino)methyl)benzoate (7)



MS Spectrum

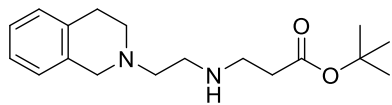


MS Spectrum Peak List

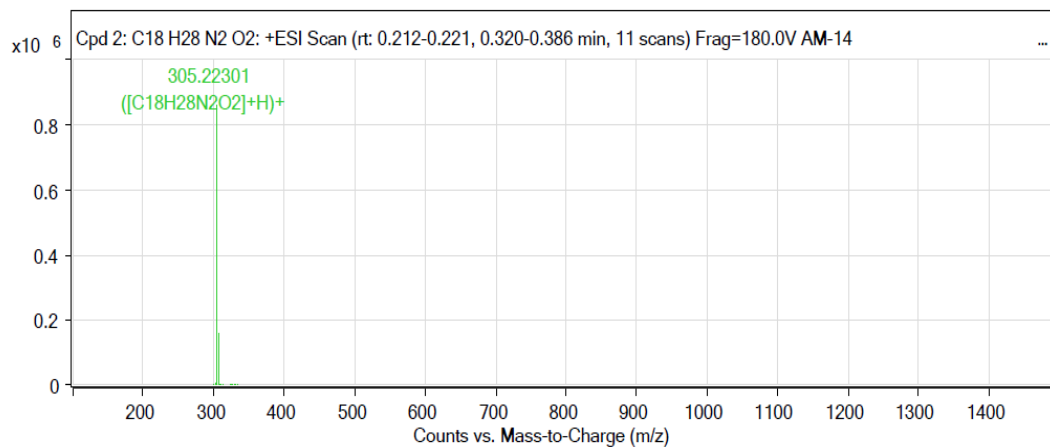
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
294.17035	294.16998	-1.26	1	342776.38	C ₁₆ H ₂₃ NO ₄	(M+H) ⁺
295.17363	295.17326	-1.24	1	58629.24	C ₁₆ H ₂₃ NO ₄	(M+H) ⁺
296.17628	296.17574	-1.83	1	7631.56	C ₁₆ H ₂₃ NO ₄	(M+H) ⁺
297.17641	297.17833	6.45	1	689.25	C ₁₆ H ₂₃ NO ₄	(M+H) ⁺
316.1519	316.15193	0.1	1	1509.43	C ₁₆ H ₂₃ NO ₄	(M+Na) ⁺
317.15368	317.15521	4.83	1	320.02	C ₁₆ H ₂₃ NO ₄	(M+Na) ⁺
318.15836	318.15768	-2.15	1	50.94	C ₁₆ H ₂₃ NO ₄	(M+Na) ⁺
332.12604	332.12587	-0.53	1	421.71	C ₁₆ H ₂₃ NO ₄	(M+K) ⁺
333.13132	333.12914	-6.55	1	95.29	C ₁₆ H ₂₃ NO ₄	(M+K) ⁺
334.12099	334.12587	14.61	1	22.01	C ₁₆ H ₂₃ NO ₄	(M+K) ⁺

--- End Of Report ---

tert-butyl 3-((2-(3,4-dihydroisoquinolin-2(1H)-yl)ethyl)amino)propanoate (**8**)



MS Spectrum

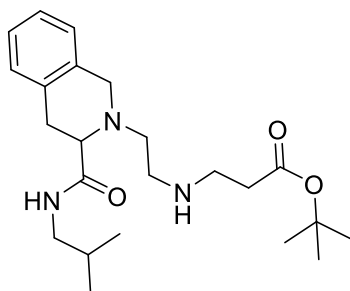


MS Spectrum Peak List

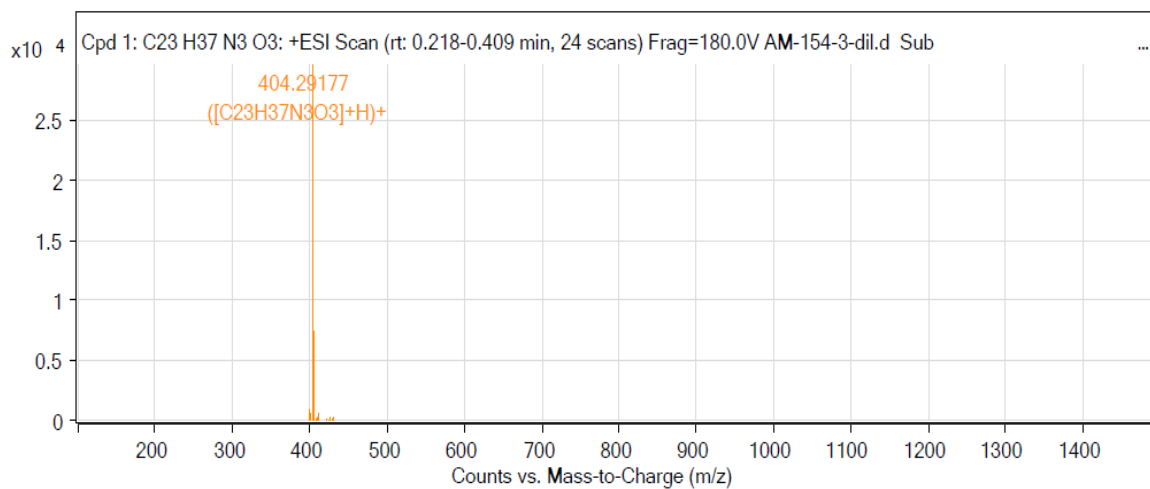
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
305.22301	305.22335	-2.15	1	863210.69	C ₁₈ H ₂₈ N ₂ O ₂	(M+H) ⁺
306.22610	306.22554	-2.12	1	162855.42	C ₁₈ H ₂₈ N ₂ O ₂	(M+H) ⁺
307.22895	307.22835	-1.95	1	17544.28	C ₁₈ H ₂₈ N ₂ O ₂	(M+H) ⁺
308.23158	308.23102	-1.8	1	1616.55	C ₁₈ H ₂₈ N ₂ O ₂	(M+H) ⁺
327.20358	327.2043	2.2	1	1100.32	C ₁₈ H ₂₈ N ₂ O ₂	(M+Na) ⁺
328.2065	328.20748	2.97	1	217.81	C ₁₈ H ₂₈ N ₂ O ₂	(M+Na) ⁺

--- End Of Report ---

tert-butyl 3-((2-(3-(isobutylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl) ethyl) amino) propanoate (**9**)



MS Spectrum

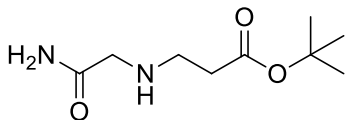


MS Spectrum Peak List

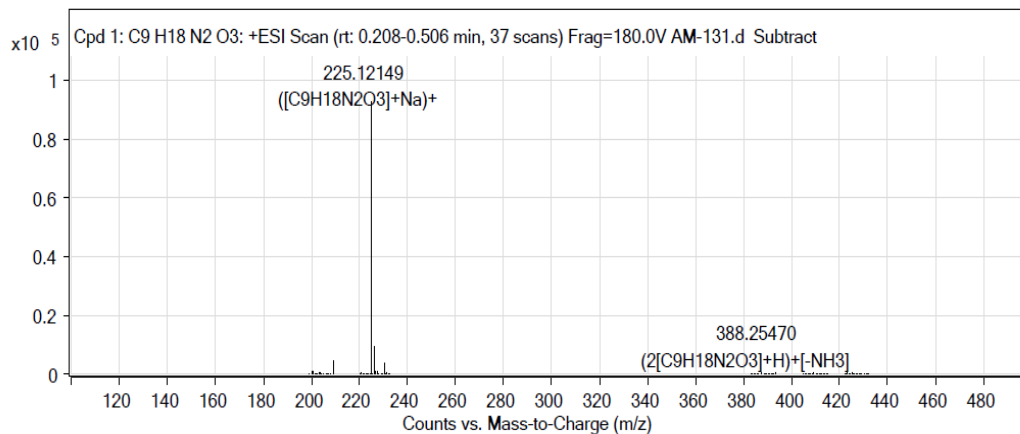
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
404.29177	404.29077	-2.48	1	29599.73	C ₂₃ H ₃₇ N ₃ O ₃	(M+H)+
405.29504	405.29391	-2.77	1	7514.09	C ₂₃ H ₃₇ N ₃ O ₃	(M+H)+
406.2981	406.29674	-3.35	1	1214.1	C ₂₃ H ₃₇ N ₃ O ₃	(M+H)+
407.29891	407.29943	1.26	1	125.24	C ₂₃ H ₃₇ N ₃ O ₃	(M+H)+
426.27382	426.27271	-2.59	1	320.25	C ₂₃ H ₃₇ N ₃ O ₃	(M+Na)+

--- End Of Report ---

tert-butyl 3-((2-amino-2-oxoethyl)amino)propanoate (**10**)



MS Spectrum



MS Spectrum Peak List

m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
203.13929	203.13902	-1.35	1	811.59	C ₉ H ₁₈ N ₂ O ₃	(M+H)+
204.14249	204.14201	-2.31	1	76.64	C ₉ H ₁₈ N ₂ O ₃	(M+H)+
225.12149	225.12096	-2.33	1	93037.34	C ₉ H ₁₈ N ₂ O ₃	(M+Na)+
226.1246	226.12396	-2.83	1	9679.17	C ₉ H ₁₈ N ₂ O ₃	(M+Na)+
227.12686	227.12599	-3.84	1	1078.29	C ₉ H ₁₈ N ₂ O ₃	(M+Na)+
228.12832	228.1285	0.81	1	54.70	C ₉ H ₁₈ N ₂ O ₃	(M+Na)+
388.2547	388.24421	-27.01	1	215.83	C ₉ H ₁₈ N ₂ O ₃	(2M+H)+[-NH ₃]
410.22591	410.22616	0.61	1	65.83	C ₉ H ₁₈ N ₂ O ₃	(2M+Na)+[-NH ₃]
427.24329	427.25271	22.03	1	78.52	C ₉ H ₁₈ N ₂ O ₃	(2M+Na)+

--- End Of Report ---

6. MALDI mass spectra of PAMAM dendrimer

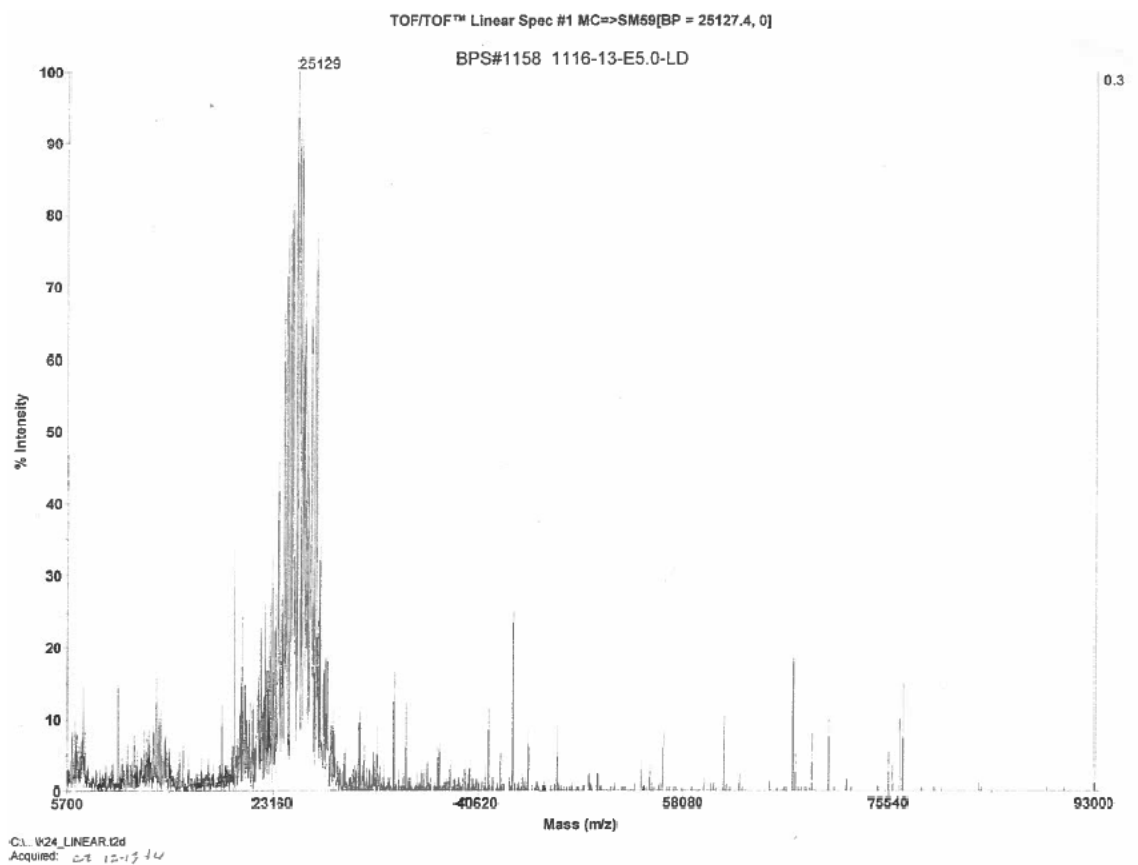


Figure S1. MALDI mass spectra of PAMAM dendrimer.

7. HSA-28D characterization

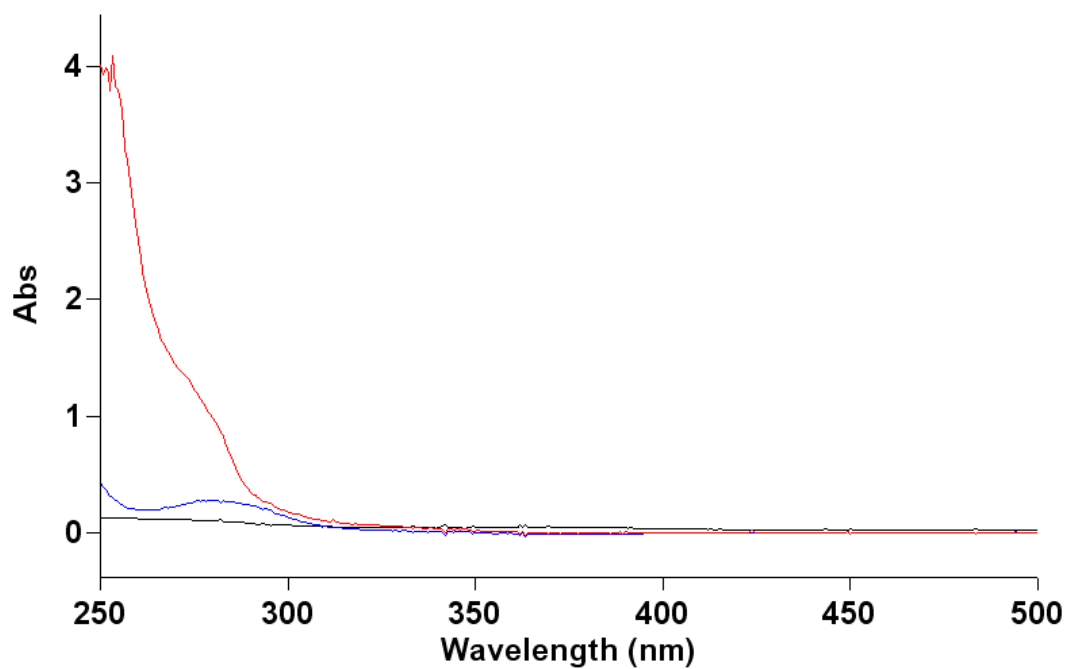


Figure S2. *UV absorption measurement.* “Naked” dendrimer (blue line) and HSA-28D (red line) both at a concentration of 0.175 mM in PBS, pH=7.4, were placed in the plate. UV spectra were recorded at 250-500 nm. The black line is a blank. An Agilent Cary 300 UV-Vis spectrophotometer with a slit of 4nm and a scan speed of 400 nm min⁻¹ and a quartz cuvette of 1 cm were used.

8. Estimation of the percentage of dendrimer coating by peptidomimetics

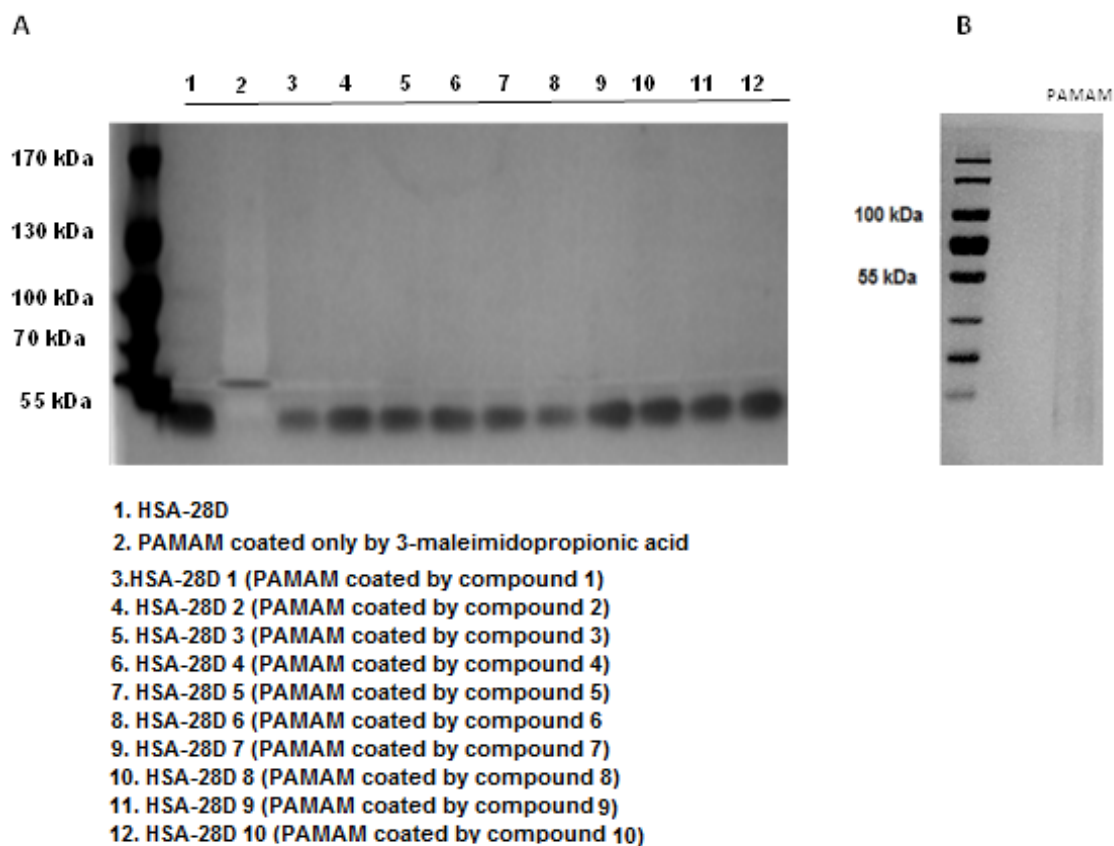


Figure S3. *Gel electrophoresis of coated PAMAMs.* **A.** Samples were loaded to Glycine 6% SDS PAGE gel, run against TTS running buffer, and stained using a silver staining procedure. **B.** Section image of the gel electrophoresis of PAMAM dendrimer, which was conducted as a control for the experiment described above.

9. Lack of biological effect of coated by peptidomimetics PAMAM dendrimer

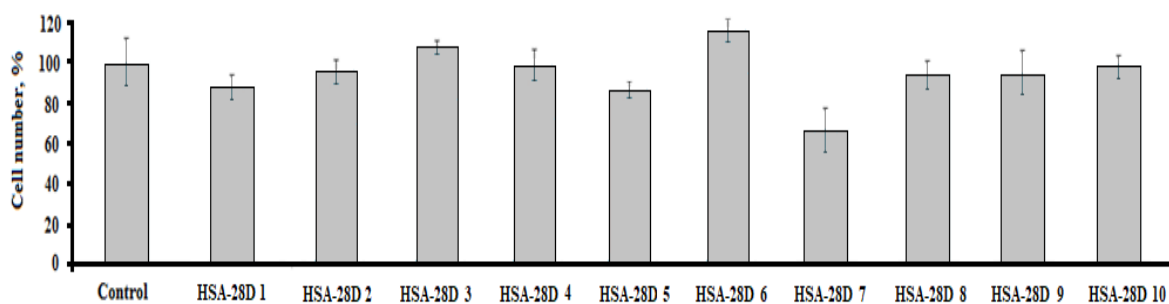


Figure S4. *The effect of coated PAMAMs on the rate of INS-1E cell proliferation.* INS-1E cells were seeded in 24-well plates and incubated for 72h with the medium supplemented with HSA-28D 1-10 ([1-10]-3 μ g/ml). After the incubation time, the cells were detached by trypsin, colored using Trypan blue and counted. The results are presented as the percentage compared to non-treated cells, n=6, *p \leq 0.05. MEAN \pm SE.