Supporting Information

Ethyl 2-cyano-2-(2-nitrobenzenesulfonyloxyimino)acetate (*o*-NosylOXY): A Recyclable Coupling Reagent for Racemization free Synthesis of Peptide, Amide, Hydroxamate and Ester

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CONTENTS

1) ^{1}H-NMR and ^{13}C-NMR Spectra of coupling reagent (*o*-NosylOXY, I):

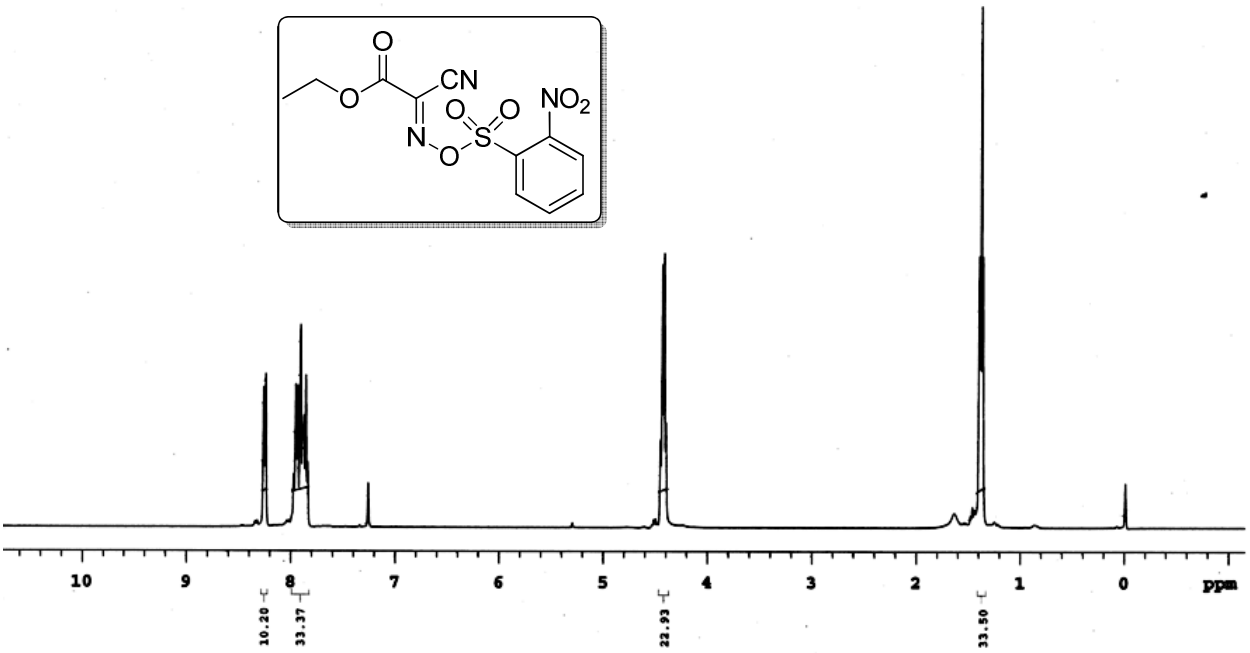


Figure S1: ^{1}H-NMR spectrum of coupling reagent (*o*-NosylOXY, **I**)

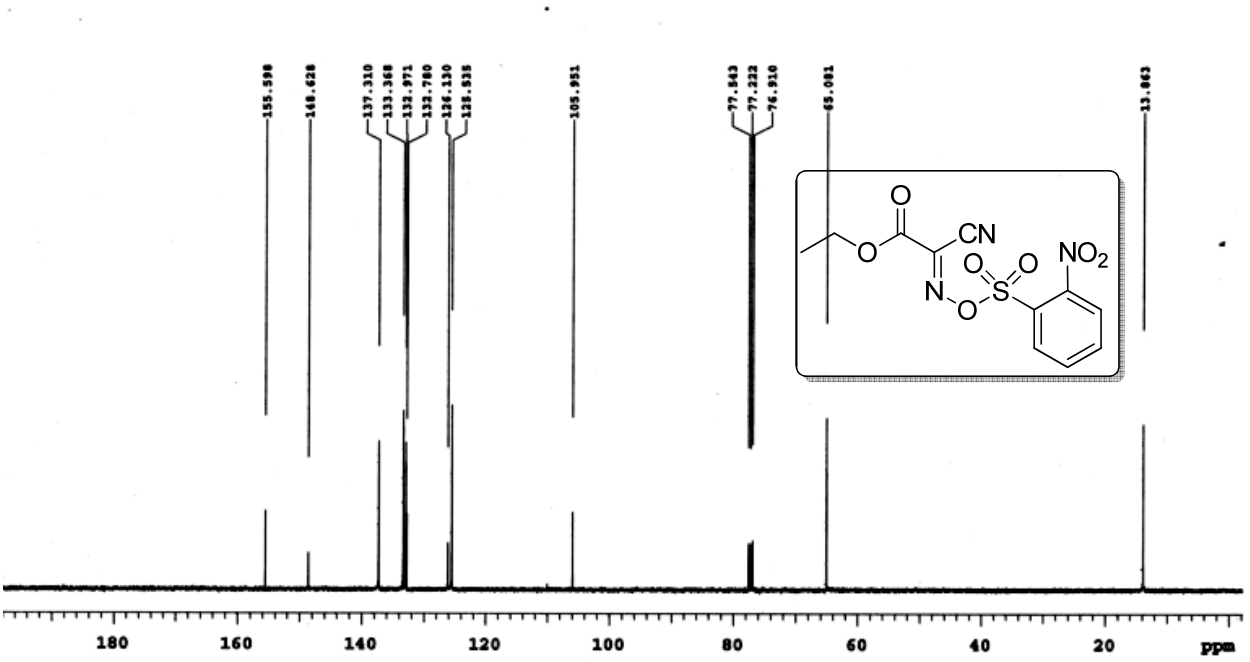
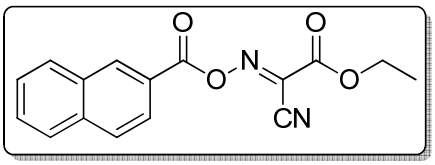


Figure S2: ^{13}C-NMR spectrum of coupling reagent (*o*-NosylOXY, **I**)

2) ^{1}H-NMR and ^{13}C-NMR spectra of intermediate V:



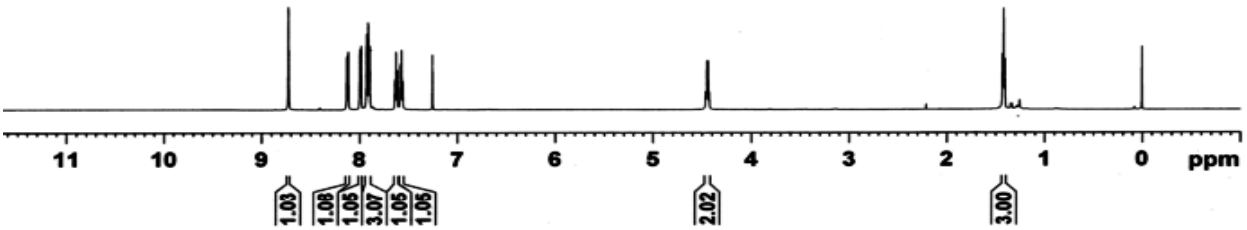
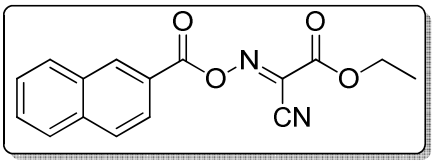


Figure S3: ^{1}H-NMR spectrum of Oxyma ester naphthanoic acid (Intermediate V in Scheme 3).



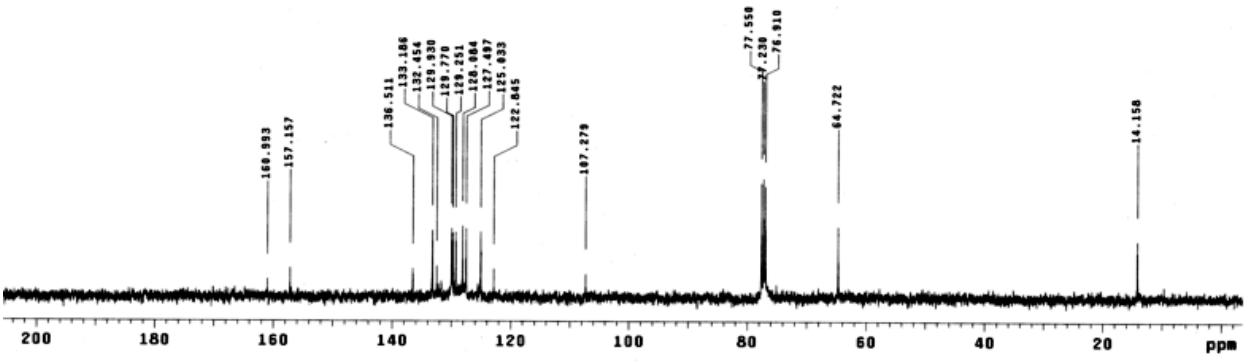


Figure S4: ^{13}C-NMR spectrum of Oxyma ester naphthanoic acid (Intermediate V in Scheme 3).

3) ^{1}H-NMR and ^{13}C-NMR spectra of amides and peptides:

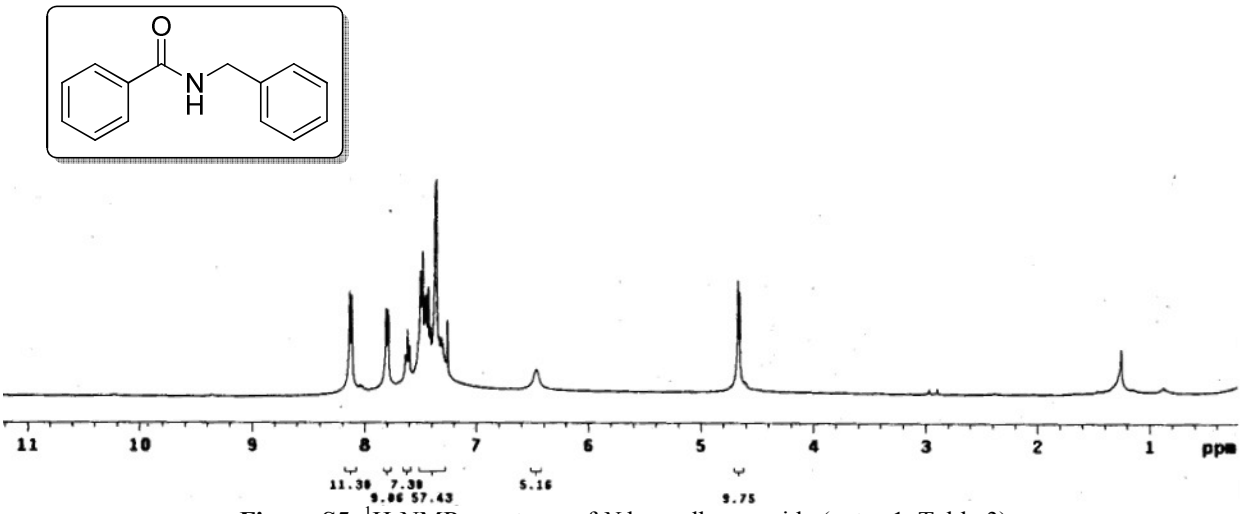


Figure S5: ^{1}H-NMR spectrum of *N*-benzylbenzamide (entry 1, Table 3).

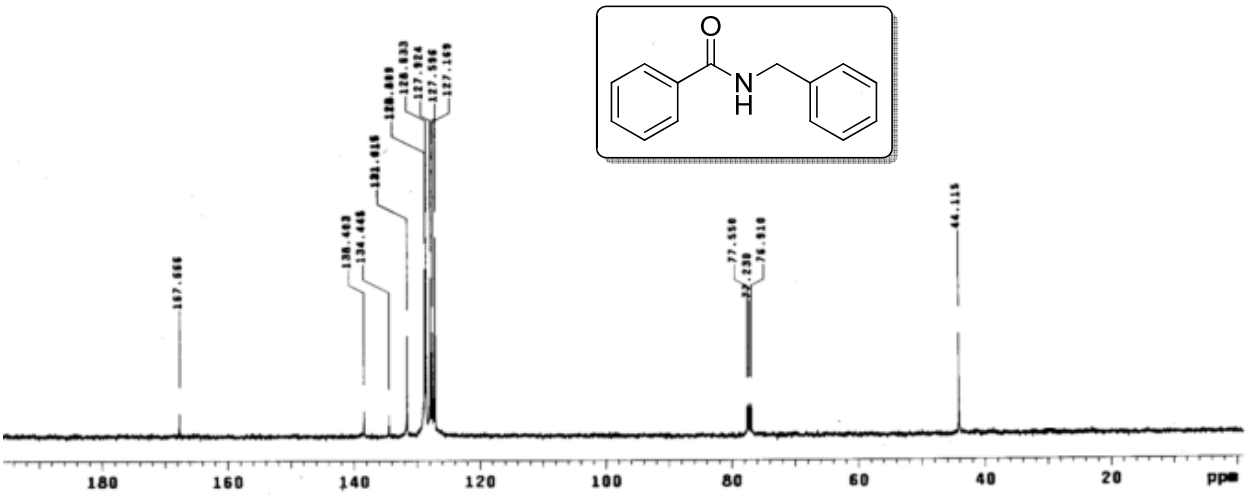


Figure S6: ^{13}C-NMR spectrum of *N*-benzylbenzamide (entry 1, Table 3).

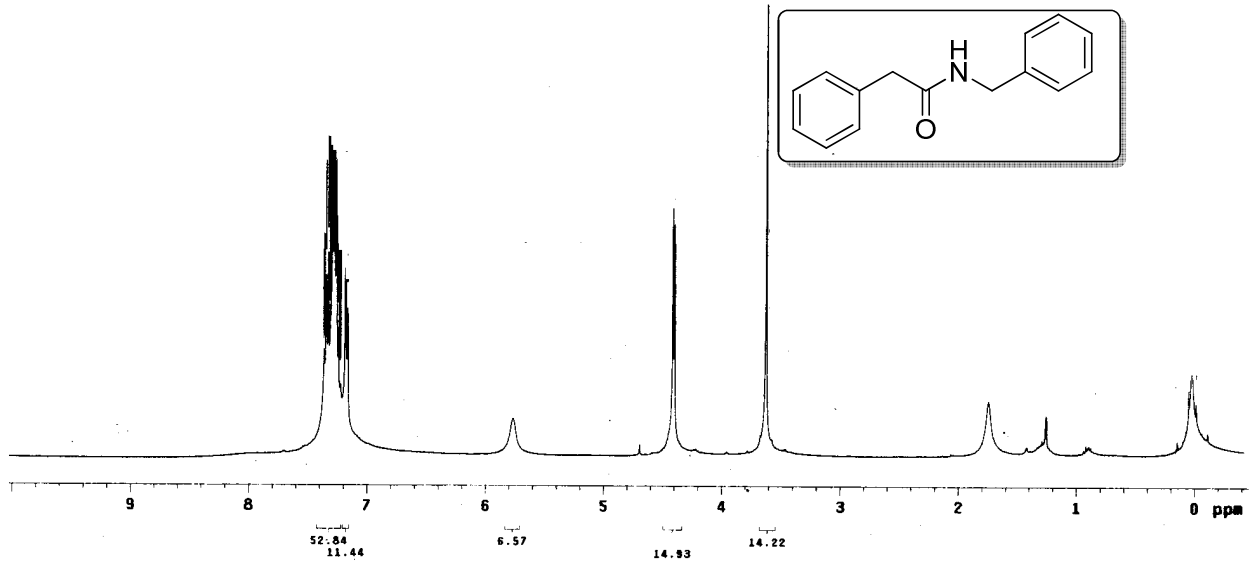


Figure S7: ^{1}H-NMR spectrum of *N*-benzyl-2-phenylacetamide (entry 2, Table 3).

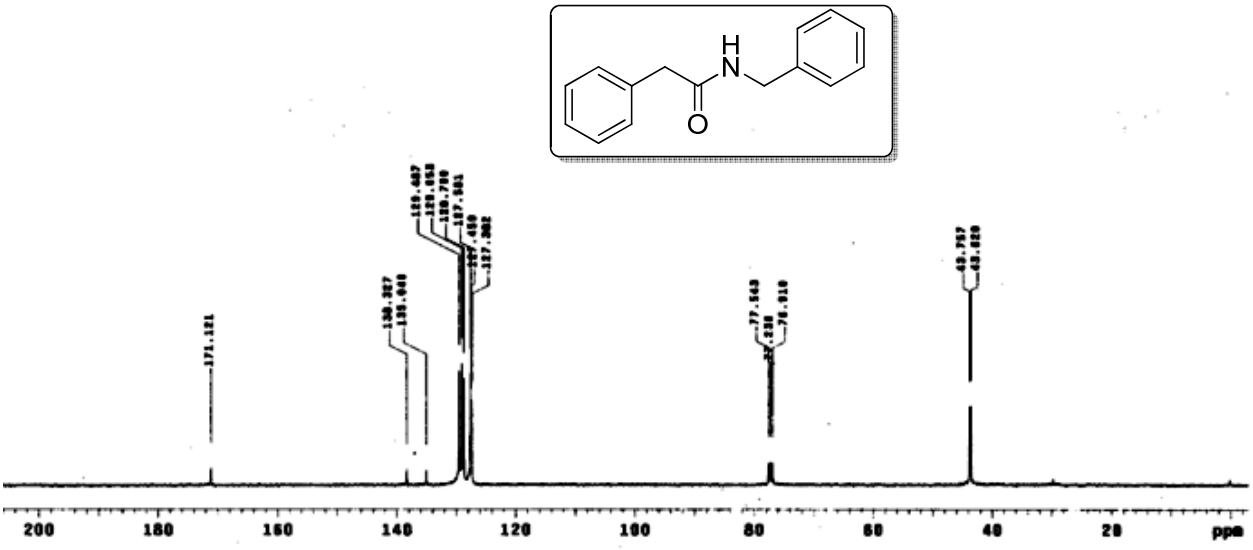


Figure S8: ^{13}C-NMR spectrum of *N*-benzyl-2-phenylacetamide (entry 2, Table 3).

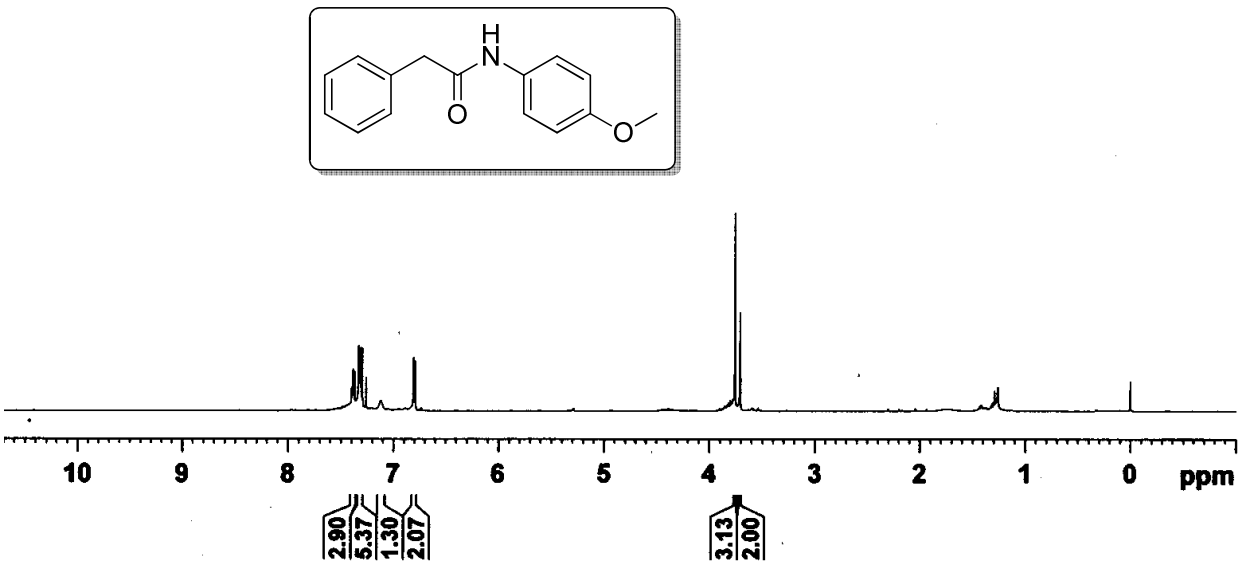


Figure S9: ^{1}H-NMR spectrum of *N*-(4-methoxyphenyl)-2-phenylacetamide (entry 3, Table 3).

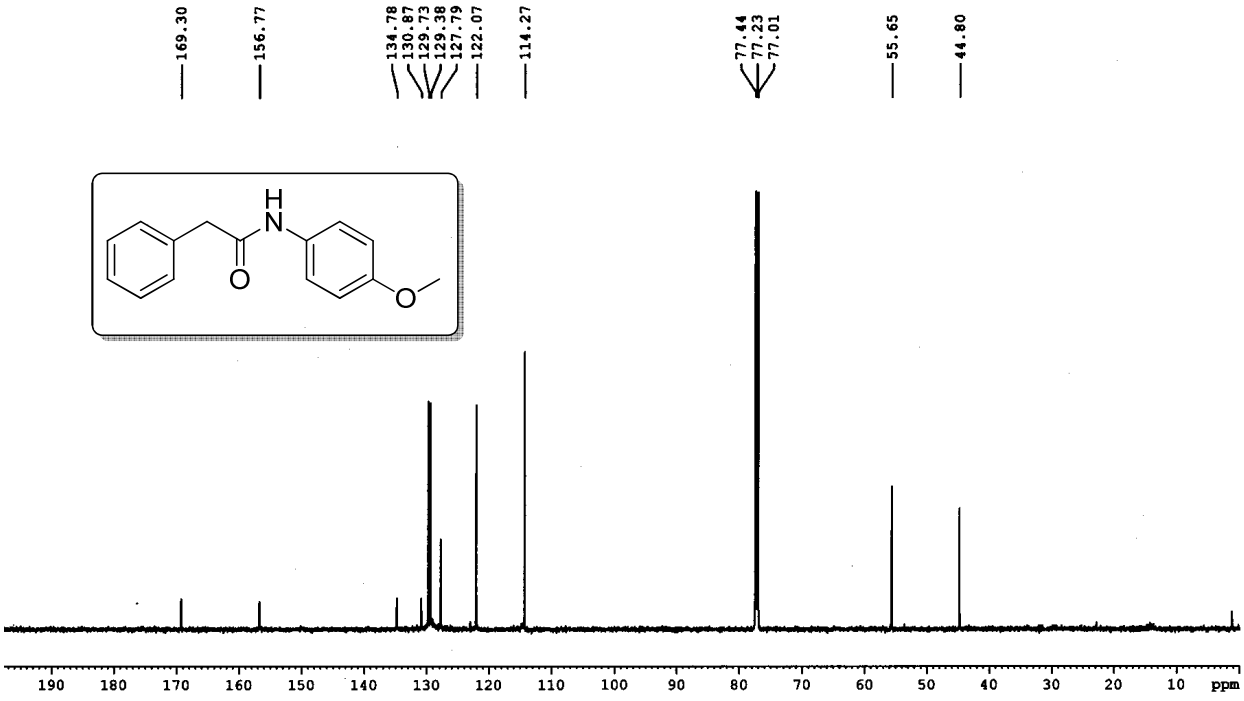


Figure S10: ^{13}C-NMR spectrum of *N*-(4-methoxyphenyl)-2-phenylacetamide (entry3, Table 3).

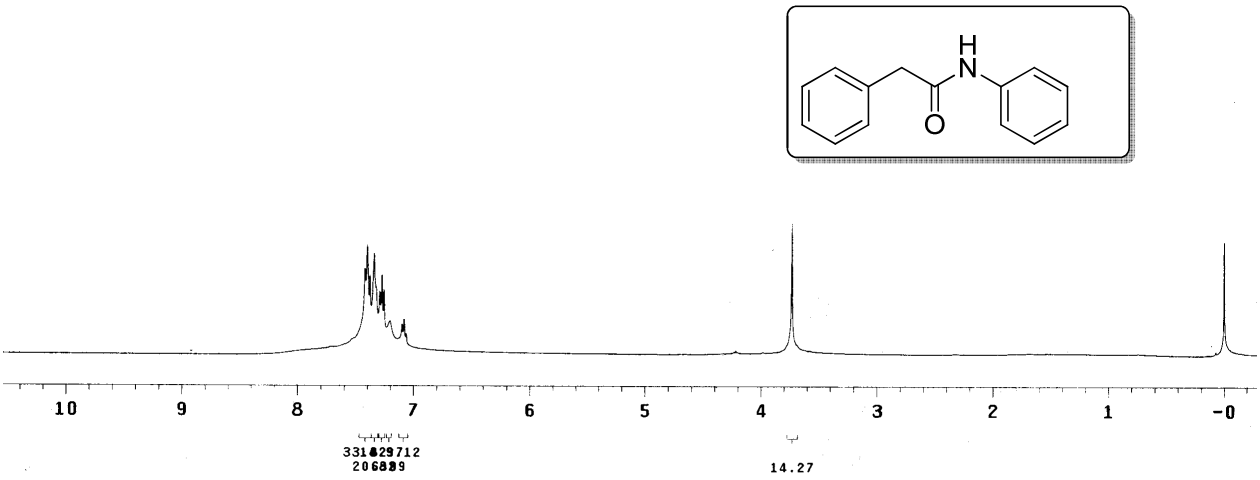


Figure S11: ^{1}H-NMR spectrum of N, 2-diphenylacetamide (entry 4, Table 3).

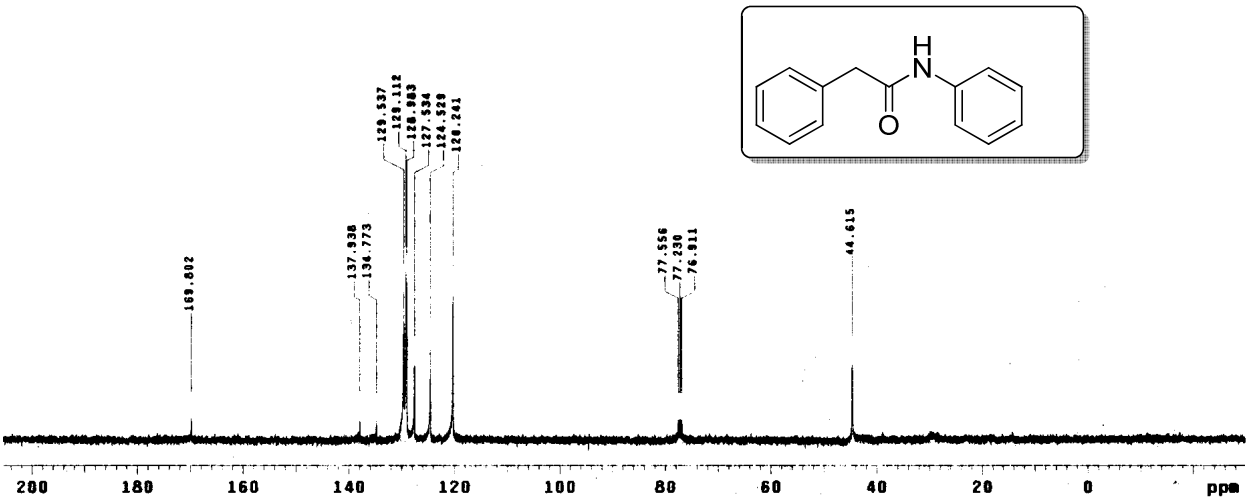


Figure S12: ^{13}C-NMR spectrum of N,2-diphenylacetamide (entry 4, Table 3).

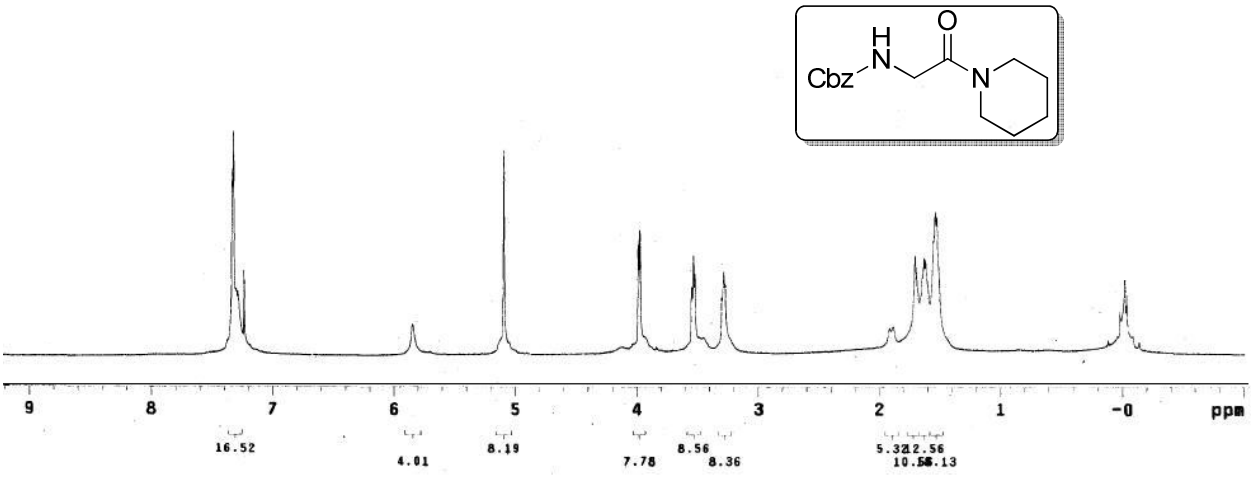


Figure S13: ^{1}H-NMR spectrum of benzyl 2-oxo-2-(piperidin-1-yl)ethylcarbamate (entry 5, Table 3).

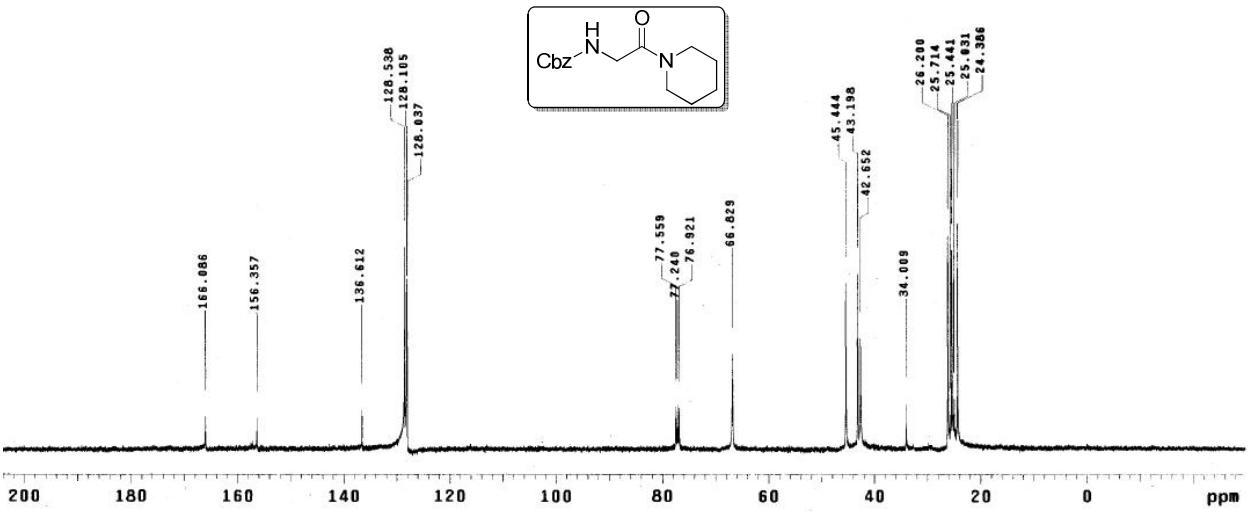


Figure S14: ^{13}C-NMR spectrum of benzyl 2-oxo-2-(piperidin-1-yl)ethylcarbamate (entry 5, Table 3).

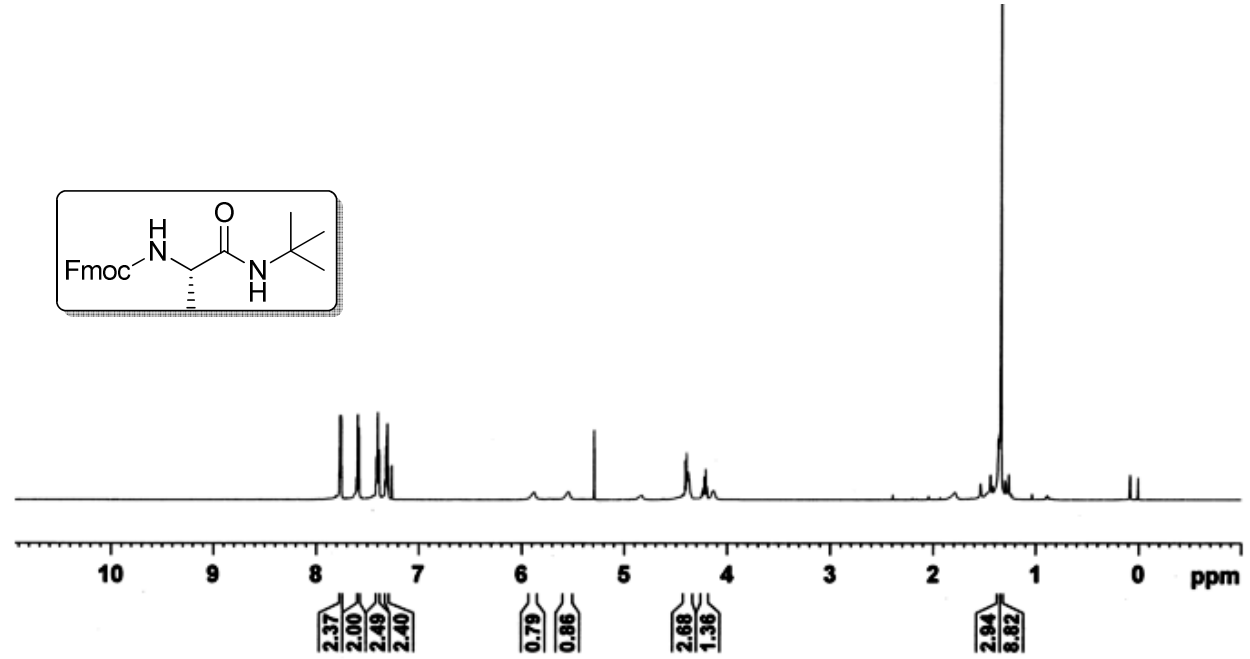


Figure S15: ^{1}H-NMR spectrum of (9H-fluoren-9-yl)methyl (1-(tert-butylamino)-1-oxopropan-2-yl)carbamate (entry 6, Table 3).

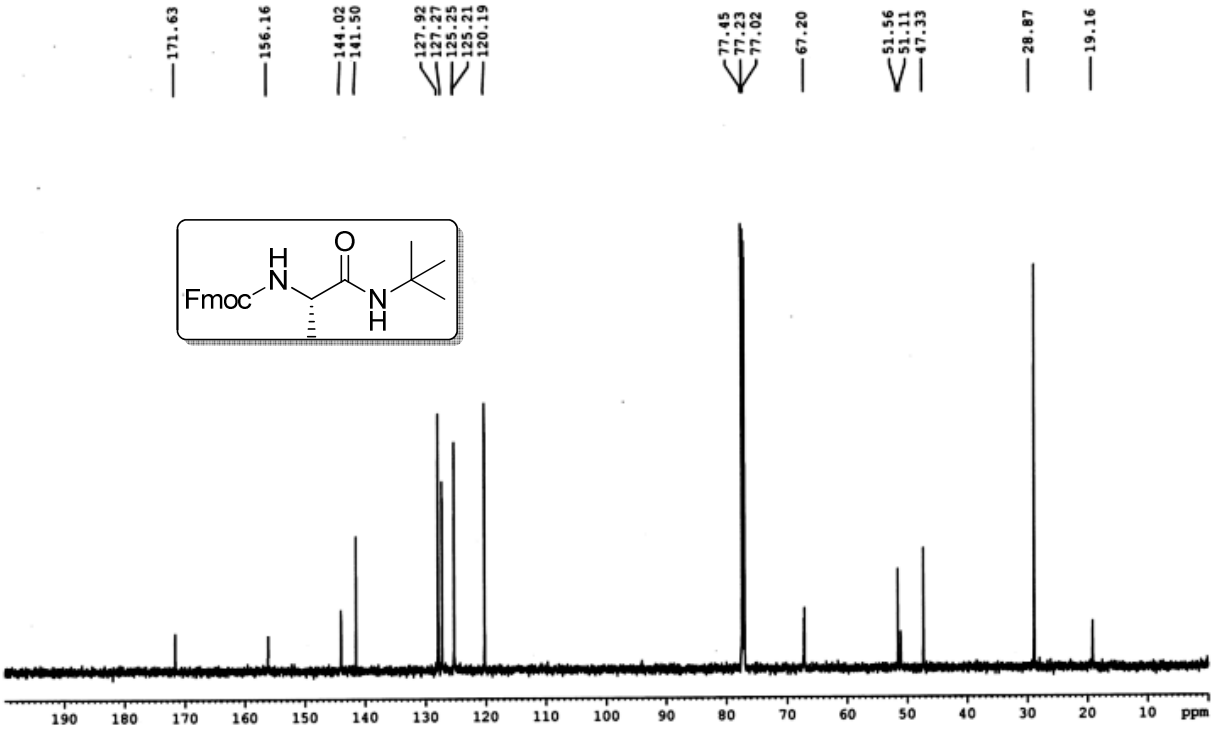


Figure S16: ^{13}C-NMR spectrum of (9H-fluoren-9-yl)methyl (1-(tert-butylamino)-1-oxopropan-2-yl)carbamate (entry 6, Table 3).

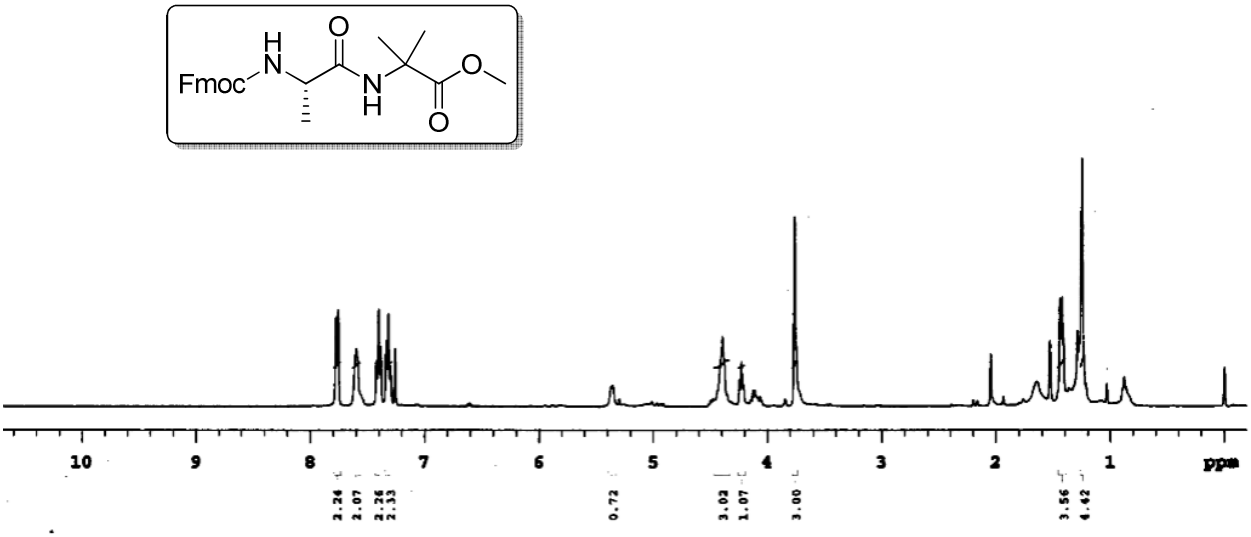


Figure S17: ^{1}H-NMR spectrum of methyl 2-(2-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)propanamido)-2-methylpropanoate (entry 7, Table 3).

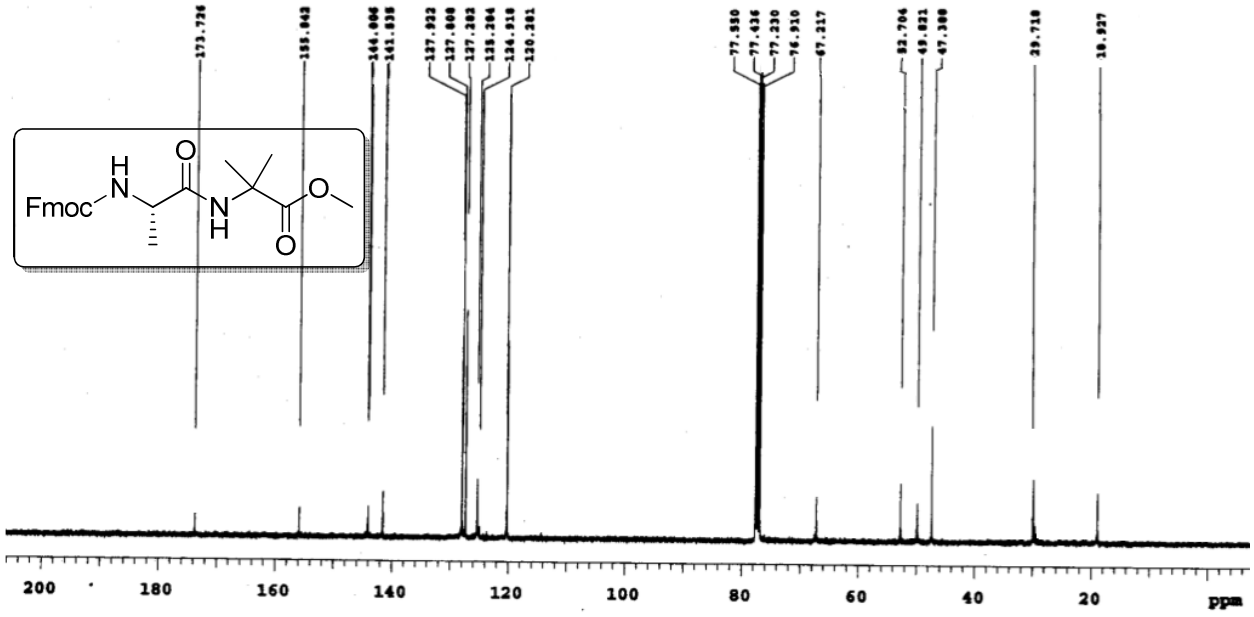


Figure S18: ^{13}C-NMR spectrum of methyl 2-(2-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)propanamido)-2-methylpropanoate (entry 7, Table 3).

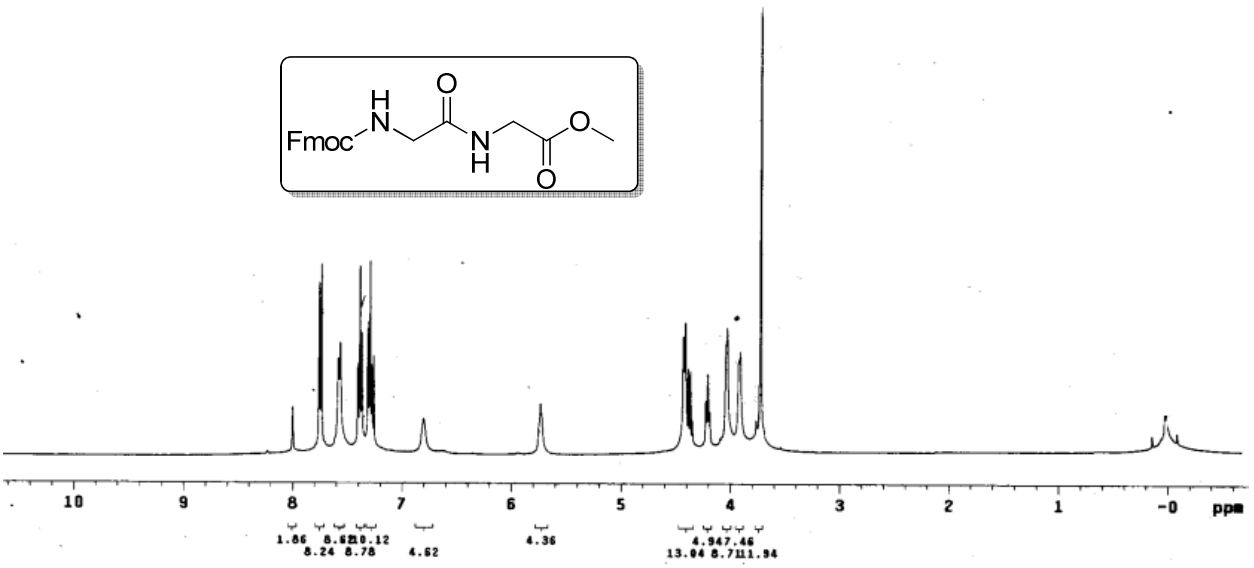


Figure S19: ^{1}H-NMR spectrum of methyl 2-(2-(((9H-fluoren-9-yl)methoxy)carbonyl)acetamido)acetate (entry 8, Table 3).

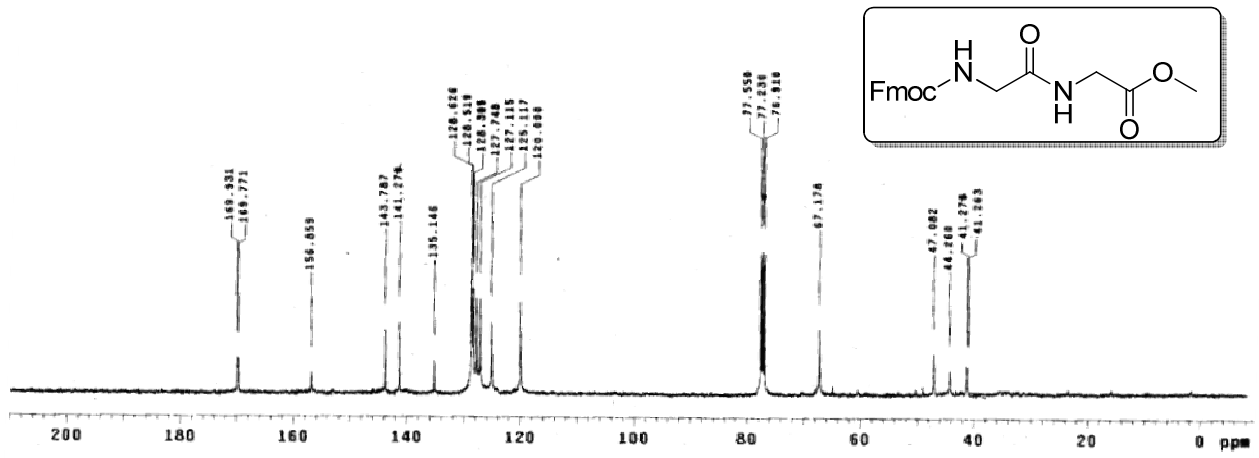


Figure S20: ^{13}C-NMR spectrum of methyl 2-(2-(((9H-fluoren-9-yl)methoxy)carbonyl)acetamido)acetate (entry 8, Table 3).

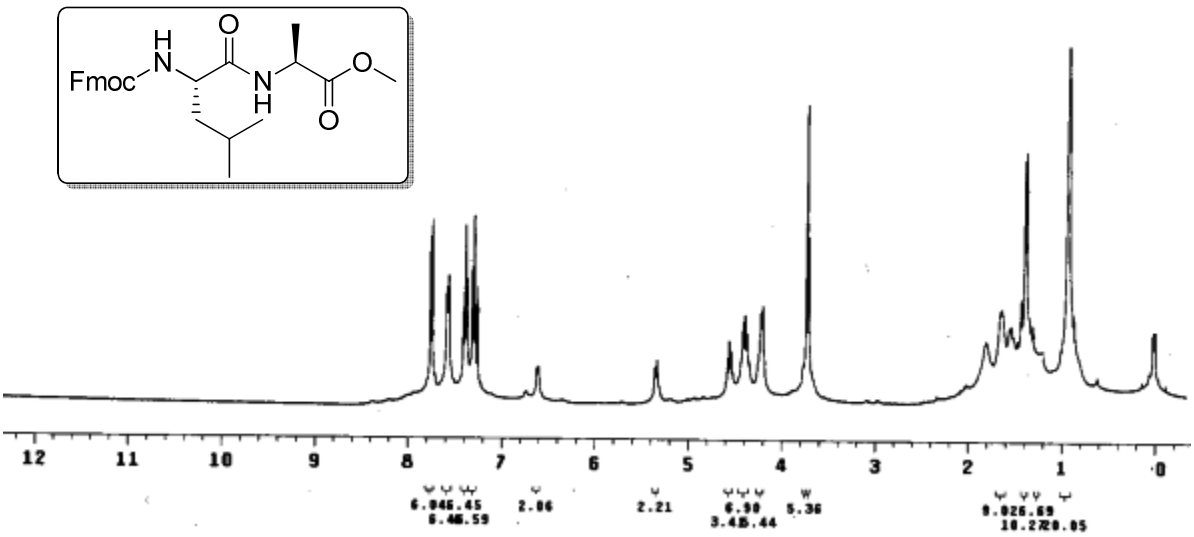


Figure S21: ^{1}H-NMR spectrum of methyl 2-(2-(((9H-fluoren-9-yl) methoxy) carbonyl)-4-methylpentanamido) propanoate (entry 9, Table3).

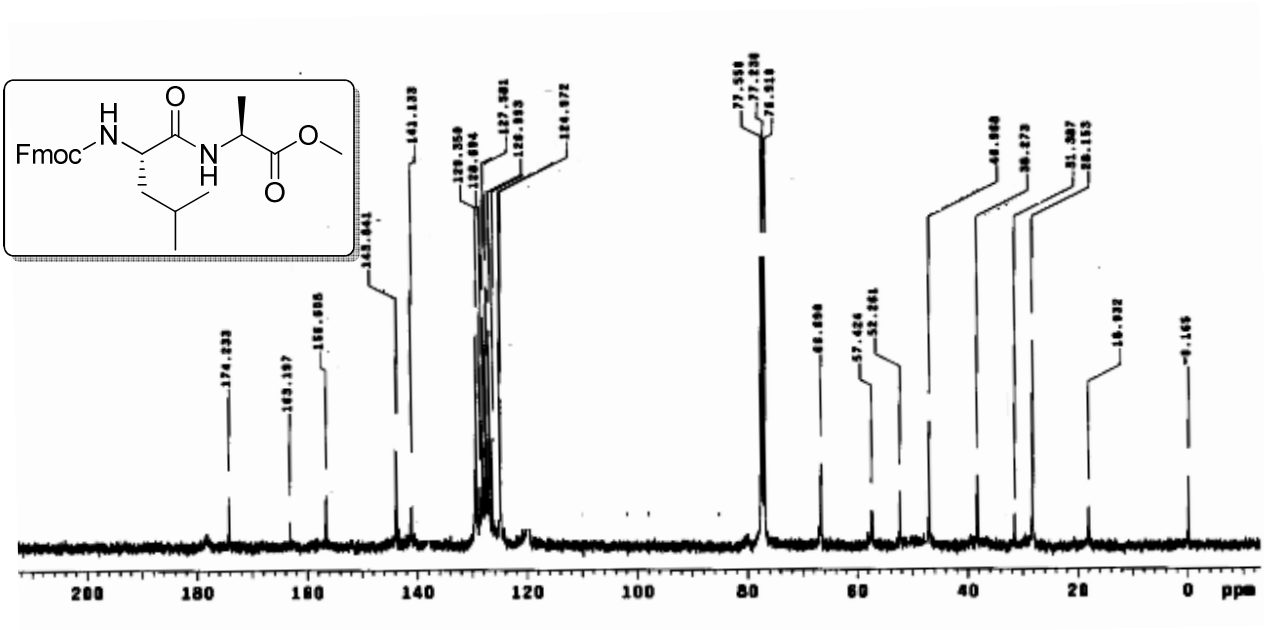


Figure S22: ^{13}C-NMR spectrum of methyl 2-(2-(((9H-fluoren-9-yl)methoxy)carbonyl)-4-methylpentanamido) propanoate (entry 9, Table 3).

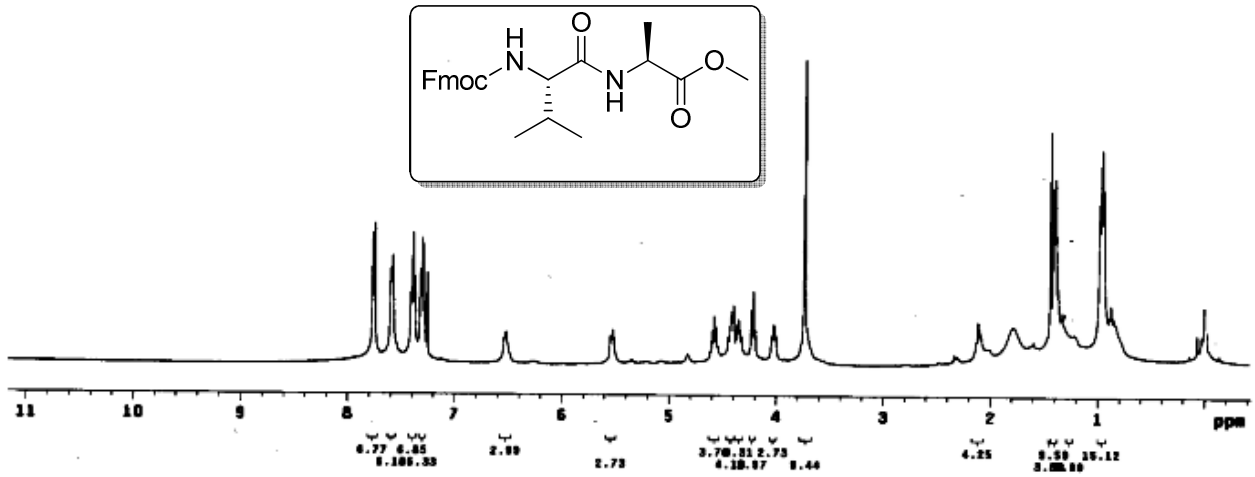


Figure S23: ^{1}H-NMR spectrum of methyl 2-(2-(((9H-fluoren-9-yl)methoxy)carbonyl)-3-methylbutanamido) propanoate (entry 10, Table 3).

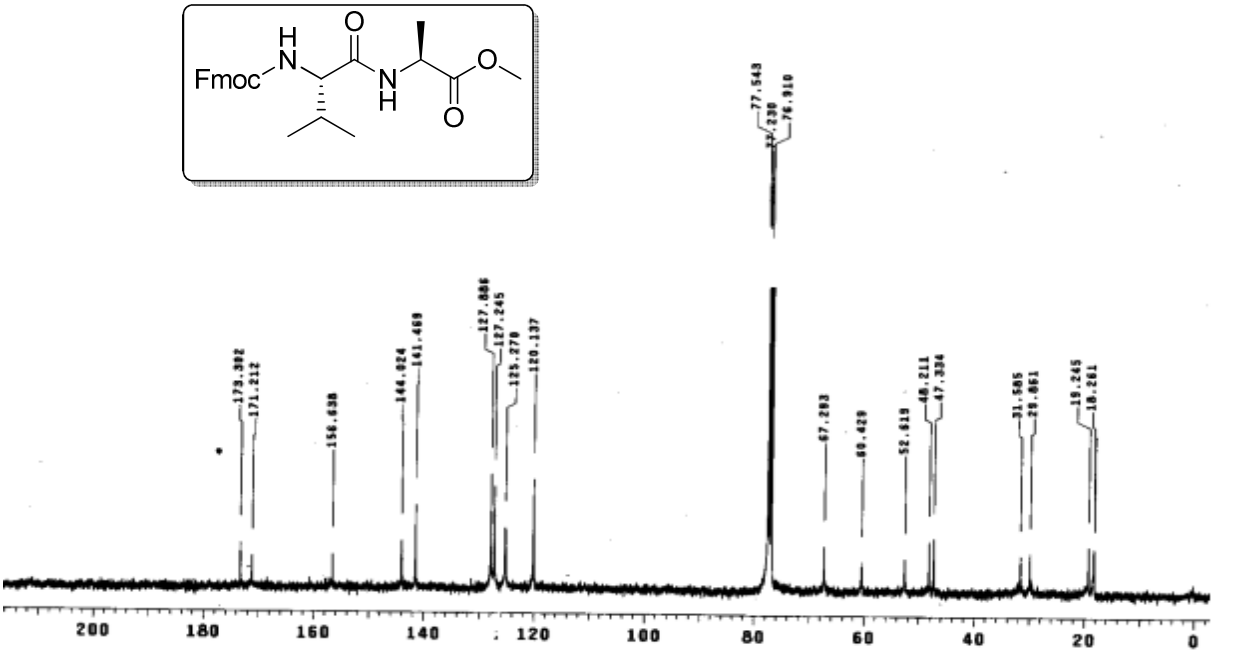


Figure S24: ^{13}C-NMR spectrum of methyl 2-(2-(((9H-fluoren-9-yl) methoxy)carbonyl)-3-methylbutanamido) propanoate (entry 10, Table 3).

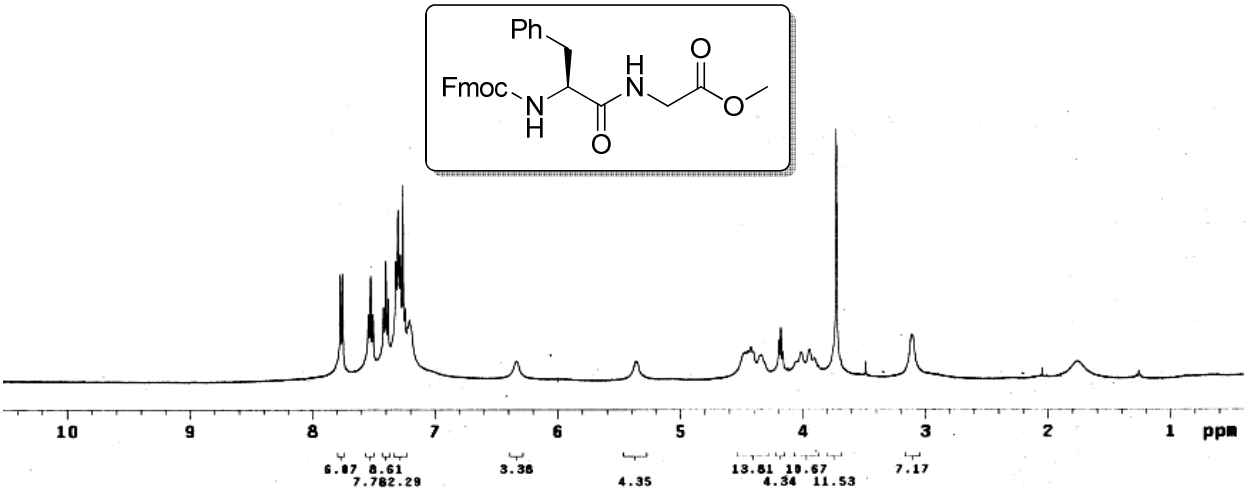


Figure S25: ^{1}H-NMR spectrum of methyl 2-(2-(((9H-fluoren-9-yl)methoxy)carbonyl)-3-phenylpropanamido) acetate (entry 11, Table 3).

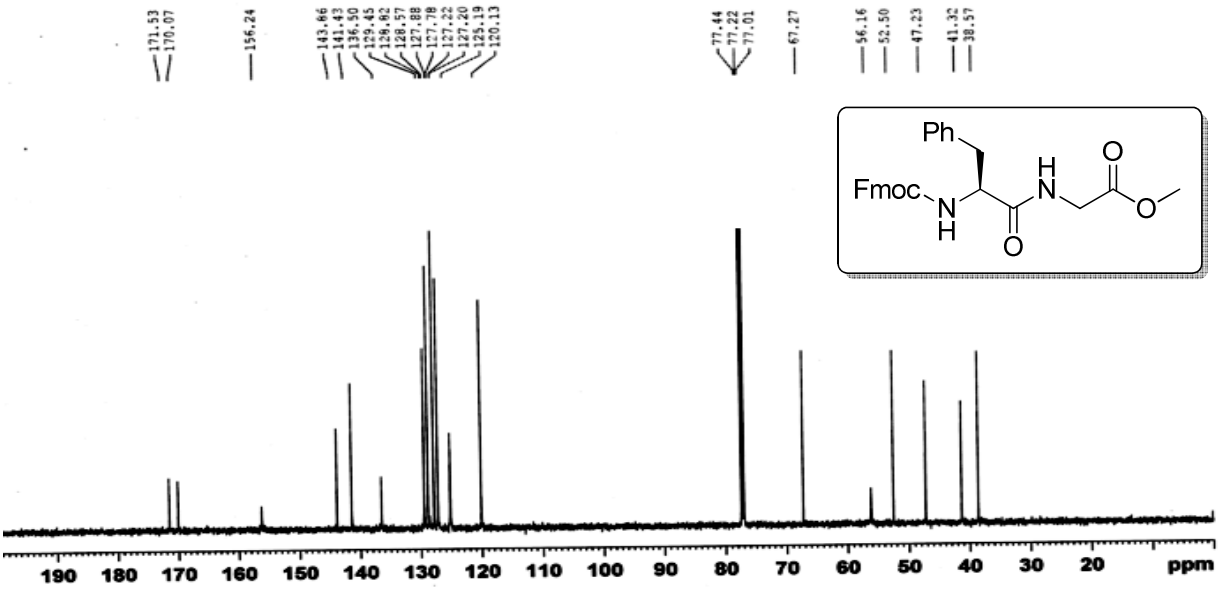


Figure S26: ^{13}C-NMR spectrum of methyl 2-(2-(((9H-fluoren-9-yl)methoxy)carbonyl)-3-phenylpropanamido) acetate (entry 11, Table 3).

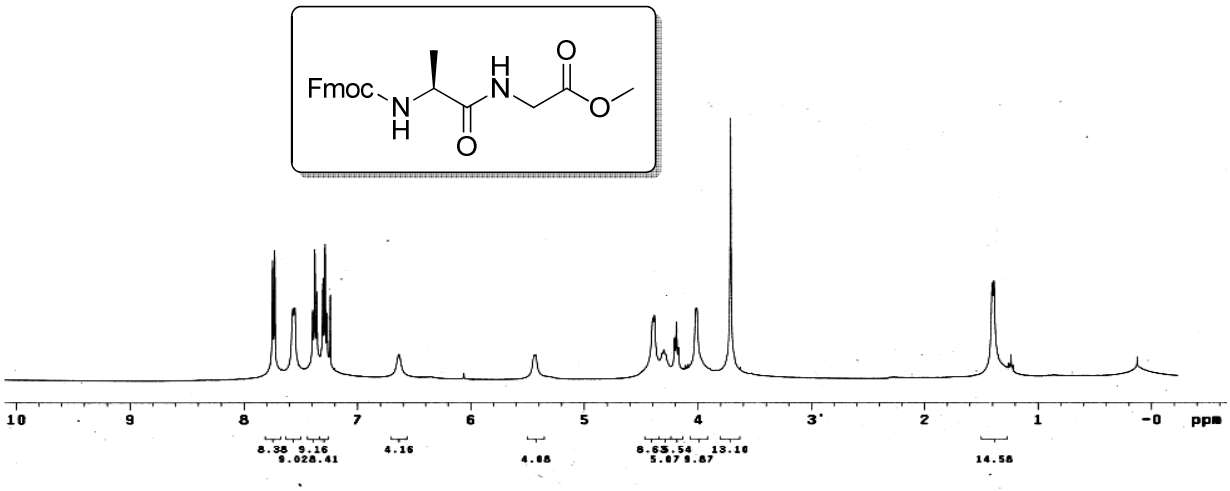


Figure S27: ^{1}H-NMR spectrum of methyl 2-(2-(((9H-fluoren-9-yl)methoxy)carbonyl) propanamido) acetate (entry 12, Table 3).

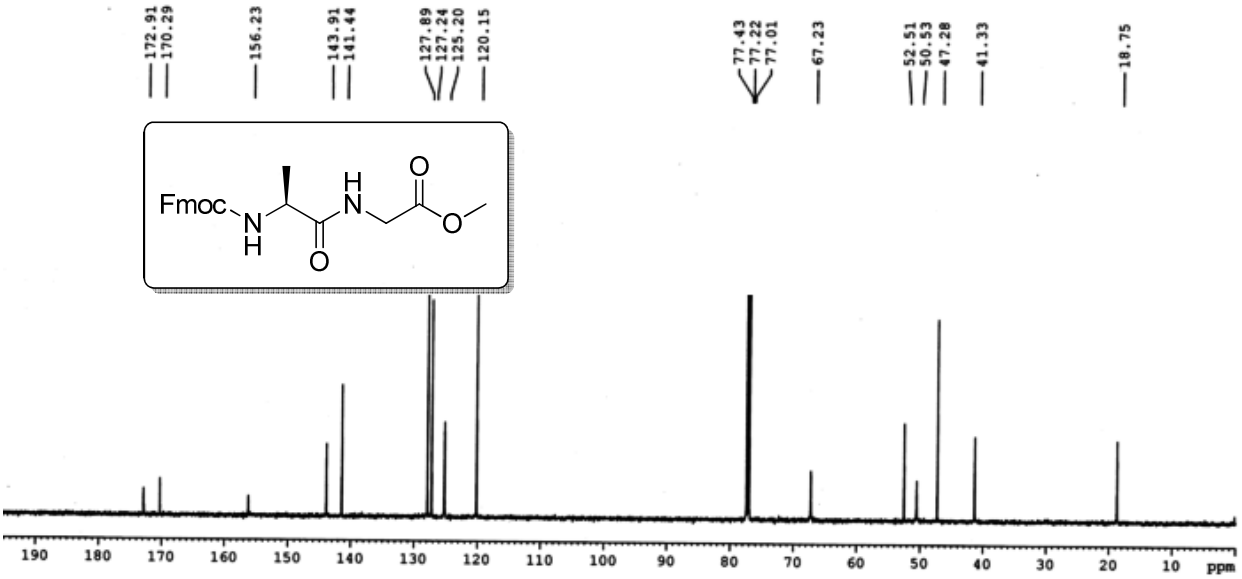


Figure S28: ^{13}C-NMR spectrum of methyl 2-(2-(((9H-fluoren-9-yl)methoxy)carbonyl) propanamido) acetate (entry 12, Table 3).

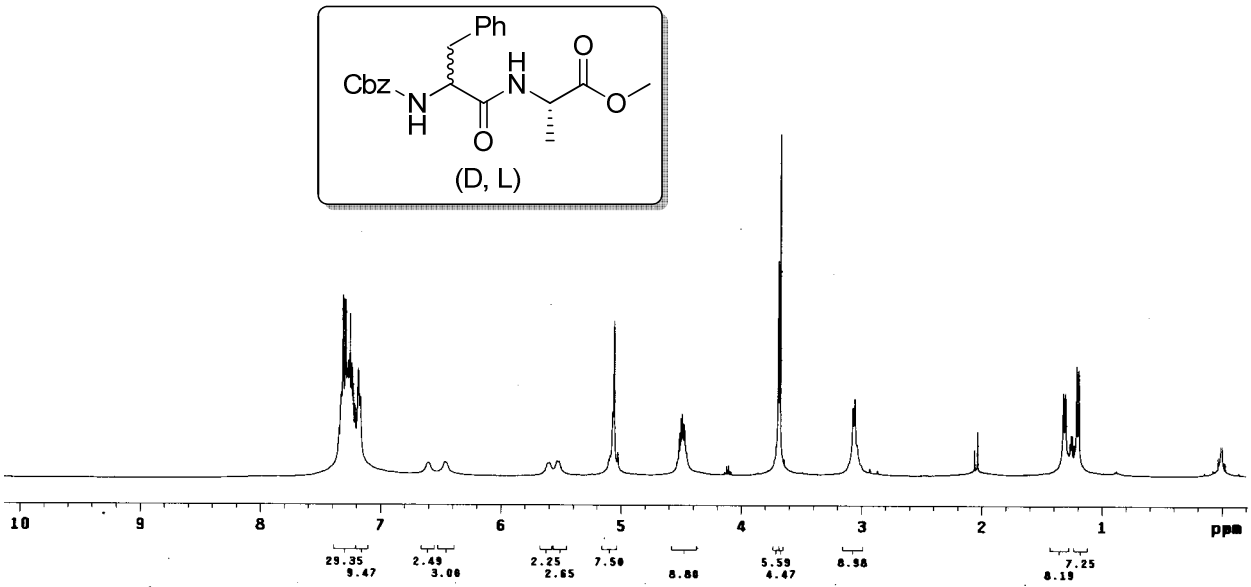


Figure S29: ^{1}H-NMR spectrum of (DL) methyl 2-(2-(benzyloxycarbonyl)-3-phenylpropanamido) propanoate (entry 13, Table 3).

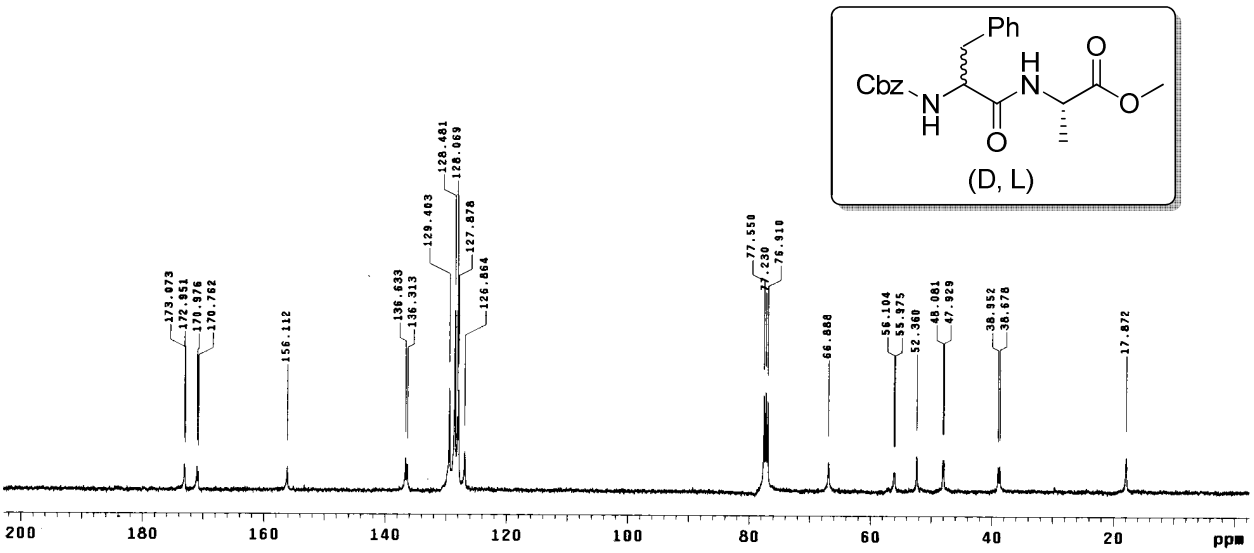


Figure S30: ^{13}C-NMR spectrum of (DL) methyl 2-(2-(benzyloxycarbonyl)-3-phenylpropanamido) propanoate (entry 13, Table 3).

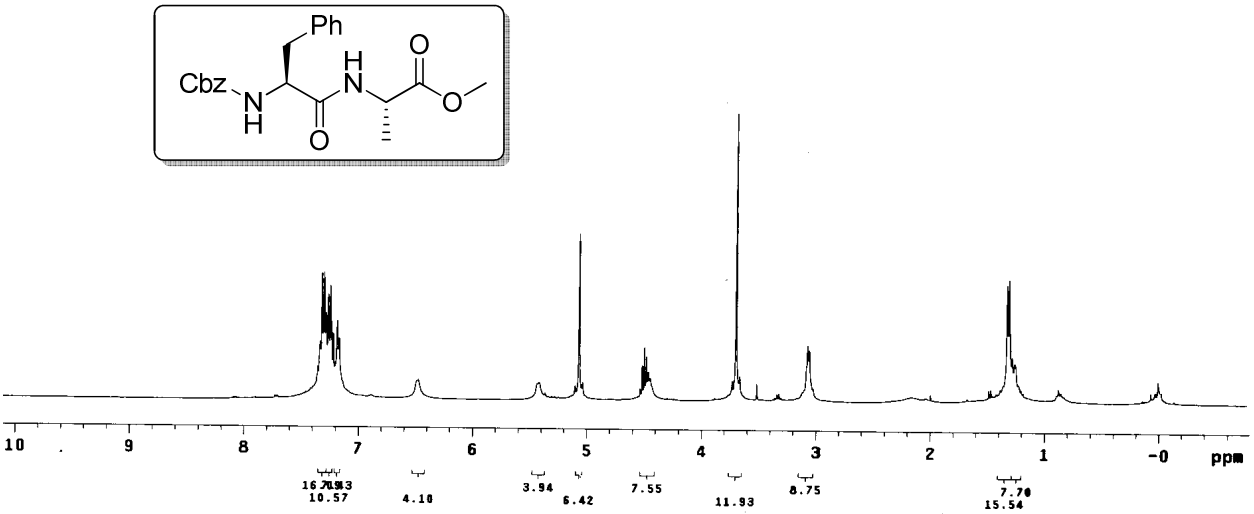


Figure S31: ^{1}H-NMR spectrum of (L) methyl 2-(2-(benzyloxycarbonyl)-3-phenylpropanamido) propanoate (entry 14, Table 3).

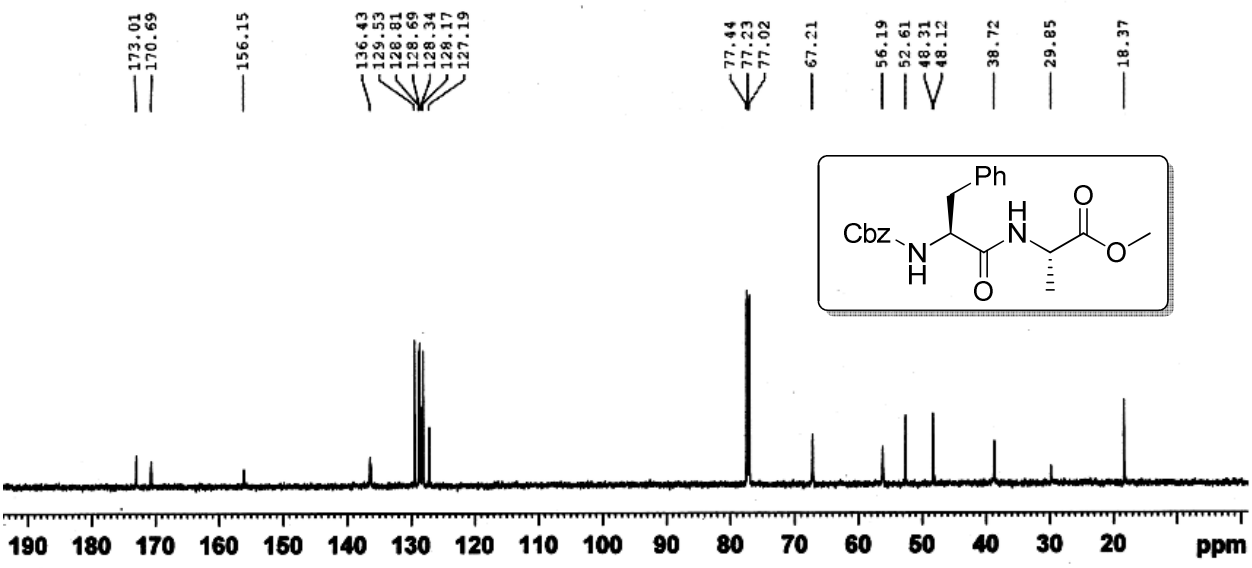


Figure S32: ^{13}C-NMR spectrum of (L) methyl 2-(2-(benzyloxycarbonyl)-3-phenylpropanamido)propanoate (entry 14, Table 3).

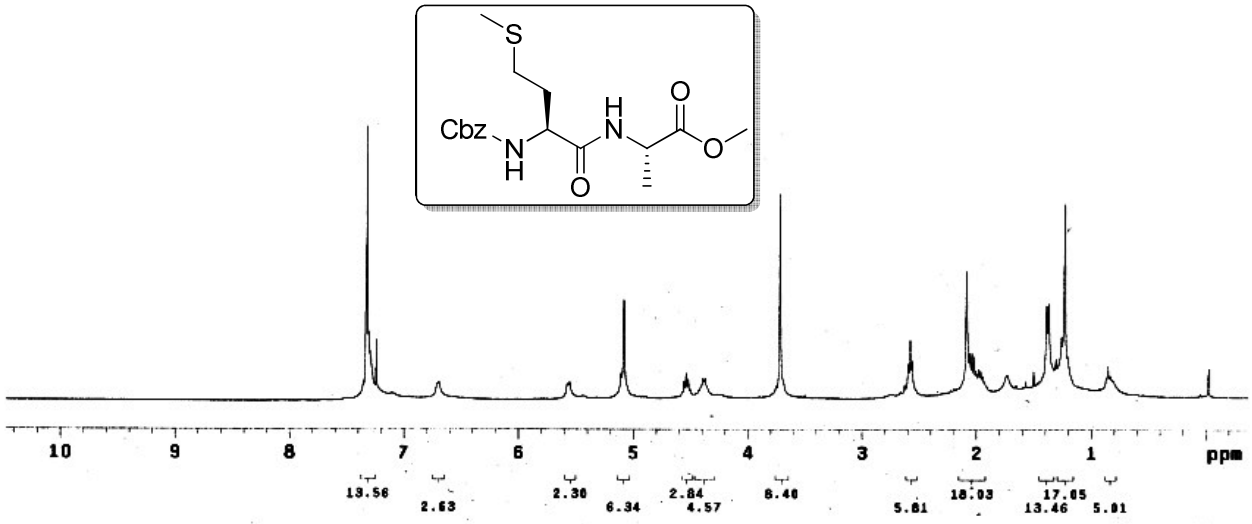


Figure S33: ^{1}H-NMR spectrum of methyl 2-(2-(benzyloxycarbonyl)-4-(methylthio)butanamido) propanoate (entry 15, Table 3).

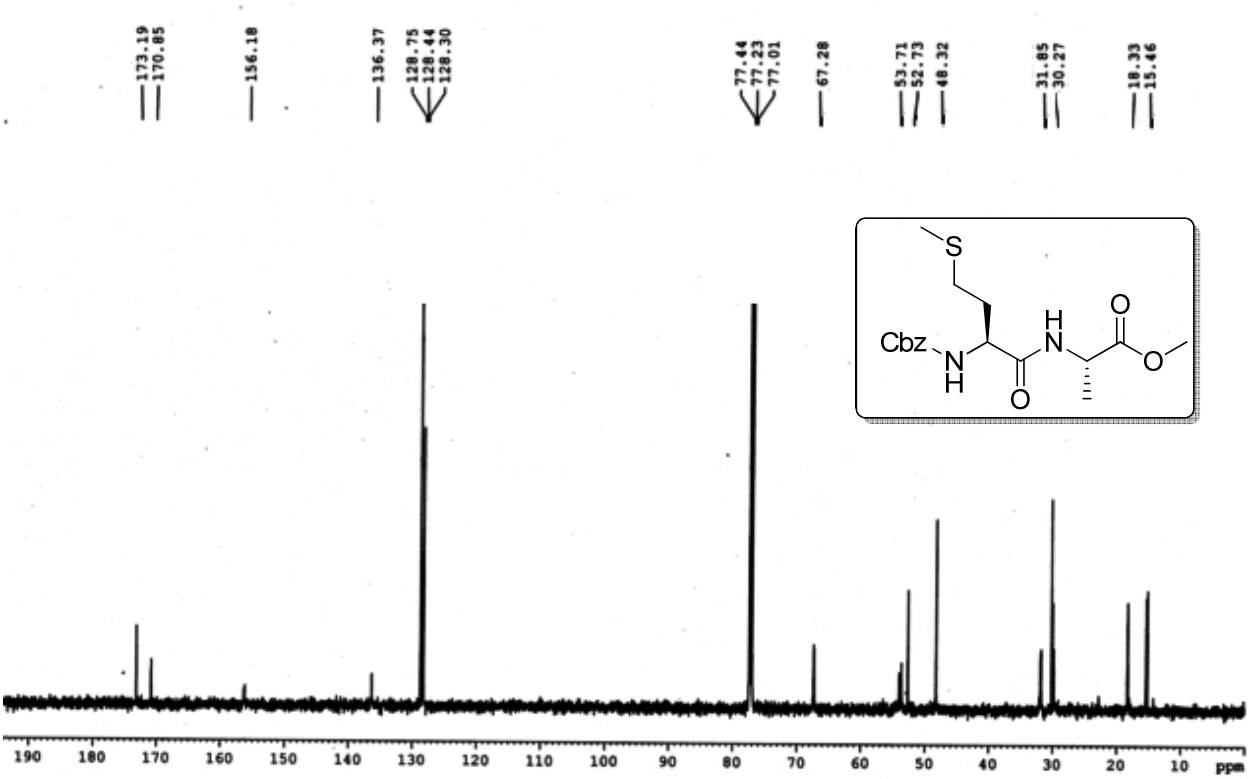


Figure S34: ^{13}C-NMR spectrum of methyl 2-(2-(benzyloxycarbonyl)-4-(methylthio)butanamido) propanoate (entry 15, Table 3).

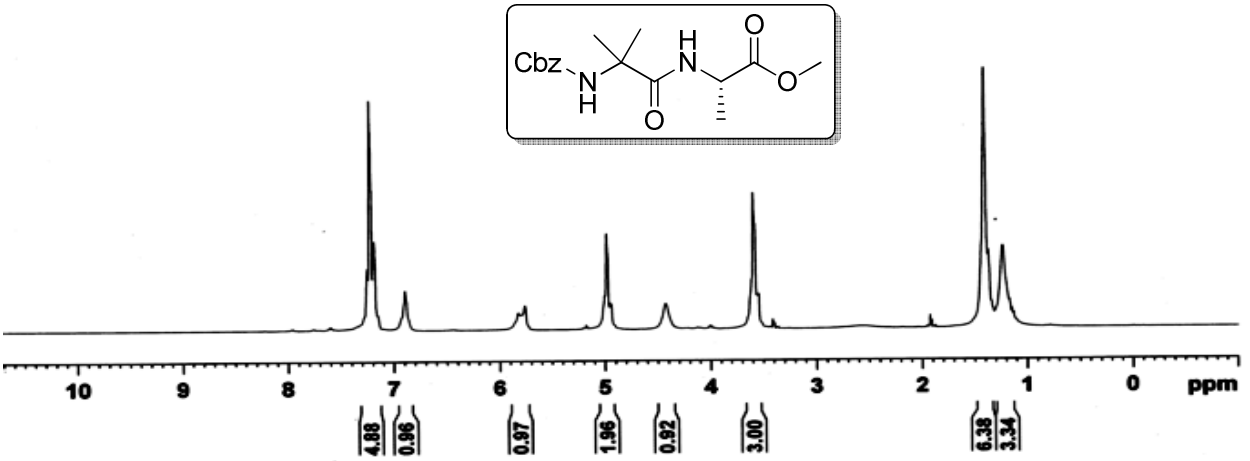


Figure S35: ^{1}H-NMR spectrum of methyl 2-(2-(benzyloxycarbonyl)-2-methylpropanamido)propanoate (entry 16, Table 3).

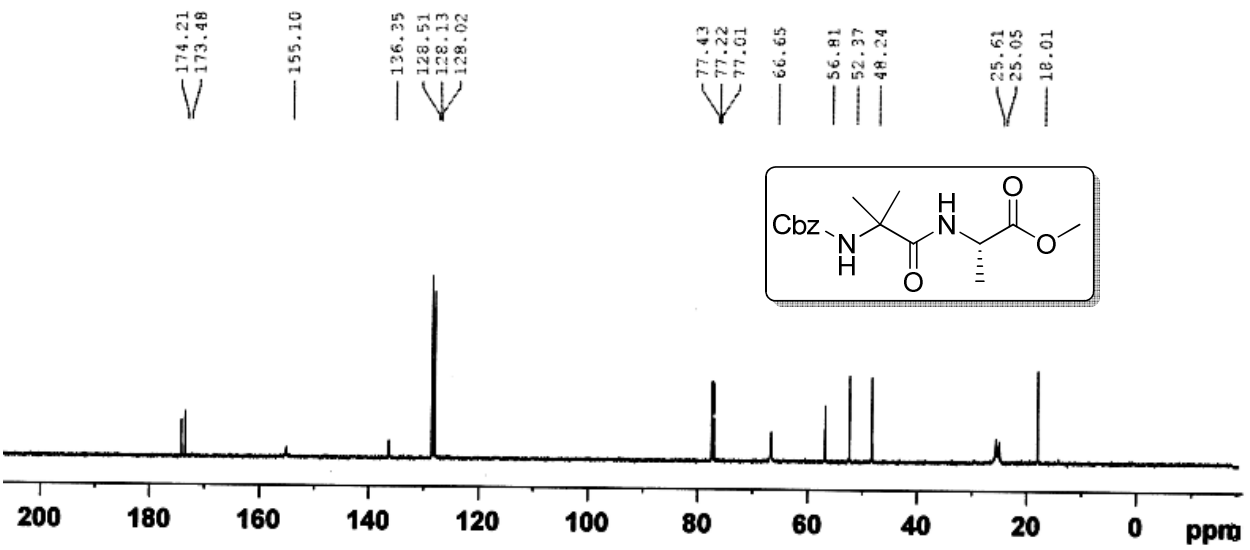


Figure S36: ^{13}C-NMR spectrum of methyl 2-(2-(benzyloxycarbonyl)-2-methylpropanamido)propanoate (entry 16, Table 3).

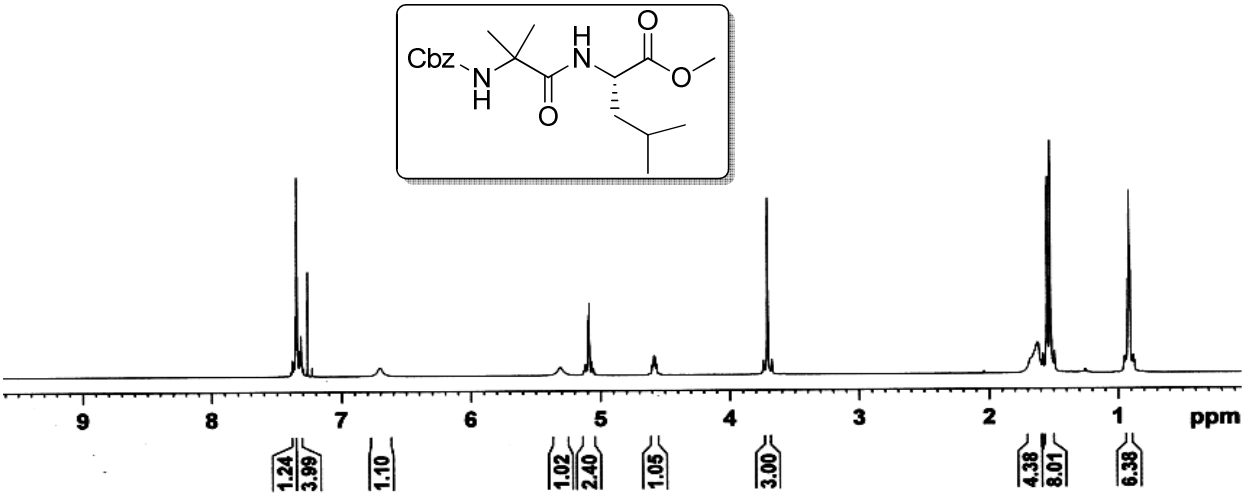


Figure S37: ^{1}H-NMR spectrum of methyl 2-(2-(benzyloxycarbonyl)-2-methylpropanamido)-4-methylpentanoate (entry 17, Table 3).

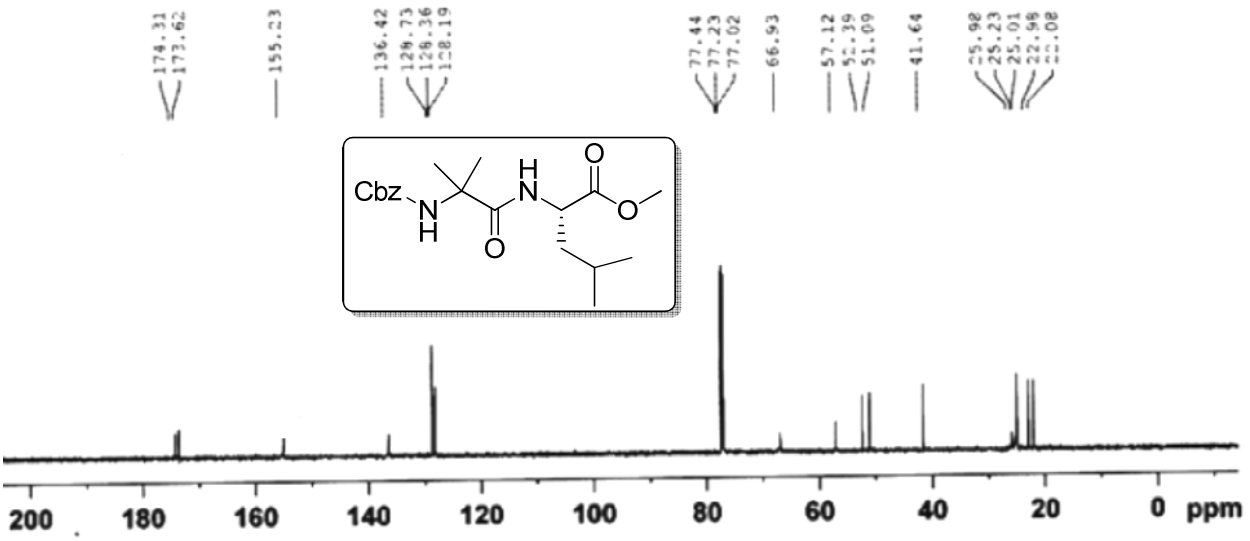


Figure S38: ^{13}C-NMR spectrum of methyl 2-(2-(benzyloxycarbonyl)-2-methylpropanamido)-4-methylpentanoate (entry 17, Table 3).

Figure S39: ^{1}H-NMR spectrum of 2-[2-(2-Benzyloxycarbonylamino-acetylamino)-3-phenyl-propionylamino]-3-methyl-butyric acid methyl ester (entry 18, Table 3).

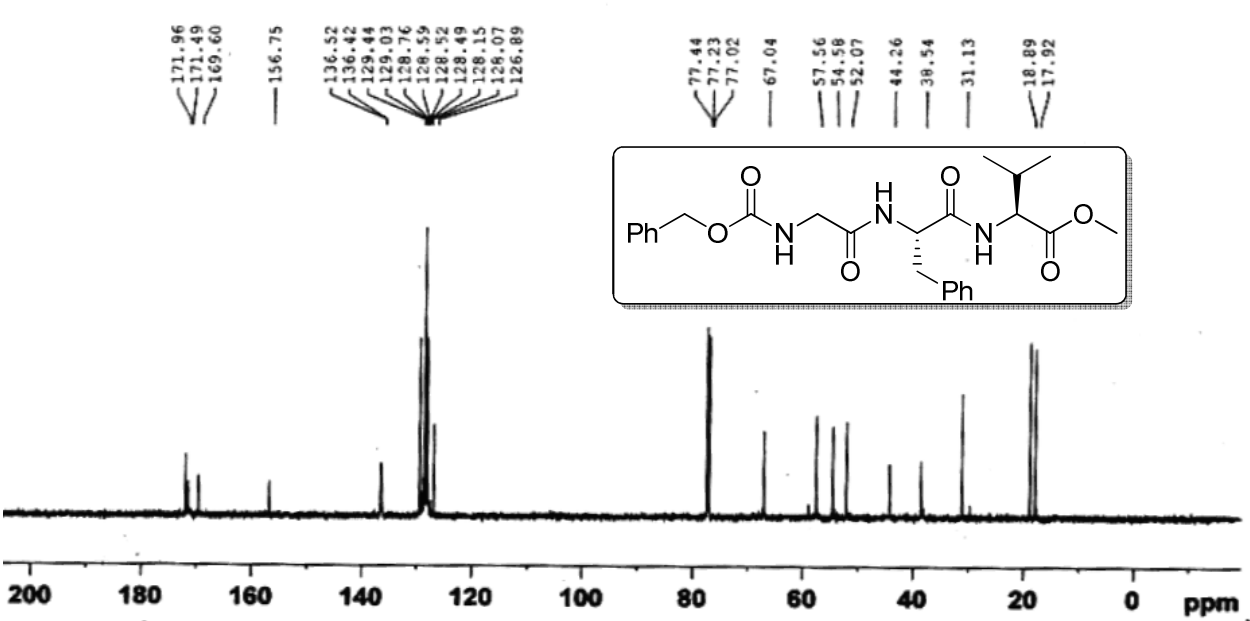


Figure S40: ^{13}C-NMR spectrum of 2-[2-(2-Benzyloxycarbonylamino-acetylamino)-3-phenyl-propionylamino]-3-methyl-butyric acid methyl ester (entry 18, Table 3).

4) ^{1}H-NMR and ^{13}C-NMR Spectra of hydroxamates:

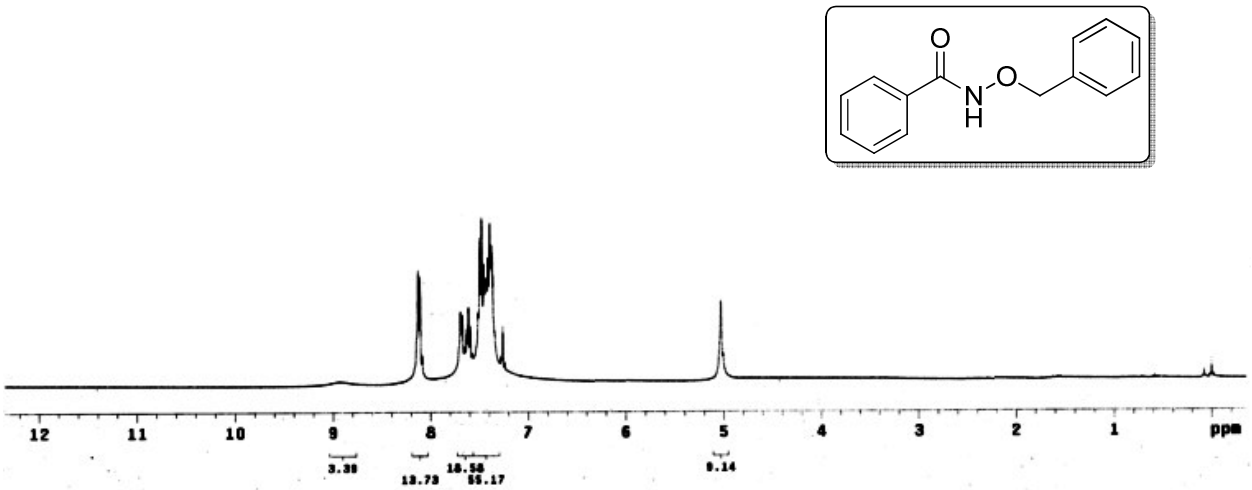


Figure S41: ^{1}H-NMR spectrum of N-(benzyloxy)benzamide (entry 1, Table 4).

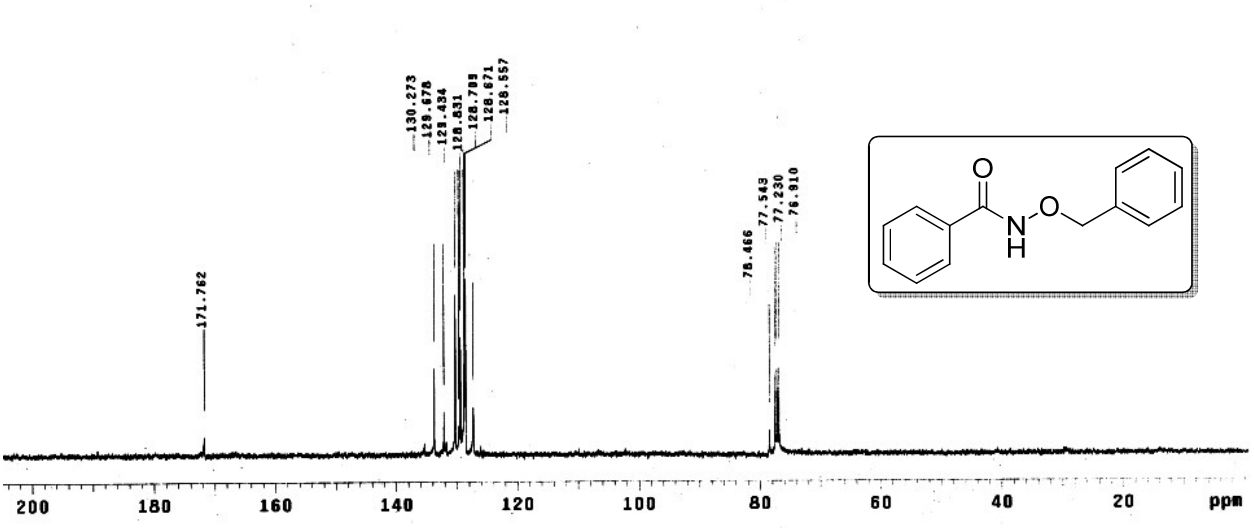


Figure S42: ^{13}C-NMR spectrum of N-(benzyloxy)benzamide (entry 1, Table 4).

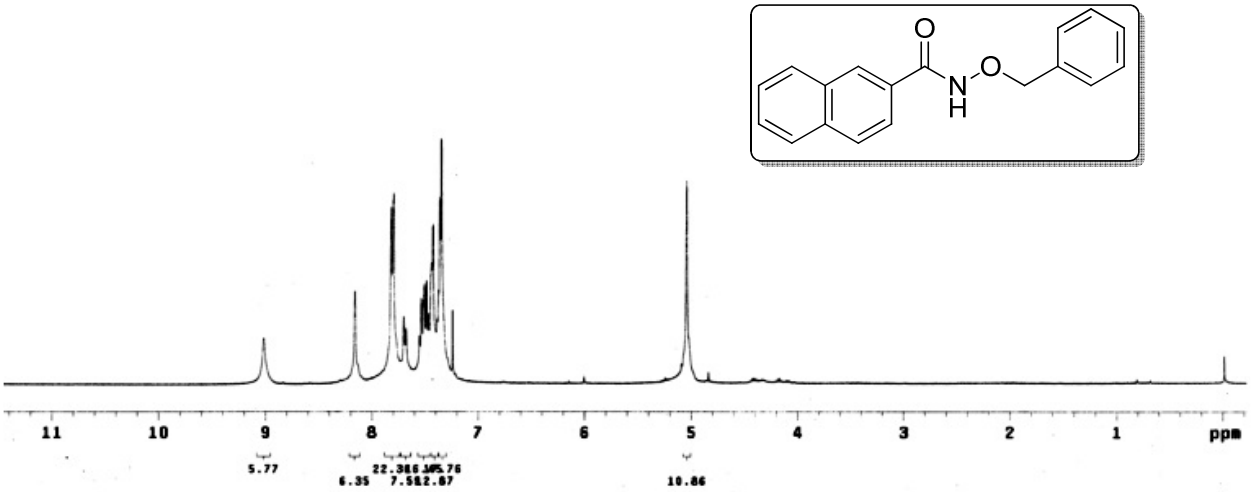


Figure S43: ^{1}H-NMR spectrum of N-(benzyloxy)-2-naphthamide (entry 2, Table 4).

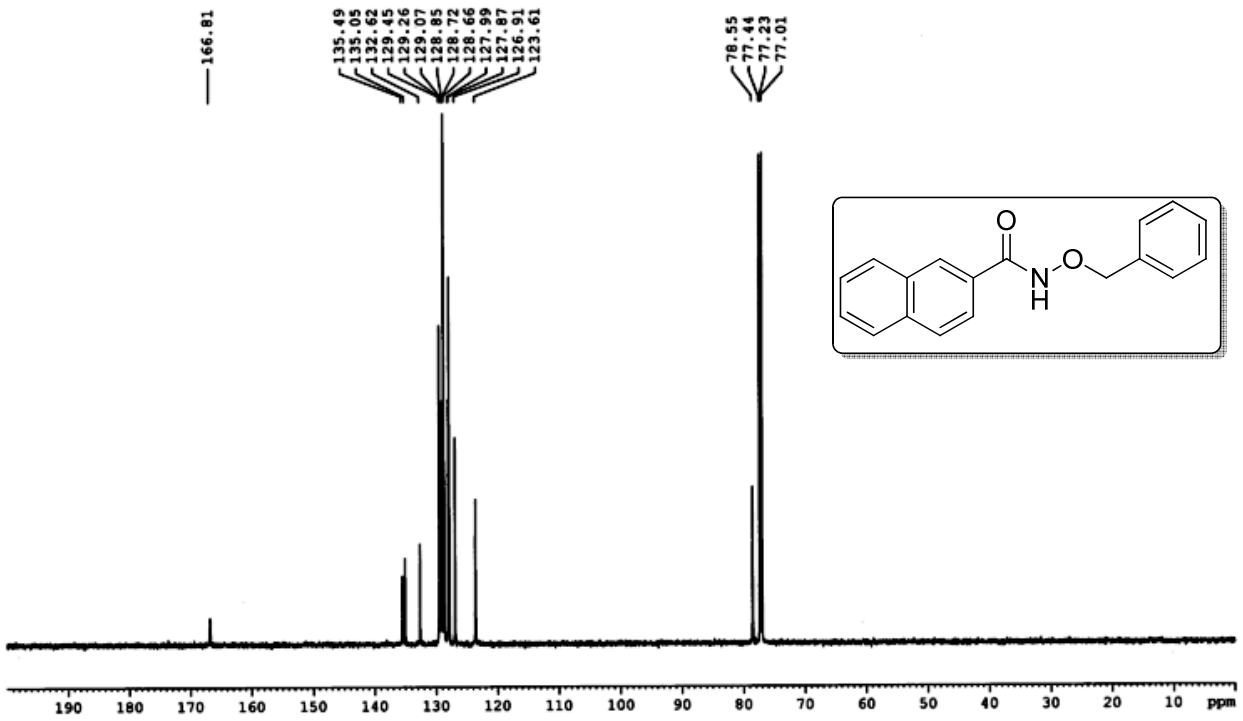


Figure S44: ^{13}C-NMR spectrum of N-(benzyloxy)-2-naphthamide (entry 2, Table 4).

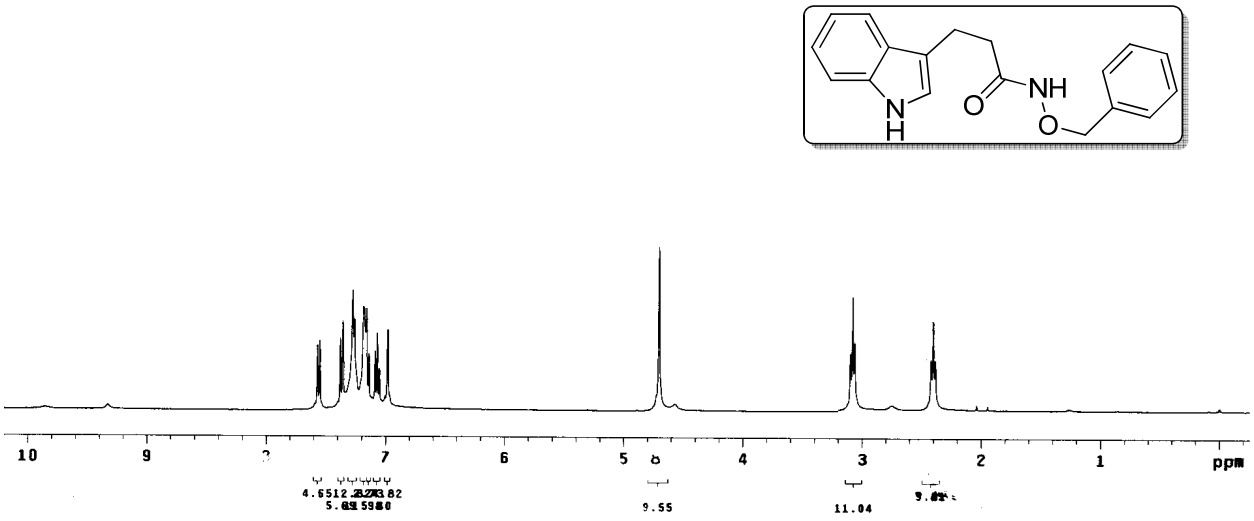


Figure S45: ^{1}H-NMR spectrum of *N*-(benzyloxy)-3-(1*H*-indol-3-yl)propanamide (entry 3, Table 4).

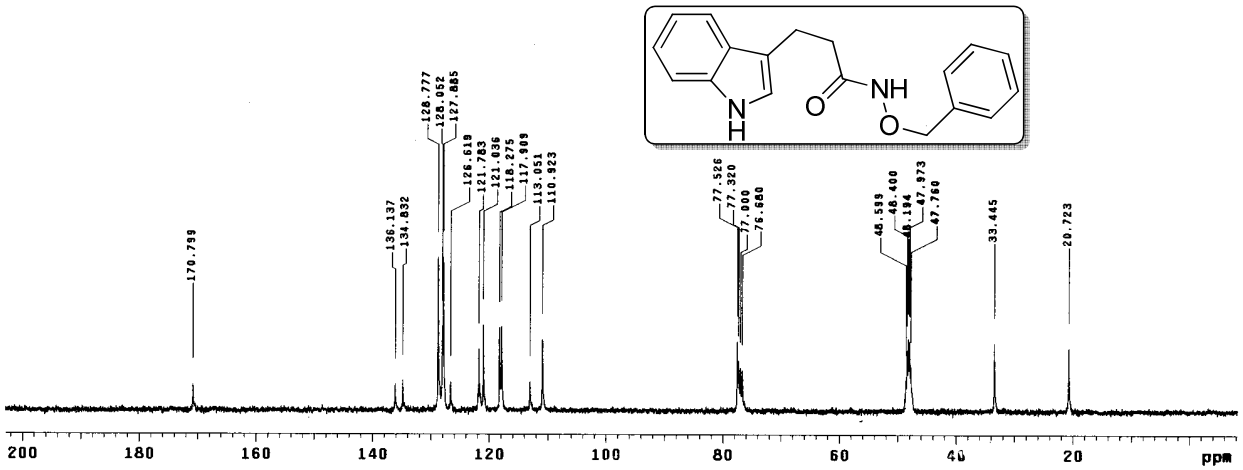


Figure S46: ^{13}C-NMR spectrum of *N*-(benzyloxy)-3-(1*H*-indol-3-yl)propanamide (entry 3, Table 4).

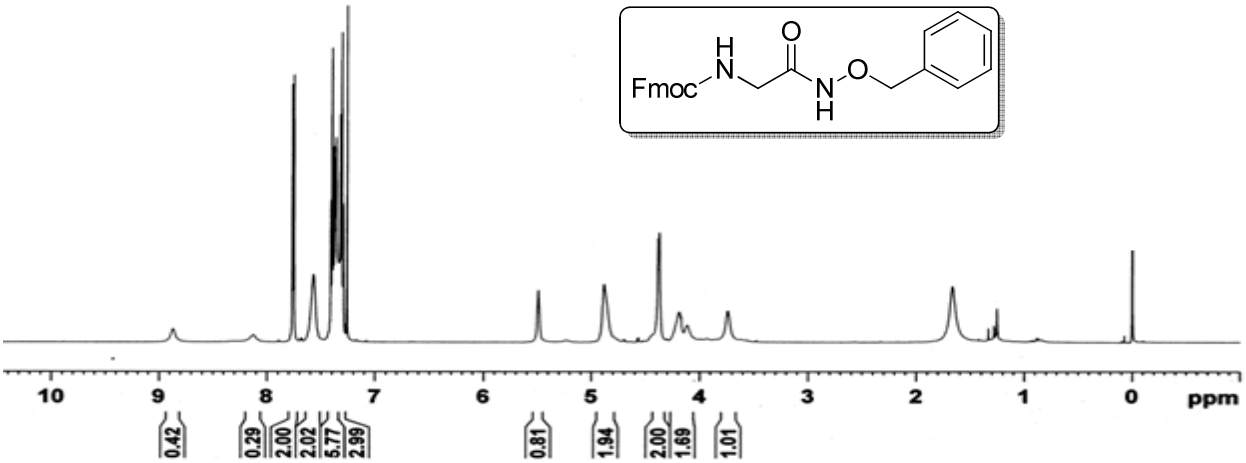


Figure S47: ^{1}H-NMR spectrum of (9H-fluoren-9-yl)methyl 2-(benzyloxyamino)-2-oxoethylcarbamate (entry 4, Table 4).

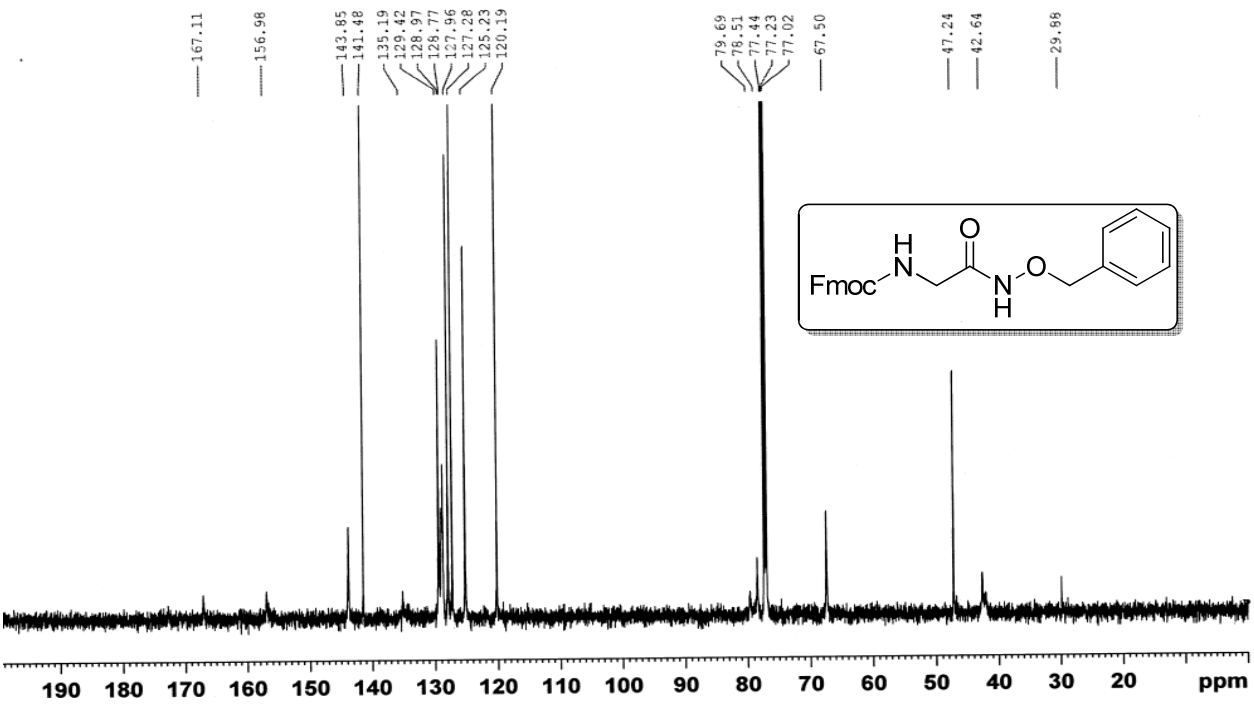


Figure S48: ^{13}C-NMR spectrum of (9H-fluoren-9-yl)methyl 2-(benzyloxyamino)-2-oxoethylcarbamate (entry 4, Table 4).

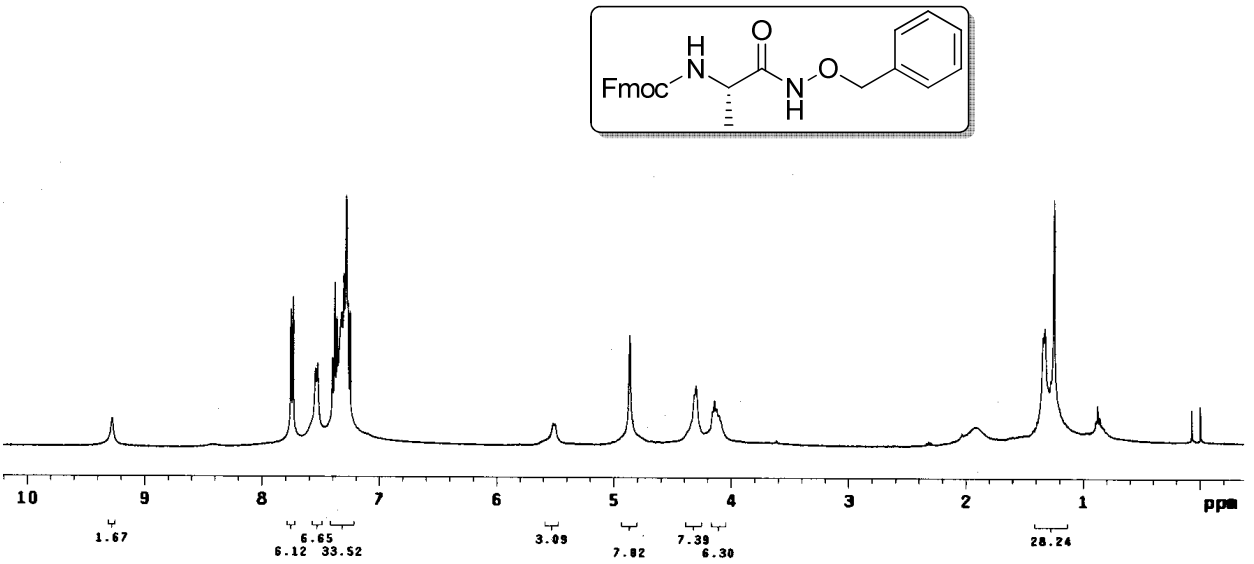


Figure S49: ^{1}H-NMR spectrum of (9H-fluoren-9-yl)methyl 1-(benzyloxyamino)-1-oxopropan-2-ylcarbamate (entry 5, Table 4).

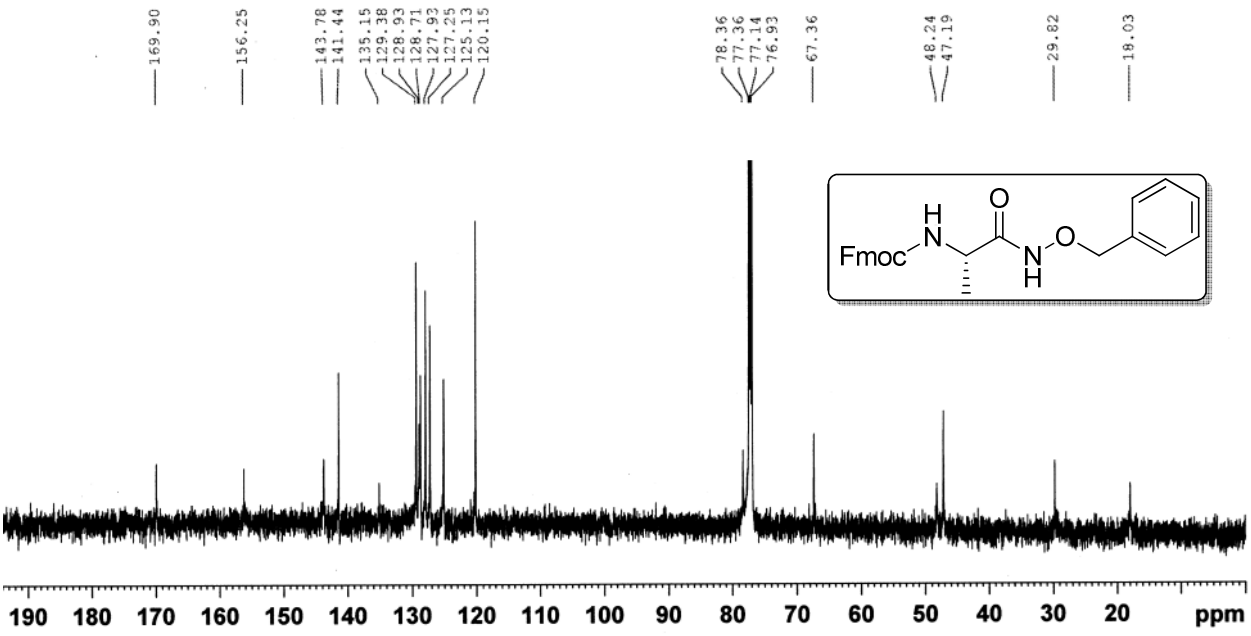


Figure S50: ^{13}C-NMR spectrum of (9H-fluoren-9-yl)methyl 1-(benzyloxyamino)-1-oxopropan-2-ylcarbamate (entry 5, Table 4).

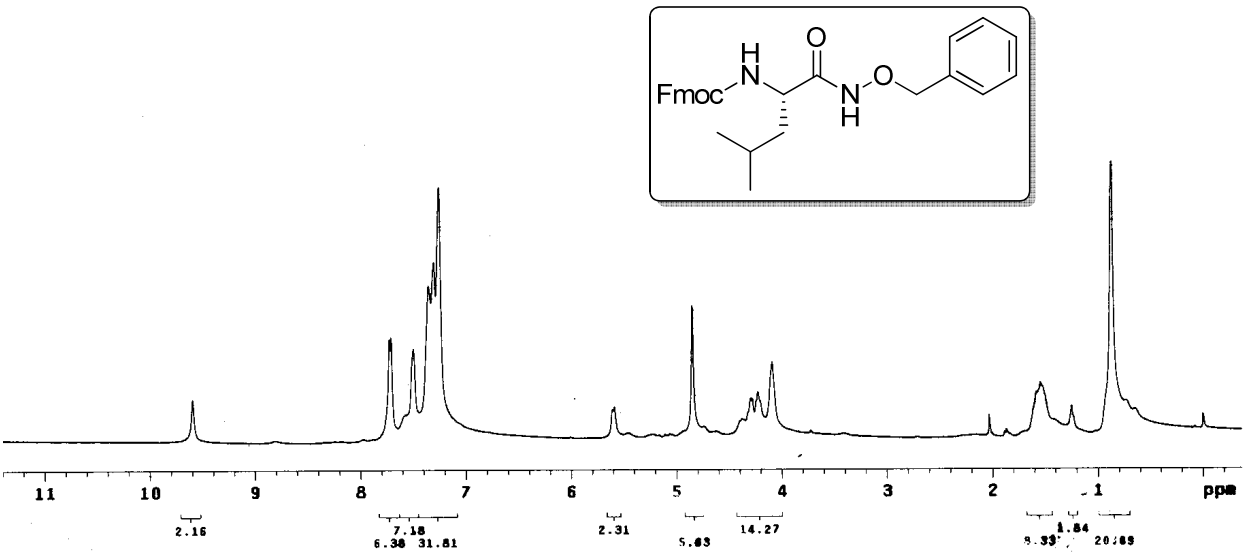


Figure S51: ^{1}H-NMR spectrum of (9H-fluoren-9-yl)methyl 1-(benzyloxyamino)-4-methyl-1-oxopentan-2-ylcarbamate (entry 6, Table 4).

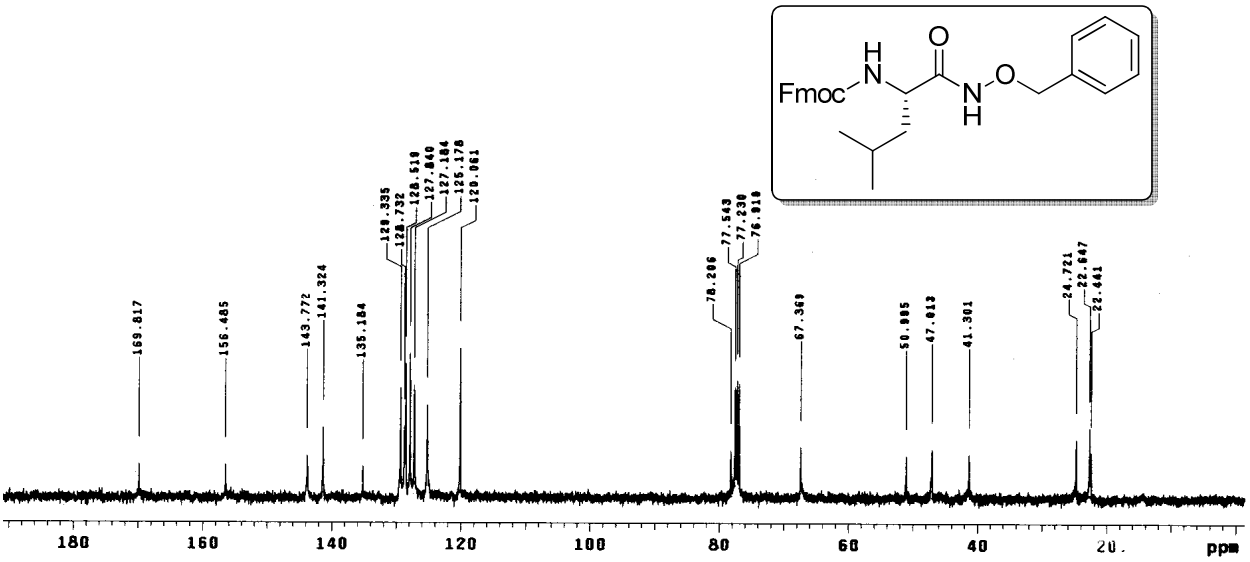


Figure S52: ^{13}C-NMR spectrum of (9H-fluoren-9-yl)methyl 1-(benzyloxyamino)-4-methyl-1-oxopentan-2-ylcarbamate (entry 6, Table 4).

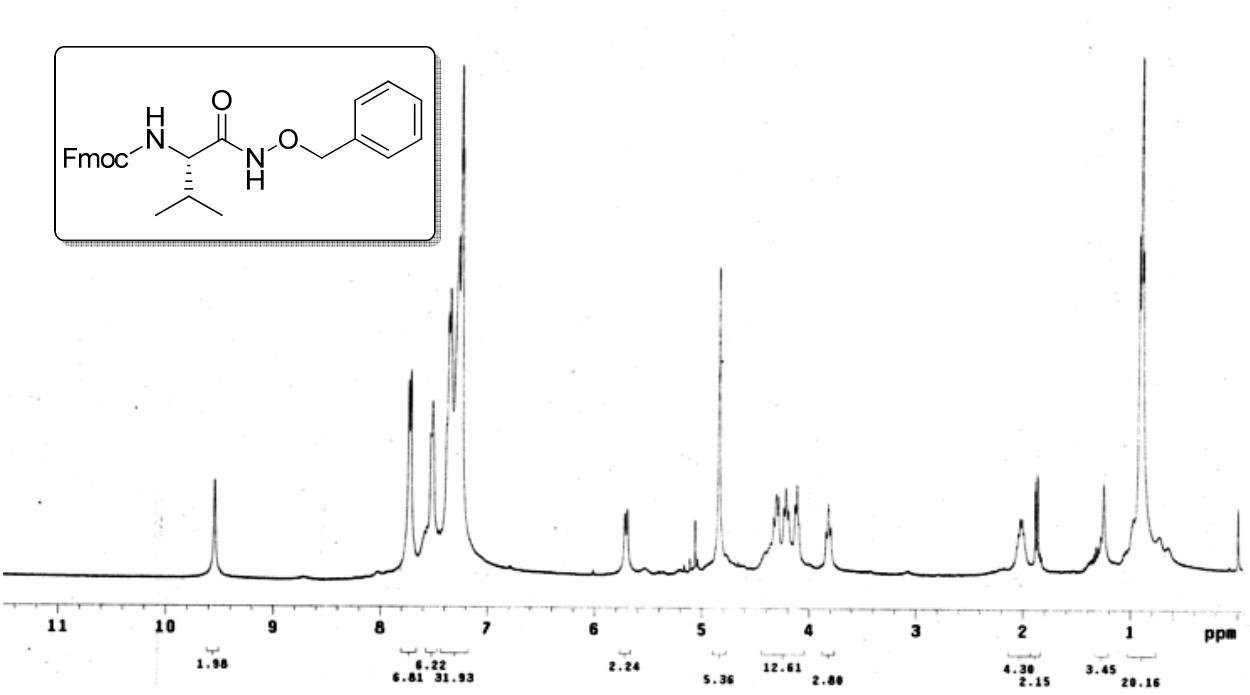


Figure S53: ^{1}H-NMR spectrum of (9H-fluoren-9-yl)methyl 1-(benzyloxyamino)-3-methyl-1-oxobutan-2-ylcarbamate (entry 7, Table 4).

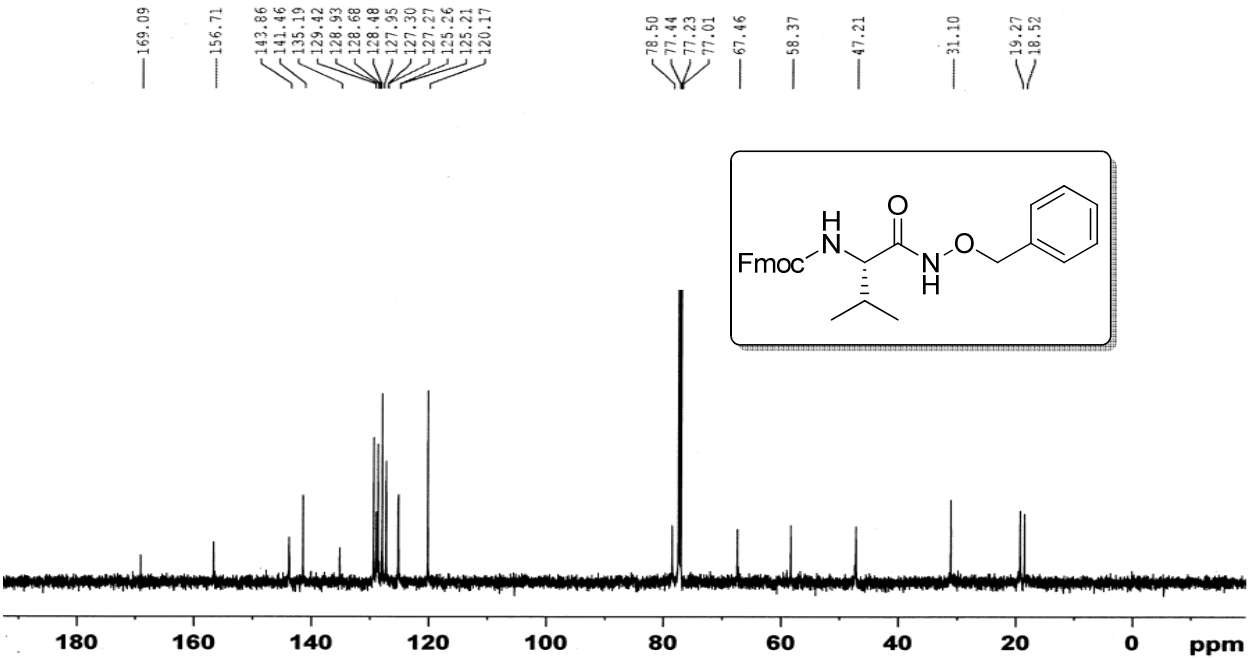


Figure S54: ^{13}C-NMR spectrum of (9H-fluoren-9-yl)methyl 1-(benzyloxyamino)-3-methyl-1-oxobutan-2-ylcarbamate (entry 7, Table 4).

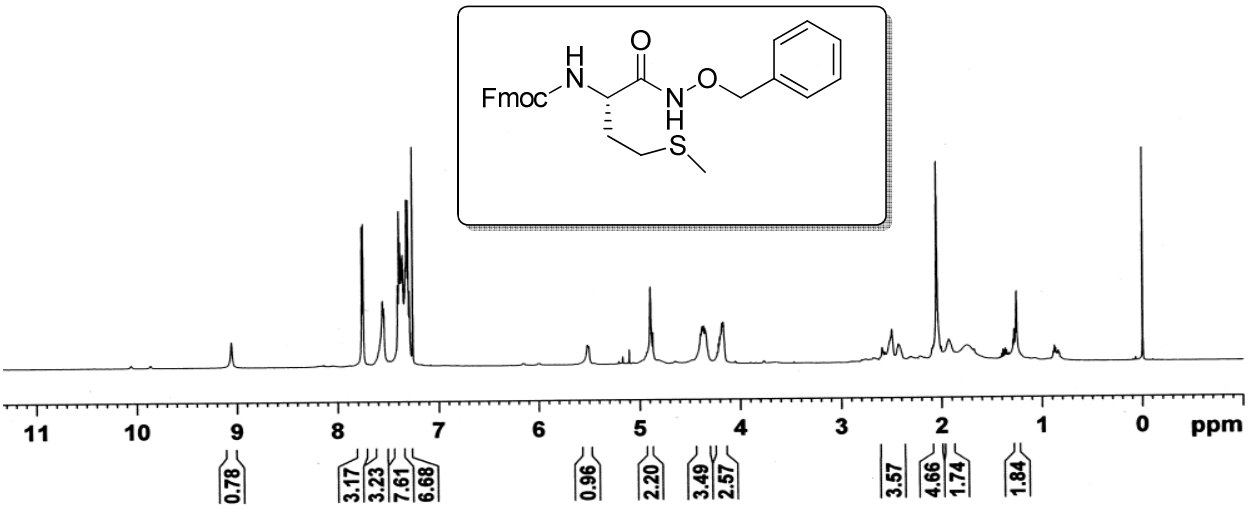


Figure S55: ^{1}H-NMR spectrum of (9H-fluoren-9-yl)methyl 1-(benzyloxyamino)-4-(methylthio)-1-oxobutan-2-ylcarbamate (entry 8, Table 4).

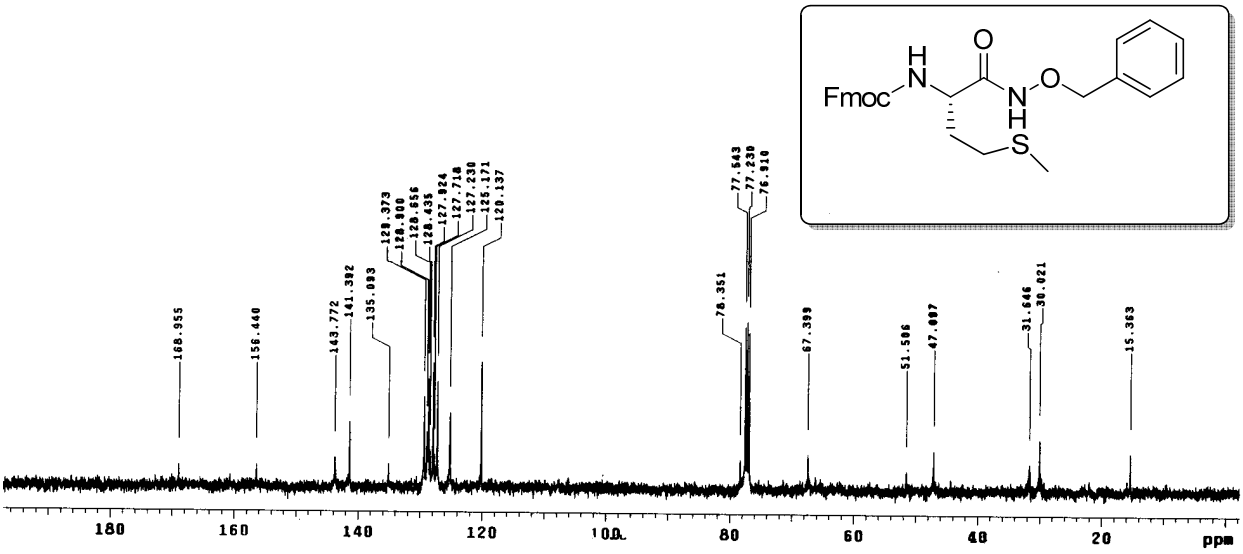


Figure S56: [1]H-NMR spectrum of (9H-fluoren-9-yl)methyl 1-(benzyloxyamino)-4-(methylthio)-1-oxobutan-2-ylcarbamate (entry 8, Table 4).

5) [1]H-NMR and [13]C-NMR Spectra of esters:

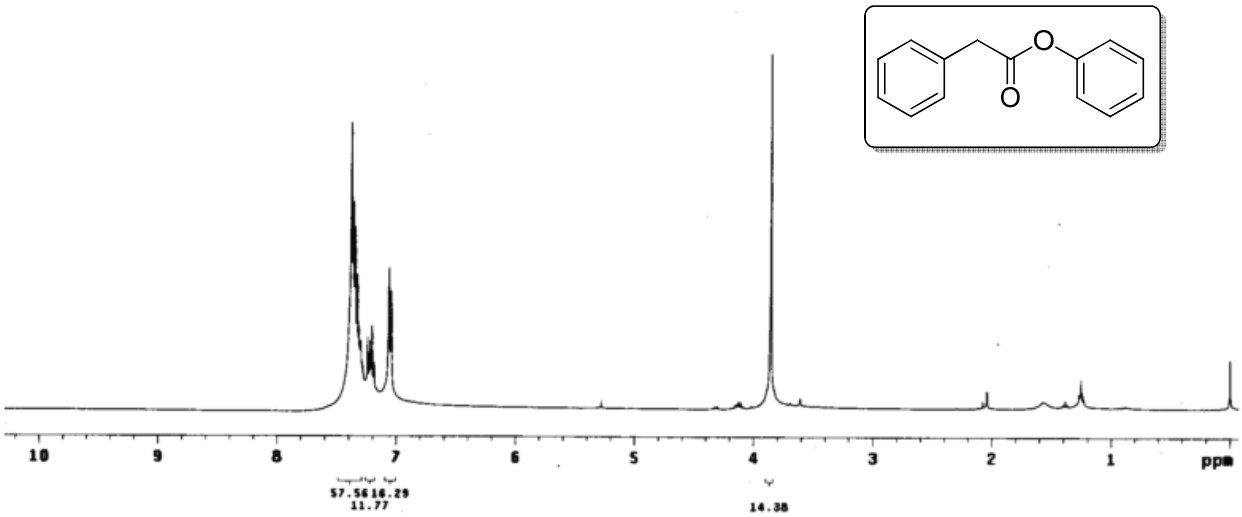


Figure S57: [1]H-NMR spectrum of phenyl 2-phenylacetate (entry 1, Table 6).

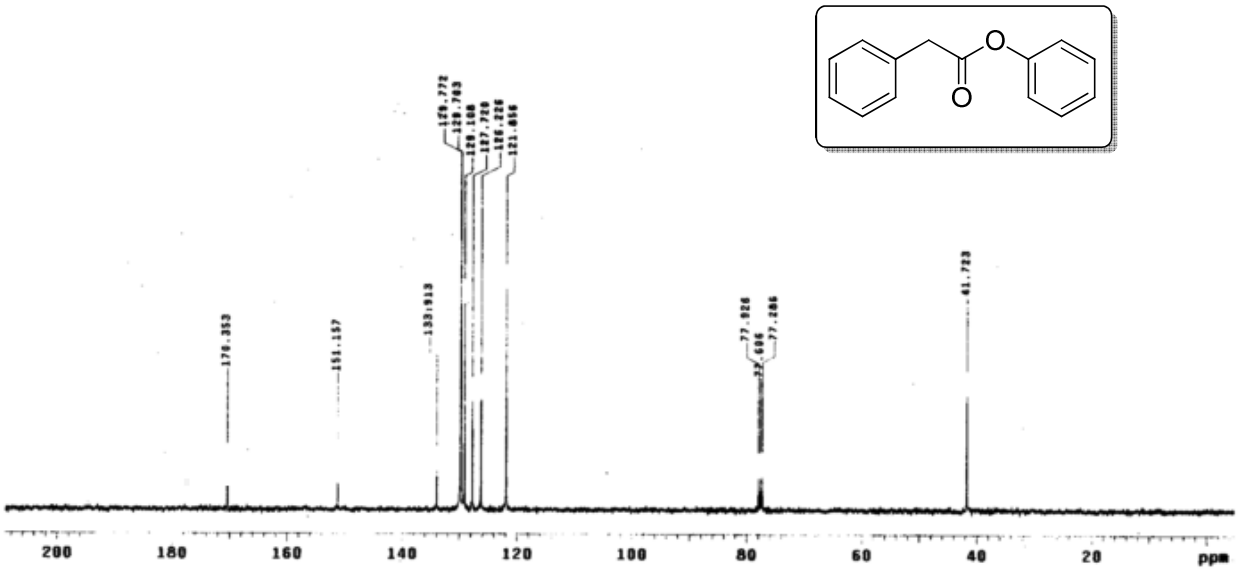


Figure S58: ^{13}C-NMR spectrum of phenyl 2-phenylacetate (entry 1, Table 6).

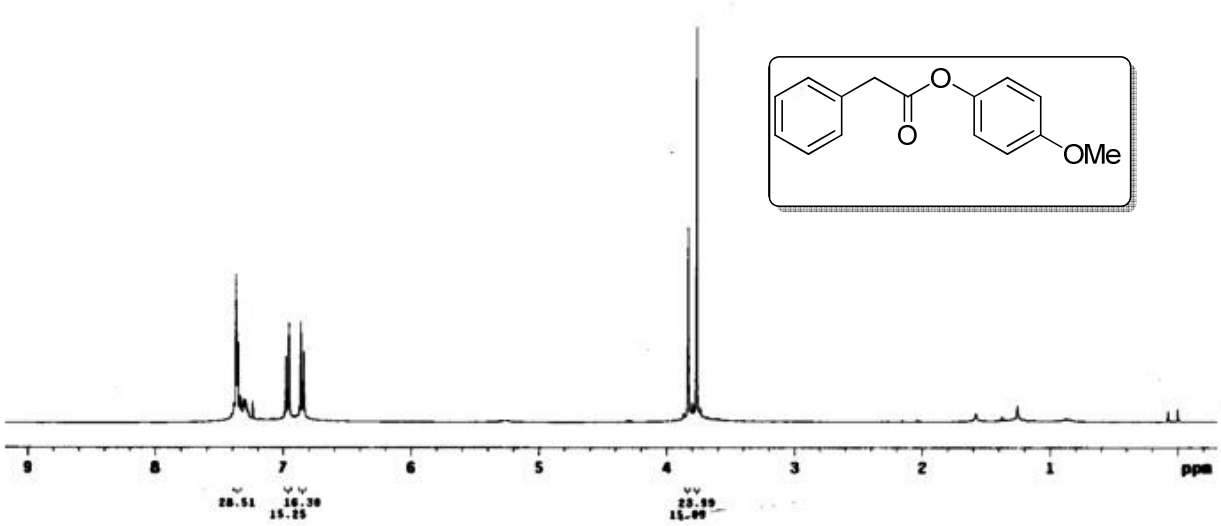


Figure S59: ^{1}H-NMR spectrum of 4-methoxyphenyl 2-phenylacetate (entry 2, Table 6).

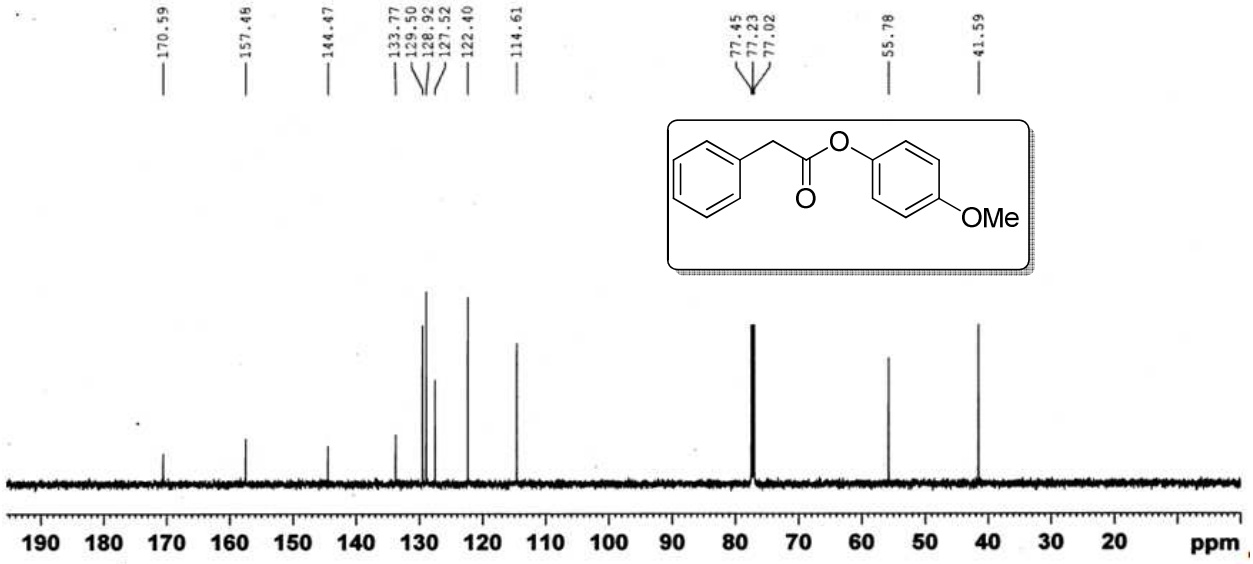


Figure S60: ^{13}C-NMR spectrum of 4-methoxyphenyl 2-phenylacetate (entry 2, Table 6).

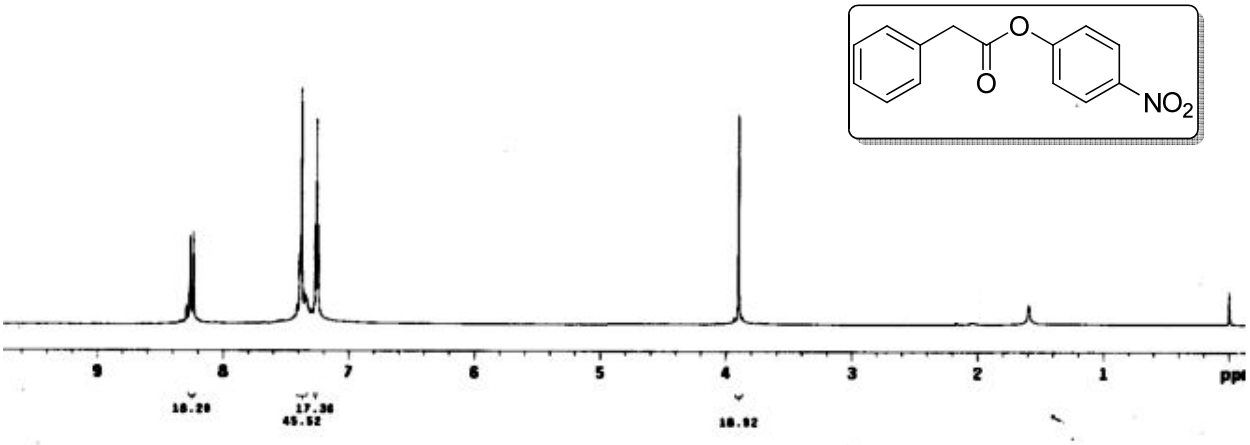


Figure S61: ^{1}H-NMR spectrum of 4-nitrophenyl 2-phenylacetate (entry 3, Table 6).

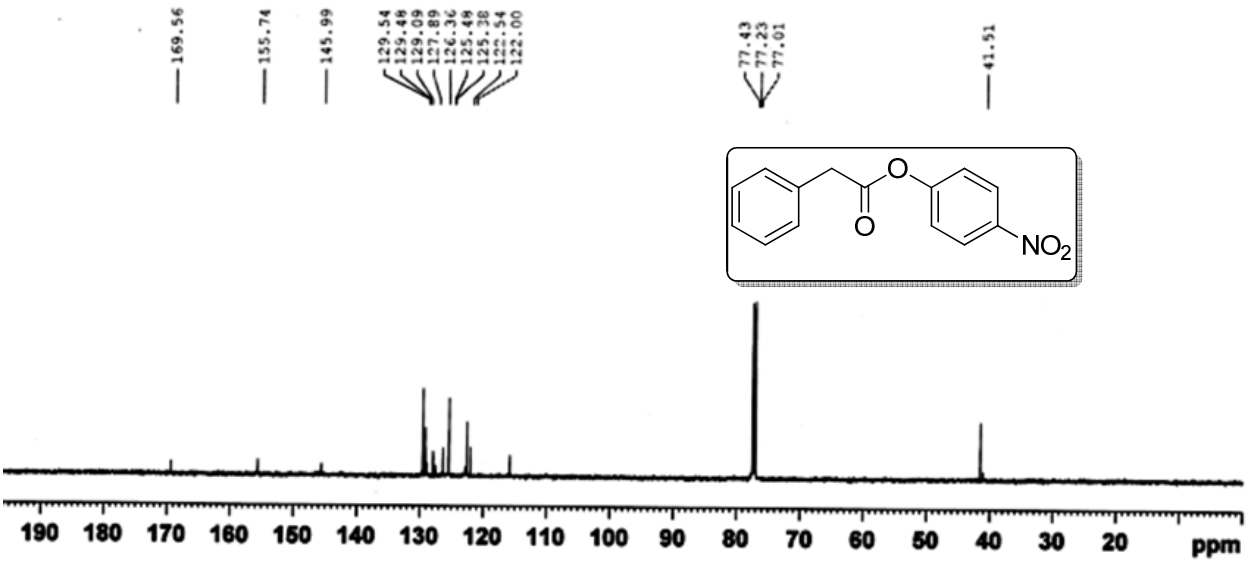


Figure S62: ^{13}C-NMR spectrum of 4-nitrophenyl 2-phenylacetate (entry 3, Table 6).

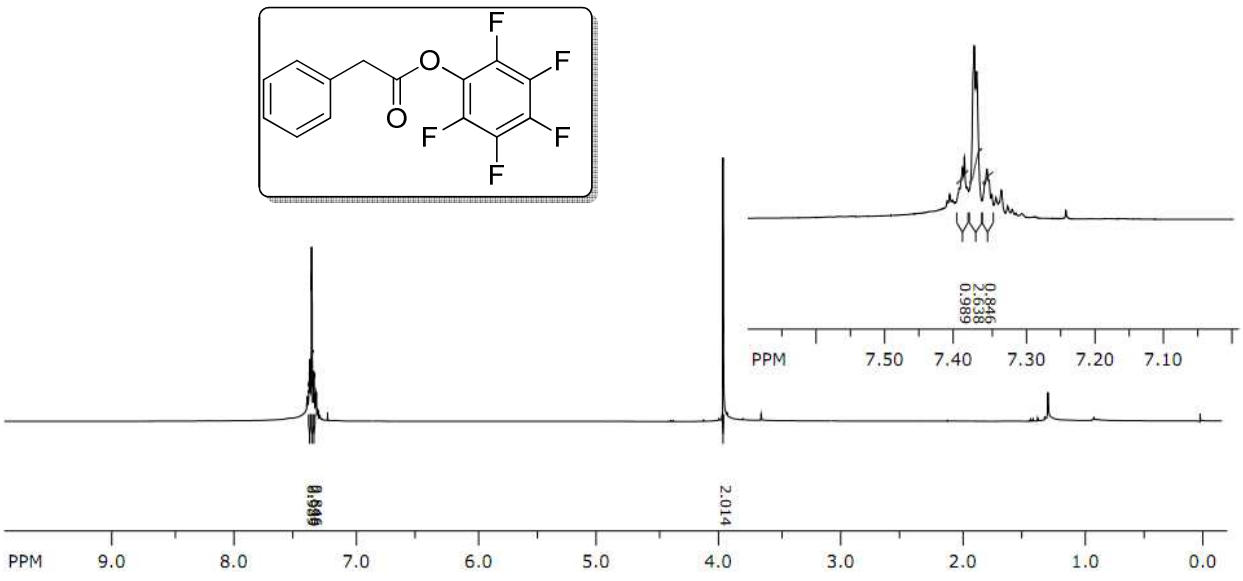


Figure S63: ^{1}H-NMR spectrum of pentafluorophenyl 2-phenylacetate (entry 4, Table 6).

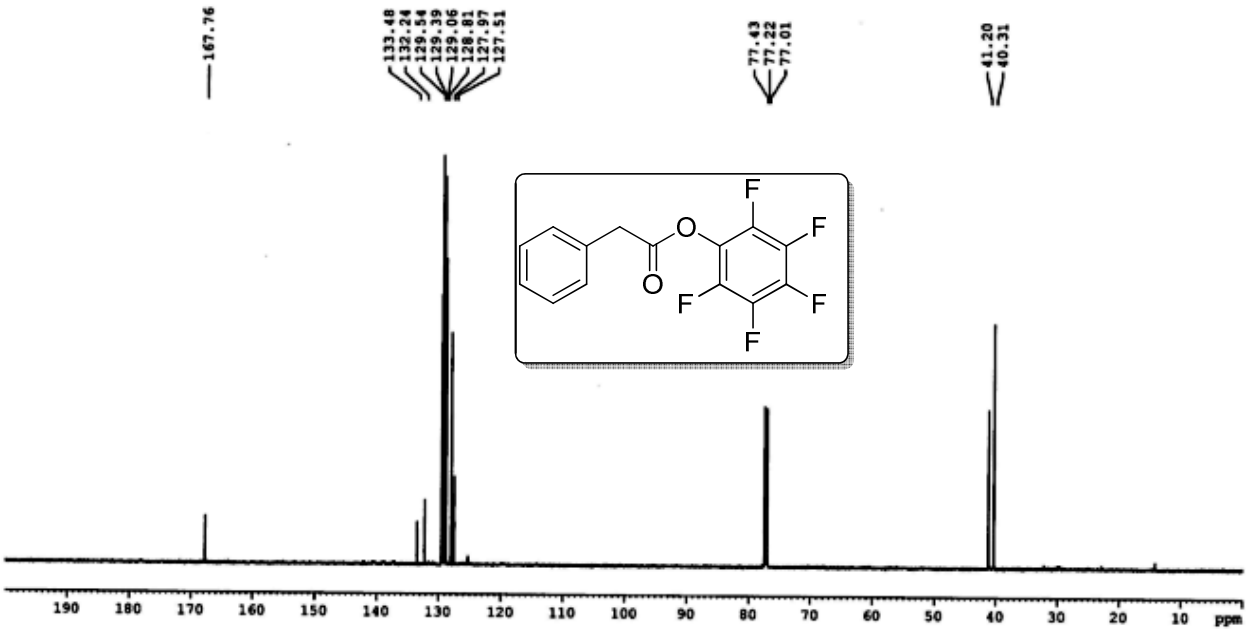


Figure S64: ^{13}C-NMR spectrum of pentafluorophenyl 2-phenylacetate (entry 4, Table 6).

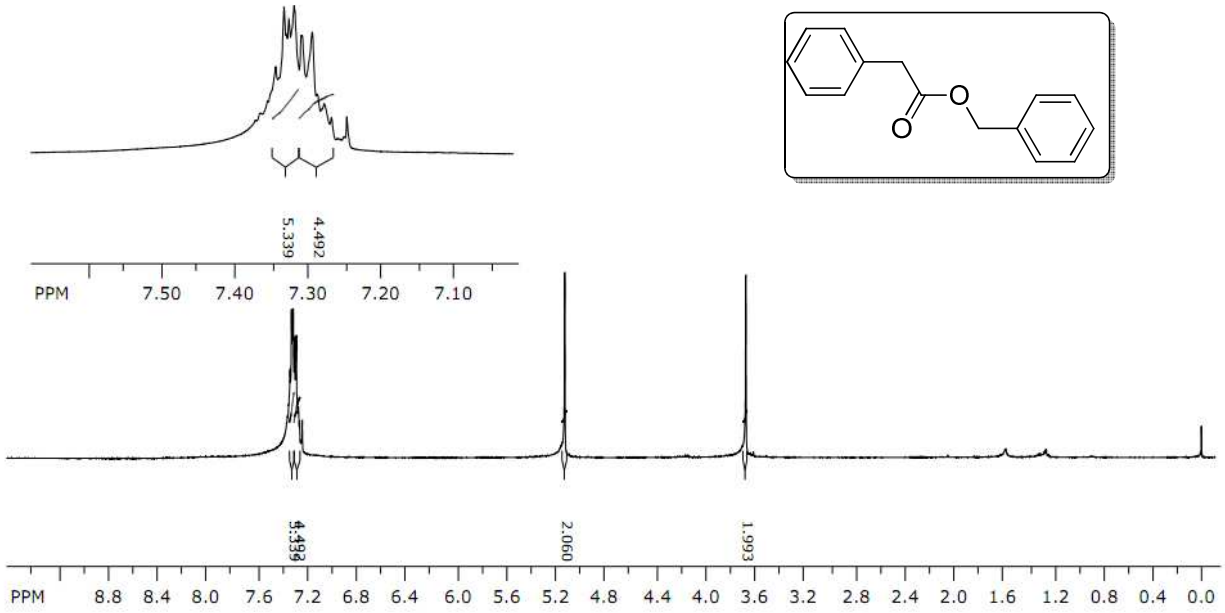


Figure S65: ^{1}H-NMR spectrum of benzyl 2-phenylacetate (entry 5, Table 6).

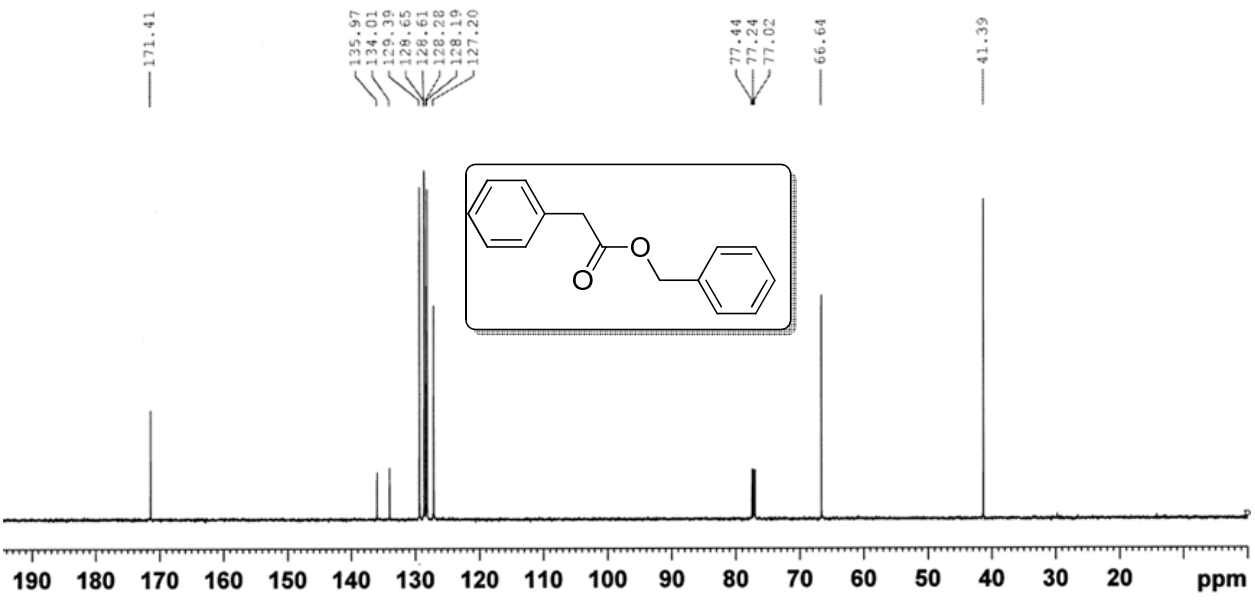


Figure S66: ^{13}C-NMR spectrum of benzyl 2-phenylacetate (entry 5, Table 6).

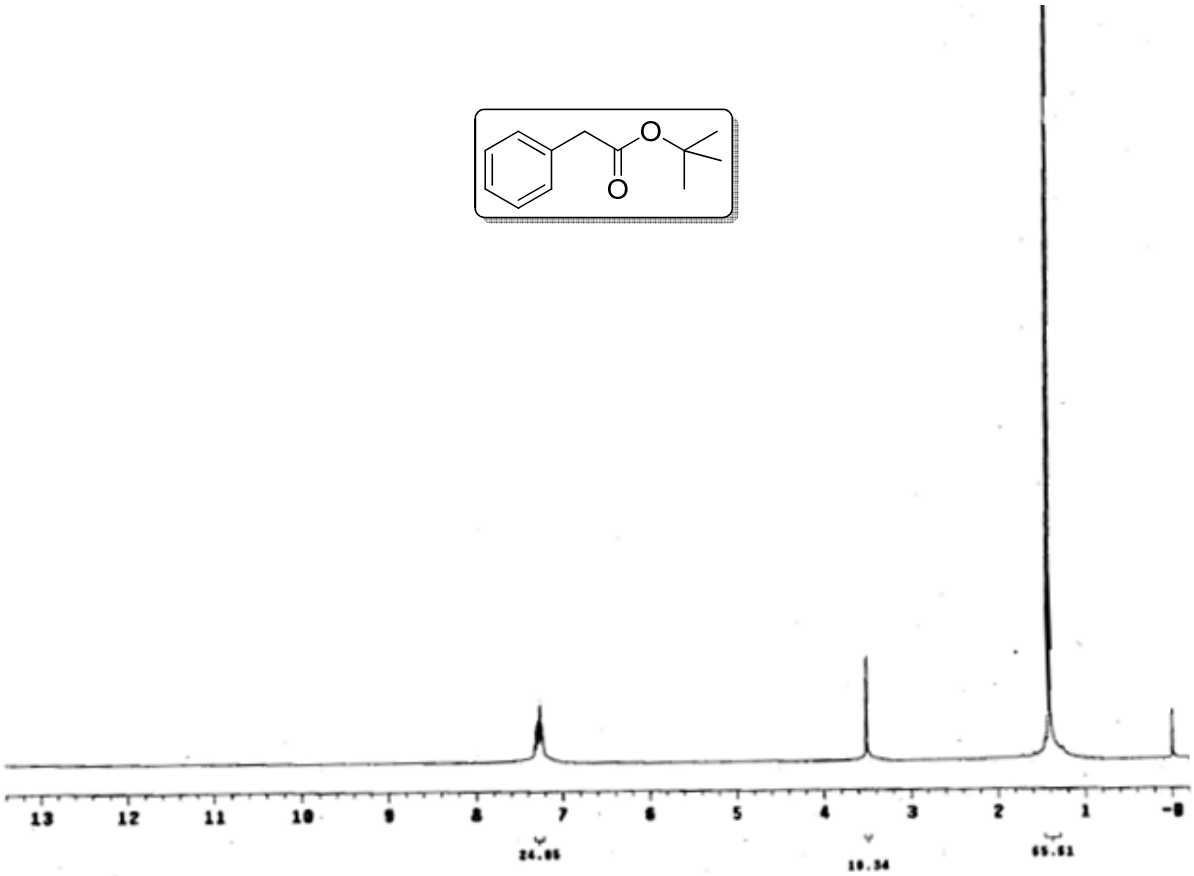


Figure S67: ^{1}H-NMR spectrum of tert-butyl 2-phenylacetate (entry 6, Table 6).

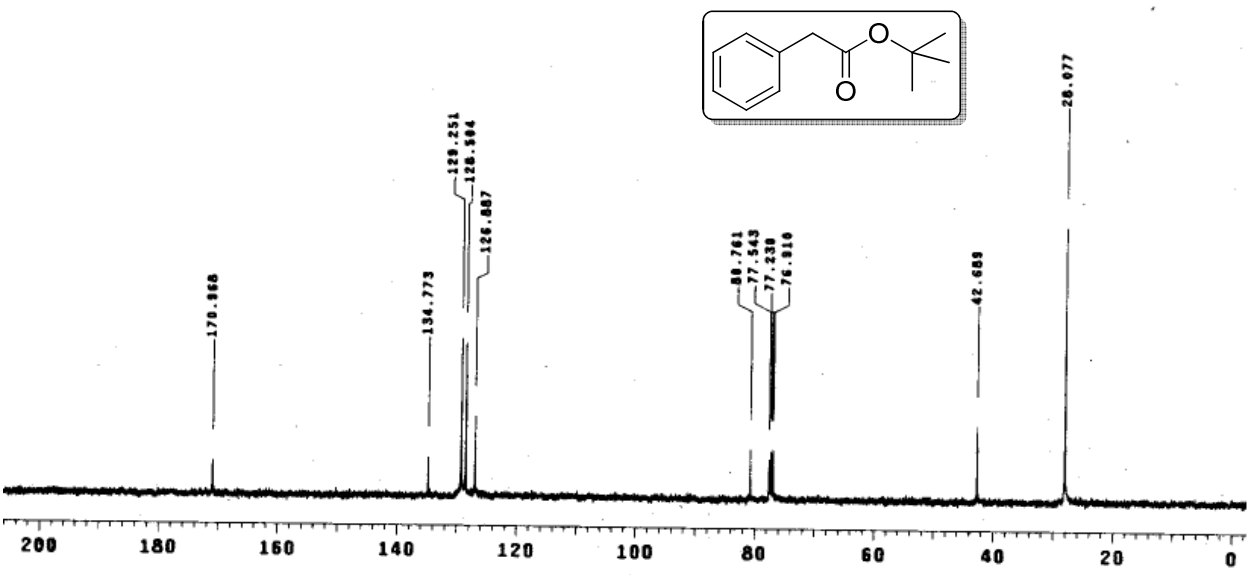


Figure S68: ^{13}C-NMR spectrum of tert-butyl 2-phenylacetate (entry 6, Table 6).

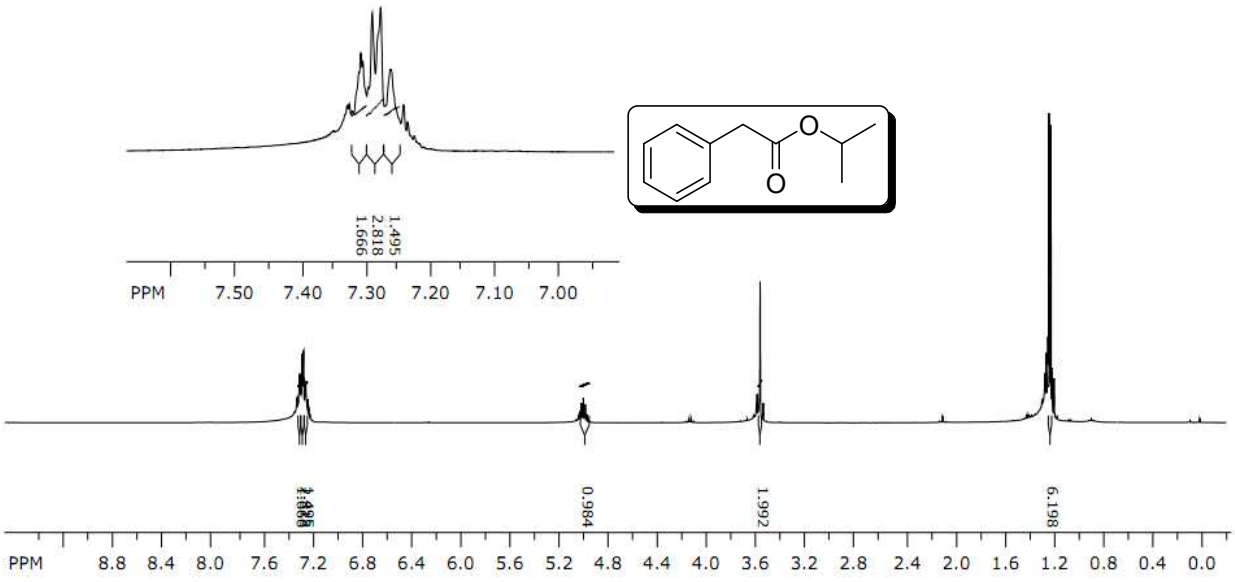


Figure S69: ^{1}H-NMR spectrum of isopropyl 2-phenylacetate (entry 7, Table 6).

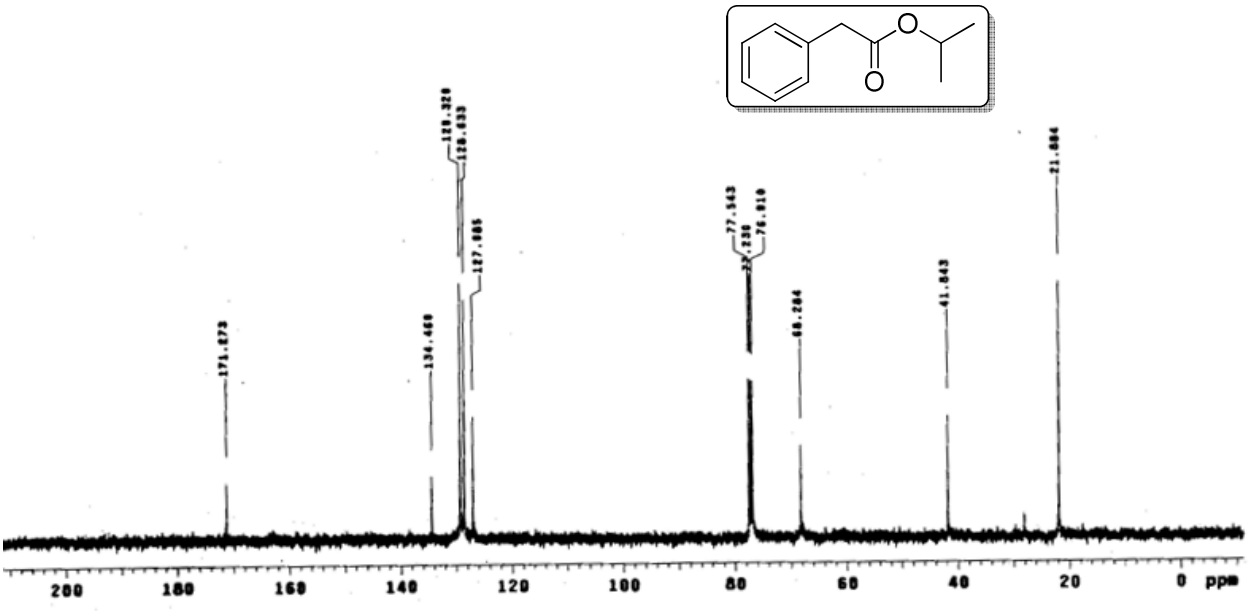


Figure S70: ^{13}C-NMR spectrum of isopropyl 2-phenylacetate (entry 7, Table 6).

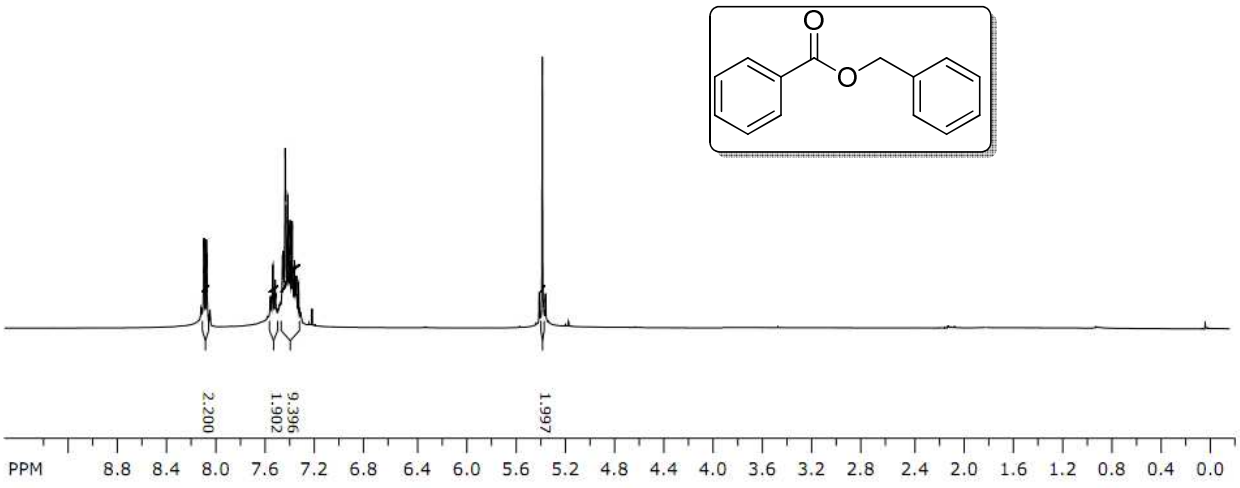


Figure S71: ^{1}H-NMR spectrum of benzyl benzoate (entry 8, Table 6).

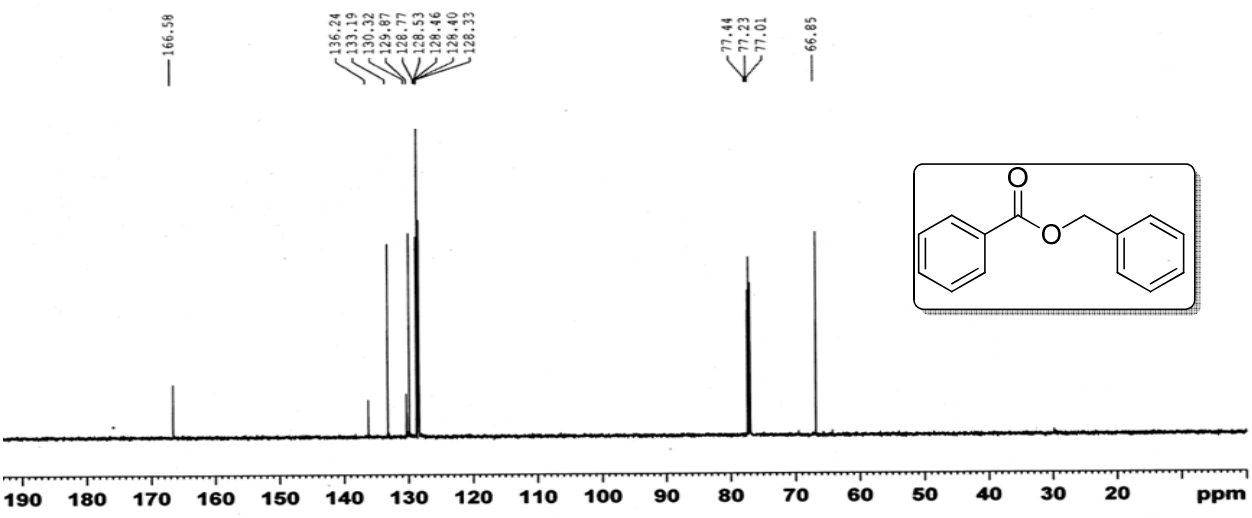


Figure S72: ^{13}C-NMR spectrum of benzyl benzoate (entry 8, Table 6).

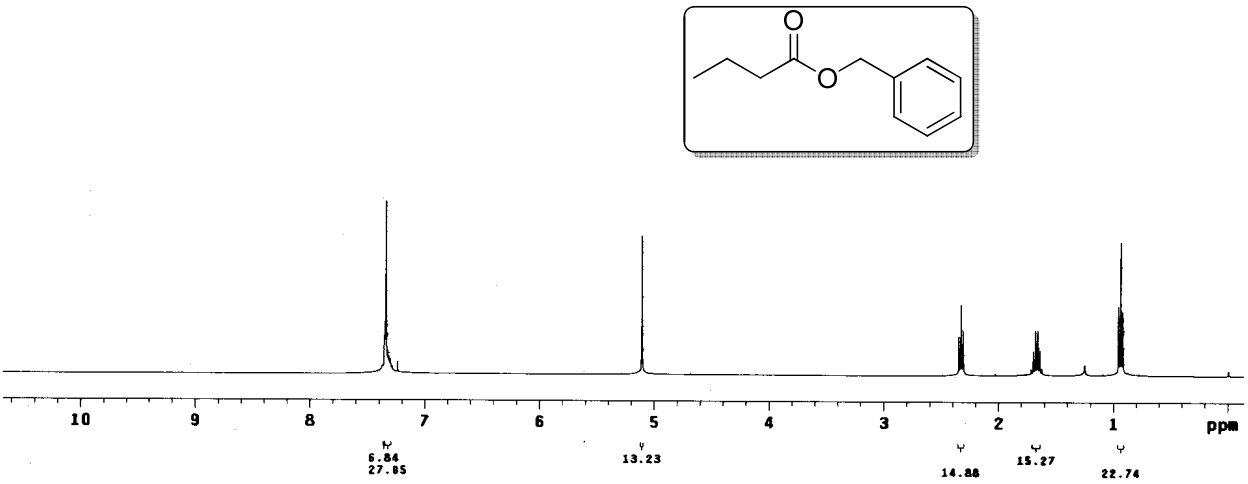


Figure S73: ^{1}H-NMR spectrum of benzyl butyrate (entry 9, Table 6).

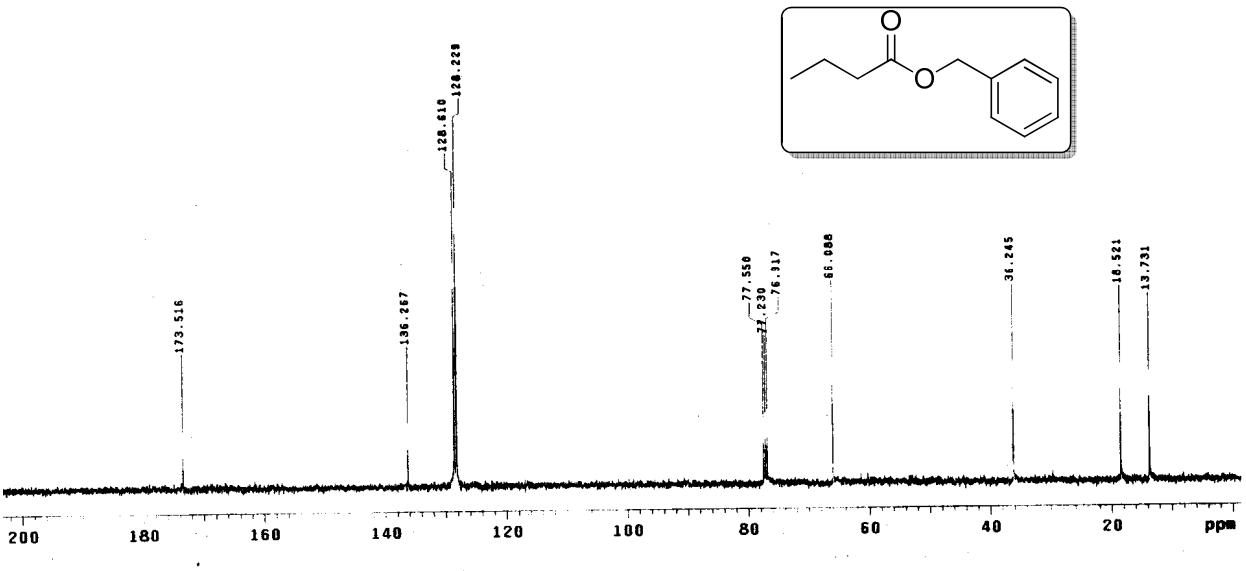


Figure S74: ^{13}C-NMR spectrum of benzyl butyrate (entry 9, Table 6).

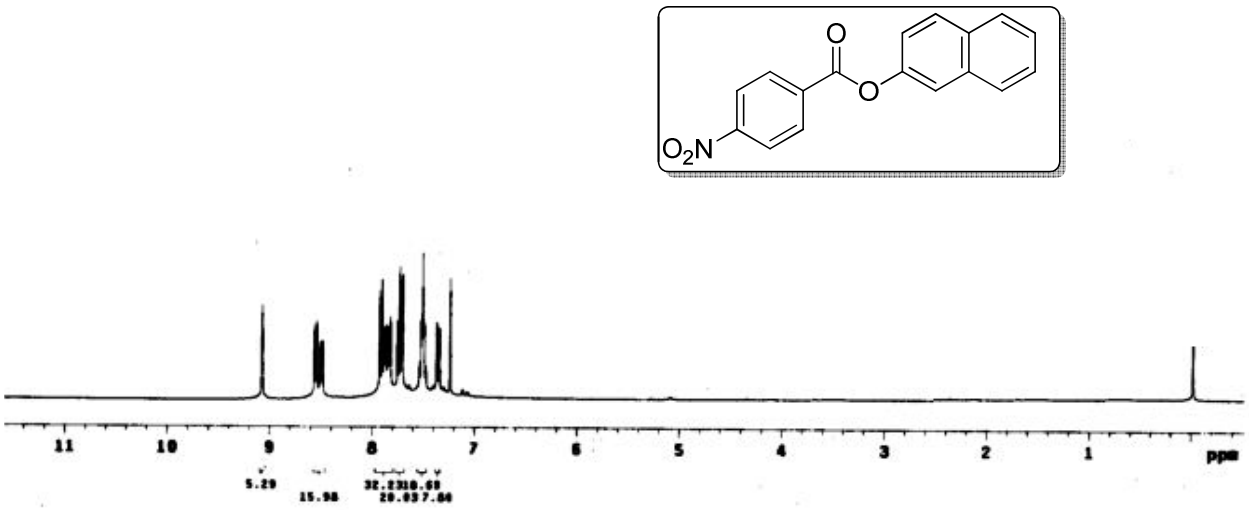


Figure S75: 1H-NMR spectrum of naphthalen-2-yl 4-nitrobenzoate (entry 10, Table 6).

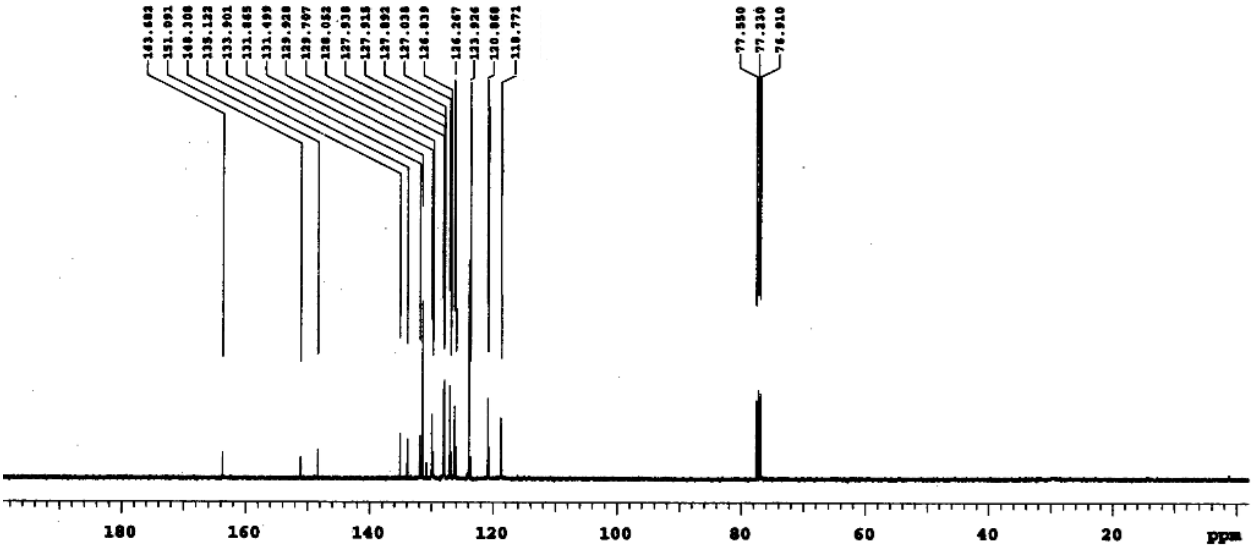


Figure S76: ^{13}C-NMR spectrum of naphthalen-2-yl 4-nitrobenzoate (entry 10, Table 6).

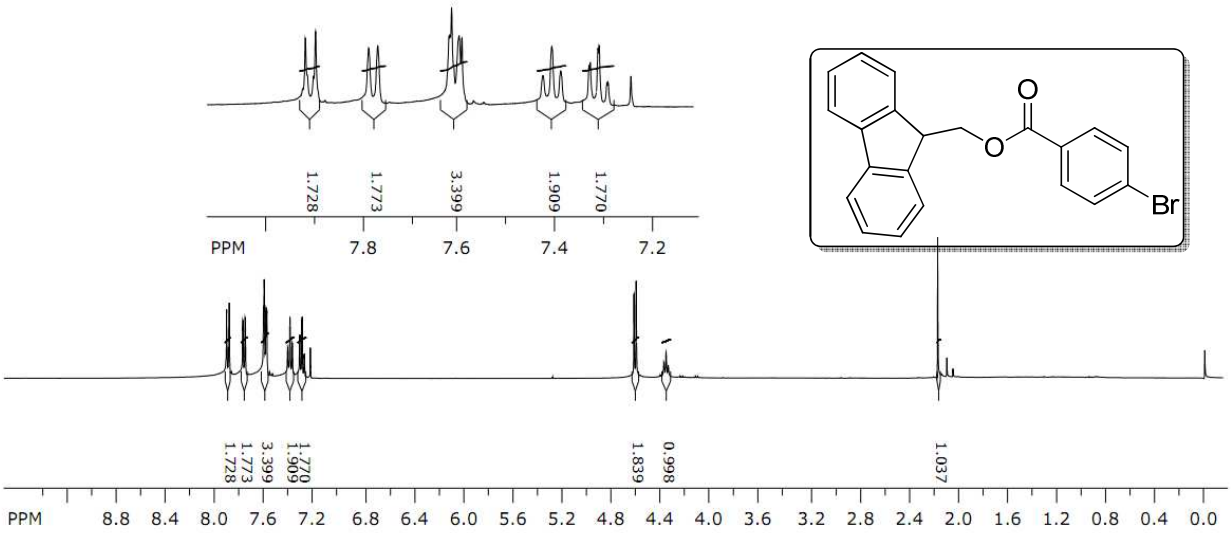


Figure S77: ^{1}H-NMR spectrum of (9H-fluoren-9-yl)methyl 4-bromobenzoate (entry 11, Table 6).

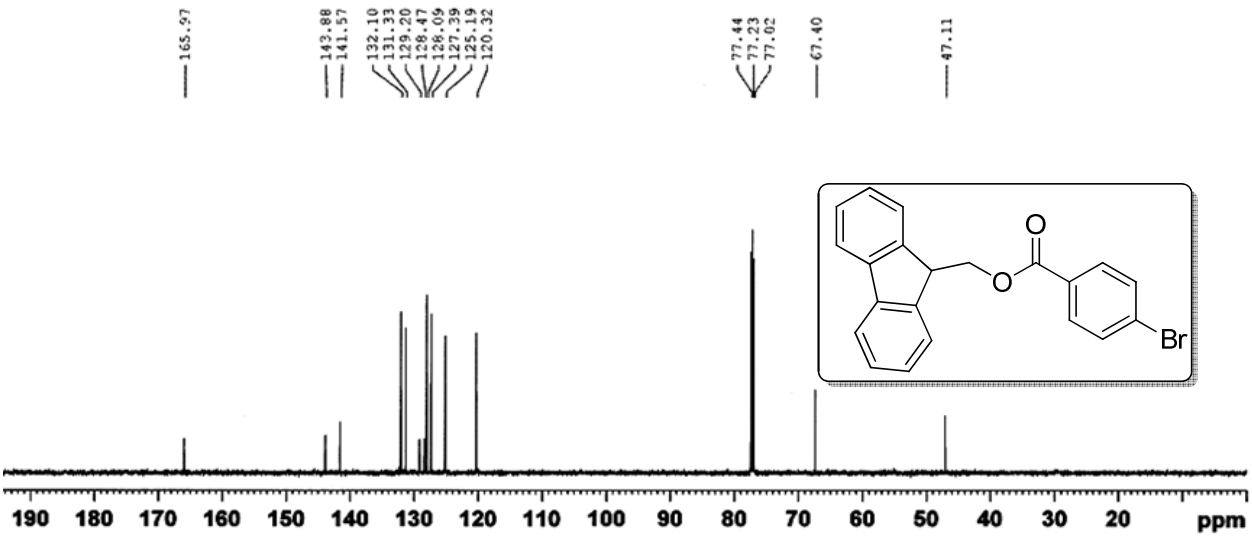


Figure S78: ^{13}C-NMR spectrum of (9H-fluoren-9-yl)methyl 4-bromobenzoate (entry 11, Table 6).

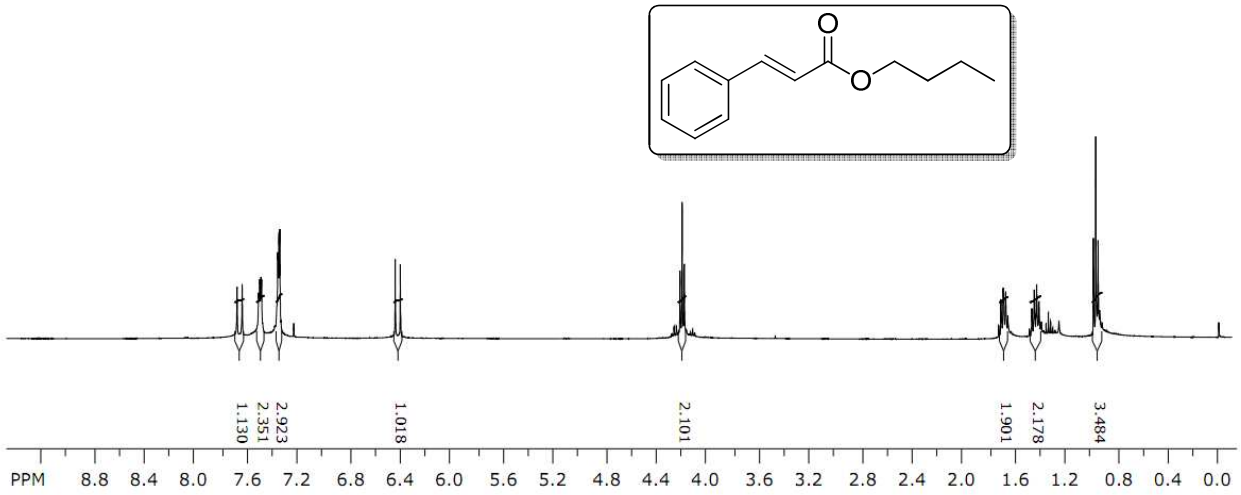


Figure S79: ^{1}H-NMR spectrum of butyl cinnamate (entry 12, Table 6).

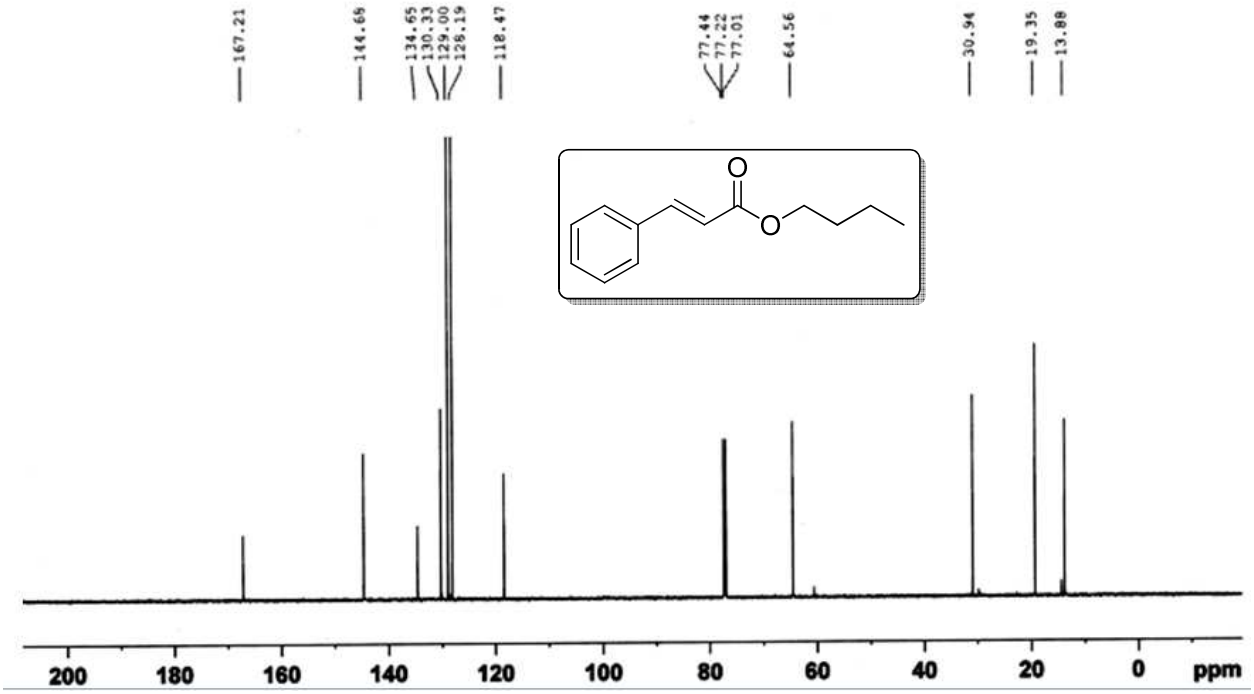


Figure S80: ^{13}C-NMR spectrum of butyl cinnamate (entry 12, Table 6).

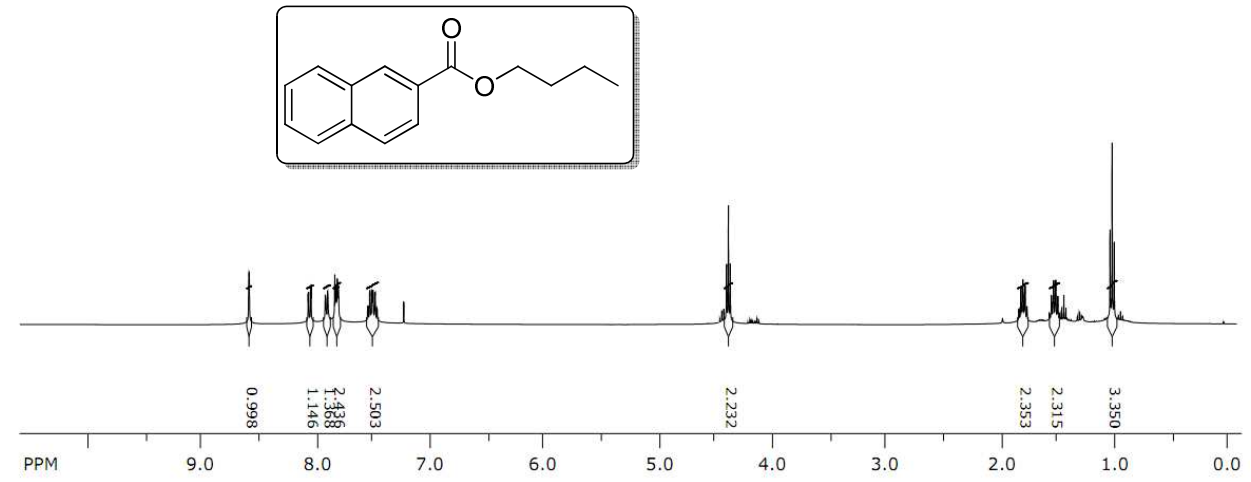


Figure S81: ^{1}H-NMR spectrum of butyl 2-naphthoate (entry 13, Table 6).

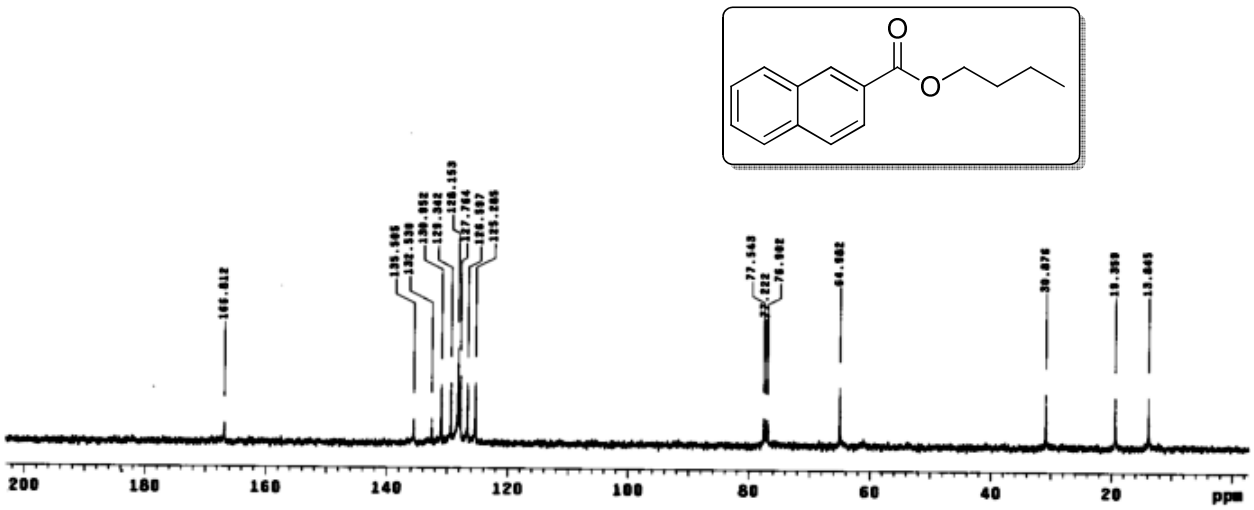


Figure S82: ^{13}C-NMR spectrum of butyl 2-naphthoate (entry 13, Table 6).

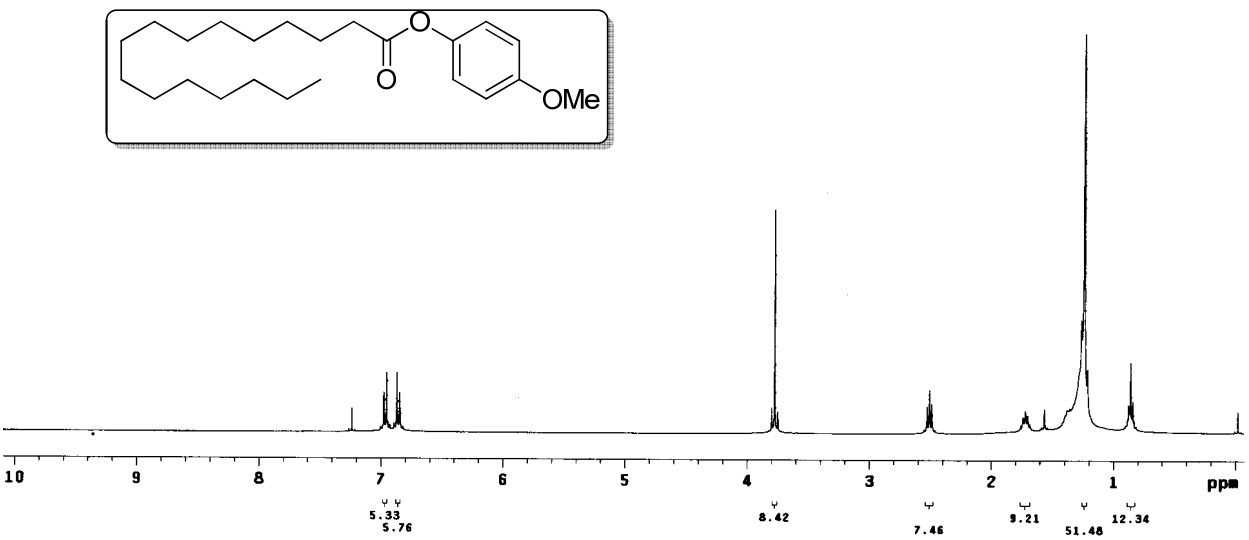


Figure S83: ^{1}H-NMR spectrum of 4-methoxyphenyl palmitate (entry 1, Table 7).

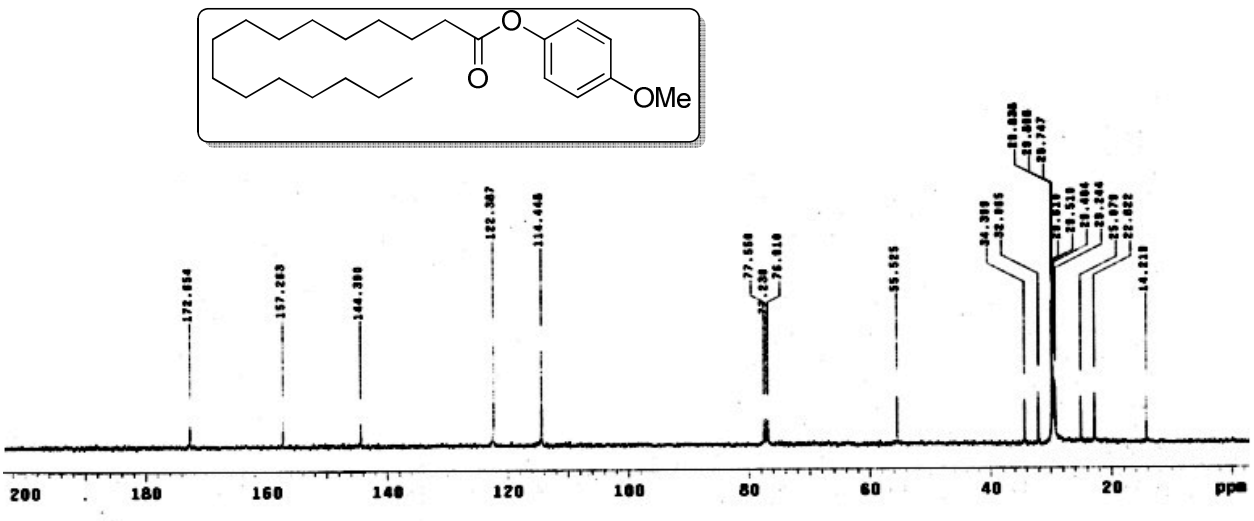


Figure S84: ^{13}C-NMR spectrum of 4-methoxyphenyl palmitate (entry 1, Table 7).

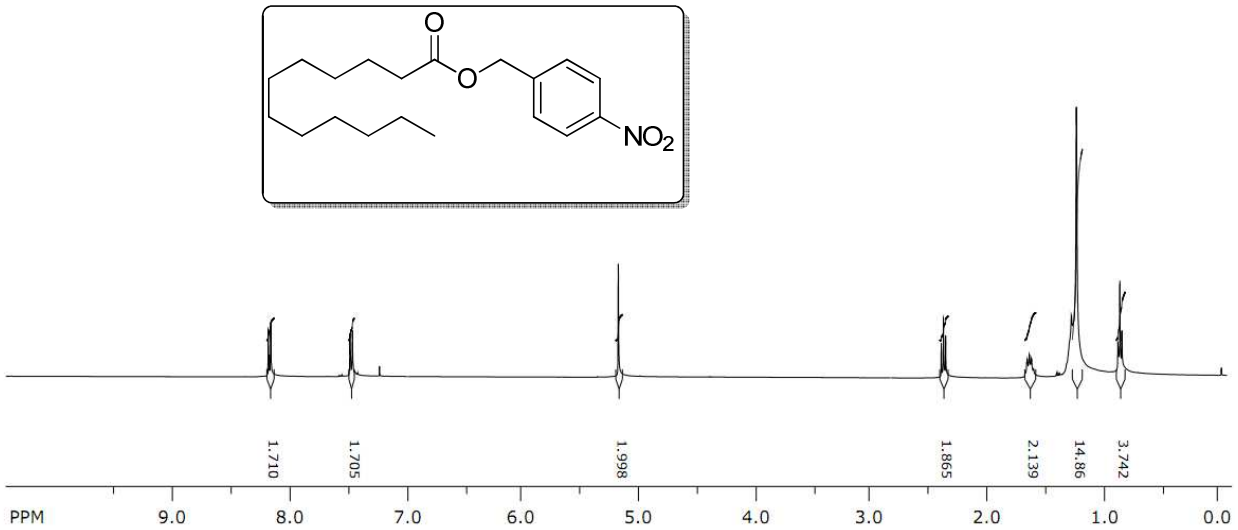


Figure S85: ^{1}H-NMR spectrum of 4-nitrobenzyl tetradecanoate (entry 2, Table 7).

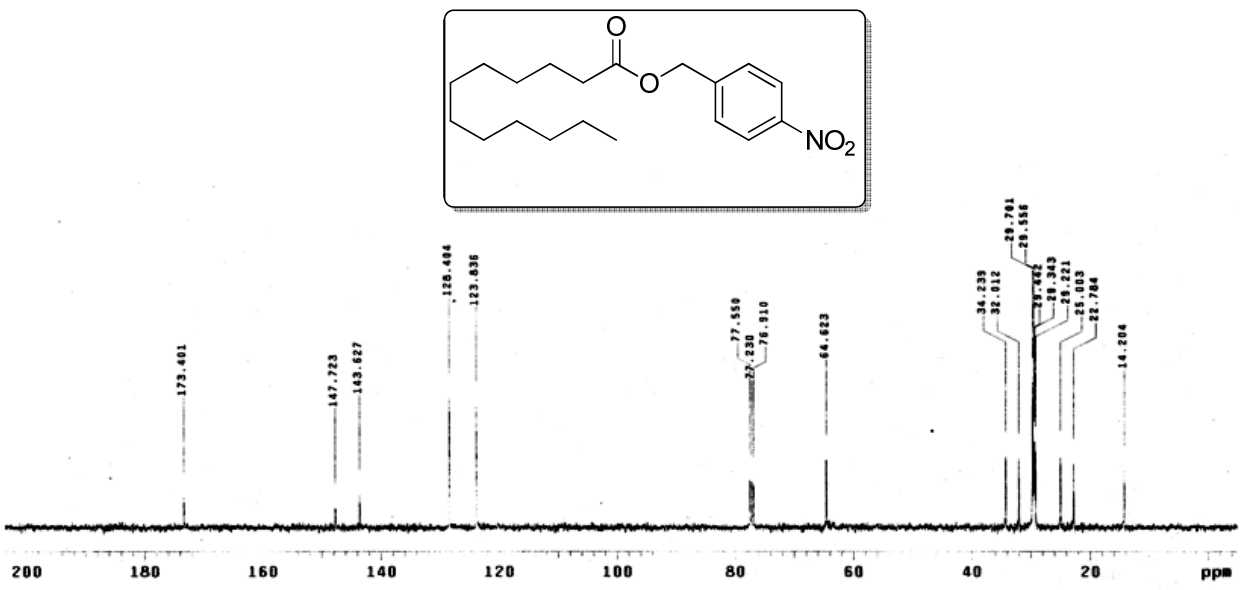


Figure S86: ^{13}C-NMR spectrum of 4-nitrobenzyl tetradecanoate (entry 2, Table 7).

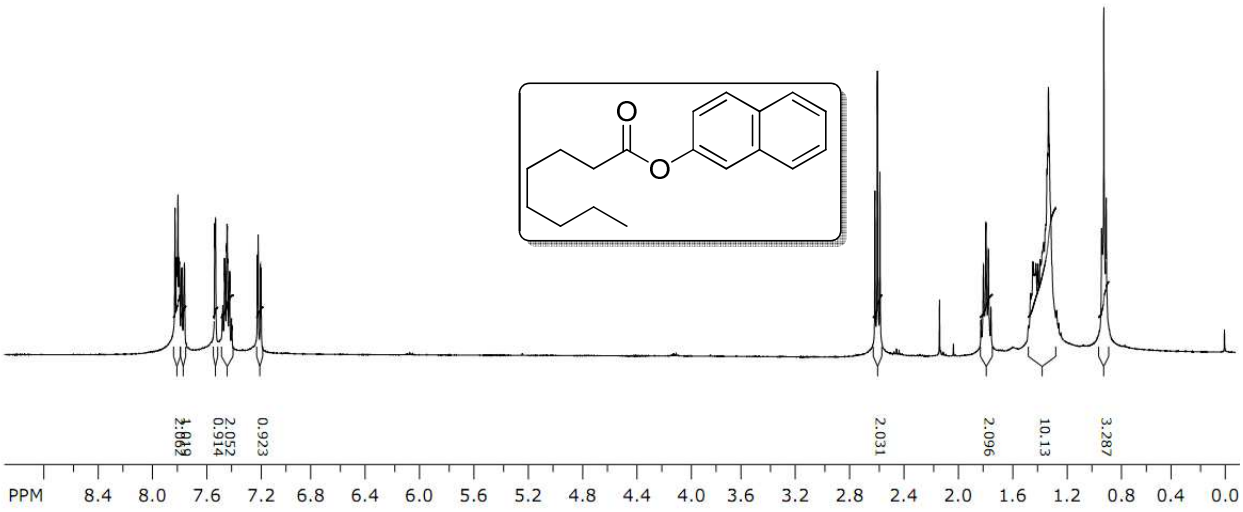


Figure S87: ^{1}H-NMR spectrum of naphthalen-2-yl octanoate (entry 3, Table 7).

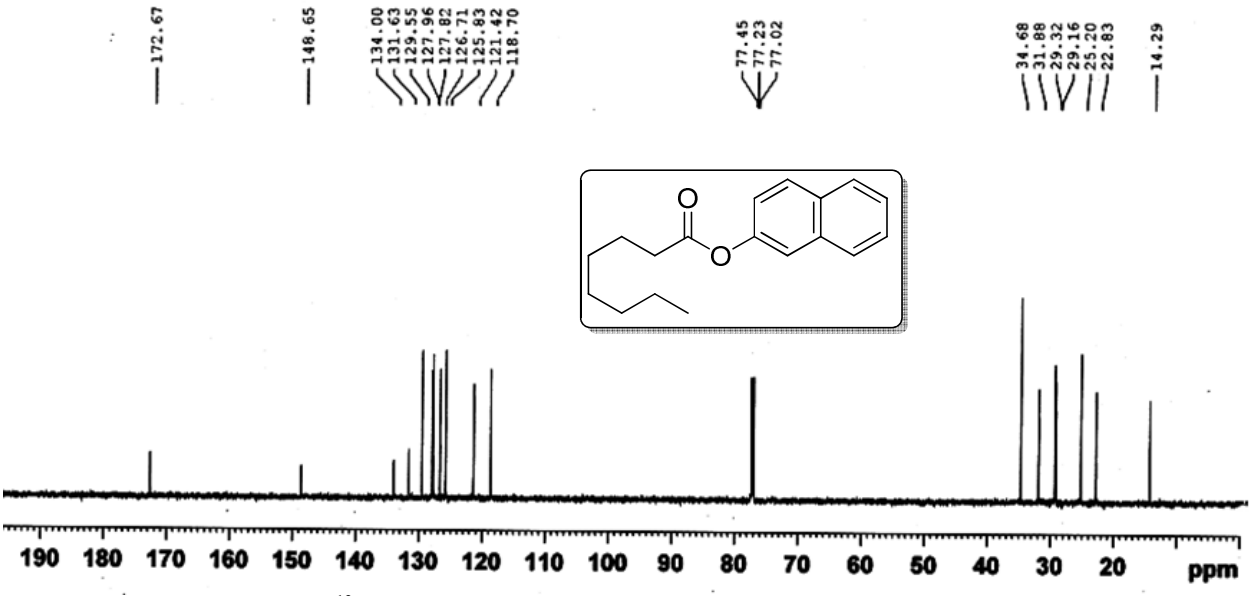


Figure S88: ^{13}C-NMR spectrum of naphthalen-2-yl octanoate (entry 3, Table 7).

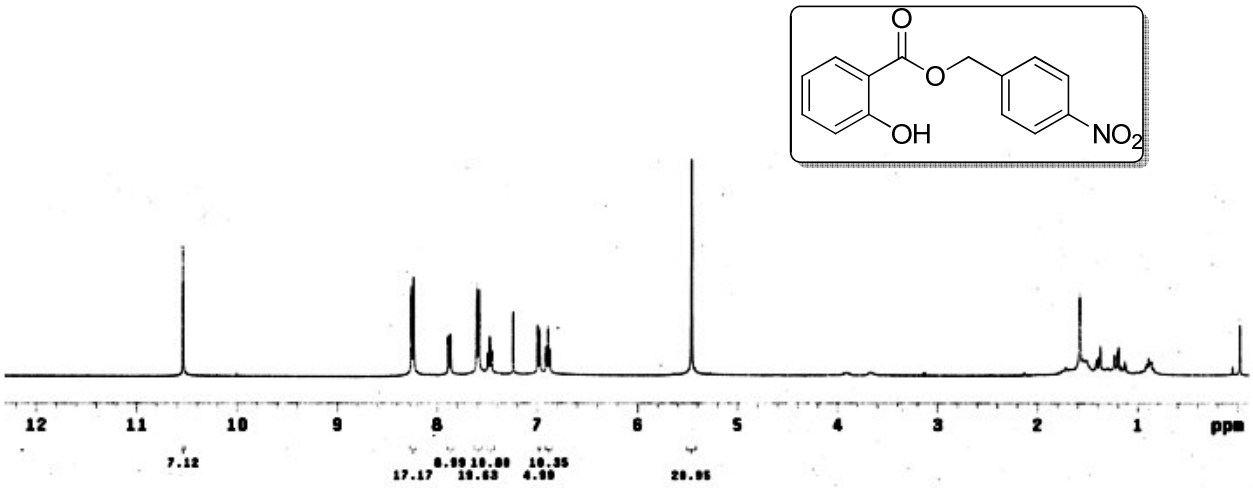


Figure S89: ^{1}H-NMR spectrum of 4-nitrobenzyl 2-hydroxybenzoate (entry 4, Table 7).

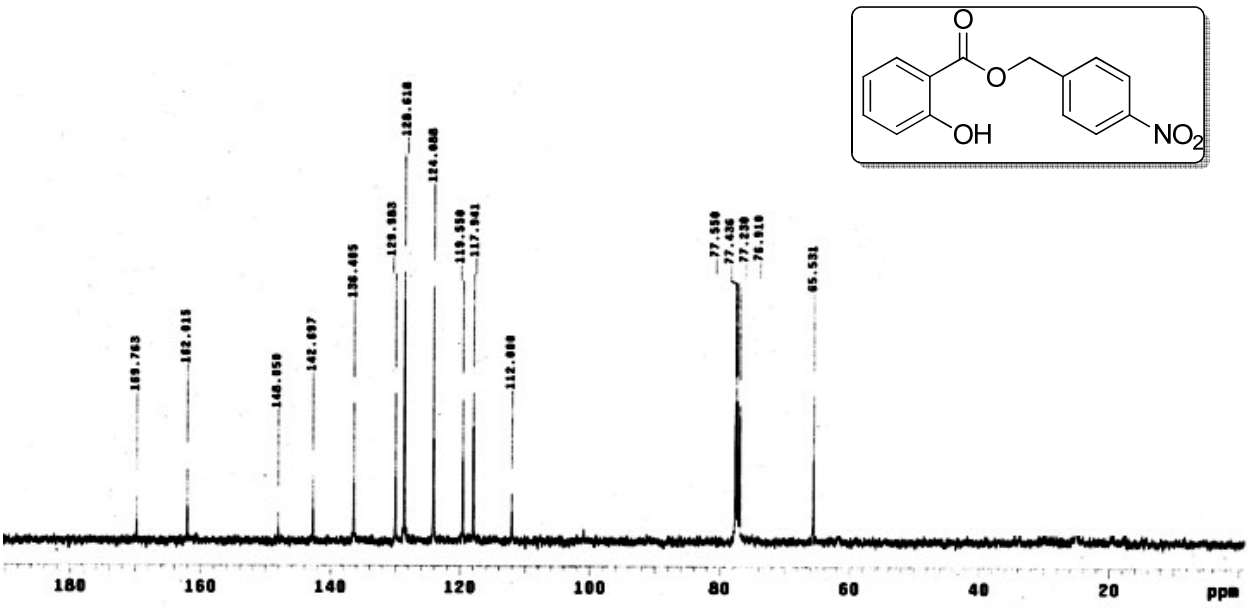


Figure S90: ^{13}C-NMR spectrum of 4-nitrobenzyl 2-hydroxybenzoate (entry 4, Table 7).

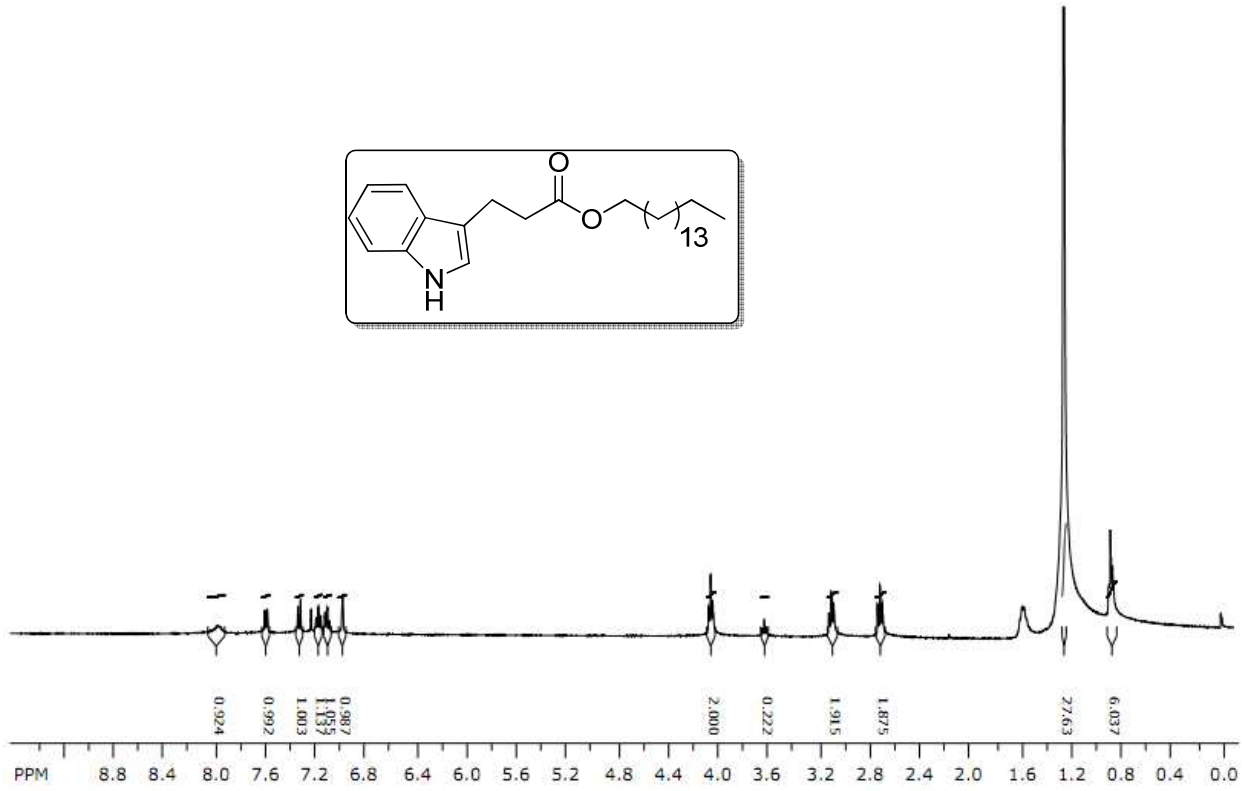


Figure S91: ^{1}H-NMR spectrum of hexadecyl 3-(1H-indol-3-yl)propanoate (entry 5, Table 7).

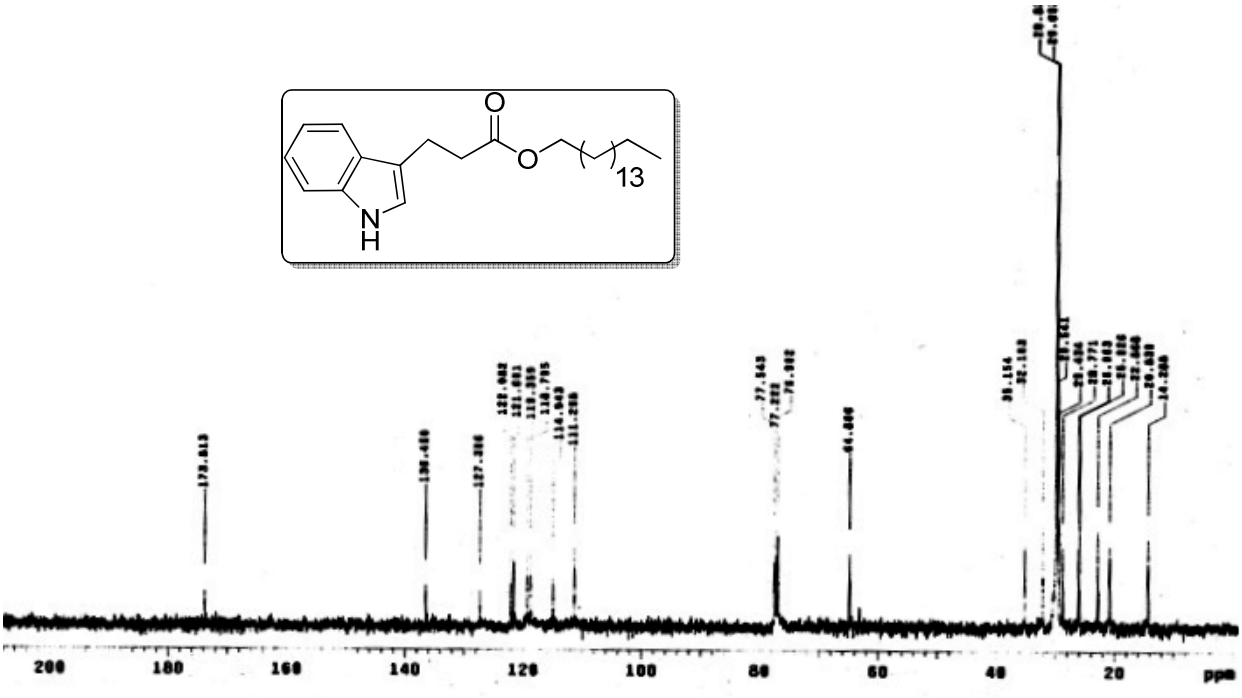


Figure S92: ^{13}C-NMR spectrum of hexadecyl 3-(1H-indol-3-yl)propanoate (entry 5, Table 7).

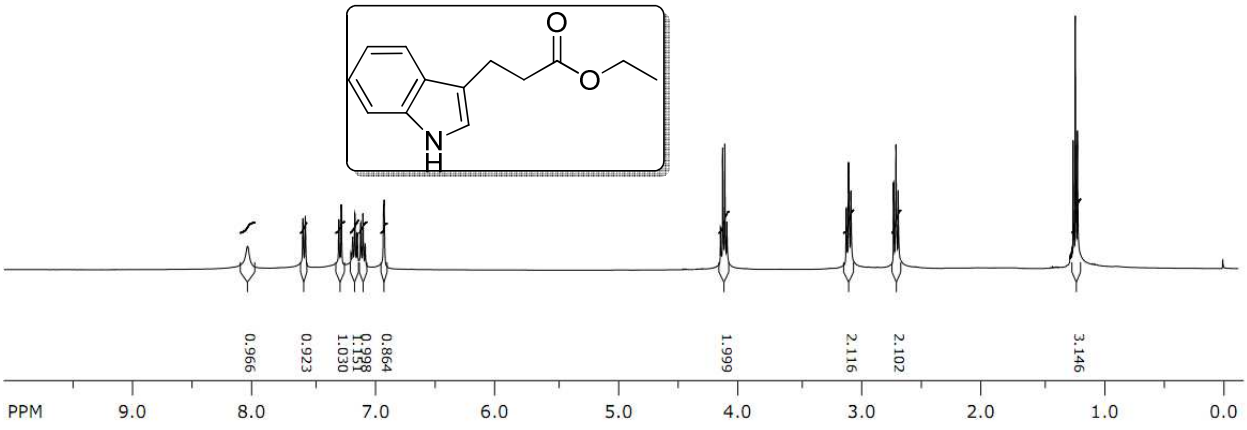


Figure S93: ^{1}H-NMR spectrum of ethyl 3-(indolin-3-yl)propanoate (entry 6, Table 7).

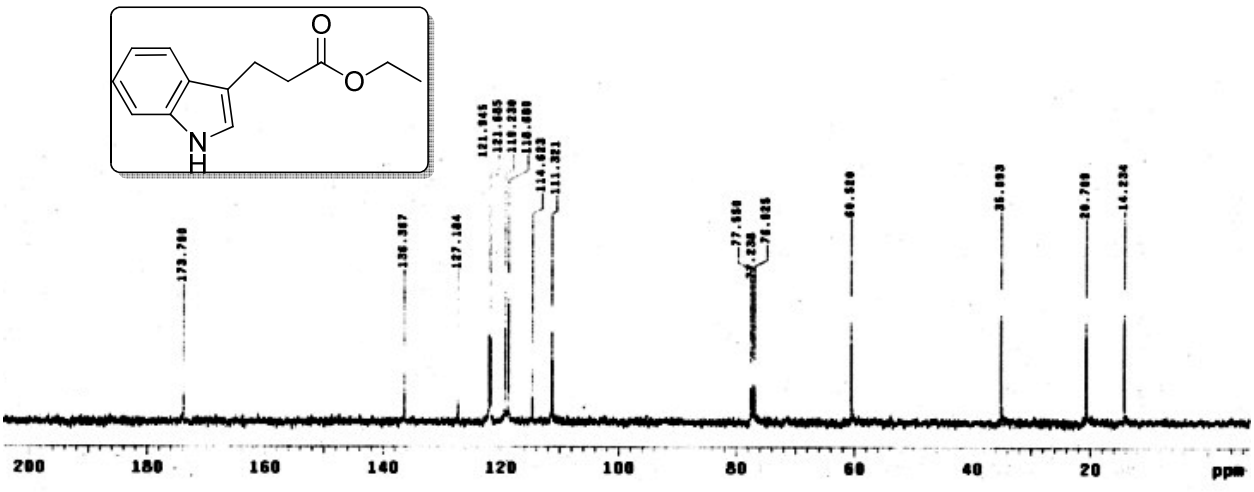


Figure S94: ^{13}C-NMR spectrum of ethyl 3-(indolin-3-yl)propanoate (entry 6, Table 7).

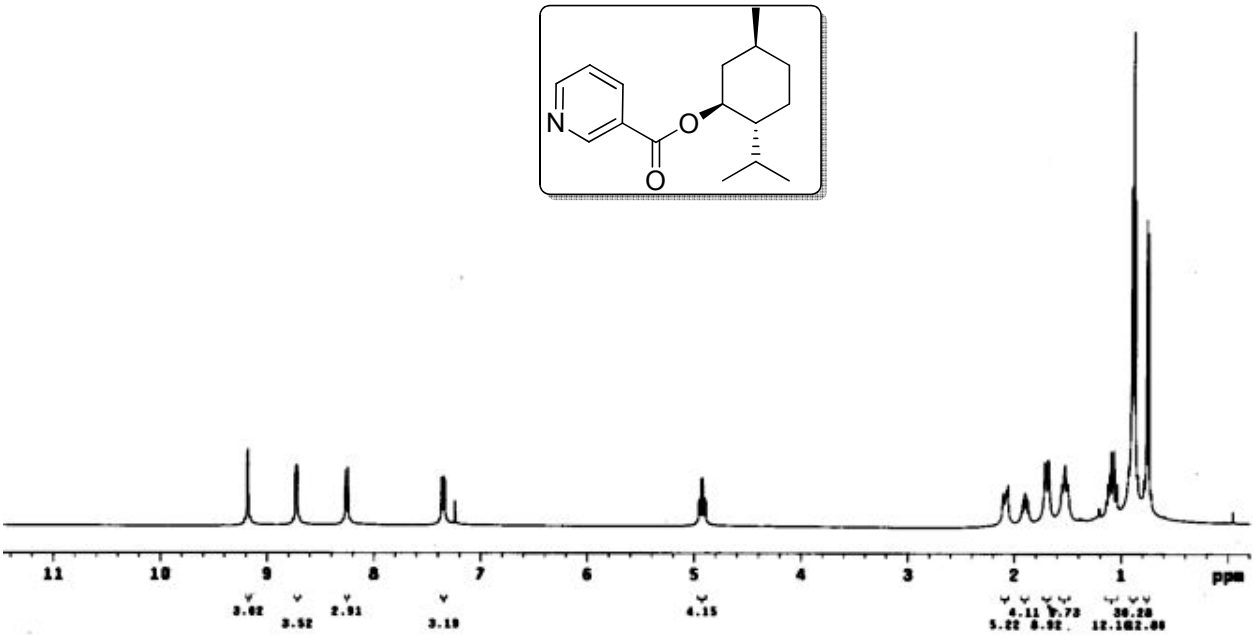


Figure S95: ^{1}H-NMR spectrum of (1S,2R,5S)-2-isopropyl-5-methylcyclohexyl nicotinate (entry 7, Table 7).

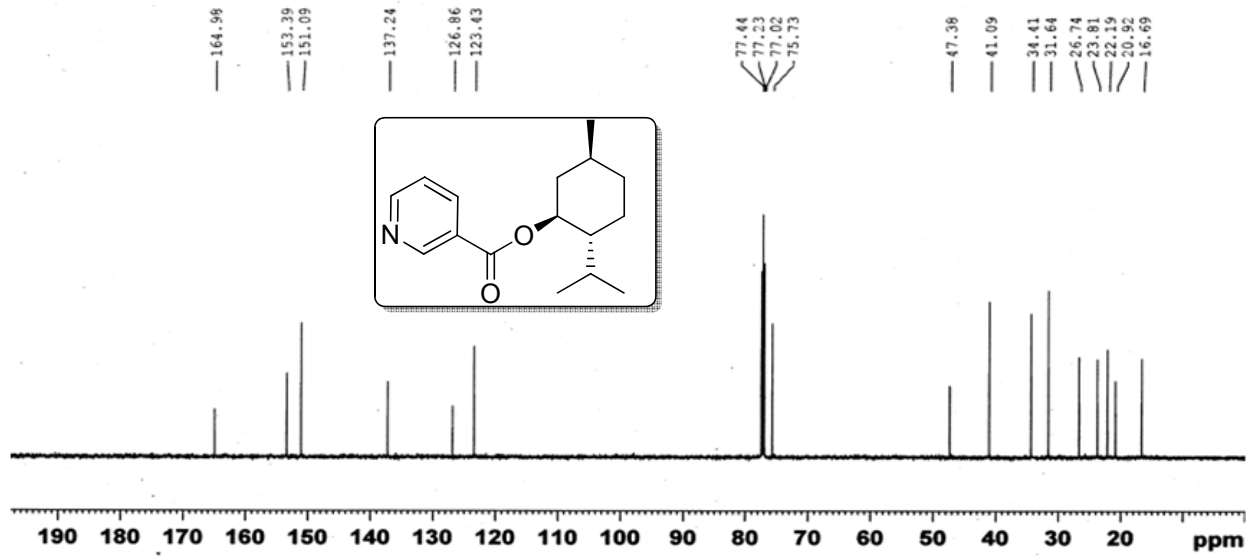


Figure S96: ^{13}C-NMR spectrum of (1S, 2R, 5S)-2-isopropyl-5-methylcyclohexyl nicotinate (entry 7, Table 7).

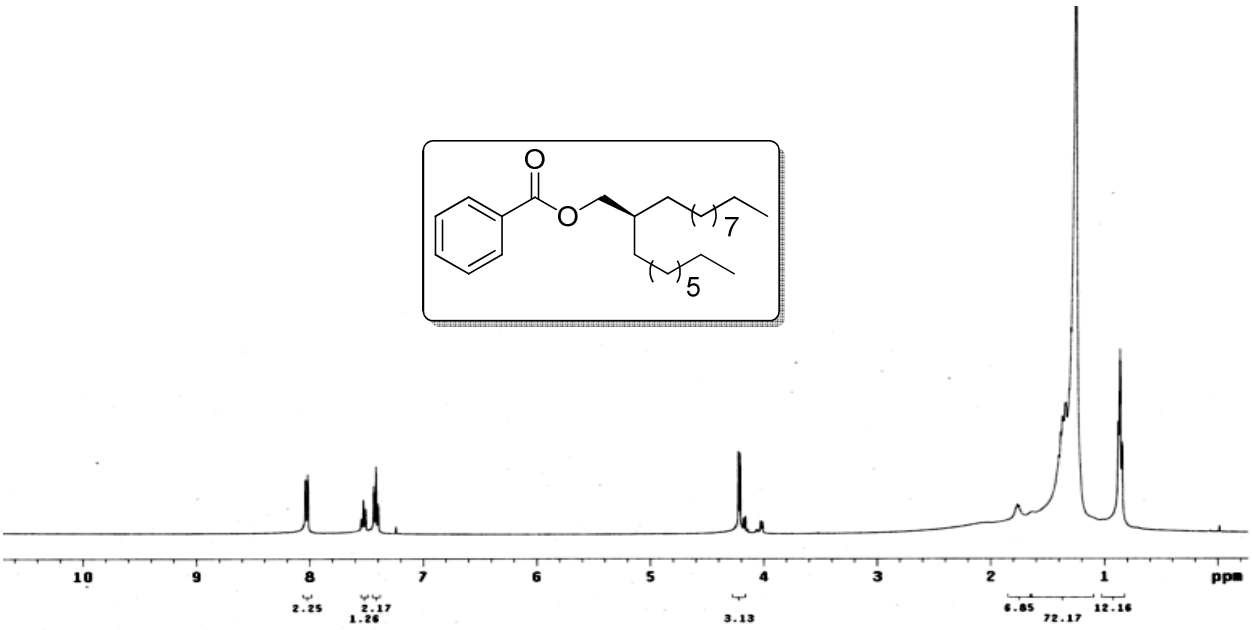


Figure S97: ^{1}H-NMR spectrum of 2-octyldodecyl benzoate (entry 8, Table 7).

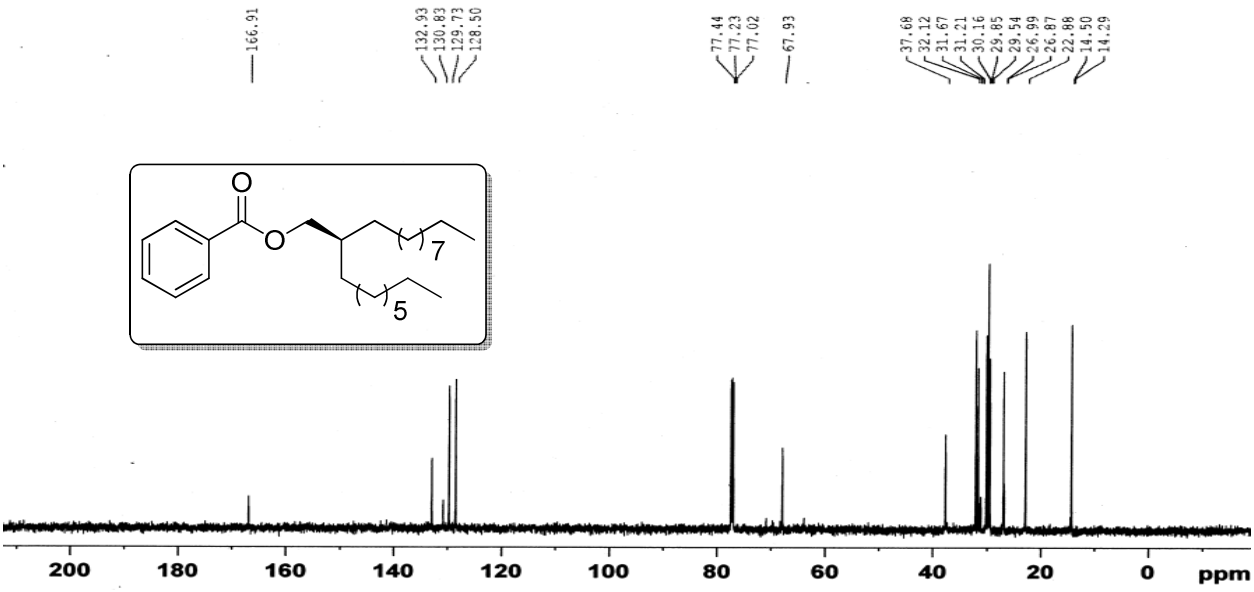


Figure S98: ^{13}C-NMR spectrum of 2-octyldodecyl benzoate (entry 8, Table 7).

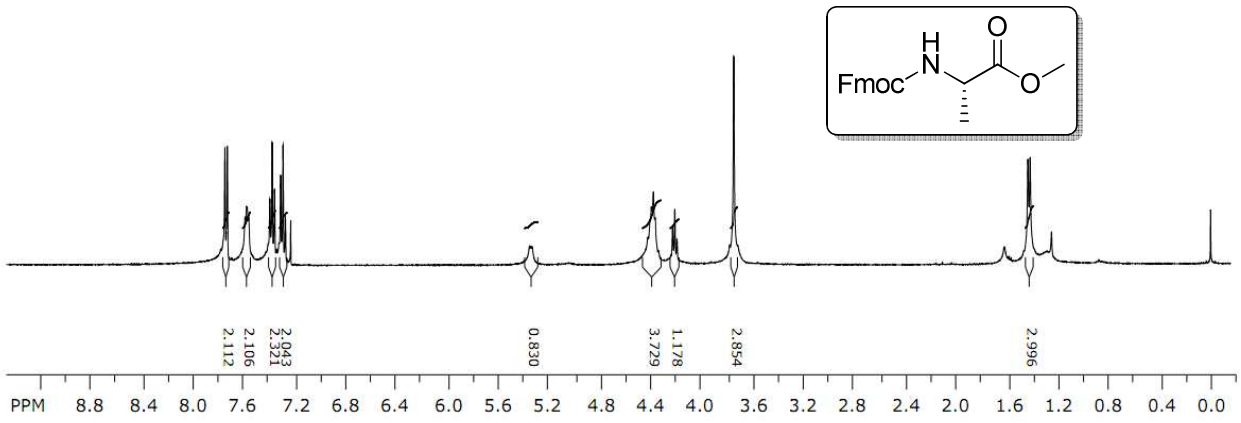


Figure S99: ^{1}H-NMR spectrum of methyl 2-(((9H-fluoren-9-yl)methoxy)carbonyl)propanoate (entry 9, Table 7).

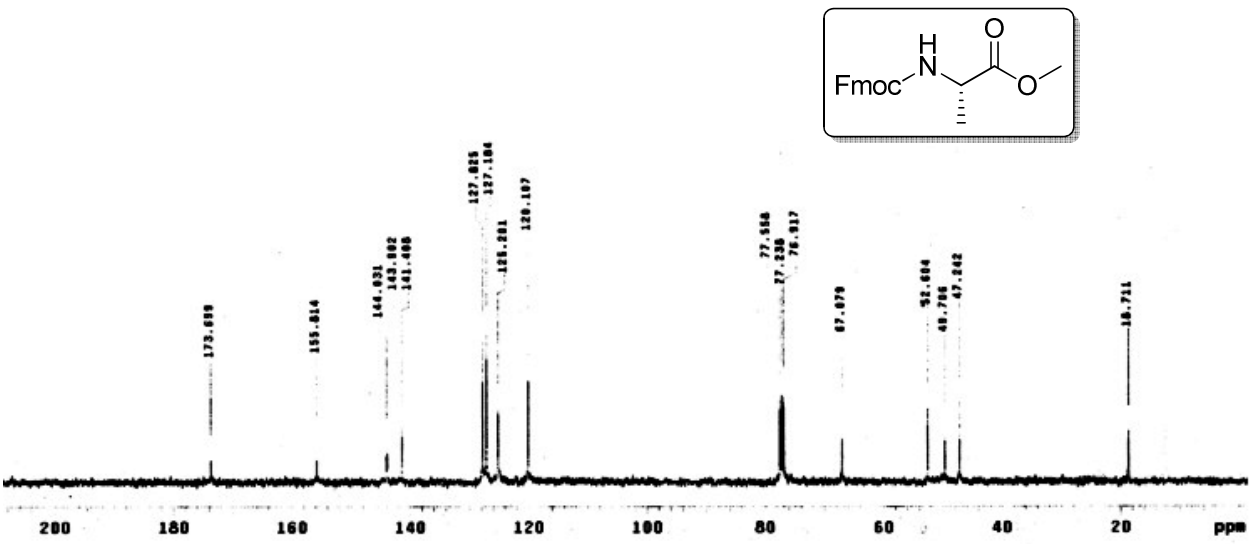


Figure S100: ^{13}C-NMR spectrum of methyl 2-(((9H-fluoren-9-yl)methoxy)carbonyl)propanoate (entry 9, Table 7).

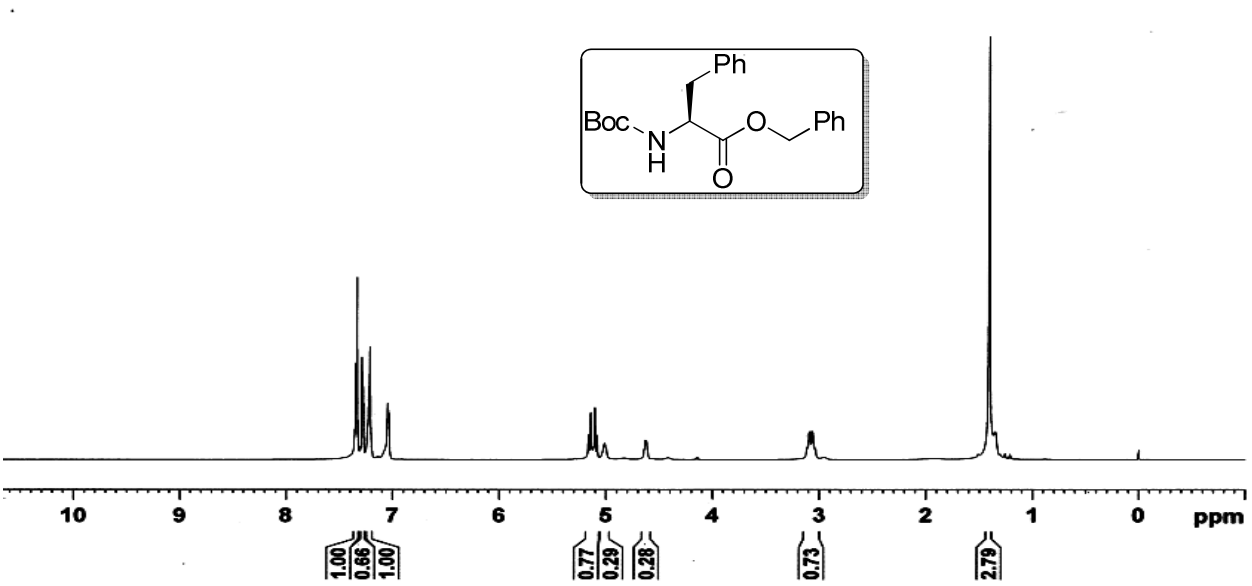


Figure S101: ^{1}H-NMR spectrum of (DL) benzyl 2-(tert-butoxycarbonyl)-3-phenylpropanoate (entry 10, Table 7).

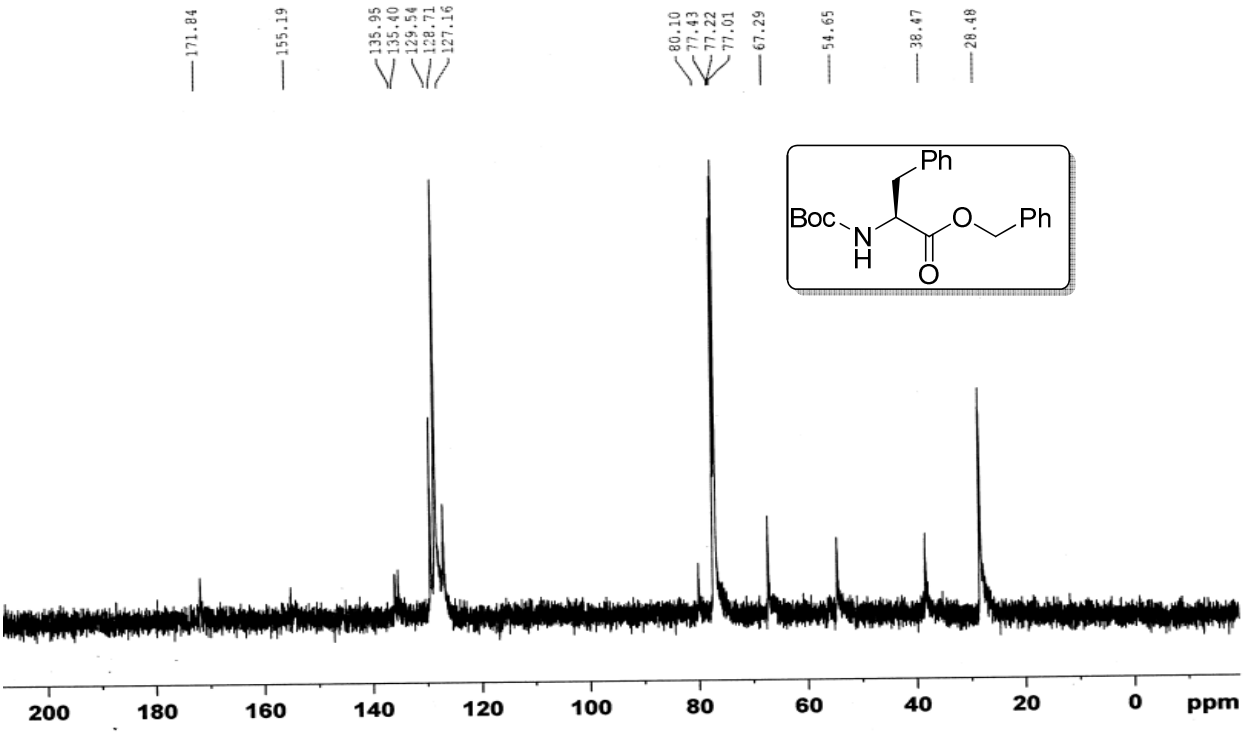


Figure S102: ^{13}C-NMR spectrum of (DL)benzyl 2-(tert-butoxycarbonyl)-3-phenylpropanoate (entry 10, Table 7).

6) ^{1}H-NMR and ^{13}C-NMR Spectra of recovered 2-nitrobenzene sulfonic acid and Oxyma:

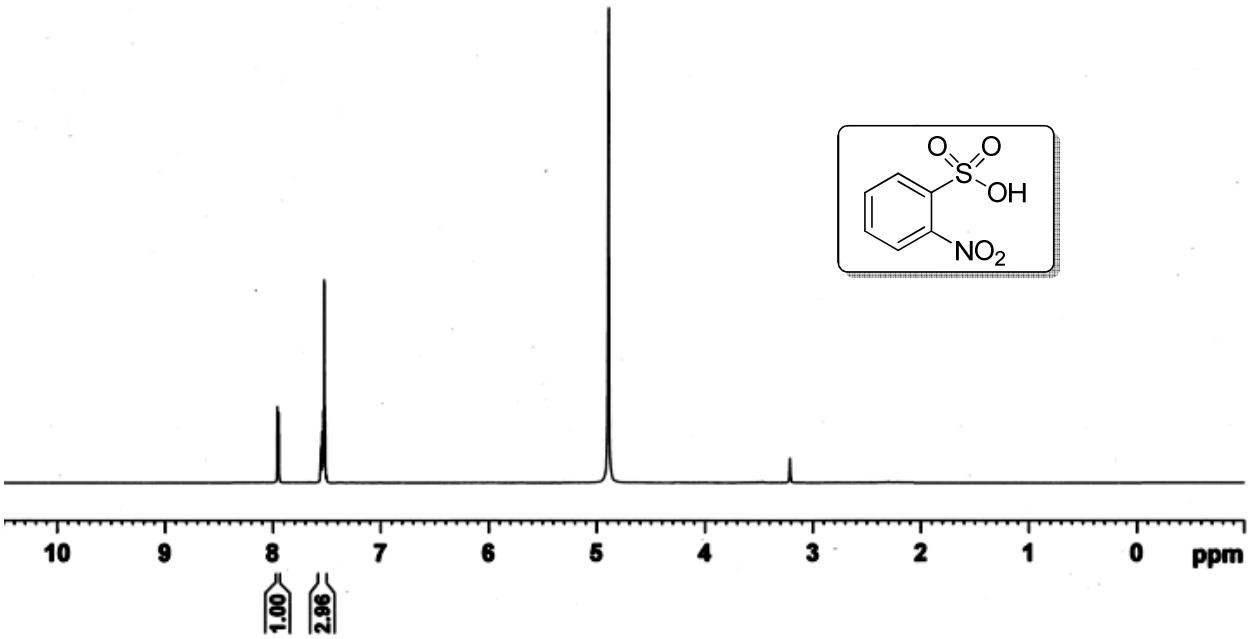


Figure S103: ^{1}H-NMR spectrum of 2-nitrobenzenesulfonic acid.

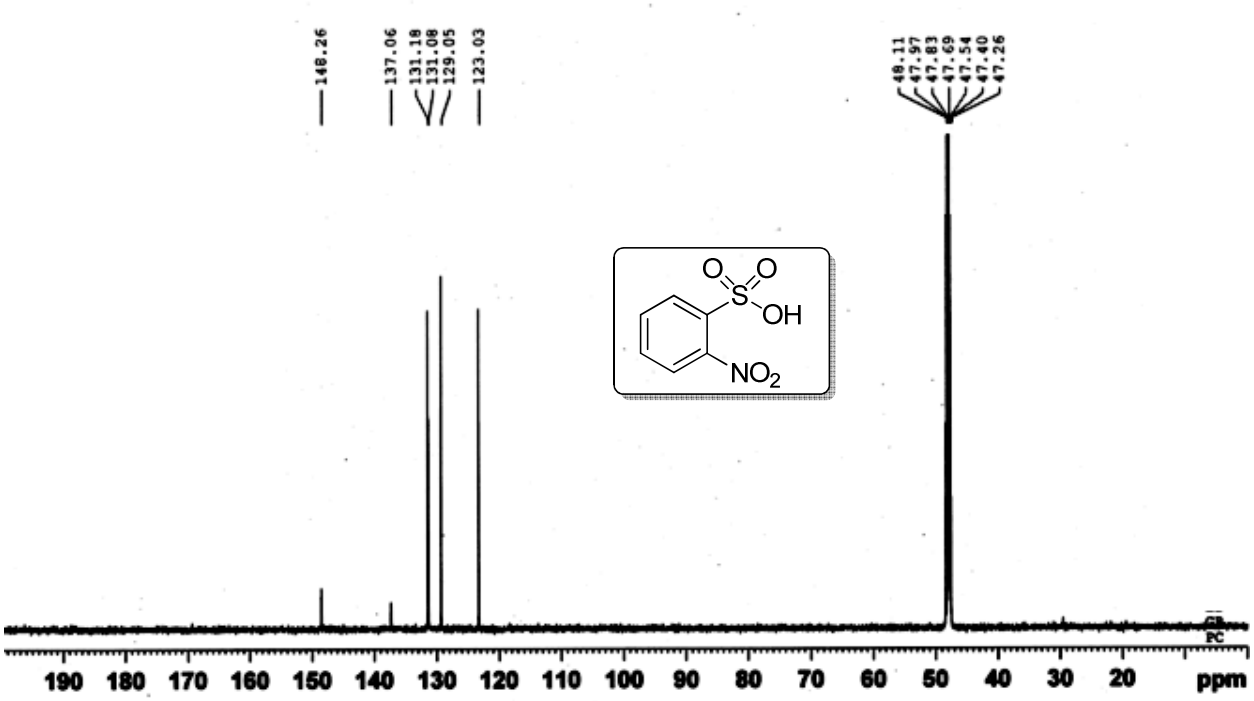


Figure S104: ^{13}C-NMR spectrum of 2-nitrobenzenesulfonic acid.

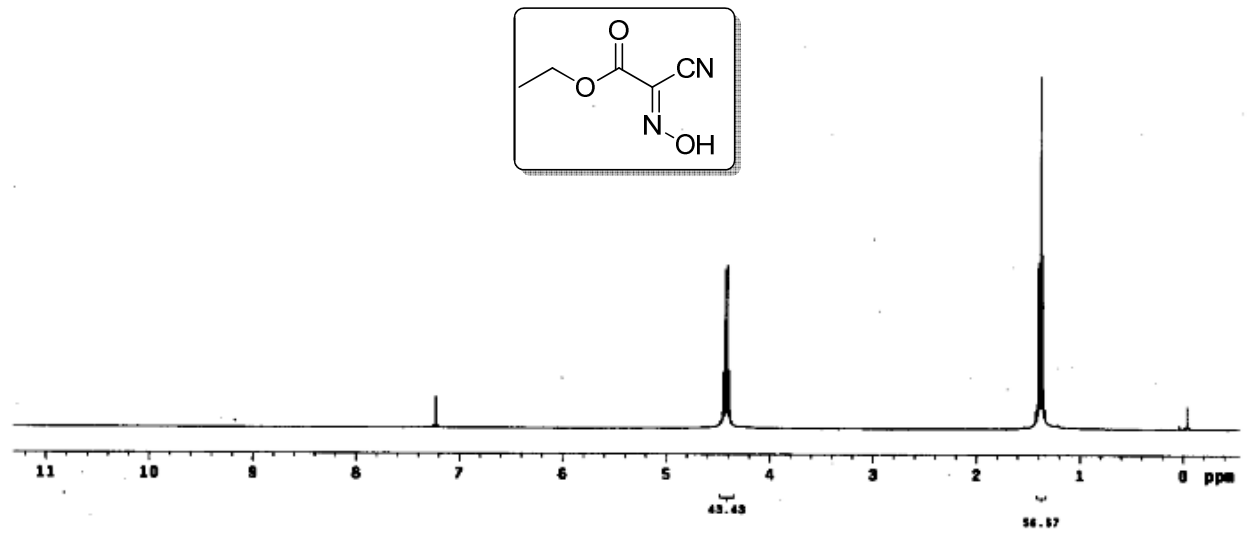


Figure S105: ^{1}H-NMR spectrum of (E)-ethyl 2-cyano-2-(hydroxyimino)acetate.

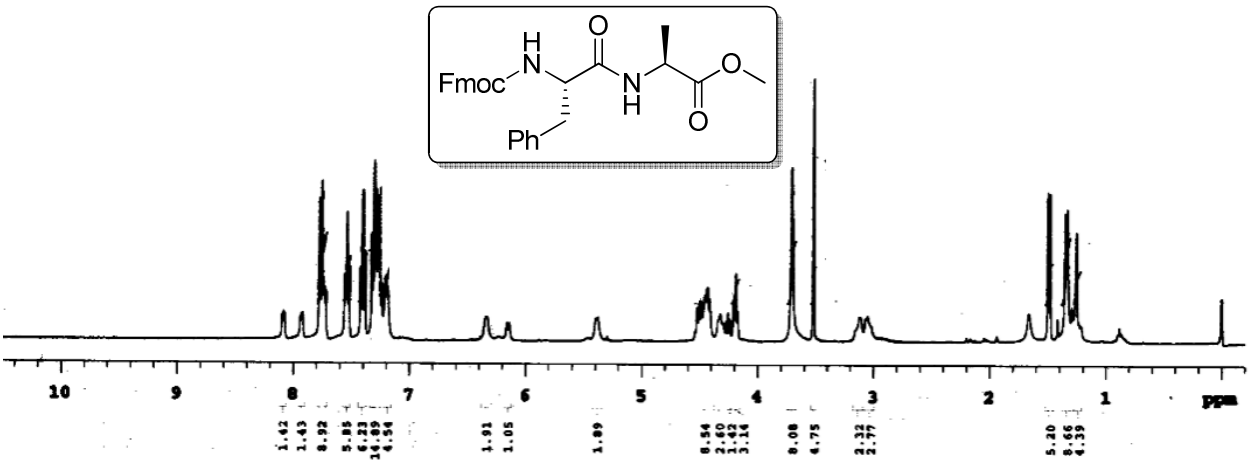


Figure S106: ^{1}H-NMR spectrum of methyl 2-(2-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-phenylpropanamido)propanoate

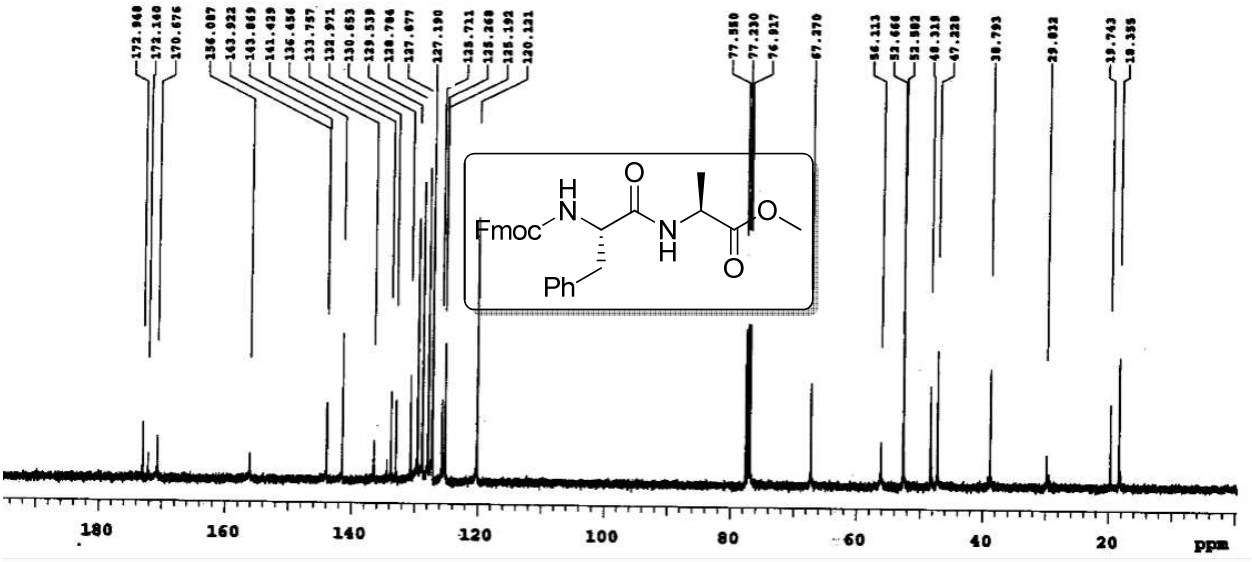


Figure S107: ^{13}C-NMR spectrum of methyl 2-(2-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-phenylpropanamido)propanoate

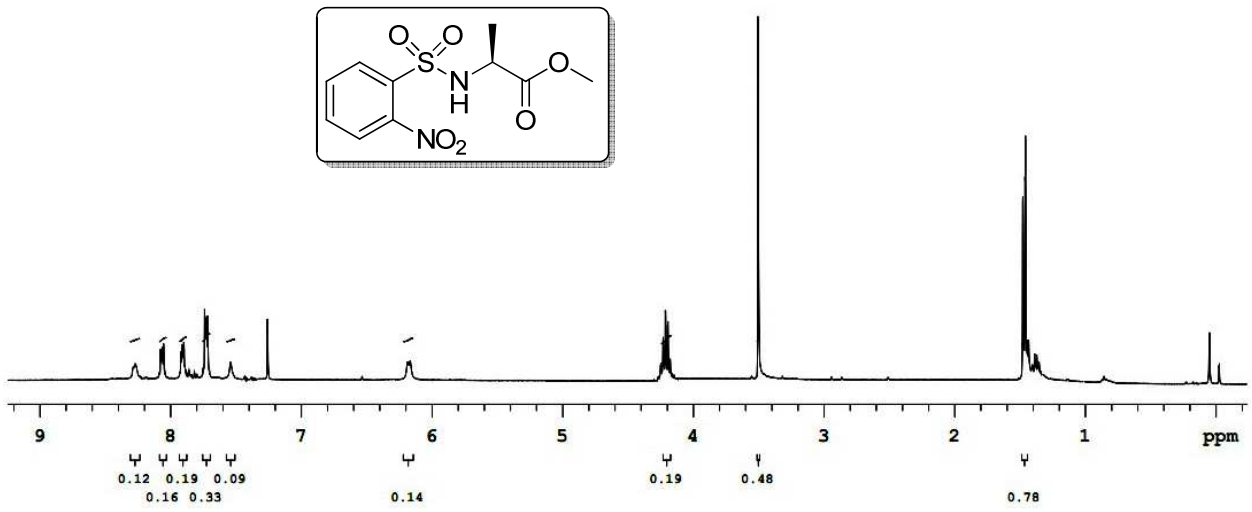


Figure S108: [1]H-NMR spectrum of methyl 2-(2-nitrophenylsulfonamido)propanoate

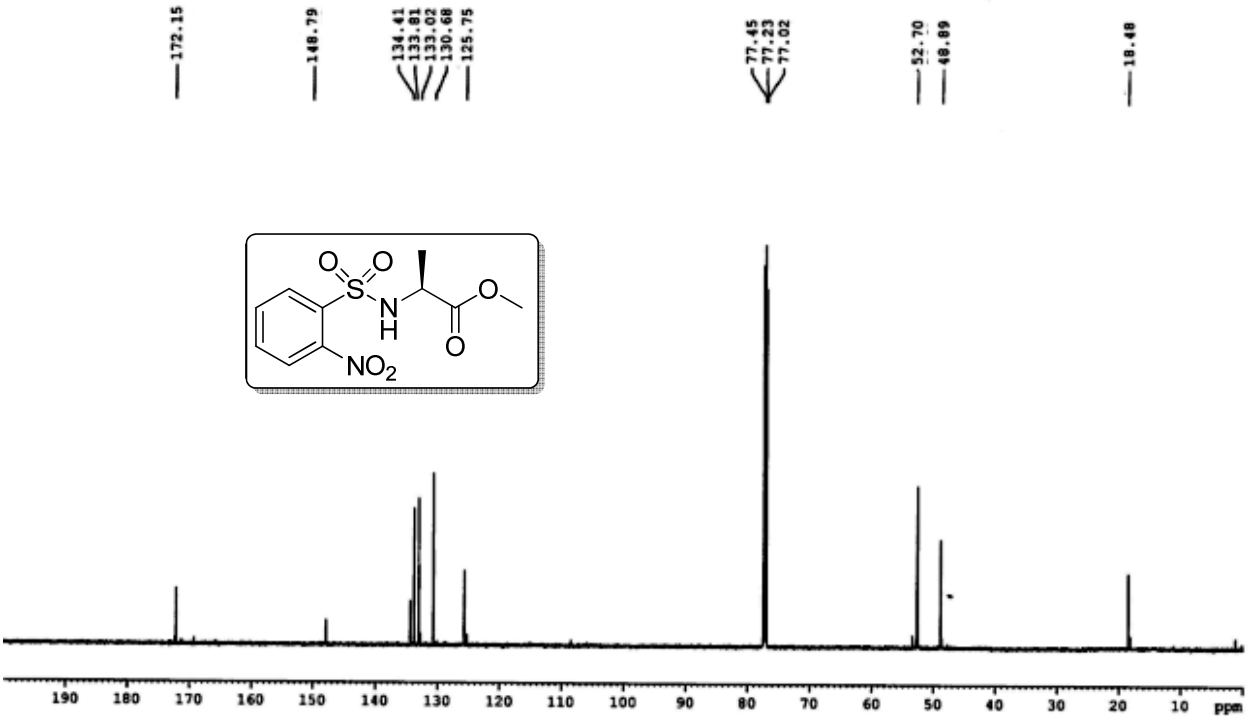


Figure S109: [13]C-NMR spectrum of methyl 2-(2-nitrophenylsulfonamido)propanoate

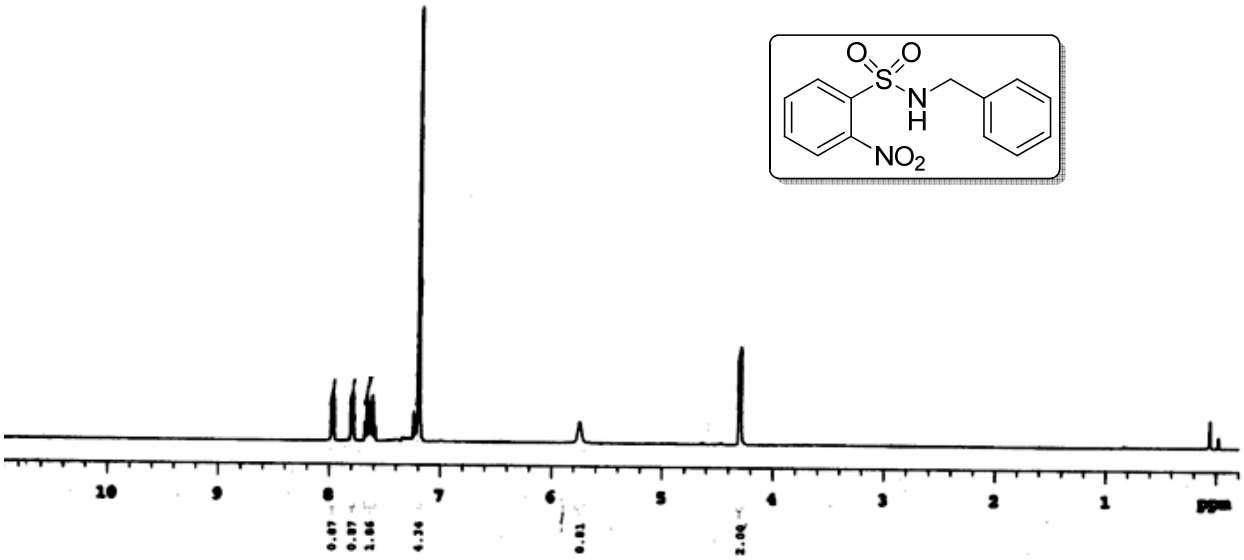


Figure S110: ^{1}H-NMR spectrum of N-benzyl-2-nitrobenzenesulfonamide (byproduct of the reaction without pre-activation).

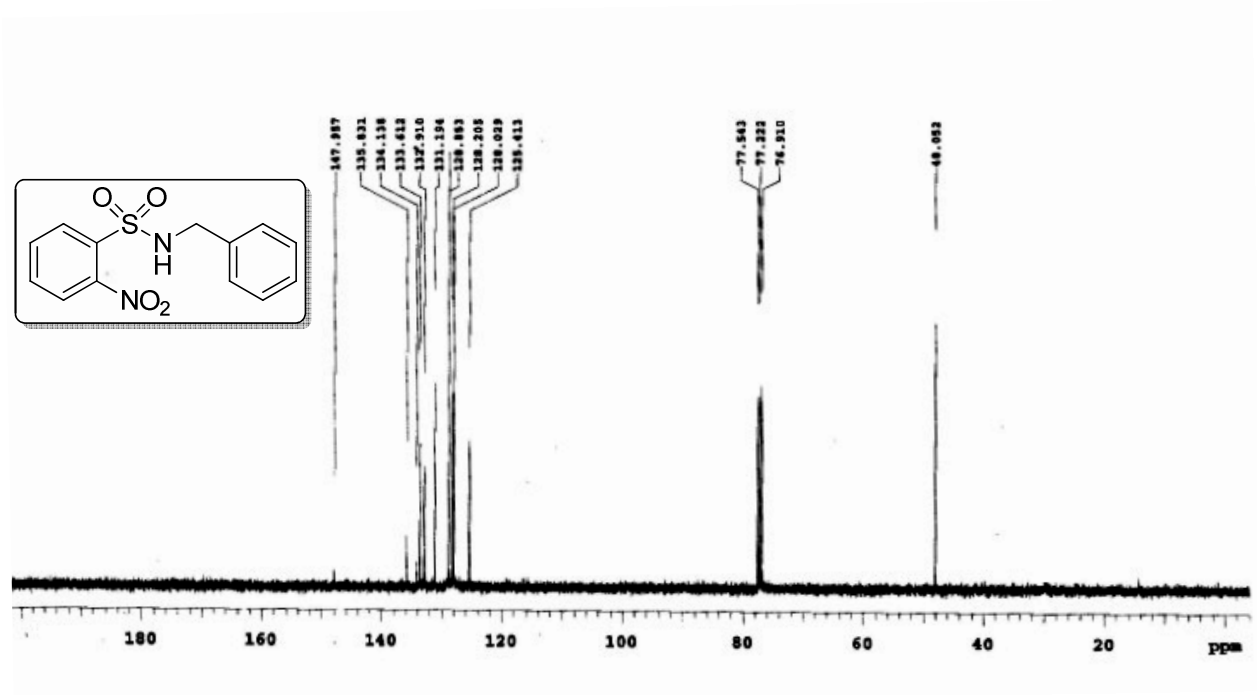


Figure S111: ^{13}C-NMR spectrum of N-benzyl-2-nitrobenzenesulfonamide (byproduct of the reaction without pre-activation).

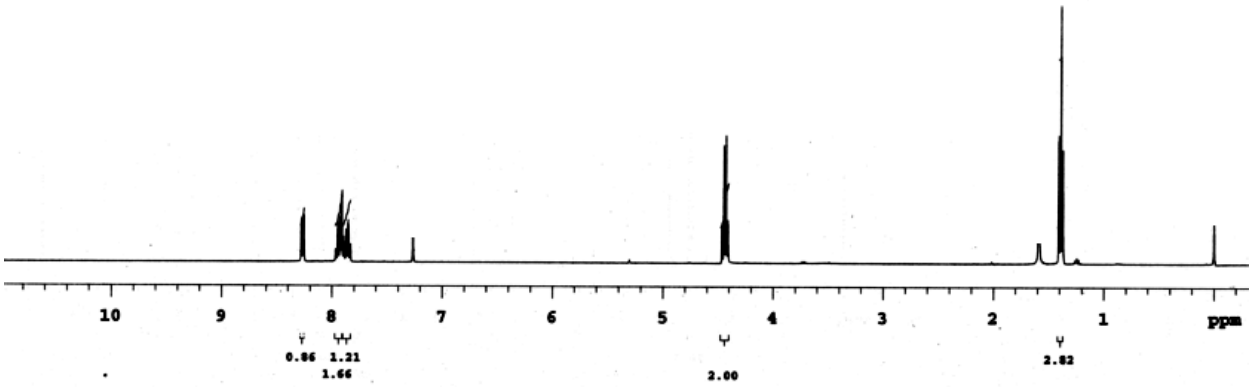


Figure S112: ^{1}H-NMR spectrum of coupling reagent **I**, first day of synthesis.

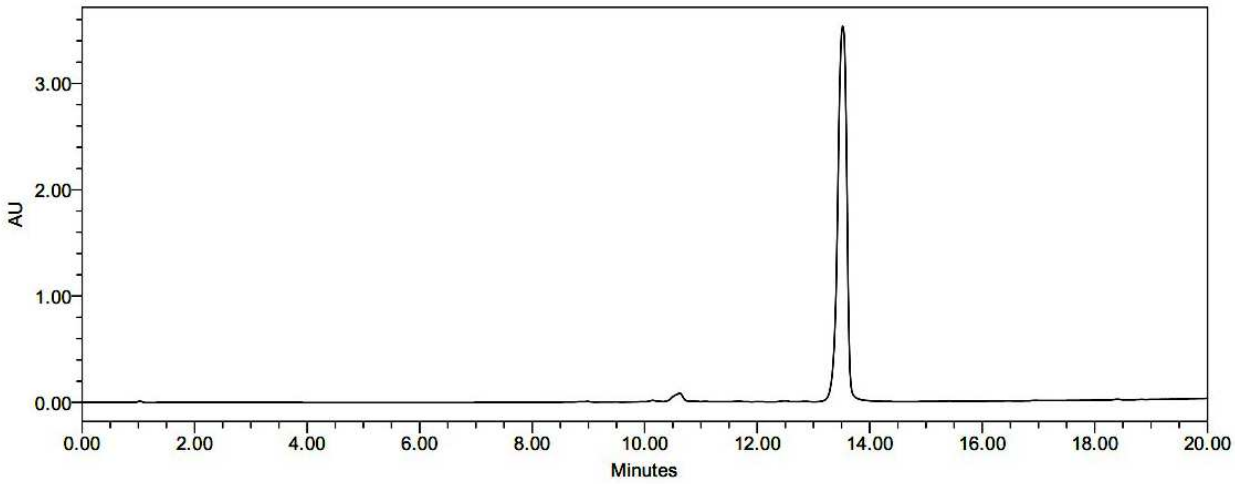


Figure113: HPLC chromatogram of **I**, first day of synthesis, run up to 20 min using Ascentis C18 reverse phase analytical (5 µm, 4.6 mm × 25 cm) column linear gradient of 0-80 %, 0-7 min. then 80-100 % upto 20 min., CH_3CN in H_2O with 0.1% formic acid.

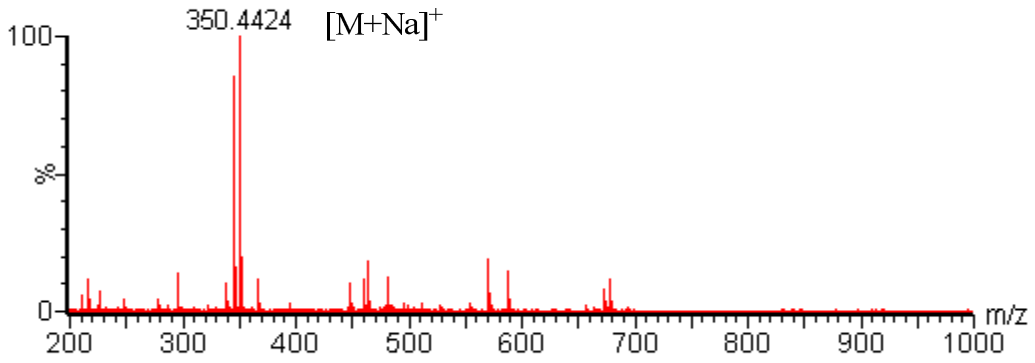


Figure S114: ESI-MS spectrum of **I**, the eluent at Rt 13.7 min of the above HPLC chromatogram.

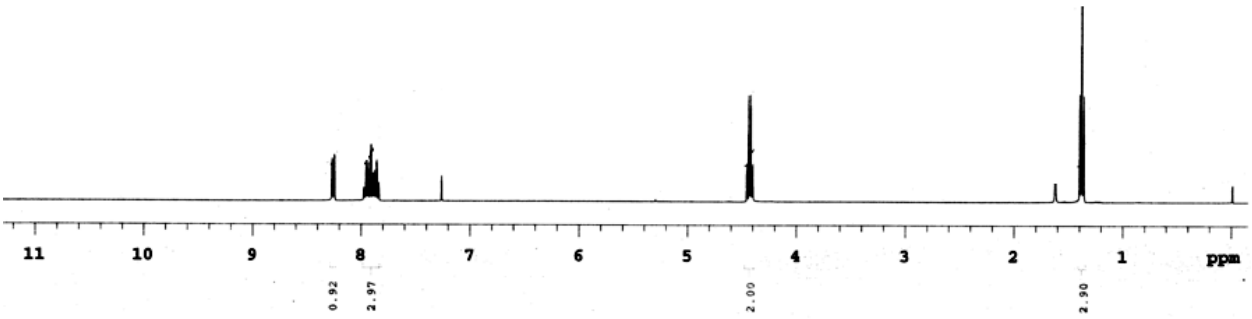


Figure S115: ^{1}H-NMR spectrum of coupling reagent **I**, after 20 day of the synthesis.

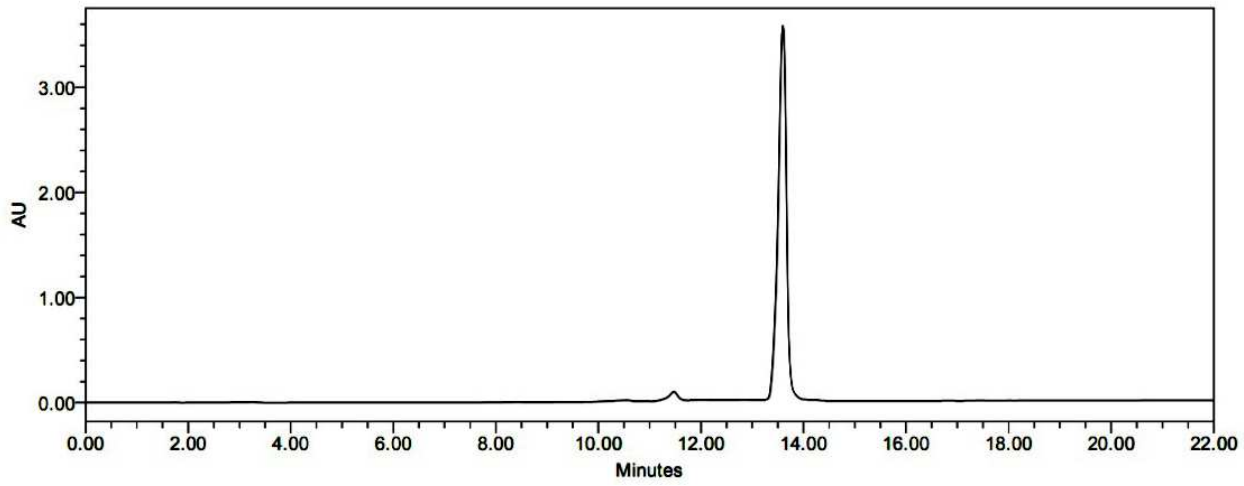


Figure 116: HPLC chromatogram of **I**, after 20 days of the synthesis, run for 20 min, using Ascentis C18 reverse phase analytical (5 µm, 4.6 mm × 25 cm) column, linear gradient of 0-80 %, 0-7 min, then 80-100 % during 20 min, CH_3CN in H_2O with 0.1% formic acid

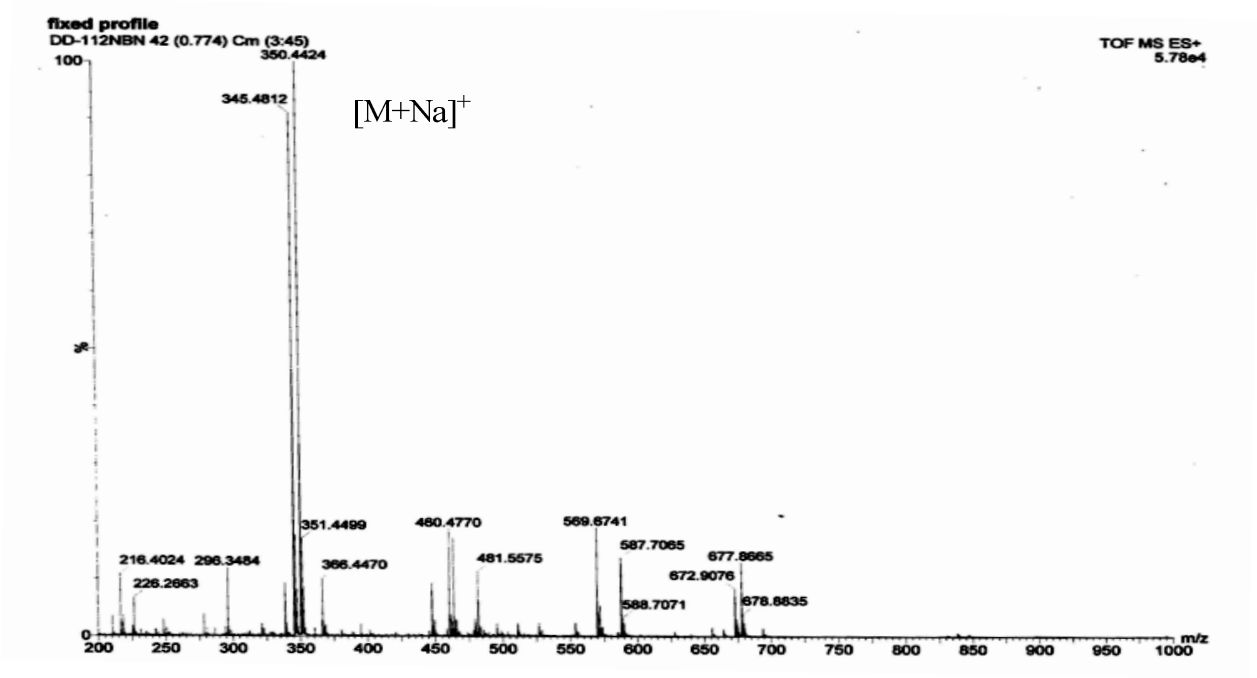


Figure S117: ESI-MS spectrum of **I**, the major peak of profile S116.

7) Data for racemization test:

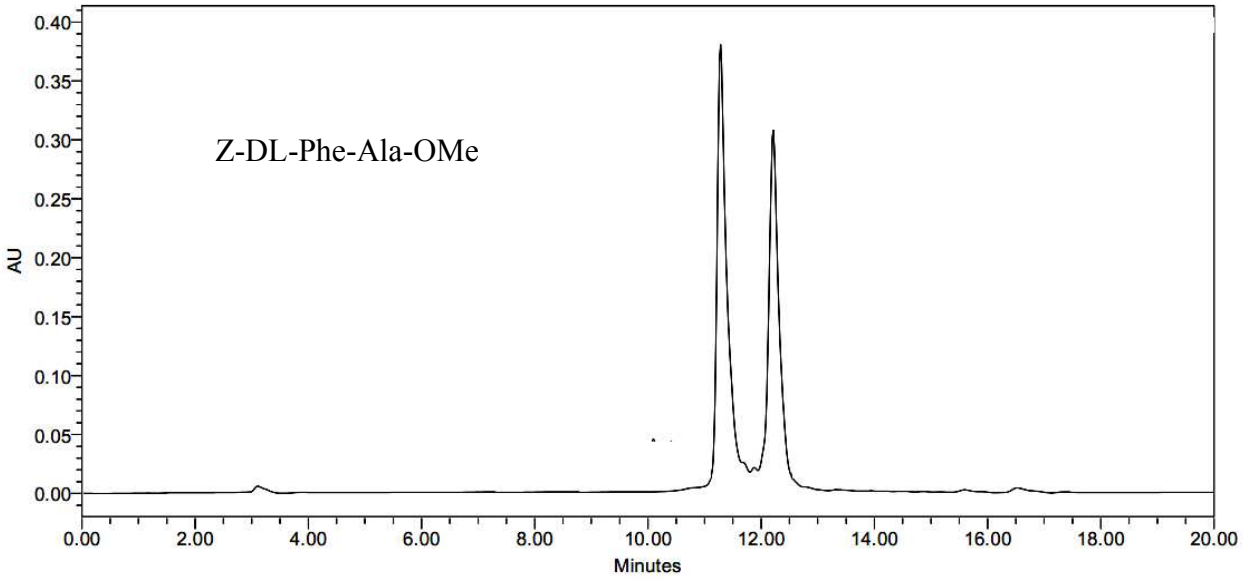


Figure S118: HPLC chromatogram of Z-DL-Phe-Ala-OMe dipeptide run upto 20 min.in Ascentis C18 reverse phase analytical (5 µm, 25 cm× 4.6 mm,) column linear gradient of 0-80 %, 0-7 min. then 80-100 % upto 20 min., CH_3CN in H_2O with 0.1% formic acid (entry 13, Table 3).

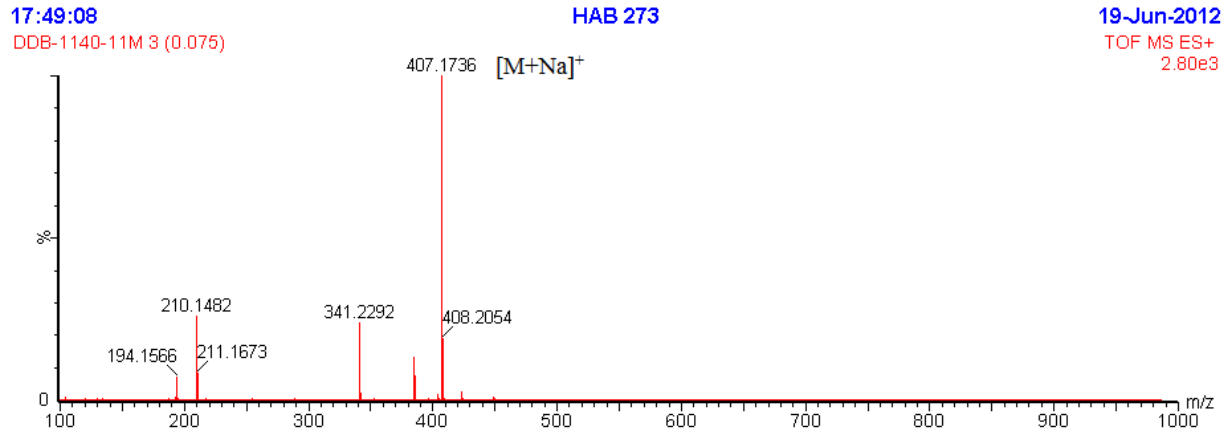


Figure S119: ESI-MS spectrum of Z-DL-Phe-Ala-OMe dipeptide, peak retention time 11.78 min of above chromatogram (entry 13, Table 3).

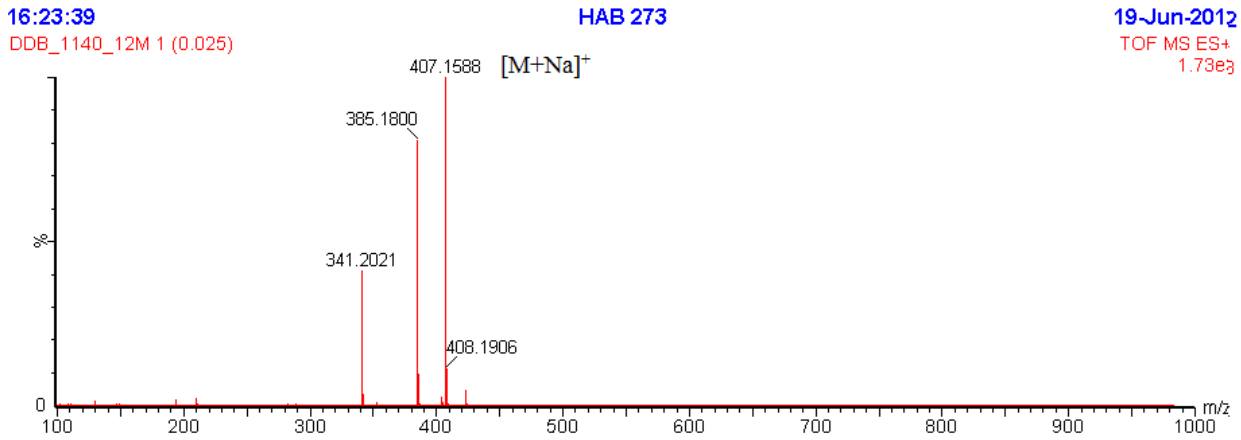


Figure S120: ESI-MS spectrum of Z-DL-Phe-Ala-OMe dipeptide, peak retention time 12.16 min of above chromatogram (entry 13, Table 3).

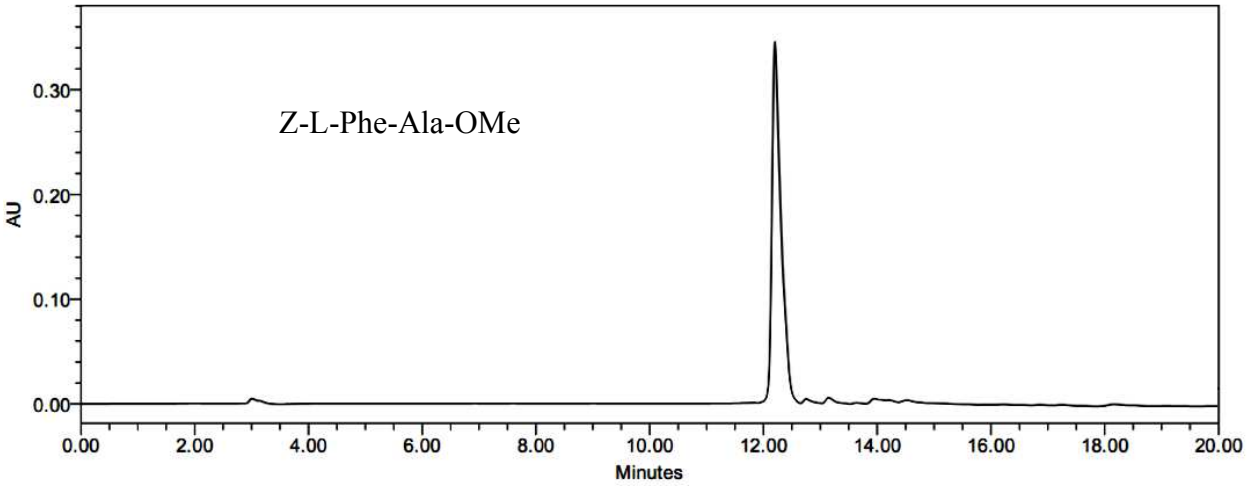


Figure S121: HPLC chromatogram of Z-L-Phe-Ala-OMe dipeptide run in Ascentis C18 reverse phase analytical (5 µm, 25 cm× 4.6 mm,) column linear gradient of 0-80 %, 0-7 min. then 80-100 % upto 20 min., CH_3CN in H_2O with 0.1% formic acid (entry 14, Table 3).

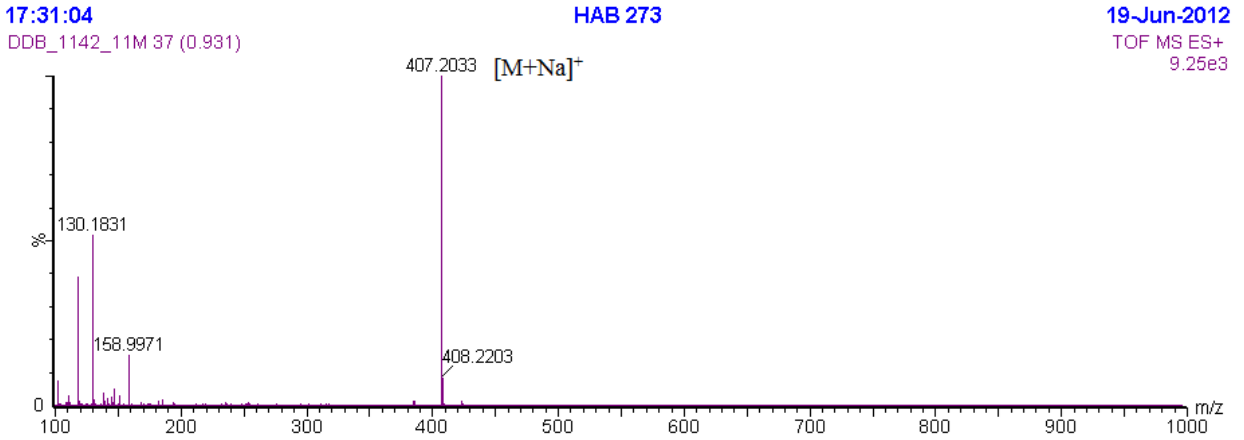


Figure S122: ESI-MS spectrum of Z-L-Phe-Ala-OMe dipeptide, peak retention time 11.76 min of above chromatogram (entry 14, Table 3).

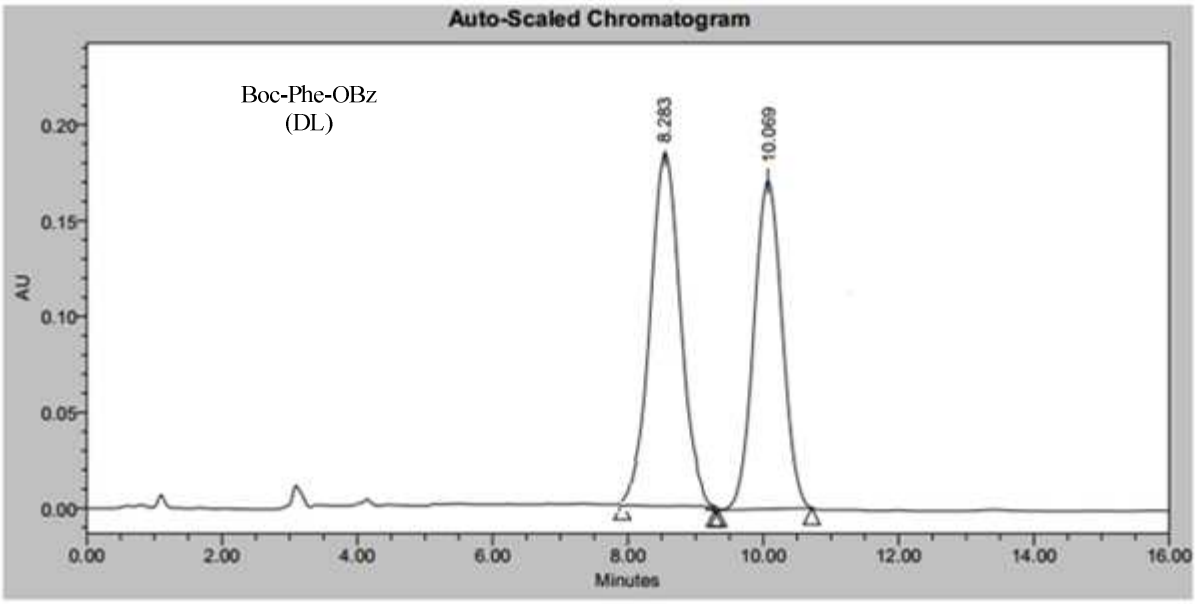


Figure S123: HPLC chromatogram of Boc-DL-Phe-OBz run in CHIRAL PAK^{R} AS-H (5 µm, 2.1×150mm) column in isocratic gradient of 10% isopropanol in hexane (entry 10, Table 8).

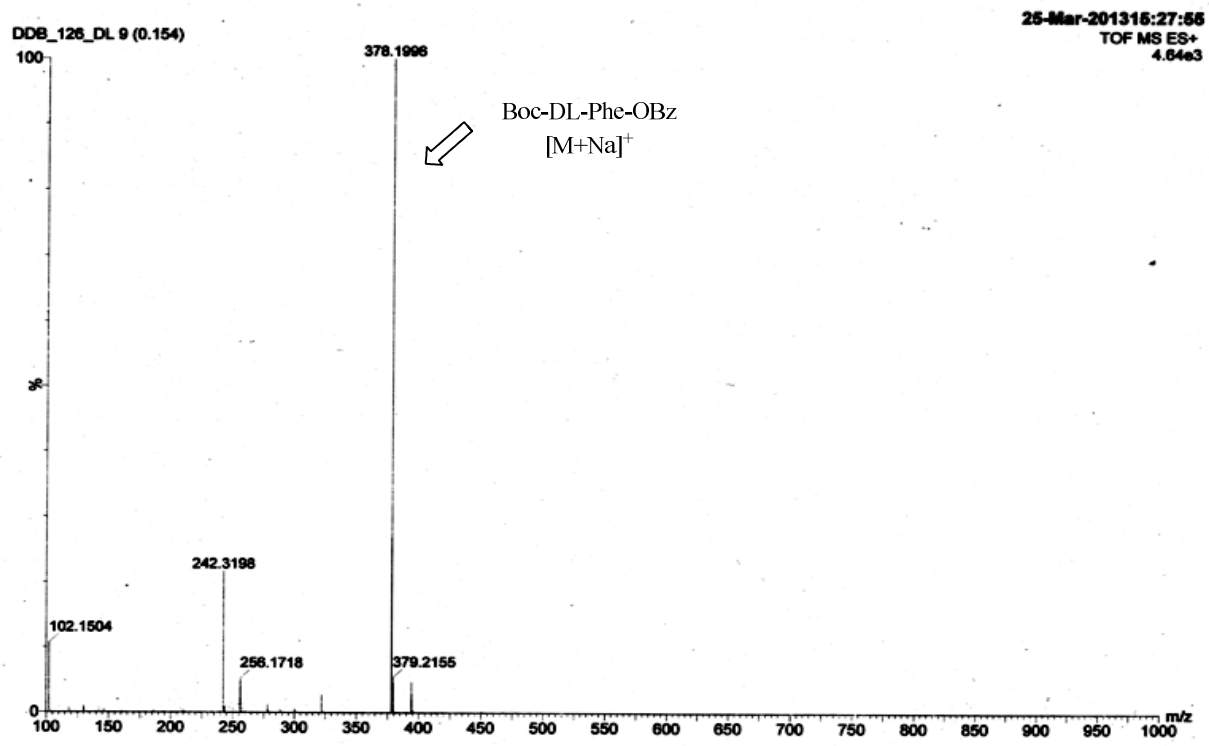


Figure S124: ESI-MS spectrum of Boc-DL-Phe-OBz ester, peak retention time 8.28 min of above chromatogram (entry 10, Table 8).

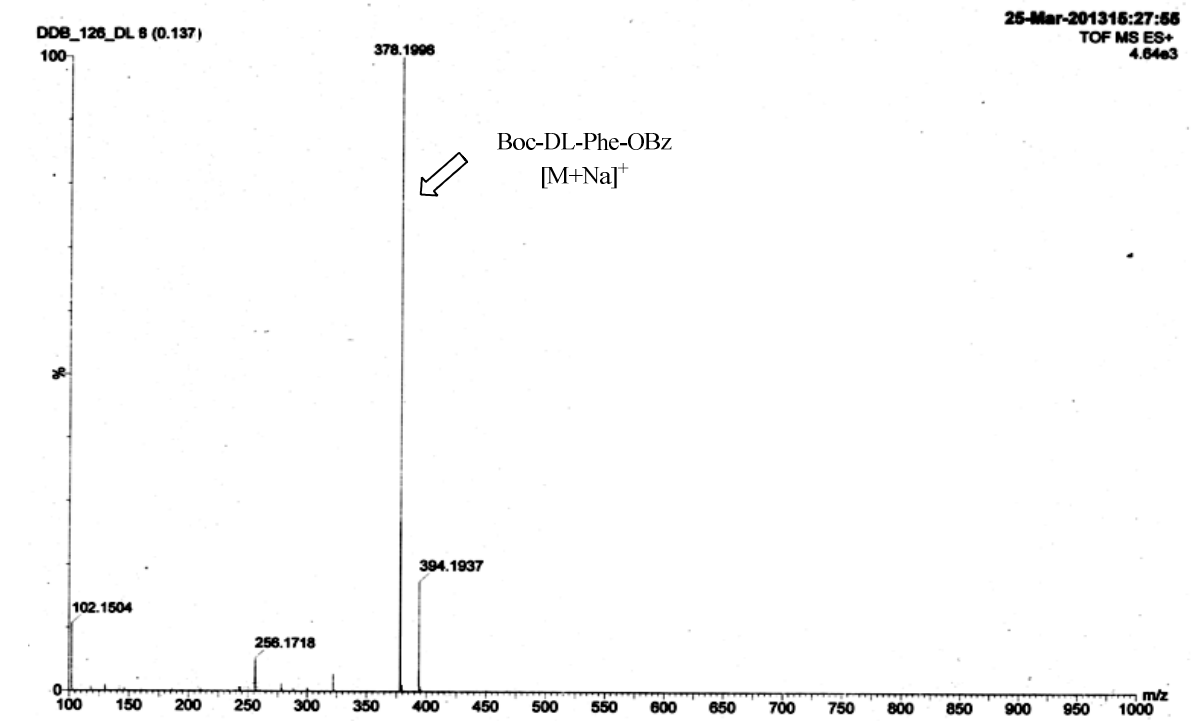


Figure S125: ESI-MS spectrum of Boc-DL-Phe-OBz ester, peak retention time 10.06 min of above chromatogram (entry 10, Table 8).

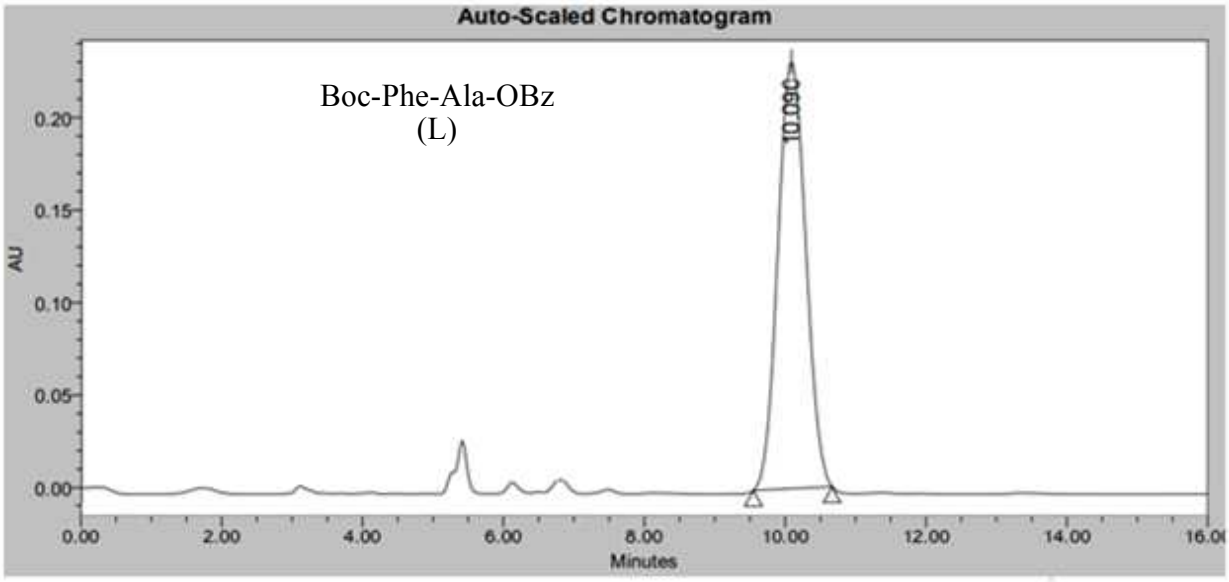


Figure S126: HPLC chromatogram of Boc-L-Phe-OBz runs in CHIRAL PAK^{R} AS-H (5 µm, 2.1×150mm) column in isocratic gradient of 10% isopropanol in hexane (entry 11, Table 8).

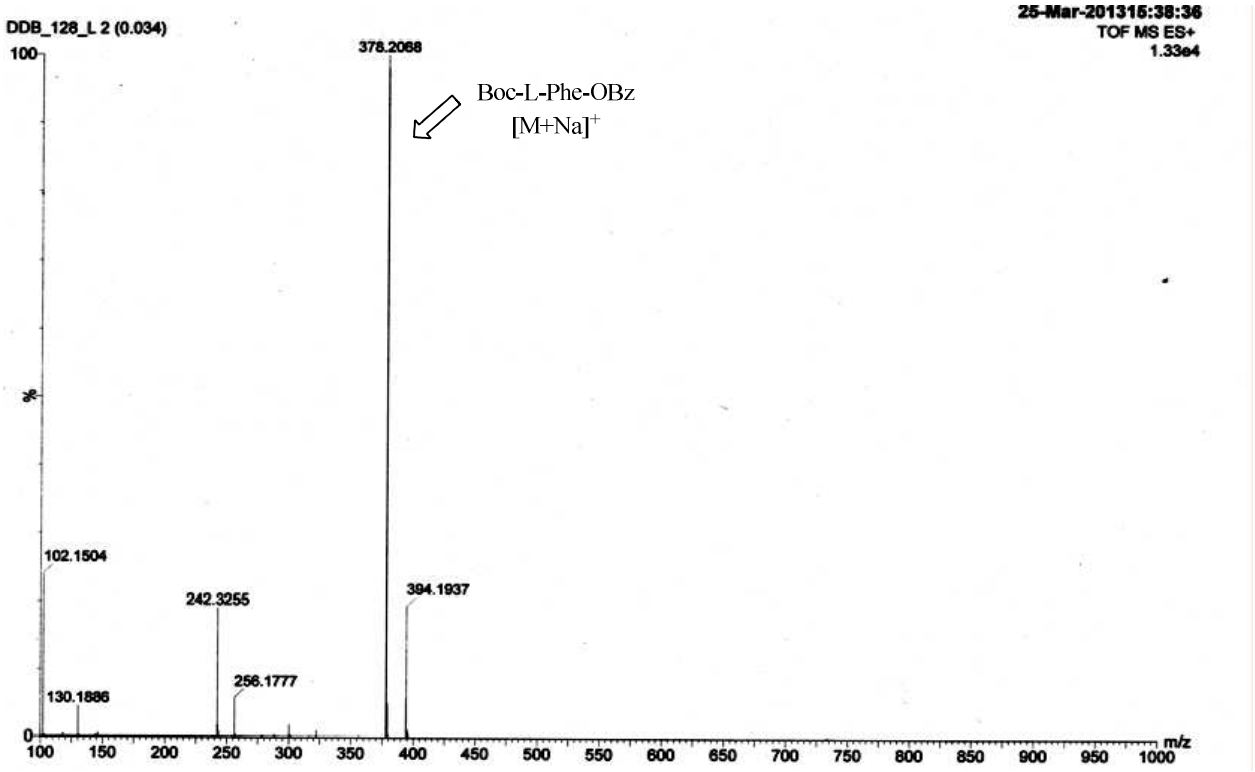


Figure S127: ESI-MS spectrum of Boc-L-Phe-OBz ester, peak retention time 10.09 min of above chromatogram (entry 11, Table 8).

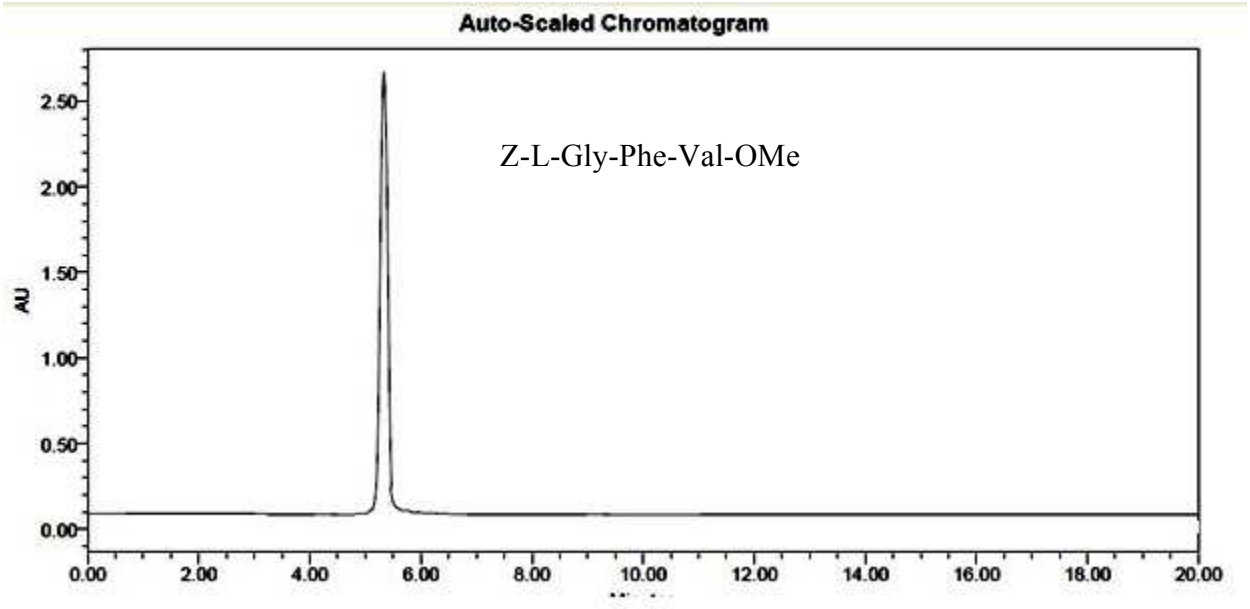


Figure S128: HPLC chromatogram of Z-Gly-Phe-Val-OMe run upto 20 min. in a symmetry C8 (5 µm, 3.5 × 150 mm) column, isocratic gradient 35 % acetonitrile in water (entry 18, Table 3).

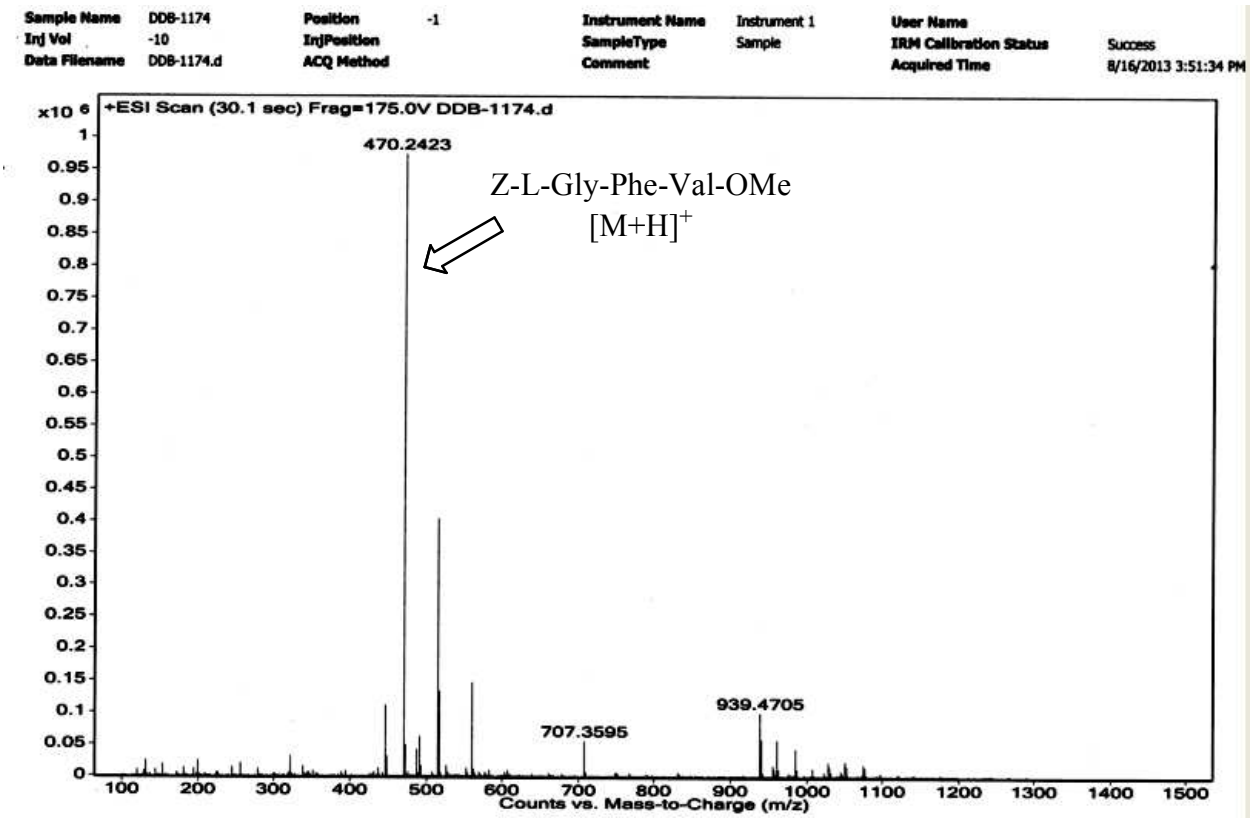


Figure S129: ESI-MS spectrum of Z-Gly-Phe-Val-OMe peptide, peak of above chromatogram (entry 18, Table 3).

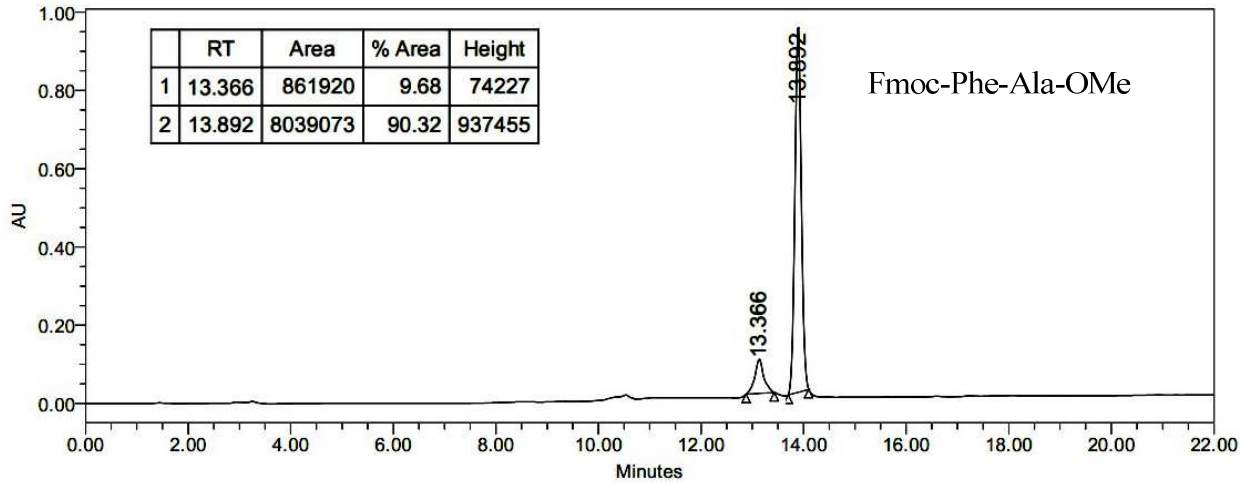


Figure S130: HPLC chromatogram of Fmoc-Phe-Ala-OMe dipeptide run in Ascentis C18 reverse phase analytical column (5 µm, 4.6 mm × 25 cm), linear gradient of 0-80 %, 0-7 min. then 80-100 % up to 22 min., CH_3CN in H_2O with 0.1% formic acid (Reaction was performed with 2-nitrobenenesulfonyl chloride).

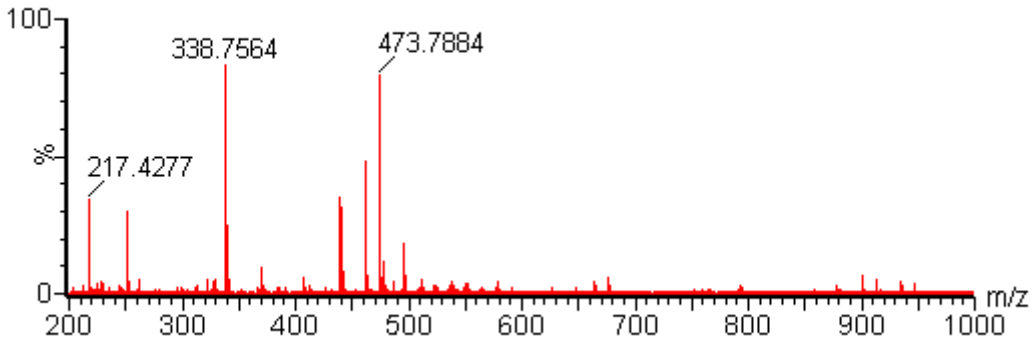


Figure S131: ESI-MS-spectrum of Fmoc-Phe-Ala-OMe dipeptide, Rt, 13.892 min (reaction was performed with 2-nitrobenenesulfonyl chloride).

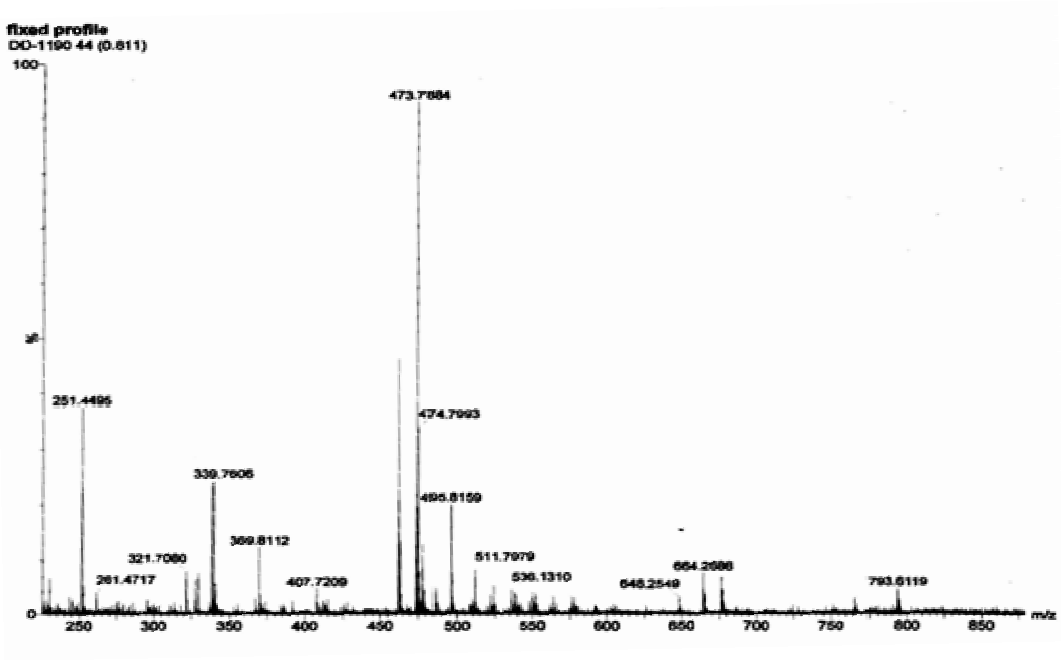


Figure S132: ESI-MS-spectra of Fmoc-Phe-Ala-OMe dipeptide, Rt 13.366 min (reaction was performed with 2-nitrobenenesulfonyl chloride).

8) HPLC Chromatogram of dipeptides:

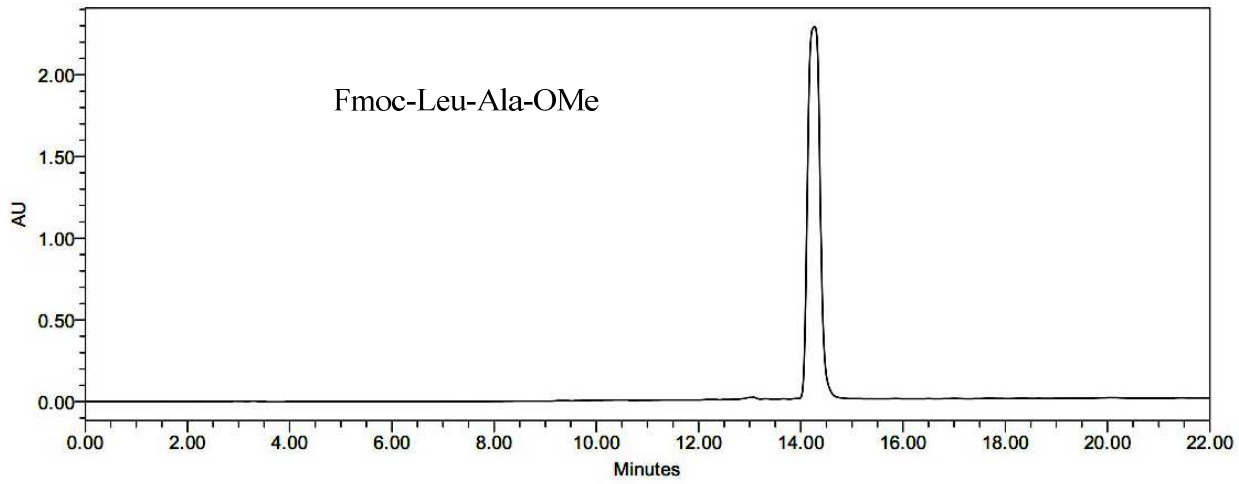


Figure S133: HPLC chromatogram of Fmoc-Leu-Ala-OMe dipeptide run in Ascentis C18 reverse phase analytical (5 µm, 25 cm× 4.6 mm,) column linear gradient of 0-80 %, 0-7 min. then 80-100 % upto 22 min., CH_3CN in H_2O with 0.1% formic acid. (entry 9, Table 3).

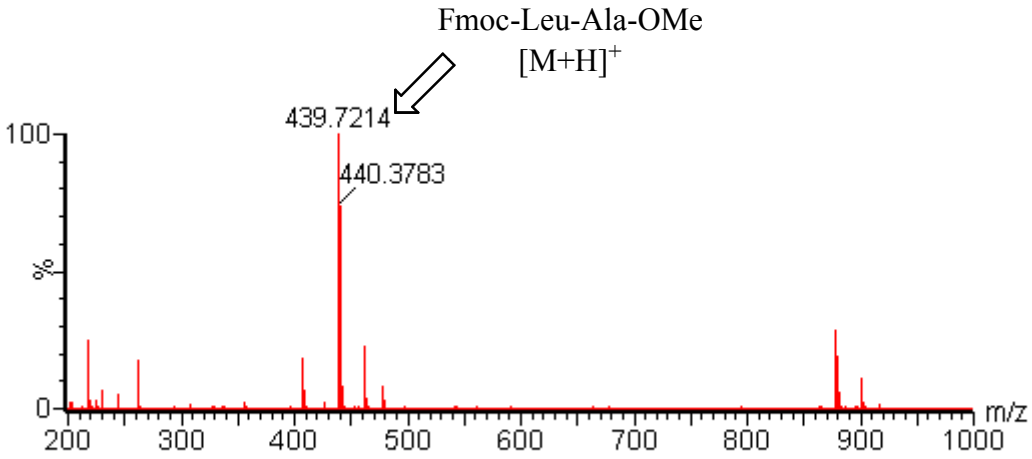


Figure S134: ESI-MS-spectra of Methyl 2-(2-(((9H-fluoren-9-yl)methoxy)carbonylamino) -4-methylpentanamido) propanoate (entry 9, Table 3).

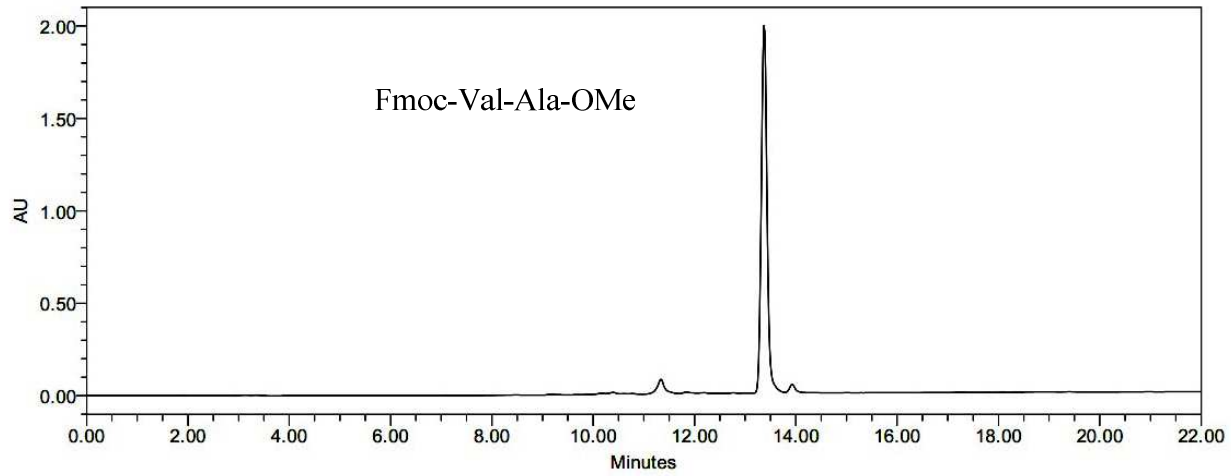


Figure S135: HPLC chromatogram of Fmoc-Val-Ala-OMe dipeptide run in Ascentis C18 reverse phase analytical (5 µm, 25 cm× 4.6 mm,) column linear gradient of 0-80 %, 0-7 min. then 80-100 % upto 22 min., CH_3CN in H_2O with 0.1% formic acid. (entry 10, Table 3).

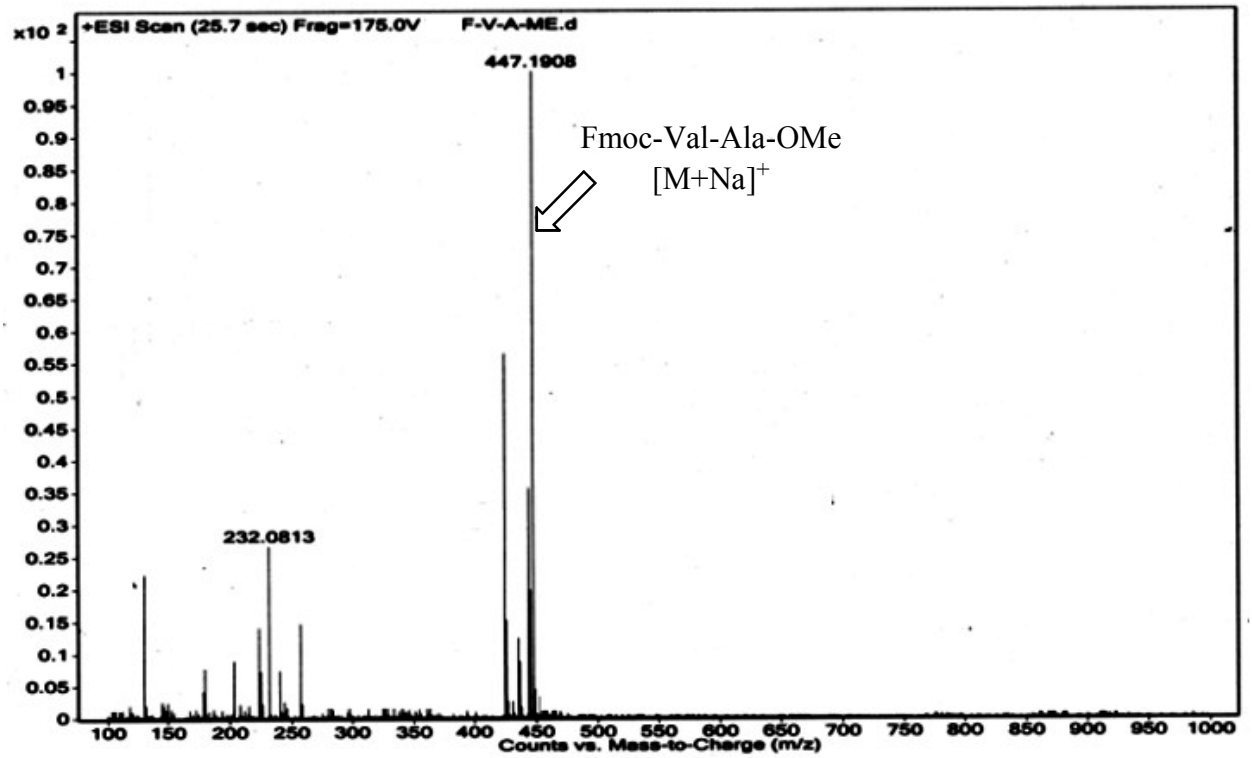


Figure S136: ESI-MS-spectra of 2-[2-(9H-Fluoren-9-ylmethoxycarbonylamino)-3-methyl-butyrylamino]-propionic acid methyl ester (entry 10, Table 3).

9) HPLC chromatogram and mass spectrum of Boc-VVIA-OMe:

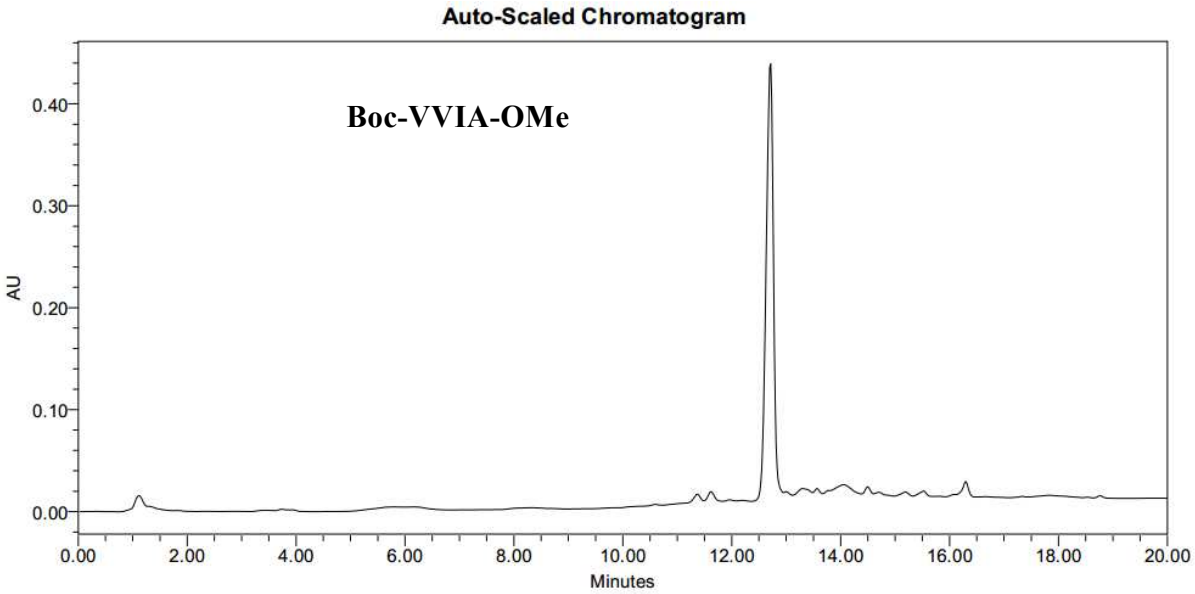


Figure S137: HPLC chromatogram of Boc-VVIA-OMe C8 analytical column (0-20min. linear gradient, 20-100% acetonitrile in water) (Figure 3c).

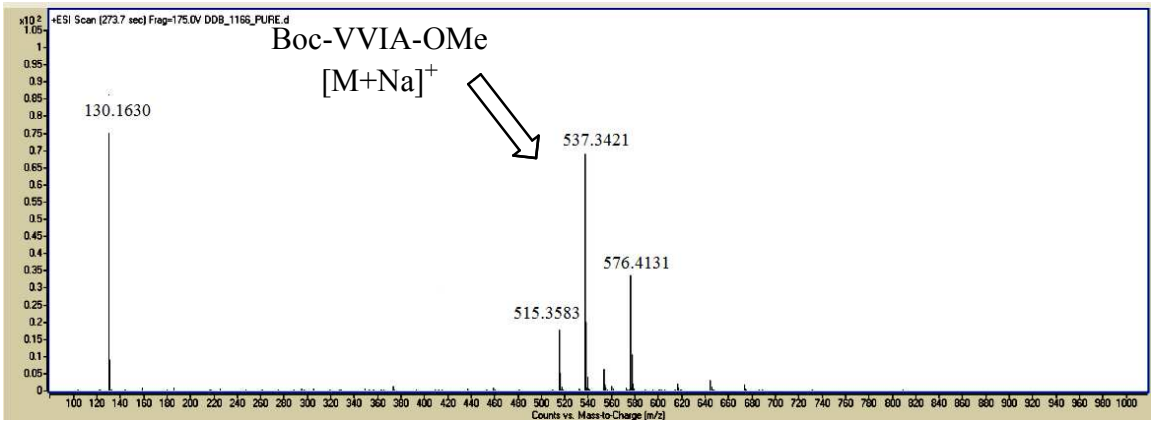


Figure S138: ESI-MS spectrum of Boc-VVIA-OMe peptide, peak of above chromatogram (Figure 3c).

10) HPLC profiles and ESI-MS spectra of products after test cleavage in solid phase synthesis of NFGAILG-NH_2 peptide:

The crude products after each coupling step were cleaved from resin and precipitated by cold ether, then analyzed by reverse phase HPLC, symmetry C8 analytical column, with linear gradient of 20 min (5 to 100 % acetonitrile in water).

Table S1. HPLC retention times and observed mass (ESI-MS) of the peptides after each coupling step for SPPS of IAPP (22-27).

Entry	Peptide	Retention time of HPLC (in min.)[a]	Expected mass (m/z)	Obsarved mass (m/z)
1	Fmoc-LG-NH_2	12.10	$[M+Na]^+$ 432.18	432.19
2	Fmoc-ILG-NH_2	12.00	$[M+H]^+$ 523.12	523.15
3	Fmoc-AILG-NH_2	11.00	$[M+H]^+$ 594.32	594.34
4	Fmoc-GAILG-NH_2	12.05	$[M+H]^+$ 651.35	651.37
5	Fmoc-FGAILG-NH_2	14.02	$[M+H]^+$ 798.41	798.44
6	Fmoc-NFGAILG-NH_2	13.30	$[M+H]^+$ 912.46	912.49
7	NFGAILG-NH_2	11.50	$[M+H]^+$ 690.39	690.39

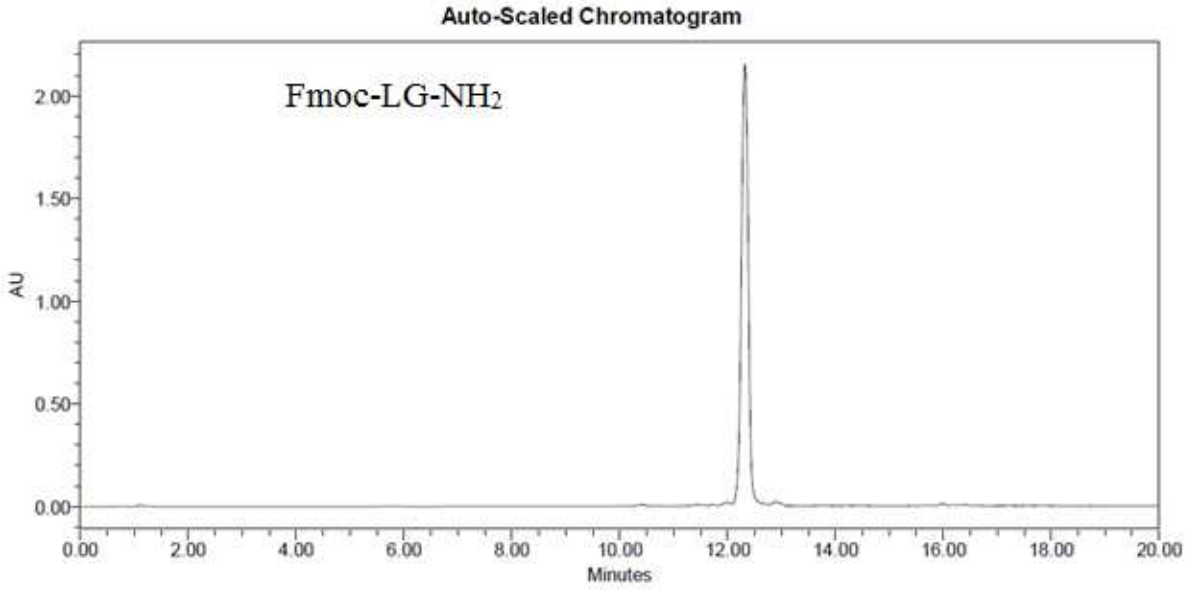


Figure S139: HPLC chromatogram of Fmoc-LG-NH_2 (entry 1, Table S1).

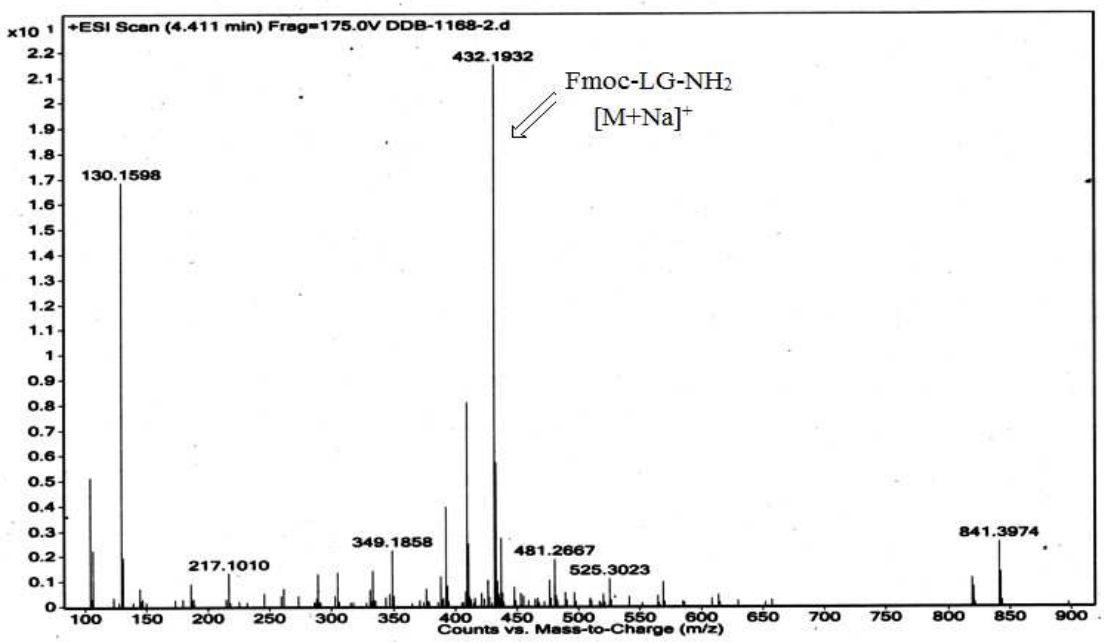


Figure S140: ESI-MS spectrum of Fmoc-LG-NH_2 peptide, peak of the above chromatogram (entry 1, Table S1).

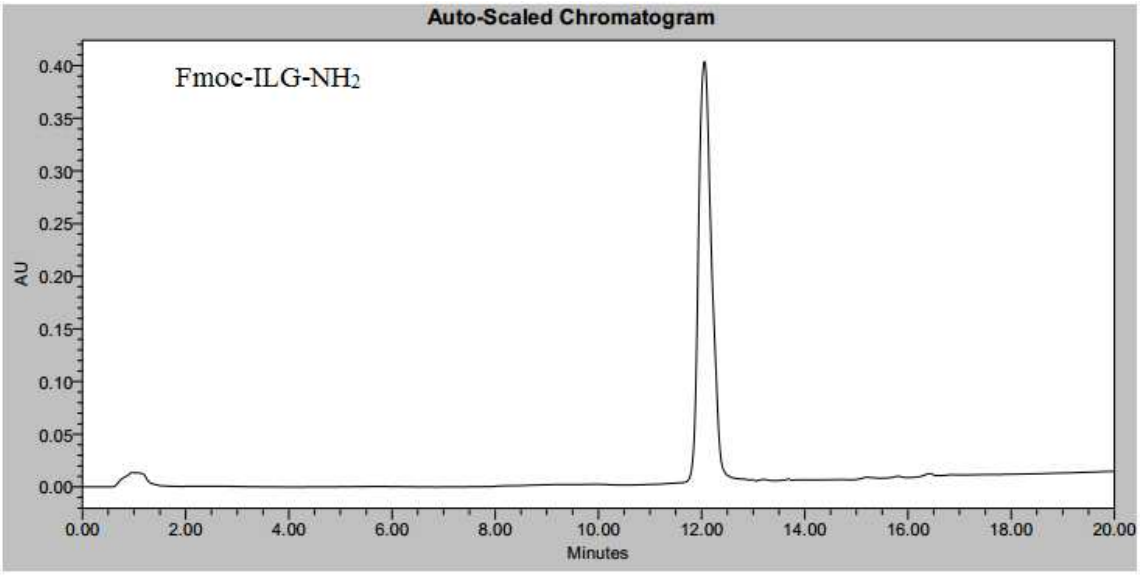


Figure S141: HPLC chromatogram of Fmoc-ILG-NH_2 (entry 2, Table S1).

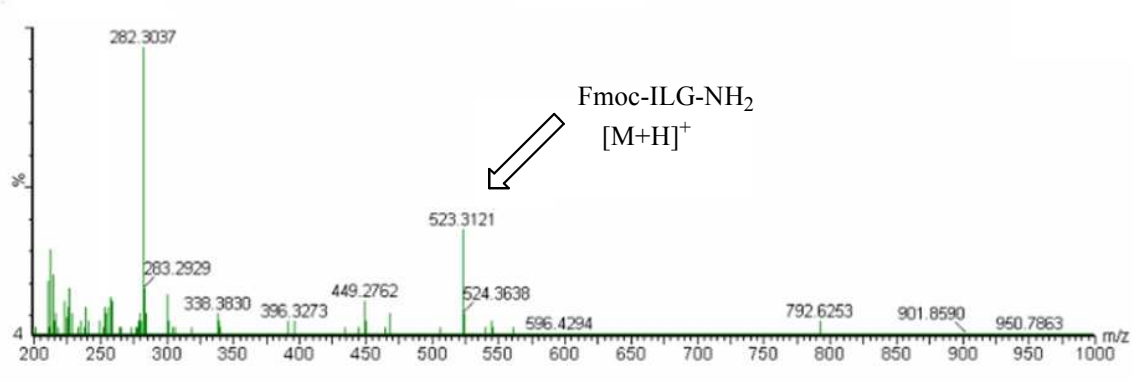


Figure S142: ESI-MS spectrum of the peak of the above chromatogram, Fmoc-ILG-NH_2 peptide (entry 2, Table S1).

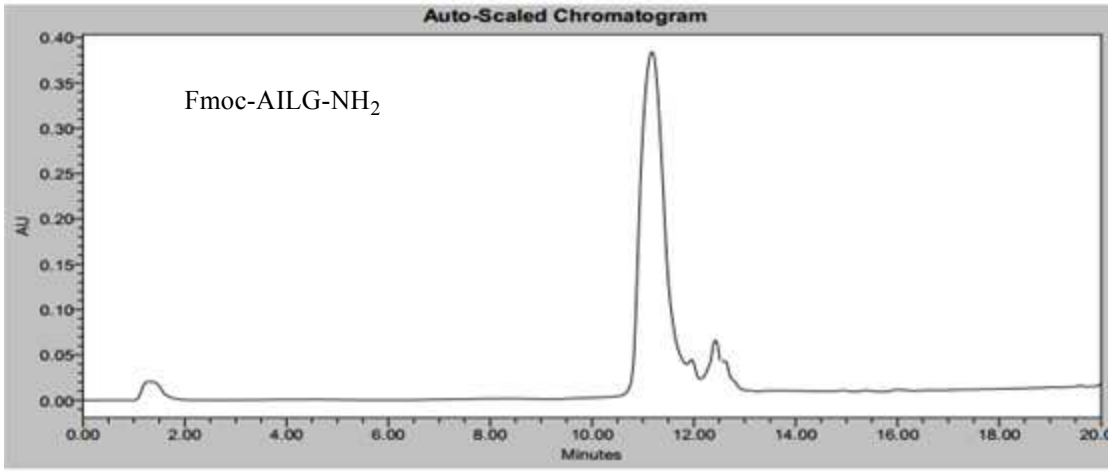


Figure S143: HPLC chromatogram of Fmoc-AILG-NH_2 (entry 3, Table S1).

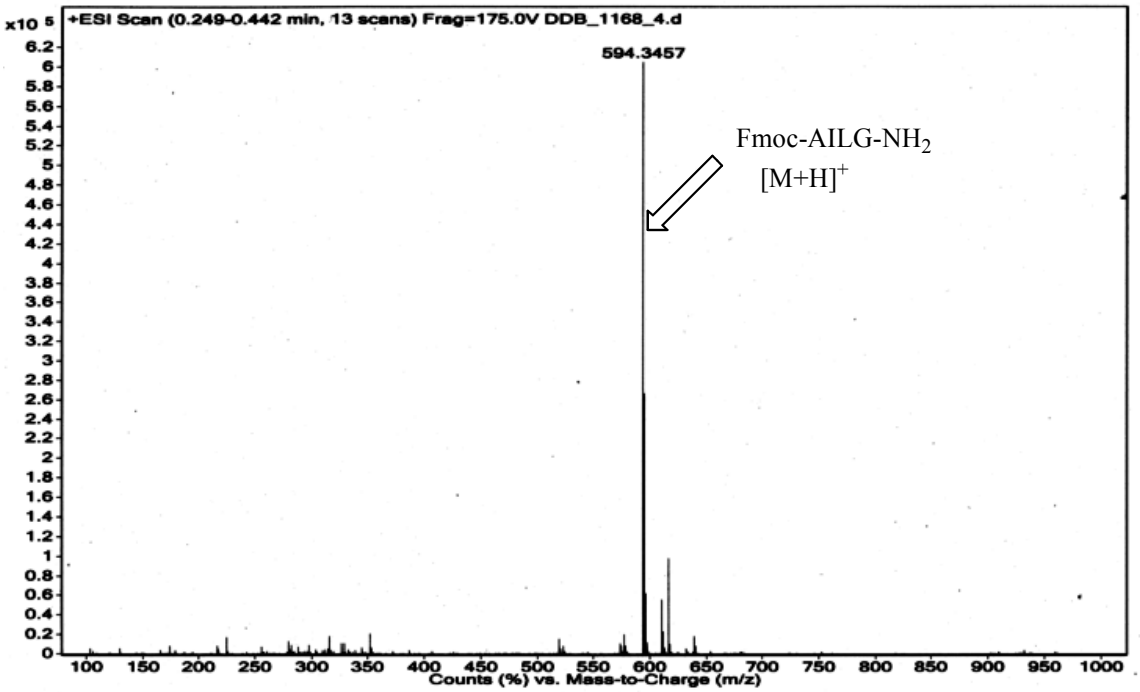


Figure S144: ESI-MS spectrum of Fmoc-AILG-NH_2 peptide, highest peak of above chromatogram (entry 3, Table S1).

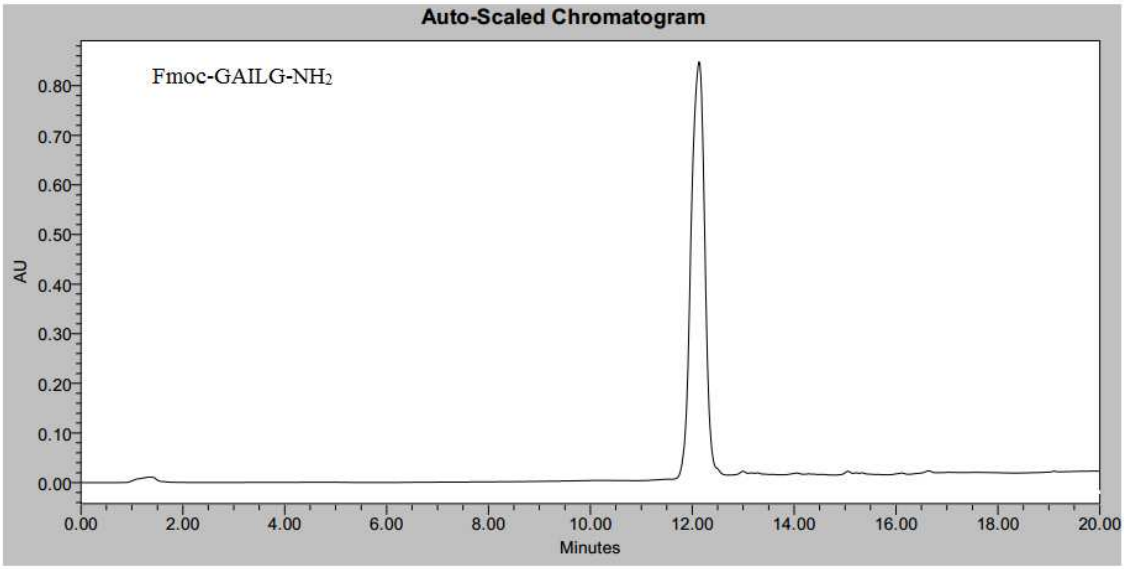


Figure S145: HPLC chromatogram of Fmoc-GAILG-NH_2 (entry 4, Table S1).

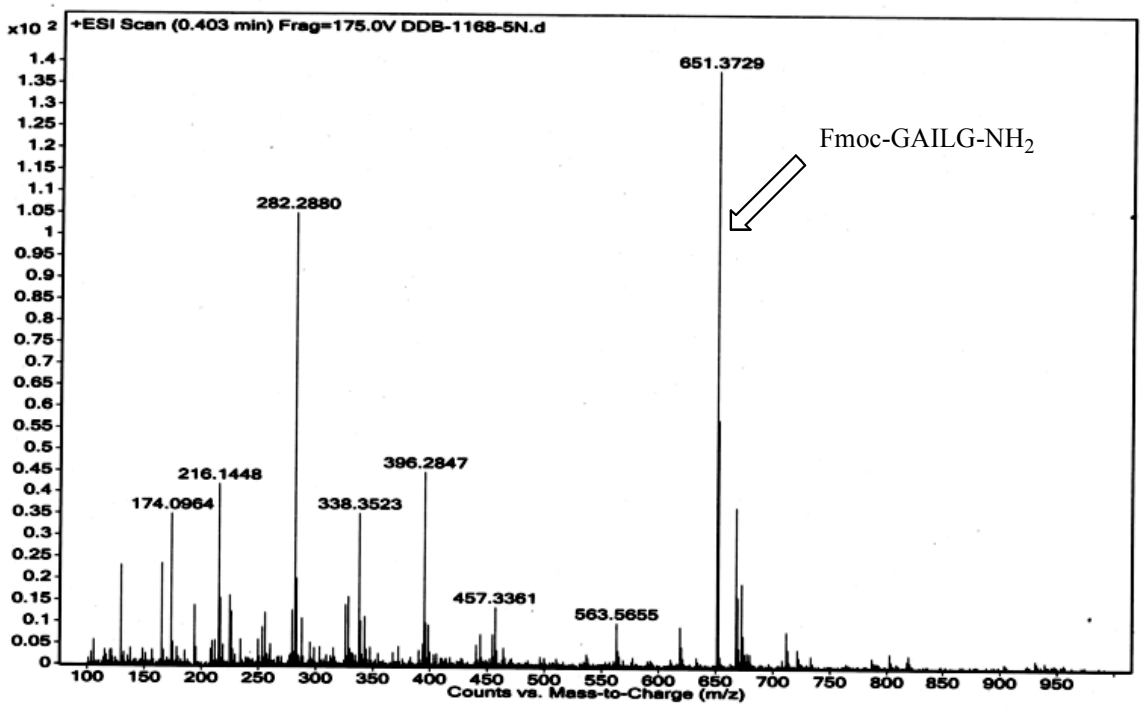


Figure S146: ESI-MS spectrum of Fmoc-GAILG-NH_2 peptide, peak of the above chromatogram (entry 4, Table S1).

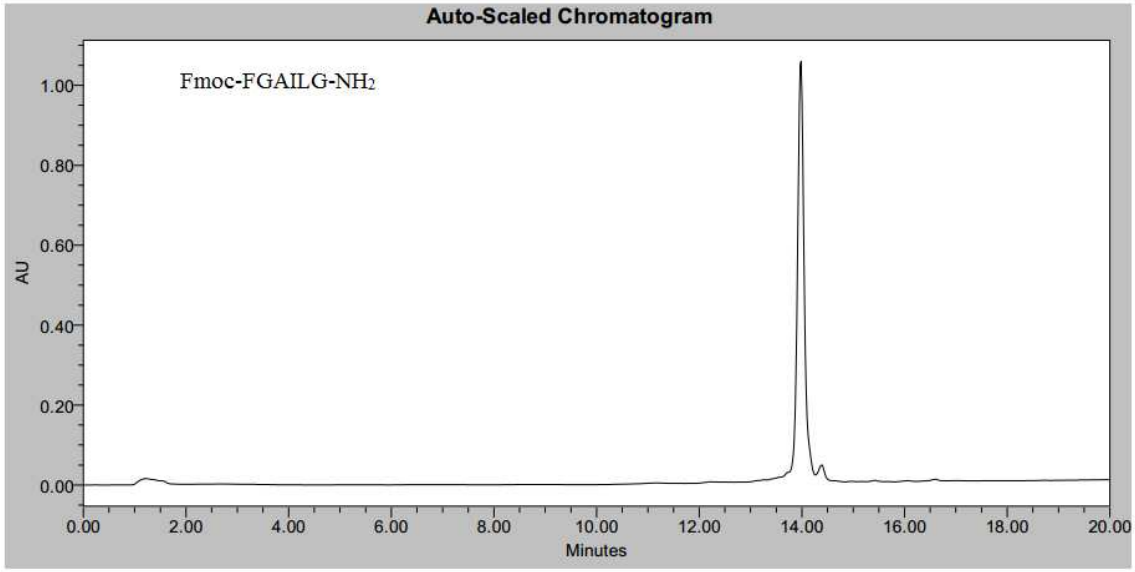


Figure S147: HPLC chromatogram of Fmoc-FGAILG-NH_2 (entry 5, Table S1).

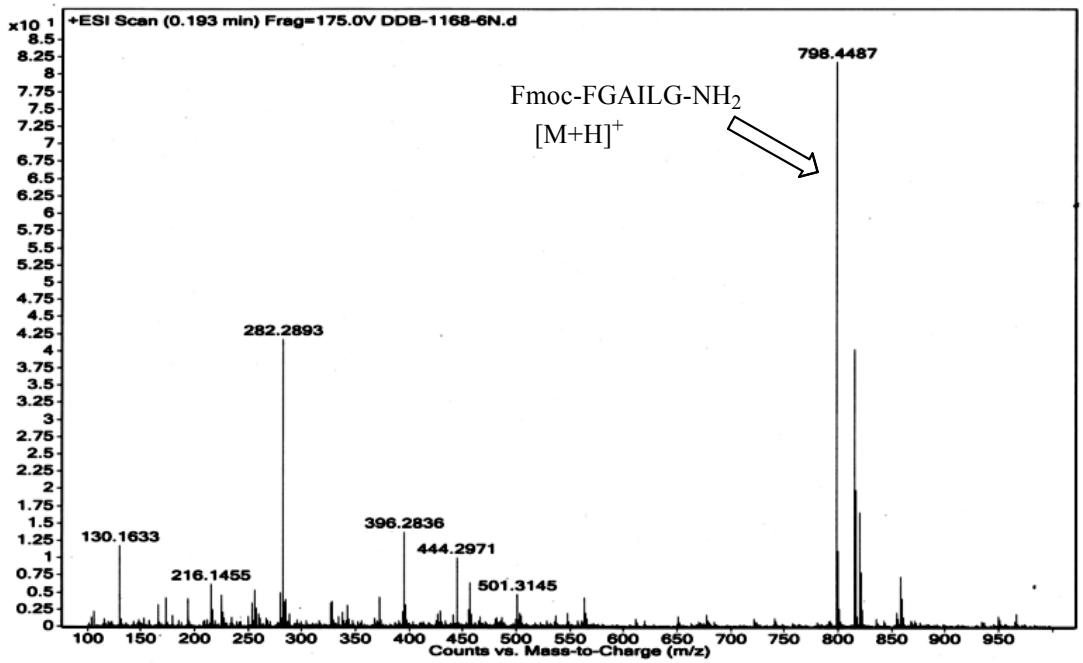


Figure S148: ESI-MS spectrum of Fmoc-FGAILG-NH_2 peptide, peak of the above chromatogram (entry 5, Table S1).

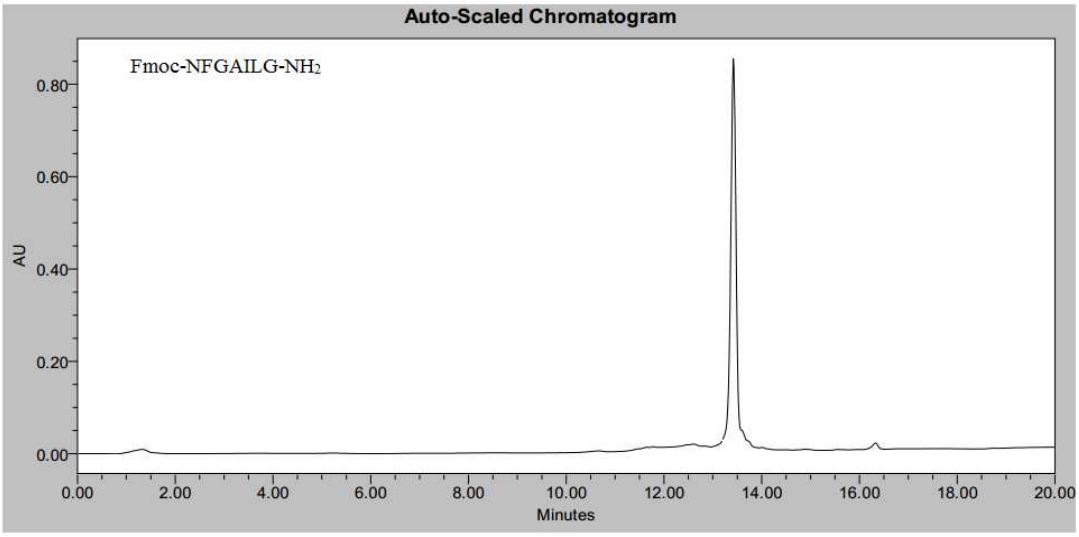


Figure S149: HPLC chromatogram of Fmoc-NFGAILG-NH_2 (entry 6, Table S1).

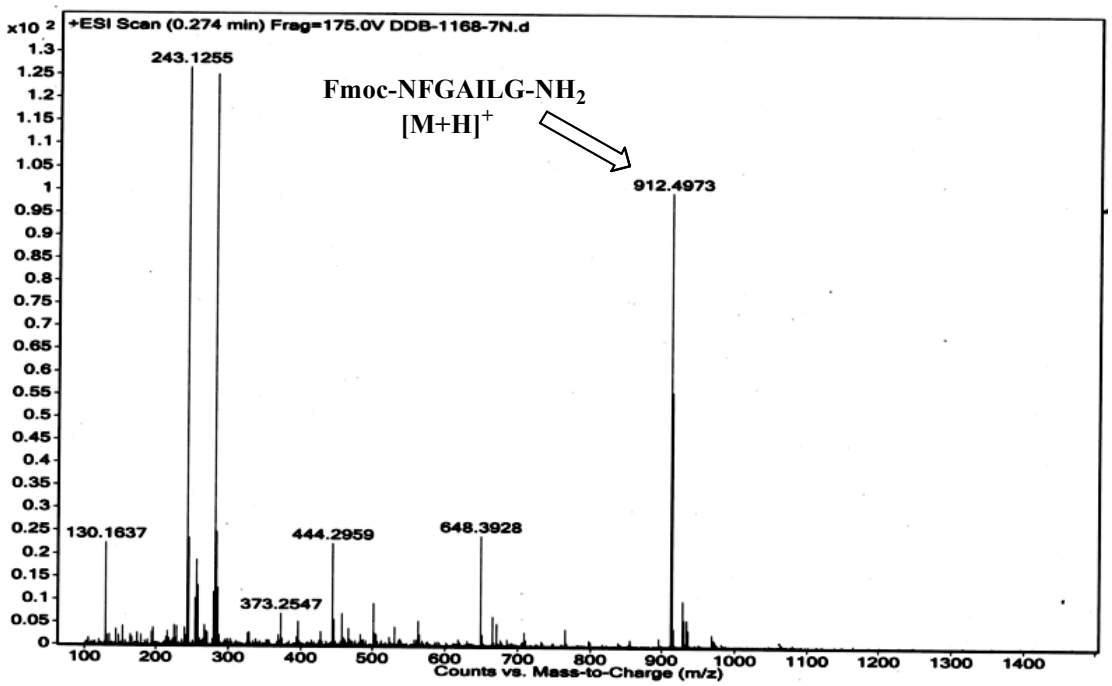


Figure S150: ESI-MS spectrum of Fmoc-NFGAILG-NH_2 peptide, peak of the above chromatogram (entry 6, Table S1).

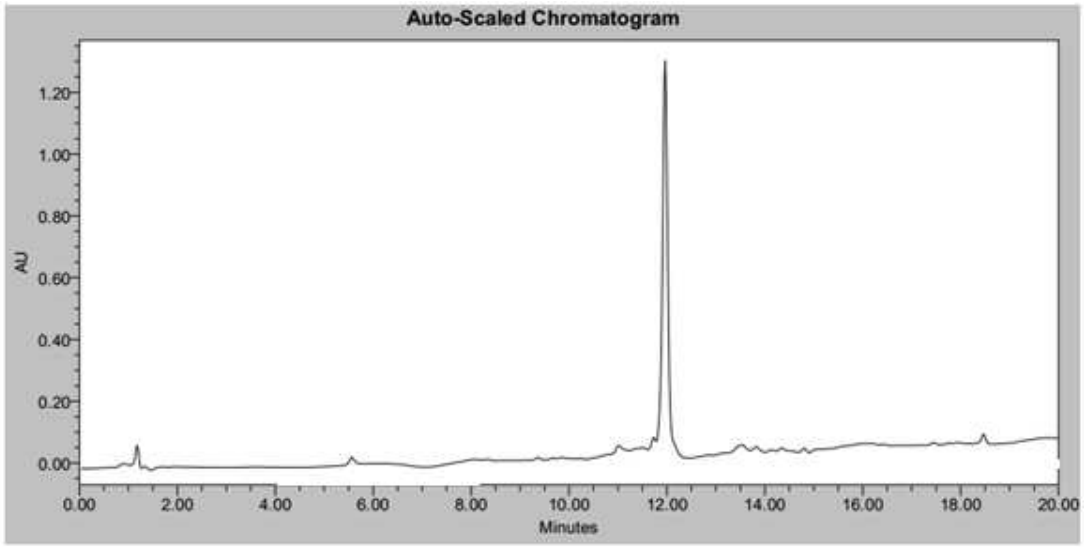


Figure S151: HPLC chromatogram NFGAIILG-NH_2 (Figure 3a, before purification).

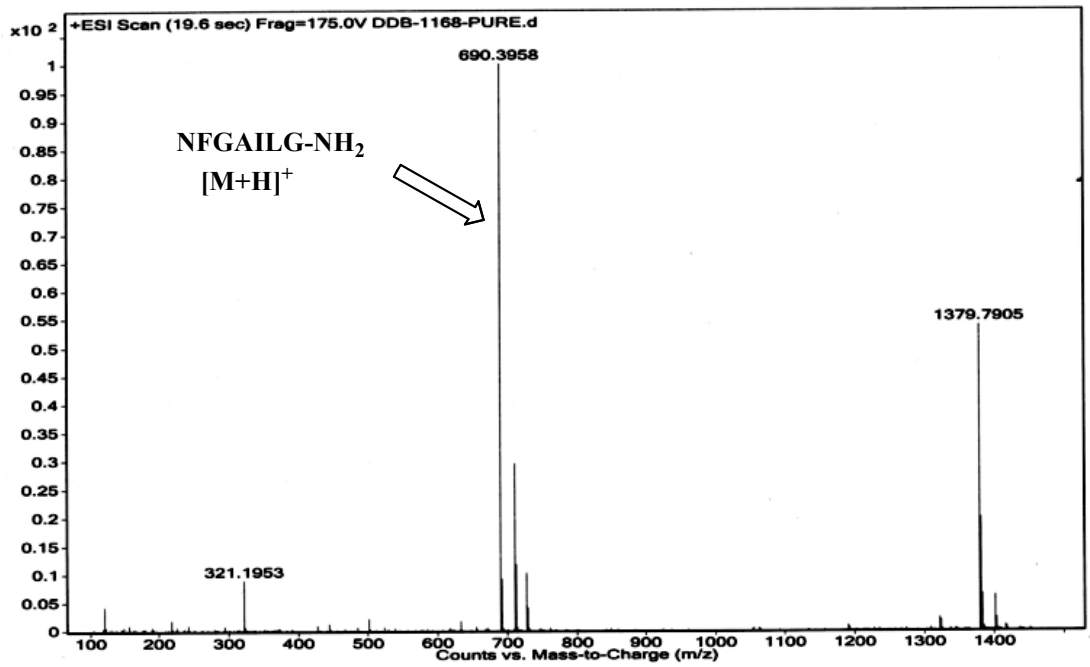


Figure S152: ESI-MS spectrum of NFGAILG-NH_2 peptide (Figure 3a), peak of above chromatogram.

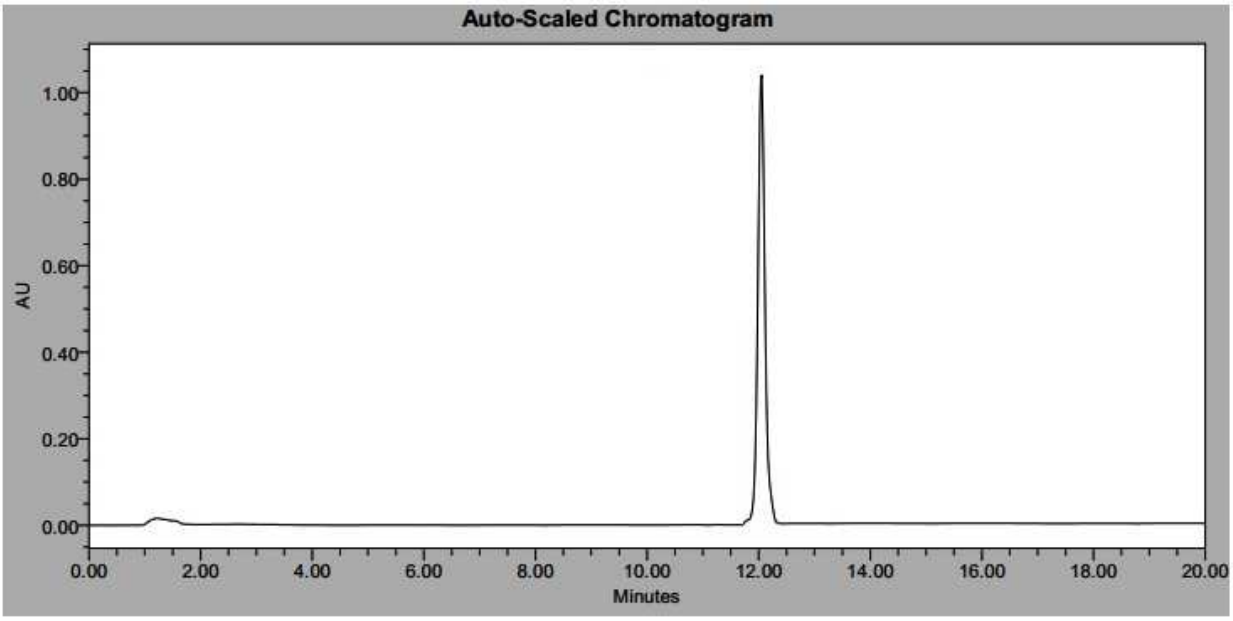


Figure S153: HPLC chromatogram of purified NFGAIILG-NH_2 (Figure 3a).

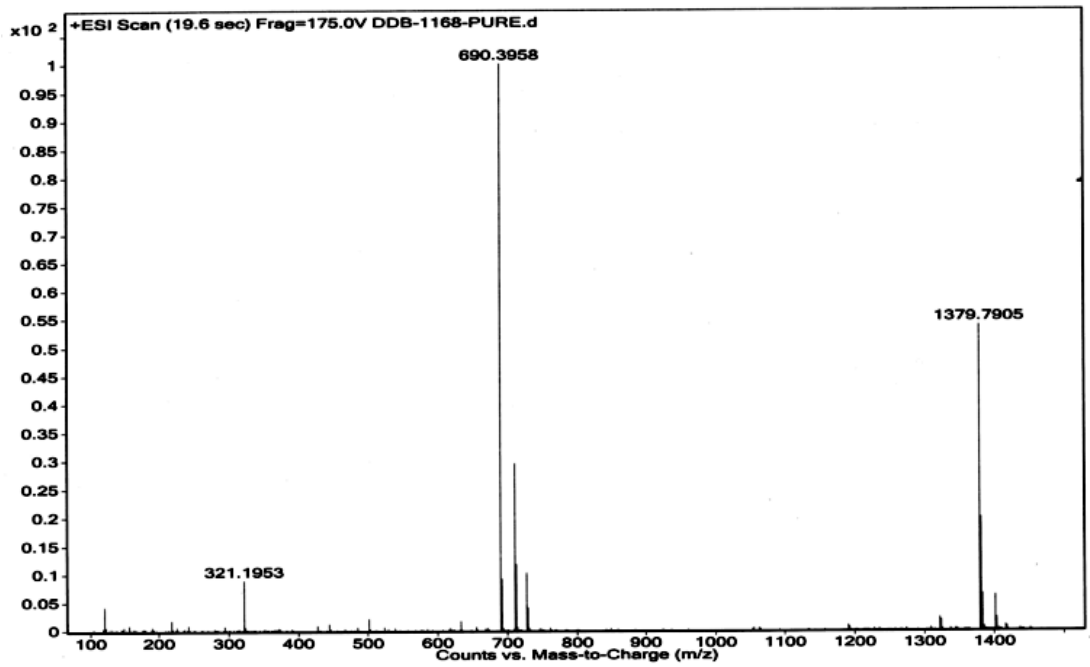


Figure S154: ESI-MS spectrum of purified NFGAILG-NH_2 peptide (Figure 3a), peak of the above chromatogram.

10) HPLC chromatograms and mass spectra of the products after test cleavage of VQAAIDYING-NH_2 (Figure 2b) via solid phase synthesis:

The crude products after each coupling step were cleaved from the resin and precipitated by cold ether, then analyzed by reverse phase HPLC, symmetry C8 analytical column, with linear gradient of 20 min (5 to 100 % acetonitrile in water).

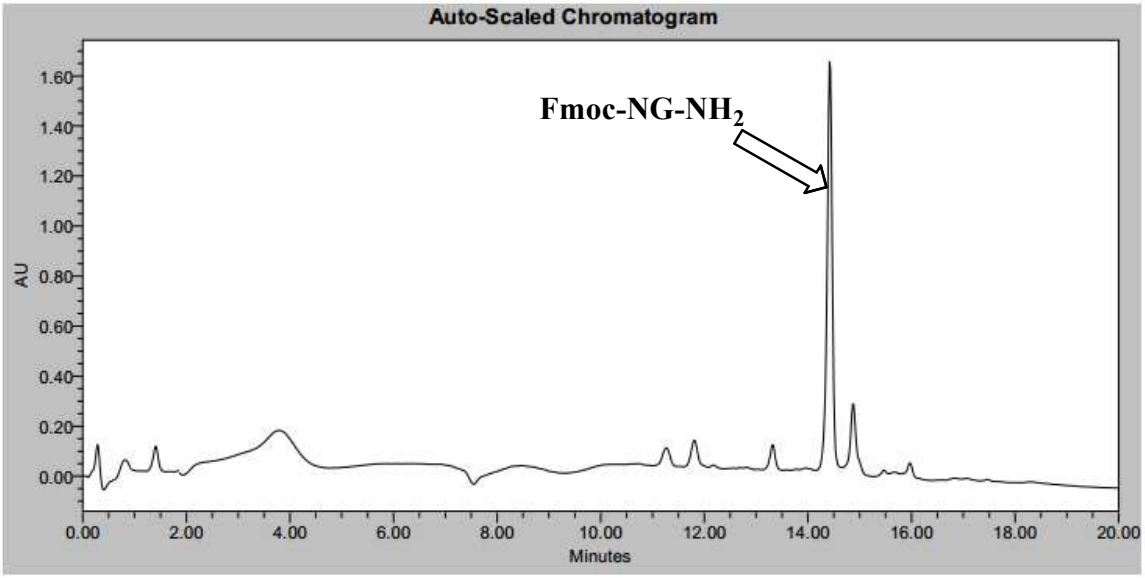


Figure S155: HPLC chromatogram of Fmoc-NG-NH_2.

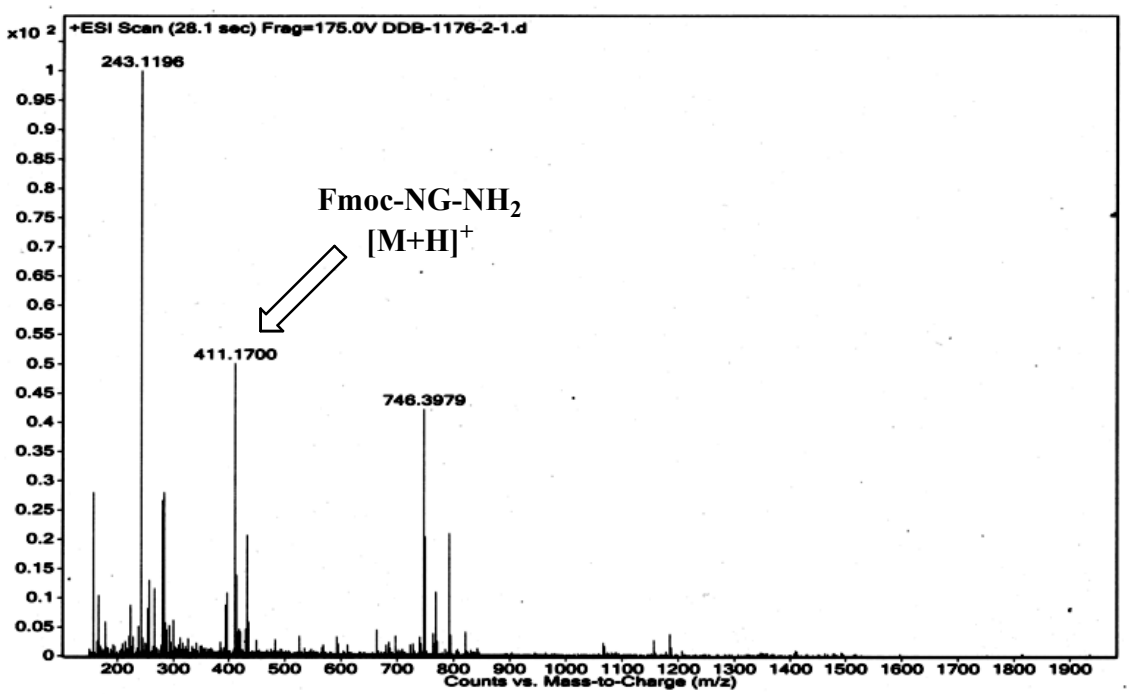


Figure S156: ESI-MS spectrum of the indicated peak of the above chromatogram, Fmoc-NG-NH_2 peptide.

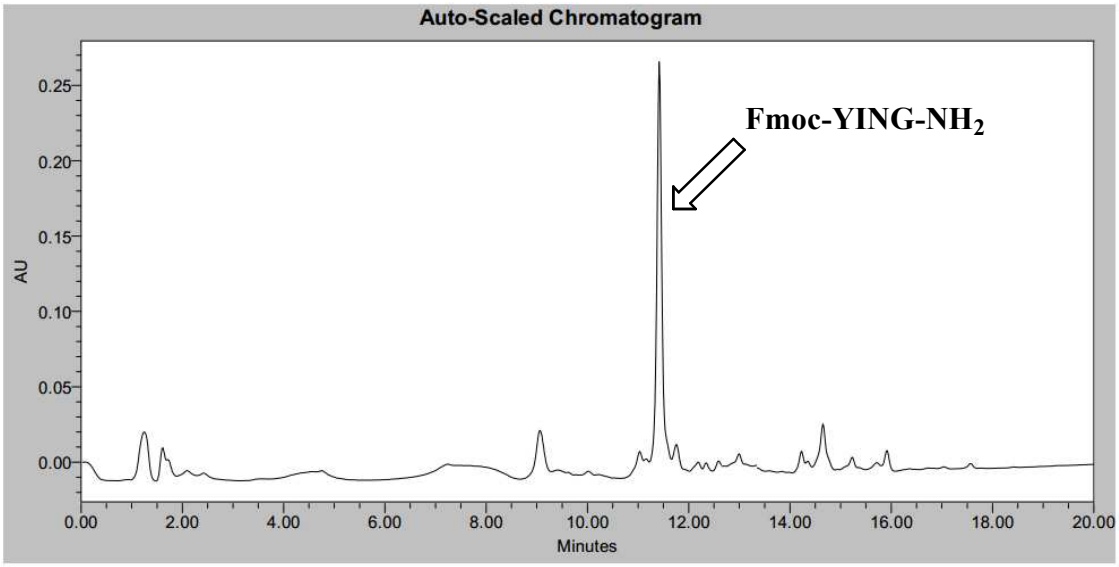


Figure S157: HPLC chromatogram of Fmoc-YING-NH_2.

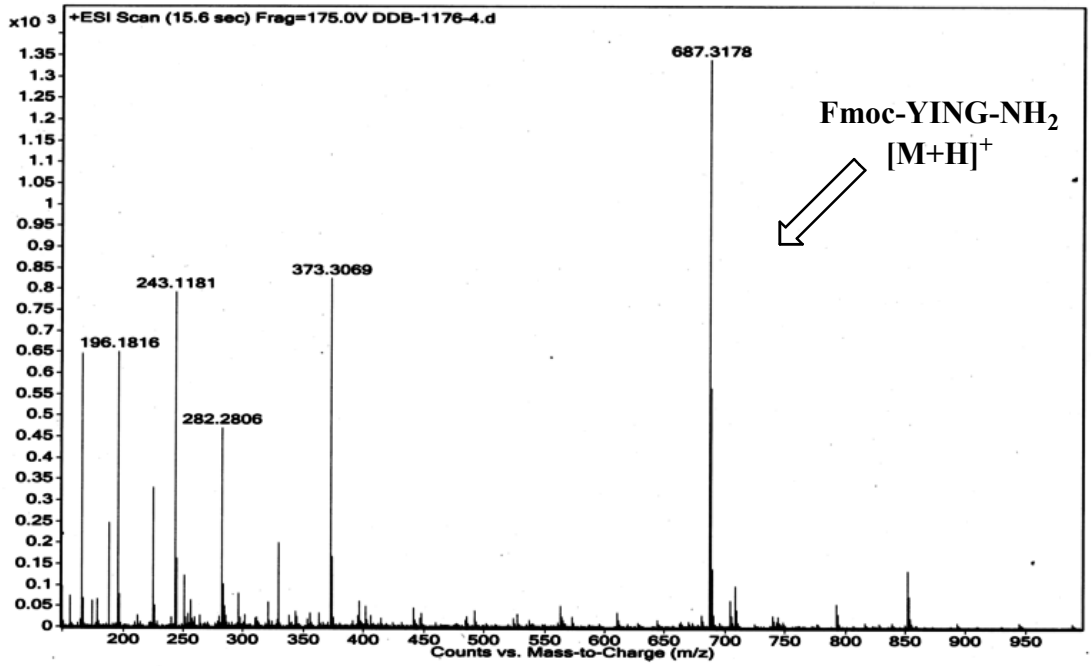


Figure S158: ESI-MS spectrum of the indicated peak in Figure S157, Fmoc-YING-NH_2 peptide.

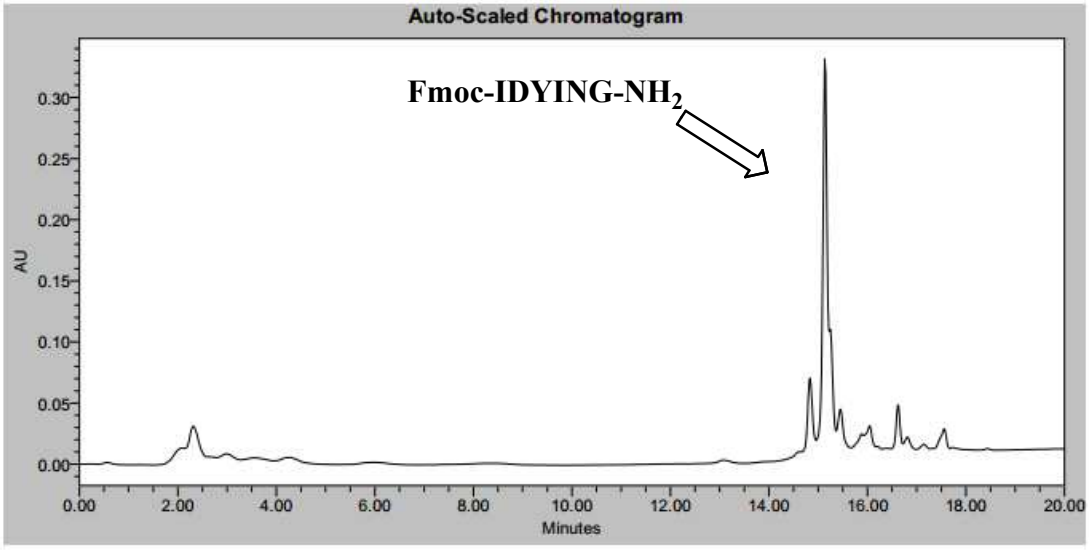


Figure S159: HPLC chromatogram of Fmoc-IDYING-NH_2.

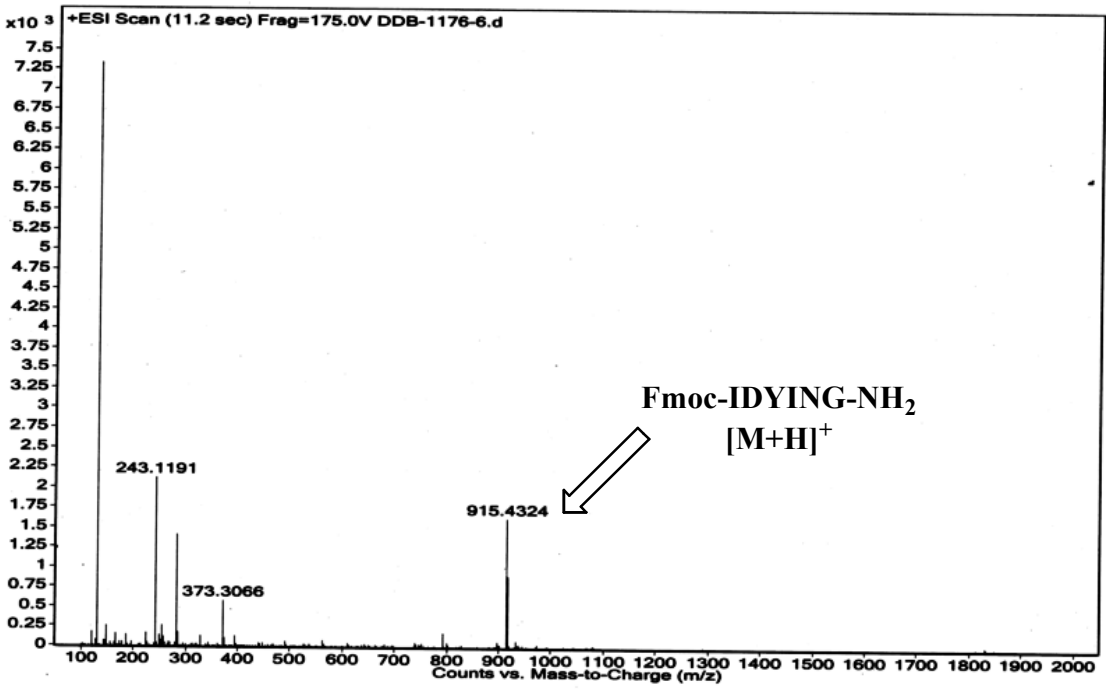


Figure S160: ESI-MS spectrum of the indicated peak in Figure S159, Fmoc-IDYING-NH_2 peptide.

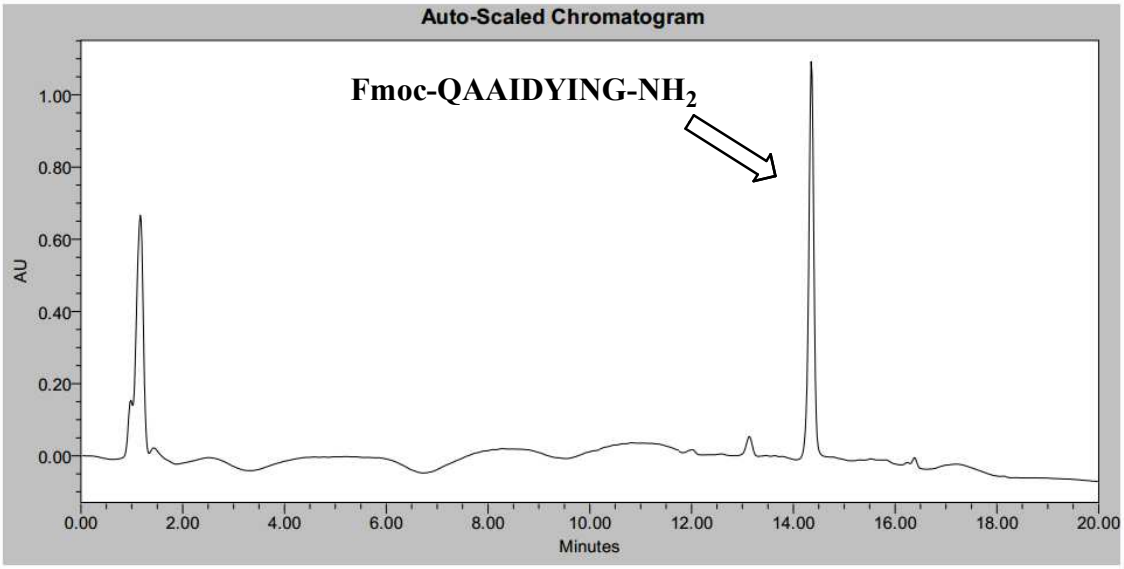


Figure S161: HPLC chromatogram of Fmoc-QAAIDYING-NH_2.

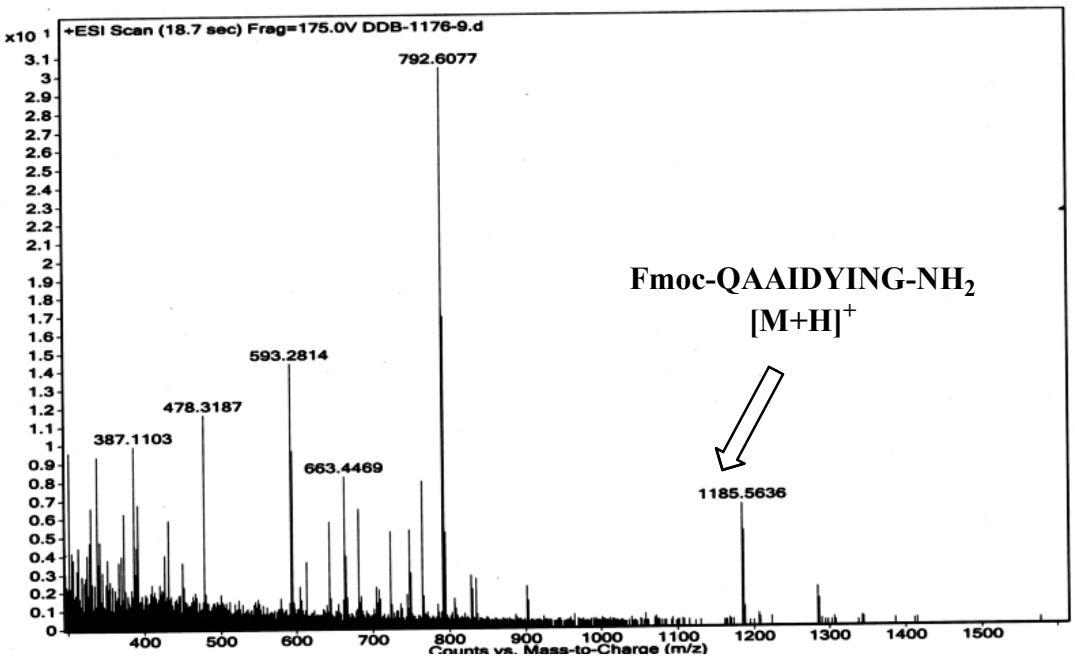


Figure S162: ESI-MS spectrum of the indicated peak in Figure S161, Fmoc-QAAIDYING-NH_2 peptide.

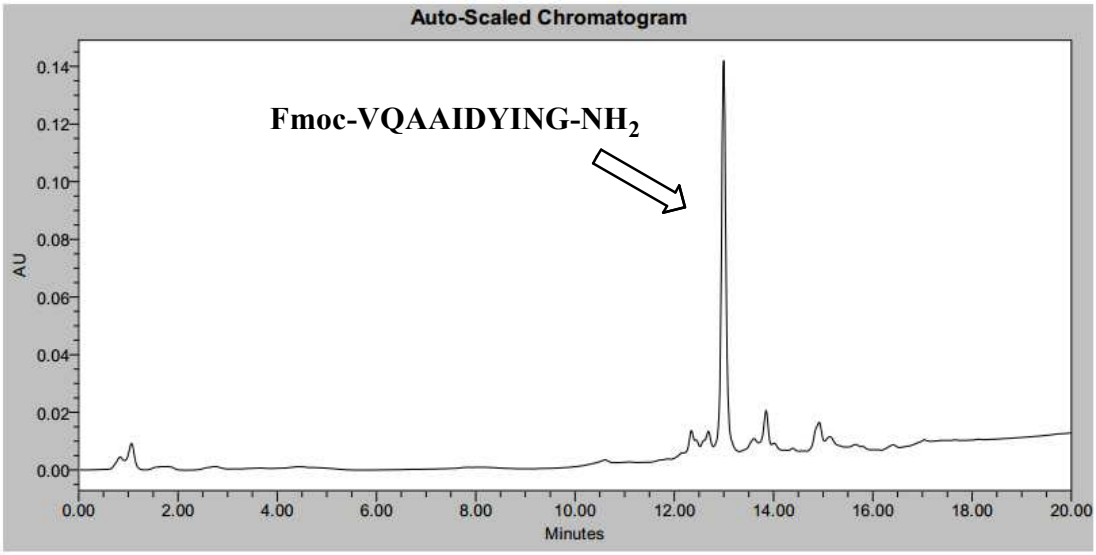


Figure S163: HPLC chromatogram of Fmoc-VQAAIDYING-NH_2.

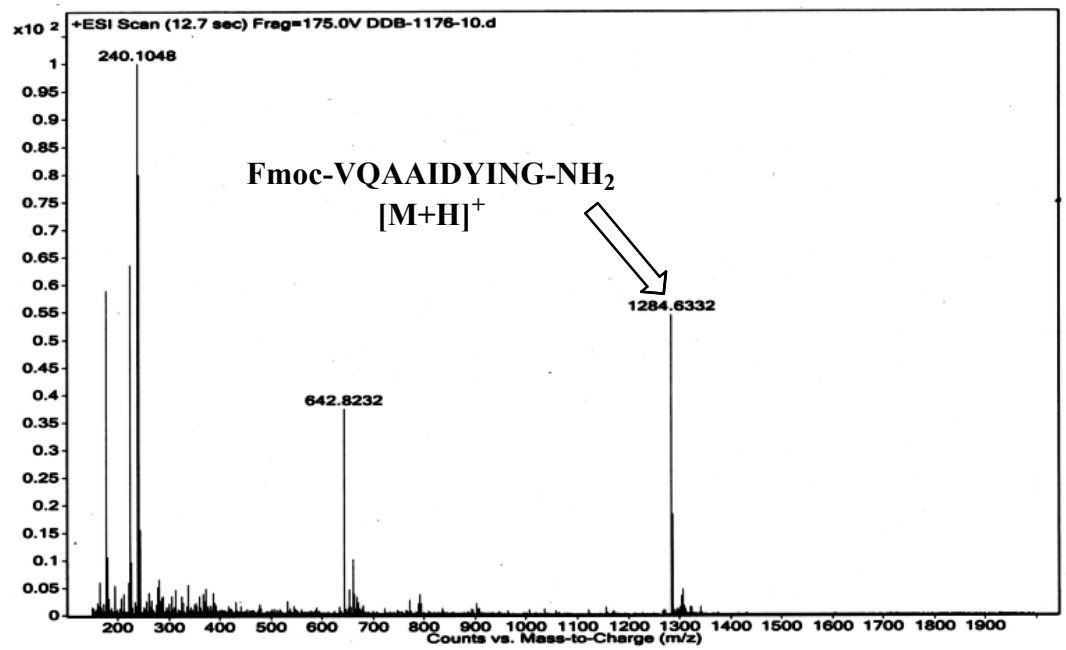


Figure S164: ESI-MS spectrum of the indicated peak in Figure S163, Fmoc-VQAAIDYING-NH_2 peptide.

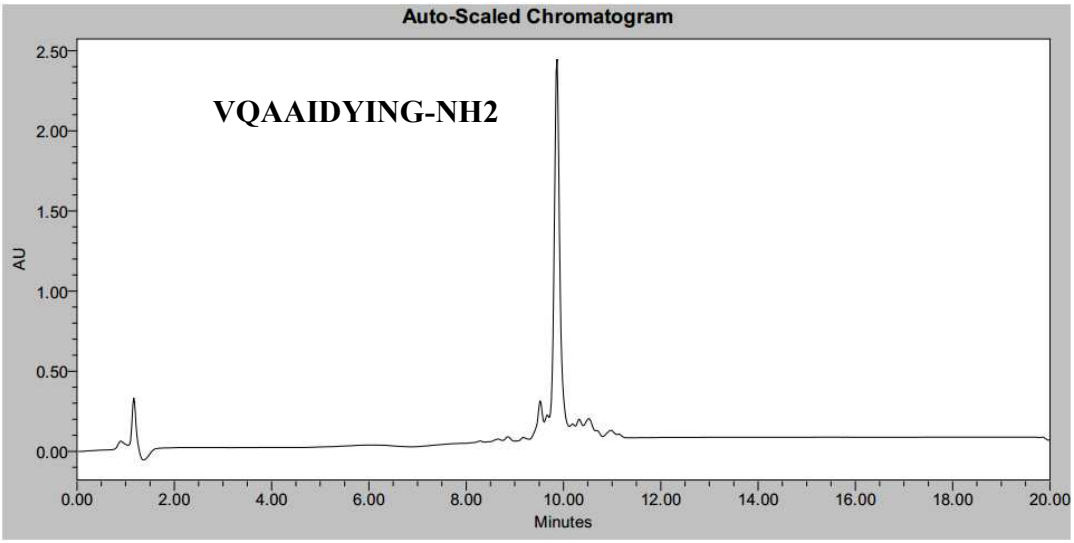


Figure S165: HPLC chromatogram of crude VQAAIDYING-NH_2 (Figure 3b).

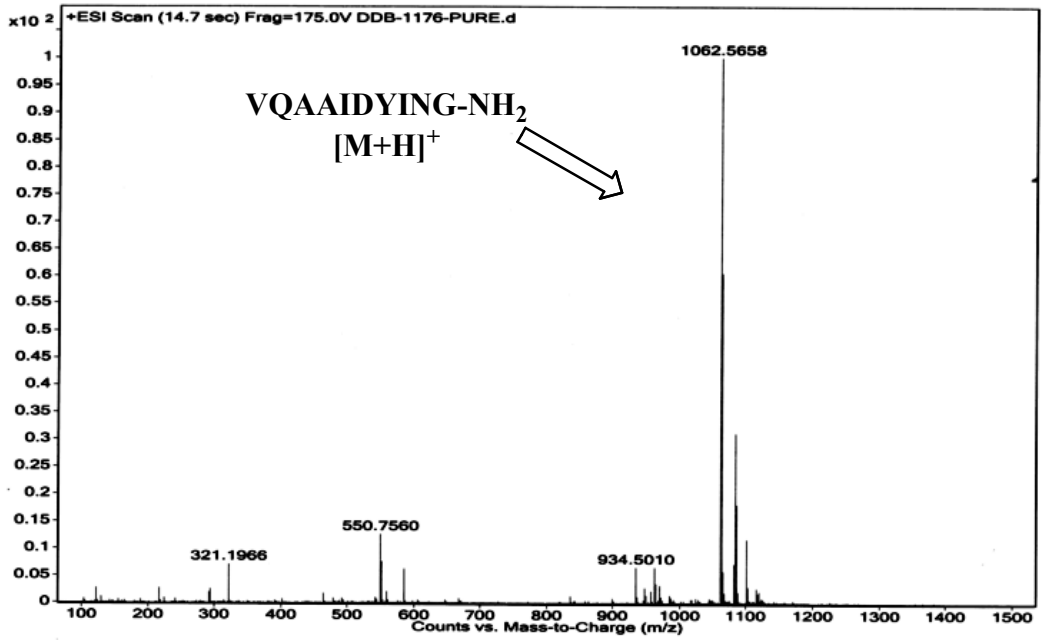


Figure S166: ESI-MS spectrum of crude VQAAIDYING-NH_2 (Figure 3b)

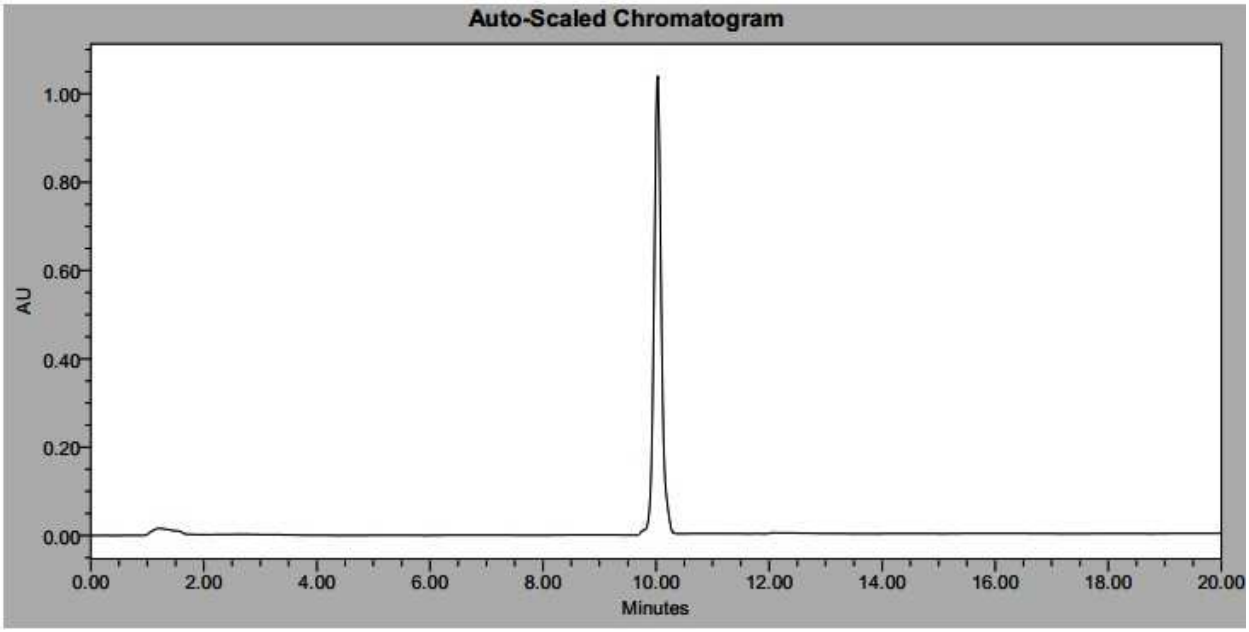


Figure S167: HPLC chromatogram of purified VQAAIDYING-NH_2 (Figure 3b).

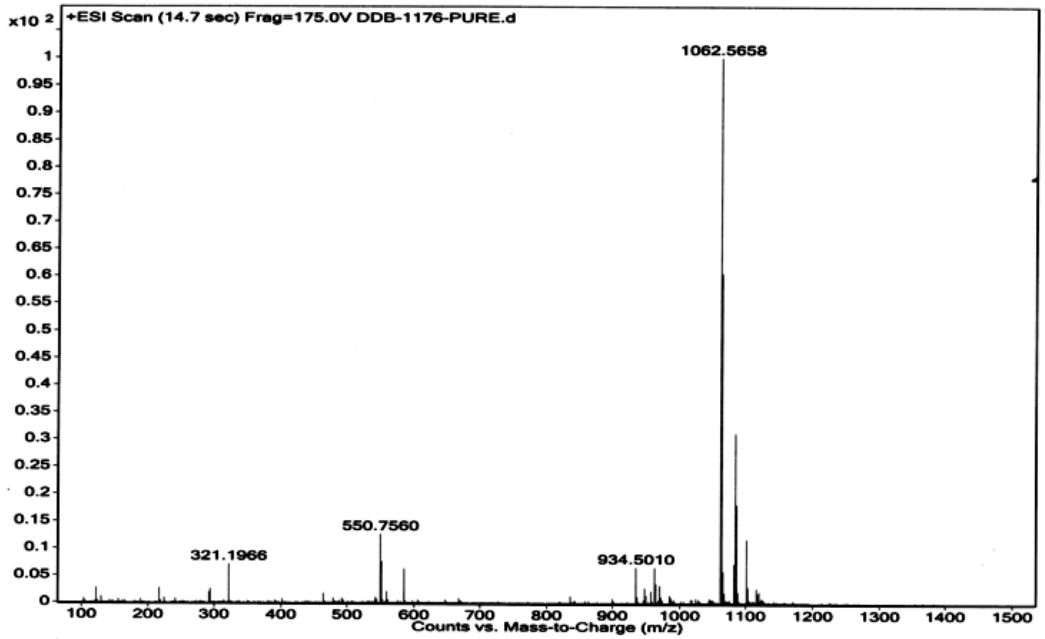


Figure S168: ESI-MS spectrum of purified VQAAIDYING-NH_2 (Figure 3b)

12) Crystal data of intermediate V (Figure 169), CCDC # 936483

	Oxyma ester of naphthanoic acid
Formula	$C_{16}H_{12}N_2O_4$
Mol. wt.	296.28
Crystal system	Orthorhombic
Space group	P2(1)2(1)2(1)
Temperature /K	296 (2)
Wavelength /Å	0.71073
a /Å	5.9579(4)
b /Å	8.2268(7)
c /Å	29.991(2)
α/°	90.00
β/°	90.00
γ/°	90.00
V/ $Å^3$	1470.0(2)
Z	4

Density/Mgm^{-3}	1.339
F(000)	616
Total no. of reflections	2425
Reflections, I > 2σ(I)	1708
Max. 2θ/°	25.00
Ranges (h, k, l)	-7<= h <=6 -7<= k <=9 -26<= l <=35
Complete to 2θ (%)	25.00
Refinement method	Full-matrix least-squares on F^2
WR_2(all data)	0.1765
Goof (F^2)	0.905
R indices [I > 2σ(I)]	0.0562
R indices (all data)	0.0801

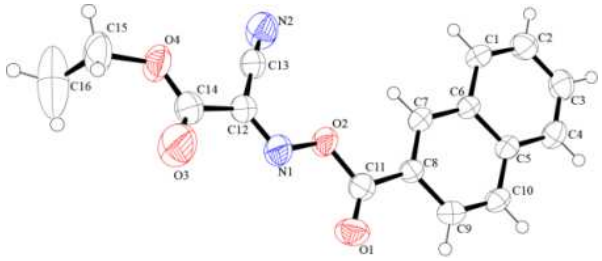


Figure S169. X-ray crystallographic structure of the intermediate **V** (ORTEP diagram with ellipsoid of 50% probability, CCDC No. 936483).