

General, Mild, and Metal-Free Synthesis of Phenyl Selenoesters from Anhydrides and Their Use in Peptide Synthesis

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Supporting Information

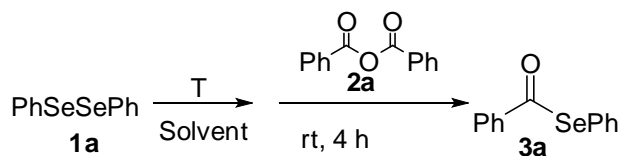
Table of Contents

Model Studies of Selenoester 3a Synthesis from Benzoic Anhydride	SI 3
Acylation of Piperidine in DMF	SI 4
Acylation of Amines 11a and 11e with 4 and 5	SI 4
Preparation of <i>N</i>-Acryloyl-proline methyl ester 26	SI 5
Potential Epimerization Studies of Dipeptides 14a	SI 6
Potential Epimerization Studies of Dipeptides 14b	SI 8
Potential Epimerization Studies of Dipeptides 14c	SI 10
Epimerization Studies of Fmoc-Phe-SePh	SI 12
HR-MALDI-MS/MS analysis of Pentapeptide 21	SI 16
Supporting references	SI 17
¹H and ¹³C-NMR Spectra	SI 18

Model Studies of Selenoester **3a** Synthesis from Benzoic Anhydride

The model reaction of benzoic anhydride **2a** with diphenyl diselenide **1a** was conducted to determine the best reaction conditions. Initially, the effect of solvents was tested. After reduction of diphenyl diselenide (characteristic yellow colour vanishing) with sodium borohydride at a fixed temperature (Table S1) in the proper solvent, the reaction mixture was cooled to room temperature (30 min) and benzoic anhydride was added. The desired selenoesters were obtained after column chromatography with yields ranging from 67% to 87%.

Table S1. Screening conditions for the acylation of diphenyl diselenide with benzoic anhydride^a in different solvents



Entry	Solvent	T (°C) ^b	t (min) ^b	Yield (%) ^c
1	DMF	90	30	76
2	THF/DMF ^d 3:1	100	60	70
3	THF	90	60	67
4	EtOAc	40	60	87

a) All reactions were run with **1a** (0.5 mmol), **2a** (1.1 mmol) and NaBH₄ (1 mmol) in solvent (6 mL) at the indicated temperature and time.

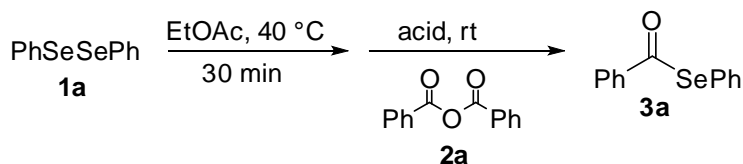
b) Values refer to the exclusive reduction of the diselenide.

c) Isolated yields

d) Sodium was employed for the reduction of diphenyl diselenide.¹

Among the solvents screened, EtOAc was the most efficient solvent for the reduction step (entry 4, table 1). However, we were delighted to find that the yield of the desired product **3a** could be improved to 94% when acetic acid was added at room temperature after the reduction of diphenyl diselenide. It is reasonable to assume that the sodium borohydride reduction of diphenyl diselenide in EtOAc seems to form less nucleophilic selenium species derived from borane byproduct complexation.² The addition of acid produced different effects on reaction yield (Table S2). To this end, after the reduction of diphenyl diselenide in EtOAc, we added an excess (5 mmol) of different acids at room temperature followed by the addition of benzoic anhydride **2a**. The addition of acid was accompanied by evolution of gas. Glacial acetic acid in EtOAc provided selenoester **3a** in 94% very high yield (entry 4, table S2). Other acids, such as concentrated hydrochloric acid, 85% phosphoric acid and powdered sodium hydrogen sulfate gave only moderate or very low yields of product. This could be due to the instability of the benzoic anhydride in presence of a strong acid.

Table S2. Variation of the acid used before benzoic anhydride^a addition



Entry	Acid	t (h) ^b	Yield (%) ^c
1	HCl	4	64
2	H ₃ PO ₄	2	35
3	NaHSO ₄	2	18
4	AcOH	5	94 ^d

a) All reactions were run with **1a** (0.5 mmol), **2a** (1.1 mmol), NaBH₄ (1 mmol) and acid (5 mmol) in Ethyl Acetate (6 mL).

b) Time employed to complete the acylation reaction at room temperature.

c) Isolated yields.

d) The reaction with BzCl gave **3a** in 80% yield.

Acylation of Piperidine in DMF

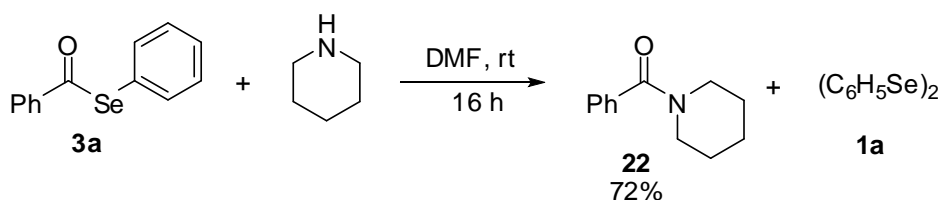


Figure S1. Benzoylation of piperidine with selenoesters **3a** in DMF

To a solution of *Se*-phenyl selenocarboxylate **3a** (60 mg, 0.23 mmol) in DMF (1 mL) piperidine (0.05 mL, 0.57 mmol) was added and the mixture left open to the air. The mixture was stirred at room temperature until the consumption of the selenoester was complete (TLC monitoring). After stirring the mixture for 16 h, HCl 1M (10 mL) was added and the mixture extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with brine (10 mL), dried over sodium sulfate anhydrous and then evaporated. The commercially available 1-benzoylpiperidine **22** (37 mg, 85% yield) was obtained after column chromatography on silica gel using a mixture of ethyl acetate-dichloromethane (2:8) as eluent.

Acylation of Amines **11a** and **11e** with **4** and **5**

Acylation of some amines with selenoesters **4** and **5** was examined (figure S2).

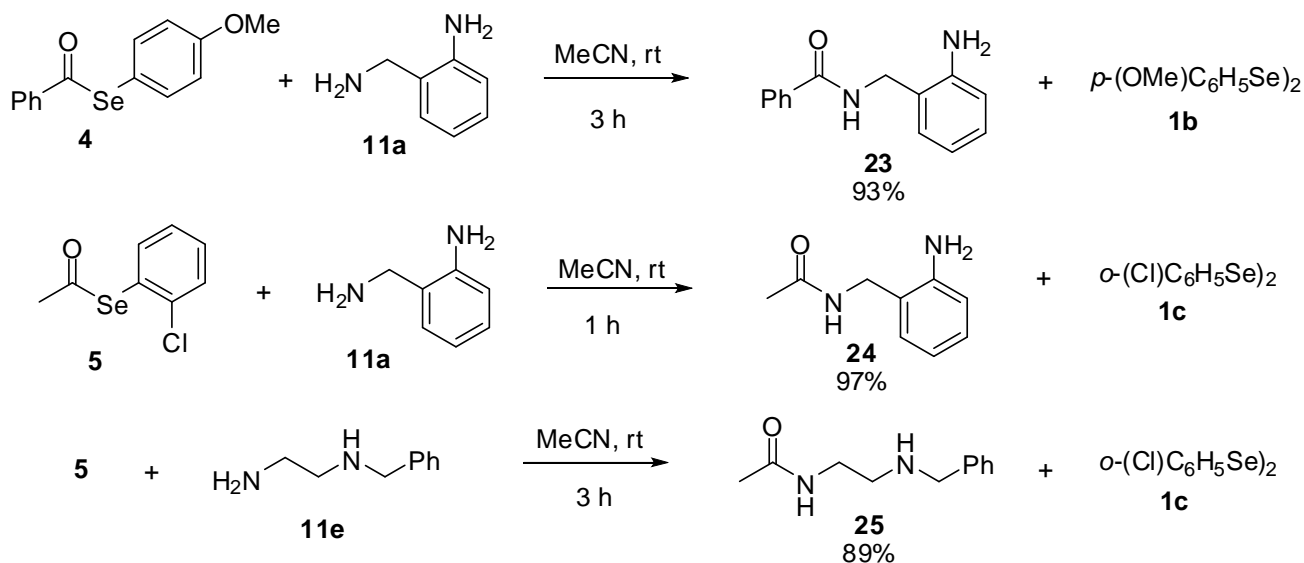


Figure 2. Acylation of amines **11a** and **11e** with selenoesters **4** and **5**

Synthesis of Amide **23**

A mixture of selenoester **4** (0.13 g, 0.44 mmol) and (2-aminobenzyl)amine **11a** (50 mg, 0.40 mmol) in MeCN (4 mL) was stirred at room temperature under air atmosphere. After 3 h the reaction mixture was evaporated. The residue was purified by chromatography on silica gel using an ethyl acetate-dichloromethane mixture (1:9) as eluent to give **23** (84 mg, 93% yield). Spectral data were in accordance with the literature.³ Notably the diselenide **1b** could be also recovered.

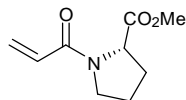
Synthesis of Amide **24**

A mixture of selenoester **5** (0.10 g, 0.44 mmol) and (2-aminobenzyl)amine **11a** (50 mg, 0.40 mmol) in MeCN (4 mL) was stirred at room temperature under air atmosphere. After 1 h the reaction mixture was evaporated. The residue was purified by chromatography on silica gel using an ethyl acetate-dichloromethane mixture (4:96) as eluent to give **24** (64 mg, 97% yield). Spectral data were in accordance with the literature.⁴ Notably the diselenide **1c** (76 mg, 98% yield) was recovered.

Synthesis of Amide 25

A mixture of selenoester **5** (0.16 g, 0.68 mmol) and *N*-benzylethane-1,2-diamine **11e** (93 mg, 0.62 mmol) in MeCN (5 mL) was stirred at room temperature under air atmosphere. After 3 h the reaction mixture was evaporated. The residue was purified by chromatography on silica gel using an ethyl acetate-dichloromethane mixture (5:95) as eluent to give **25** (105 mg, 89% yield). Spectral data were in accordance with the literature.⁵ Notably the diselenide **1c** could be recovered.

Preparation of *N*-Acryloyl-proline methyl ester **26**



Reaction of selenoester **31** with *L*-proline methyl ester hydrochloride **13c** gave the corresponding amide intermediate which was further elaborated. Thus, oxidation of the crude intermediate amide occurred smoothly in MeOH at 0 °C with an excess of hydrogen peroxide to give the corresponding selenoxide. The spontaneous *syn*-elimination finally gave the acrylamide derivative **26** in good global yield.

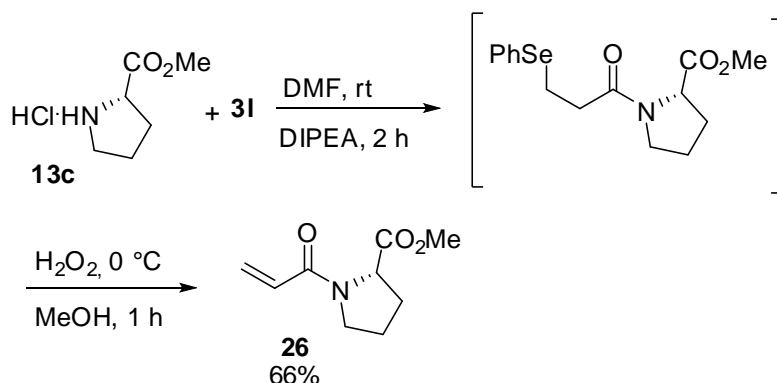
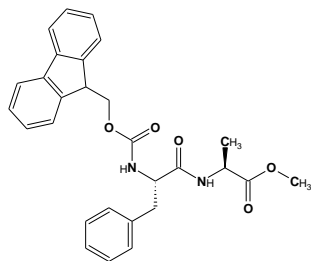


Figure S3. Preparation of *N*-acryloyl-proline methyl ester **26**

To a solution of *Se*-Phenyl 3-(phenylseleno)propaneselenoate **31** (1.11 g, 3 mmol) in 15 mL of DMF *L*-Proline methyl ester hydrochloride **13c** (1.00 g, 6.00 mmol) and DIPEA (1.32 mL, 7.5 mmol) were added and the resulting mixture was stirred (2 h) at room temperature under an atmosphere of air. Then the reaction mixture was poured into 5% hydrochloric acid solution (30 mL) and extracted with EtOAc (3 x 40 mL). The organic layer was washed with brine (10 mL), dried over sodium sulfate and evaporated. The work-up procedure yielded an oily residue which was passed through a silica pad and washed with ethyl acetate-dichloromethane mixture (1:9) to recover the diphenyl diselenide. Elution with a mixture of ethyl acetate-dichloromethane (4:6) gave the oily crude amide of sufficient purity for use in subsequent manipulation. This amide was dissolved in MeOH (16 mL) and hydrogen peroxide 30% was added (3.0 mL) at 0 °C. The progress of the reaction was monitored by TLC. After 1 h the reaction was quenched by addition of water (10 mL). The reaction mixture was then extracted with CH₂Cl₂ (3 x 30 mL) and the combined organic layers were washed with brine (10 mL), dried over sodium sulfate anhydrous and then evaporated. The pure amide **26** (0.37 g, 66% global yield) was obtained as a light yellow oil after column chromatography on silica gel using a methanol-dichloromethane mixture (6:94) as eluent. Spectral data were in accordance with the literature.⁶

Potential Epimerization Studies of Dipeptides 13a-c

Three sets of dipeptides were prepared and tested to evaluate the extent of epimerization of the amino acid selenophenyl esters: (i) Fmoc-Phe-Ala-OMe and its expected epimerization product, Fmoc-D-Phe-Ala-OMe. (ii) Fmoc-Val-TrpOMe and its expected epimerization product, Fmoc-D-Val-TrpOMe. (iii) Fmoc-Phe-ProOMe and its expected epimerization product, Fmoc-D-Phe-ProOMe.



Fmoc-Phe-Ala-OMe

The DL-diastereoisomer of Fmoc-Phe-Ala-OMe (**14a**) was prepared from D-Fmoc-Phe-OH with the procedure employed for the LL-diastereoisomer. Methyl *N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-L-phenylalanyl-L-alaninate **14a** was analyzed by chiral HPLC and compared with a sample of Fmoc-D-Phe-L-Ala-OMe as reference. The analysis revealed a 0.5% of epimerization confirming the very low racemization degree of our protocol (Figure S4).

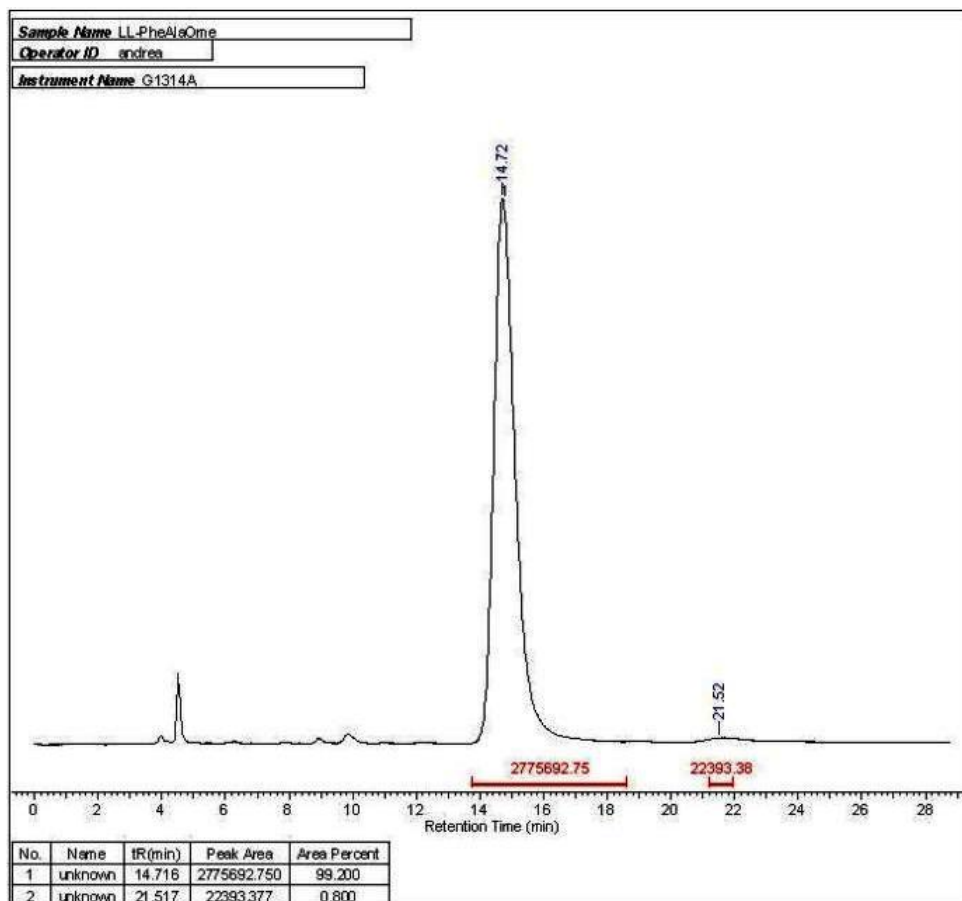


Figure S4. HPLC trace of dipeptide (LL)-**14a**. Phenomenex® Lux Cellulose-2, 4.6x250 mm; 1 mL/min hexane/i-PrOH 80:20, obs: 254 nm; retention times: 14.7 min (LL-diastereoisomer, major), 21.5 min (DL-diastereoisomer, minor), dr = 95.5:0.5.

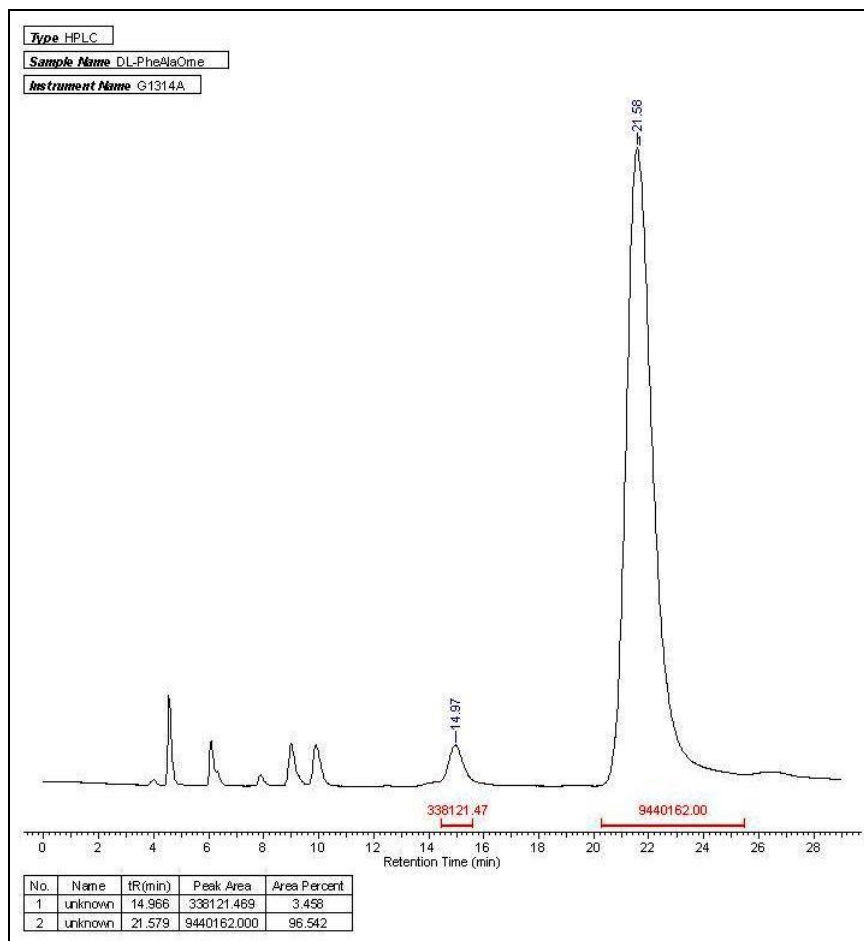


Figure S5. HPLC trace of (DL)-**14a** distereoisomer. Phenomenex® Lux Cellulose-2, 4.6x 250mm; 1 mL/min hexane/i-PrOH 80/20, obs: 254 nm; retention times: 14.9 min (LL-diastereoisomer, minor), 21.6 min (DL-diastereoisomer, major), dr = 3.5:96.5.

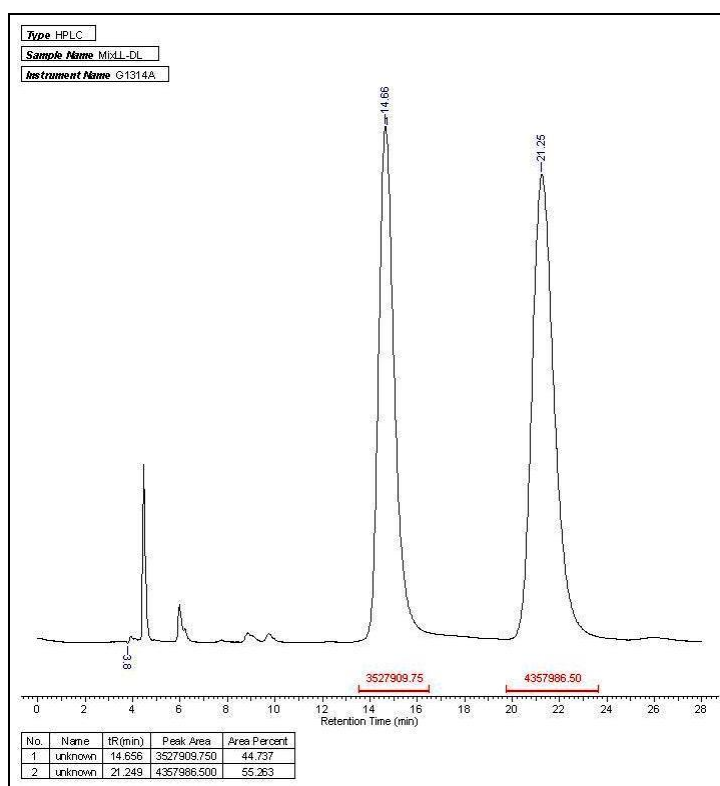
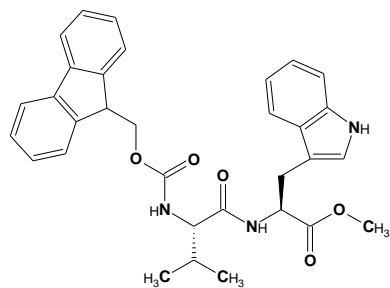


Figure S6. Representative HPLC trace of dipeptide (LL)-**14a** spiked with dipeptide epimer (DL)-**14a**. Phenomenex® Lux Cellulose-2, 4.6x250 mm; 1 mL/min hexane/i-PrOH 80/20, obs: 254 nm: retention times: 14.7 min (LL-diastereoisomer), 21.3 min (DL-diastereoisomer).



Fmoc-Val-TrpOMe

The procedure for the LL-diastereoisomer **14b** was followed to prepare the DL-diastereoisomer starting from D-Fmoc-Val-OH. Methyl *N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-L-valyl-L-tryptophanate **14b** was analyzed by chiral HPLC and compared with a sample of Fmoc-D-Val-L-Trp-OMe as reference. The analysis revealed no epimerization (Figure S7) confirming the very low racemization degree of our protocol.

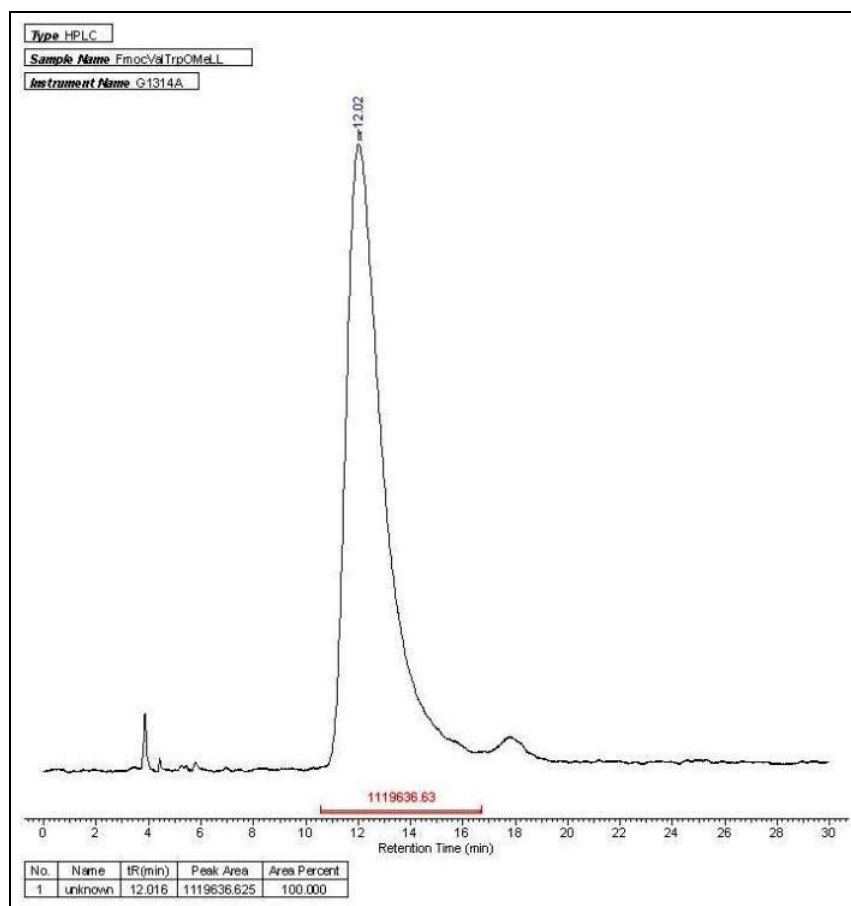


Figure S7. HPLC trace of dipeptide (LL)-**13b**. Phenomenex® Lux Amylose-2, 4.6x250 mm; 1 mL/min hexane/*i*-PrOH/EtOH 70:20:10, obs: 254 nm; retention times: 12.0 min (LL-diastereoisomer, major), 21.1 min (DL-diastereoisomer, minor), dr > 99.9:0.1.

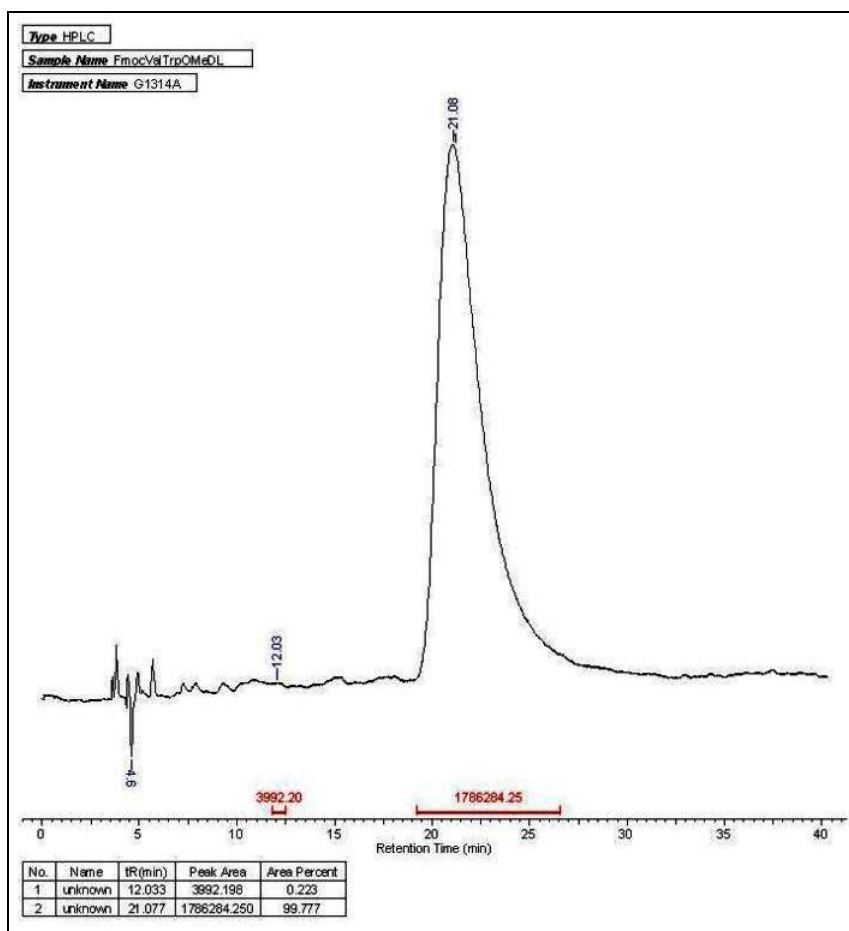


Figure S8. HPLC trace of dipeptide (DL)-**14b**. Phenomenex® Lux Amylose-2, 4.6x250 mm; 1 mL/min hexane/i-PrOH/EtOH 70:20:10, obs: 254 nm; retention times: 12.0 min (LL-diastereoisomer, minor), 21.1 min (DL-diastereoisomer, major), dr = 0.2:99.8

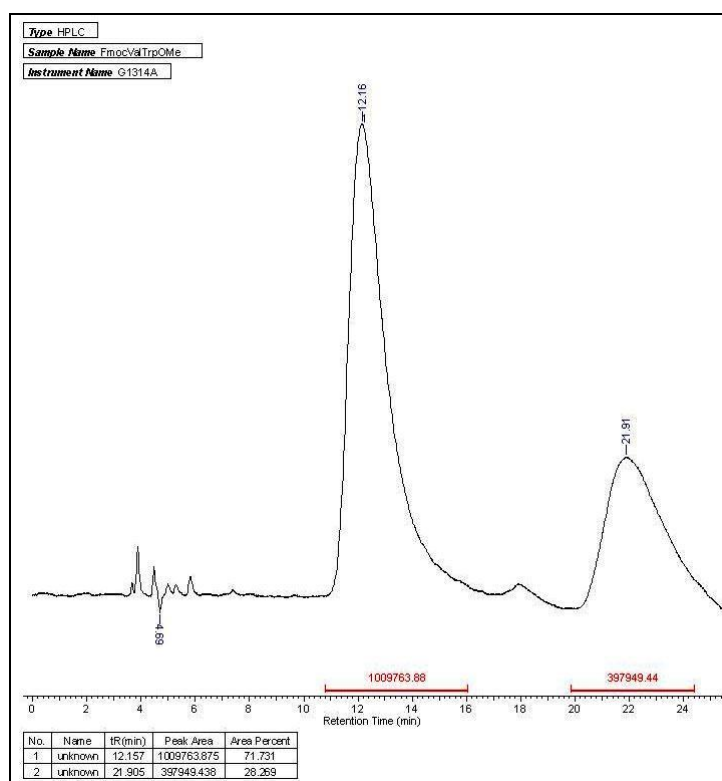
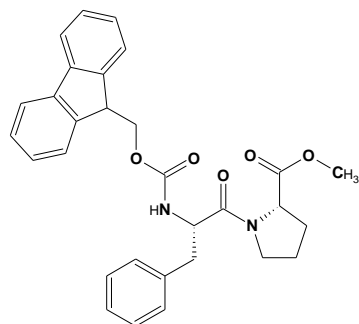


Figure S9. Representative HPLC trace of dipeptide (LL)-**14b** spiked with dipeptide epimer (DL)-**14b**. Phenomenex® Lux Amylose-2, 4.6x250 mm; 1 mL/min hexane/i-PrOH/EtOH 70:20:10, obs: 254 nm; retention times: 12.2 min (LL-diastereoisomer), 21.9 min (DL-diastereoisomer).



Fmoc-Phe-Pro-OMe

The procedure for the LL-diastereoisomer **14c** was followed to prepare the DL-diastereoisomer starting from D-Fmoc-Phe-OH. Methyl *N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-L-phenylalanyl-L-prolinate **14c** was analyzed by chiral HPLC and compared with a sample of Fmoc-D-Phe-L-Pro-OMe as reference. The analysis revealed a 1.7% of epimerization which is common to proline coupling (Figure S10).

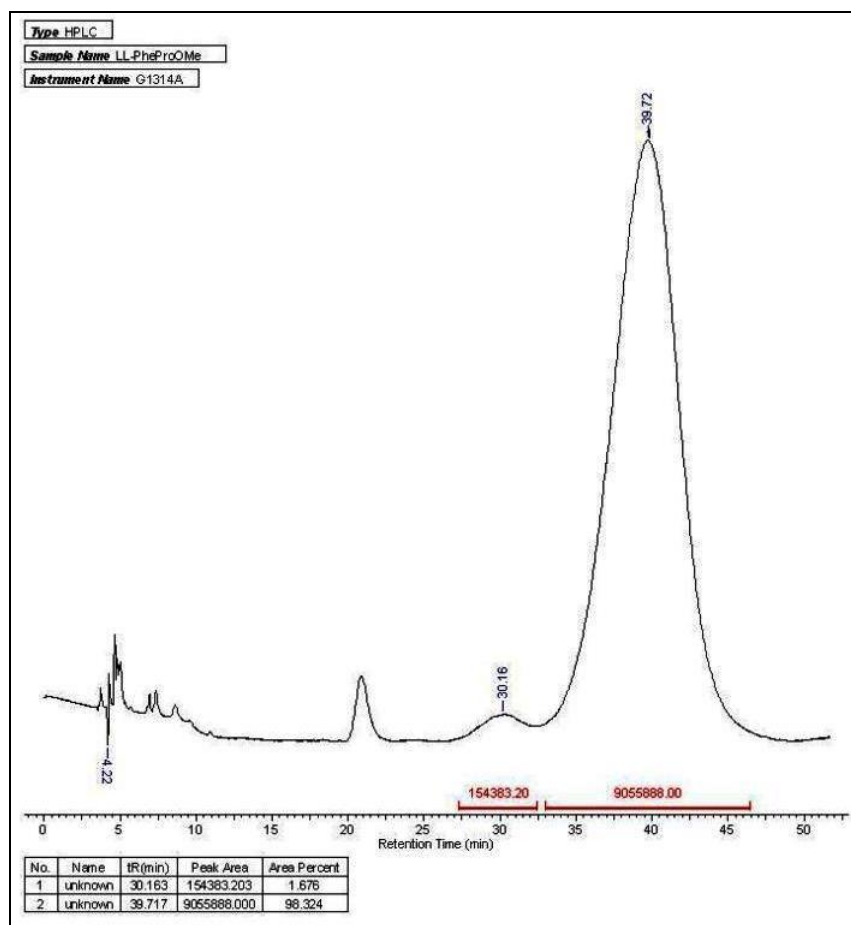


Figure S10. HPLC trace of dipeptide (LL)-**14c**. Phenomenex® Lux Amylose-2, 4.6x250 mm; 1 mL/min hexane/*i*-PrOH/EtOH 70:22:8, obs: 254 nm; retention times: 30.2 min (DL-diastereoisomer, minor), 39.7 min (LL-diastereoisomer, minor), dr = 1.7:98.3.

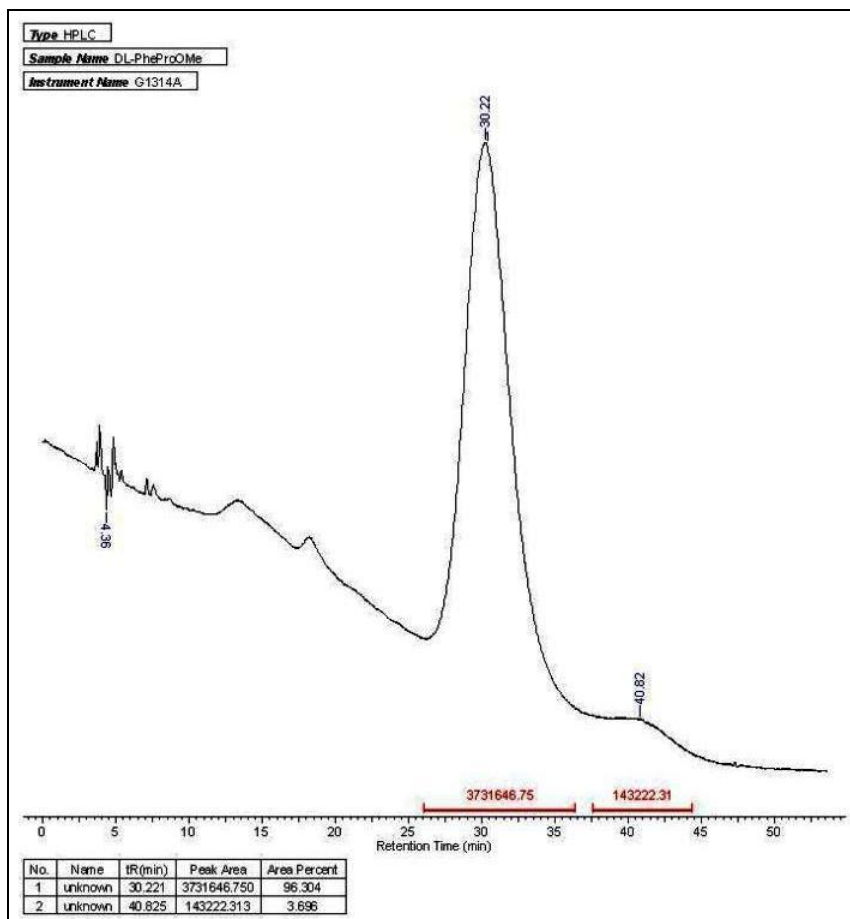


Figure S11. HPLC trace of dipeptide (DL)-**14c**. Phenomenex® Lux Amylose-2, 4.6x250 mm; 1 mL/min hexane/i-PrOH/EtOH 70:20:10, obs: 254 nm; retention times: 30.2 min (DL-diastereoisomer, major), 40.8 min (LL-diastereoisomer, minor), dr = 96.3:3.7.

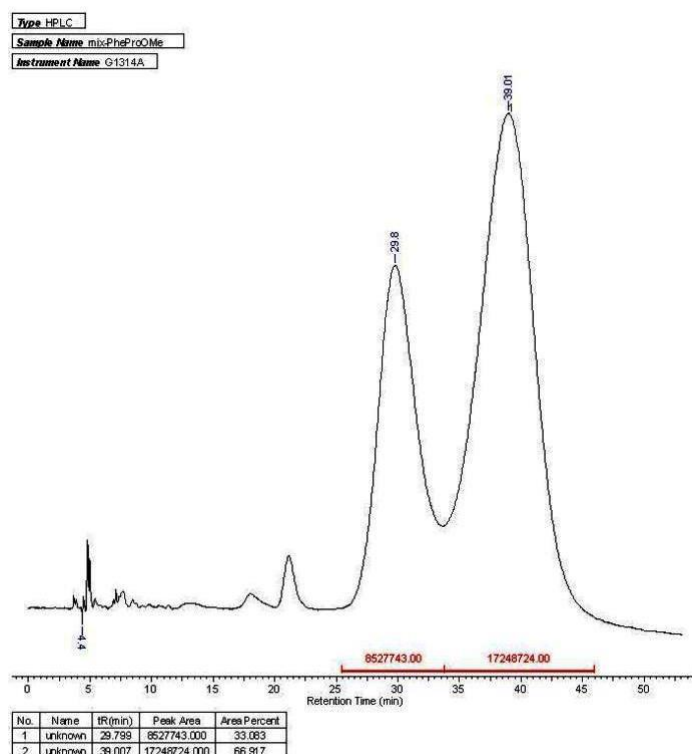
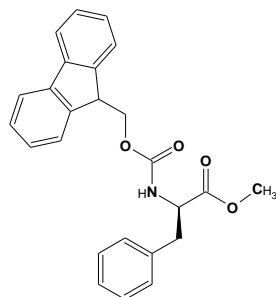


Figure S12. Representative HPLC trace of dipeptide (LL)-**14c** spiked with dipeptide epimer (DL)-**14c**. Phenomenex® Lux Amylose-2, 4.6x250 mm; 1 mL/min hexane/i-PrOH/EtOH 70:20:10, obs: 254 nm; retention times: 29.8 min (DL-diastereoisomer), 39.0 min (LL-diastereoisomer).



Epimerization Studies of Fmoc-Phe-SePh

The enantiomeric ratio of *N*-Fmoc-*D*-phenylalanine methyl esters obtained by methanolysis⁷ of a sample of (*D*)-**8e** stored at room temperature for six months and from a sample of (*D*)-**8e** stored at 0 °C for the same period of time were compared by HPLC analysis on chiral stationary phase. *Se*-Phenyl (2*R*)-2-[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino-3-phenylpropaneselenoate (*D*)-**8e** was prepared according to **GP** for the synthesis of **8e**. Product (*D*)-**8e** was obtained in 87% yield starting from *D*-Fmoc-Phe-OH; mp = 163–165 °C; $[\alpha]_D^{21} +80.61$ (*c* 0.39, CHCl₃);

Thus, freshly synthesized (*D*)-**8e** was reacted with methanol⁷ in the presence of copper chloride (II) to give the corresponding (*R*) methyl ester⁸ (Figure S13). The same procedure applied for the (*R*)-enantiomer was followed to prepare an analytical sample of (*S*) Methyl *N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-phenylalaninate [mp = 130–131 °C; $[\alpha]_D^{21} +34.33$ (*c* 0.35, CHCl₃)] starting from freshly synthesized selenoesters (*L*)-**8e**.

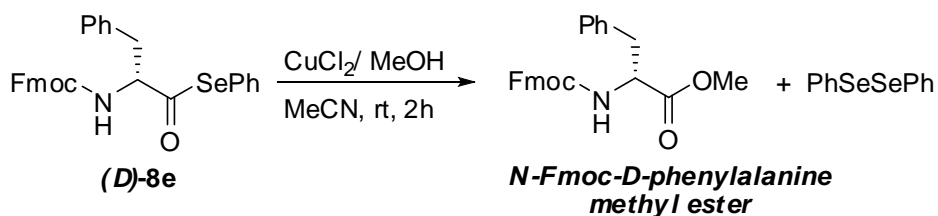


Figure S13. (*R*) *N*-Fmoc-phenylalanine methyl ester synthesis from selenoesters (*D*)-**8e**

The above prepared (*R*) *N*-Fmoc-phenylalanine methyl ester⁸ was analyzed by chiral HPLC and compared with a sample of (*L*)- ester as reference. The analysis revealed an e.r. > 99.9:0.1 (Figure S14).

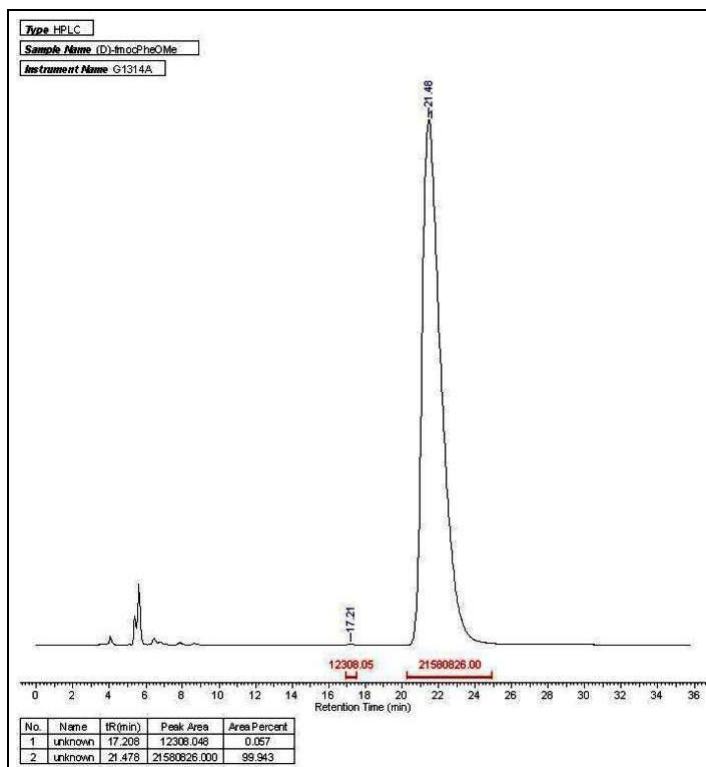


Figure S14. HPLC trace of (*R*) Methyl *N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-phenylalaninate prepared from freshly synthesized selenoester (*D*)-**8e**. Phenomenex® Lux Cellulose-2, 1 mL/min hexane/*i*-PrOH 80/20, obs: 254 nm): retention times: 17.2 min (*L*-enantiomer, minor), 21.5 min (*D*-enantiomer, major), er > 99.9:0.1.

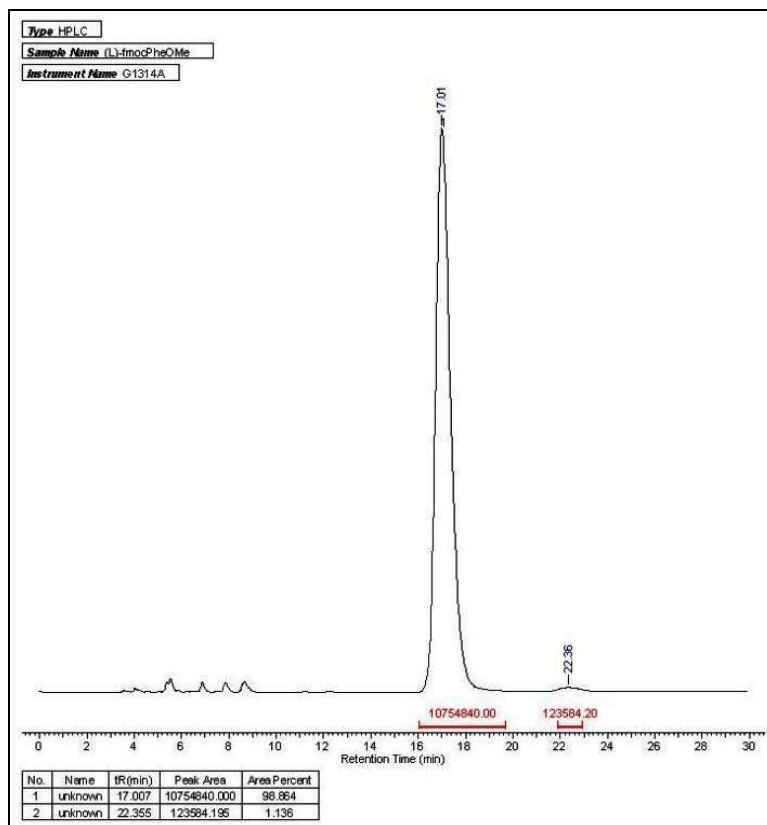


Figure S15. HPLC trace of (*S*) Methyl *N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-phenylalaninate prepared from freshly selenoester (*L*)-**8e**. Phenomenex® Lux Cellulose-2, 1 mL/min hexane/*i*-PrOH 80/20, obs: 254 nm): retention times: 17.0 min (*L*-enantiomer, major), 22.4 min (*D*-enantiomer, minor), er = 98.9:1.1.

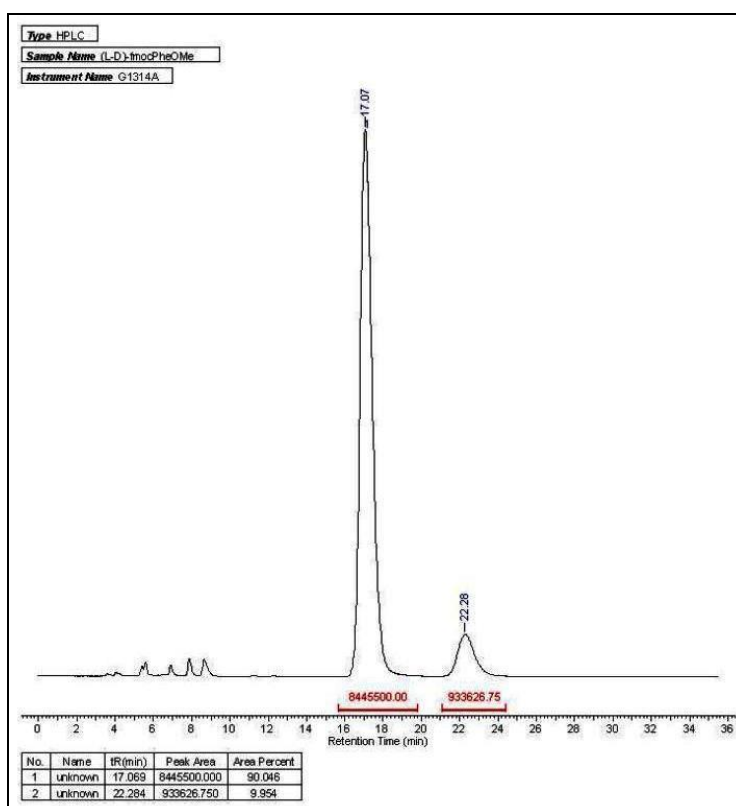


Figure S16. Representative HPLC trace of (*S*) Methyl *N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-phenylalaninate spiked with its enantiomer (*D*) to determinate retention times for each enantiomer. Phenomenex® Lux Cellulose-2, 1 mL/min hexane/*i*-PrOH 80/20, obs: 254 nm): retention times: 17.1 min (*L*-enantiomer), 22.3 min (*D*-enantiomer).

Selenoester (*D*)-**8e** (0.20 mmol) stored at **room temperature** for six months was reacted with methanol as described above to give the corresponding (*R*) *Methyl N-[(9H-fluoren-9-ylmethoxy)carbonyl]-phenylalaninate*. A sample was analyzed by chiral HPLC (Figure S17) showing a very low racemization (e. r. = 99.6:0.4).

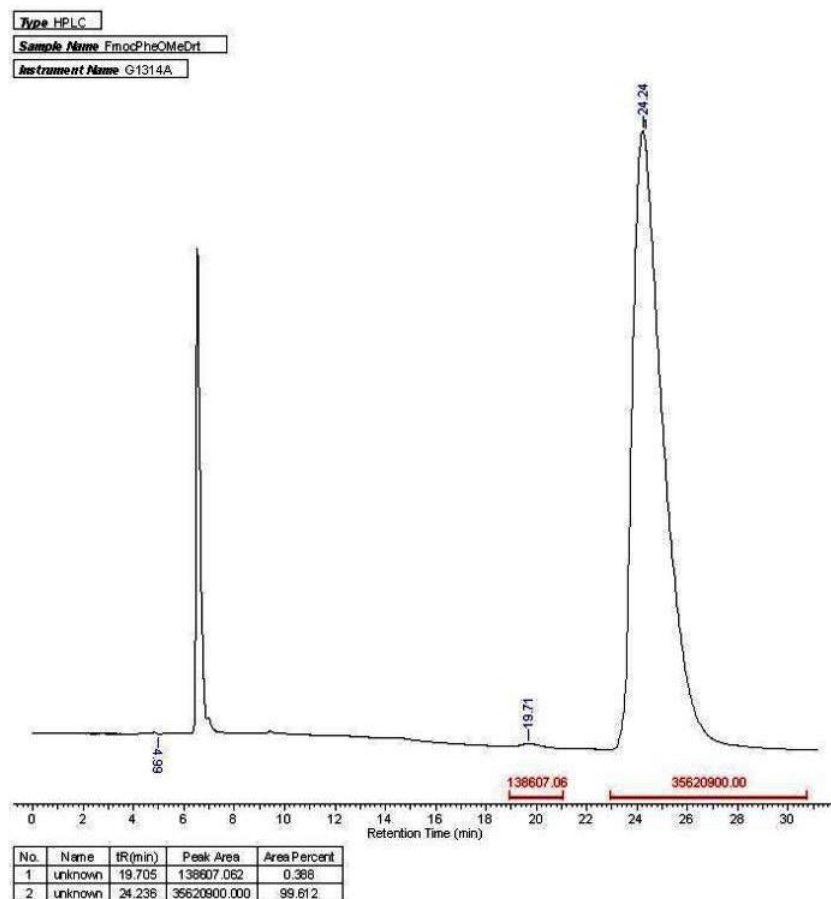


Figure S17. HPLC trace of (*R*) *Methyl N-[(9H-fluoren-9-ylmethoxy)carbonyl]-phenylalaninate* obtained from (*D*)-**8e** maintained at room temperature for six months. Phenomenex® Lux Cellulose-2, 1 mL/min hexane/*i*-PrOH 80/20, obs: 254 nm; retention times: 19.7 min (L-enantiomer, minor), 24.2 min (D-enantiomer, major), er = 99.6:0.4.

Selenoester (*D*)-**8e** (0.20 mmol) **stored at 0 °C** for six months was reacted with methanol as described above to give the corresponding (*R*) *Methyl N-[(9H-fluoren-9-ylmethoxy)carbonyl]-phenylalaninate*. A sample was analyzed (Figure S18) by chiral HPLC showing a very low racemization (e. r. = 99.4:0.6).

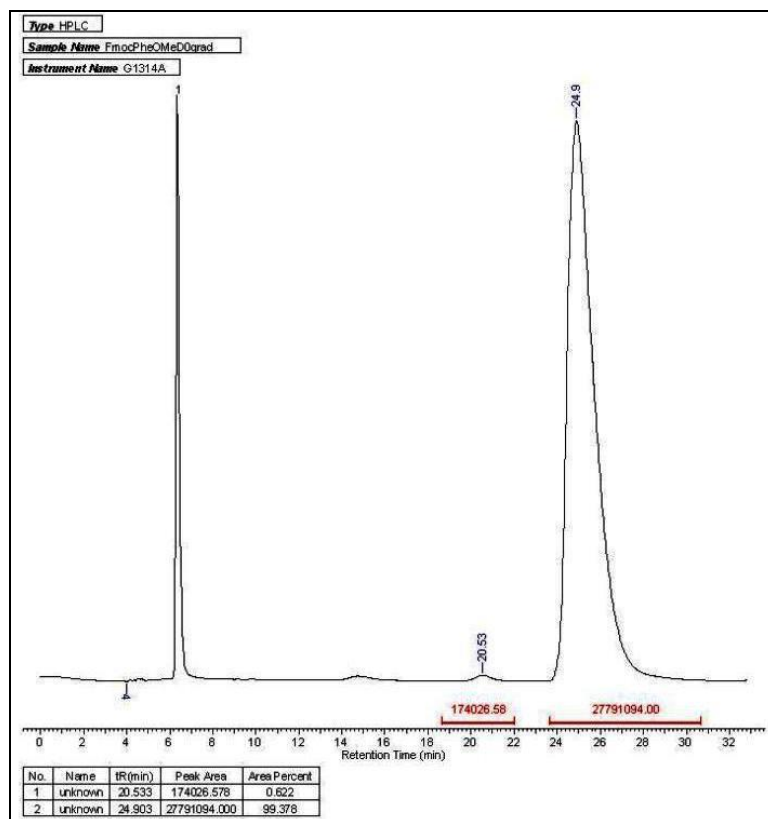


Figure S18. HPLC trace of (*R*) Methyl *N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-phenylalaninate prepared from (*D*)-**8e** maintained at 0 °C for six months. Phenomenex® Lux Cellulose-2, 1 mL/min hexane/*i*-PrOH 80/20, obs: 254 nm): retention times: 20.5 min (L-diastereoisomer, major), 24.9 min (D-diastereoisomer, minor), er = 83.5:16.5.

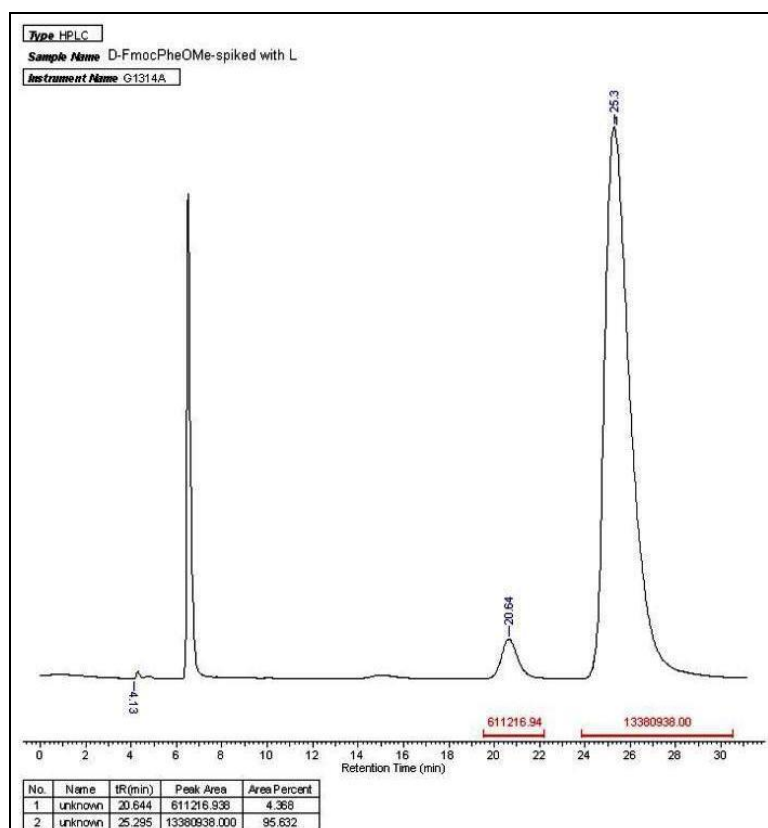
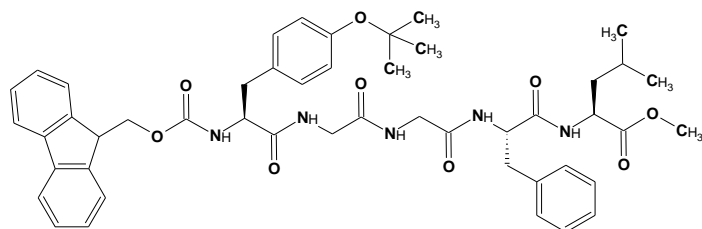


Figure S19. Representative HPLC trace of (*R*) Methyl *N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-phenylalaninate prepared from (*D*)-**8e** maintained at 0 °C for six months spiked with its enantiomer (*L*). Phenomenex® Lux Cellulose-2, 1 mL/min hexane/*i*-PrOH 80/20, obs: 254 nm): retention times: 20.6 min (L-enantiomer), 25.3 min (D-enantiomer).

HR-MALDI-MS/MS analysis⁹ of Pentapeptide 21



A 1 μ L portion of a premixed solution of peptide **21** and α -CHCA (5mg/mL, ACN:0.3% in TFA, 1:1) was spotted on the matrix target, dried at room temperature, and directly analyzed by MALDI mass spectrometry. Mass spectrometric analyses were performed using a 5800 MALDI-TOF-TOF Analyzer (AB SCIEX, Darmstadt, Germany) equipped with an Nd:YLF Laser with $\lambda = 345$ -nm wavelength of <500 ps pulse length and up to 1000 Hz repetition rate, in reflectron positive mode with a mass accuracy of 3 ppm. At least 4000 laser shots are typically accumulated with a laser pulse rate of 400 Hz in the MS mode, whereas in the MS/MS mode spectra up to 5000 laser shots are acquired and averaged with a pulse rate of 1000 Hz. MS/MS experiments were performed at a collision energy of 1 kV, ambient air is used as collision gas at a pressure of 10^{-6} Torr. The potential difference between the source acceleration voltage and the collision cell was set as 1 kV. After acquisition, spectra were handled using Data Explorer version 4.11 (AB Sciex).

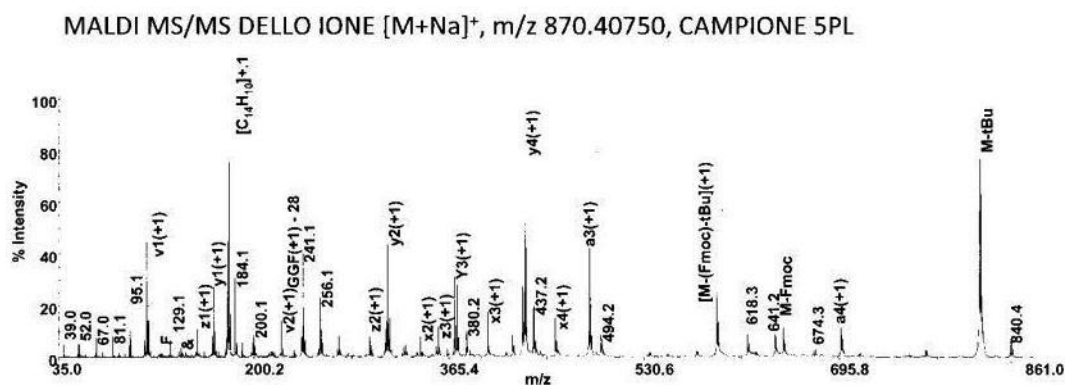
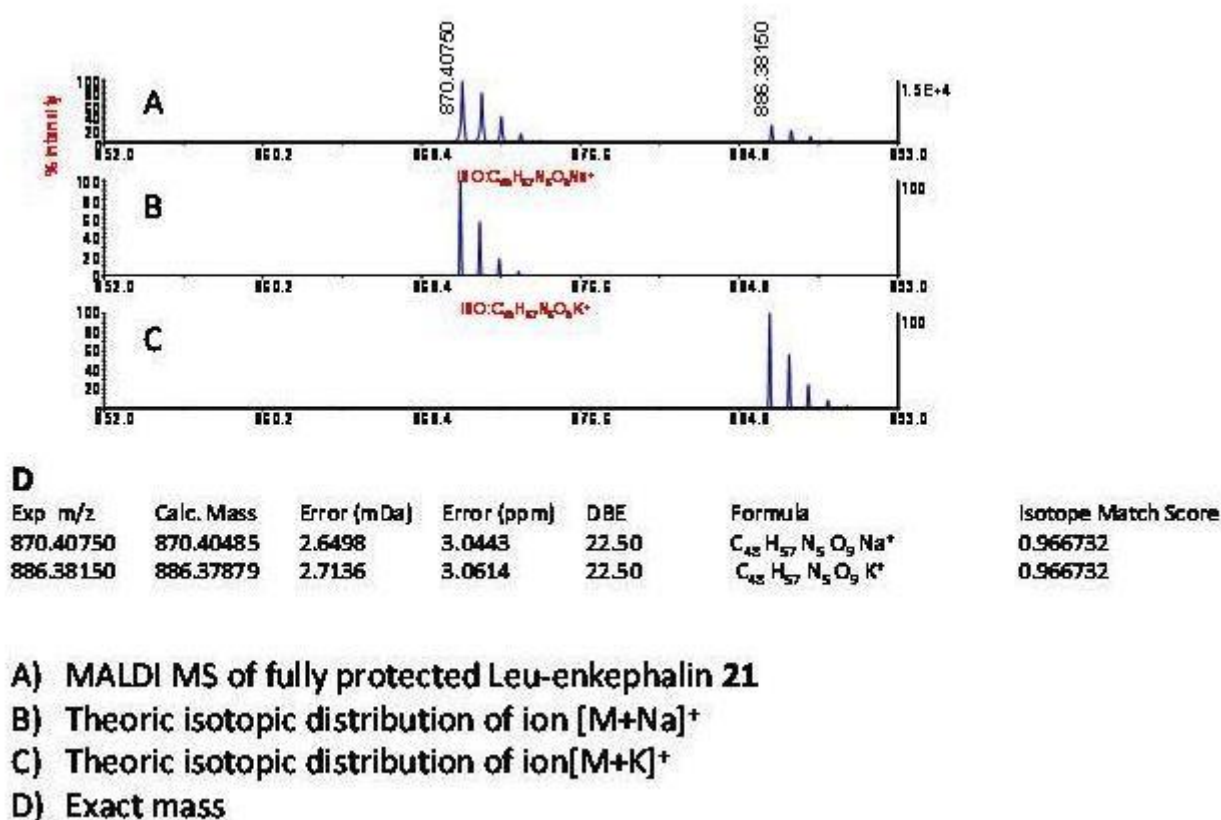
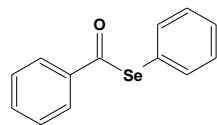


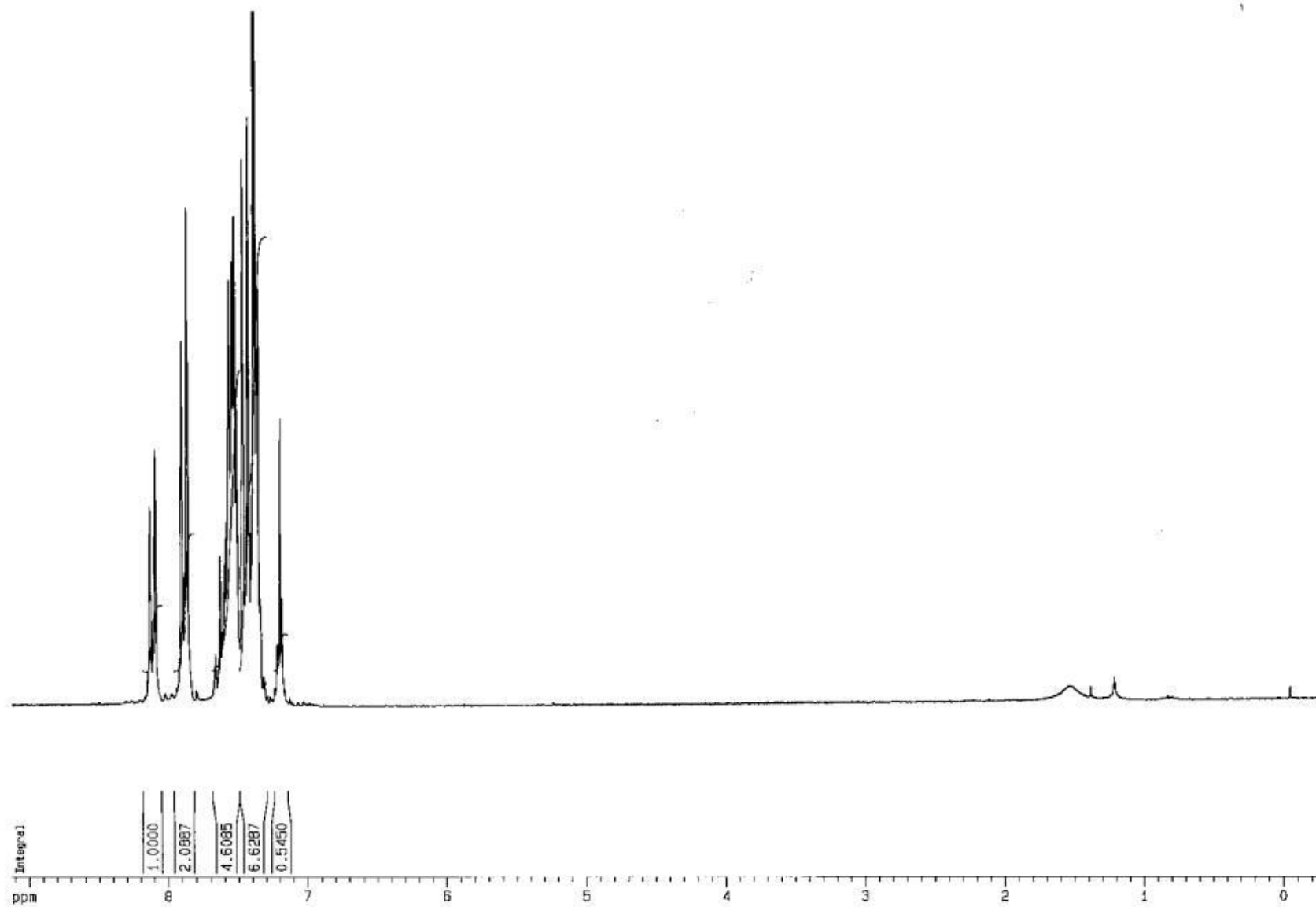
Figure S20. MALDI-TOF-TOF of pentapeptide **21** and MS/MS experiment.

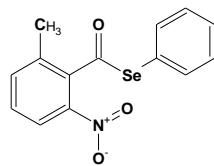
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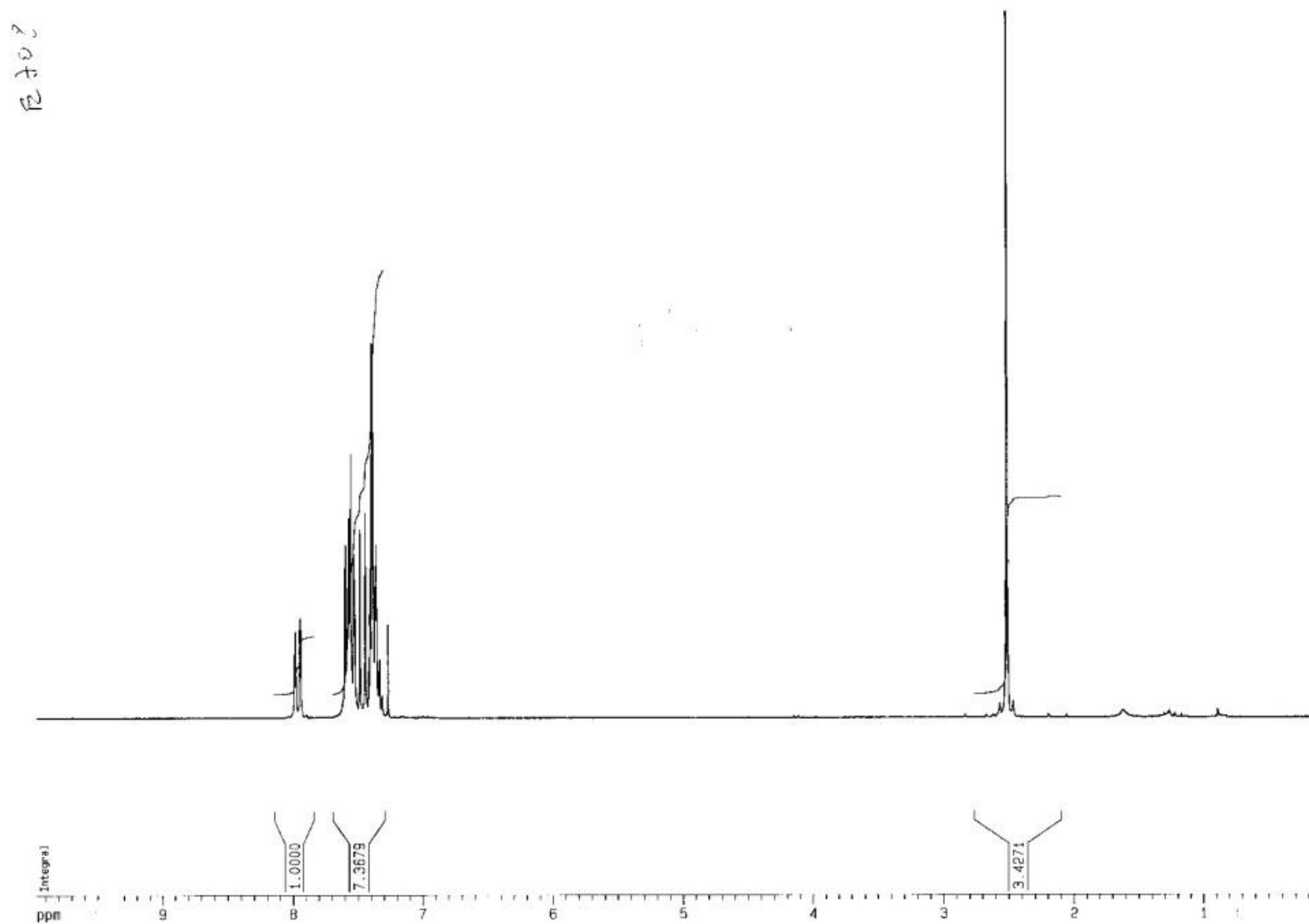


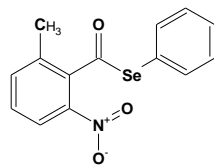
Se-Phenyl benzenecarboselenoate (**3a**): ^1H NMR (200 MHz, CDCl_3)



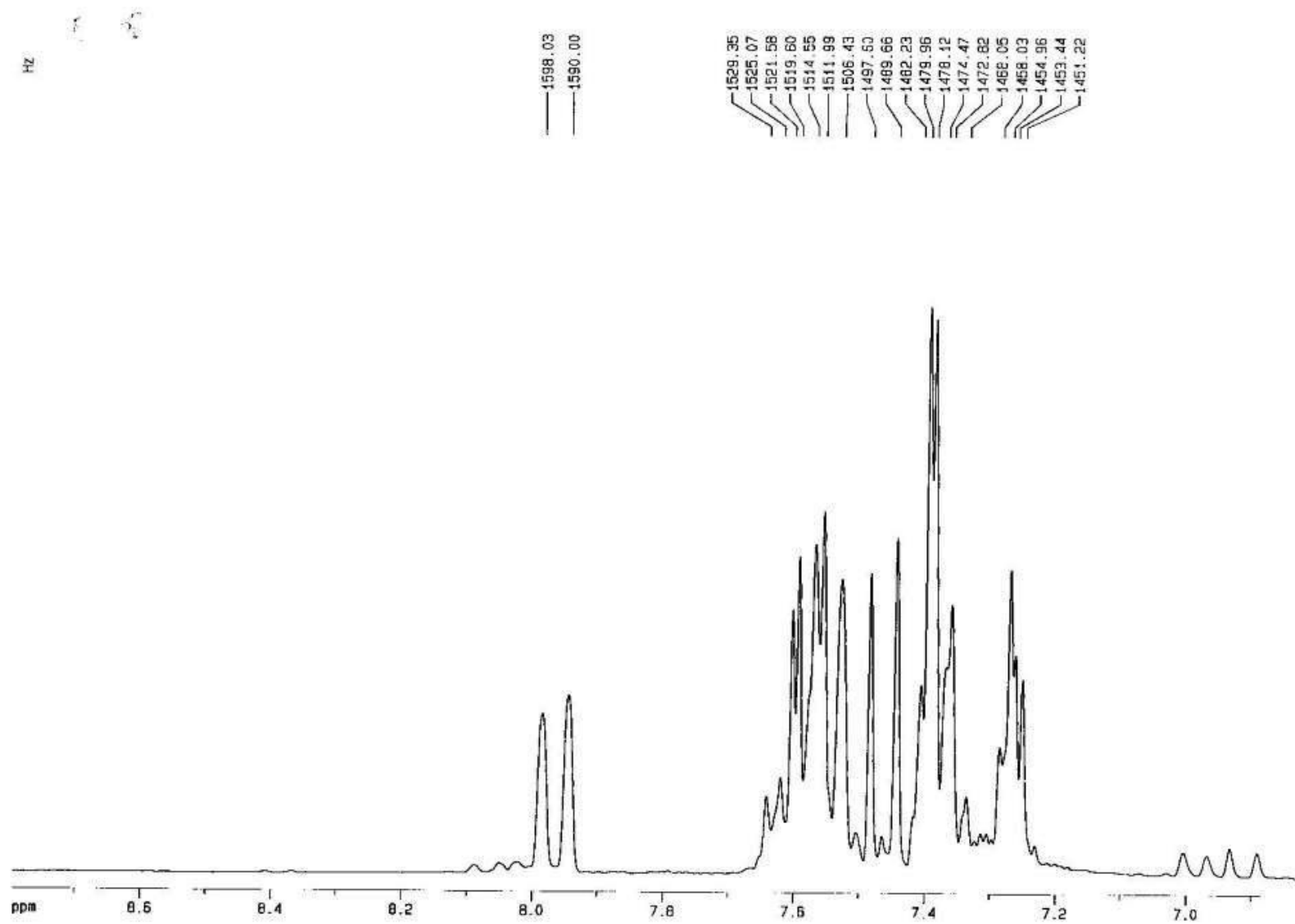


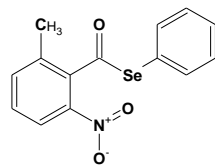
Se-Phenyl 2-methyl-6-nitrobenzenecarbosenoate (**3b**) ^1H NMR (200 MHz, CDCl_3)



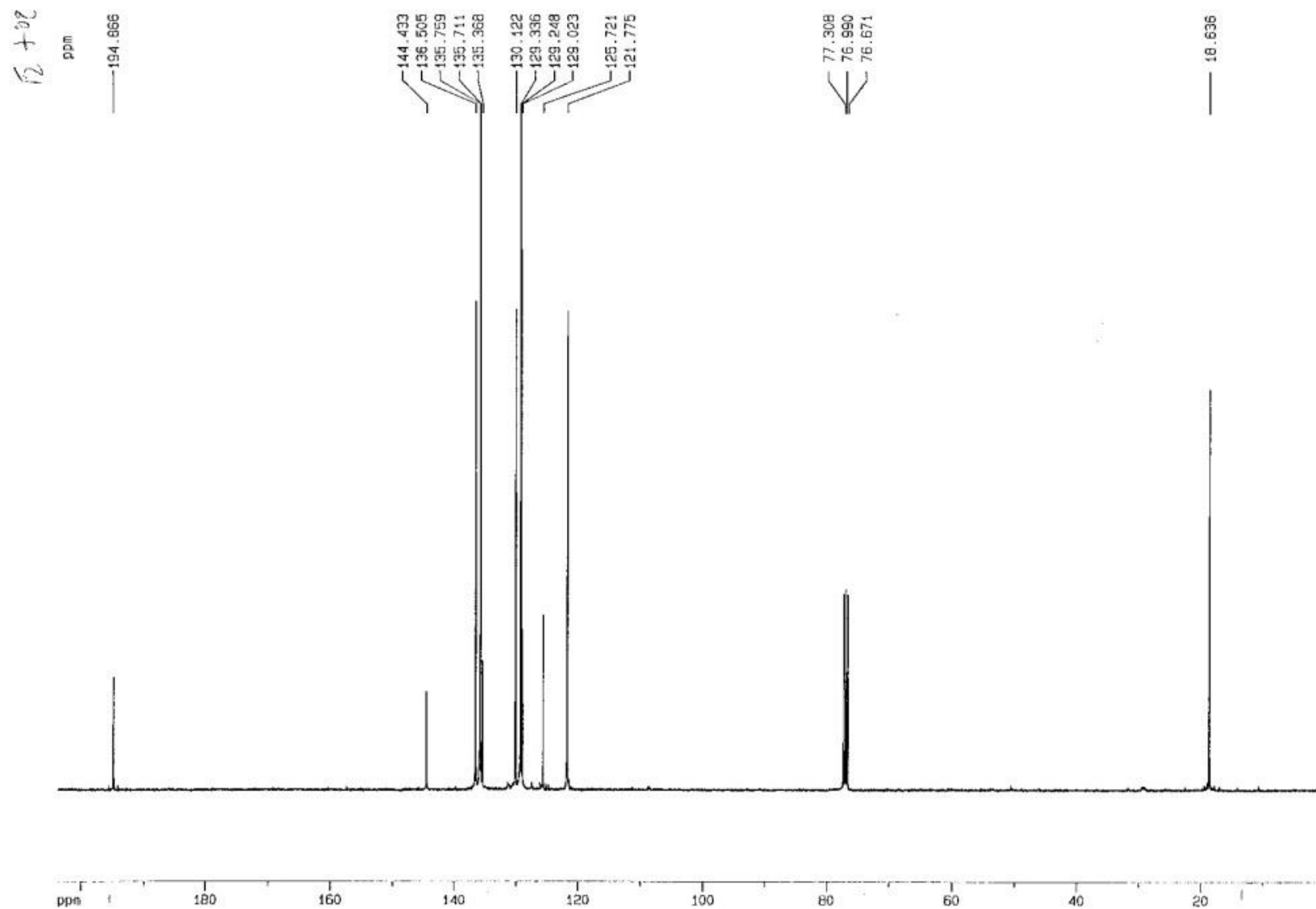


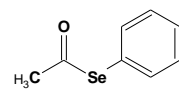
Se-Phenyl 2-methyl-6-nitrobenzenecarbosenoate (**3b**) ^1H NMR (200 MHz, CDCl_3)



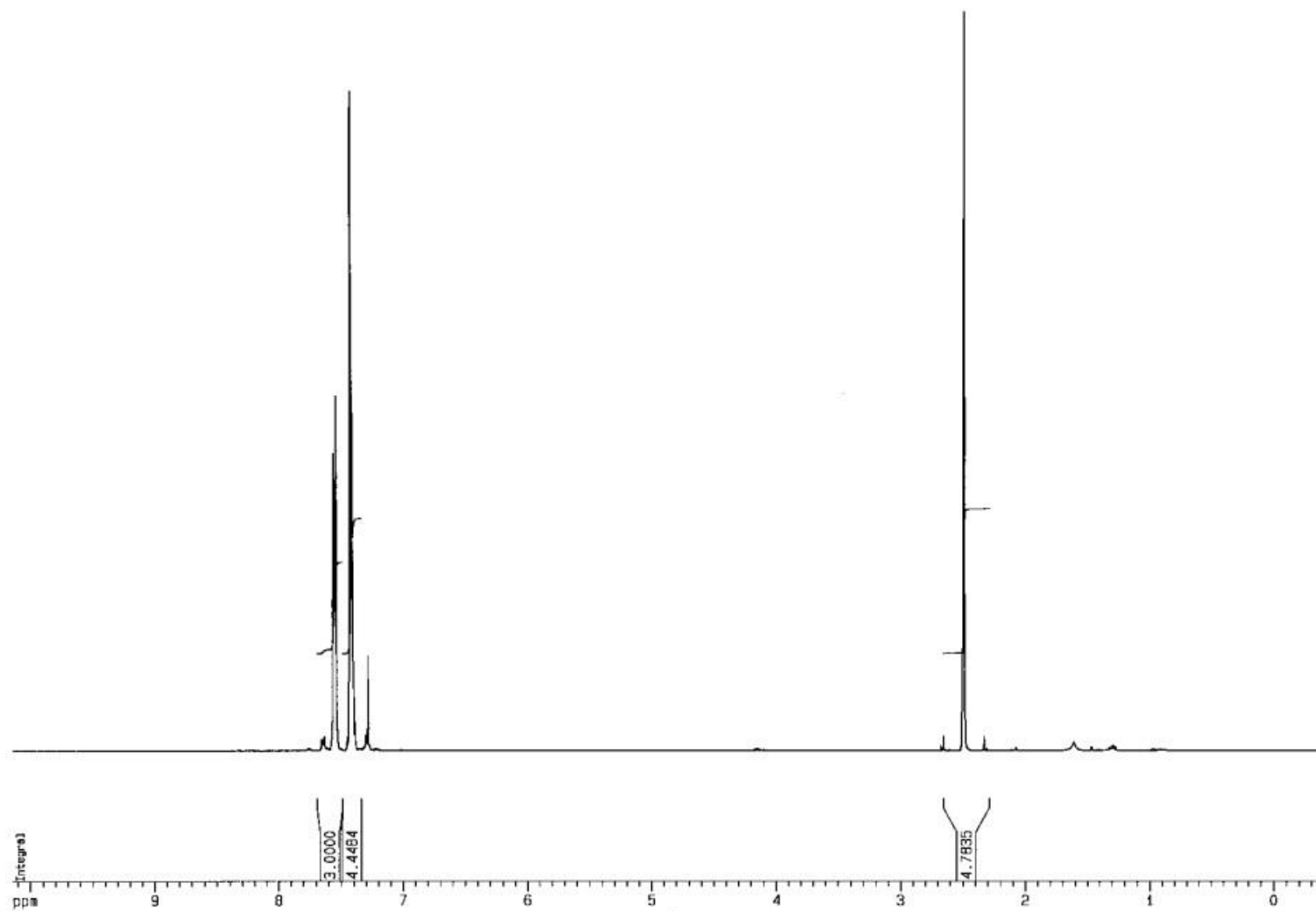


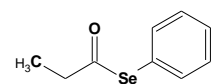
Se-Phenyl 2-methyl-6-nitrobenzenecarbosenoate (**3b**) ^{13}C NMR (100 MHz, CDCl_3)



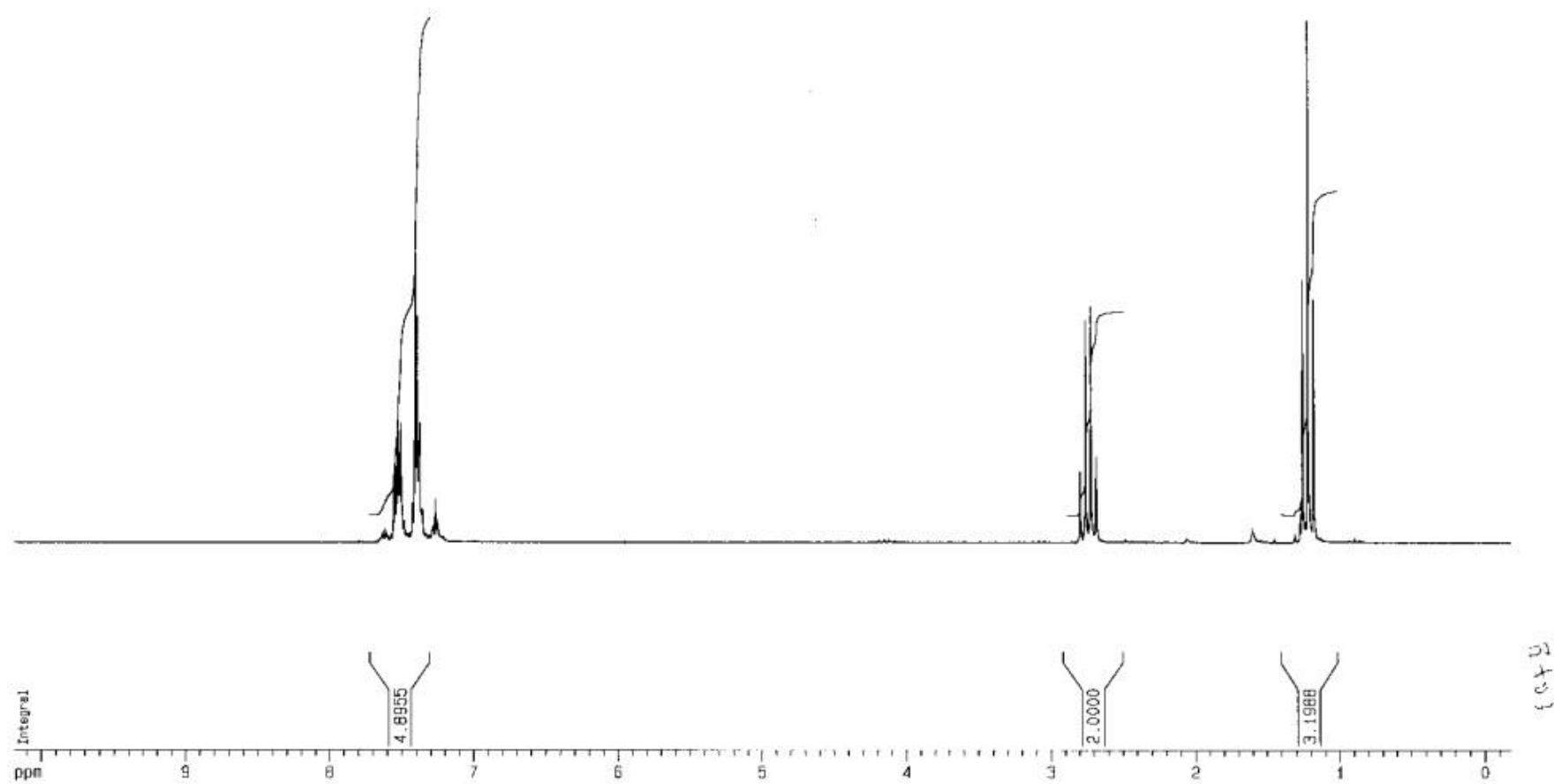


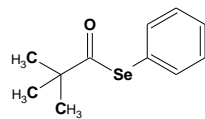
Se-Phenyl ethaneselenoate (**3c**) ^1H NMR (200 MHz, CDCl_3)



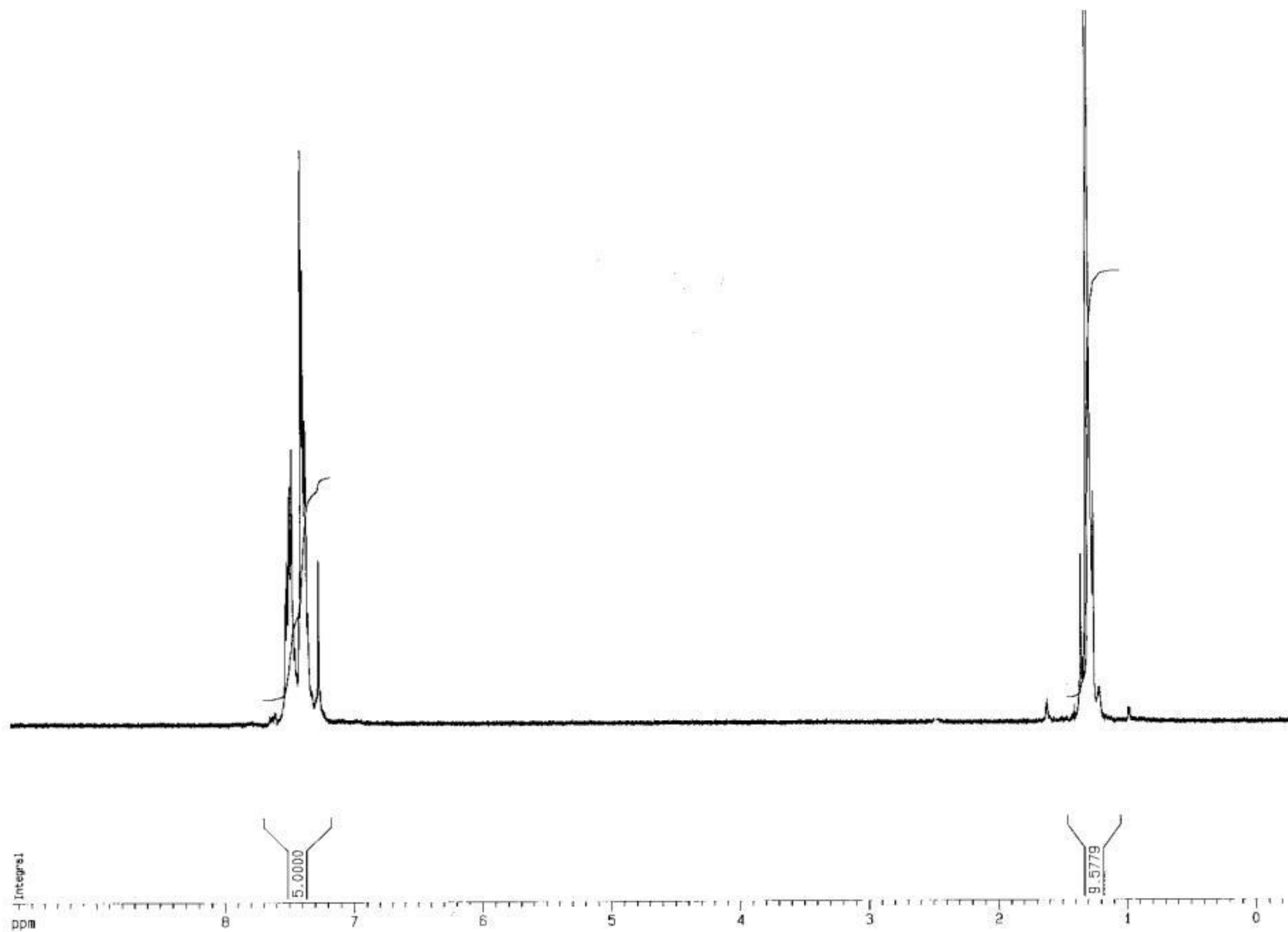


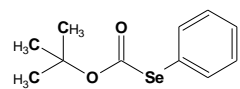
Se-Phenyl propaneselenoate (**3d**) ^1H NMR (200 MHz, CDCl_3)





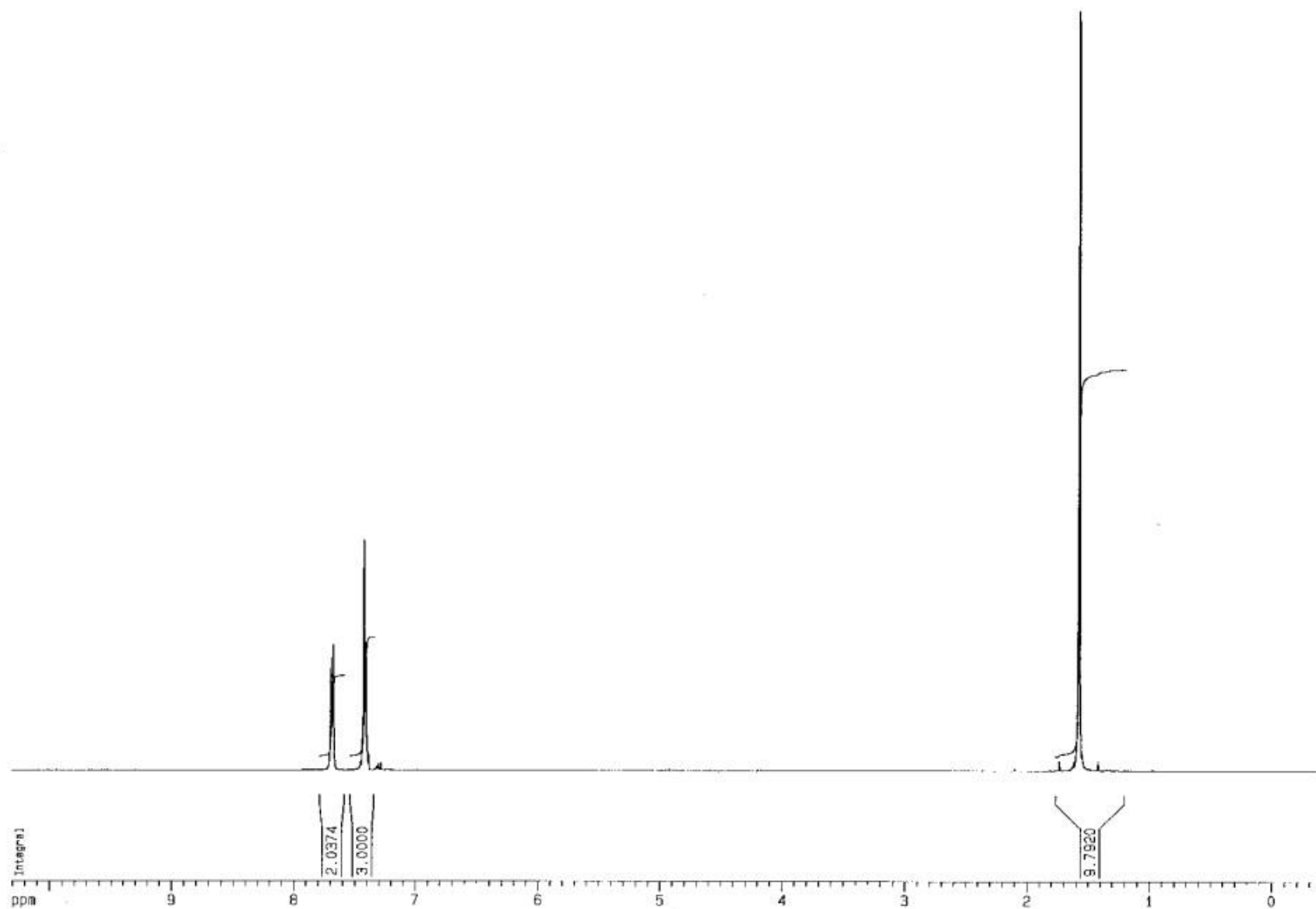
Se-Phenyl 2,2-dimethylpropaneselenoate (**3e**) ^1H NMR (200 MHz, CDCl_3)

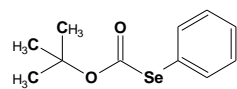




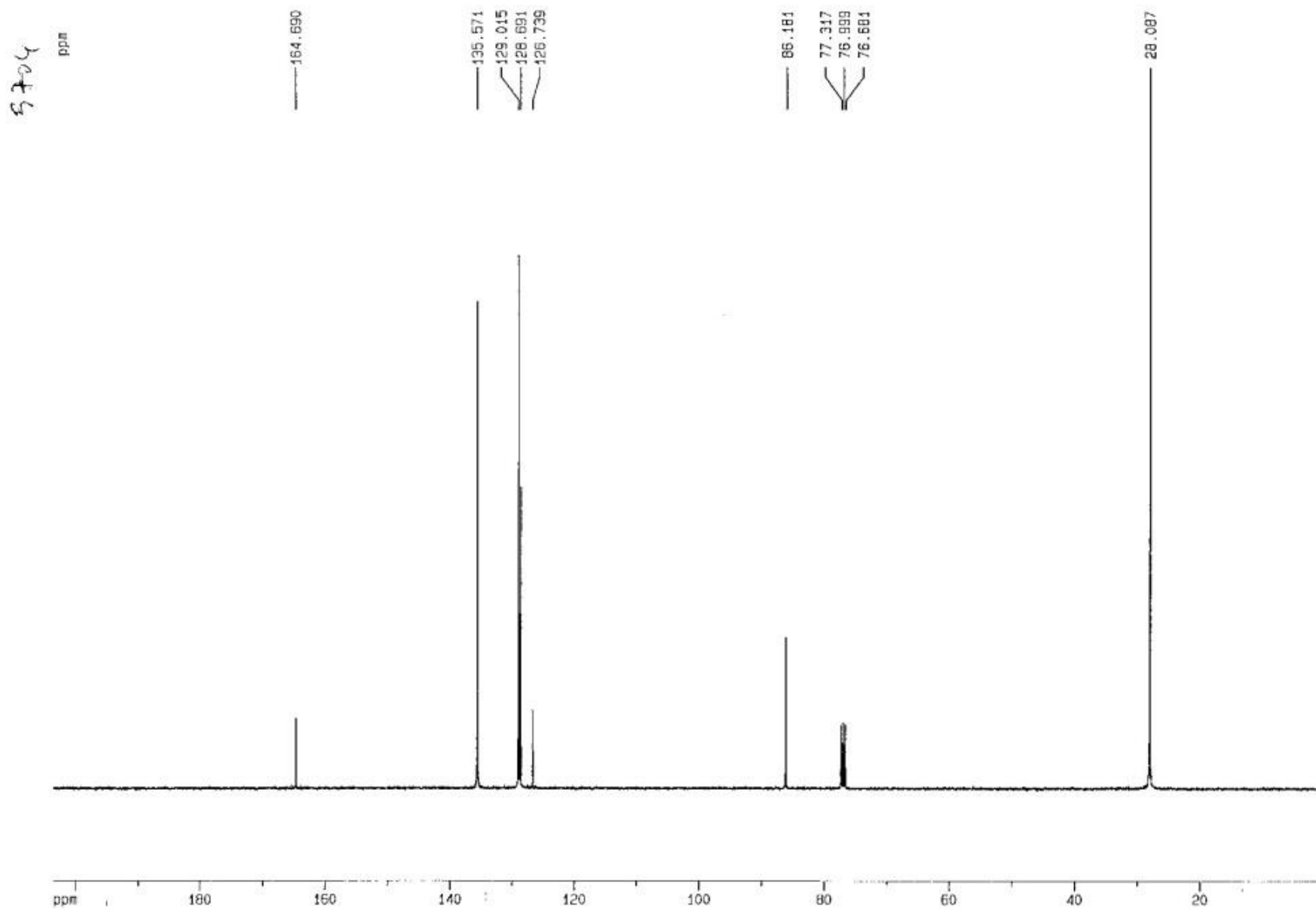
O-(*tert*-Butyl) Se-phenyl selenocarbonate (3f) ^1H NMR (200 MHz, CDCl_3)

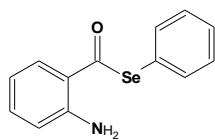
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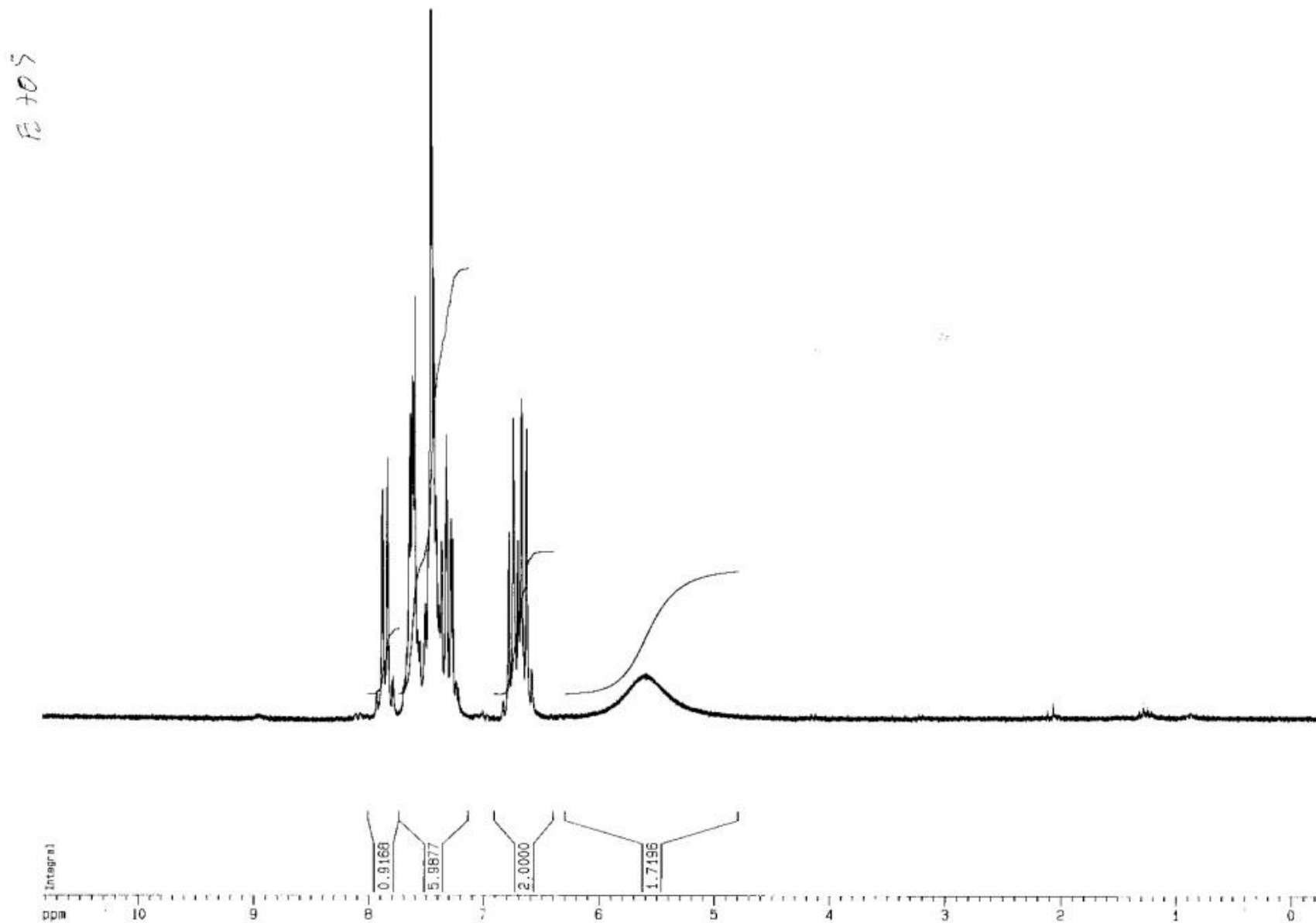


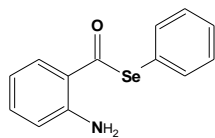
O-(*tert*-Butyl) Se-phenyl selenocarbonate (3f) ^{13}C NMR (50 MHz, CDCl_3)



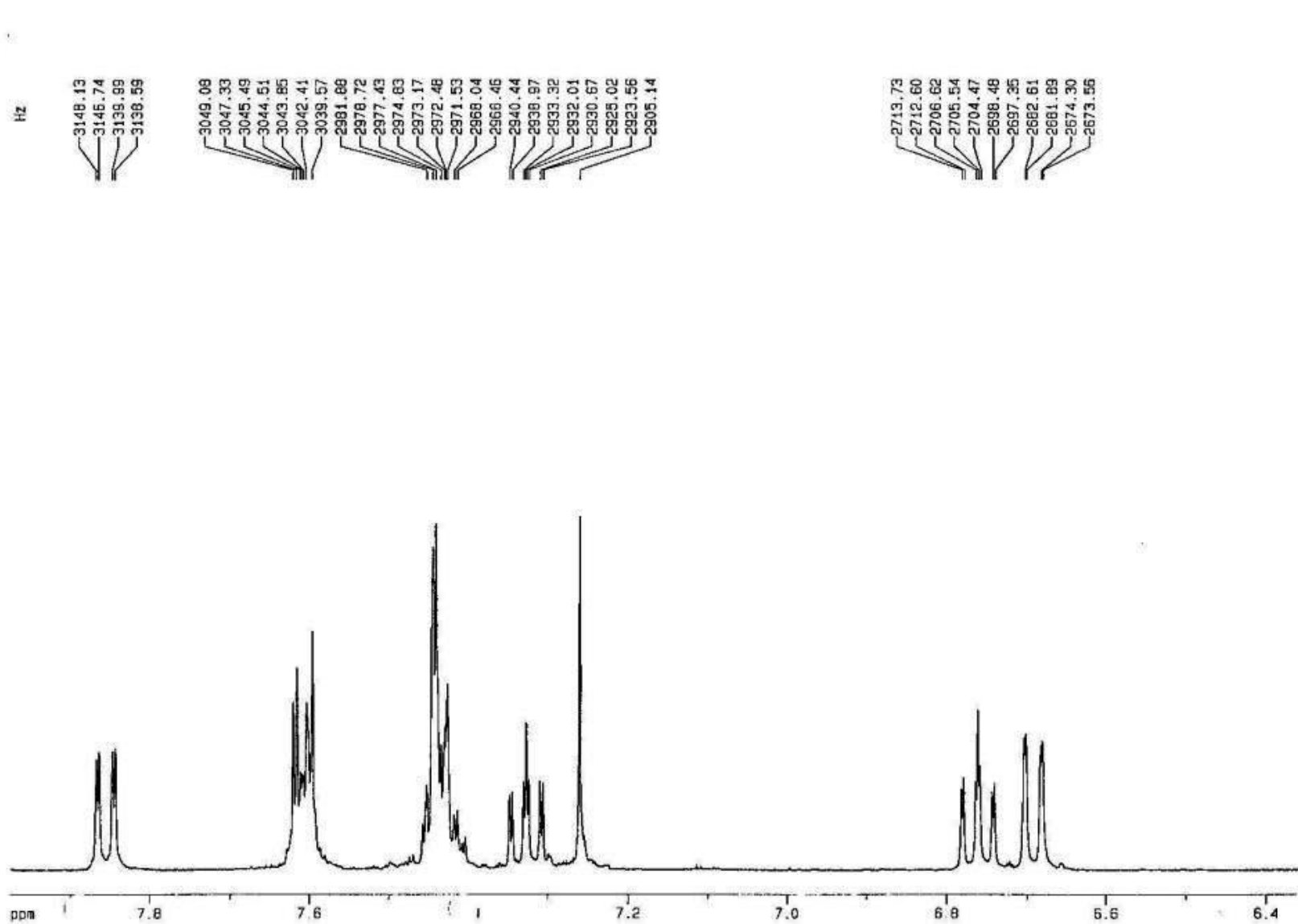


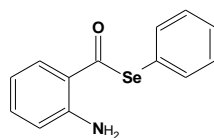
Se-Phenyl 2-aminobenzenecarboselenoate (3g) ^1H NMR (200 MHz, CDCl_3)



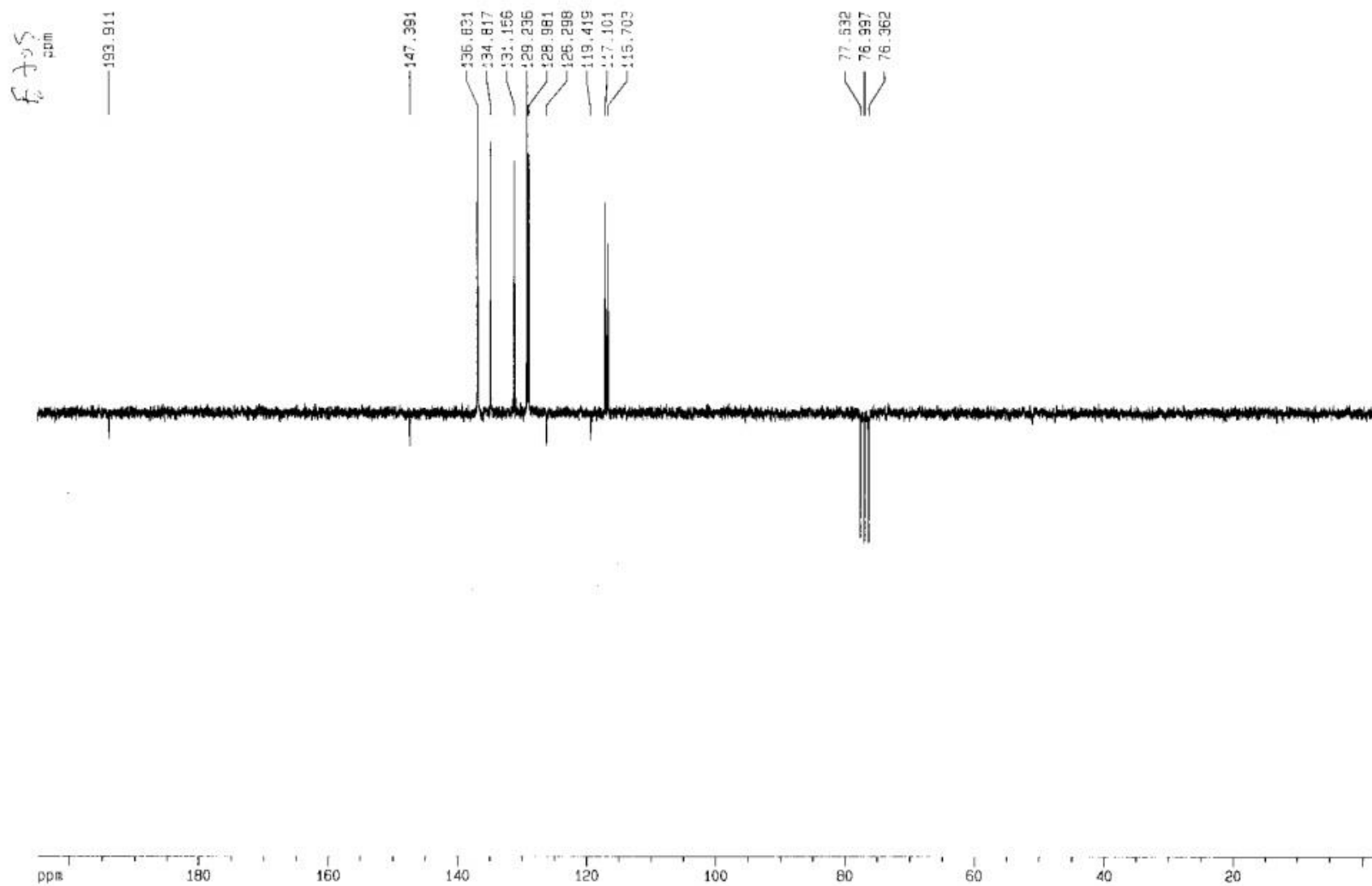


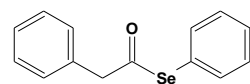
Se-Phenyl 2-aminobenzenecarboselenoate (3g) ^1H NMR (200 MHz, CDCl_3)



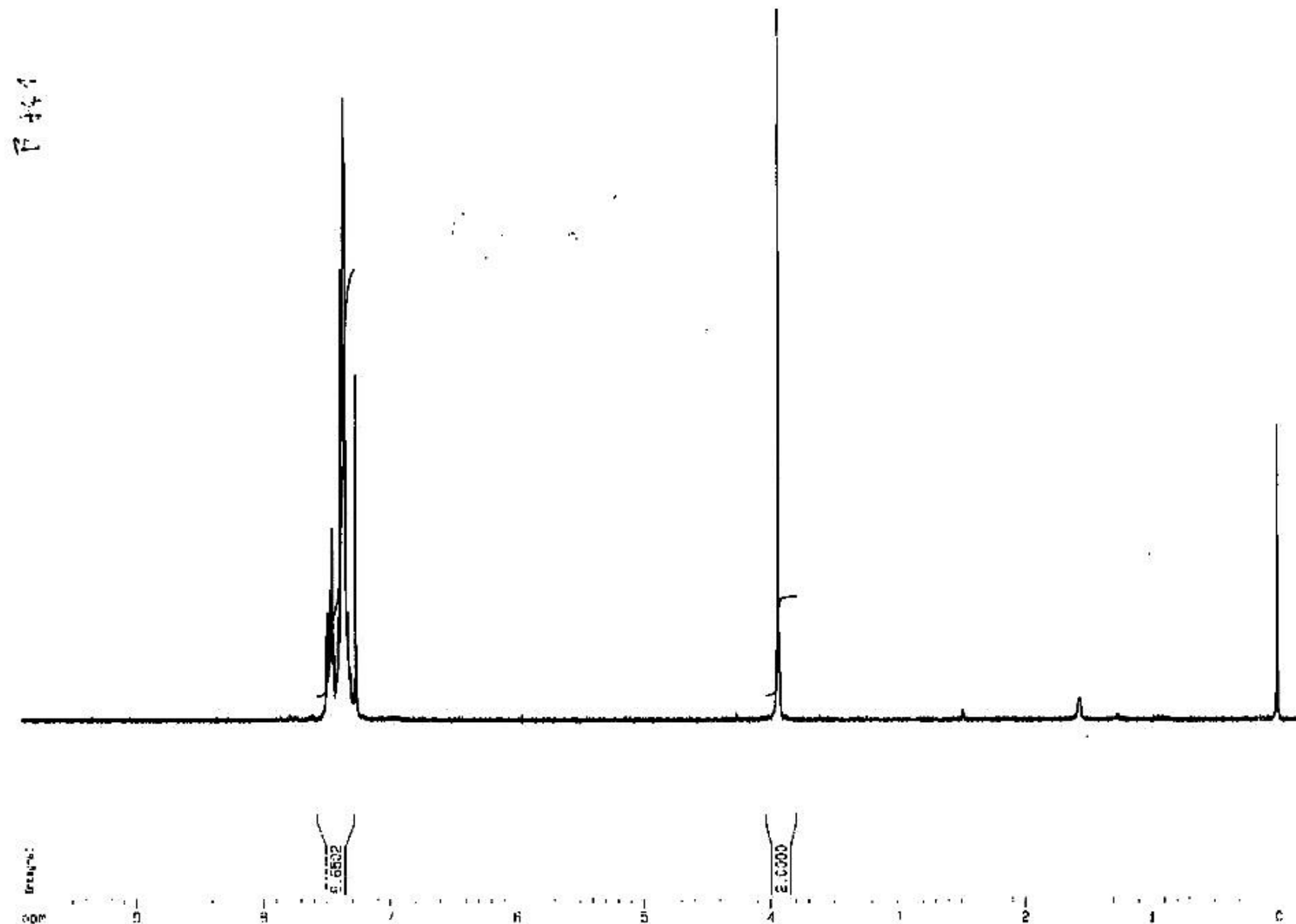


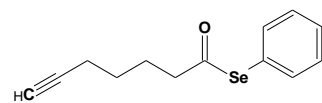
Se-Phenyl 2-aminobenzenecarboselenoate (3g) ^{13}C NMR (50 MHz, CDCl_3)



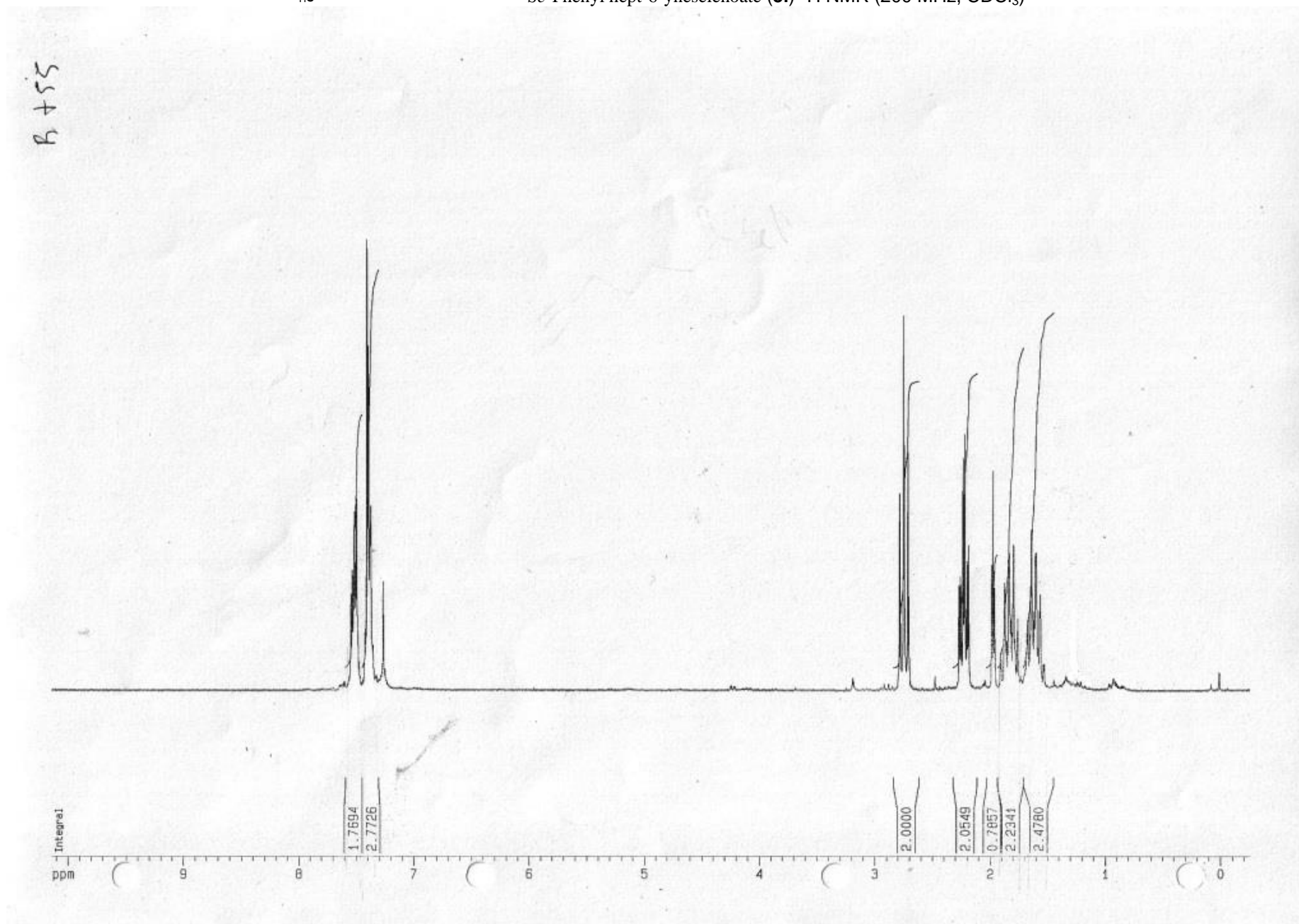


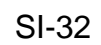
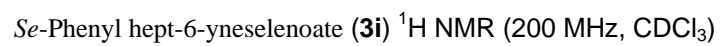
Se-Phenyl phenylethaneselenoate (**3h**) ^1H NMR (200 MHz, CDCl_3)

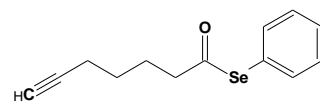




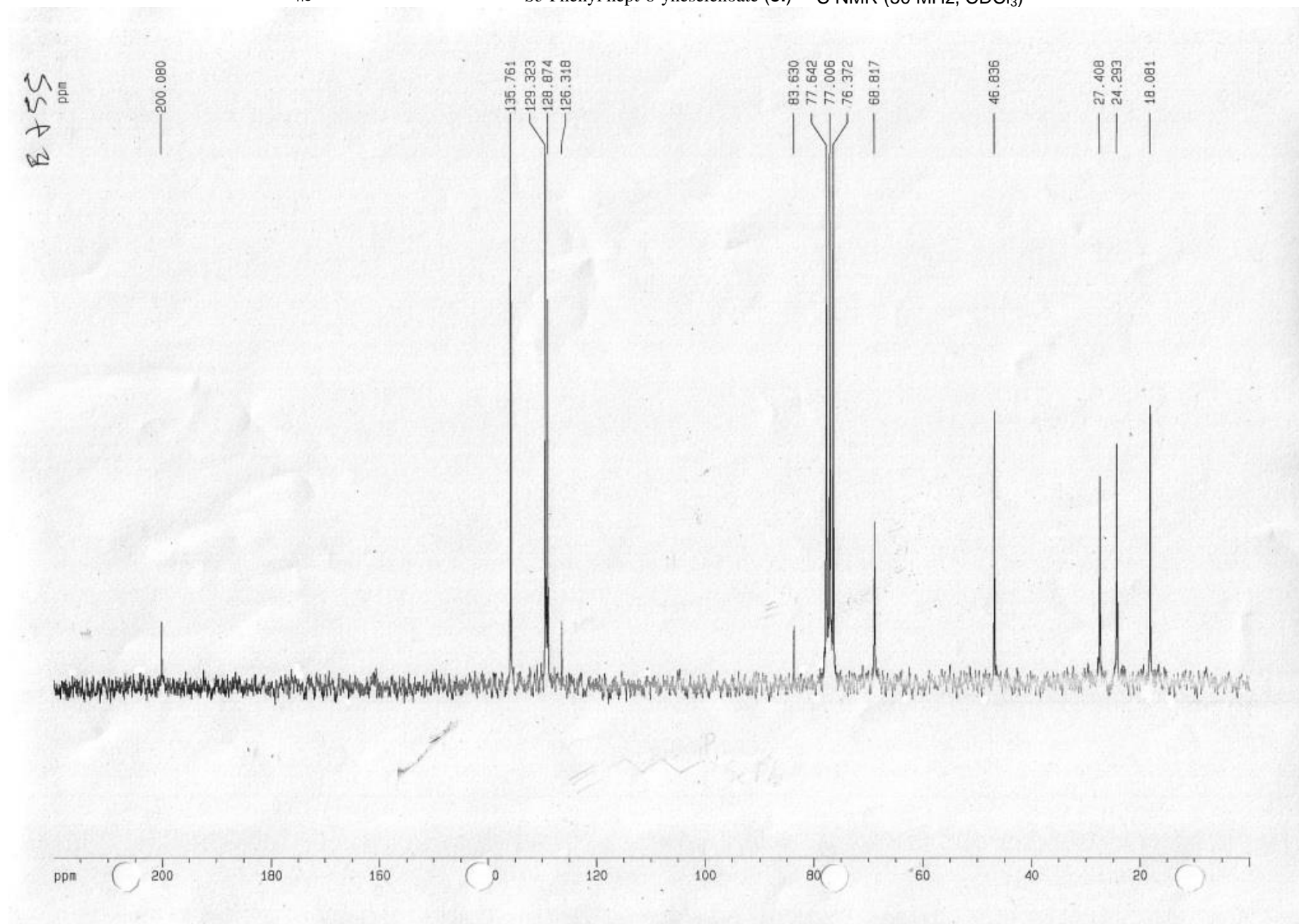
Se-Phenyl hept-6-yneselenoate (**3i**) ^1H NMR (200 MHz, CDCl_3)

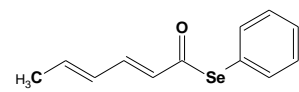






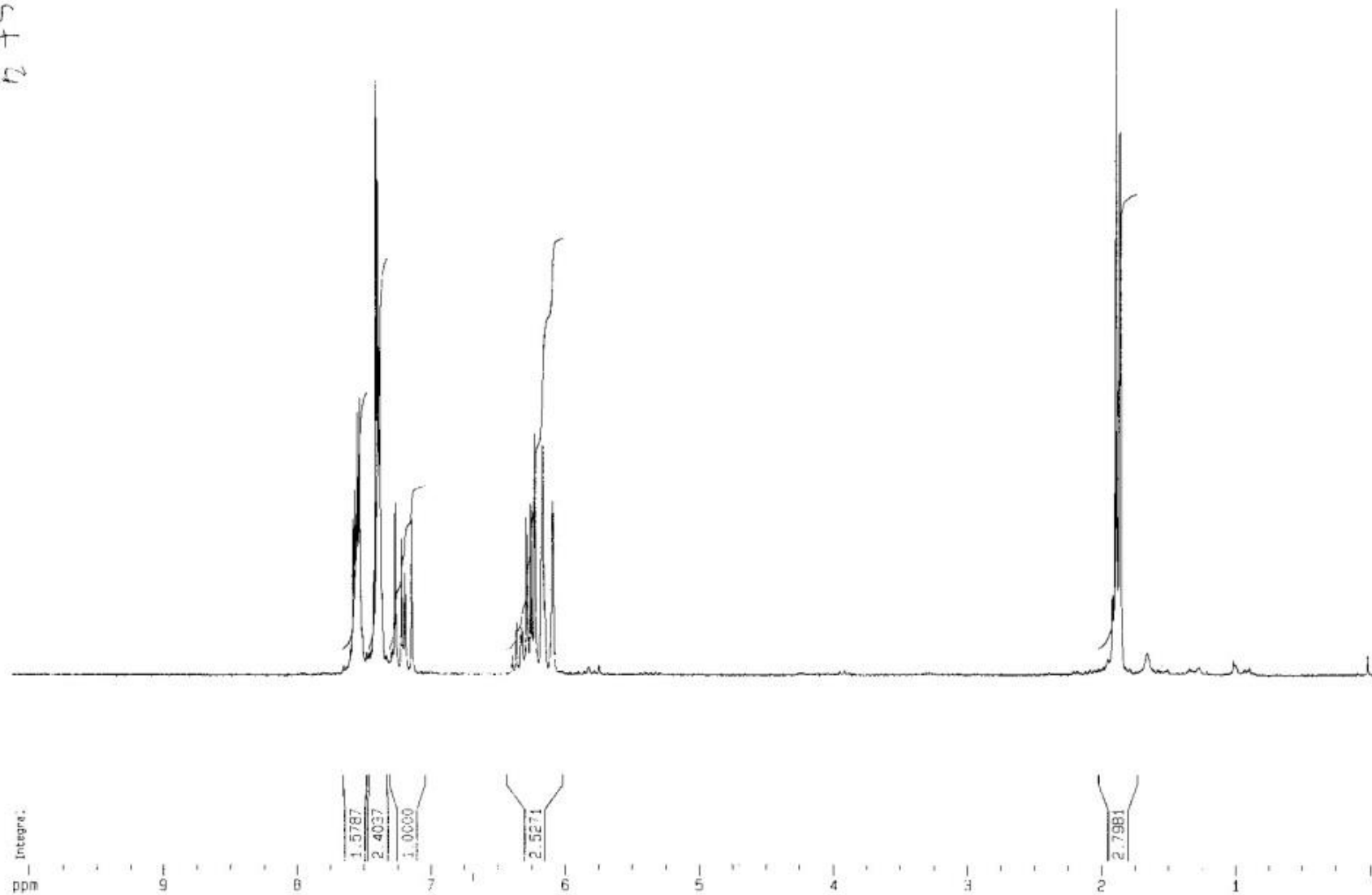
Se-Phenyl hept-6-yne-selenoate (**3i**) ^{13}C NMR (50 MHz, CDCl_3)

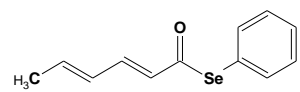




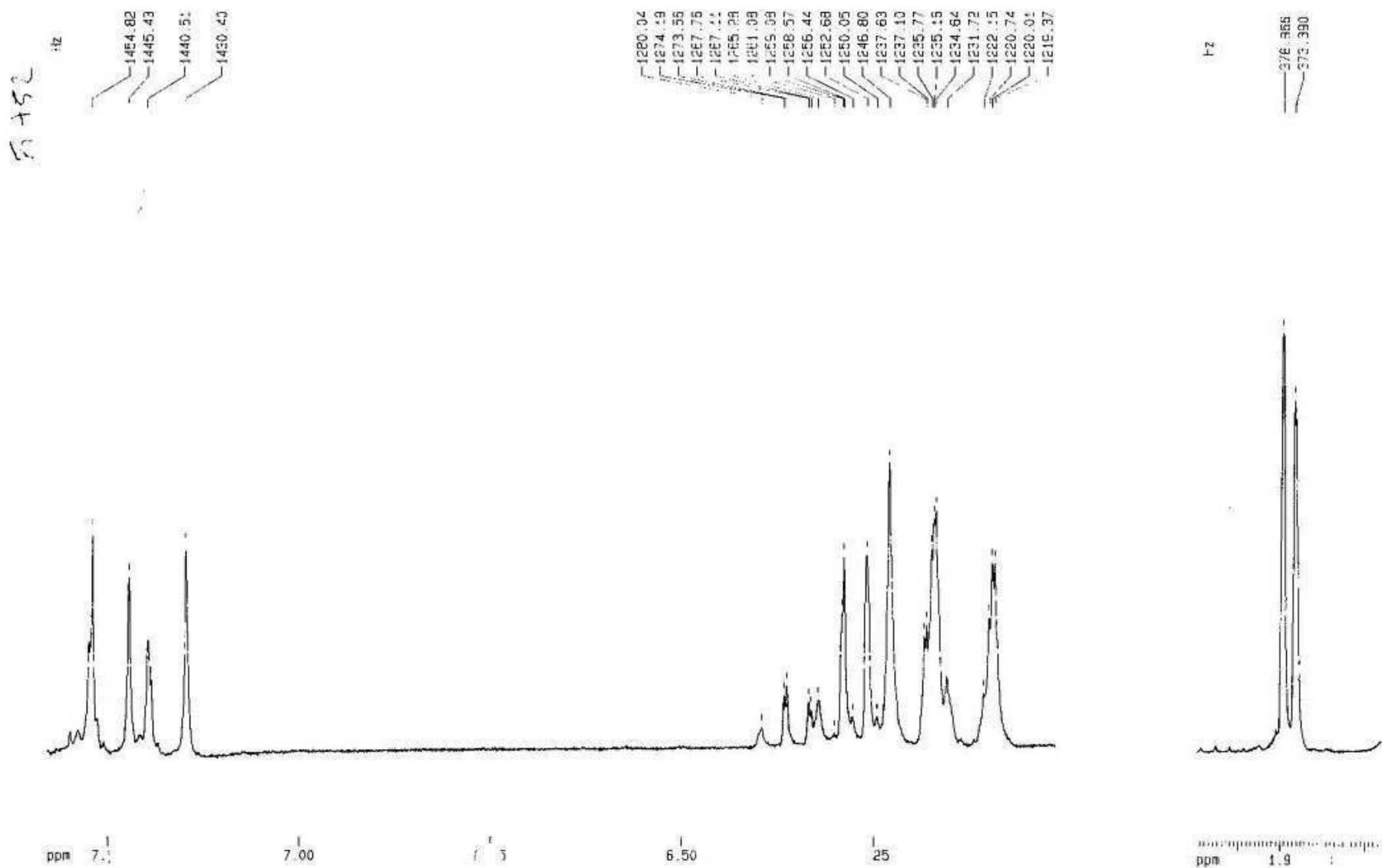
Se-Phenyl (2*E*,4*E*)-hexa-2,4-dieneselenoate (**3j**) ^1H NMR (200 MHz, CDCl_3)

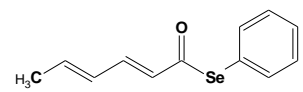
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72



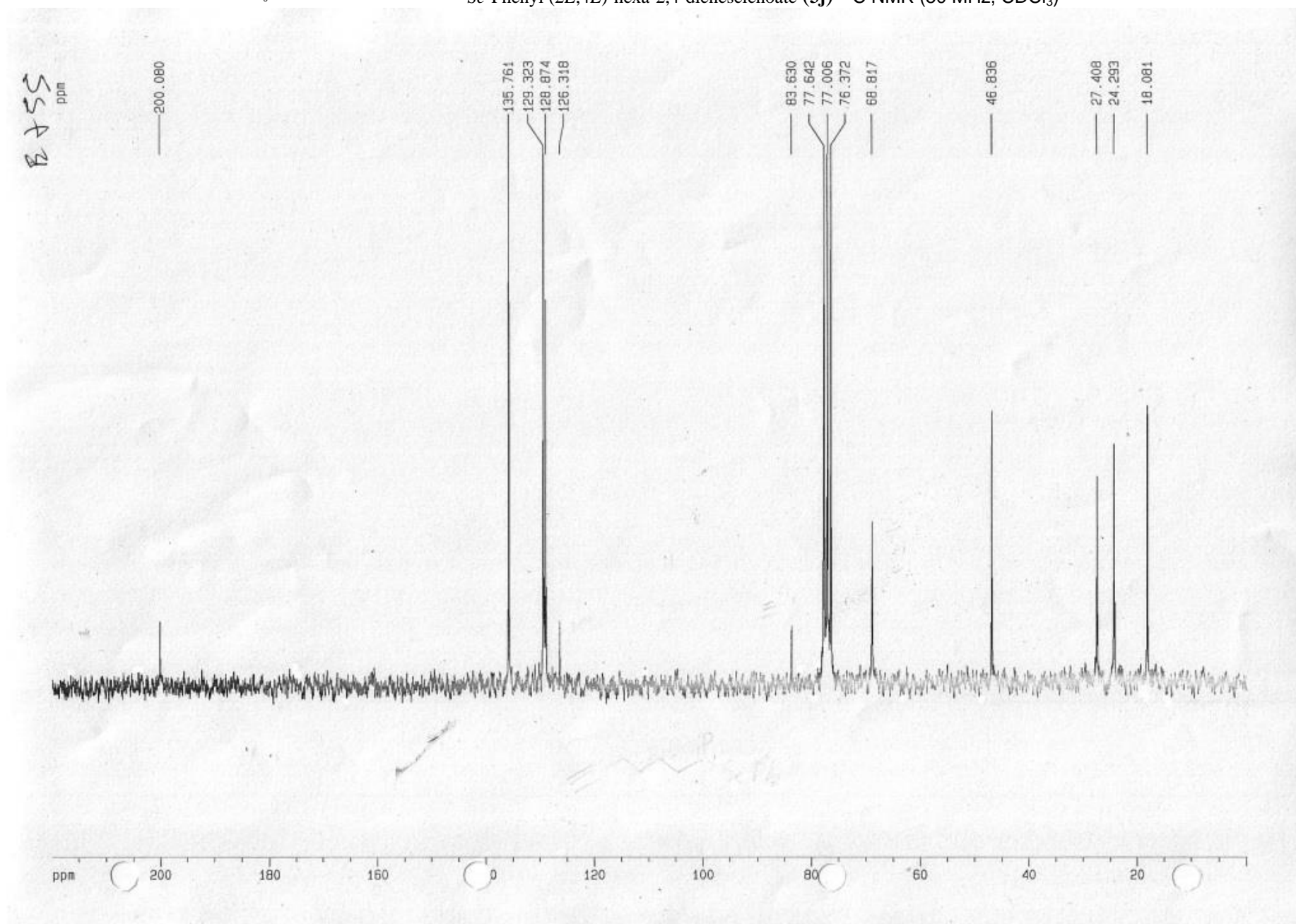


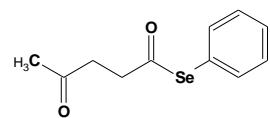
Se-Phenyl (2*E*,4*E*)-hexa-2,4-dieneselenoate (**3j**) ^1H NMR (200 MHz, CDCl_3)



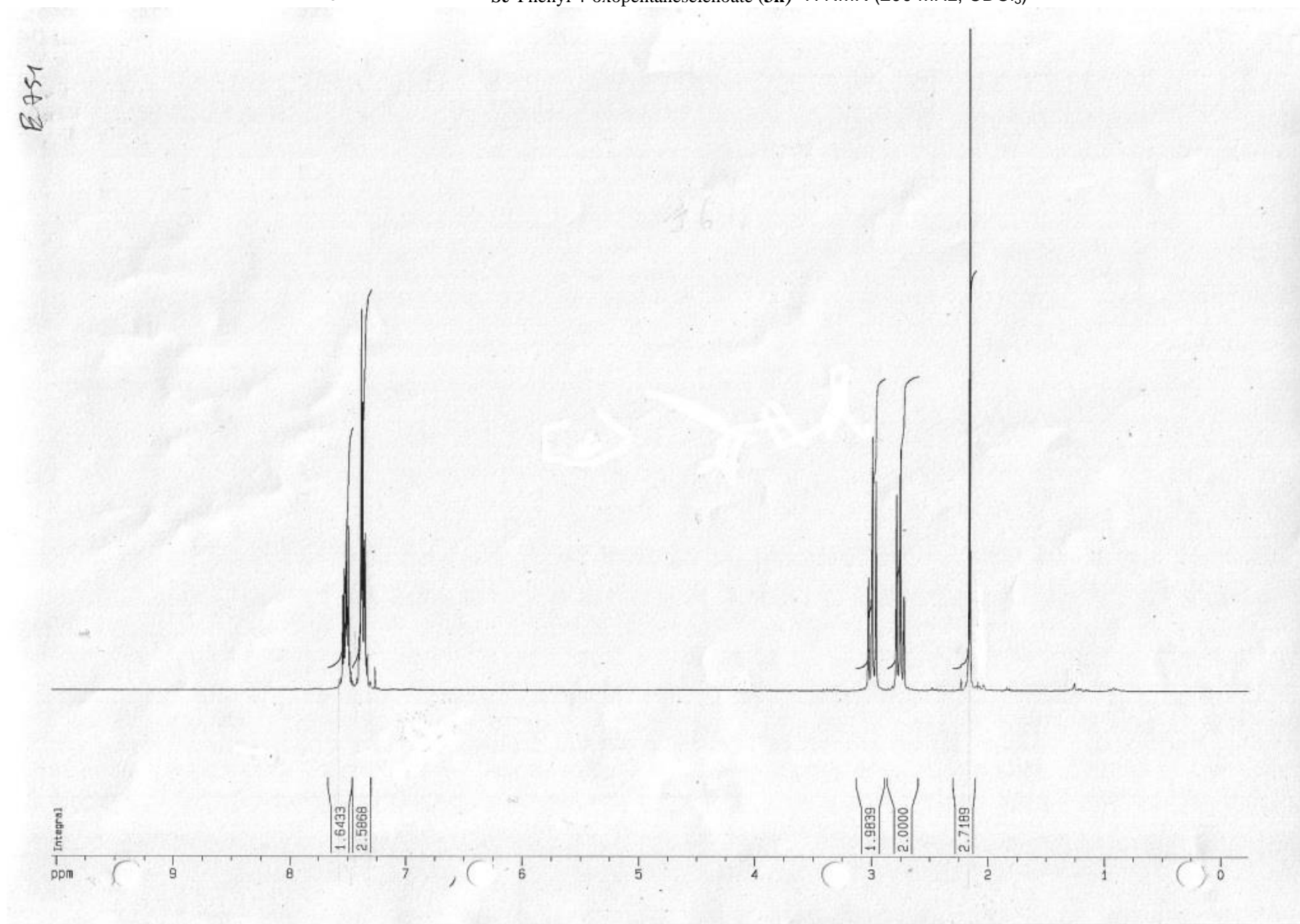


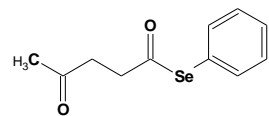
Se-Phenyl (2*E*,4*E*)-hexa-2,4-dieneselenoate (**3j**) ^{13}C NMR (50 MHz, CDCl_3)



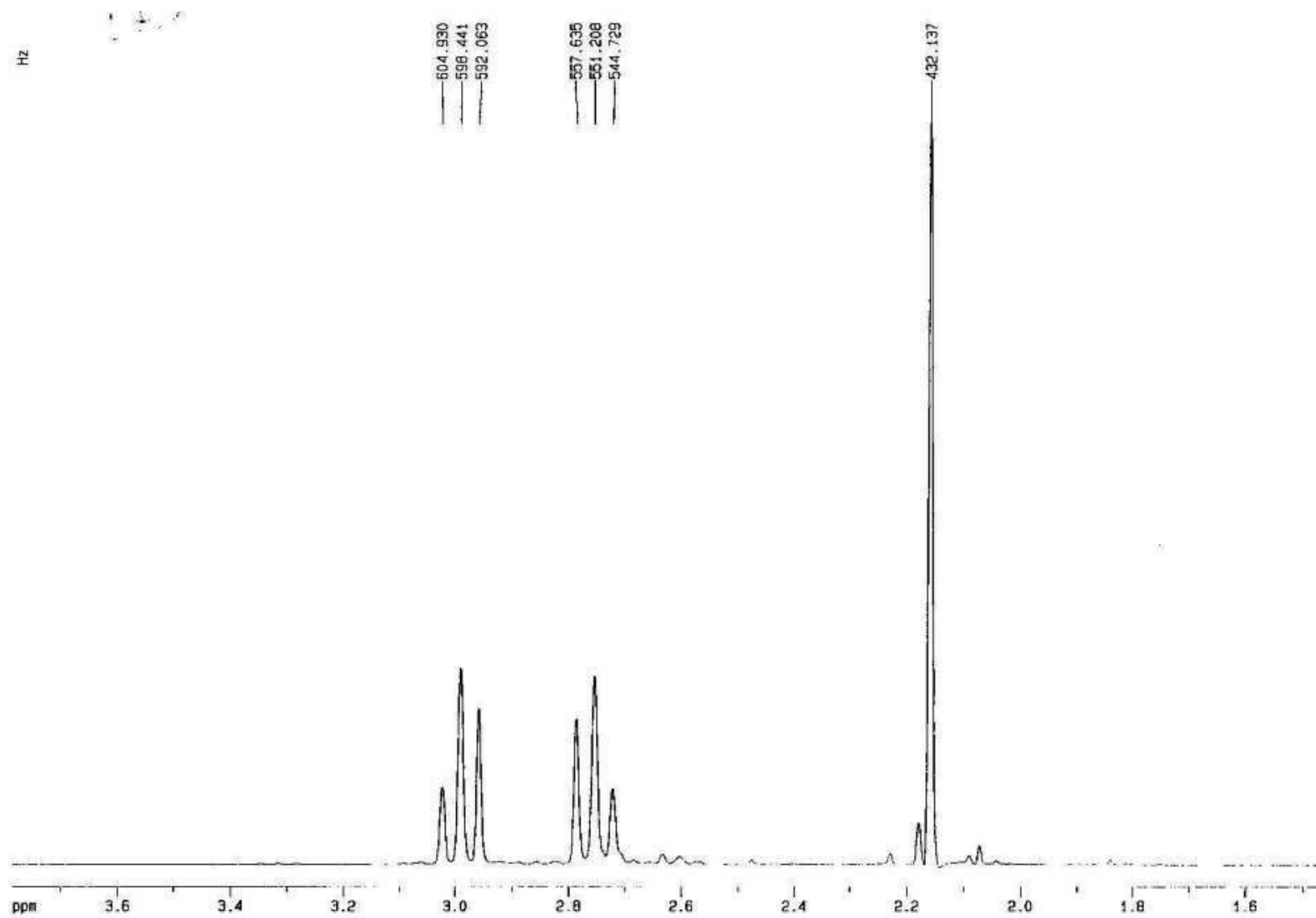


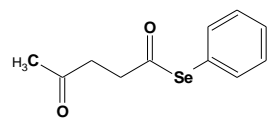
Se-Phenyl 4-oxopentaneselenoate (**3k**) ^1H NMR (200 MHz, CDCl_3)



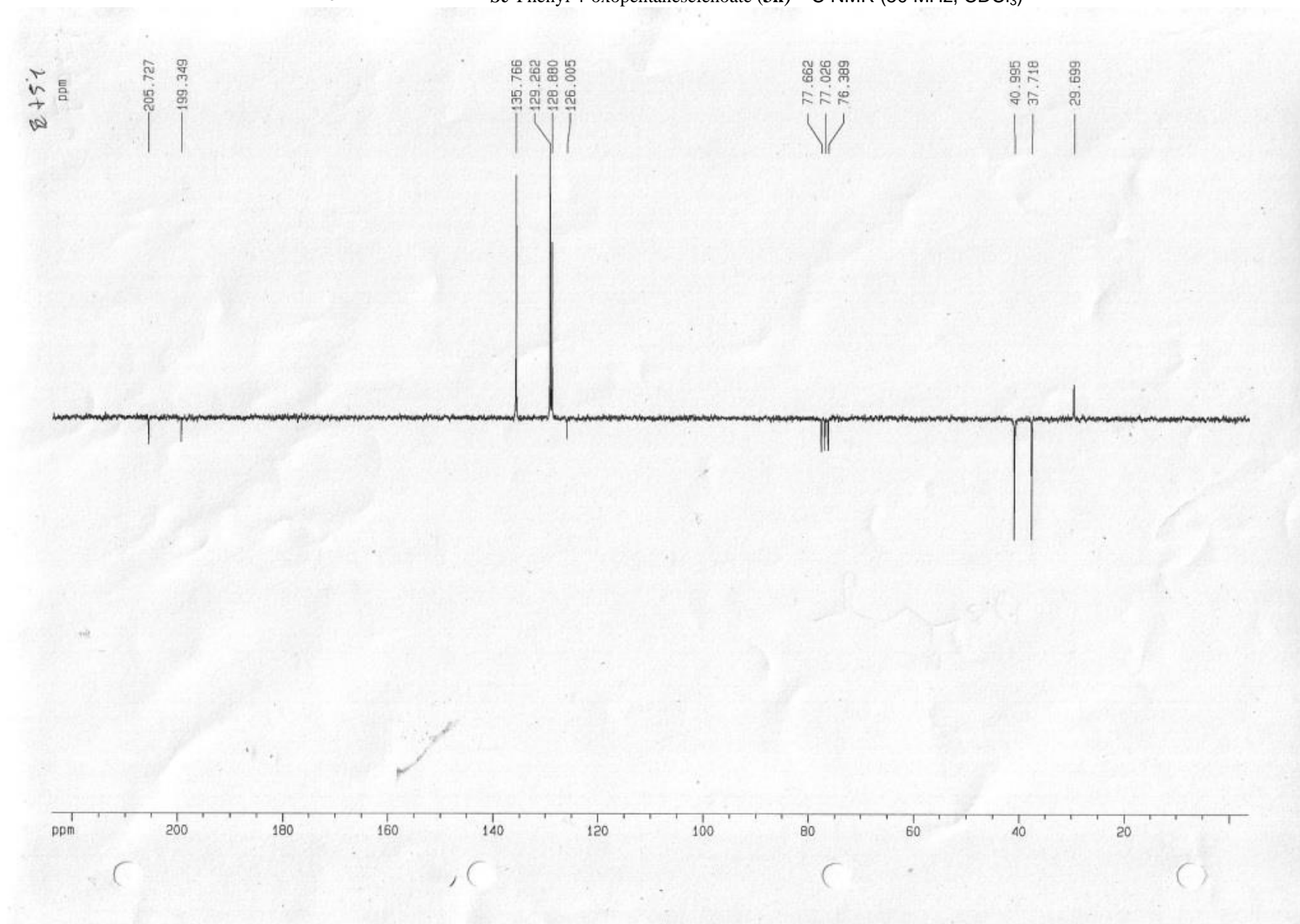


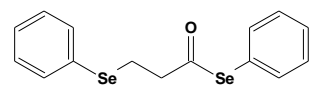
Se-Phenyl 4-oxopentaneselenoate (**3k**) ^1H NMR (200 MHz, CDCl_3)





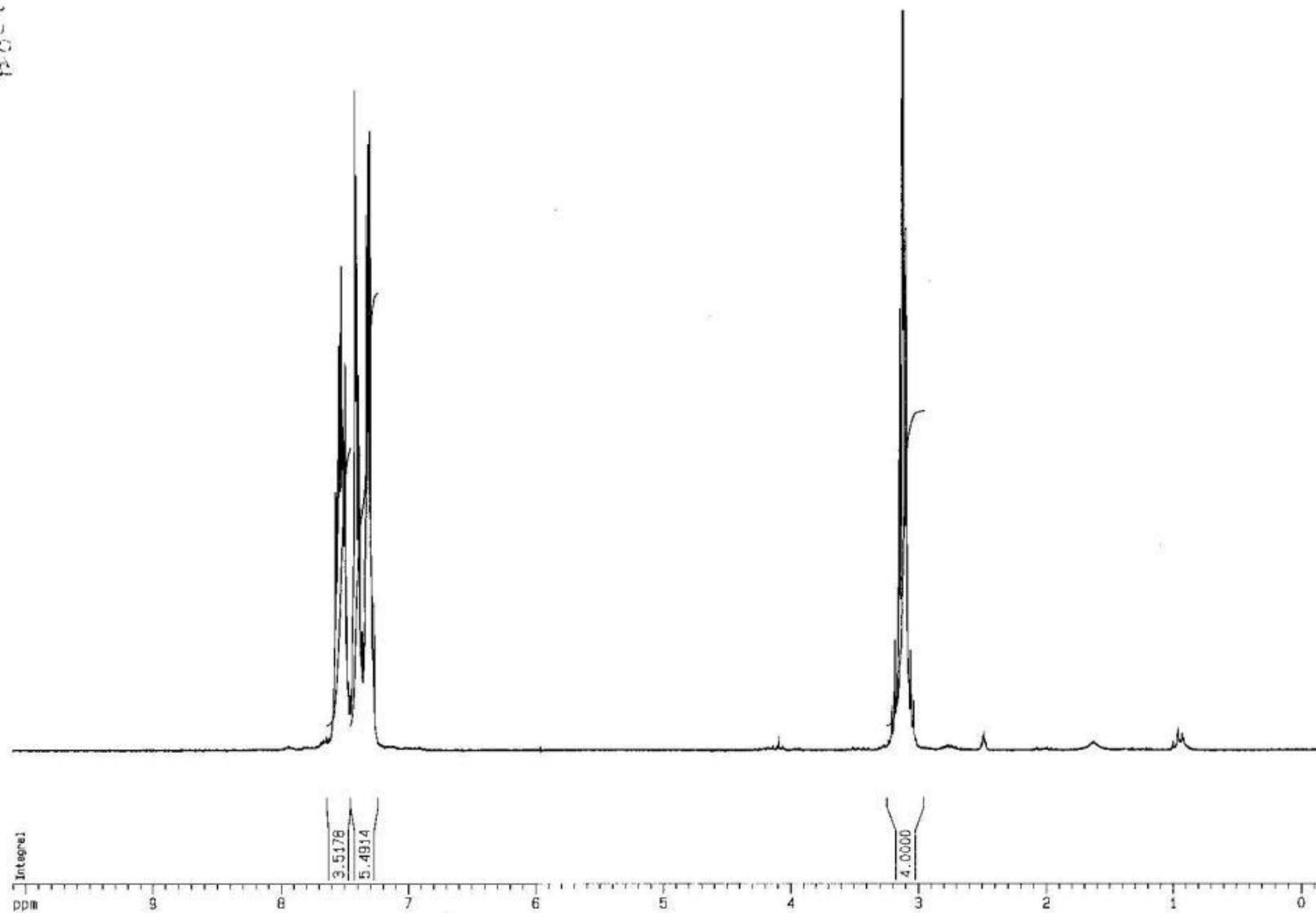
Se-Phenyl 4-oxopentaneselenoate (**3k**) ^{13}C NMR (50 MHz, CDCl_3)

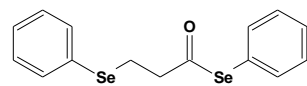




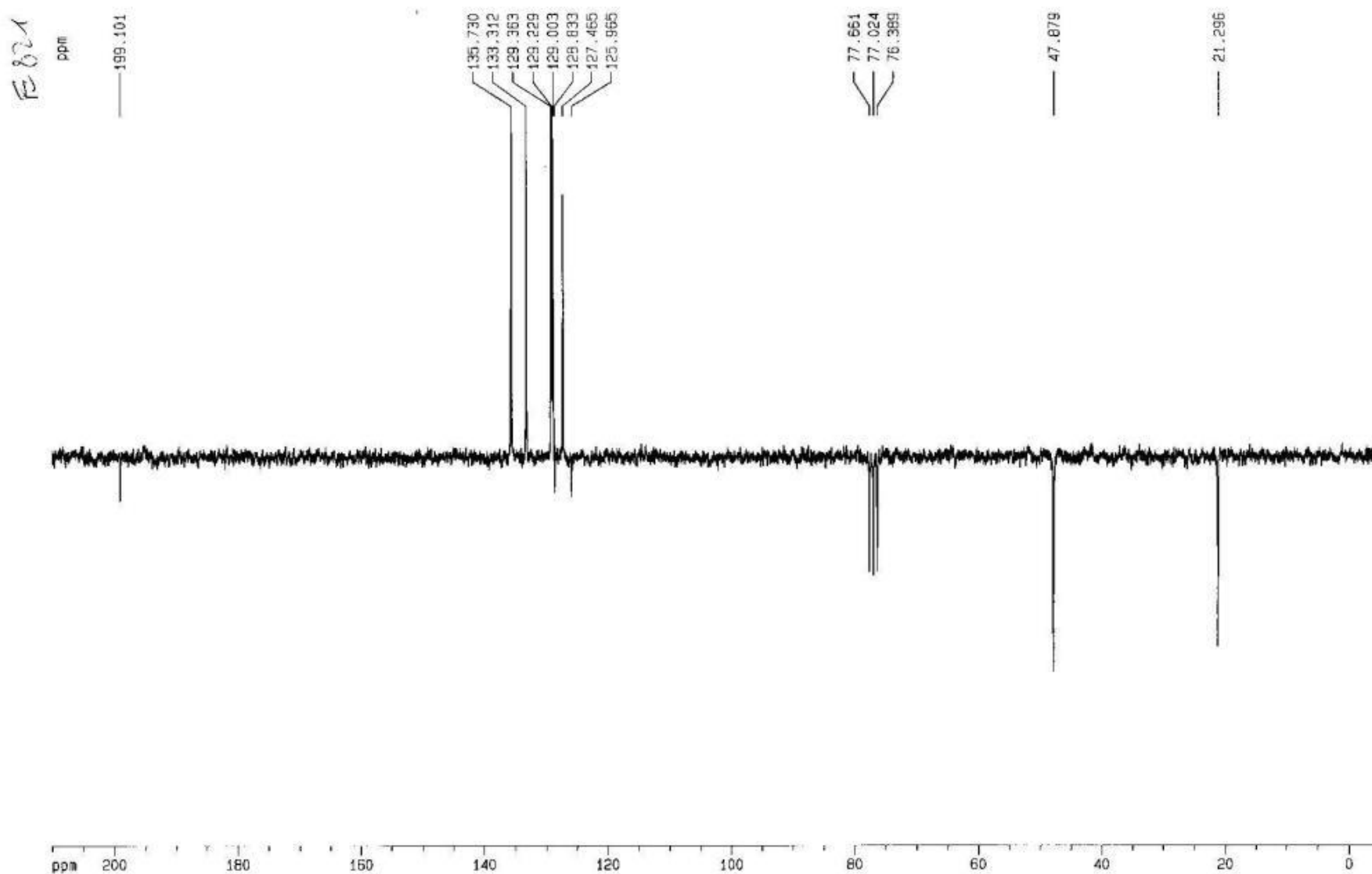
Se-Phenyl 3-(phenylseleno)propaneselenoate (31) ^1H NMR (200 MHz, CDCl_3)

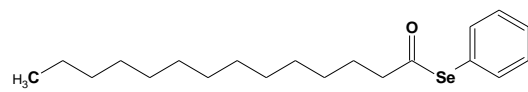
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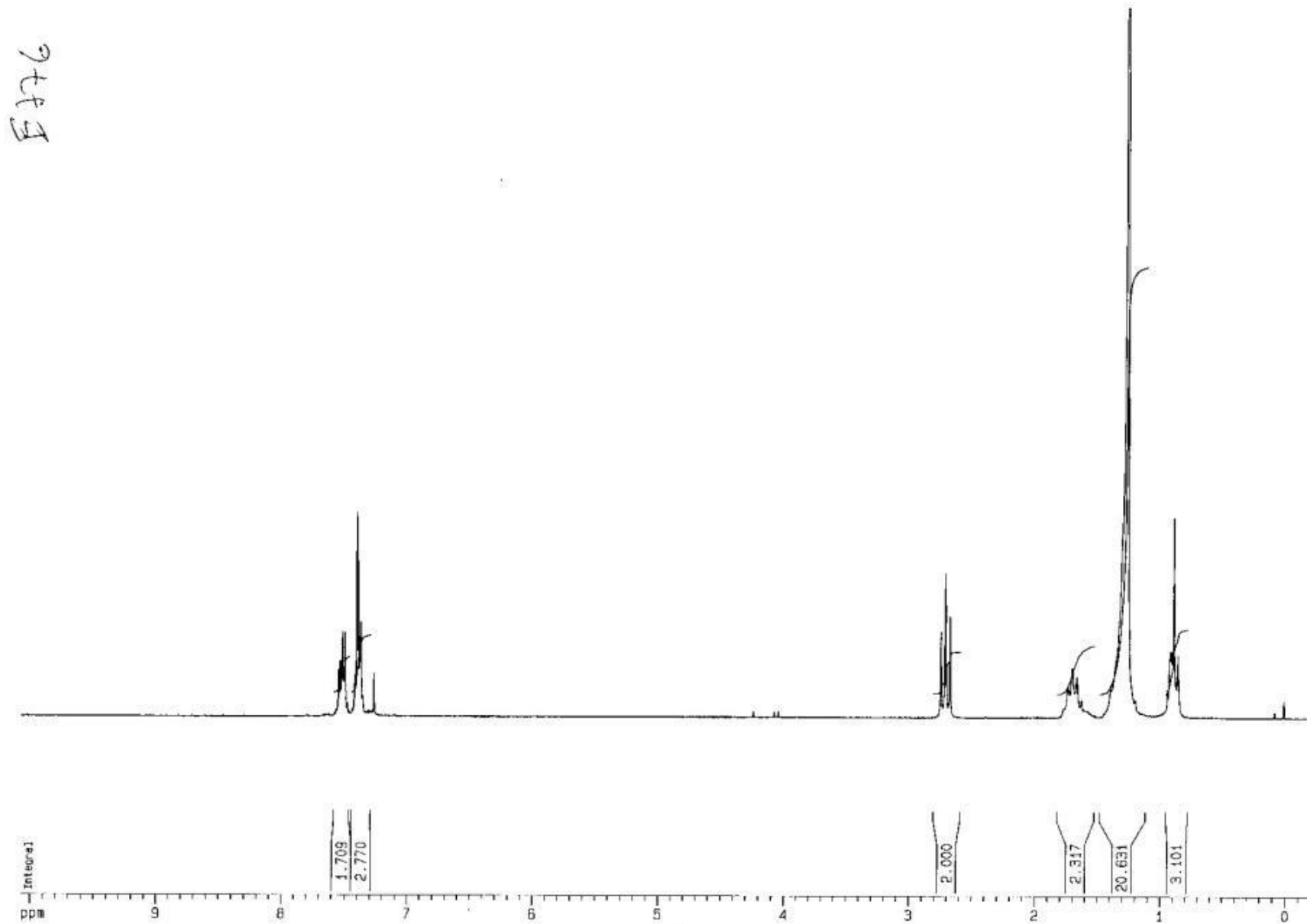


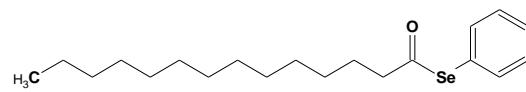
Se-Phenyl 3-(phenylseleno)propaneselenoate (31) ^{13}C NMR (50 MHz, CDCl_3)



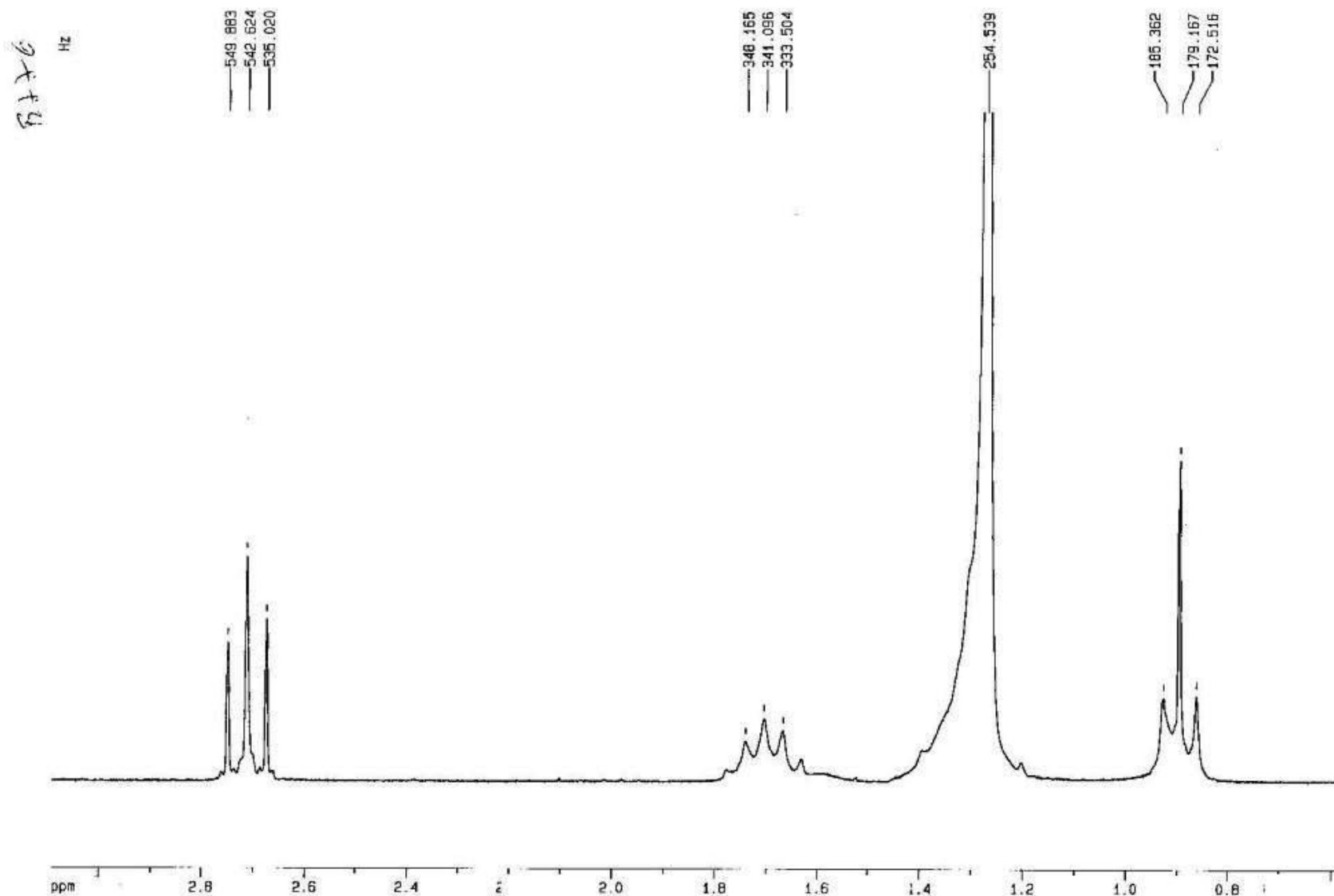


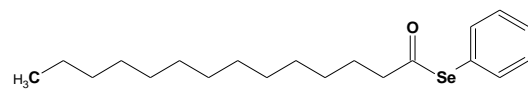
Se-Phenyl tetradecaneselenoate (**3m**) ^1H NMR (200 MHz, CDCl_3)



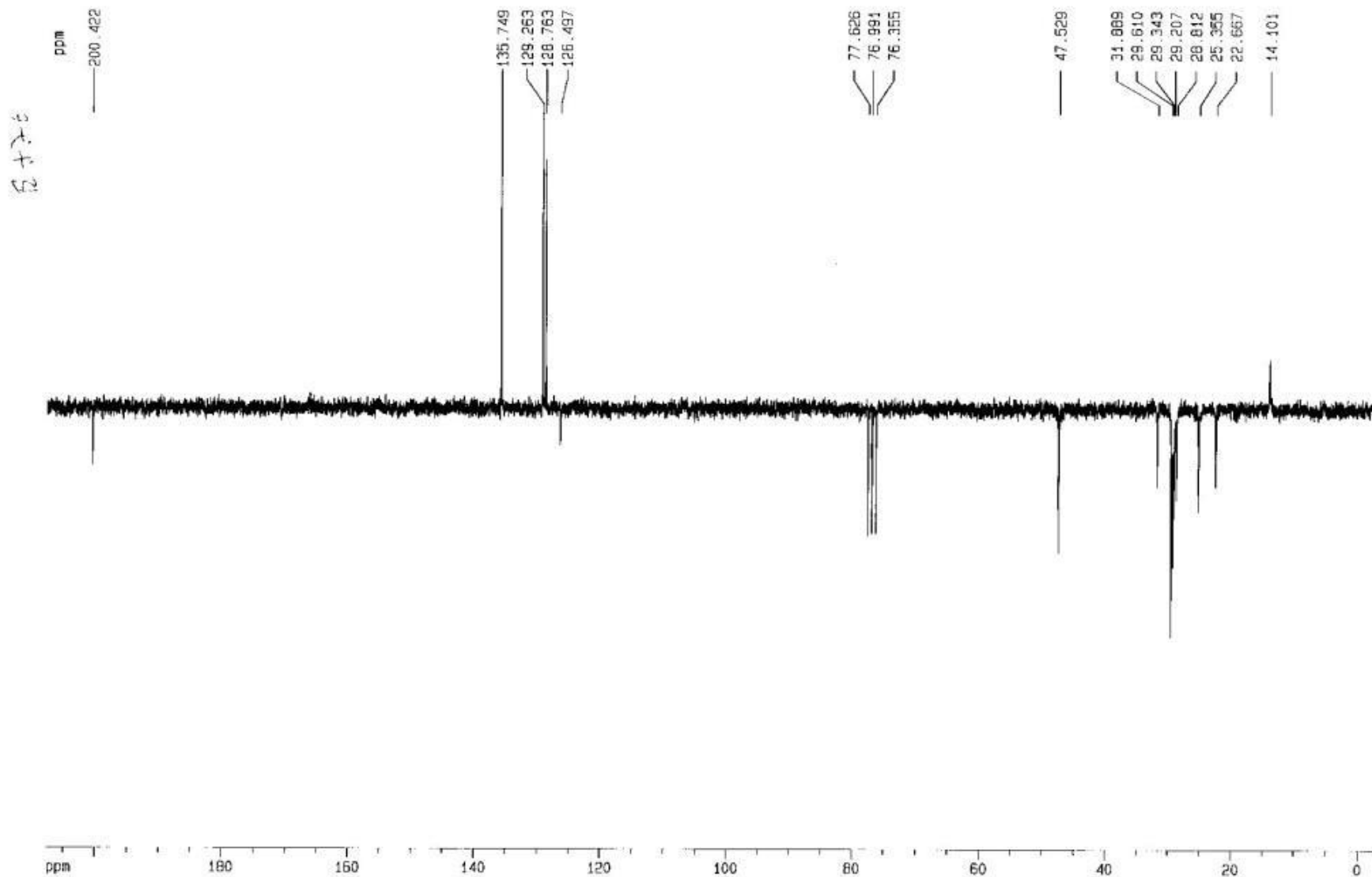


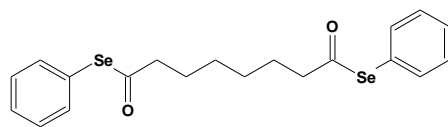
Se-Phenyl tetradecaneselenoate (**3m**) ^1H NMR (200 MHz, CDCl_3)



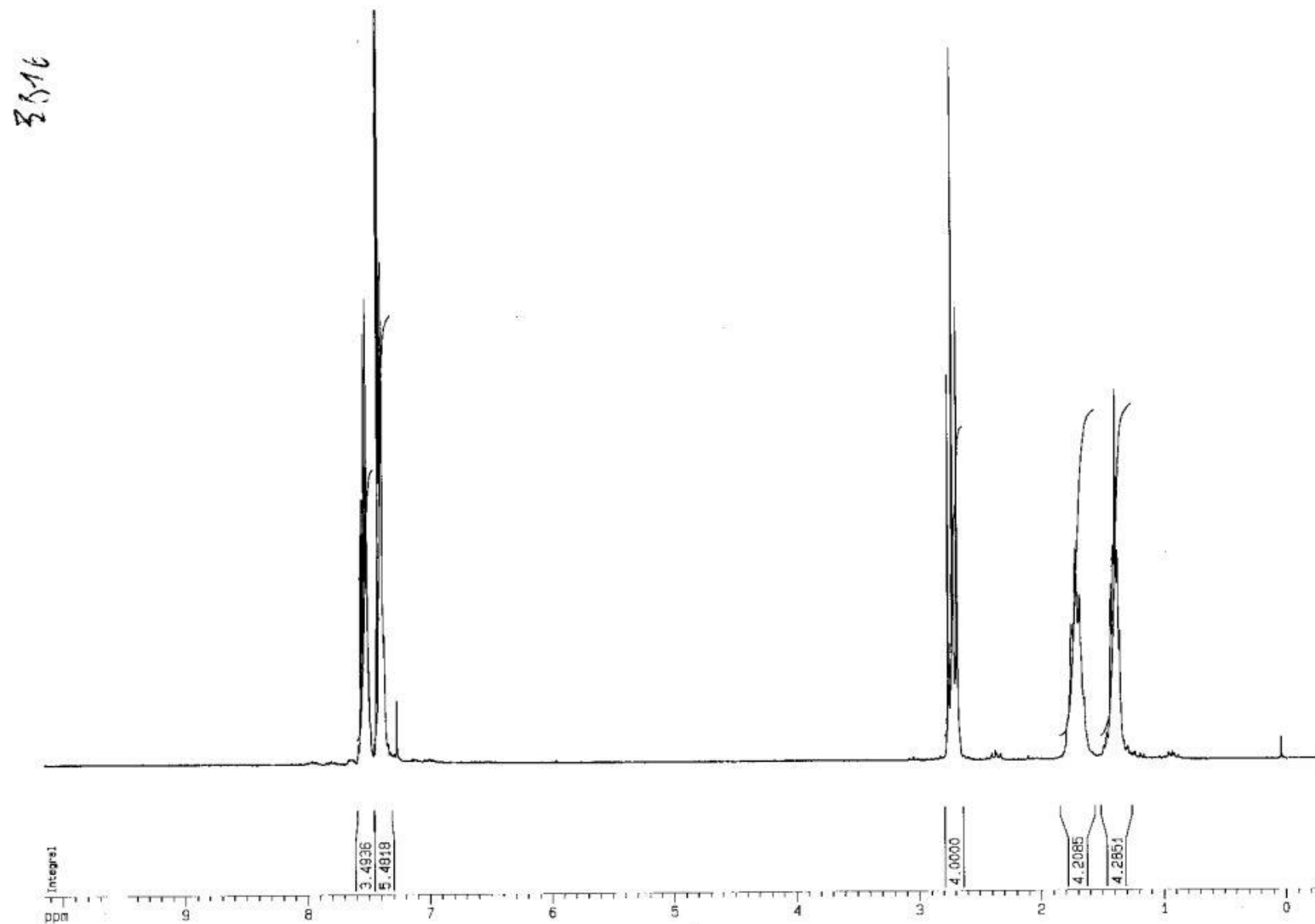


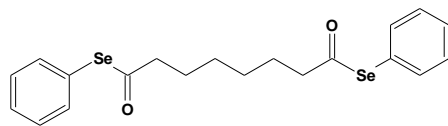
Se-Phenyl tetradecaneselenoate (**3m**) ^{13}C NMR (50 MHz, CDCl_3)



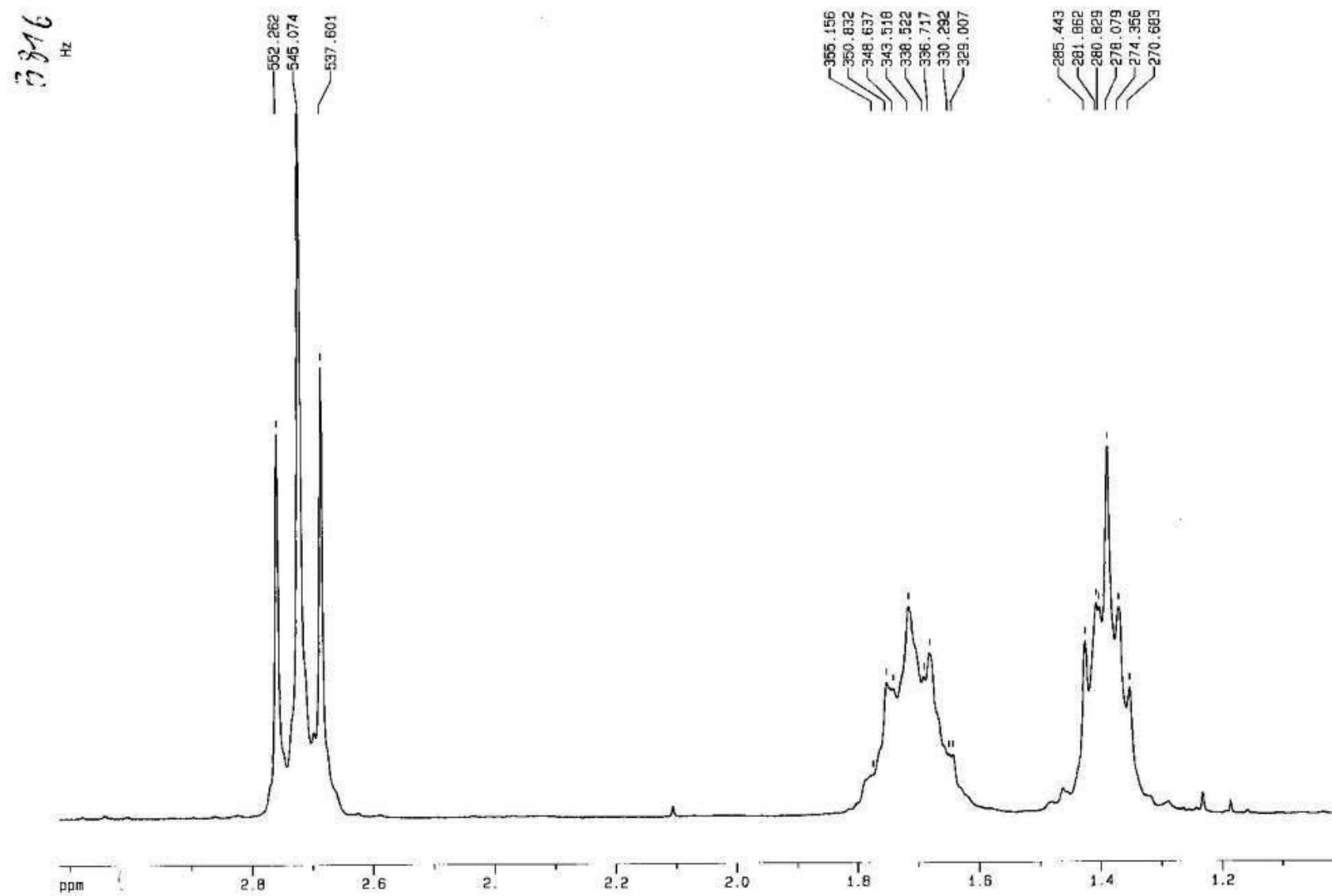


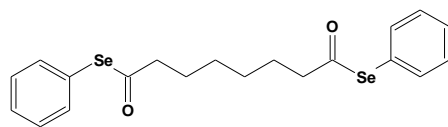
Se^1, Se^8 -Diphenyl octanebis(selenoate) (**3n**) 1H NMR (200 MHz, $CDCl_3$)



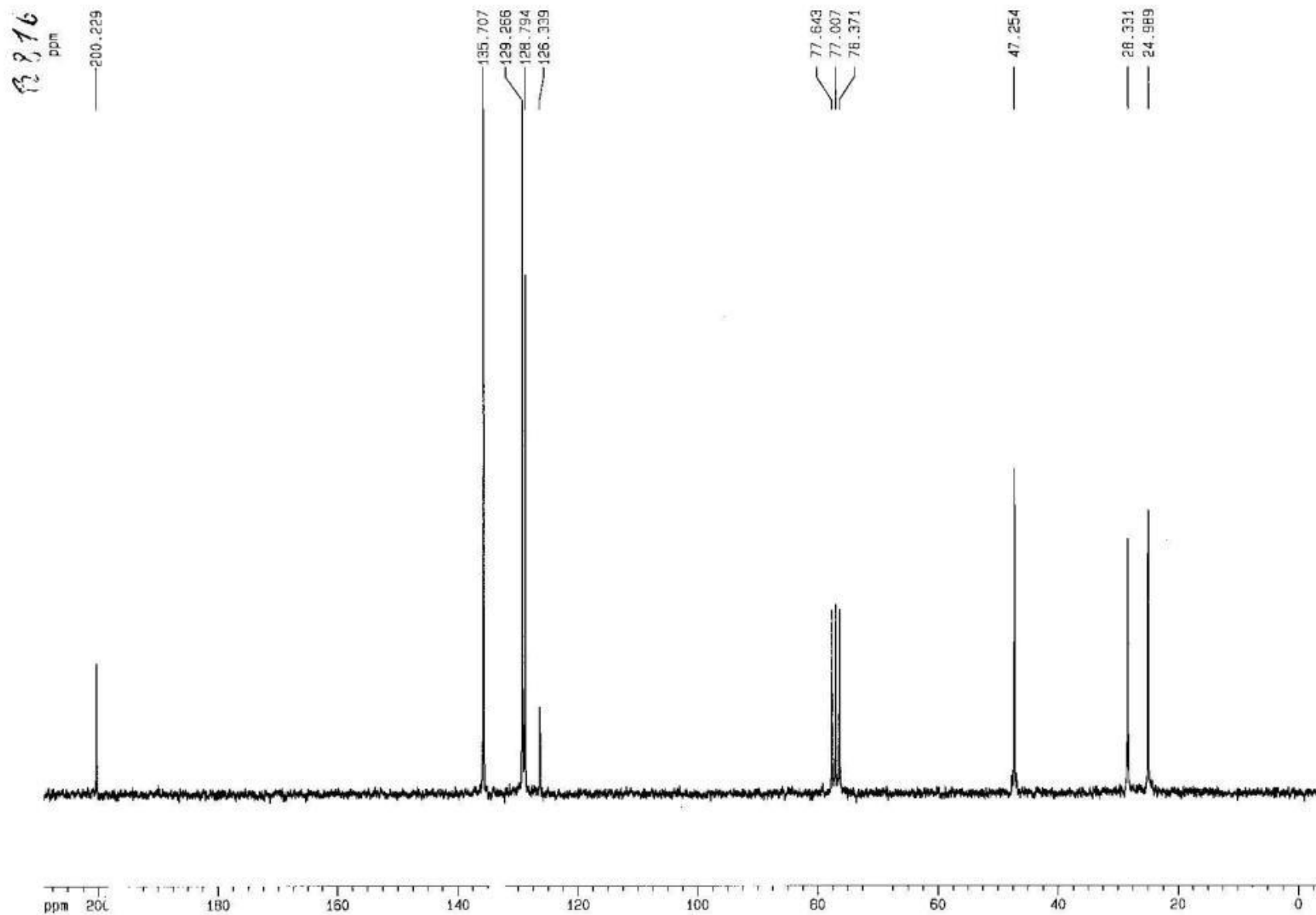


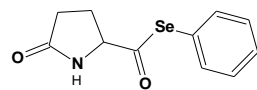
*Se*¹,*Se*⁸-Diphenyl octanebis(selenoate) (**3n**) ¹H NMR (200 MHz, CDCl₃)





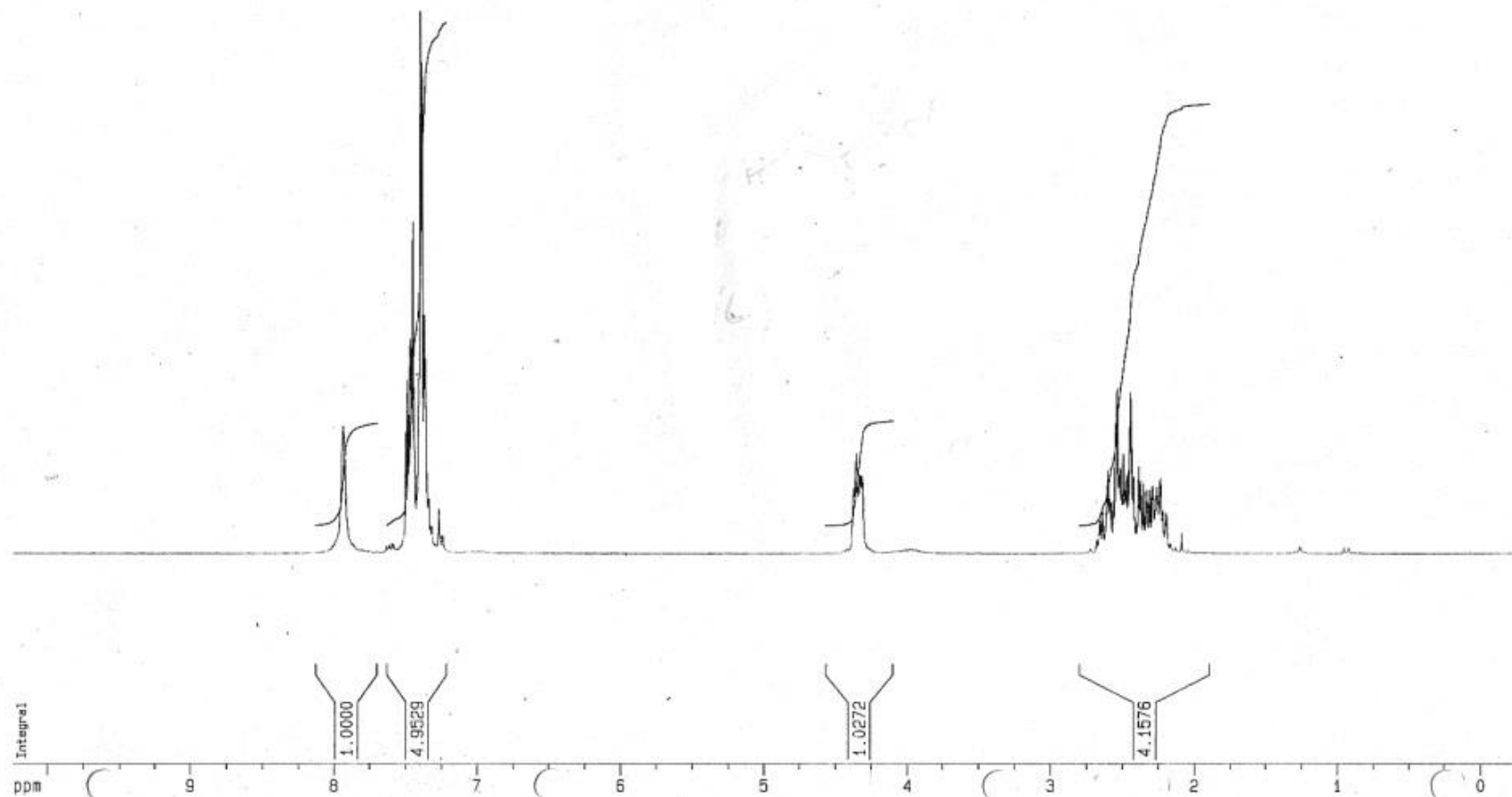
Se^1, Se^8 -Diphenyl octanebis(selenoate) (**3n**) ^{13}C NMR (50 MHz, $CDCl_3$)

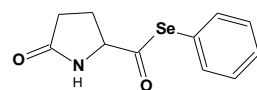




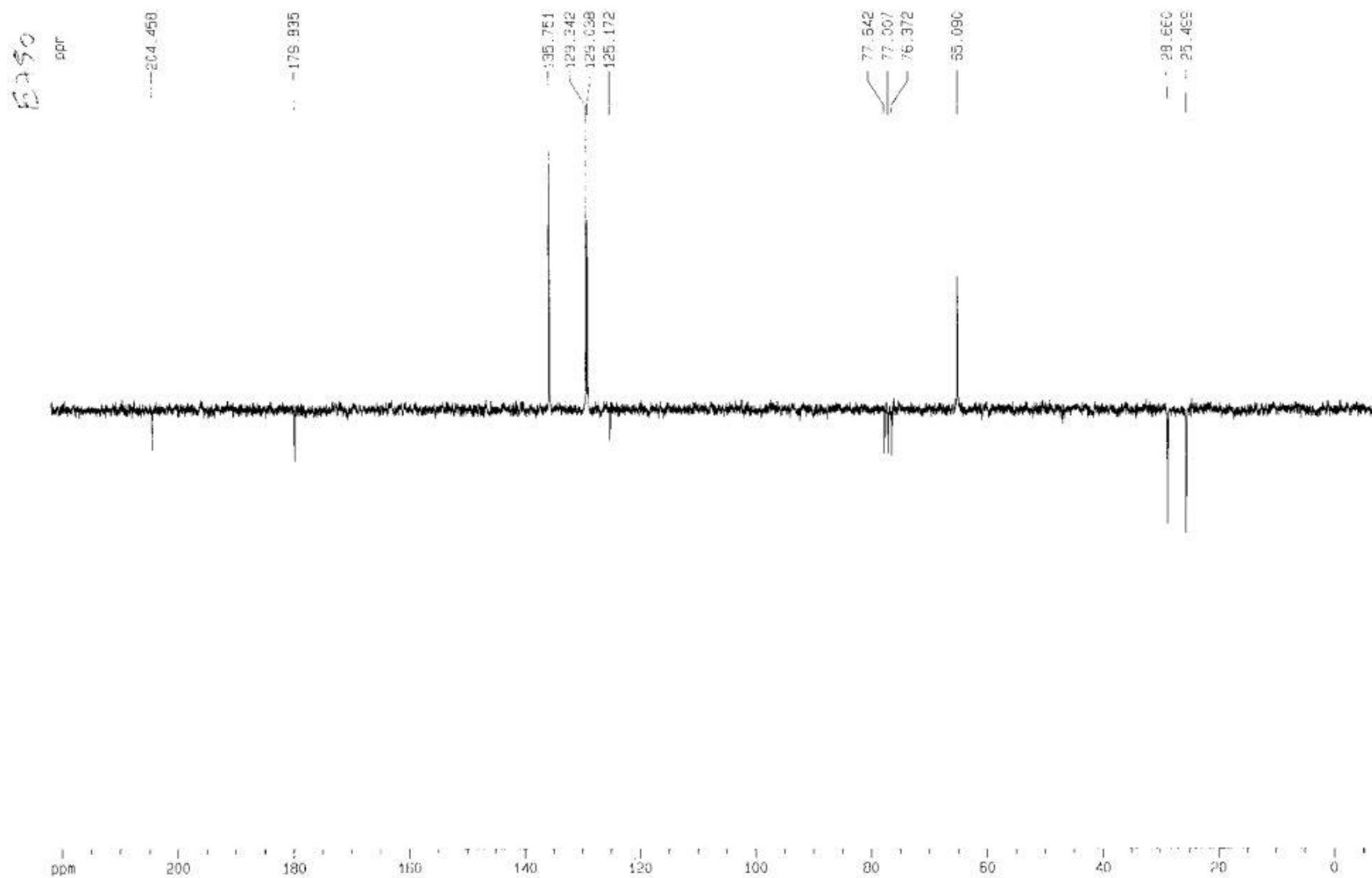
Se-Phenyl 5-oxopyrrolidine-2-carboselenoate (**3o**) ^1H NMR (200 MHz, CDCl_3)

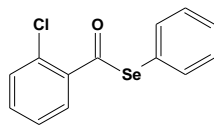
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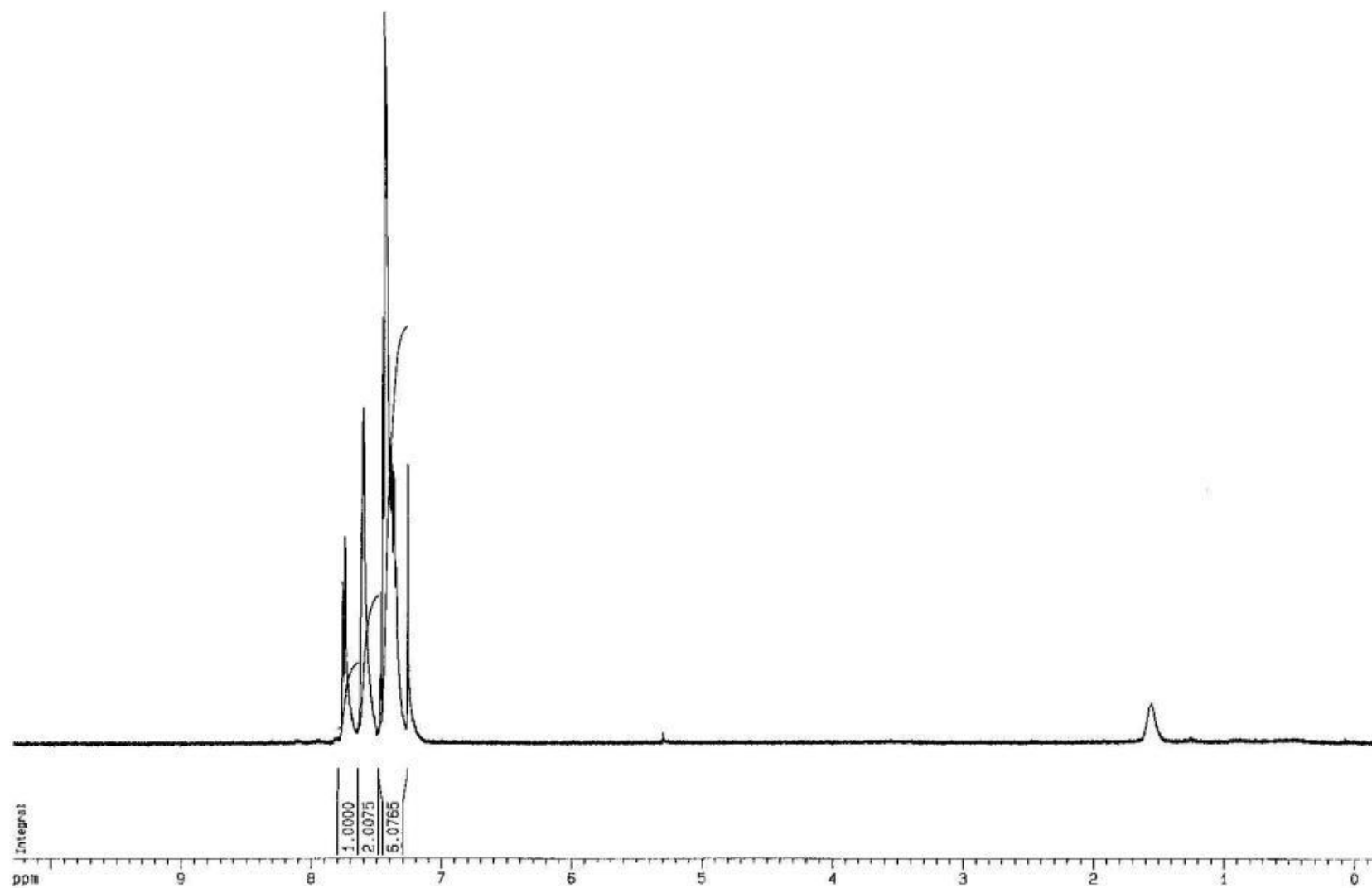


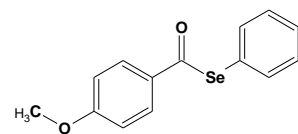
Se-Phenyl 5-oxopyrrolidine-2-carboselenoate (**3o**) ^{13}C NMR (50 MHz, CDCl_3)



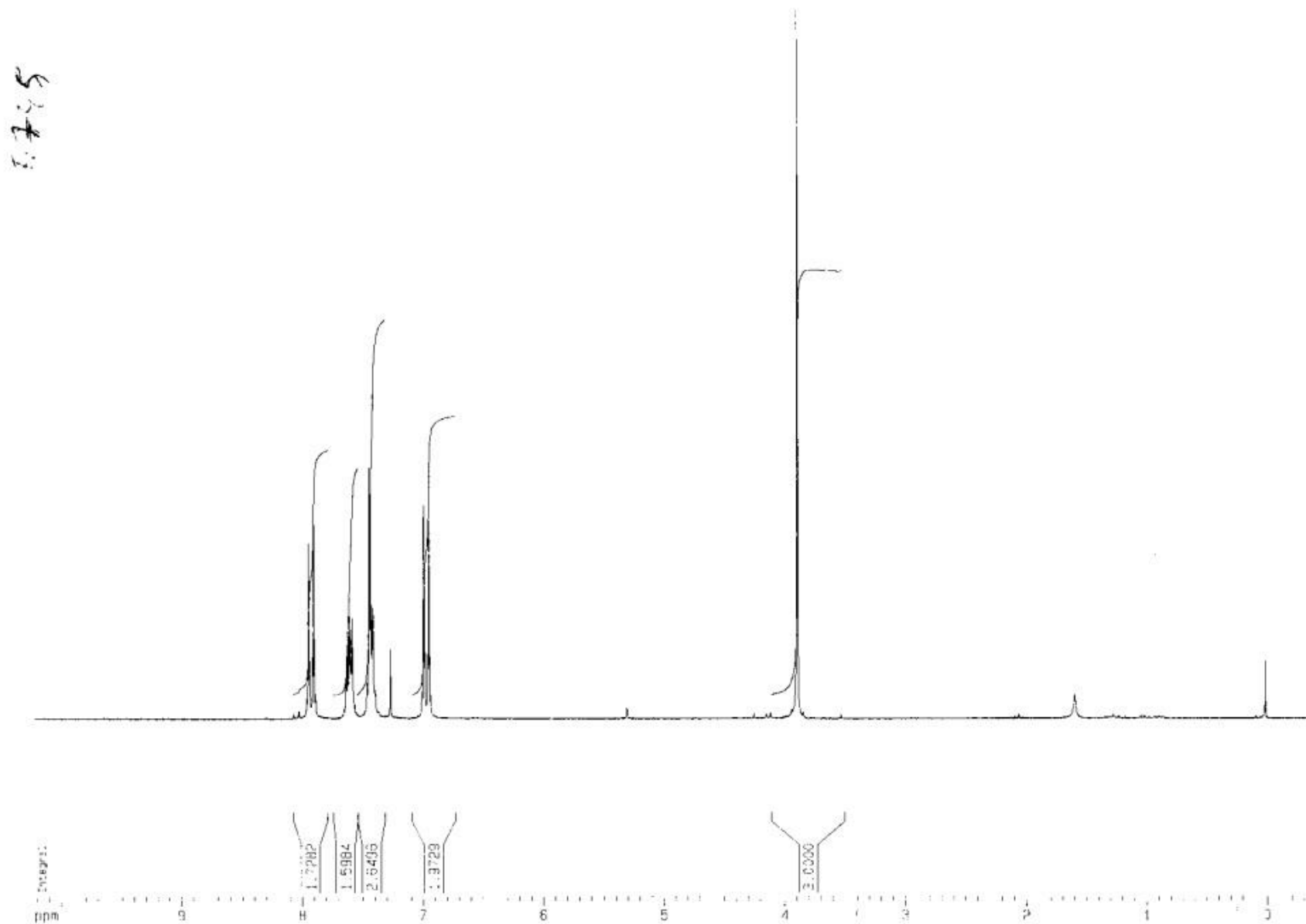


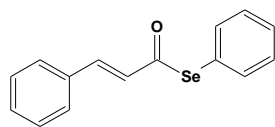
Se-Phenyl 2-chlorobenzenecarboselenoate (**3p**): ^1H NMR (200 MHz, CDCl_3)



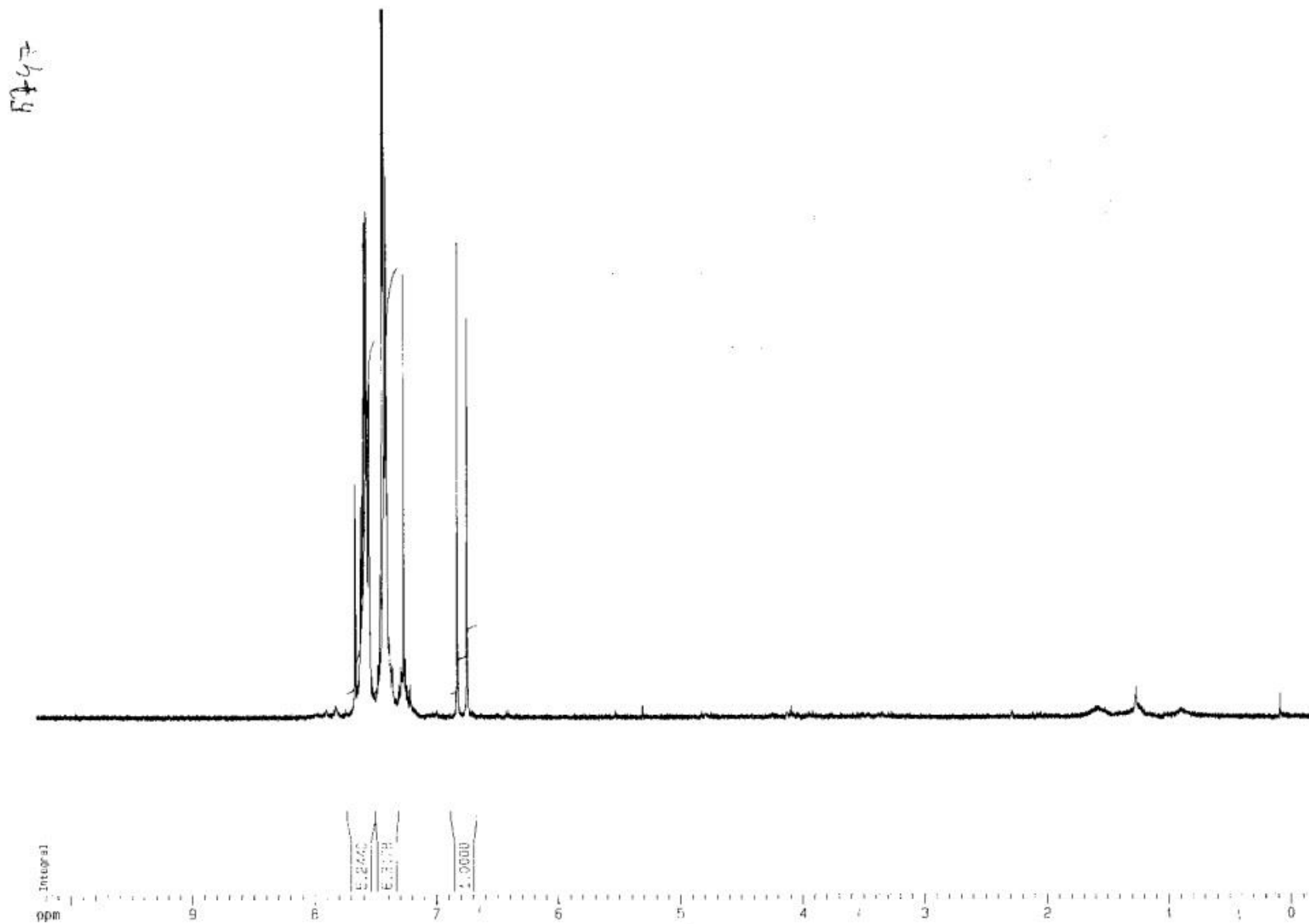


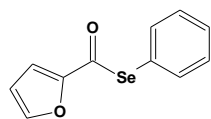
Se-Phenyl 4-methoxybenzenecarboselenoate (**3q**) ^1H NMR (200 MHz, CDCl_3)





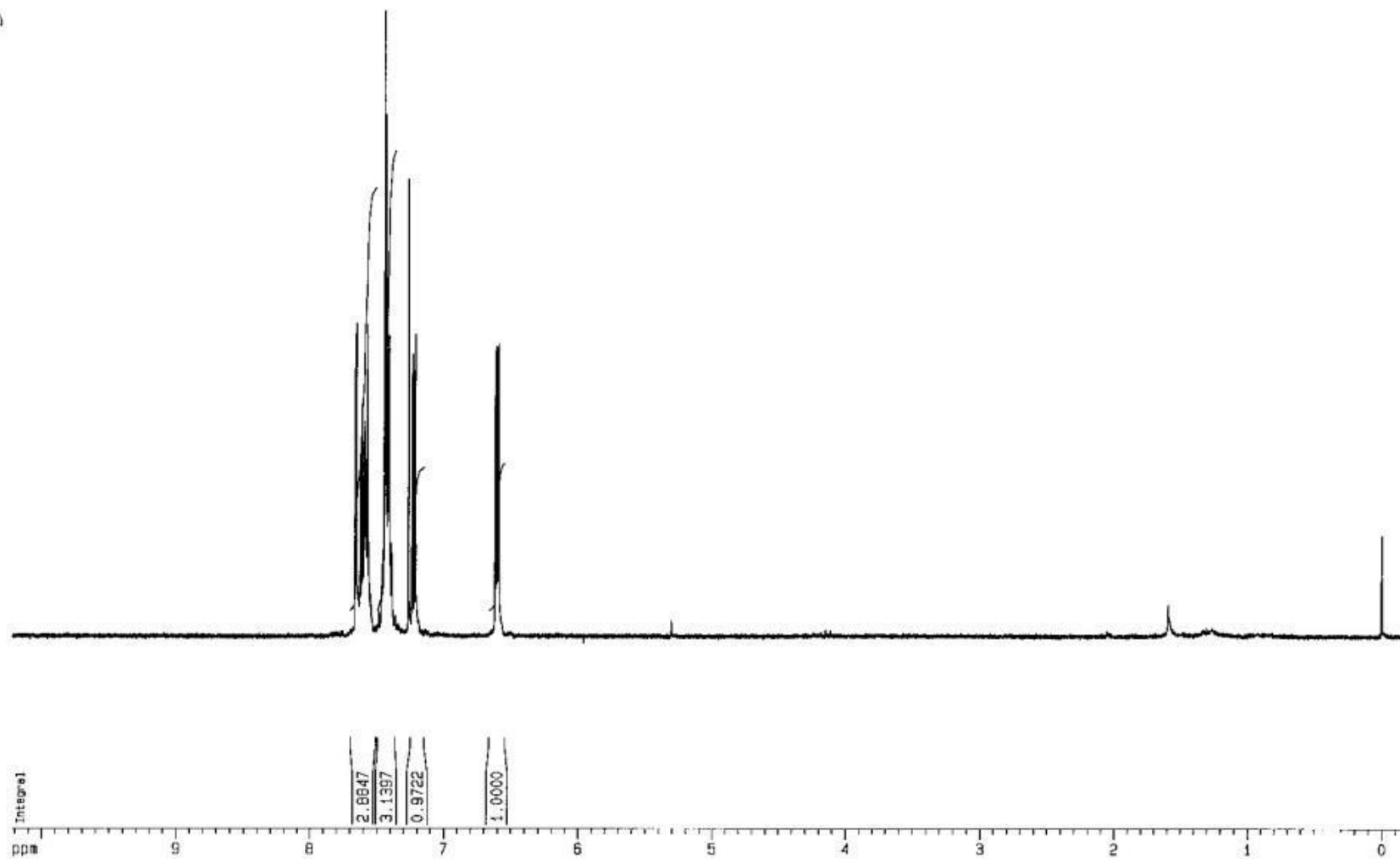
Se-Phenyl (2*E*)-3-phenylprop-2-eneselenoate (**3r**) ^1H NMR (200 MHz, CDCl_3)

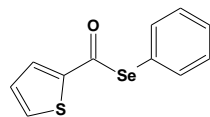




Se-Phenyl furan-2-carboselenoate (**3s**) ^1H NMR (200 MHz, CDCl_3)

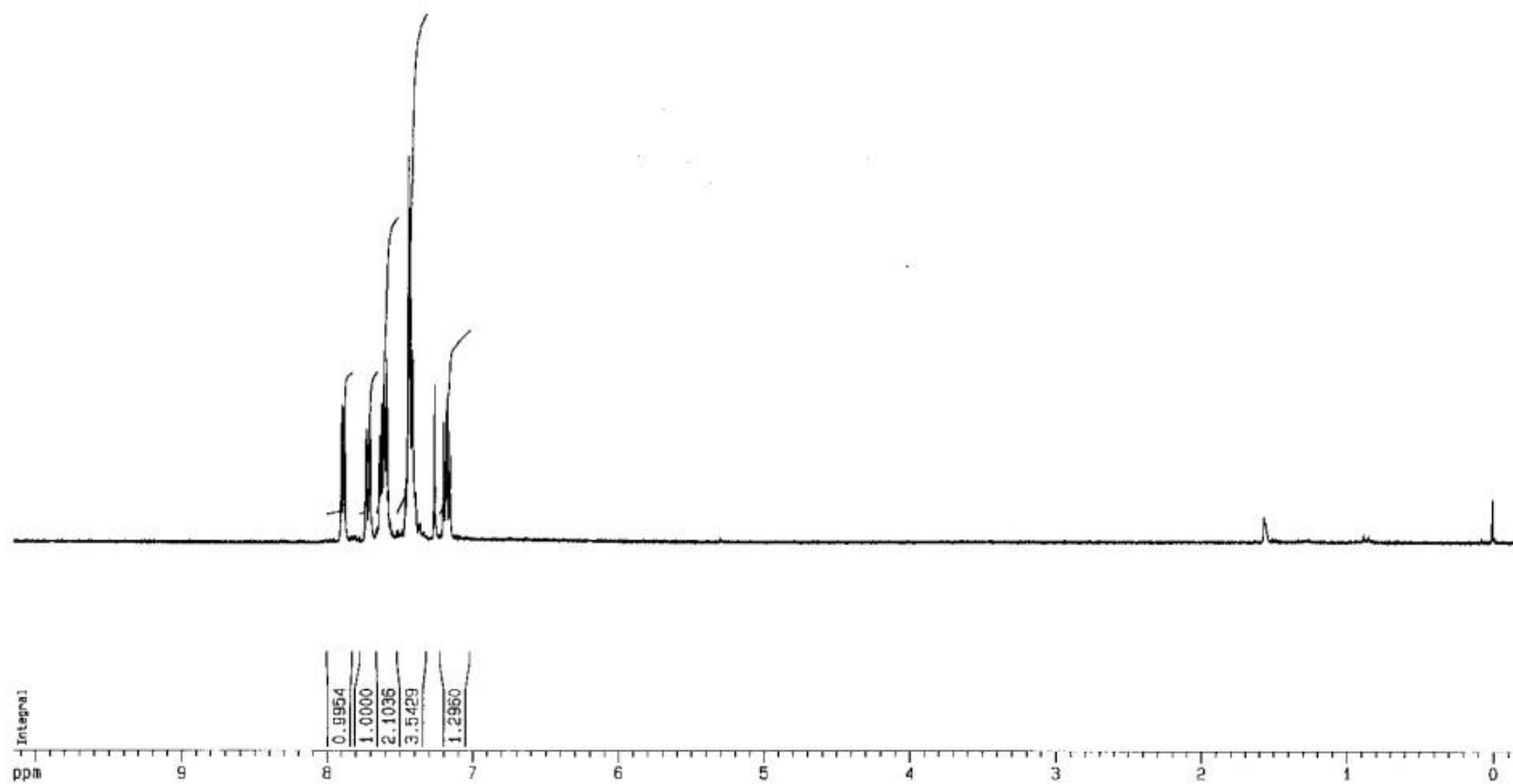
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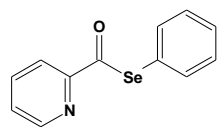




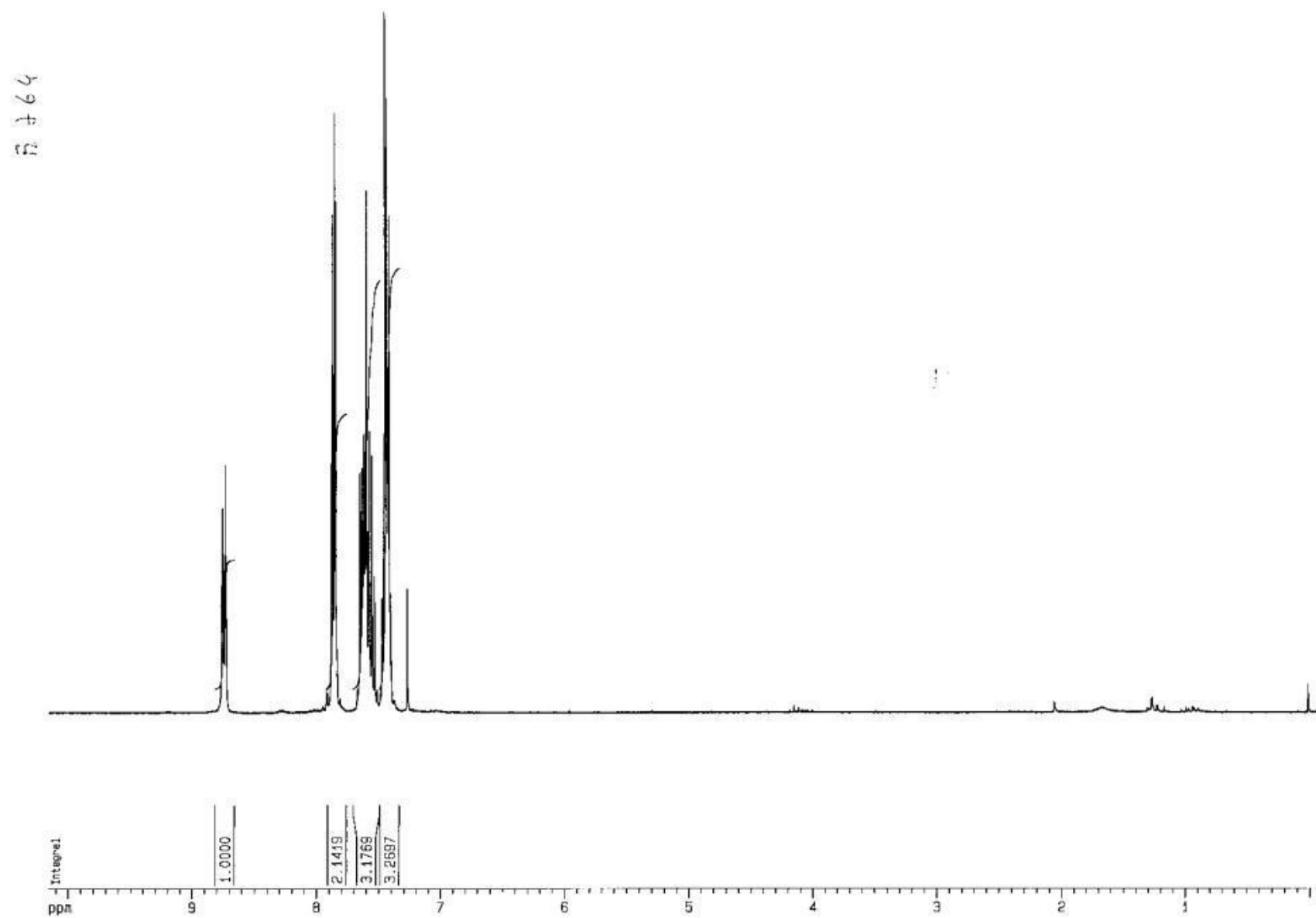
Se-Phenyl thiophene-2-carboselenoate (**3t**) ^1H NMR (200 MHz, CDCl_3)

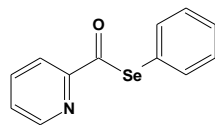
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#758



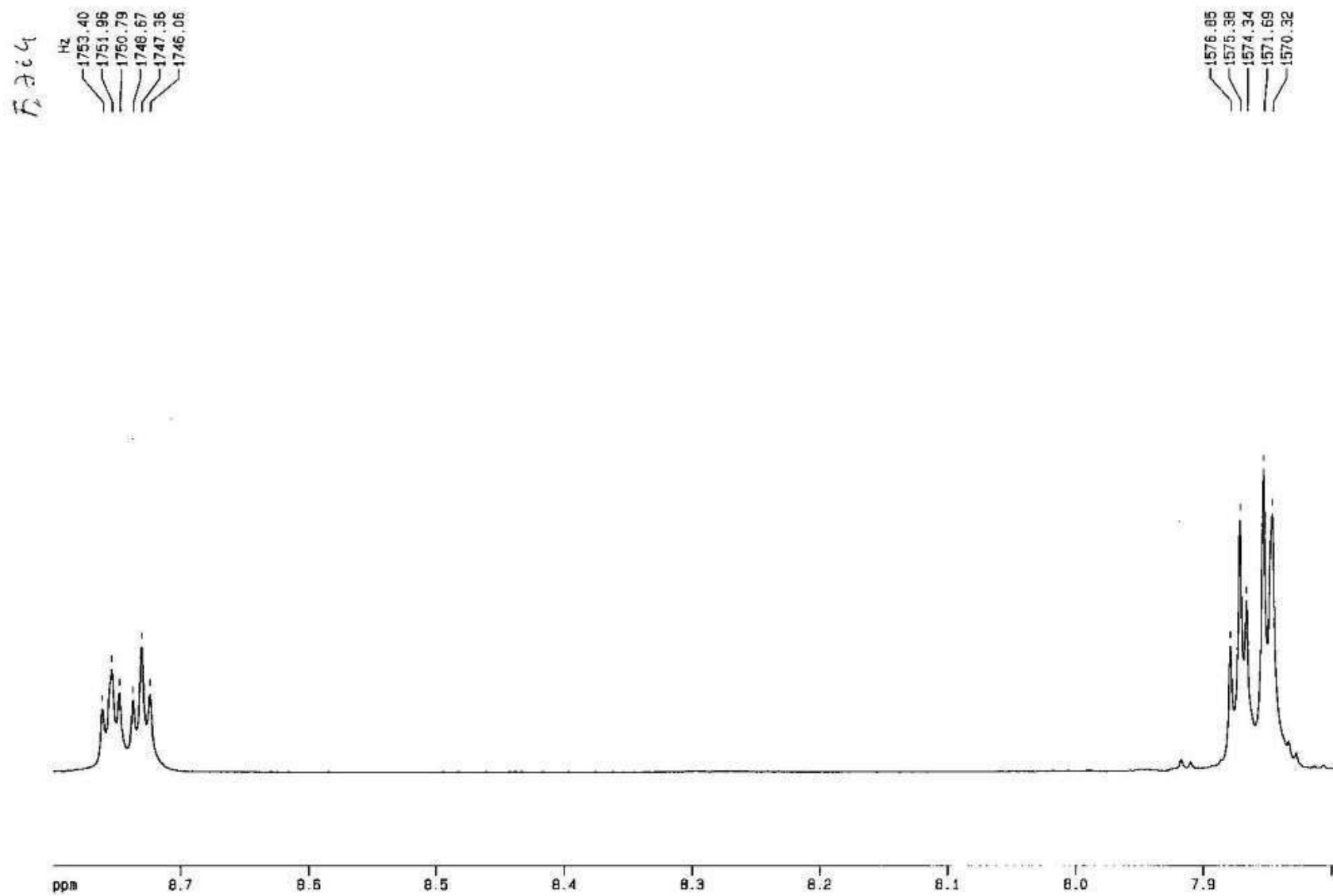


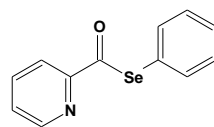
Se-Phenyl pyridine-2-carboselenoate (**3u**) ^1H NMR (400 MHz, CDCl_3)



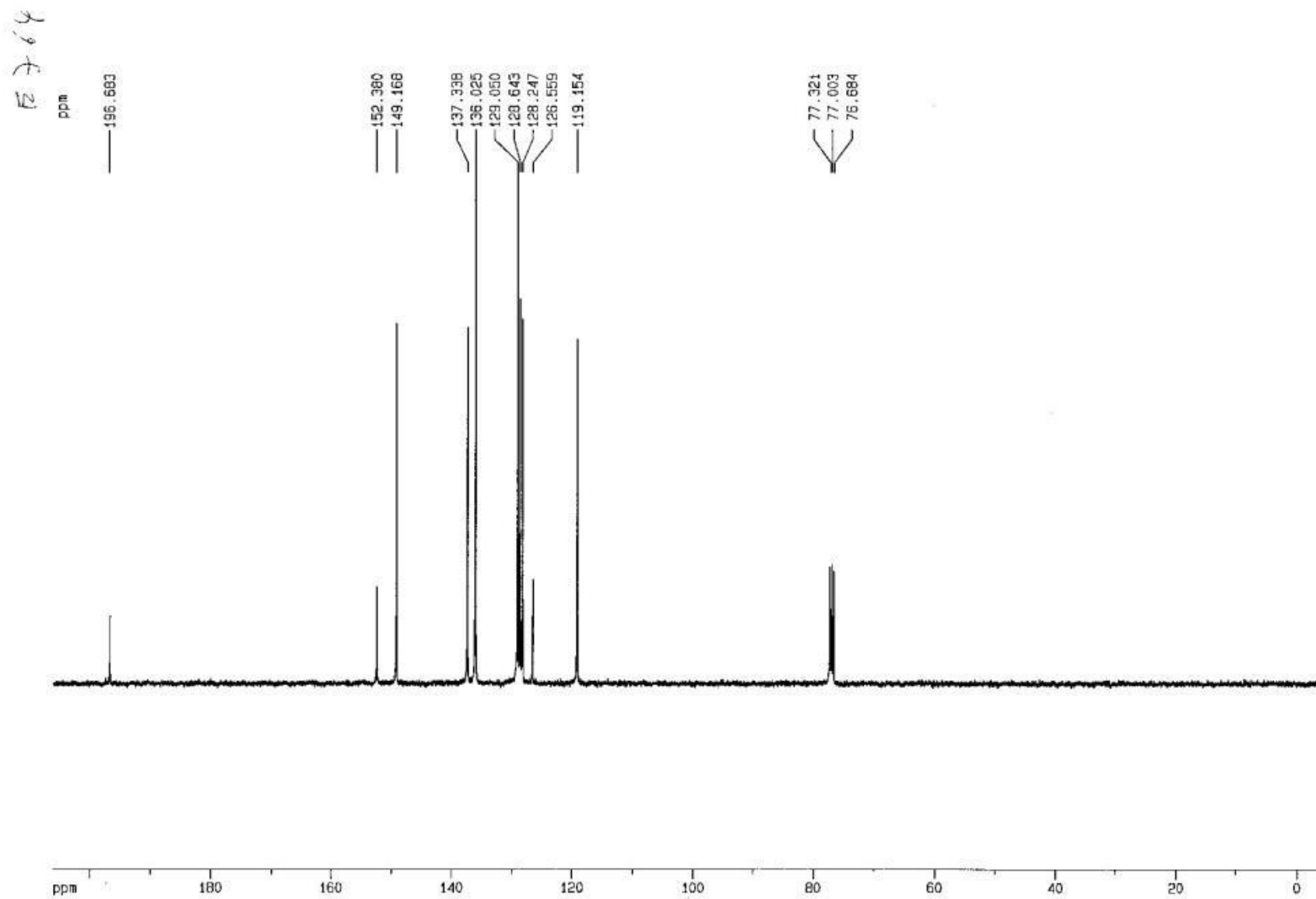


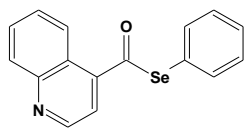
Se-Phenyl pyridine-2-carboselenoate (**3u**) ^1H NMR (400 MHz, CDCl_3)





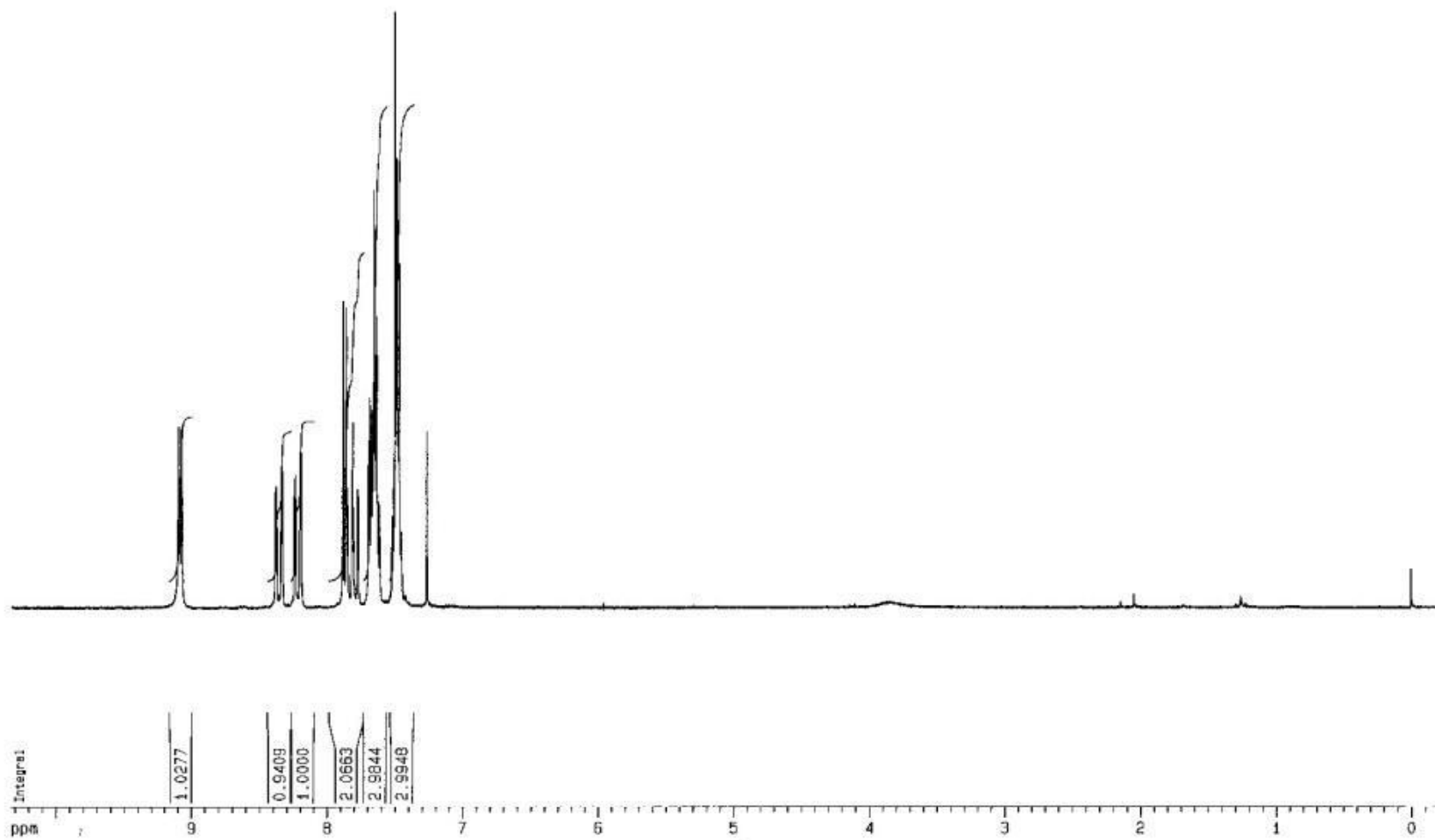
Se-Phenyl pyridine-2-carboselenoate (**3u**) ^{13}C NMR (100 MHz, CDCl_3)

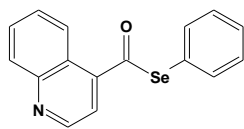




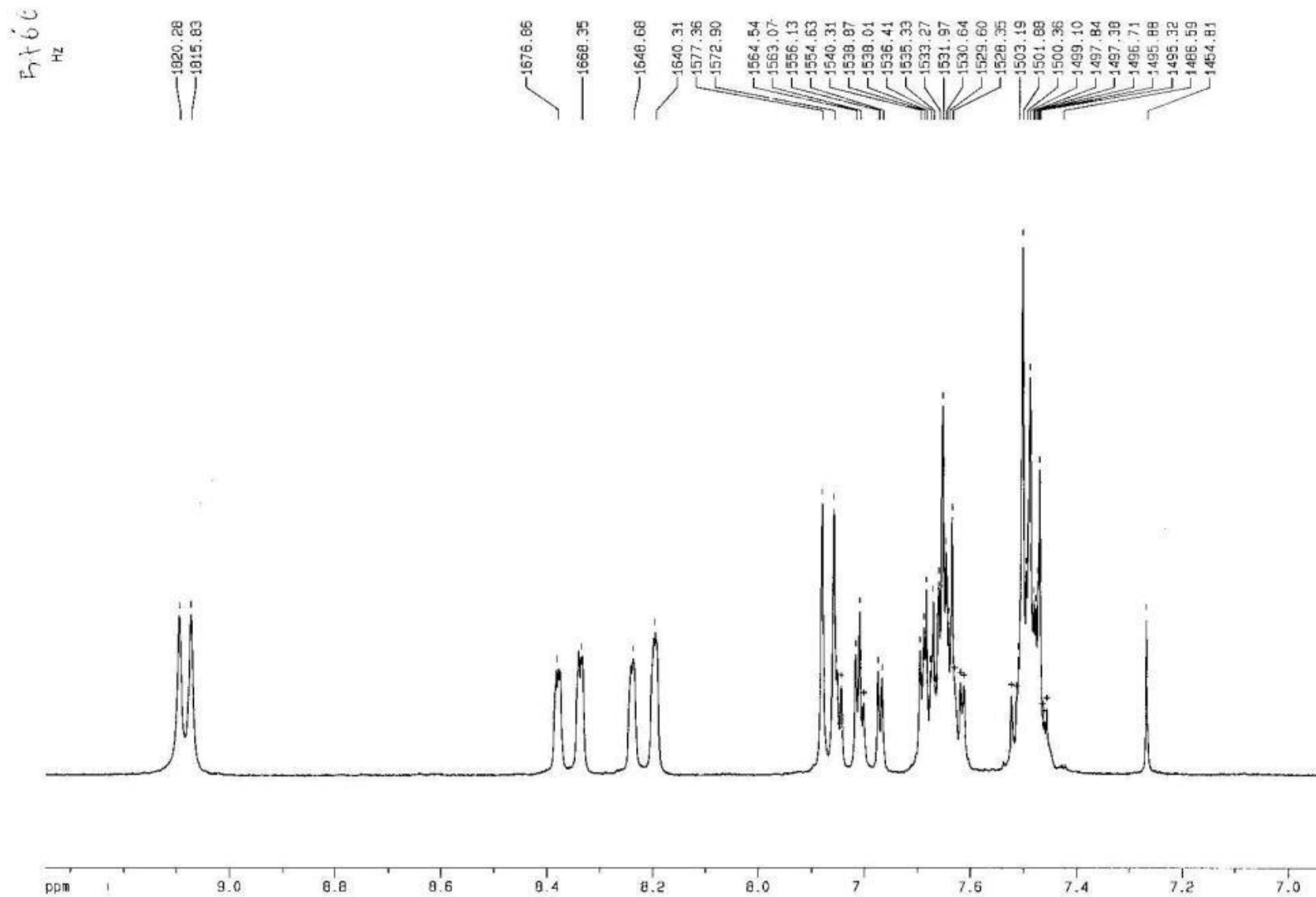
Se-Phenyl quinoline-4-carboselenoate (**3v**) ^1H NMR (200 MHz, CDCl_3)

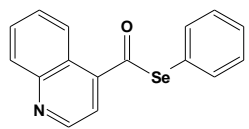
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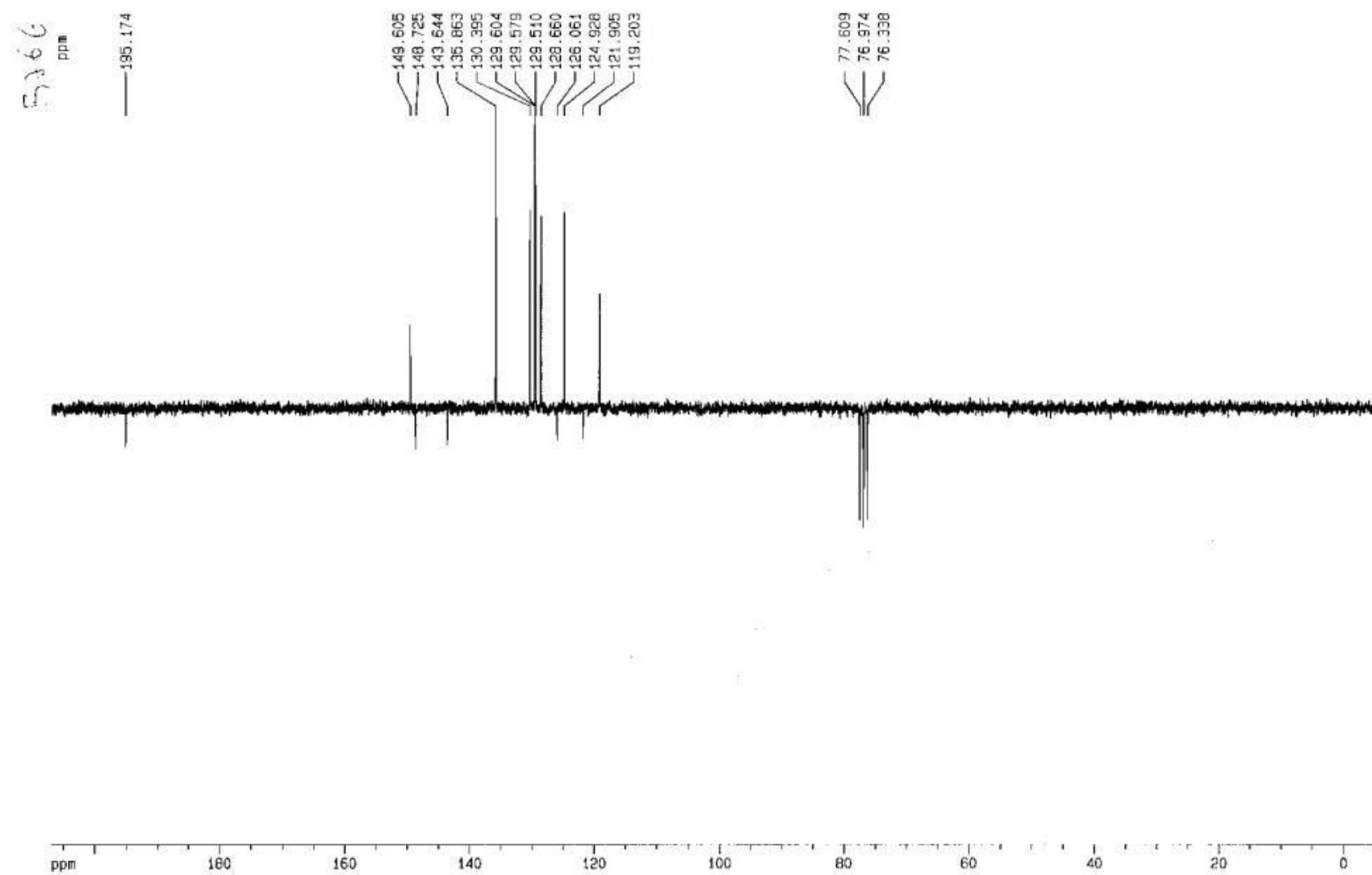


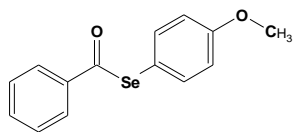
Se-Phenyl quinoline-4-carboselenoate (**3v**) ^1H NMR (200 MHz, CDCl_3)



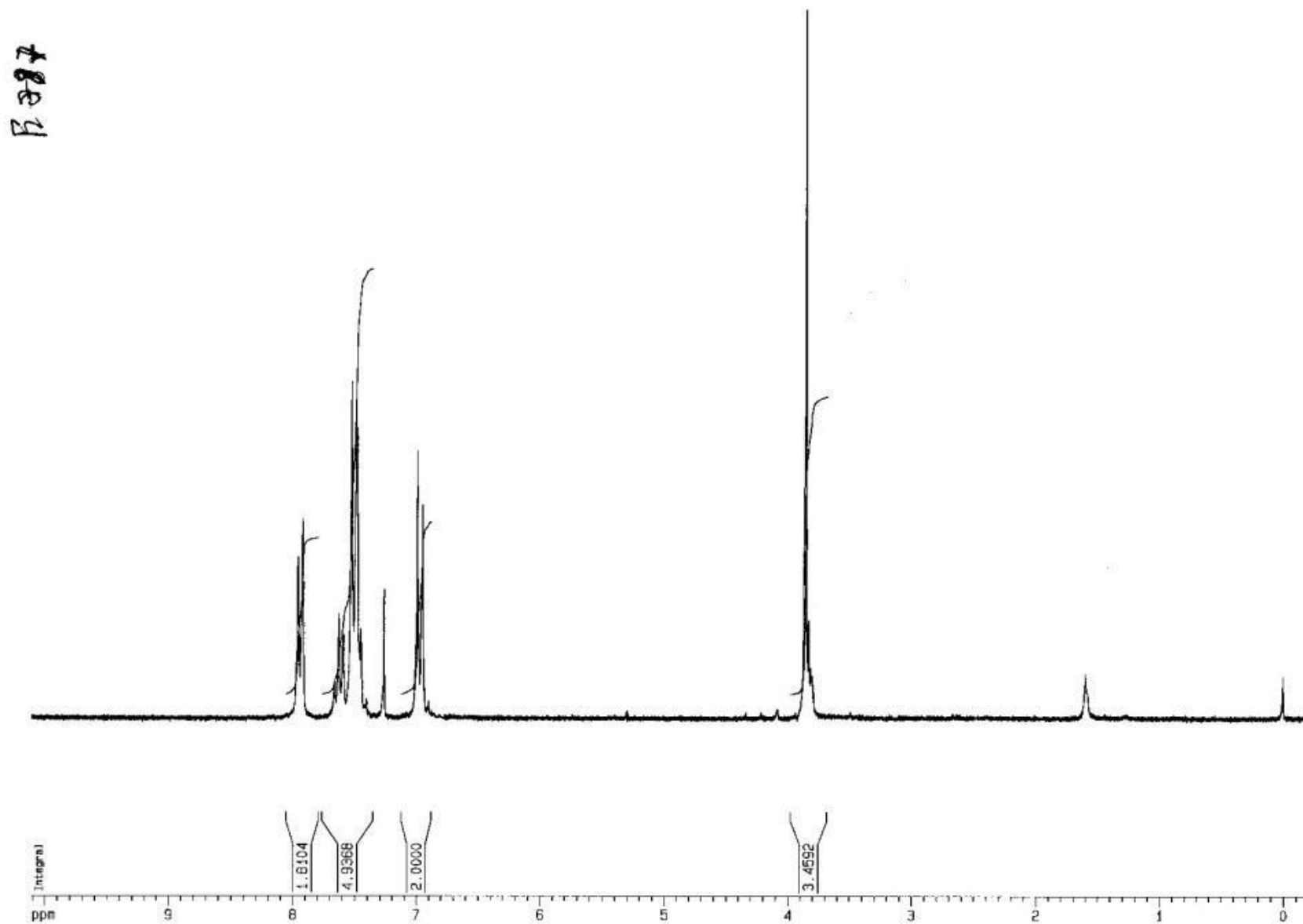


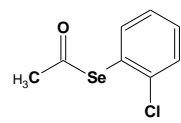
Se-Phenyl quinoline-4-carboselenoate (**3v**) ^{13}C NMR (50 MHz, CDCl_3)





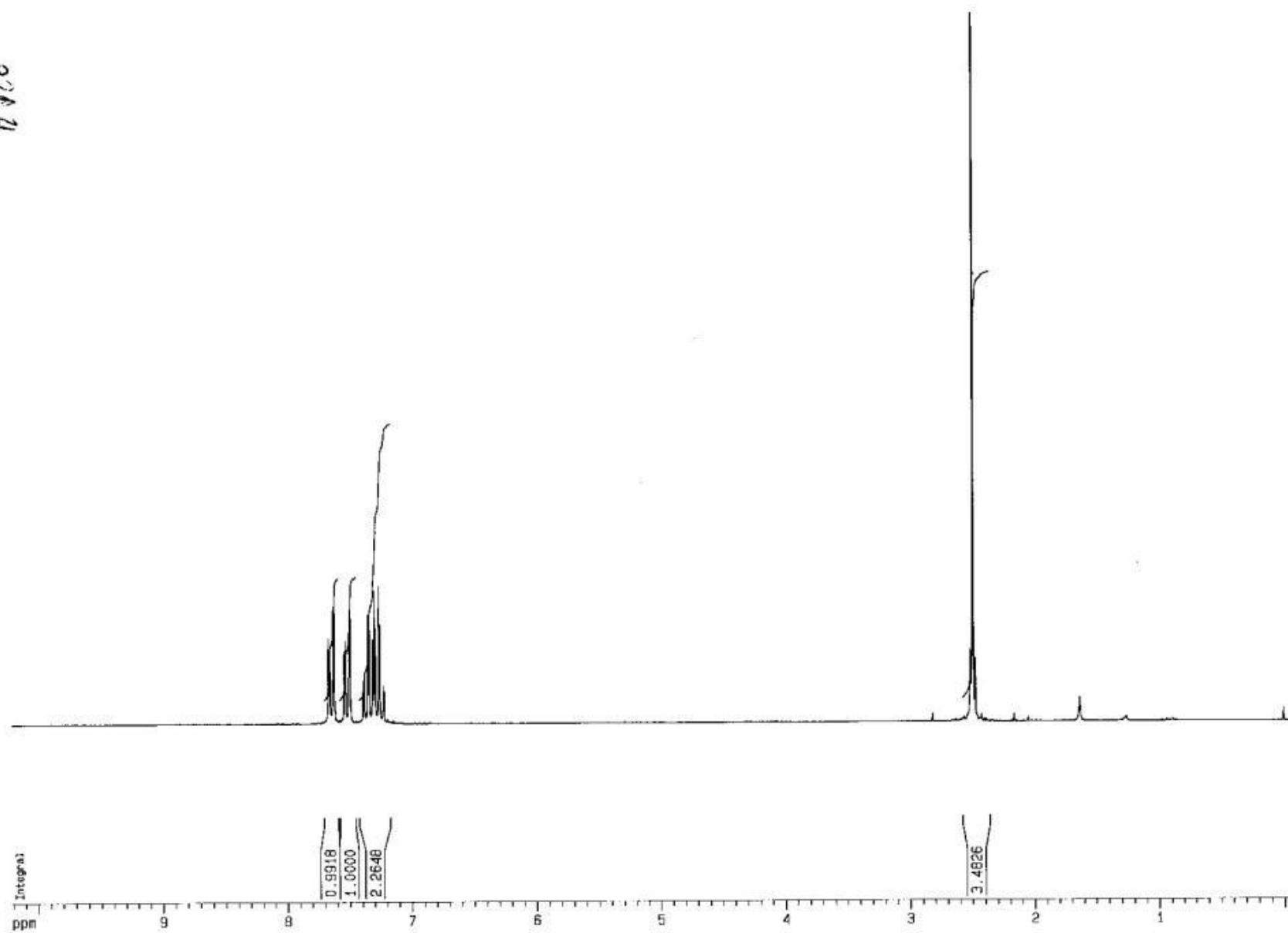
Se-(4-methoxyphenyl) benzenecarbosenoate (**4**) ^1H NMR (200 MHz, CDCl_3)

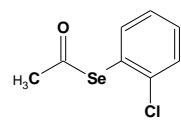




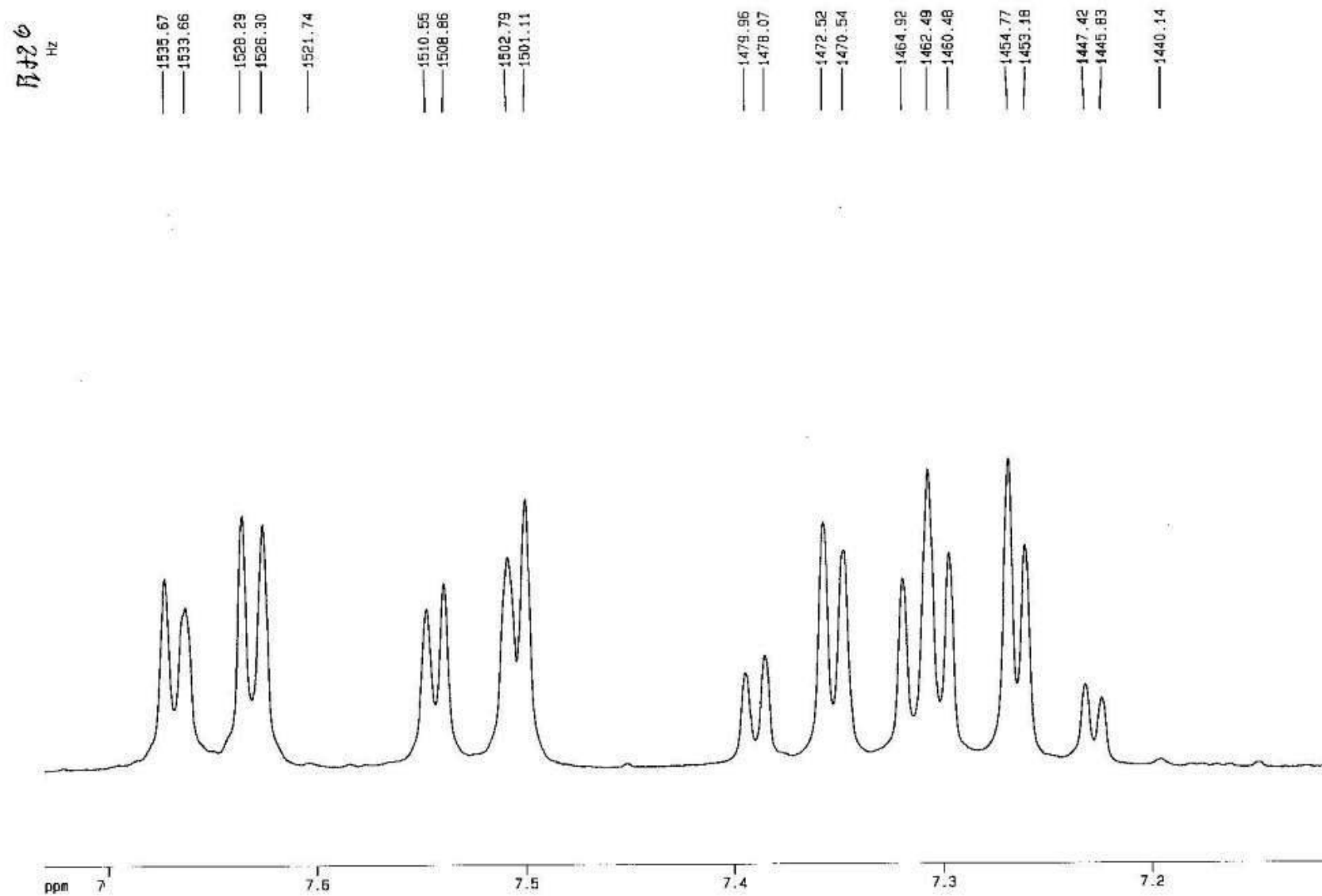
Se-(2-chlorophenyl) ethaneselenoate (**5**) ^1H NMR (200 MHz, CDCl_3)

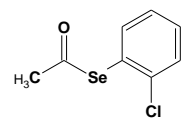
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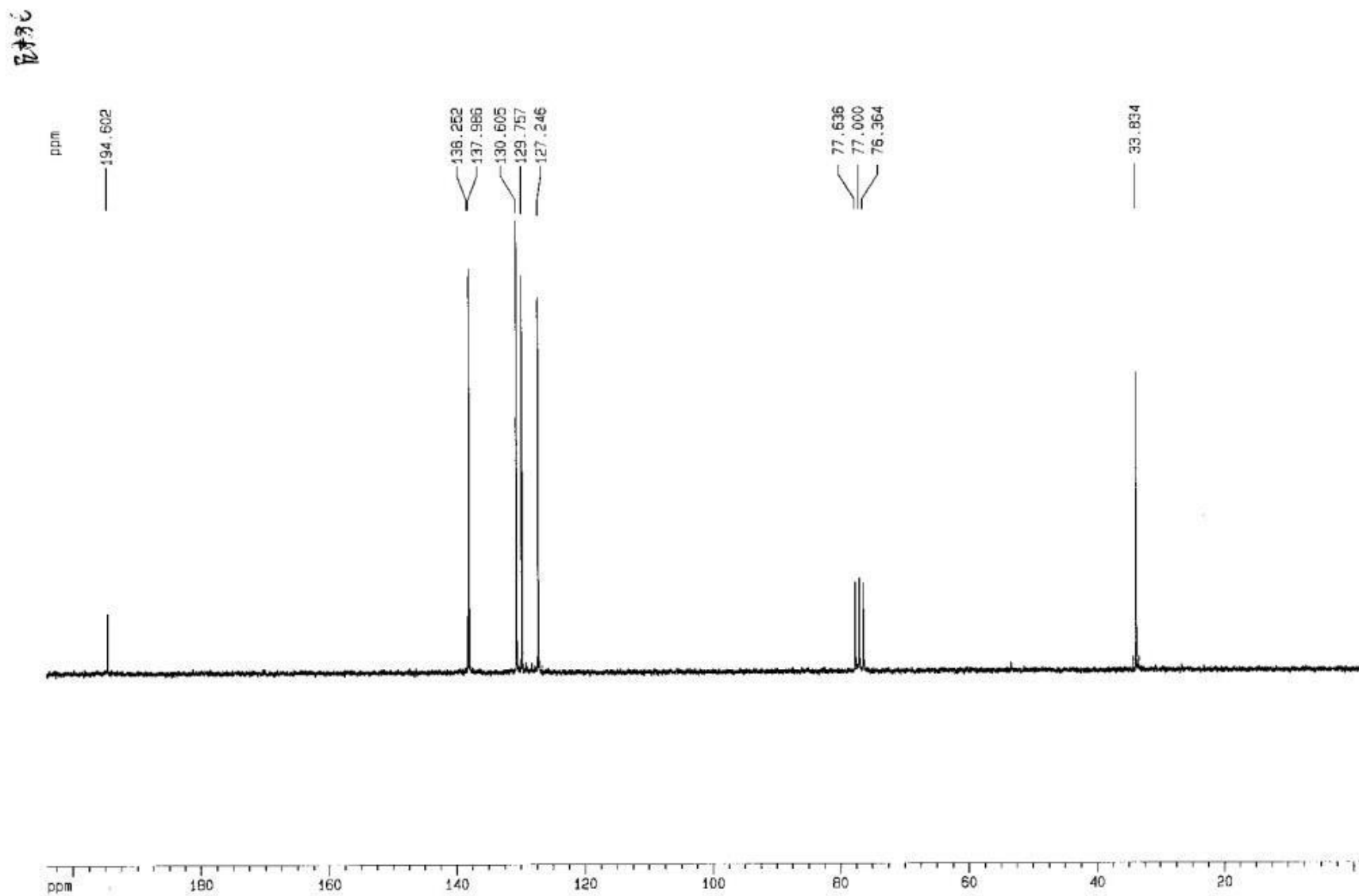


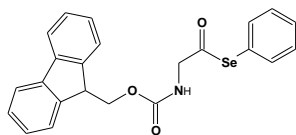
Se-(2-chlorophenyl) ethaneselenoate (**5**) ^1H NMR (200 MHz, CDCl_3)



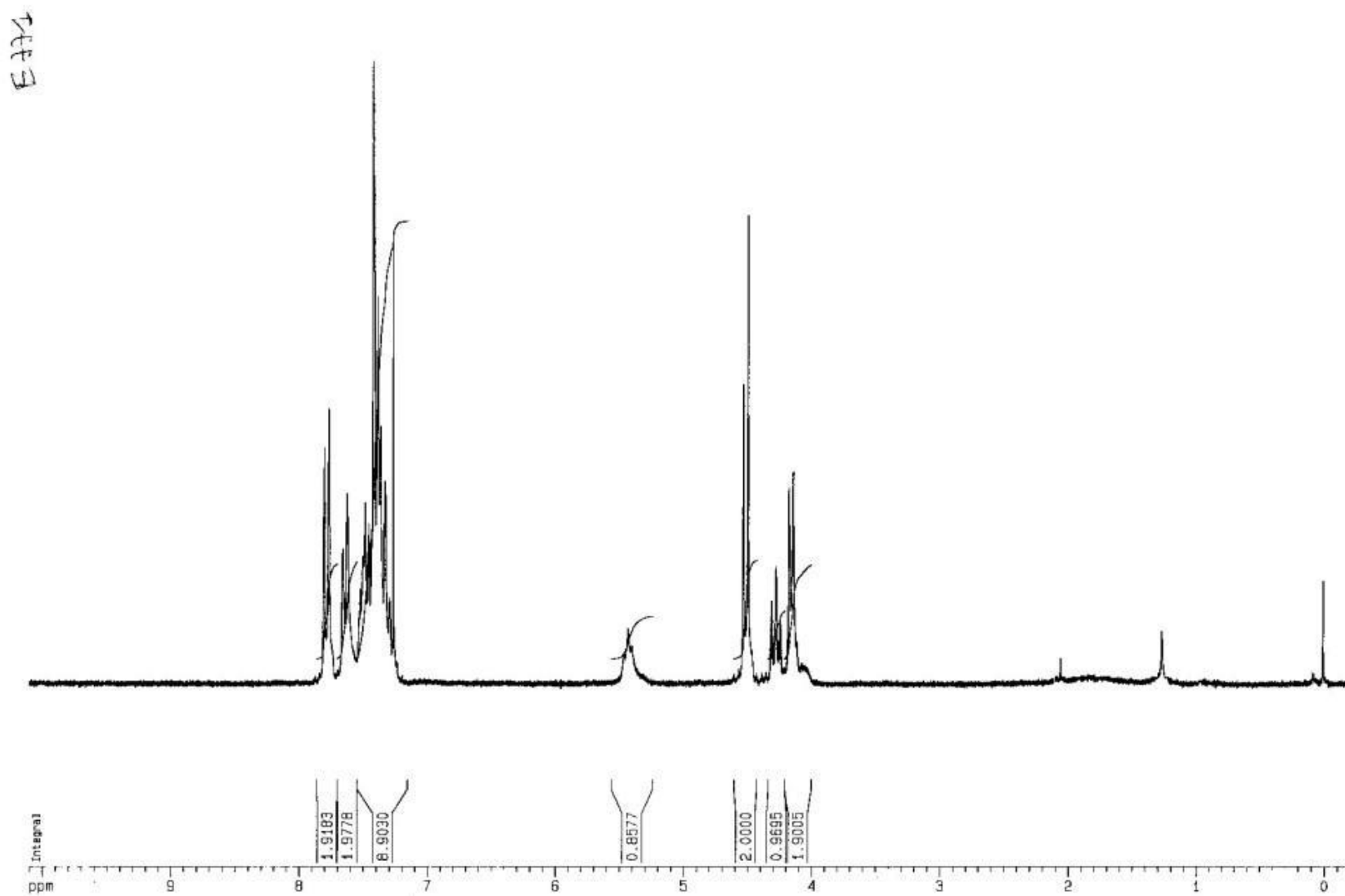


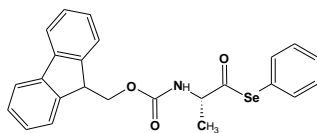
Se-(2-chlorophenyl) ethaneselenoate (**5**) ^{13}C NMR (50 MHz, CDCl_3)



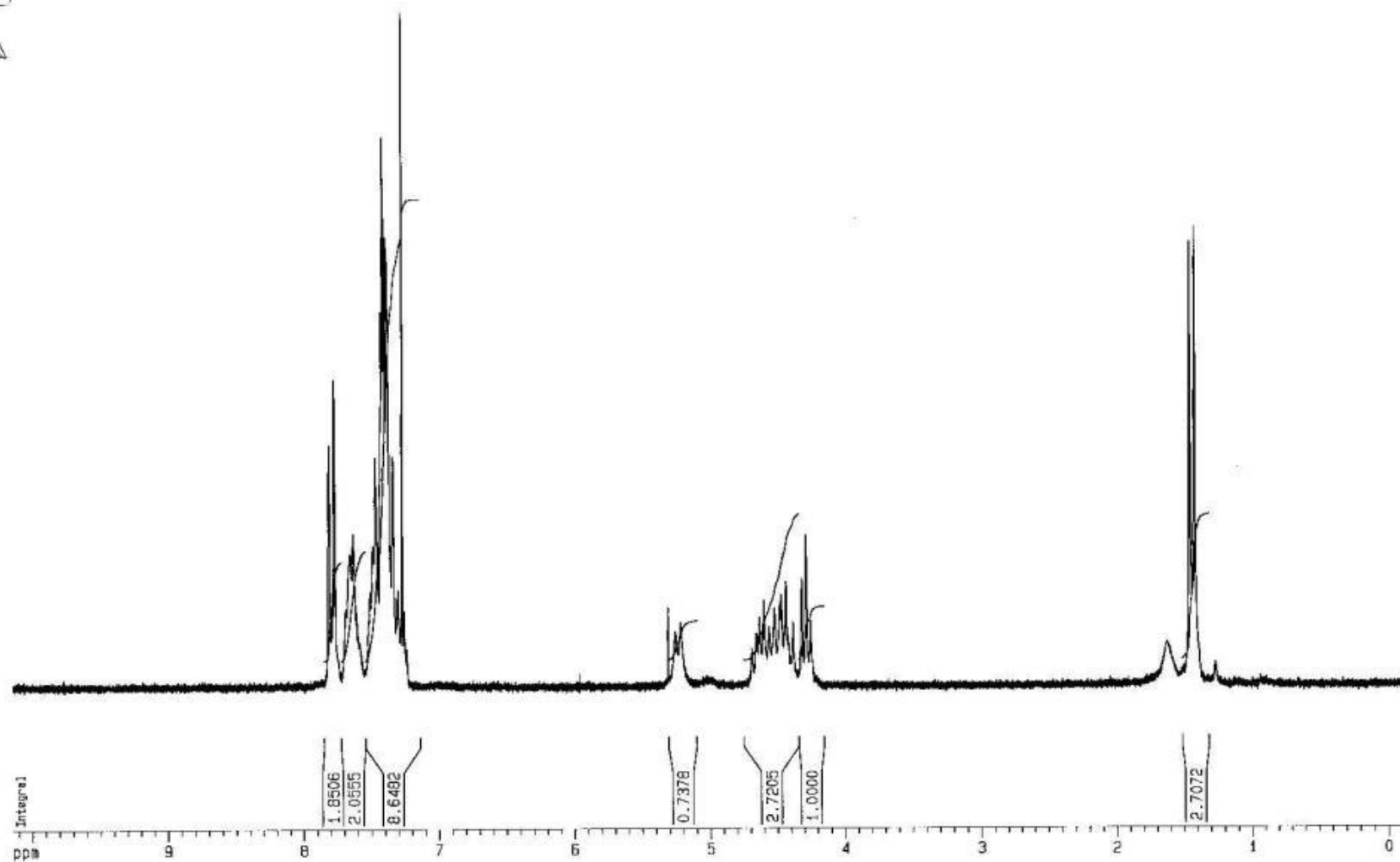


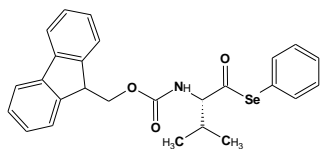
Se-Phenyl {[(9H-fluoren-9-ylmethoxy)carbonyl]amino }ethaneselenoate (**8a**) ^1H NMR (200 MHz, CDCl_3)



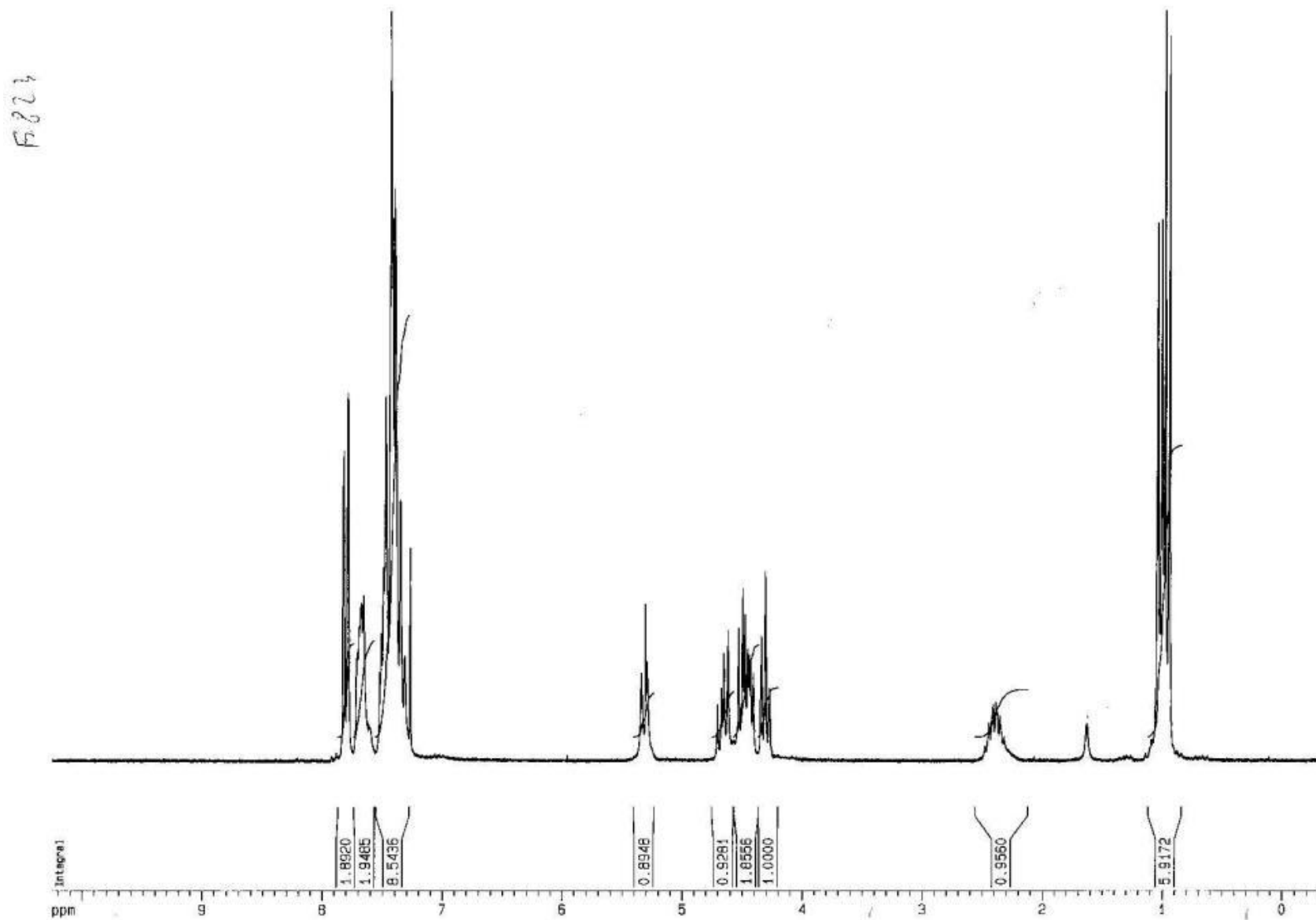


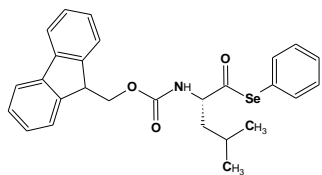
Se-Phenyl (2*S*)-2-[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino}propaneselenoate (**8b**) ^1H NMR (200 MHz, CDCl_3)



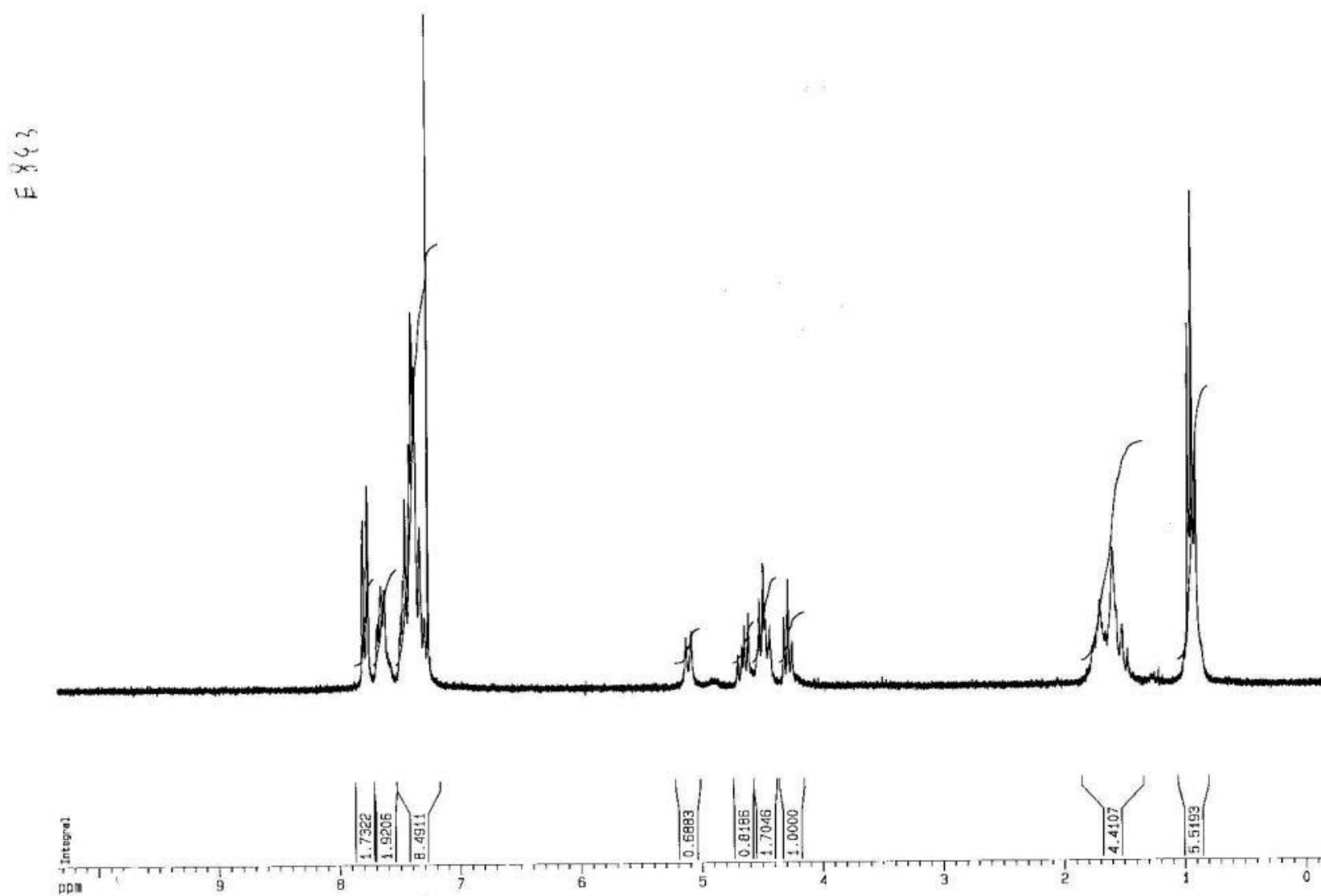


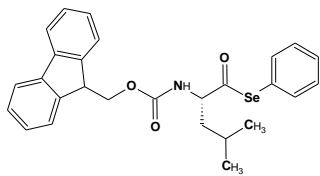
Se-Phenyl (2*S*)-2-[[[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-3-methylbutaneselenoate (**8c**) ^1H NMR (200 MHz, CDCl_3)



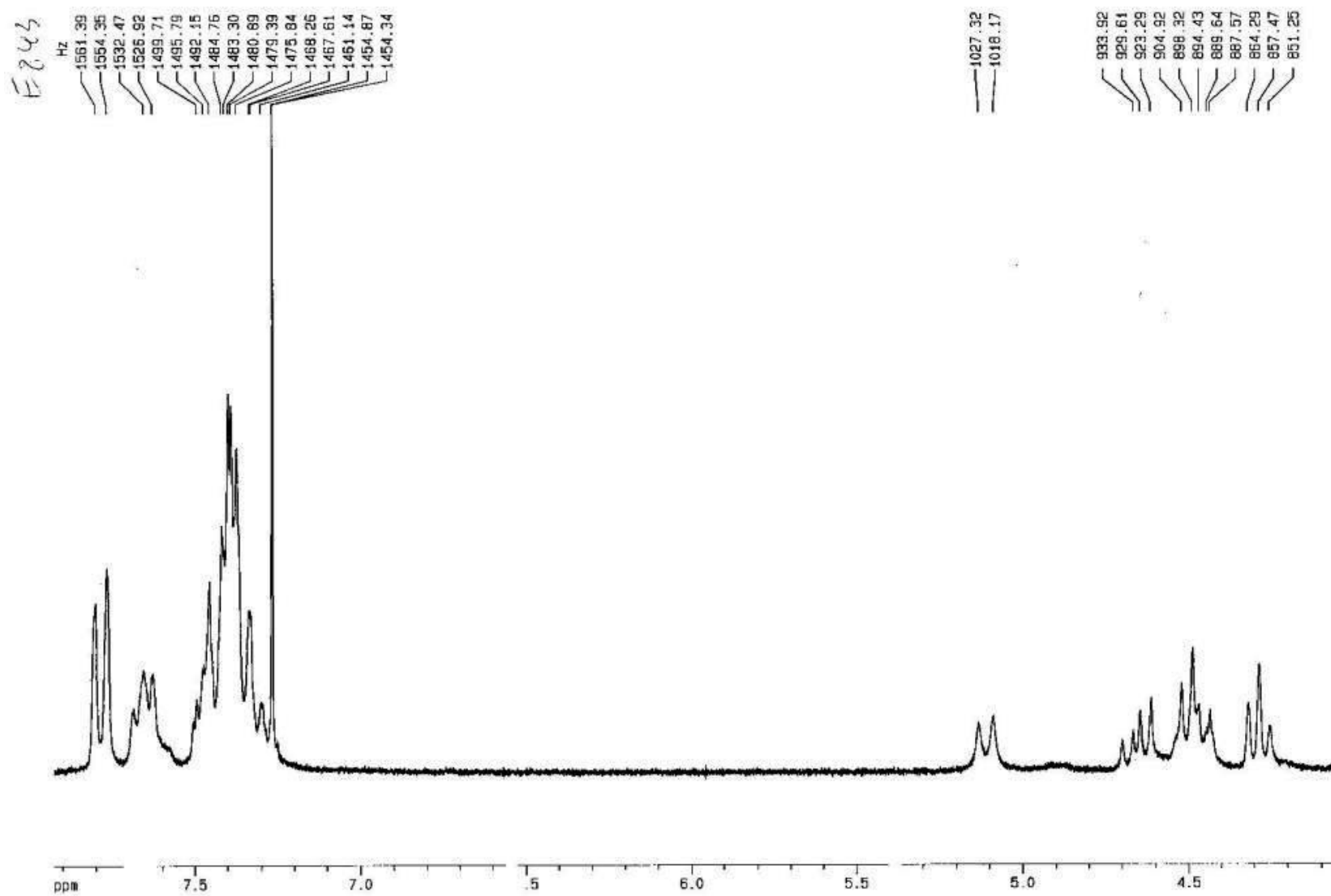


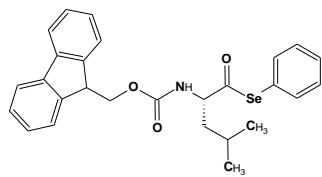
Se-Phenyl (2*S*)-2-[[[9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-4-methylpentaneselenoate (**8d**) ^1H NMR (200 MHz, CDCl_3)



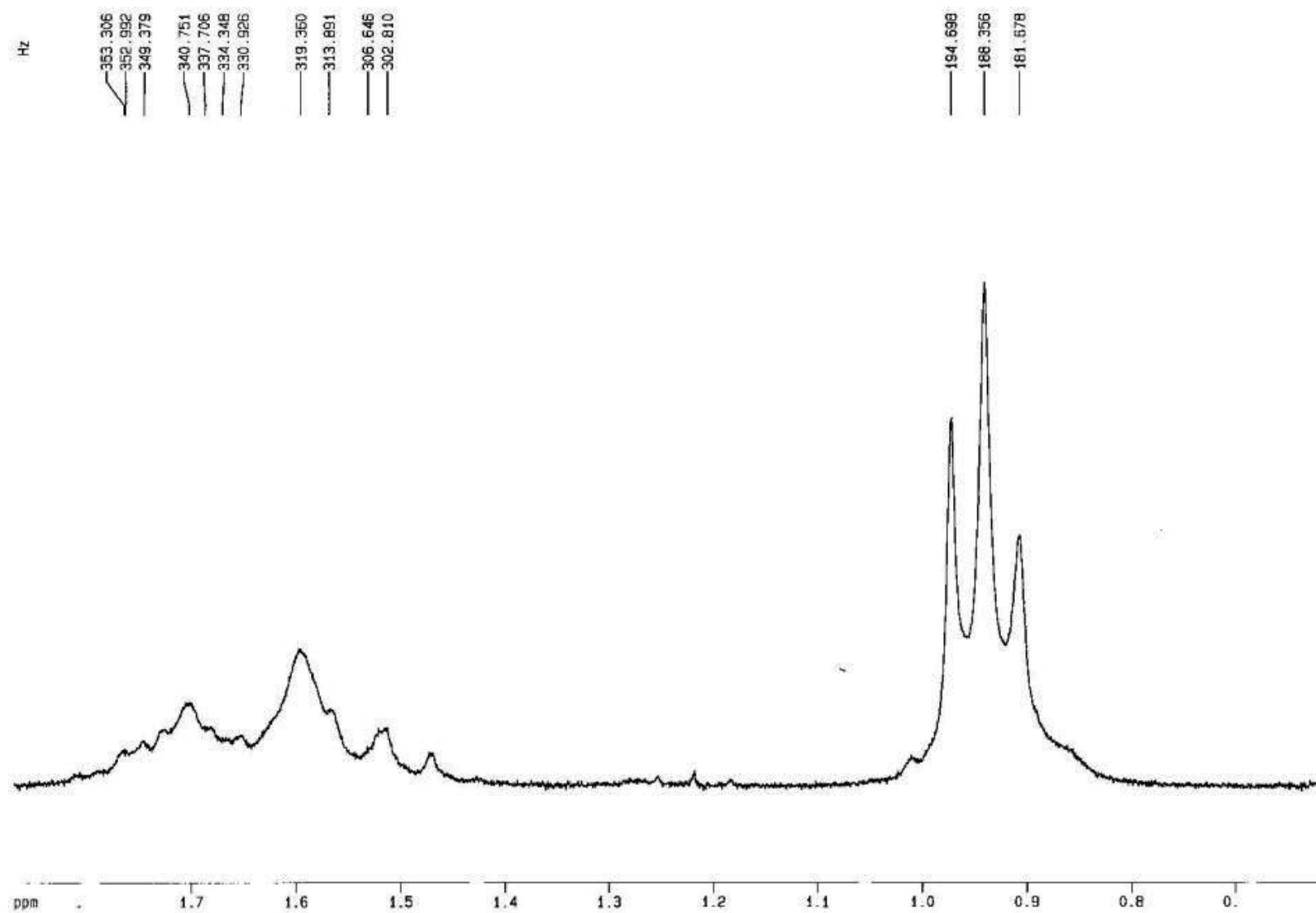


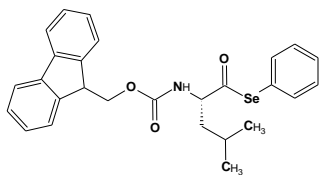
Se-Phenyl (2*S*)-2-[[[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-4-methylpentaneselenoate (**8d**) ^1H NMR (200 MHz, CDCl_3)



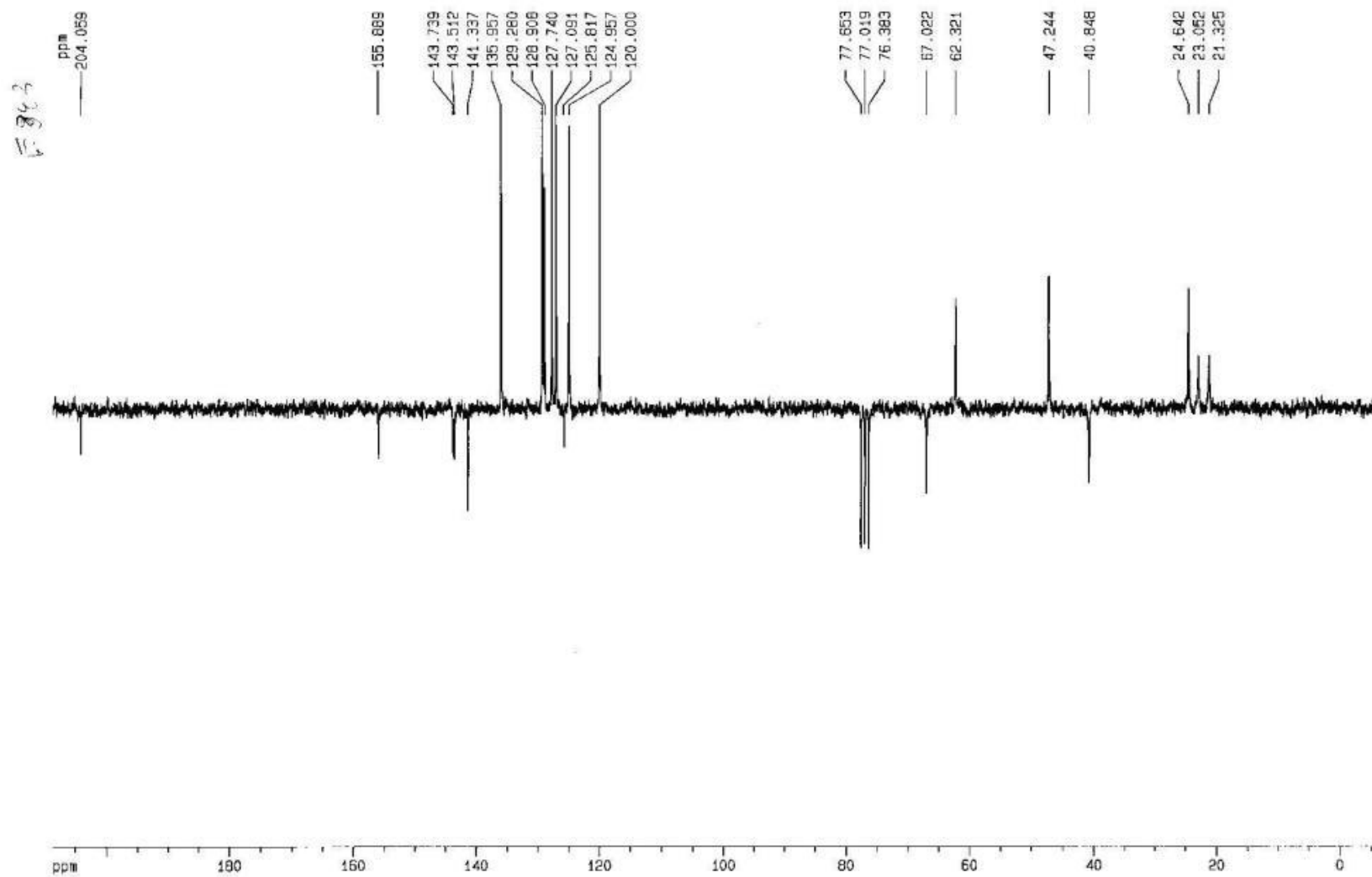


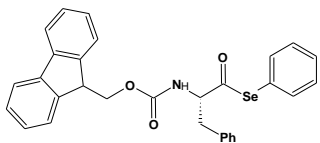
Se-Phenyl (2*S*)-2-[[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-4-methylpentaneselenoate (**8d**) ^1H NMR (200 MHz, CDCl_3)





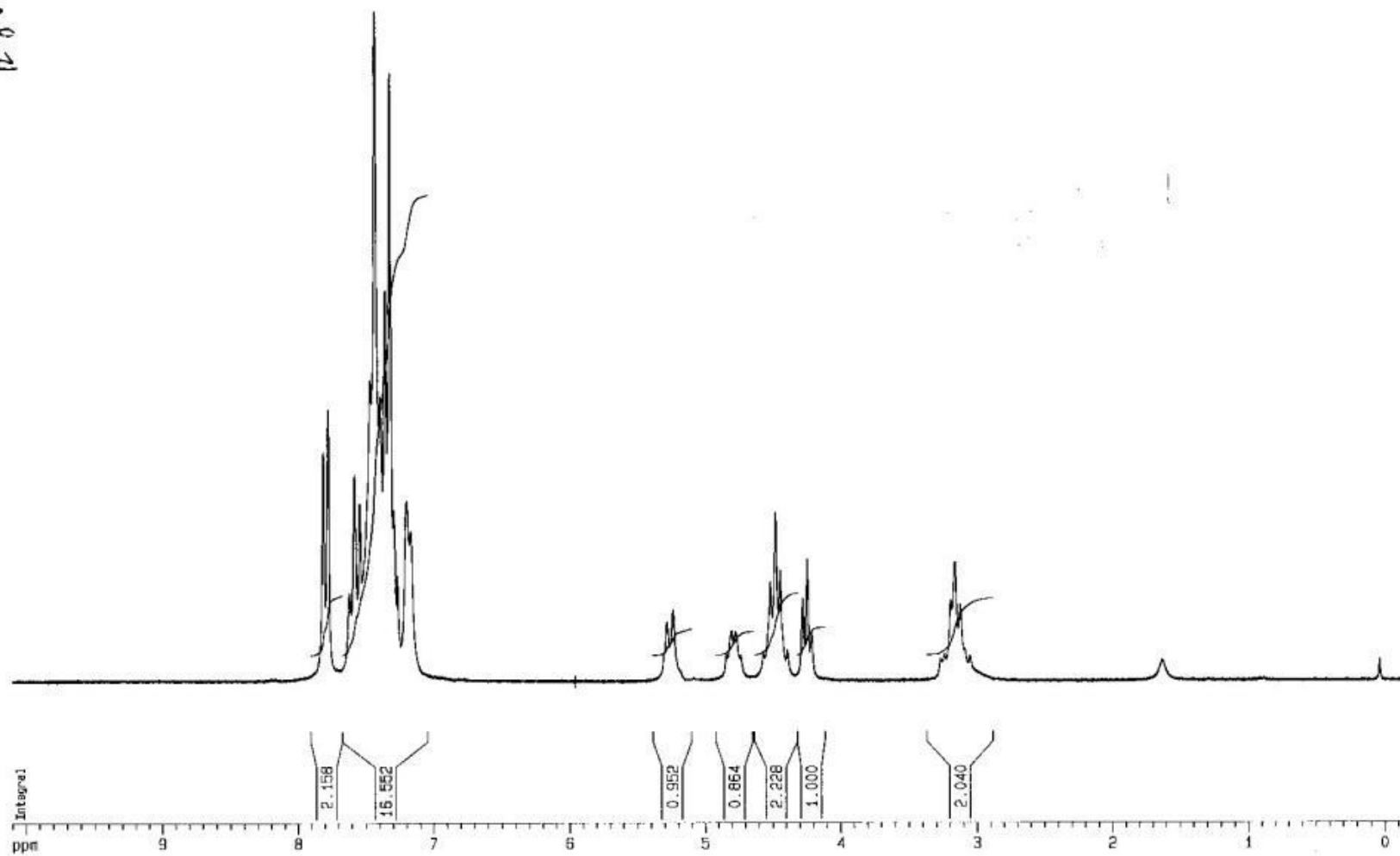
Se-Phenyl (2*S*)-2-[[[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-4-methylpentaneselenoate (**8d**) ^{13}C NMR (50 MHz, CDCl_3)

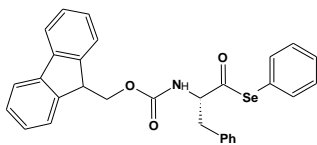




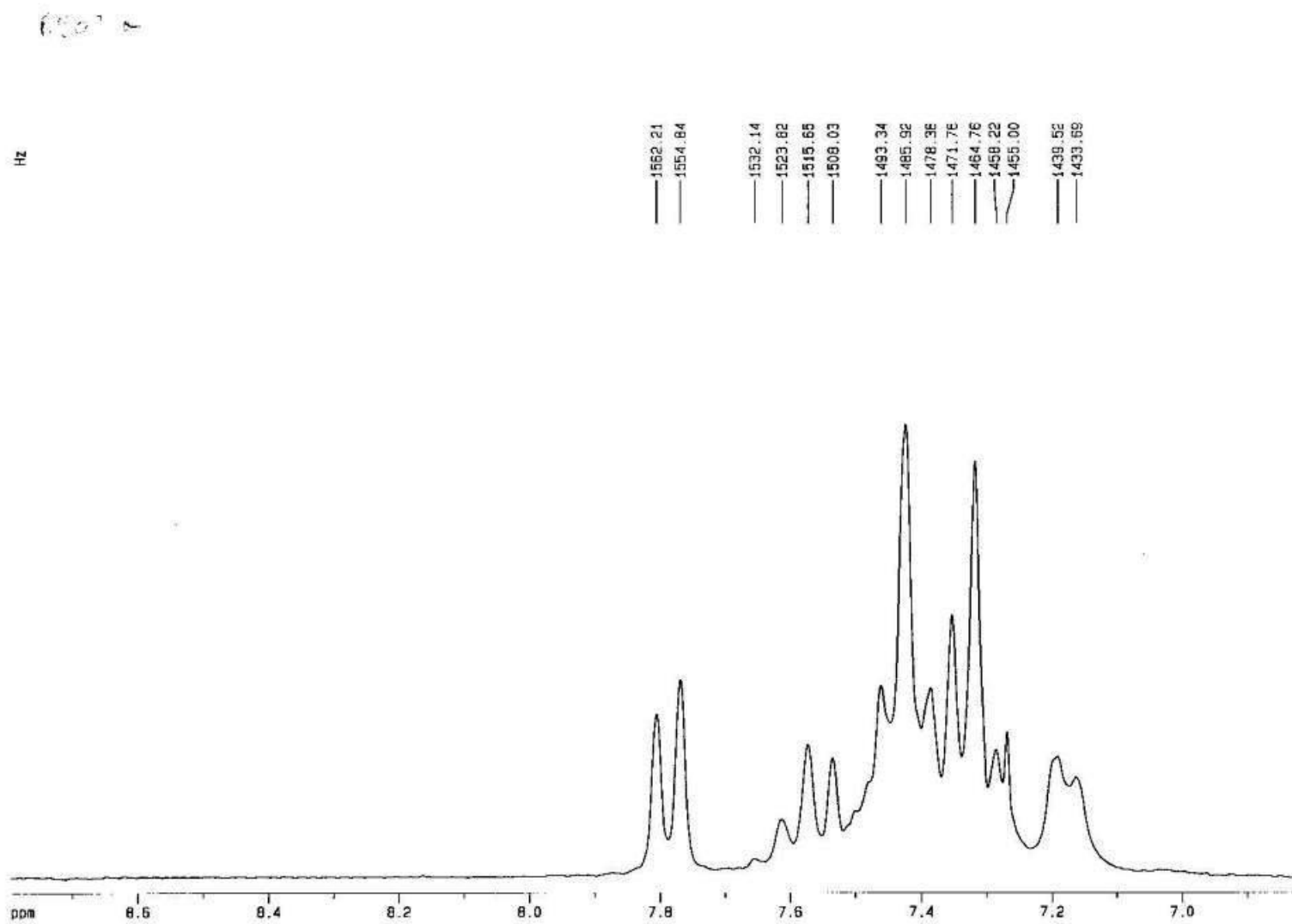
Se-Phenyl (2*S*)-2-[[[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-3-phenylpropaneselenoate (**8e**) ^1H NMR (200 MHz, CDCl_3)

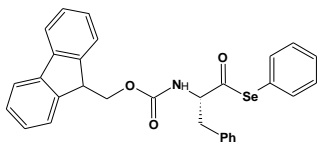
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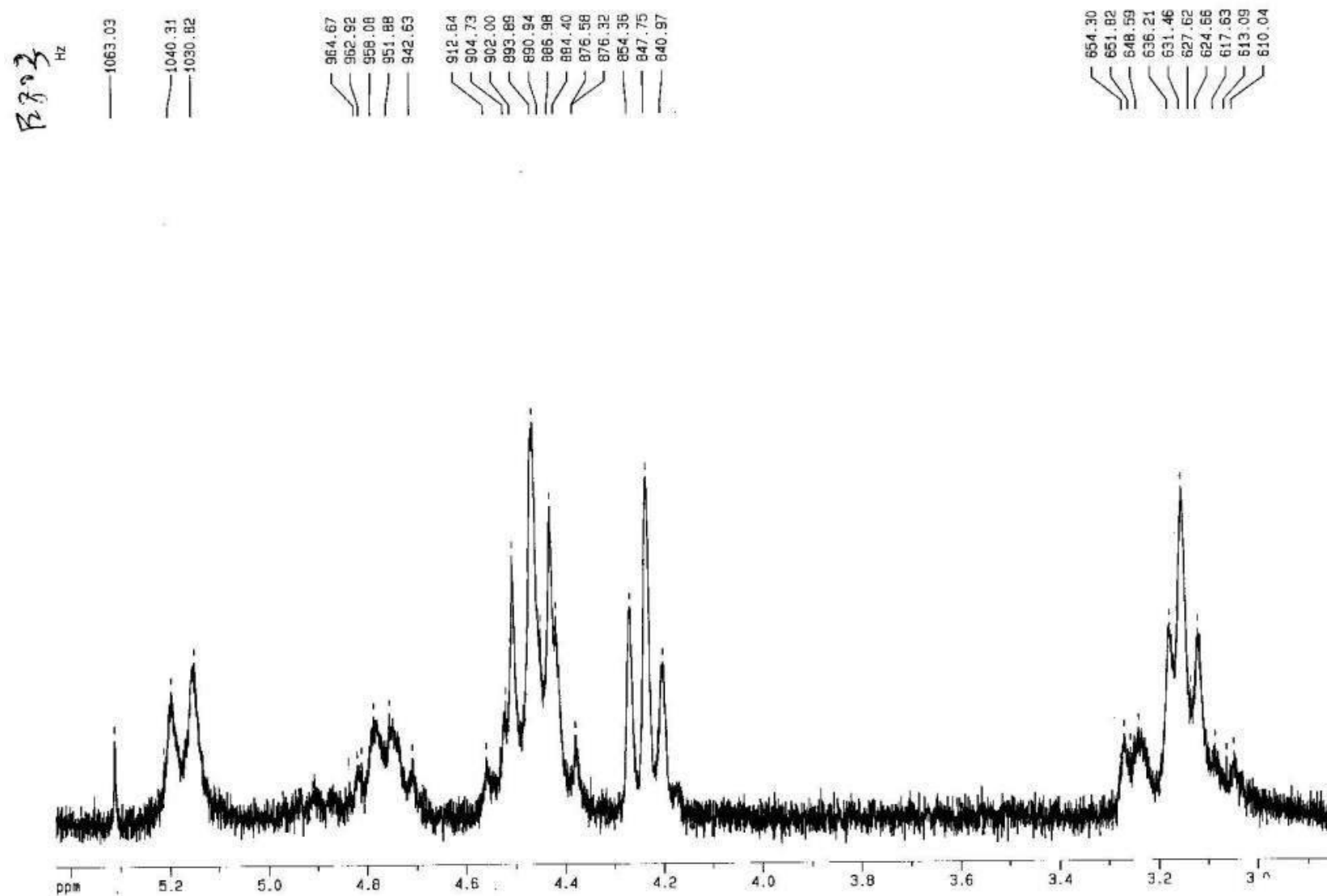


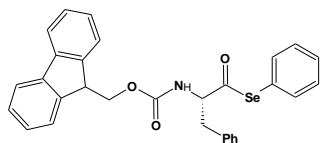
Se-Phenyl (2*S*)-2-[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino-3-phenylpropaneselenoate (**8e**) ^1H NMR (200 MHz, CDCl_3)



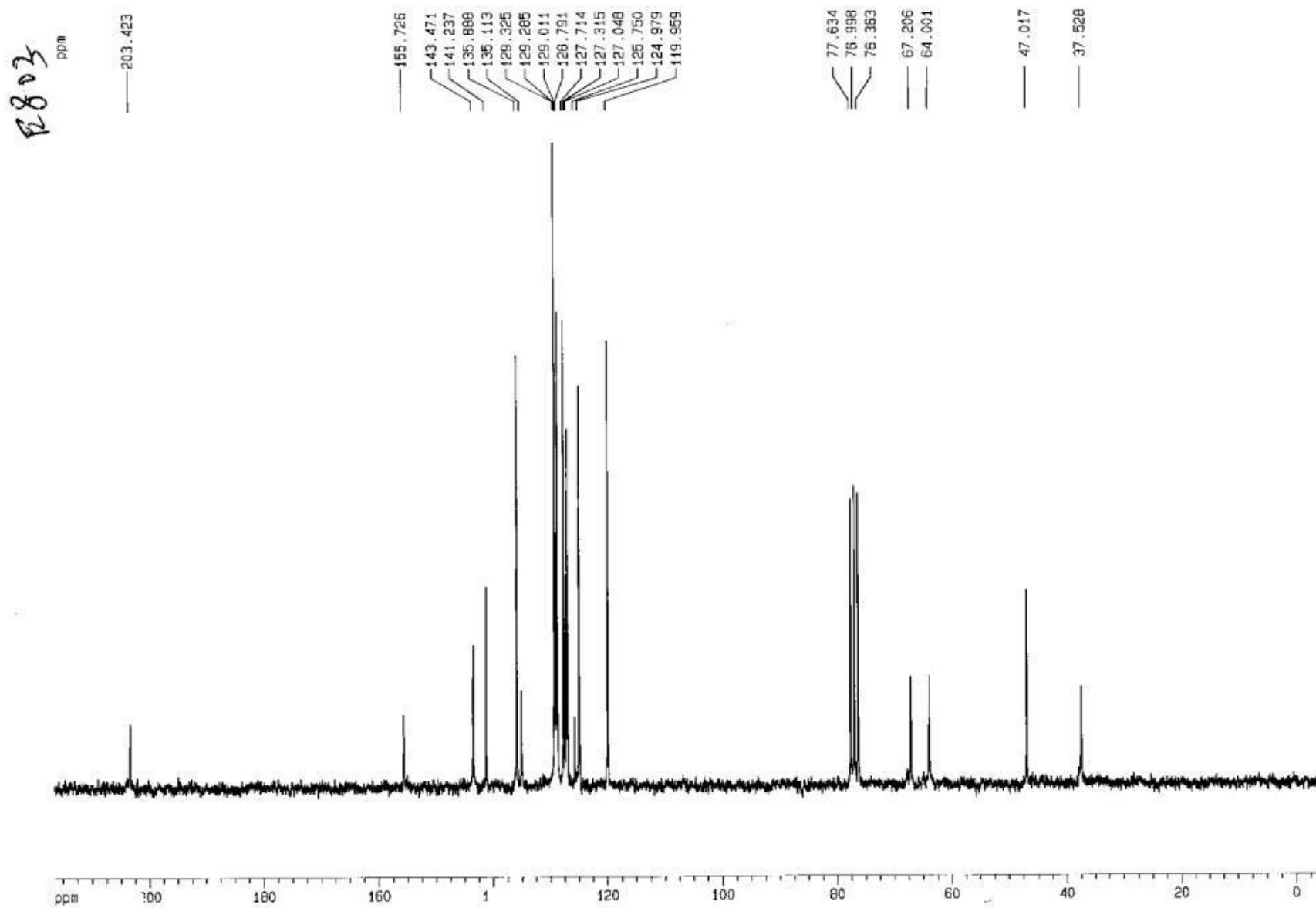


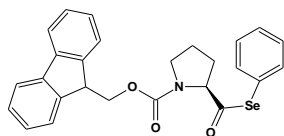
Se-Phenyl (2*S*)-2-[[[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-3-phenylpropaneselenoate (**8e**) ^1H NMR (200 MHz, CDCl_3)



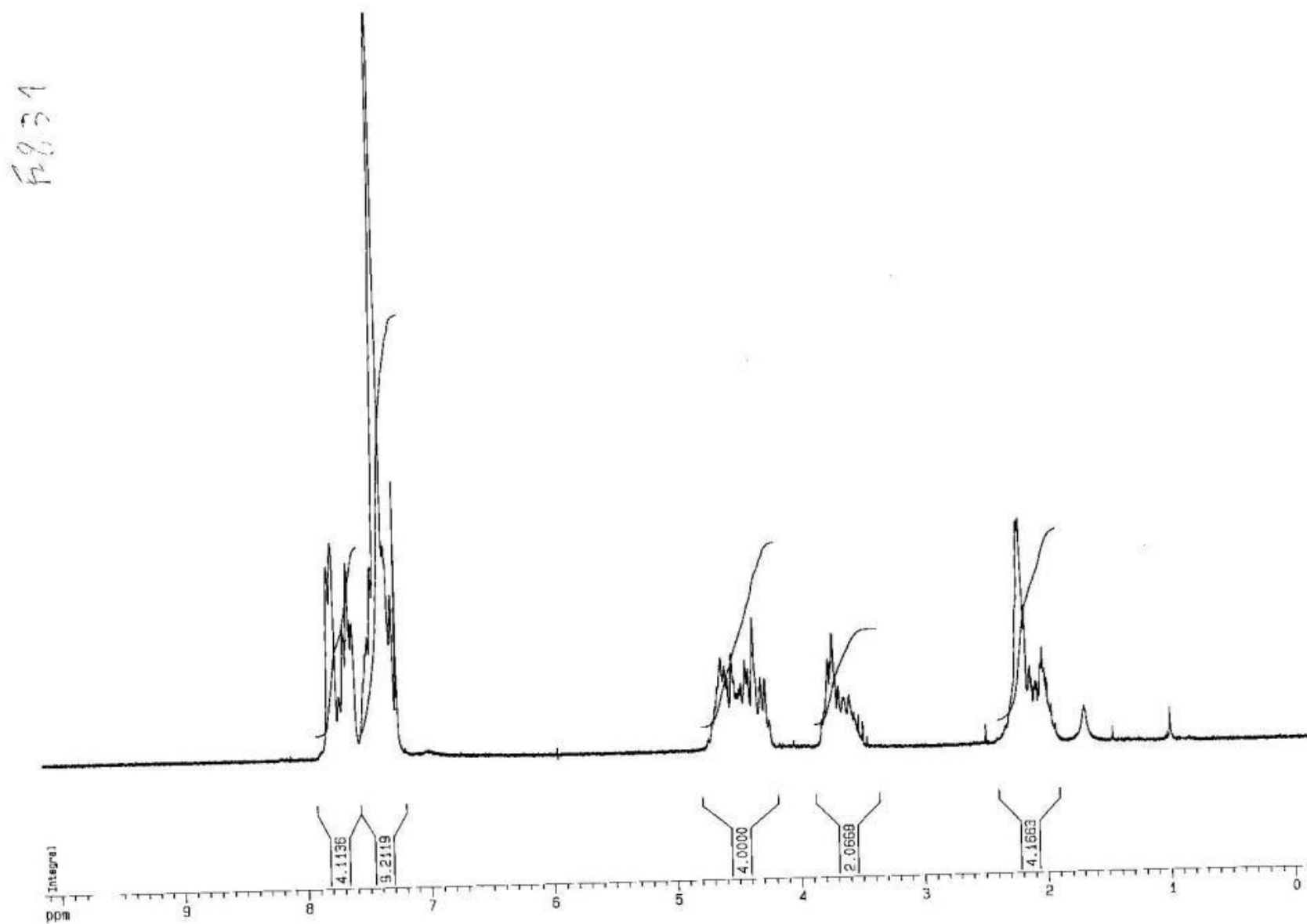


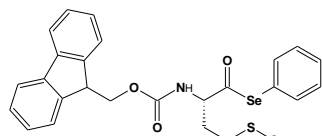
Se-Phenyl (2*S*)-2-[[[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-3-phenylpropaneselenoate (**8e**) ^{13}C NMR (50 MHz, CDCl_3)



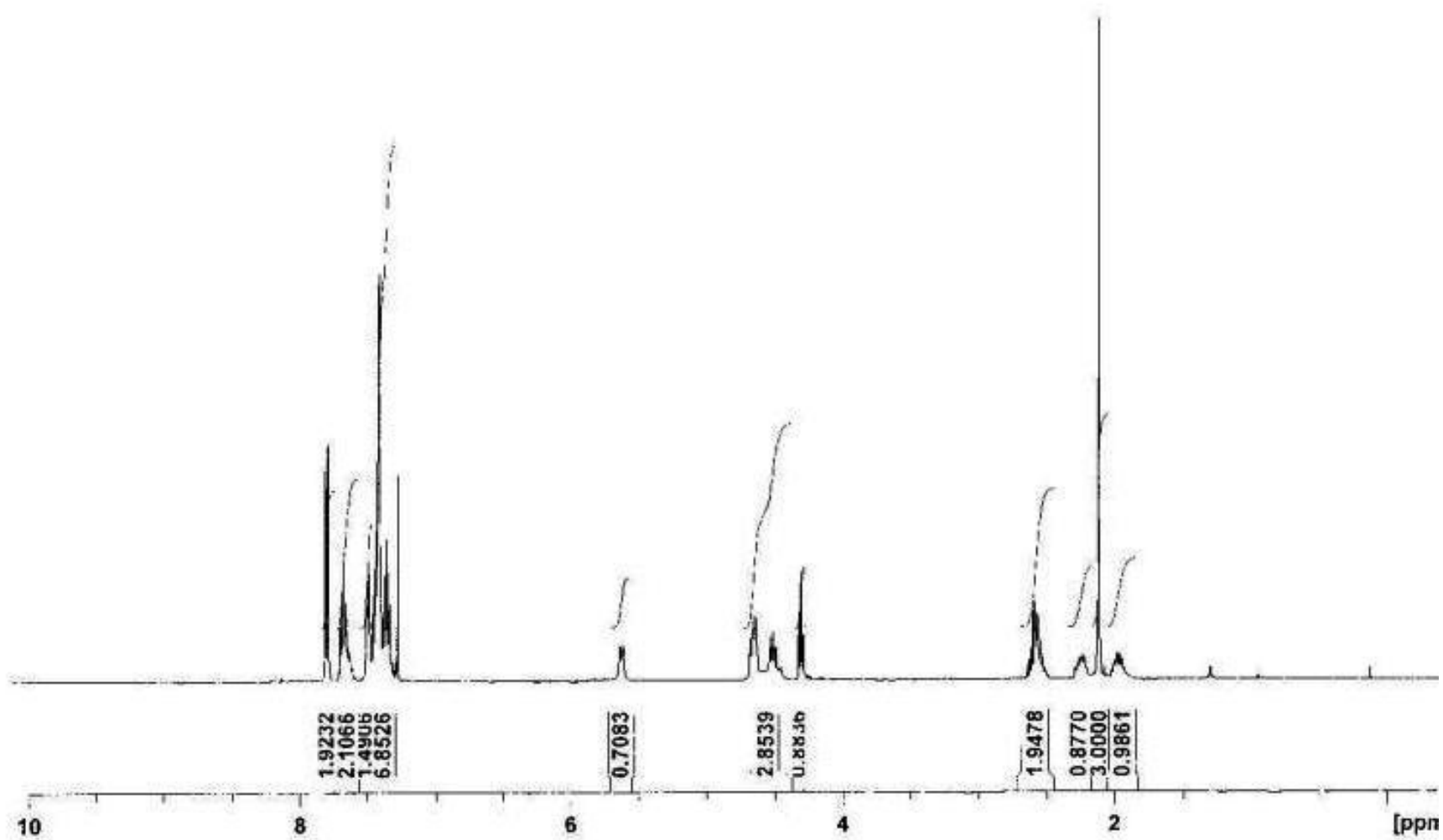


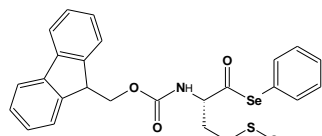
9H-Fluoren-9-ylmethyl (2S)-2-[(phenylseleno)carbonyl]pyrrolidine-1-carboxylate (**8f**) ^1H NMR (200 MHz, CDCl_3)



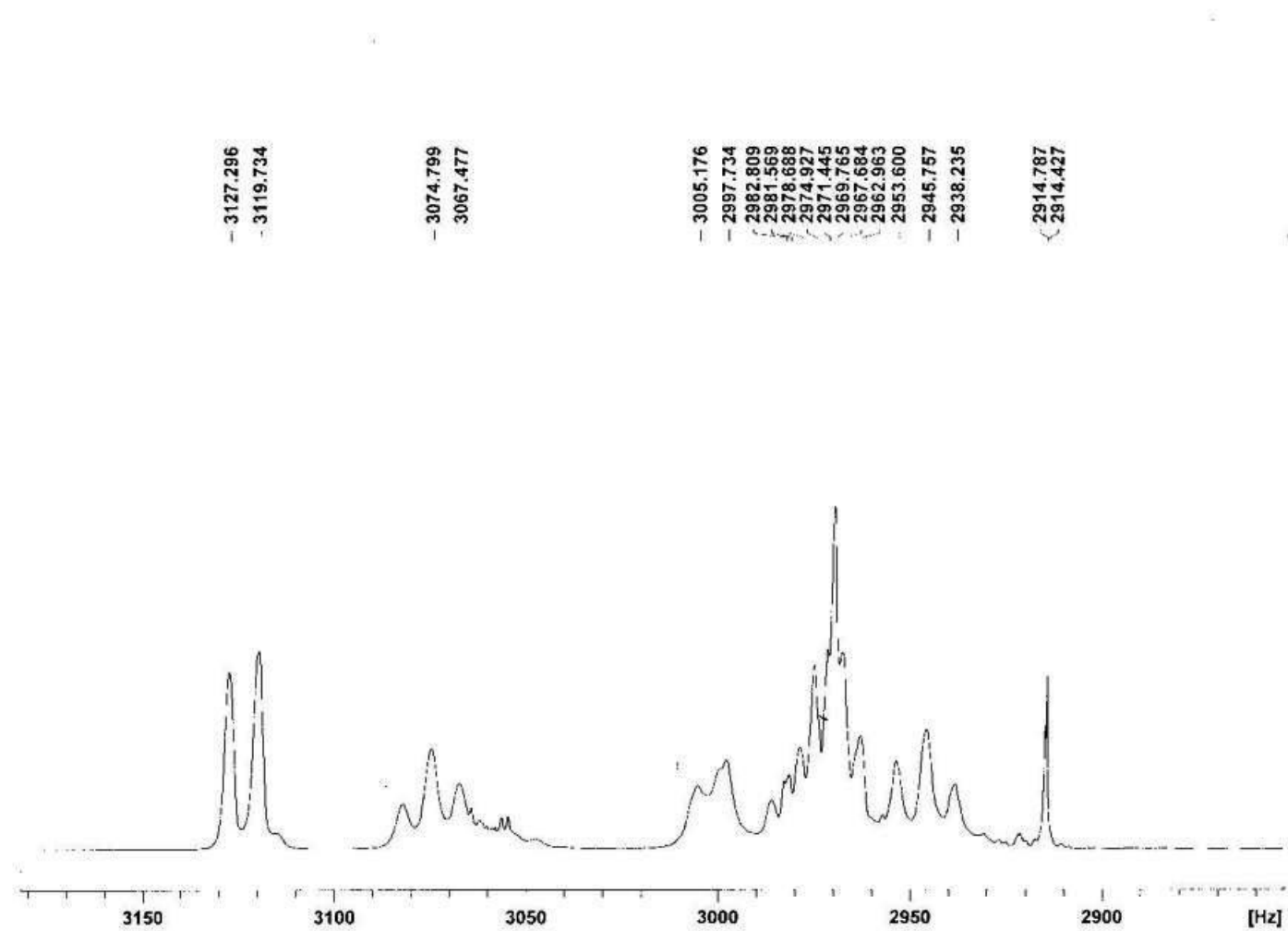


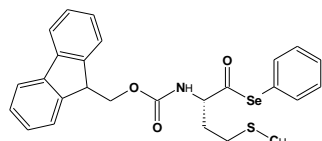
Se-phenyl (2S)-2-[[[9H-fluoren-9-ylmethoxy)carbonyl]amino]-4-(methylthio)butaneselenoate (**8g**) ^1H NMR (400 MHz, CDCl_3)



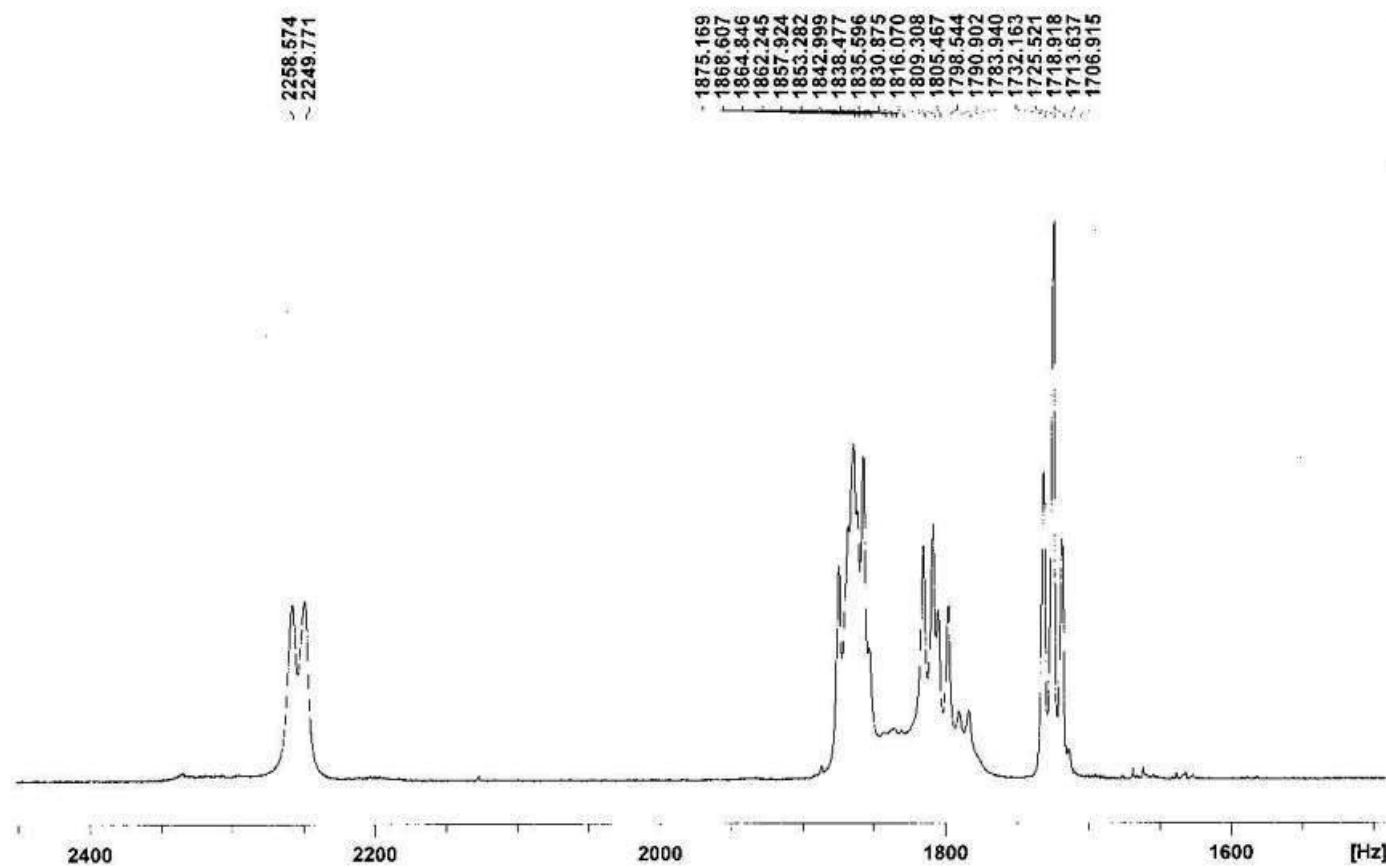


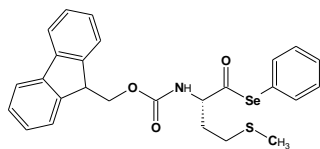
Se-phenyl (2*S*)-2-[[[9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-4-(methylthio)butaneselenoate (**8g**) ^1H NMR (400 MHz, CDCl_3)



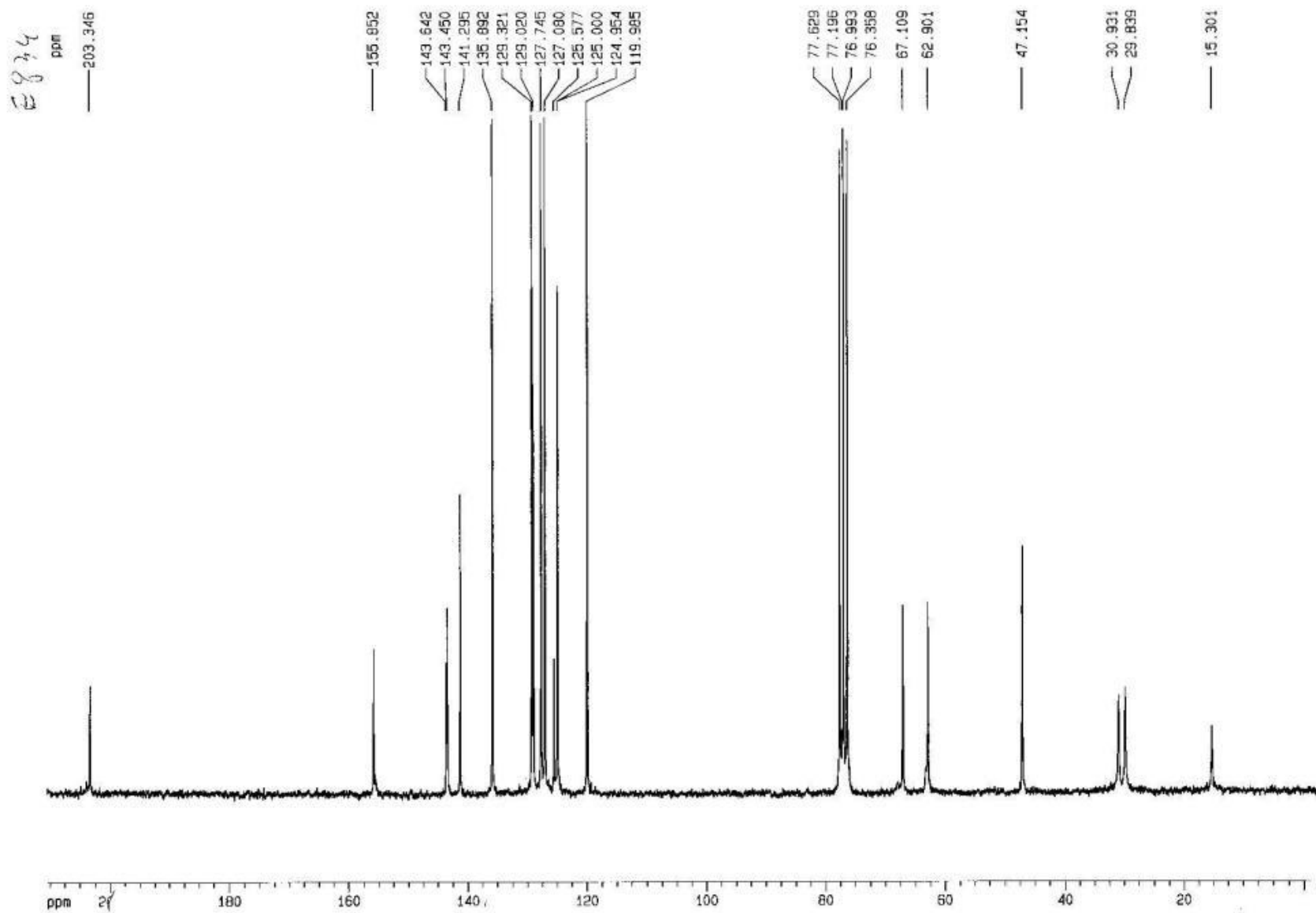


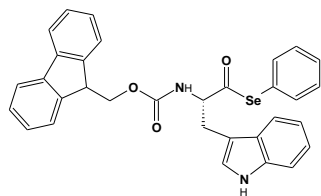
Se-phenyl (2S)-2-[[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-4-(methylthio)butaneselenoate (**8g**) ^1H NMR (400 MHz, CDCl_3)



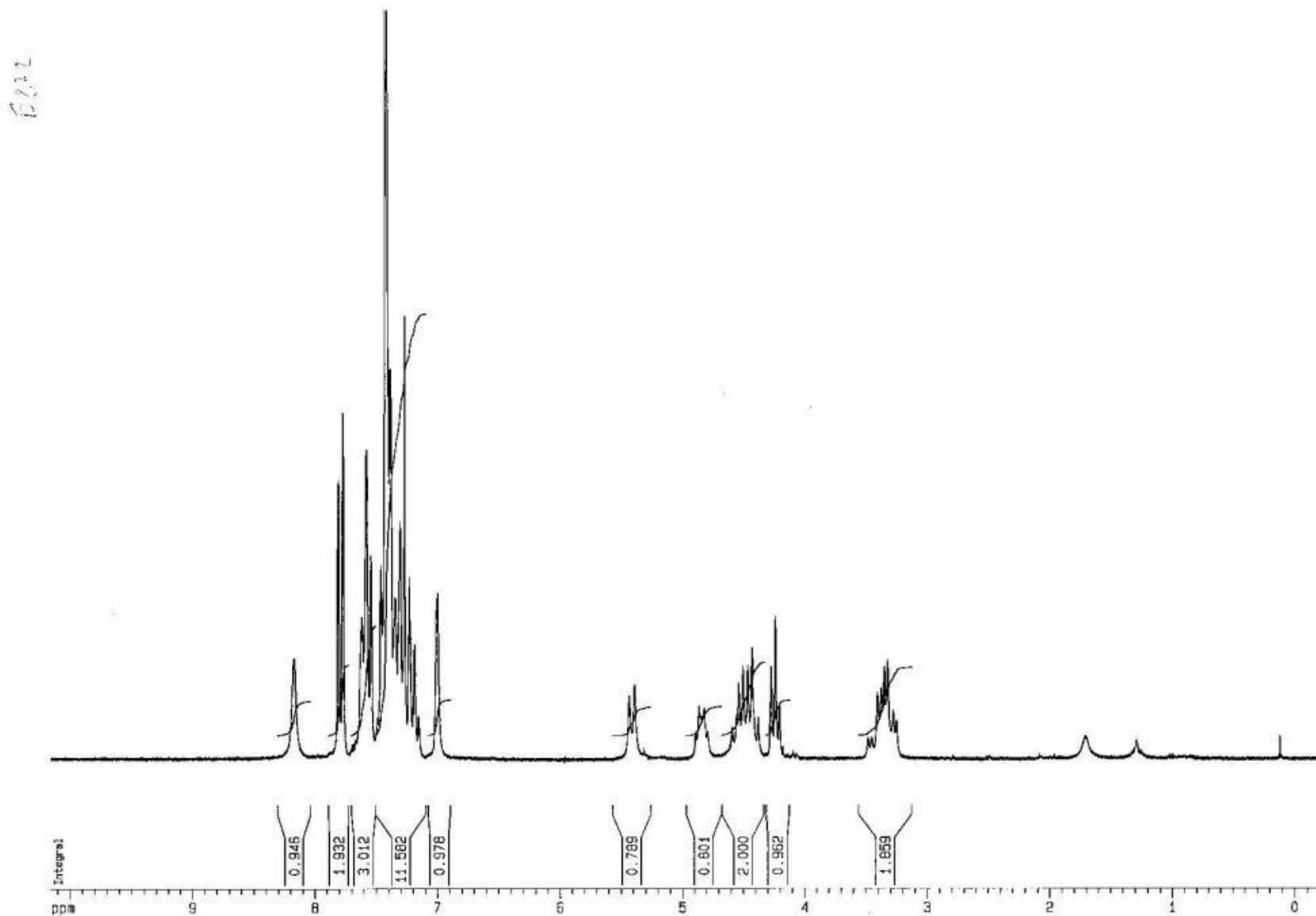


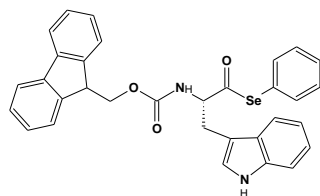
Se-phenyl (2*S*)-2-[[[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-4-(methylthio)butaneselenoate (**8g**) ^{13}C NMR (100 MHz, CDCl_3)



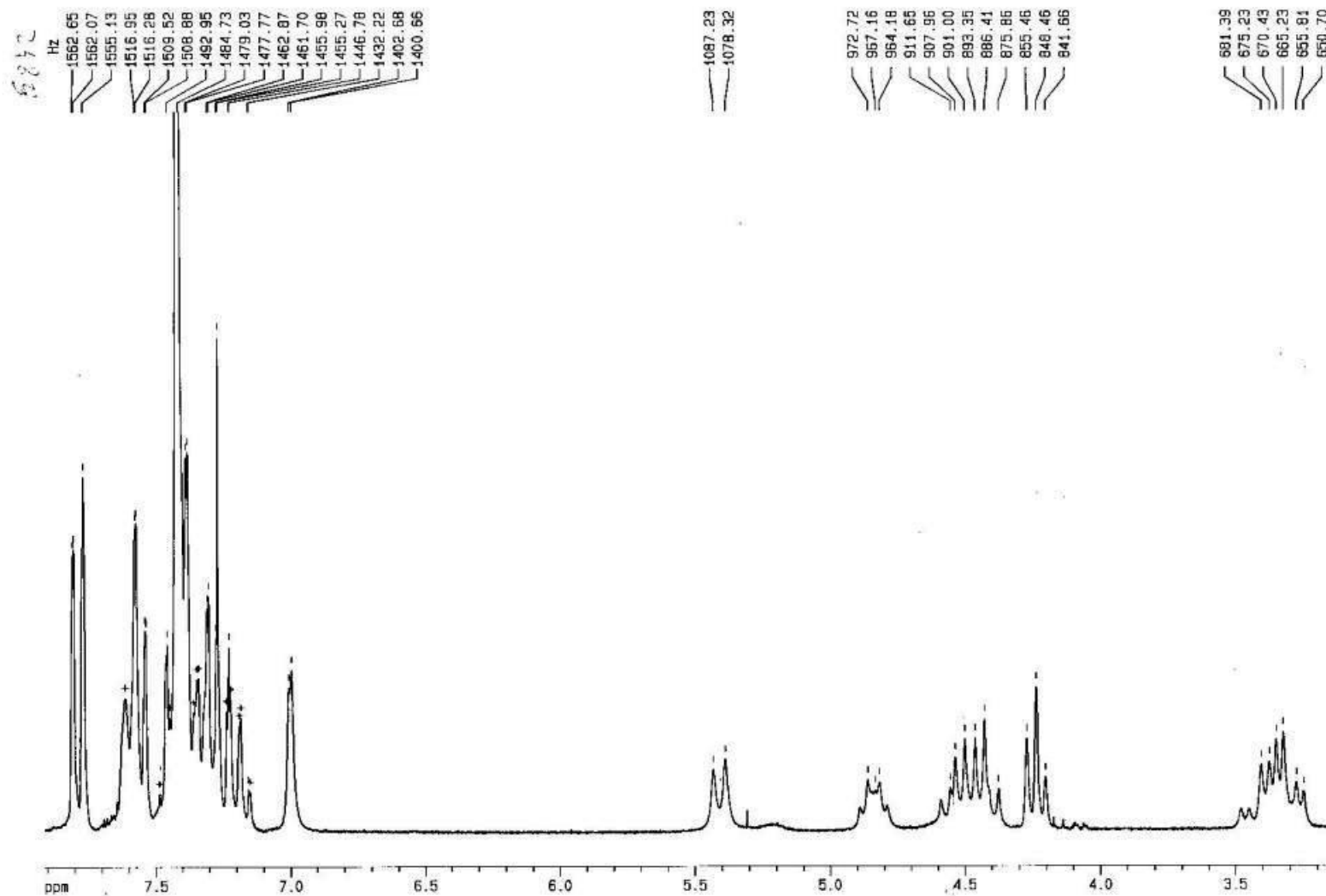


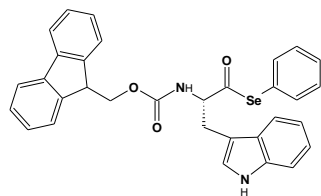
Se-Phenyl (2*S*)-2-[[[9*H*-fluoren-9-ylmethoxy]carbonyl]amino}-3-(1*H*-indol-3-yl)propaneselenoate (**8h**) ^1H NMR (200 MHz, CDCl_3)



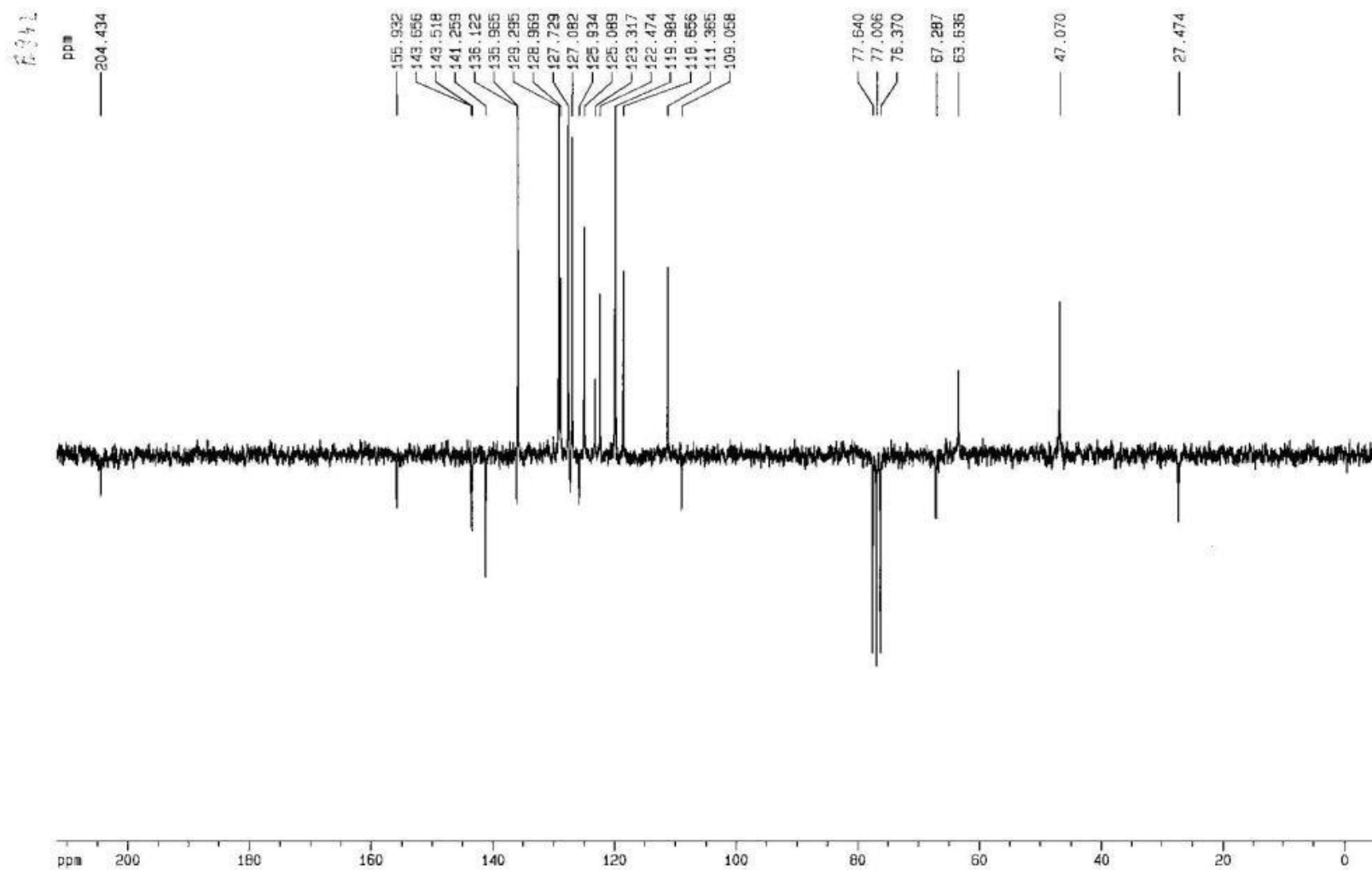


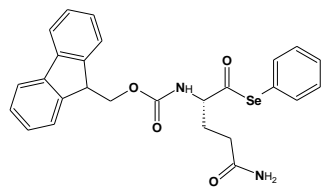
Se-Phenyl (2S)-2-[[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-3-(1H-indol-3-yl)propaneselenoate (**8h**) ^1H NMR (200 MHz, CDCl_3)





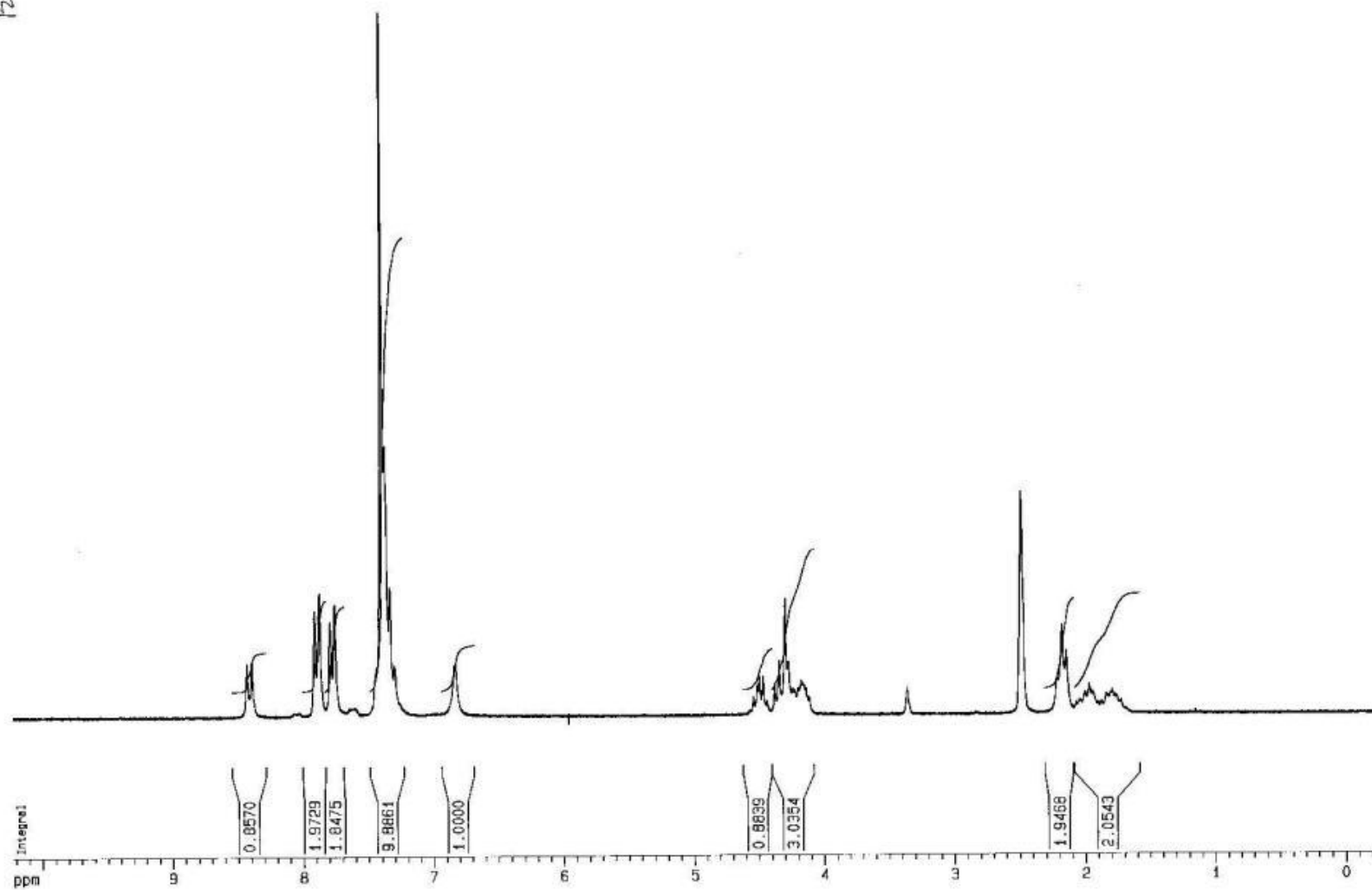
Se-Phenyl (2*S*)-2-([(9*H*-fluoren-9-ylmethoxy)carbonyl]amino)-3-(1*H*-indol-3-yl)propaneselenoate (**8h**) ^{13}C NMR (50 MHz, CDCl_3)

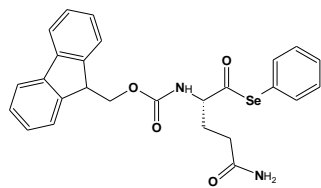




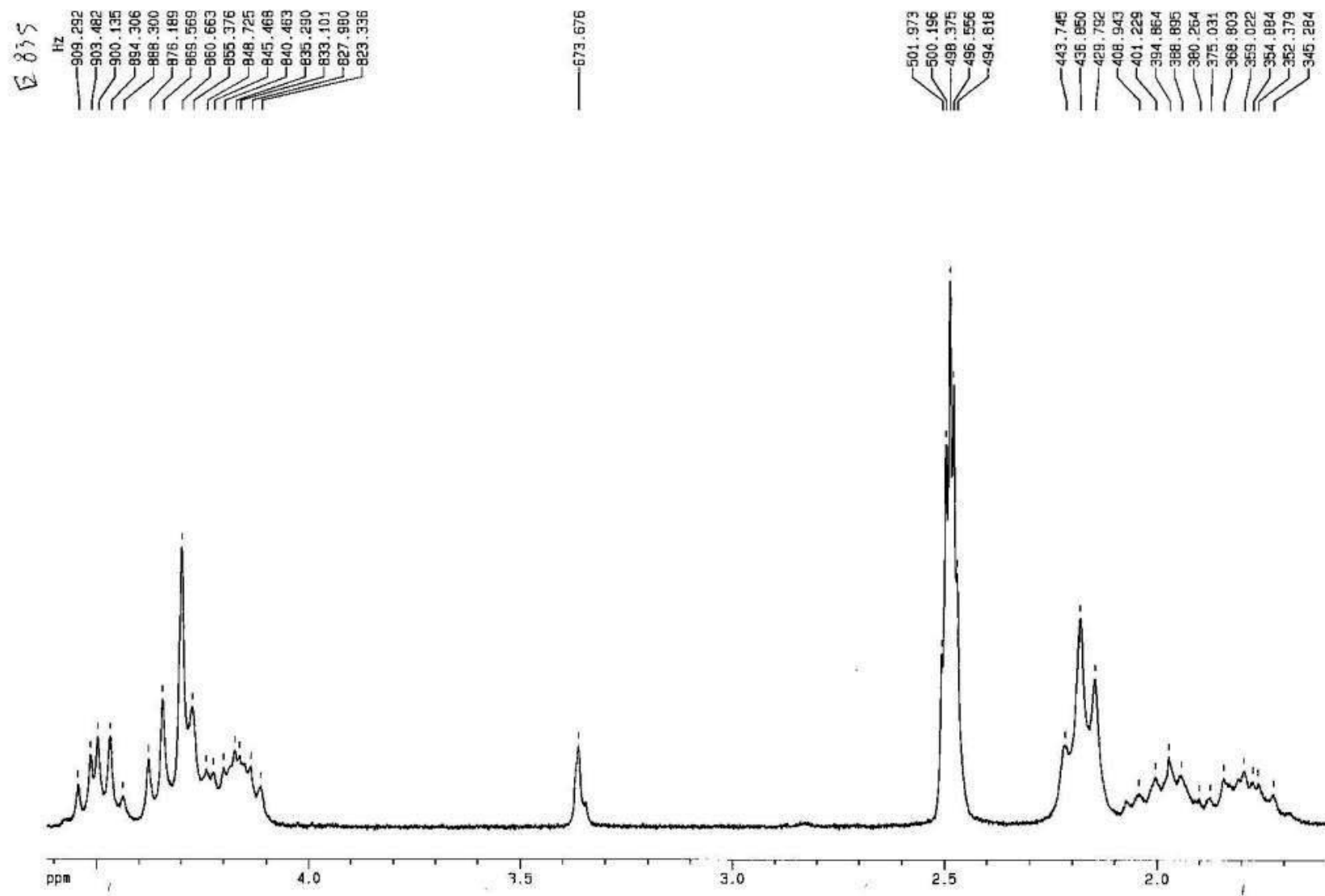
Se-Phenyl (2*S*)-5-amino-2-[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino-5-oxopentaneselenoate (**8i**) ^1H NMR (200 MHz, DMSO-d_6)

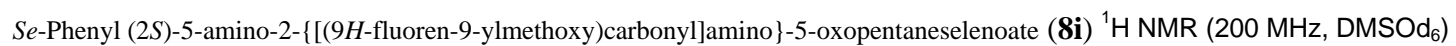
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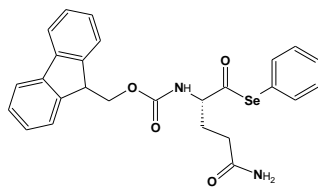




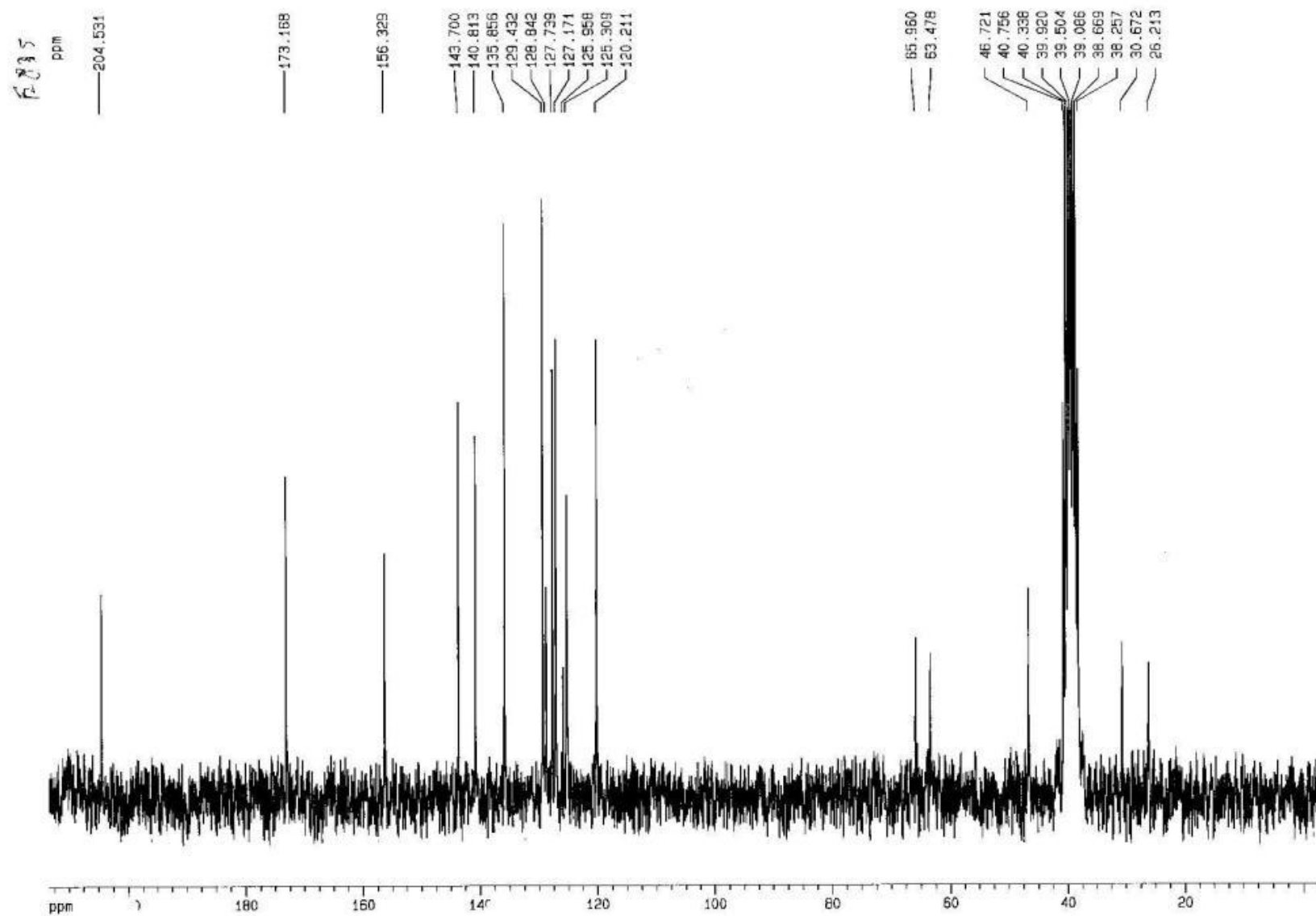
Se-Phenyl (2*S*)-5-amino-2-([(9*H*-fluoren-9-ylmethoxy)carbonyl]amino)-5-oxopentaneselenoate (**8i**) ^1H NMR (200 MHz, DMSO-d_6)

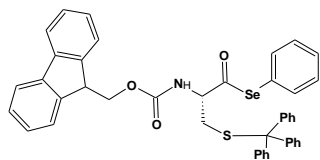






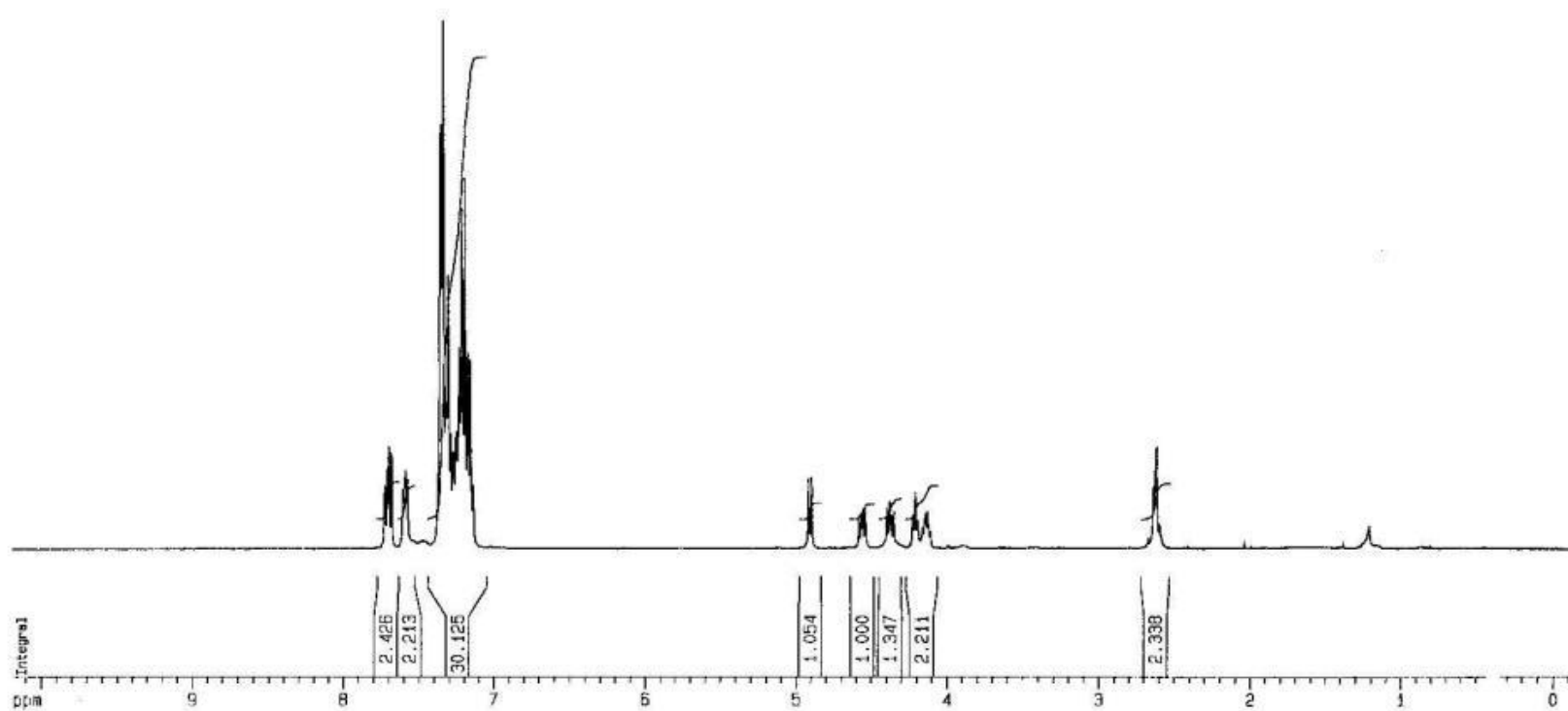
Se-Phenyl (2*S*)-5-amino-2-[[[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-5-oxopentaneselenoate (**8i**) ^{13}C NMR (50 MHz, DMSO-d_6)

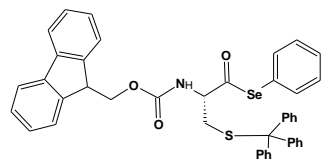




Se-Phenyl (2*S*)-2-[[[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-3-(tritylthio)propaneselenoate (**8j**) ^1H NMR (200 MHz, CDCl_3)

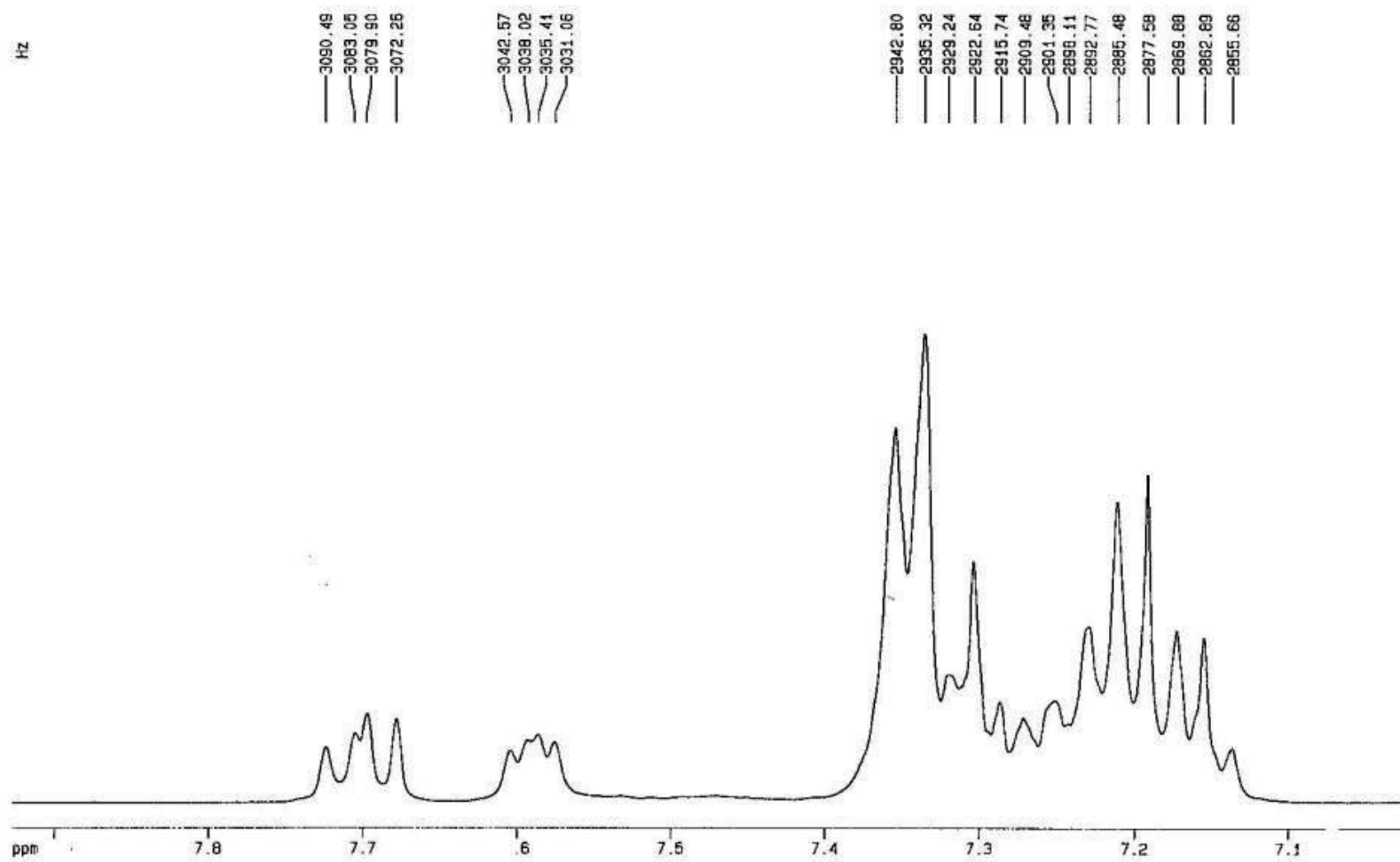
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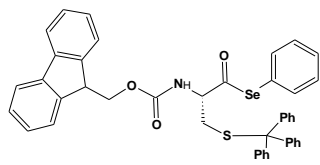




Se-Phenyl (2*S*)-2-[[[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-3-(tritylthio)propaneselenoate (**8j**) ^1H NMR (200 MHz, CDCl_3)

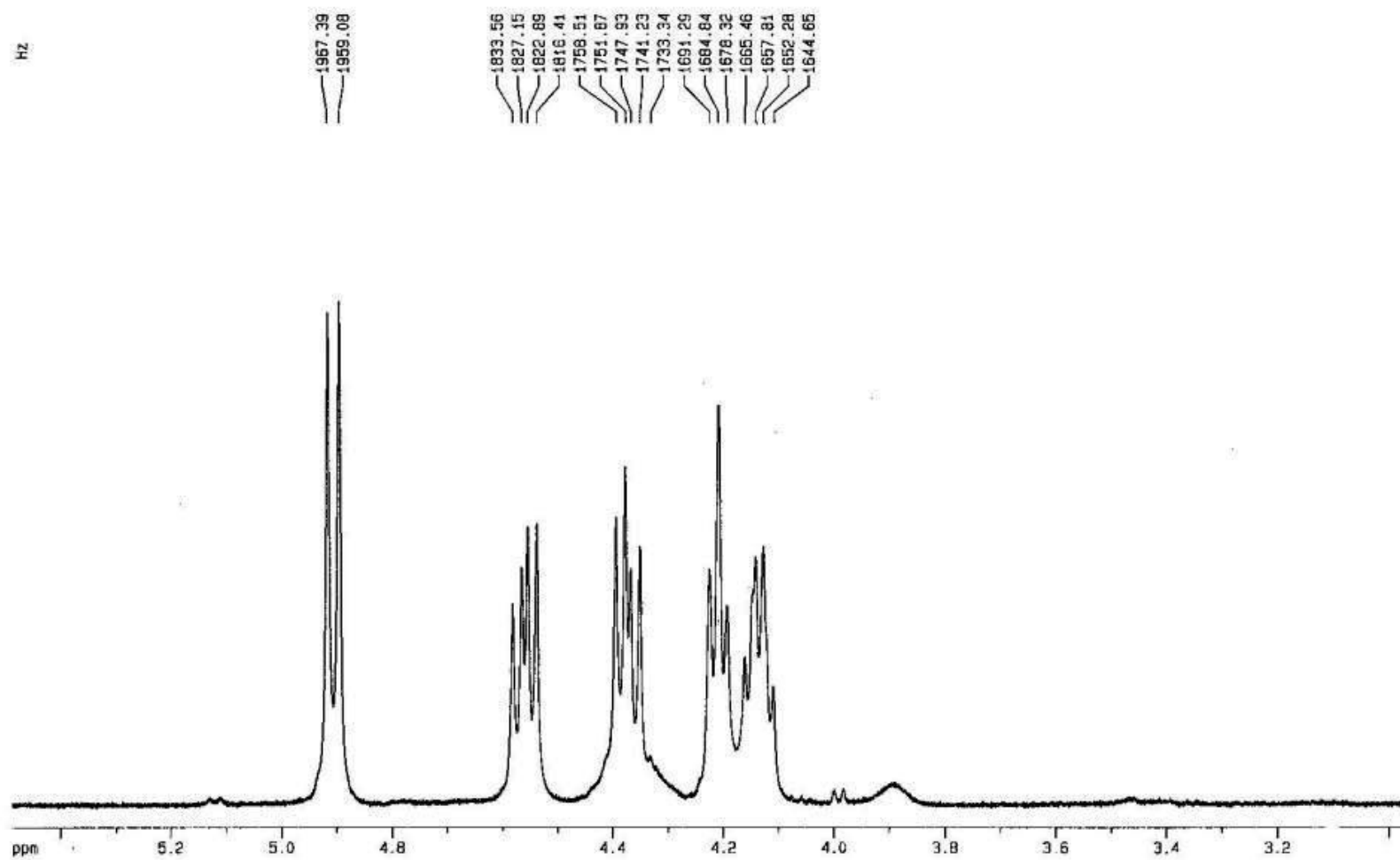
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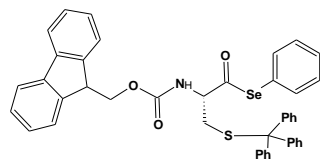




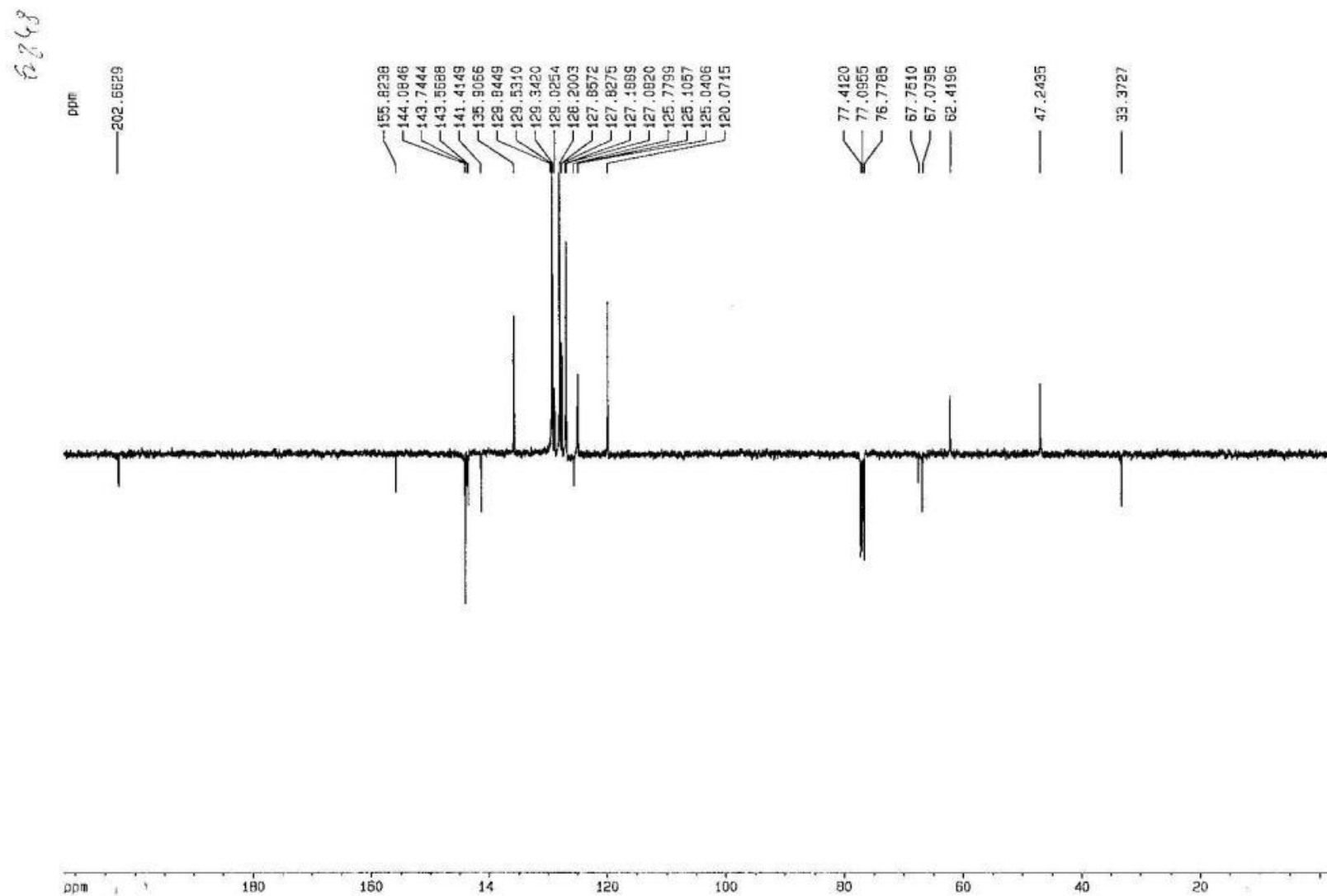
Se-Phenyl (2*S*)-2-[[[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-3-(tritylthio)propaneselenoate (**8j**) ^1H NMR (200 MHz, CDCl_3)

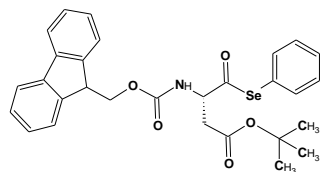
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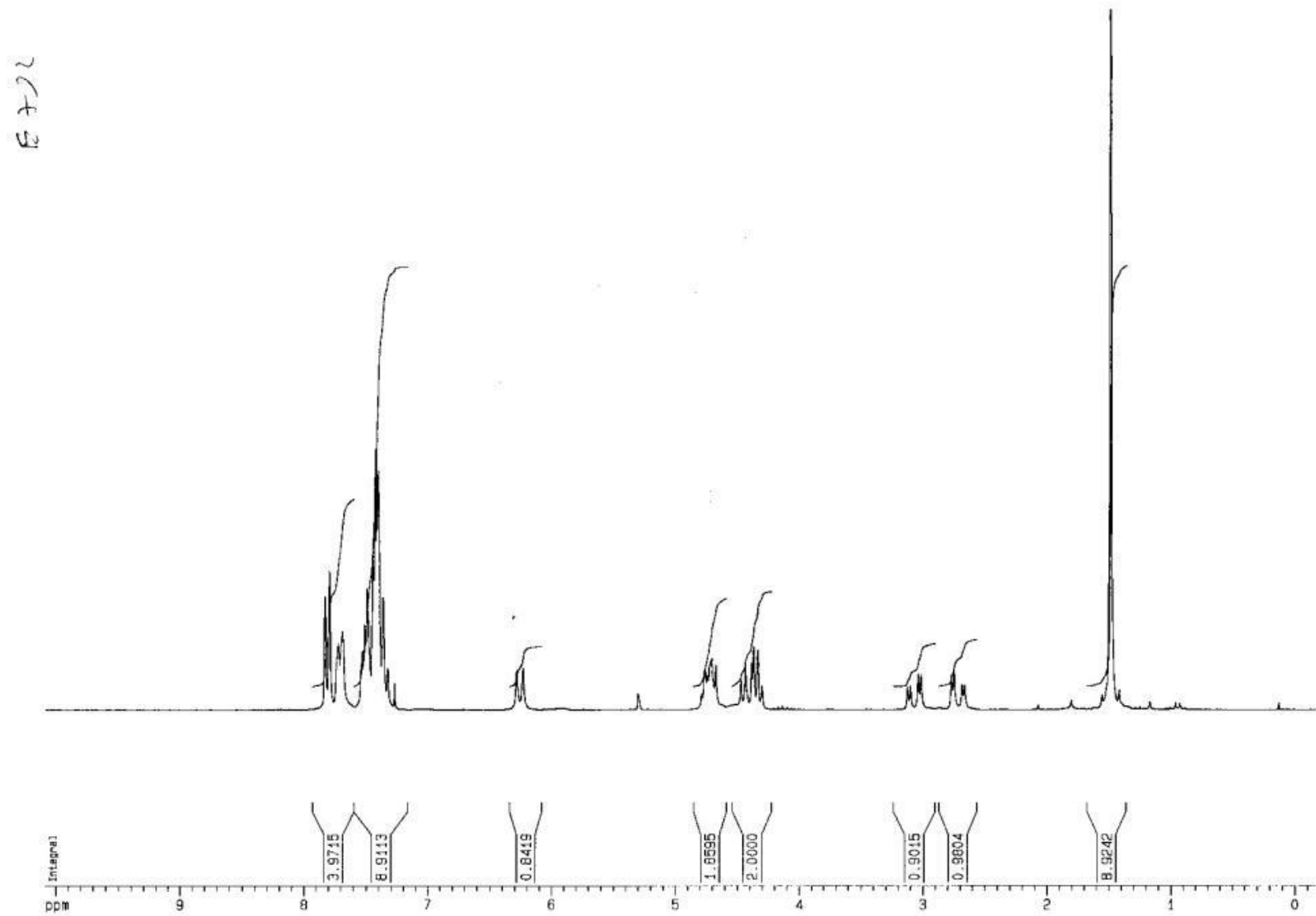


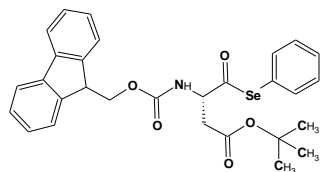
Se-Phenyl (2*S*)-2-[[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-3-(tritylthio)propaneselenoate (**8j**) ^{13}C NMR (50 MHz, CDCl_3)



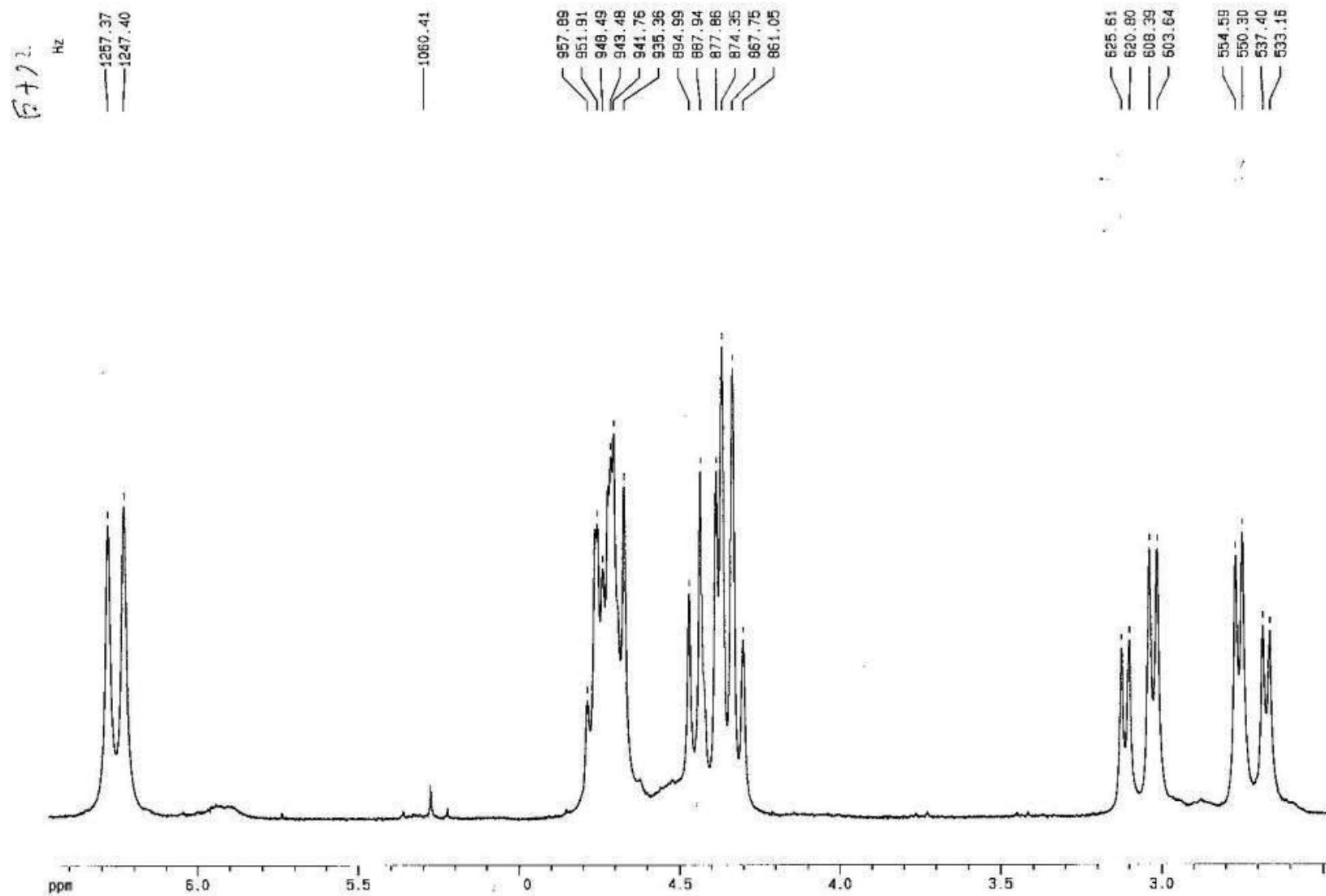


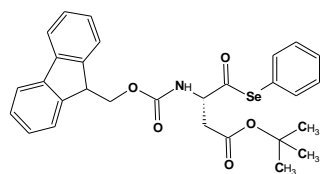
tert-Butyl (3*S*)-3-[[[9*H*-fluoren-9-ylmethoxy]carbonyl]amino]-4-oxo-4-(phenylseleno)butanoate (**8k**) ^1H NMR (200 MHz, CDCl_3)



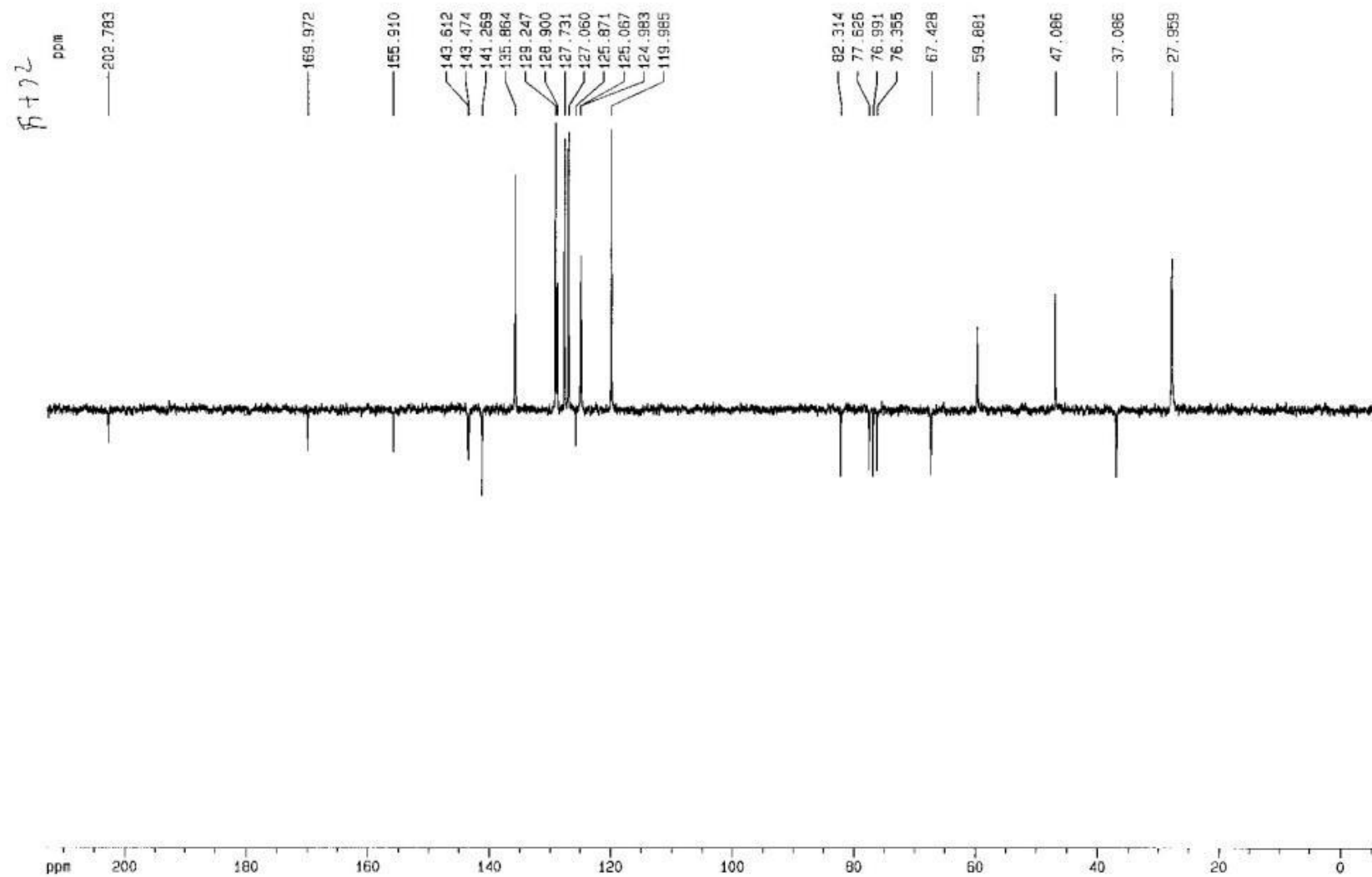


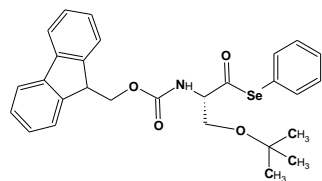
tert-Butyl (3*S*)-3-[[[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-4-oxo-4-(phenylseleno)butanoate (**8k**) ^1H NMR (200 MHz, CDCl_3)





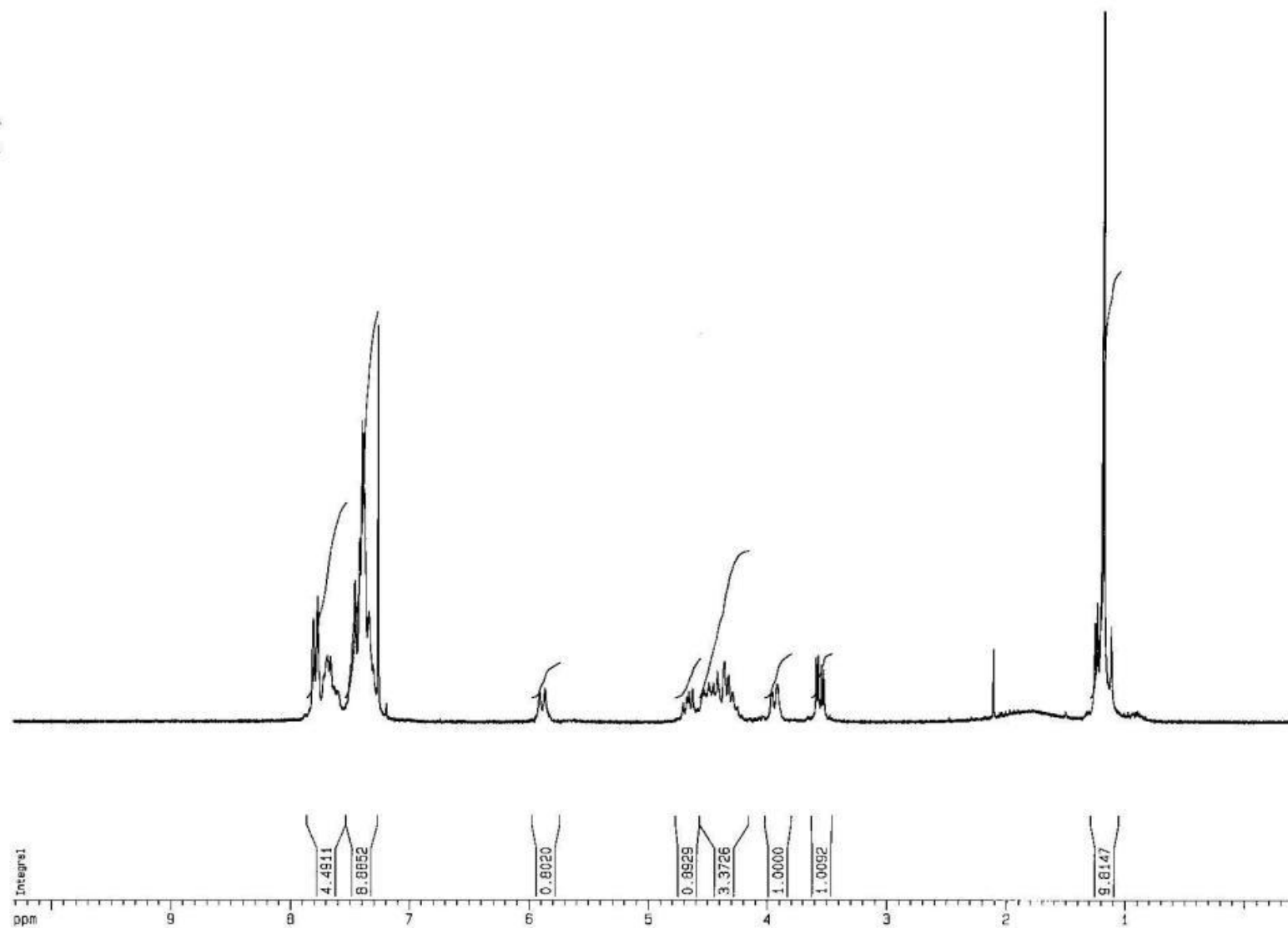
tert-Butyl (3*S*)-3-[[[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-4-oxo-4-(phenylseleno)butanoate (**8k**) ^{13}C NMR (50 MHz, CDCl_3)

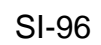


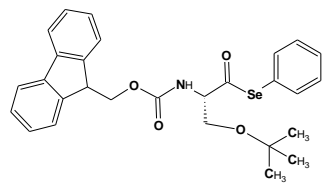


Se-Phenyl (2*S*)-3-*tert*-butoxy-2-[[*(9H*-fluoren-9-ylmethoxy)carbonyl]amino}propaneselenoate (**8I**) ^1H NMR (200 MHz, CDCl_3)

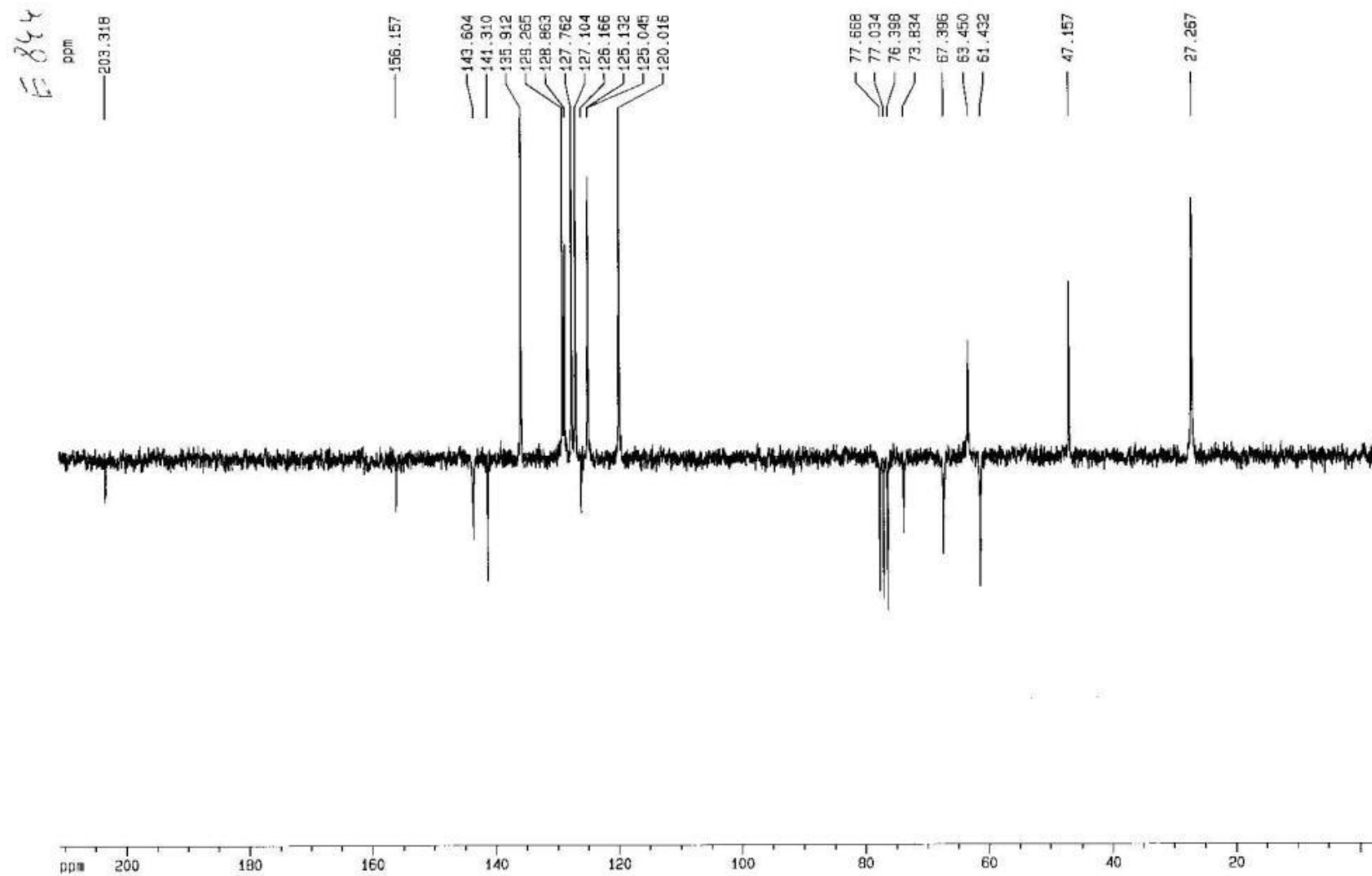
5844

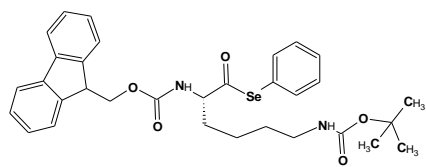




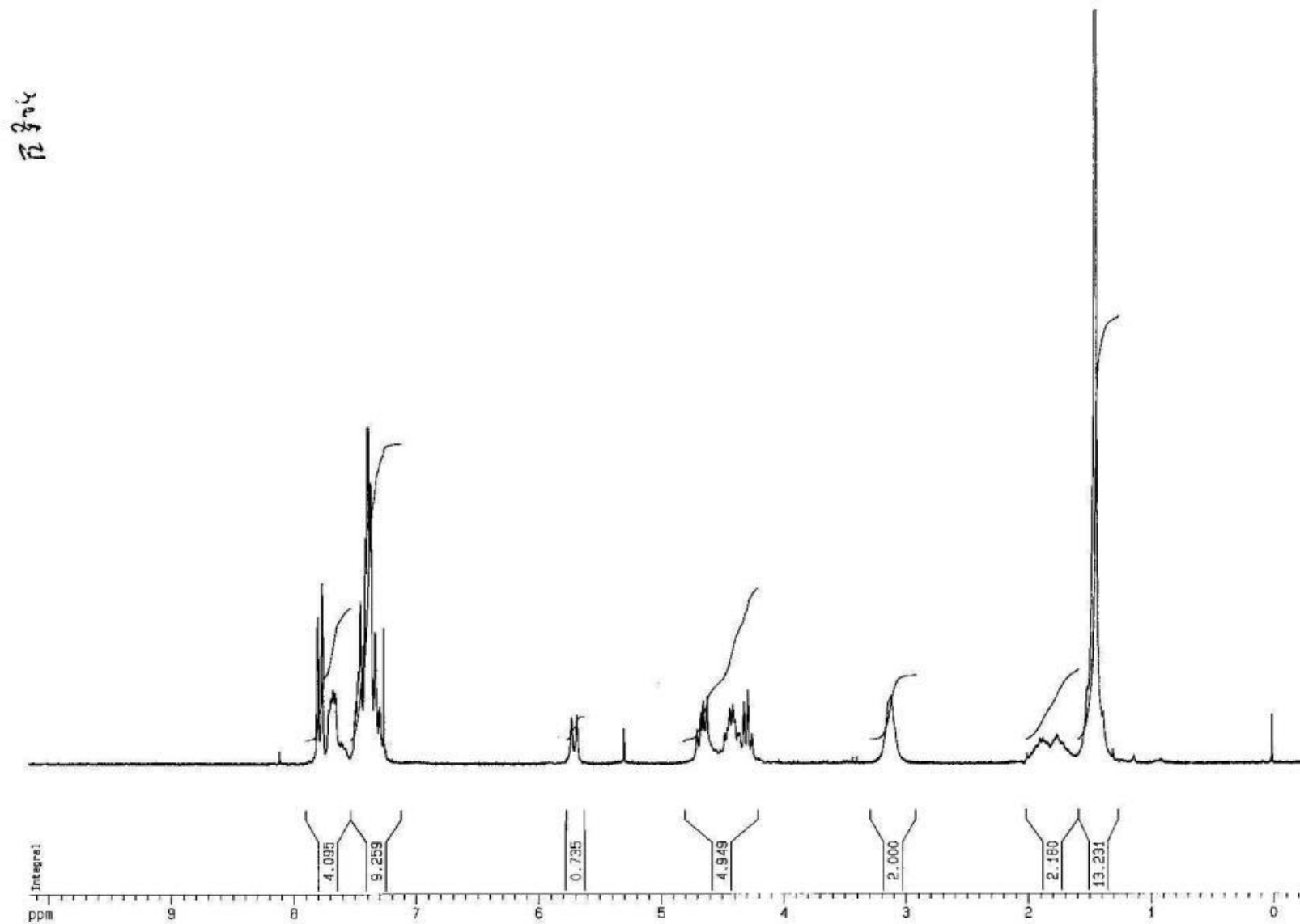


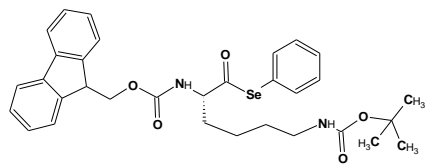
Se-Phenyl (2S)-3-*tert*-butoxy-2-[[9*H*-fluoren-9-ylmethoxy]carbonyl]amino}propaneselenoate (**81**) ^{13}C NMR (50 MHz, CDCl_3)



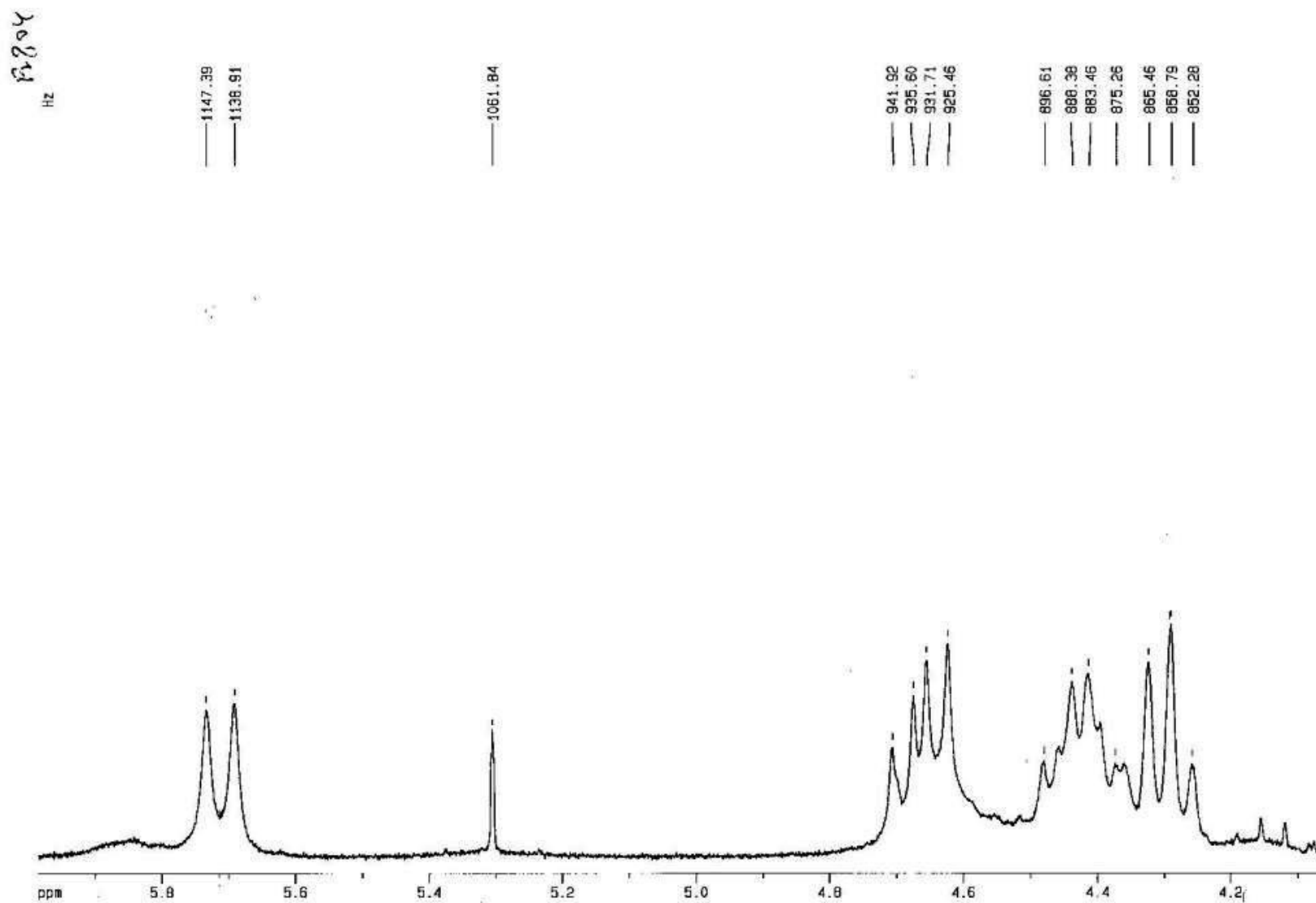


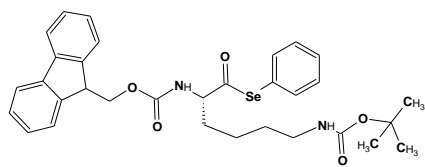
Se-Phenyl (2*S*)-6-[(*tert*-butoxycarbonyl)amino]-2-[[9*H*-fluoren-9-ylmethoxy)carbonyl]amino}hexaneselenoate (**8m**) ^1H NMR (200 MHz, CDCl_3)



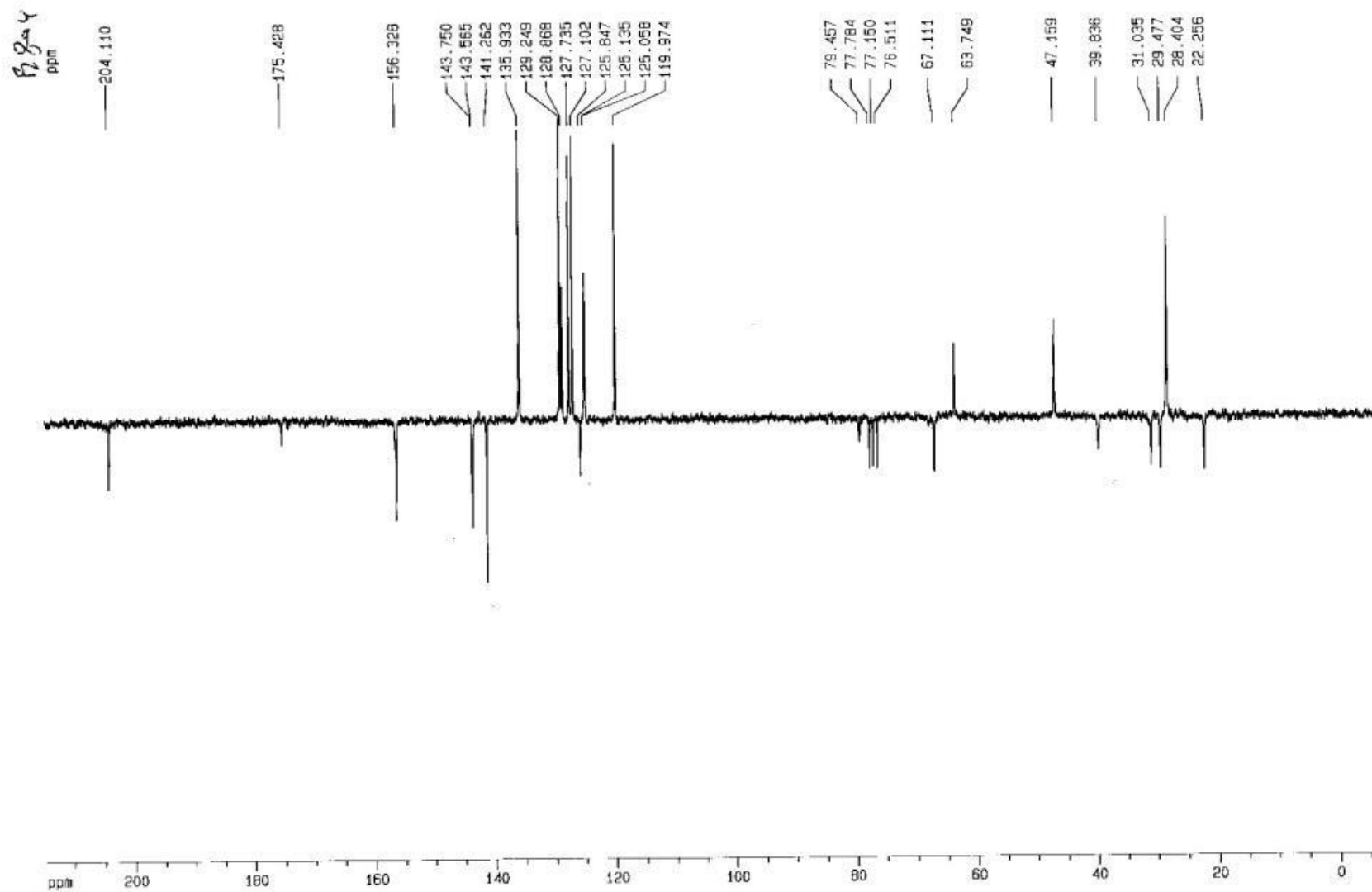


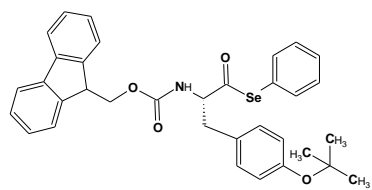
Se-Phenyl (2*S*)-6-[(*tert*-butoxycarbonyl)amino]-2-[[9*H*-fluoren-9-ylmethoxy]carbonyl]amino}hexaneselenoate (**8m**) ^1H NMR (200 MHz, CDCl_3)



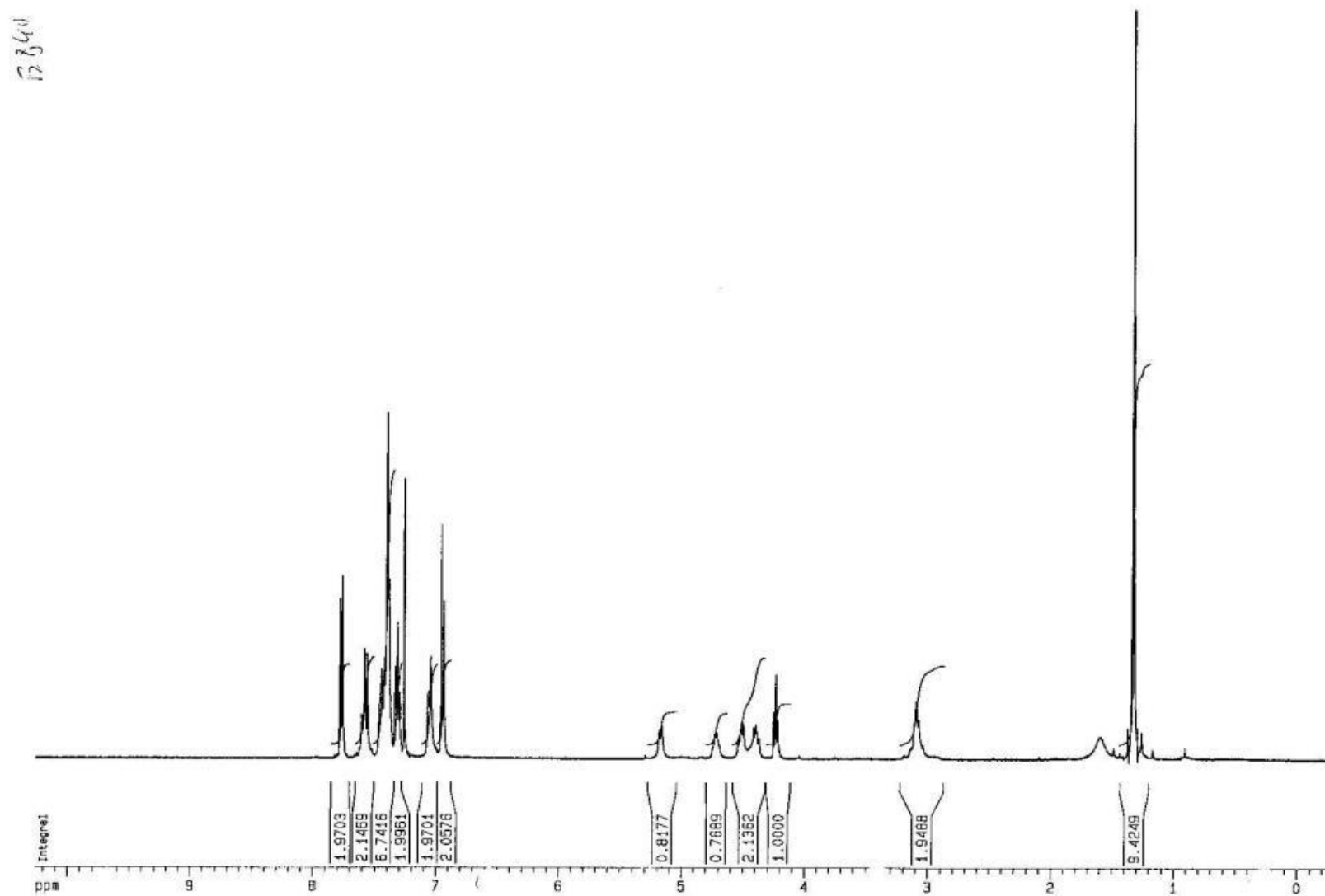


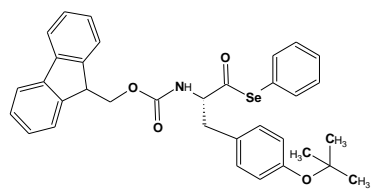
Se-Phenyl (2*S*)-6-[(*tert*-butoxycarbonyl)amino]-2-[[[9*H*-fluoren-9-ylmethoxy)carbonyl]amino]hexaneselenoate (**8m**) ^{13}C NMR (50 MHz, CDCl_3)



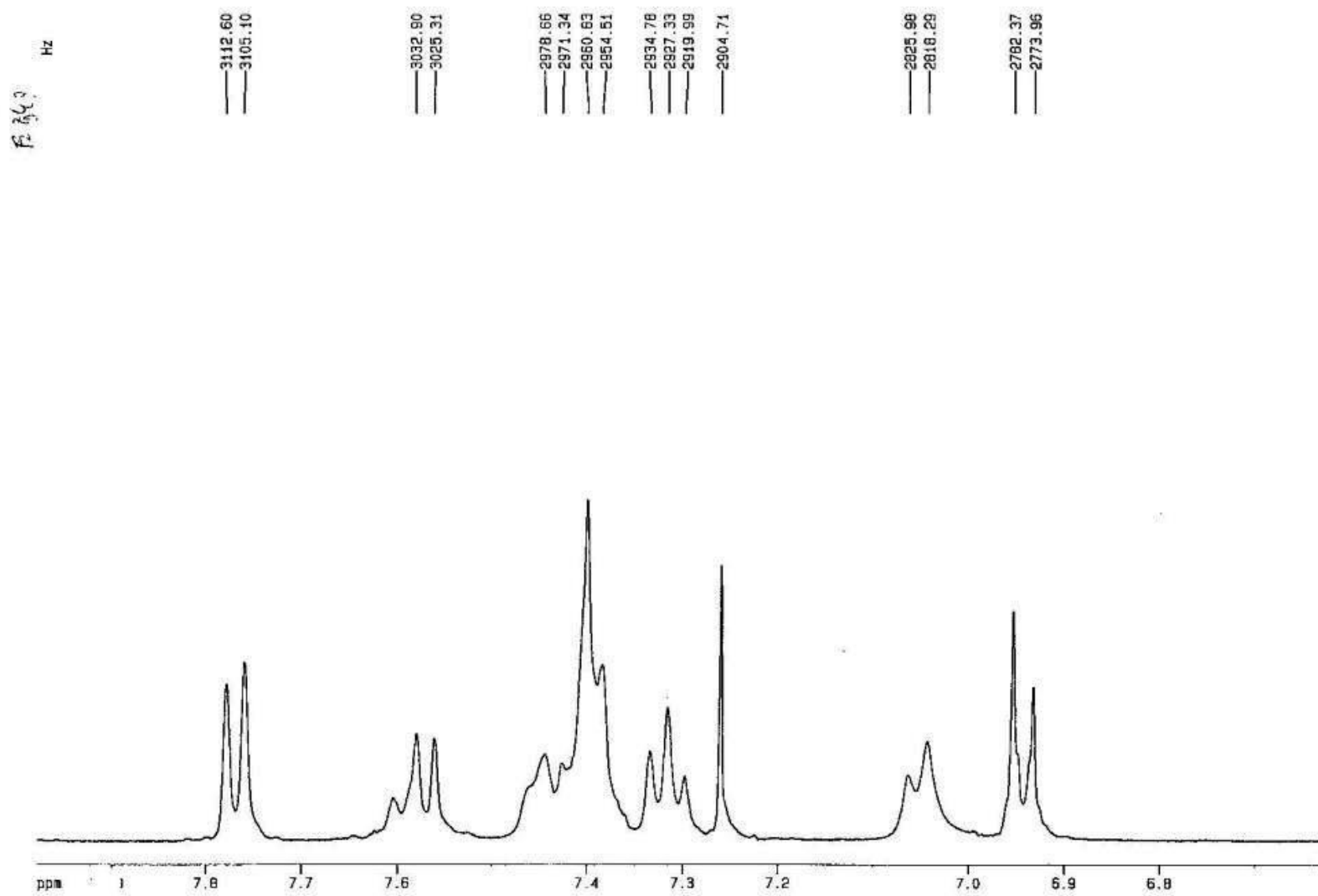


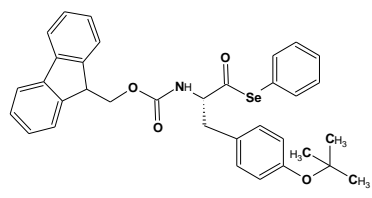
Se-Phenyl (2*S*)-3-(4-*tert*-butoxyphenyl)-2-([(9*H*-fluoren-9-ylmethoxy)carbonyl]amino)propaneselenoate (**8n**) ^1H NMR (200 MHz, CDCl_3)



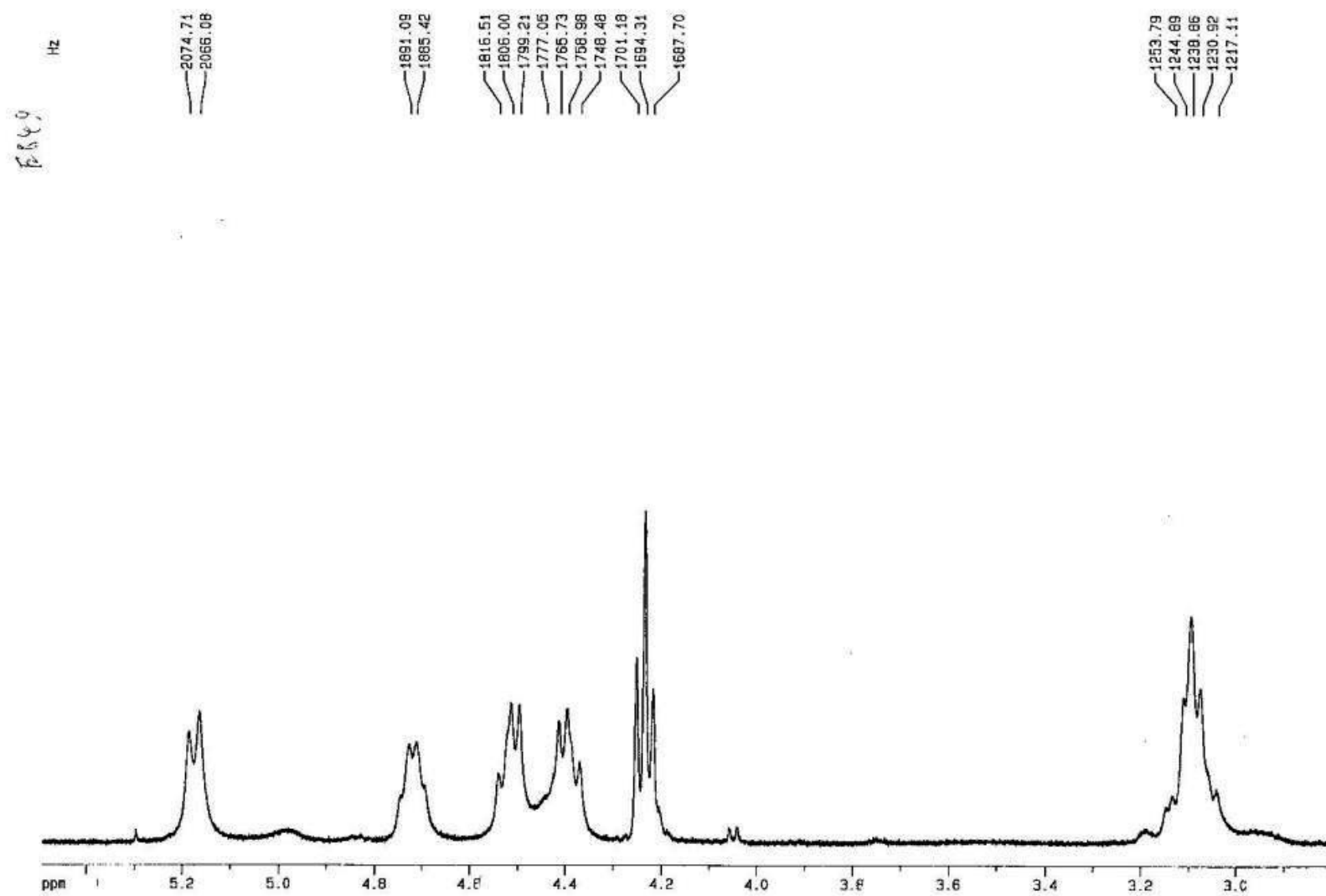


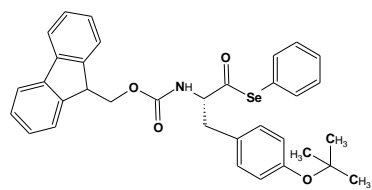
Se-Phenyl (2S)-3-(4-*tert*-butoxyphenyl)-2-[[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino}propaneselenoate (**8n**) ^1H NMR (200 MHz, CDCl_3)



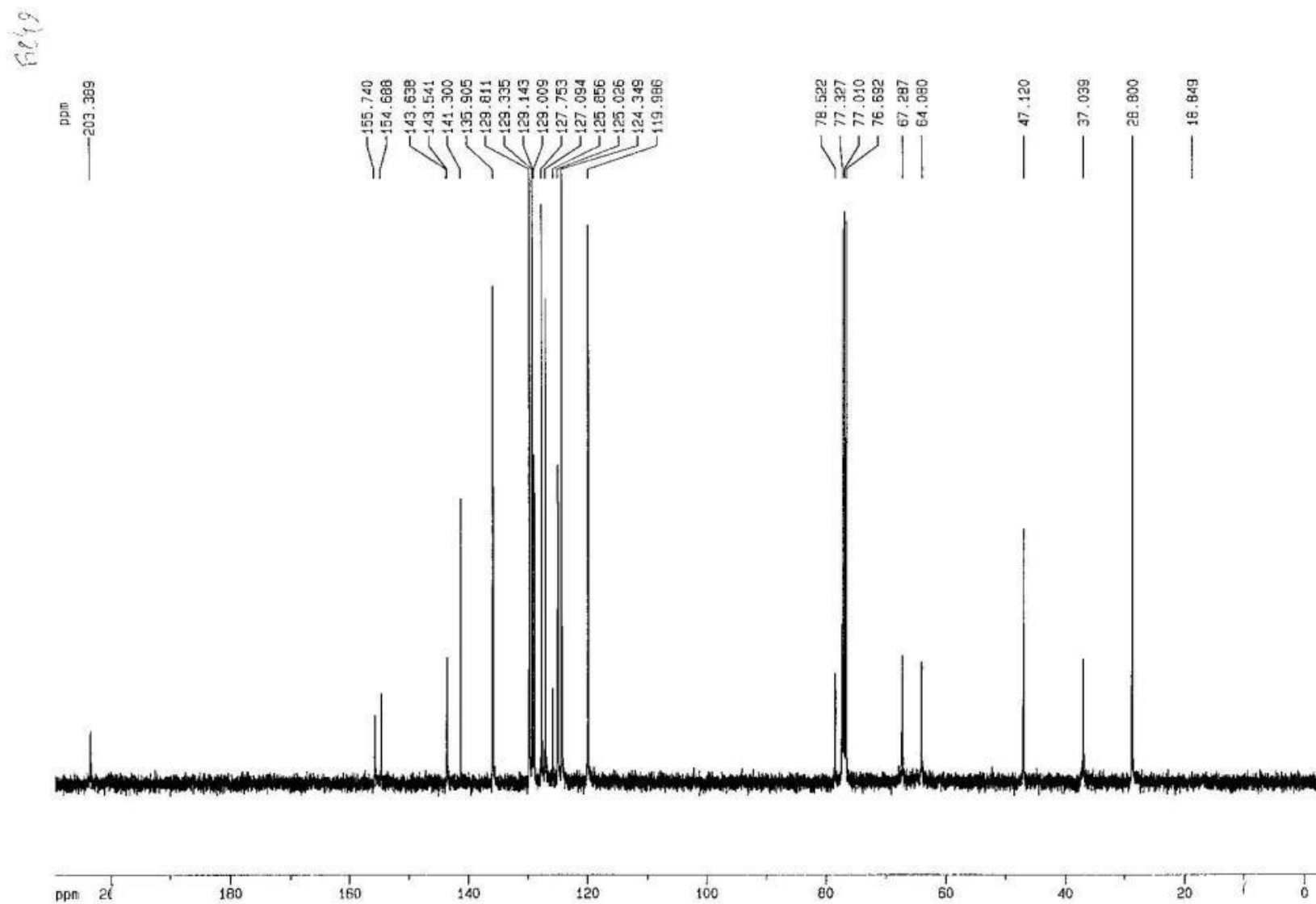


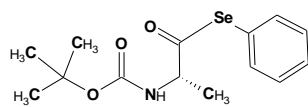
Se-Phenyl (2*S*)-3-(4-*tert*-butoxyphenyl)-2-[[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino}propaneselenoate (**8n**) ^1H NMR (200 MHz, CDCl_3)





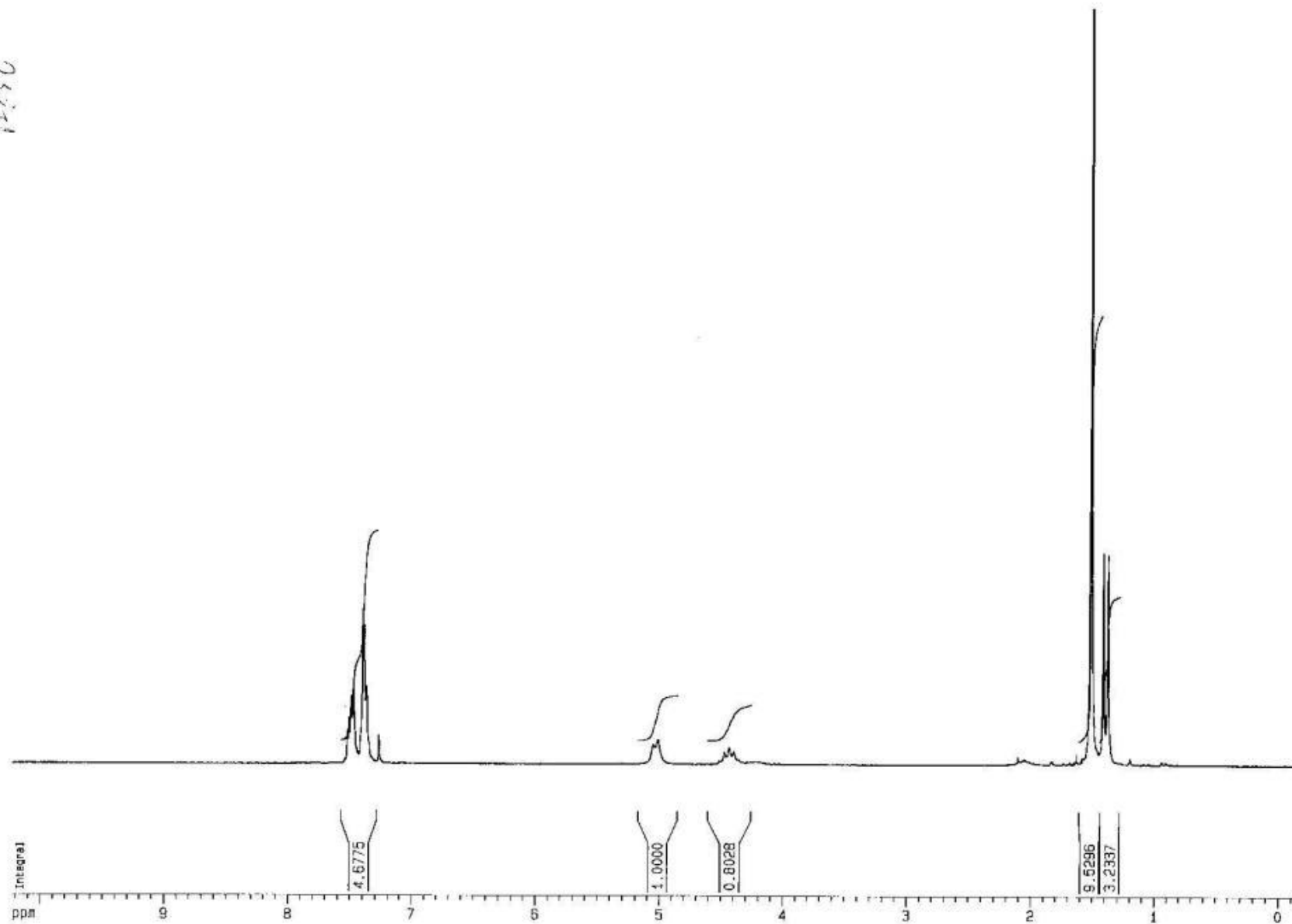
Se-Phenyl (2S)-3-(4-*tert*-butoxyphenyl)-2-[[[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]propaneselenoate (**8n**) ^{13}C NMR (50 MHz, CDCl_3)

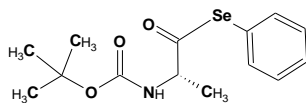




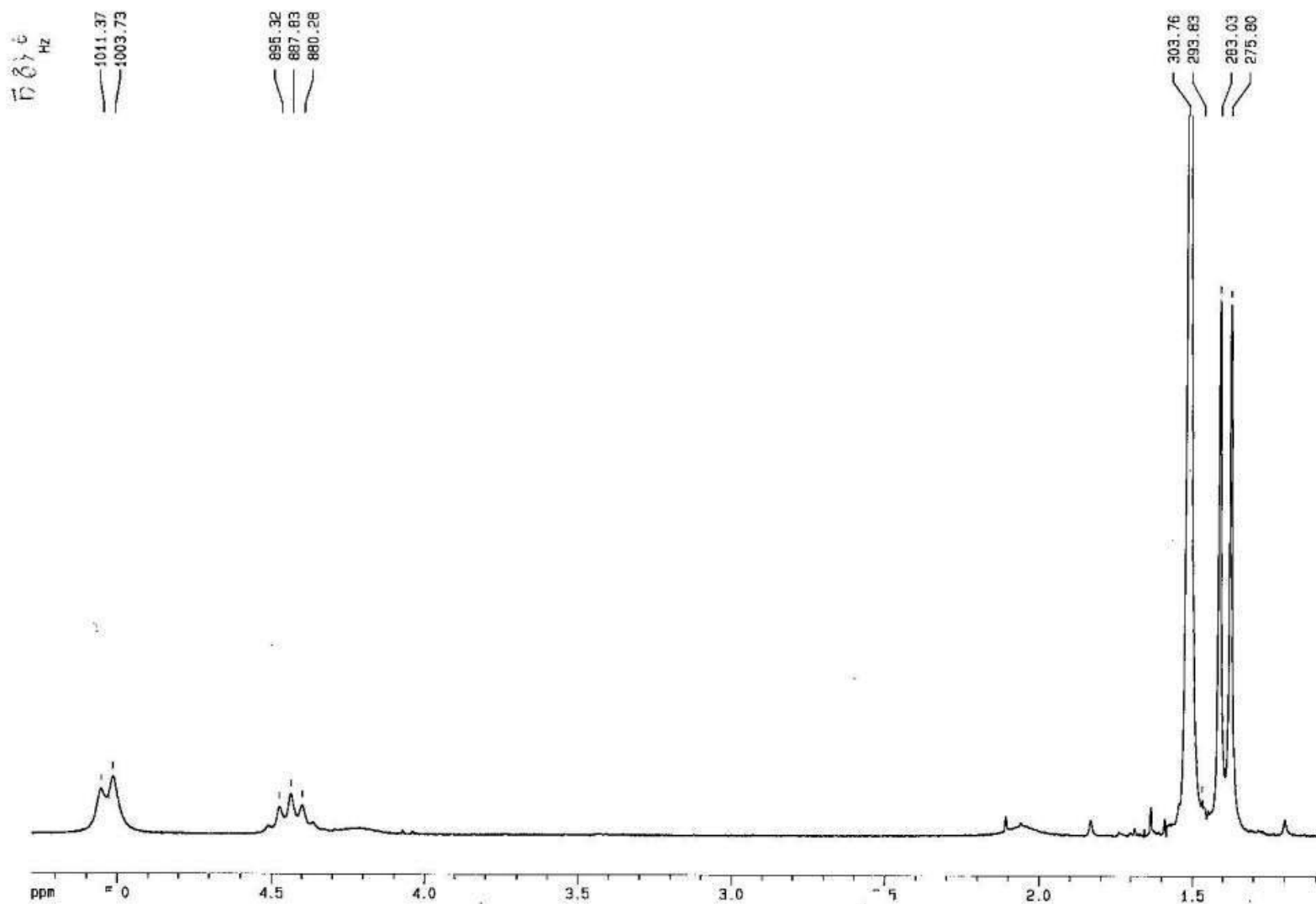
Se-phenyl (2*S*)-2-[(*tert*-butoxycarbonyl)amino]propaneselenoate (**10**) ^1H NMR (200 MHz, CDCl_3)

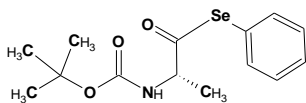
5.836





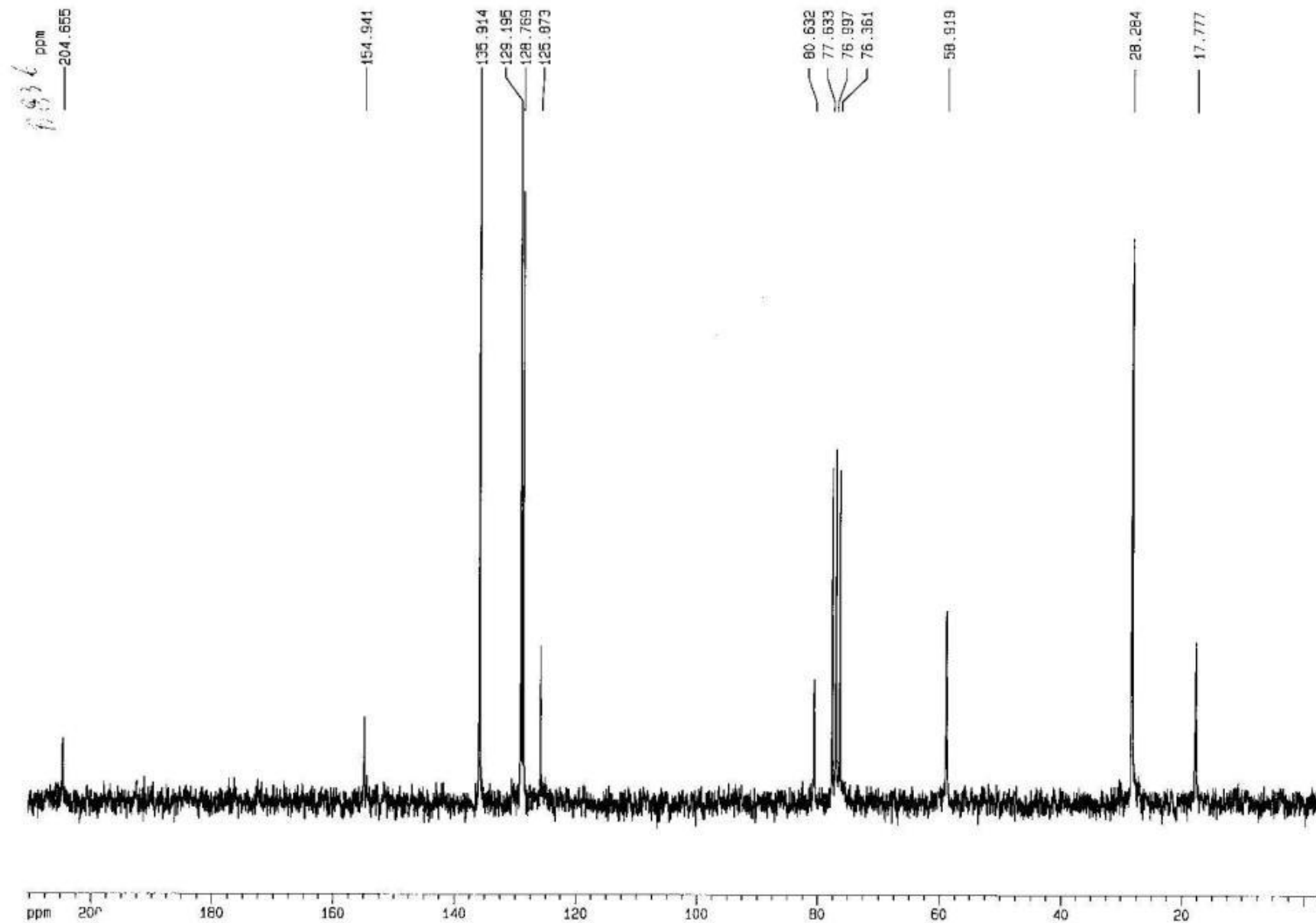
Se-phenyl (2*S*)-2-[(*tert*-butoxycarbonyl)amino]propaneselenoate (**10**) ^1H NMR (200 MHz, CDCl_3)

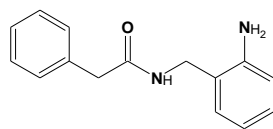




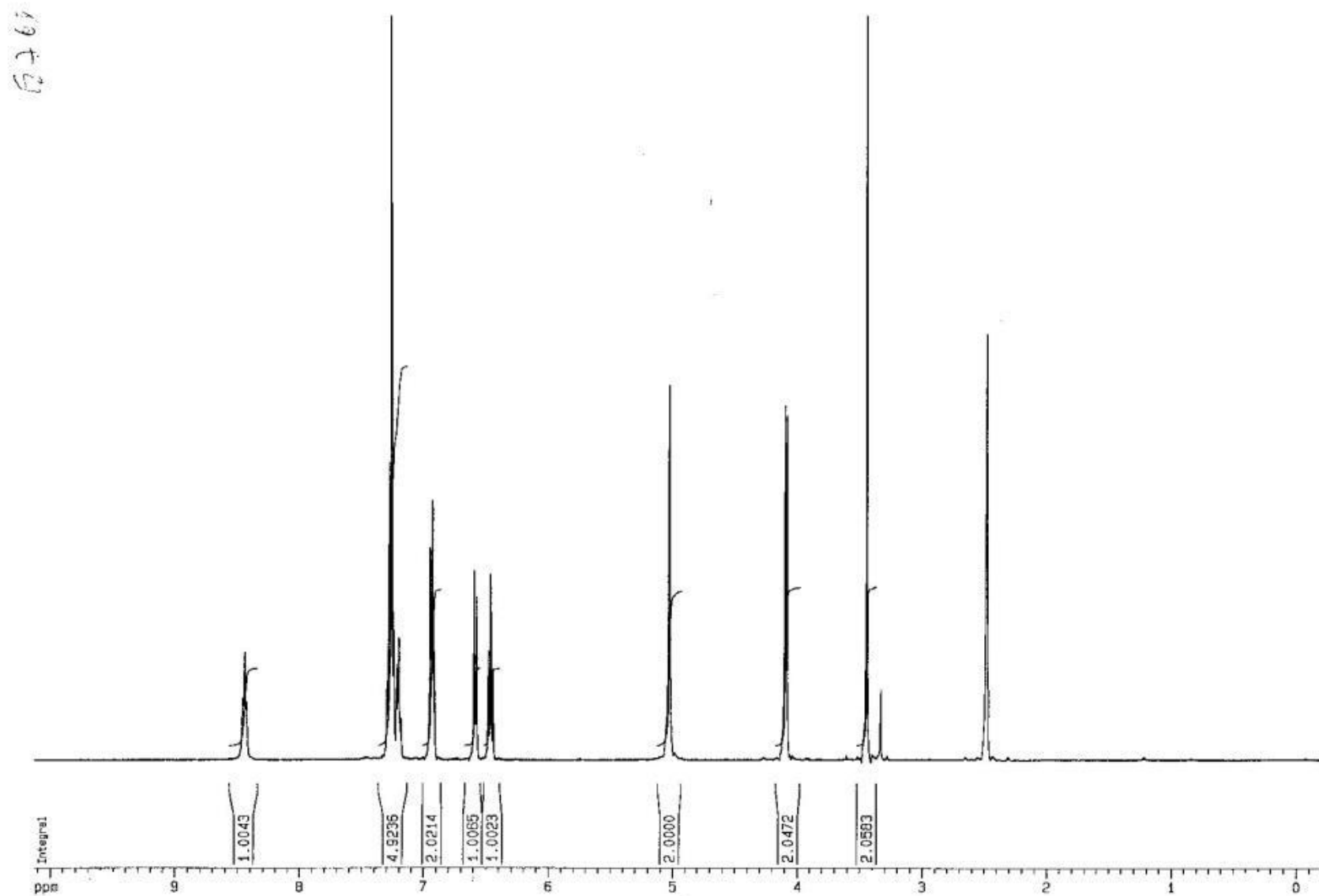
Se-phenyl (2*S*)-2-[(*tert*-butoxycarbonyl)amino]propaneselenoate (**10**)

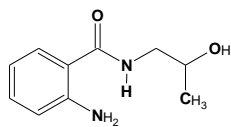
^{13}C NMR (50 MHz, CDCl_3)



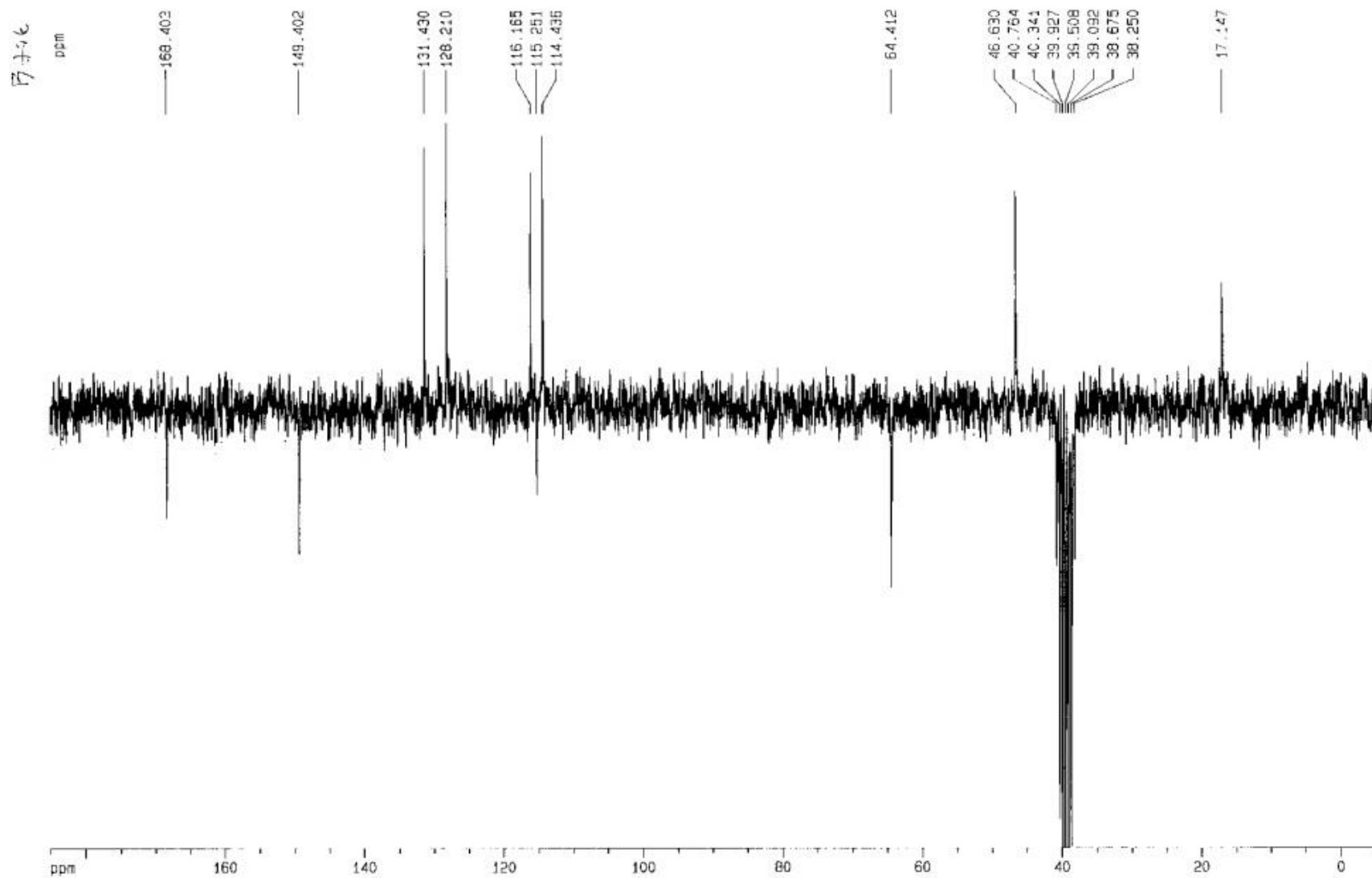


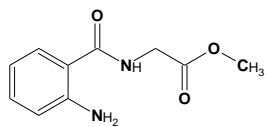
N-(2-Aminobenzyl)-2-phenylacetamide (**12a**) ^1H NMR (400 MHz, DMSO-d_6)



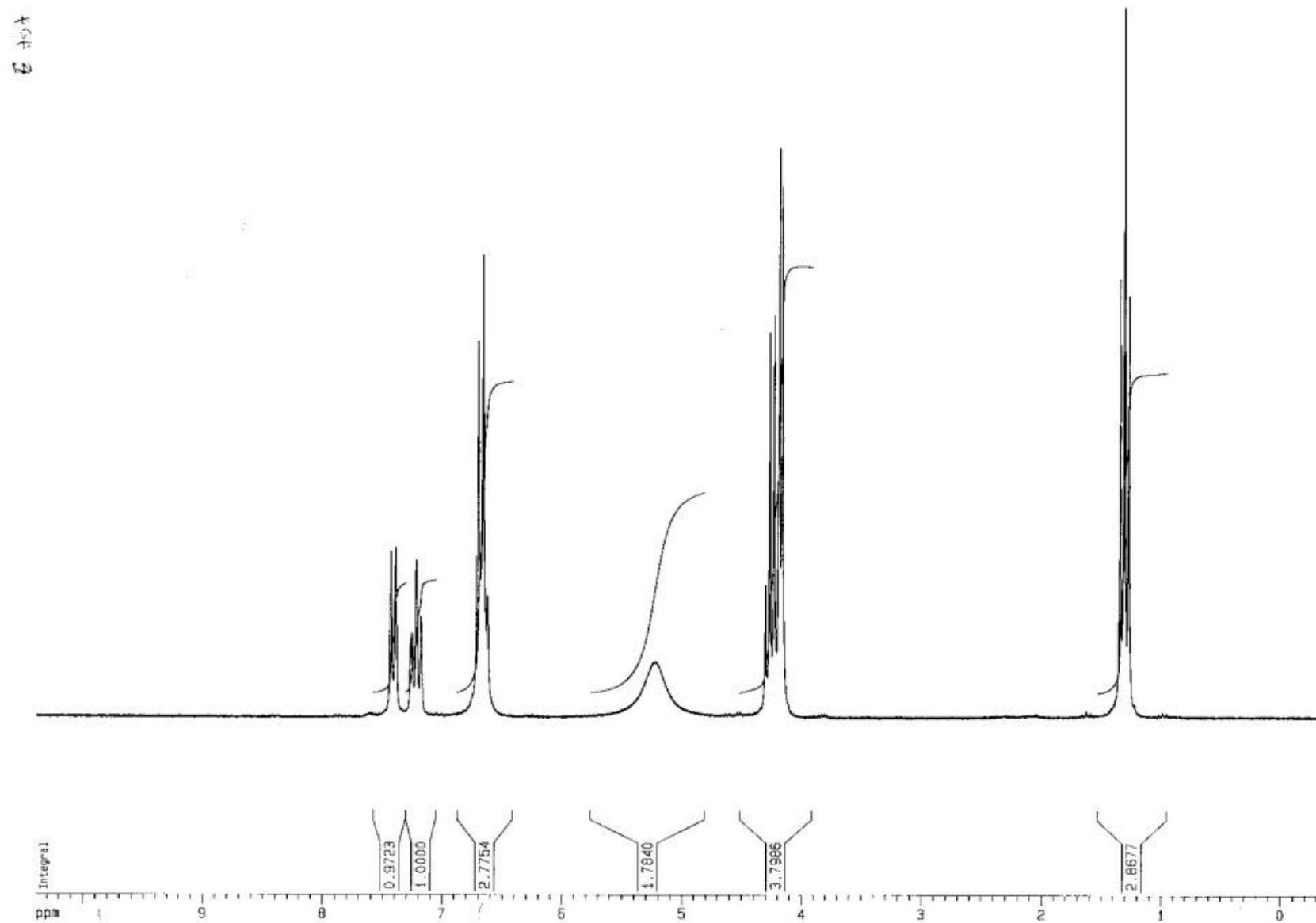


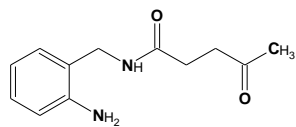
2-Amino-*N*-(2-hydroxypropyl)benzamid (**12b**) ^{13}C NMR (50 MHz, DMSO-d_6)



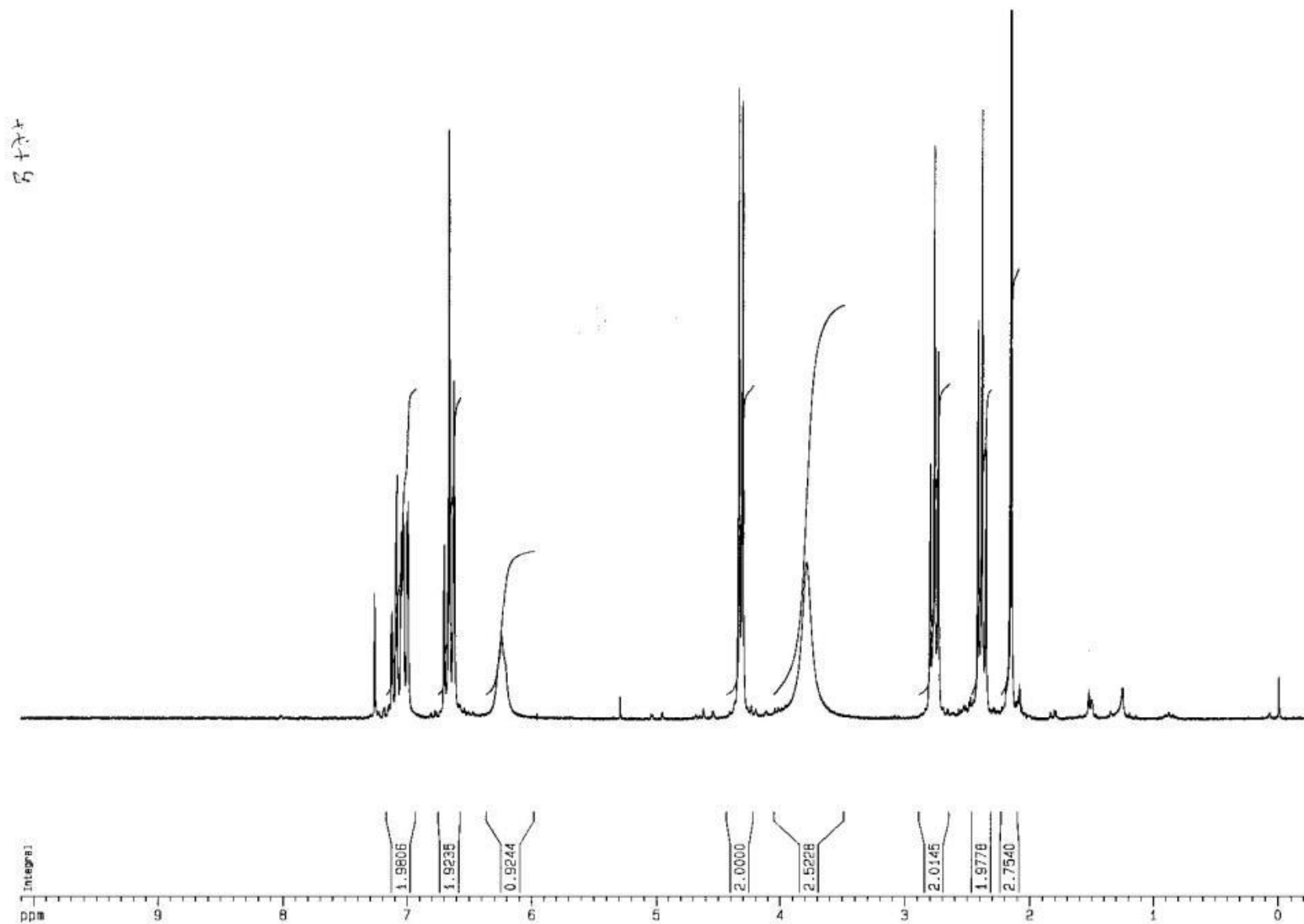


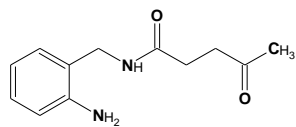
Methyl *N*-(2-aminobenzoyl)glycinate (**12c**) ^1H NMR (200 MHz, CDCl_3)



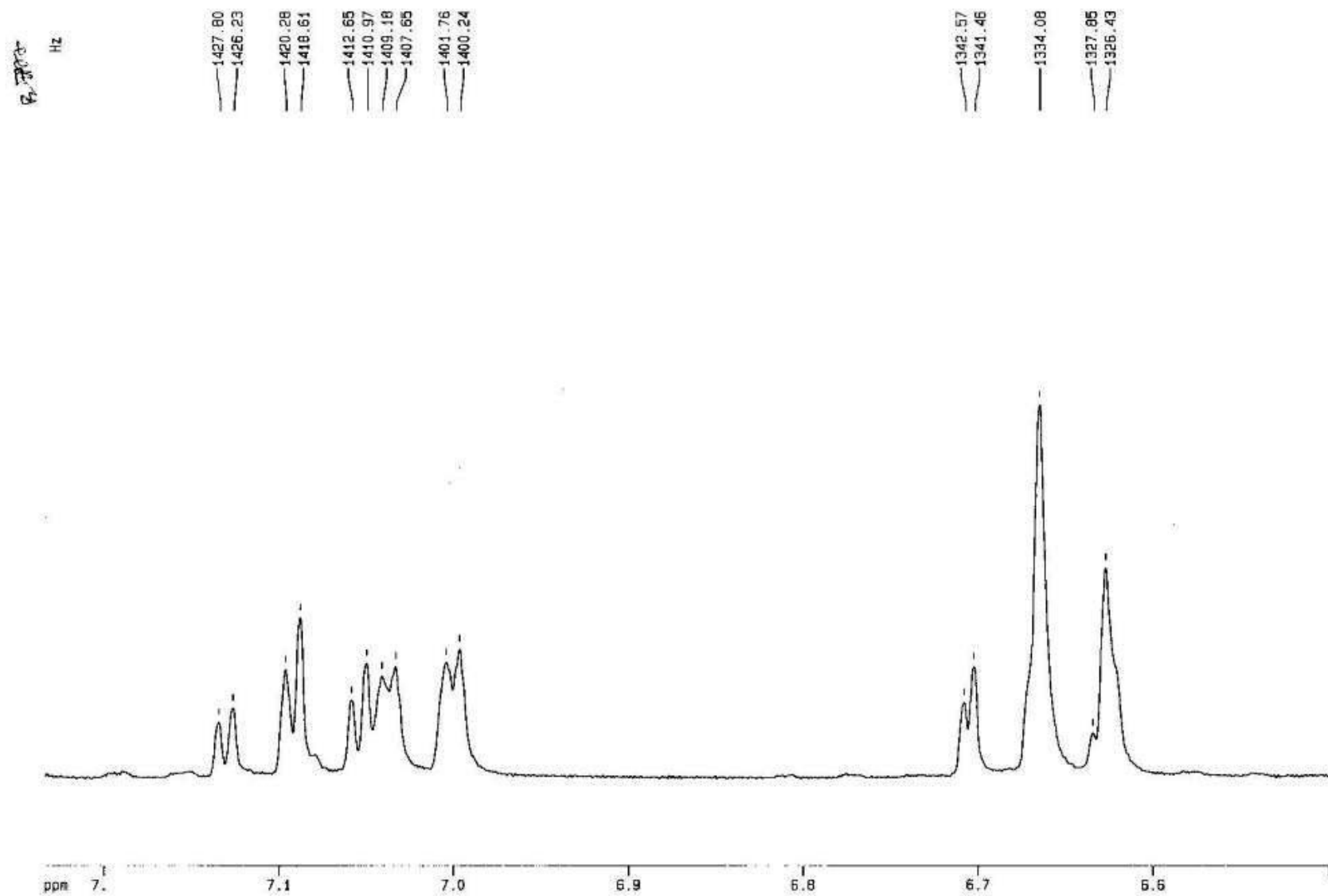


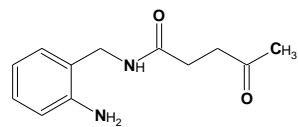
N-(2-aminobenzyl)-4-oxopentanamide (**12d**) ^1H NMR (200 MHz, CDCl_3)



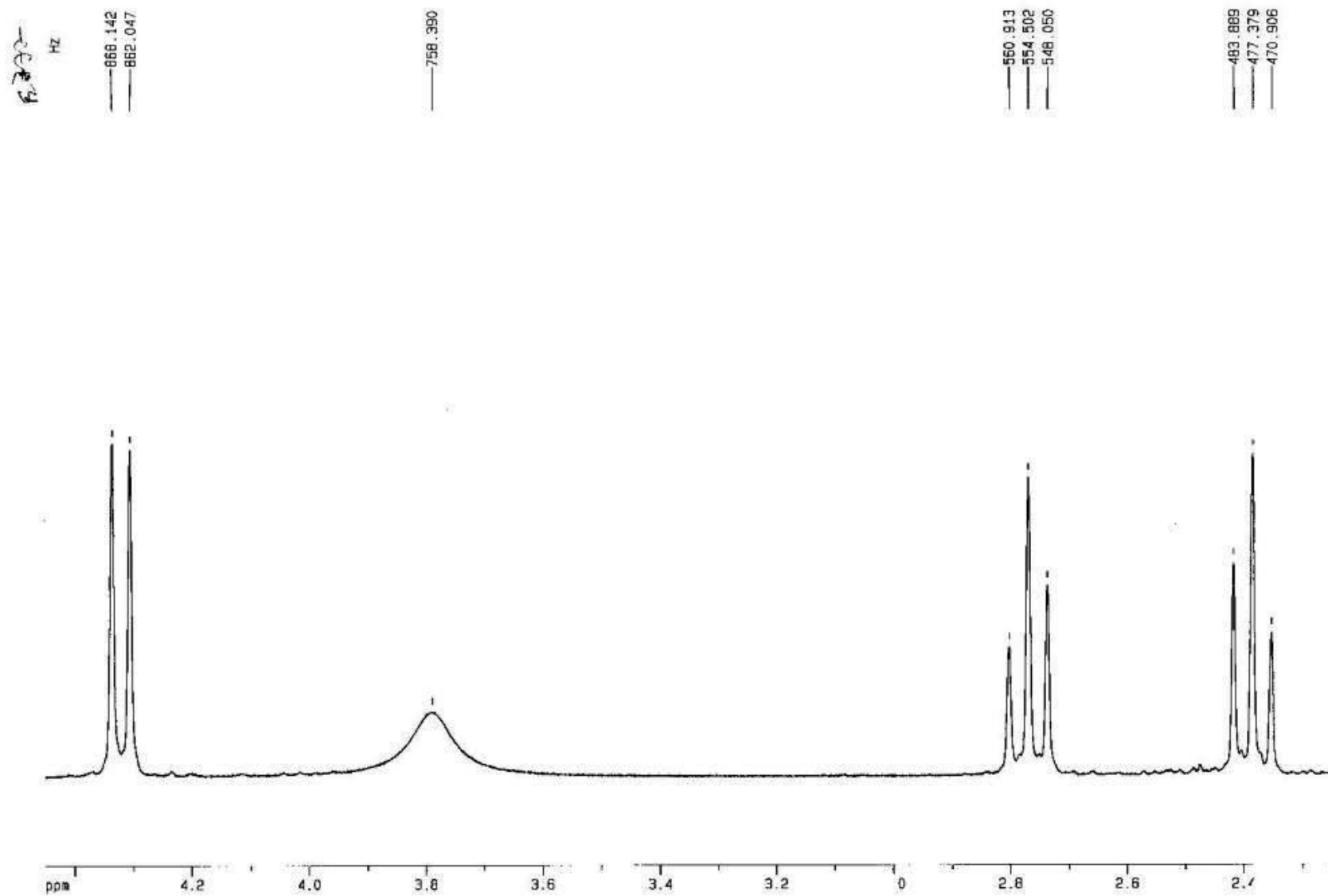


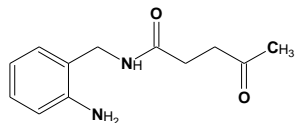
N-(2-aminobenzyl)-4-oxopentanamide (**12d**) ^1H NMR (200 MHz, CDCl_3)



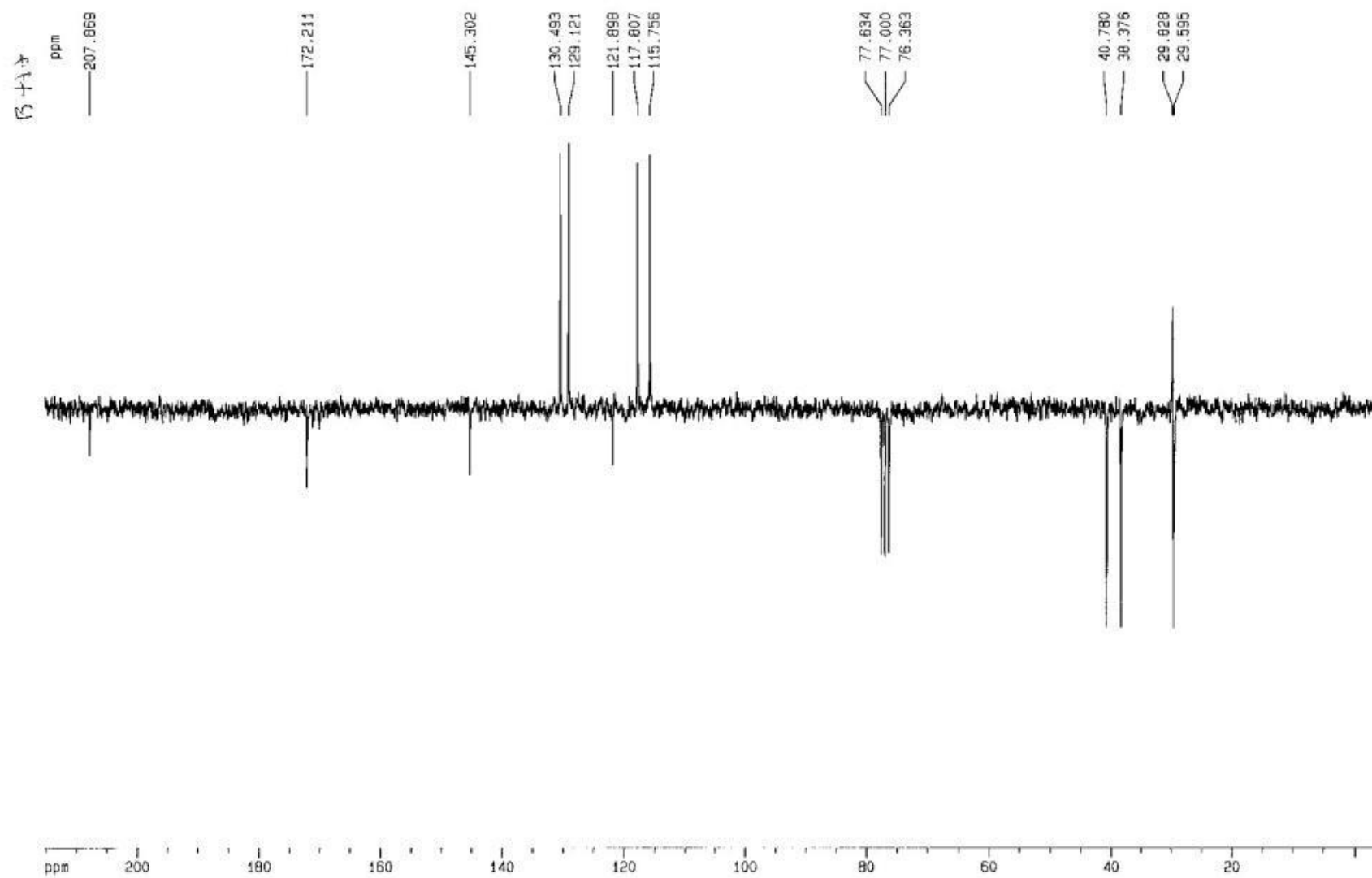


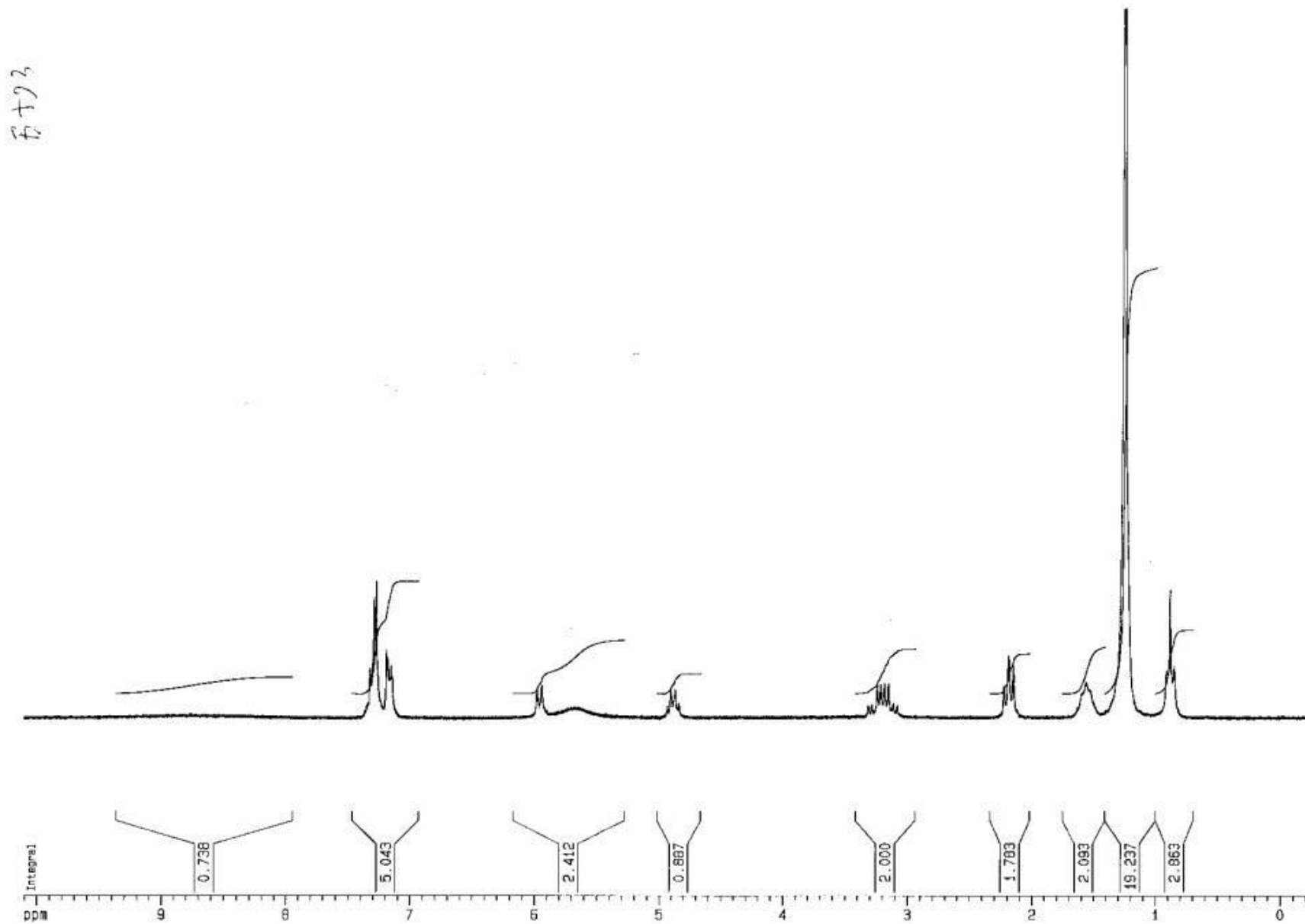
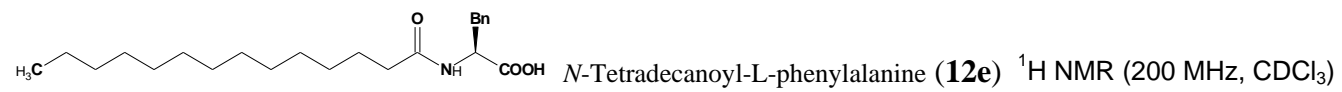
N-(2-aminobenzyl)-4-oxopentanamide (**12d**) ^1H NMR (200 MHz, CDCl_3)

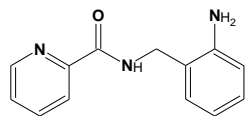




N-(2-aminobenzyl)-4-oxopentanamide (**12d**) ^{13}C NMR (50 MHz, CDCl_3)

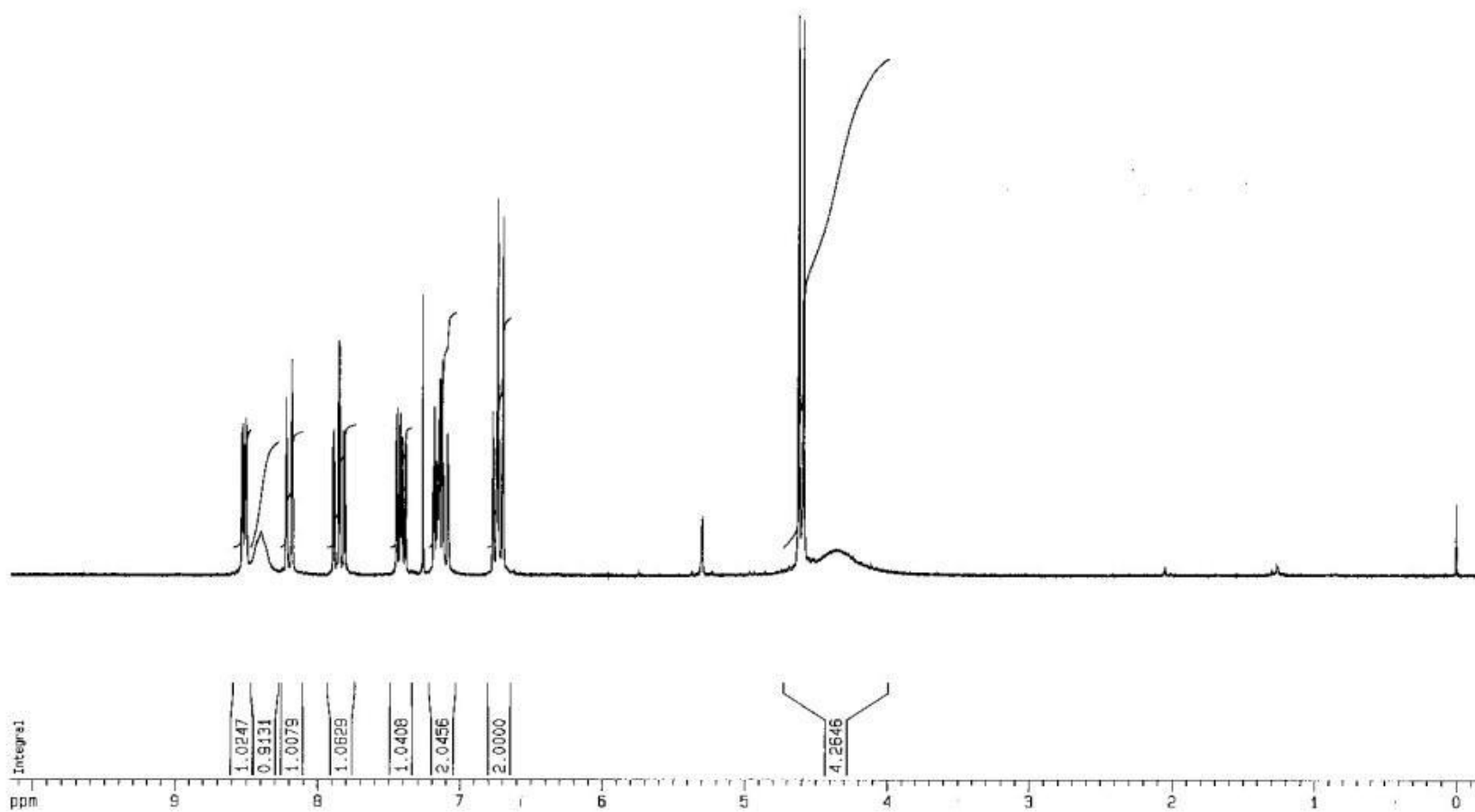


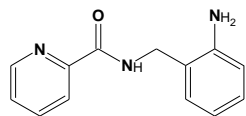




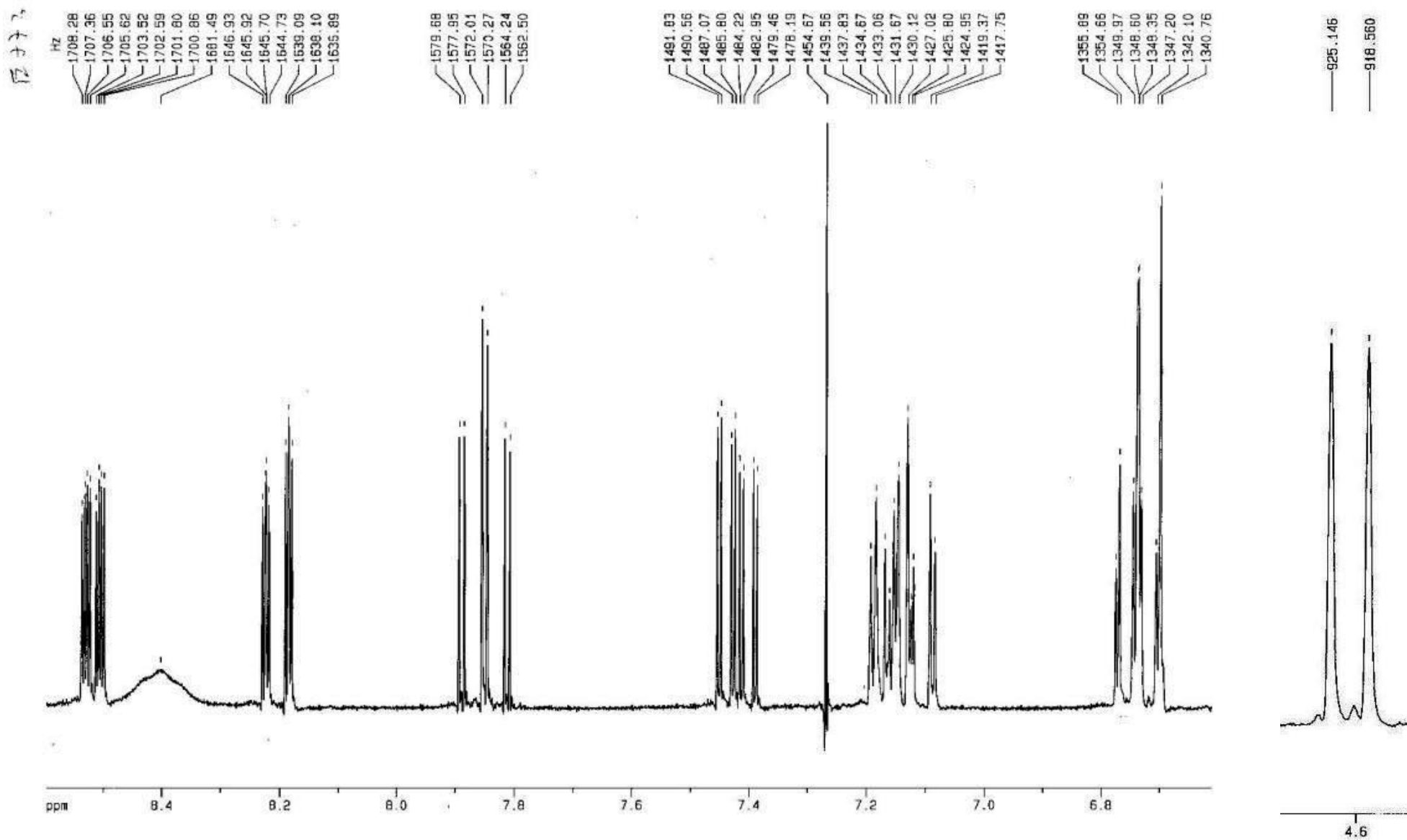
N-(2-Aminobenzyl)pyridine-2-carboxamide (**12f**) ^1H NMR (200 MHz, CDCl_3)

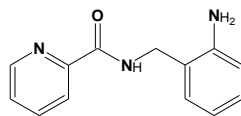
SI-116



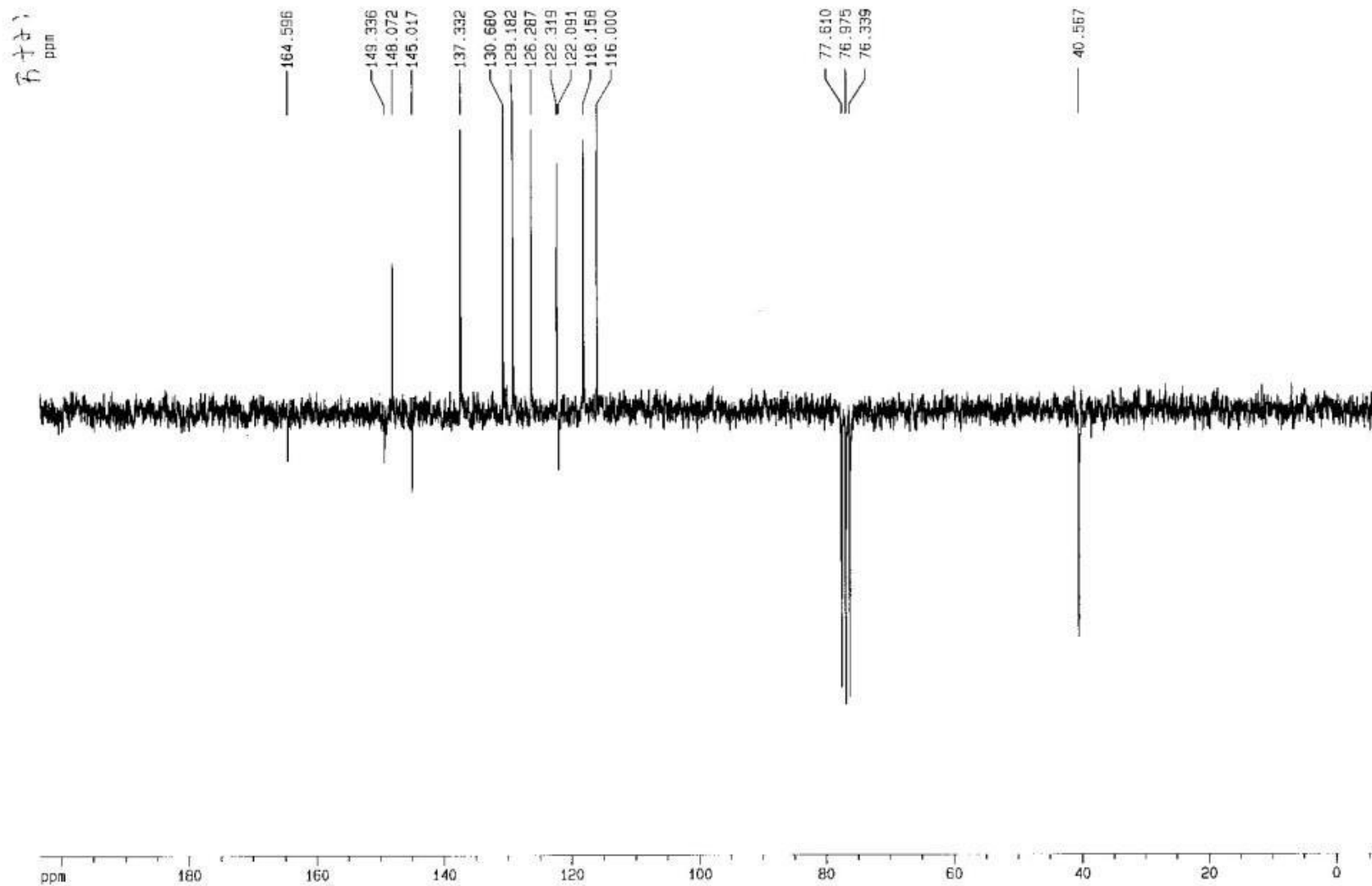


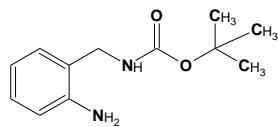
N-(2-Aminobenzyl)pyridine-2-carboxamide (**12f**) ^1H NMR (200 MHz, CDCl_3)





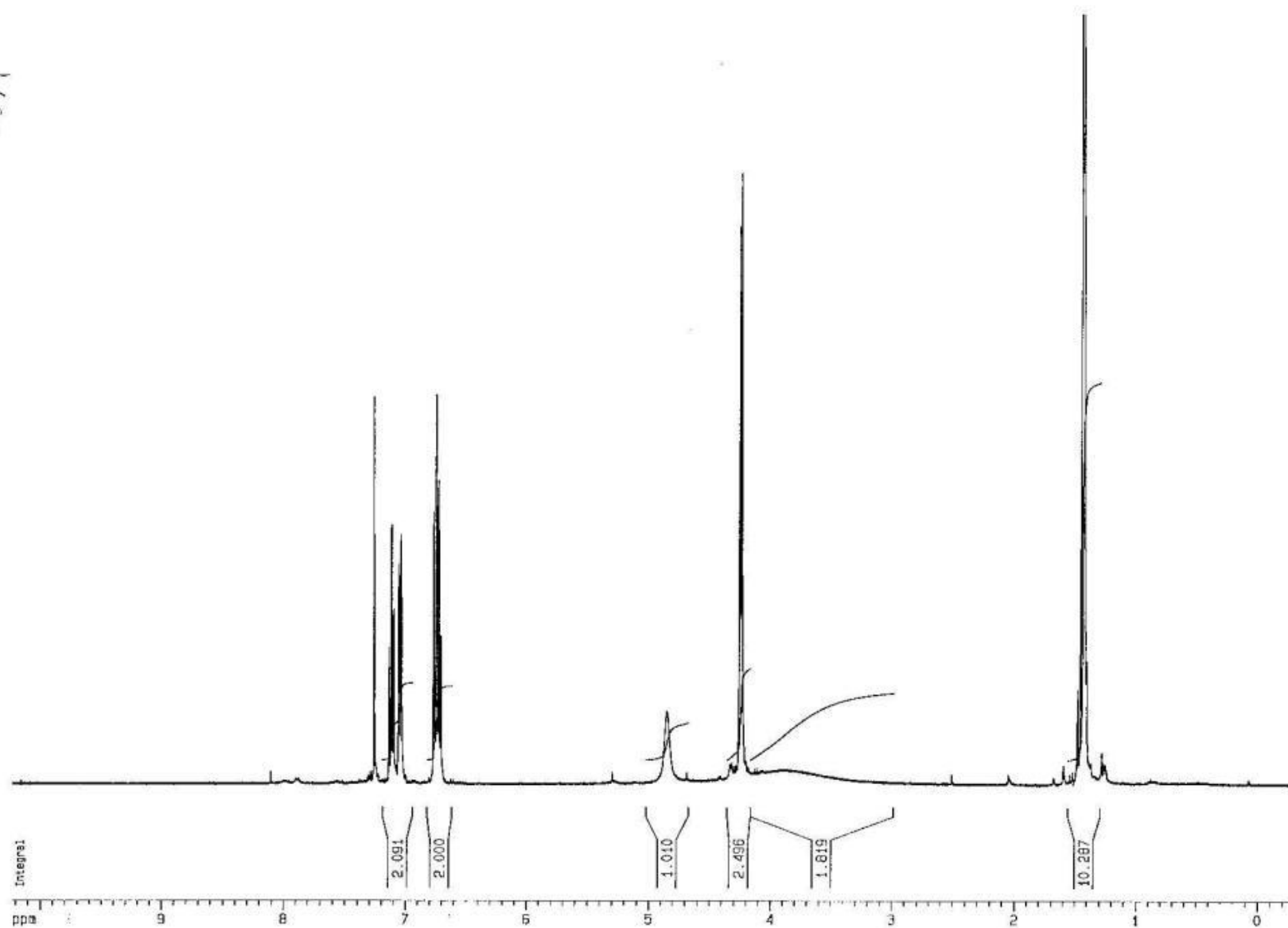
N-(2-Aminobenzyl)pyridine-2-carboxamide (**12f**) ^{13}C NMR (50 MHz, CDCl_3)

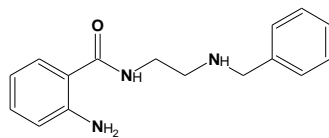




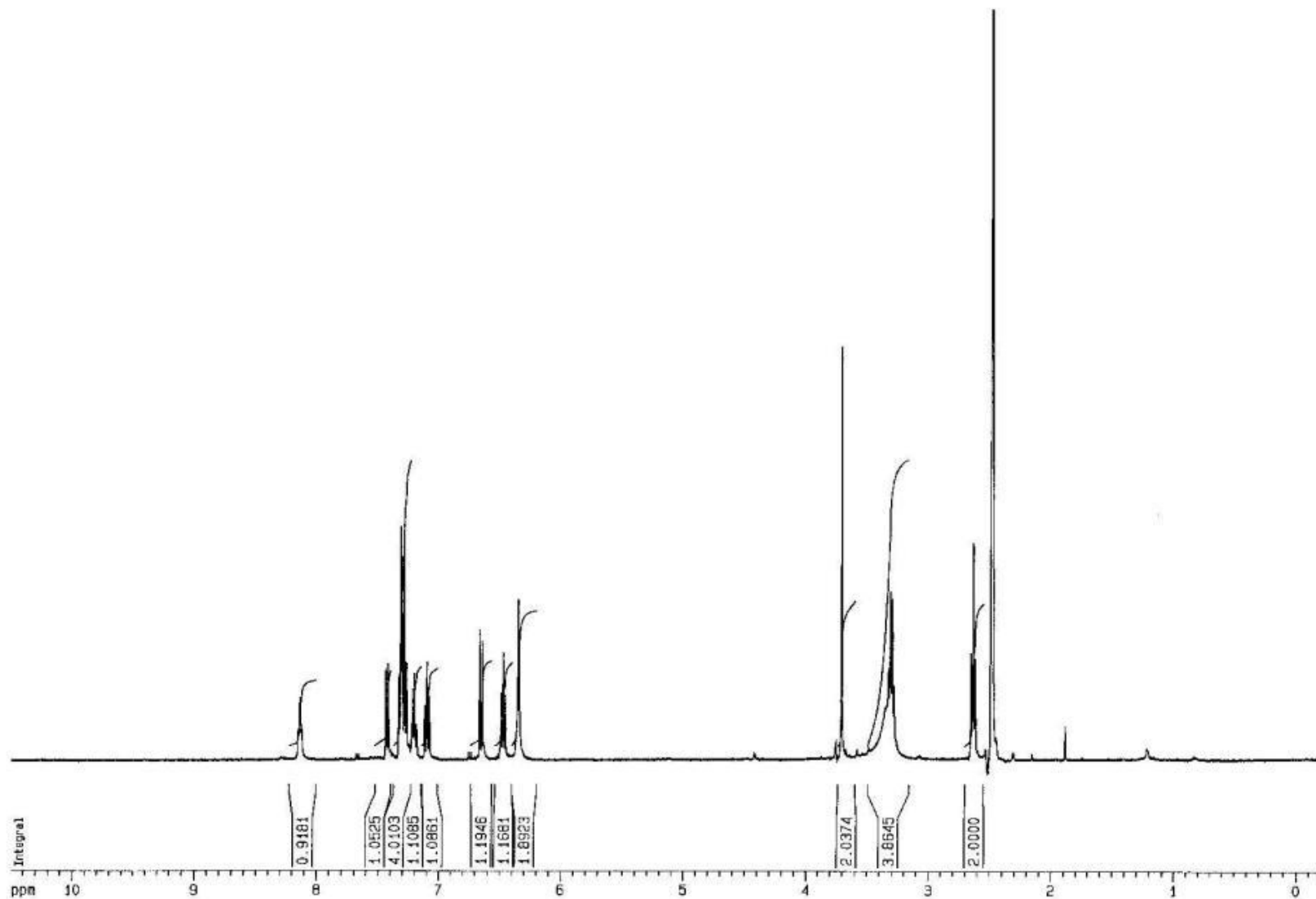
tert-Butyl (2-aminobenzyl)carbamate (**12g**) ^1H NMR (200 MHz, CDCl_3)

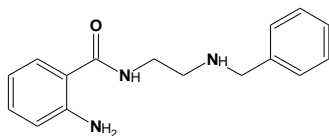
7854





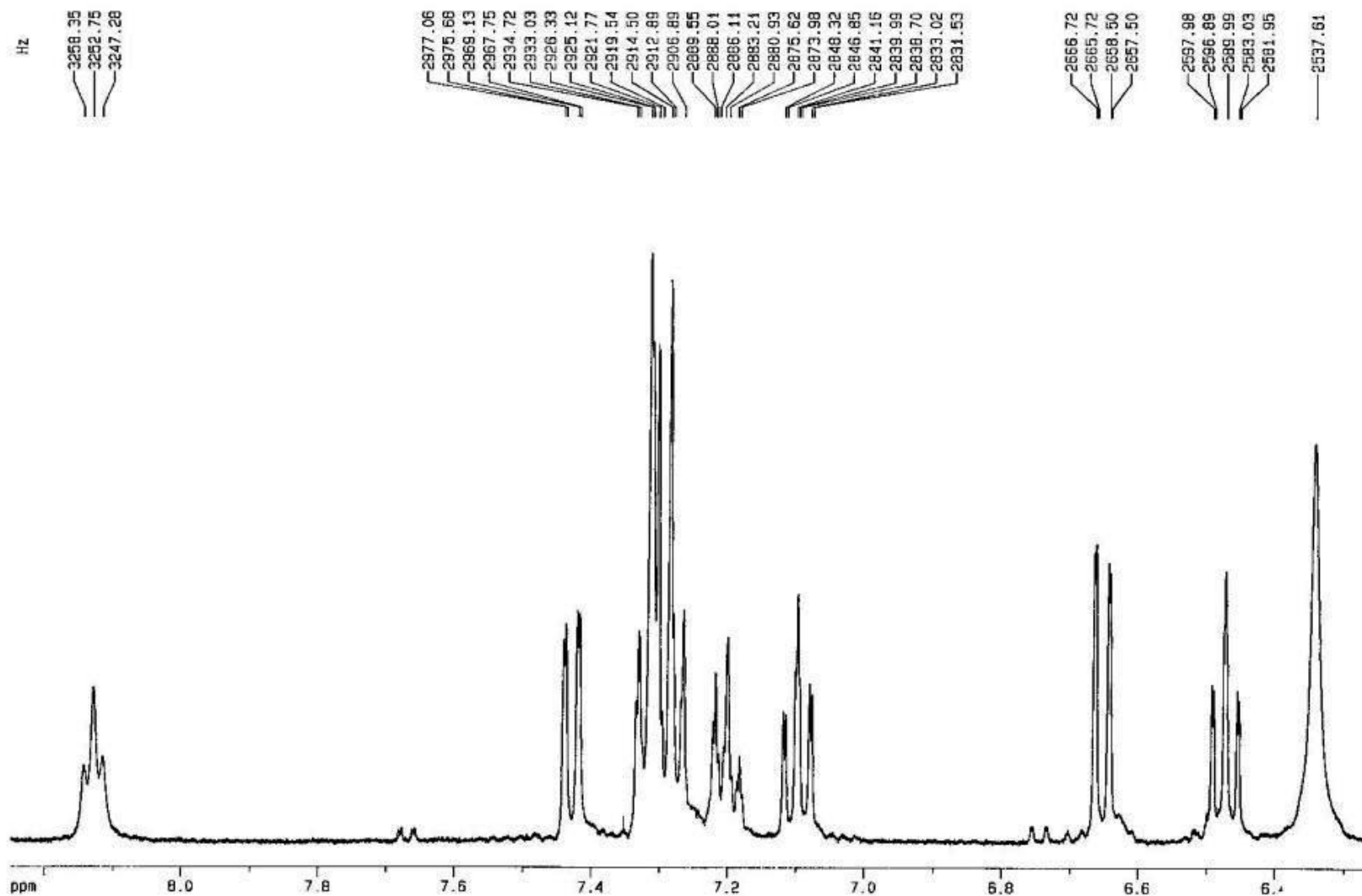
2-Amino-*N*-[2-(benzylamino)ethyl]benzamide (**12h**) ^1H NMR (400 MHz, DMSO-d_6)

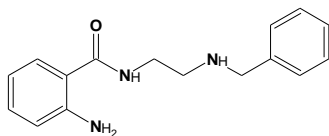




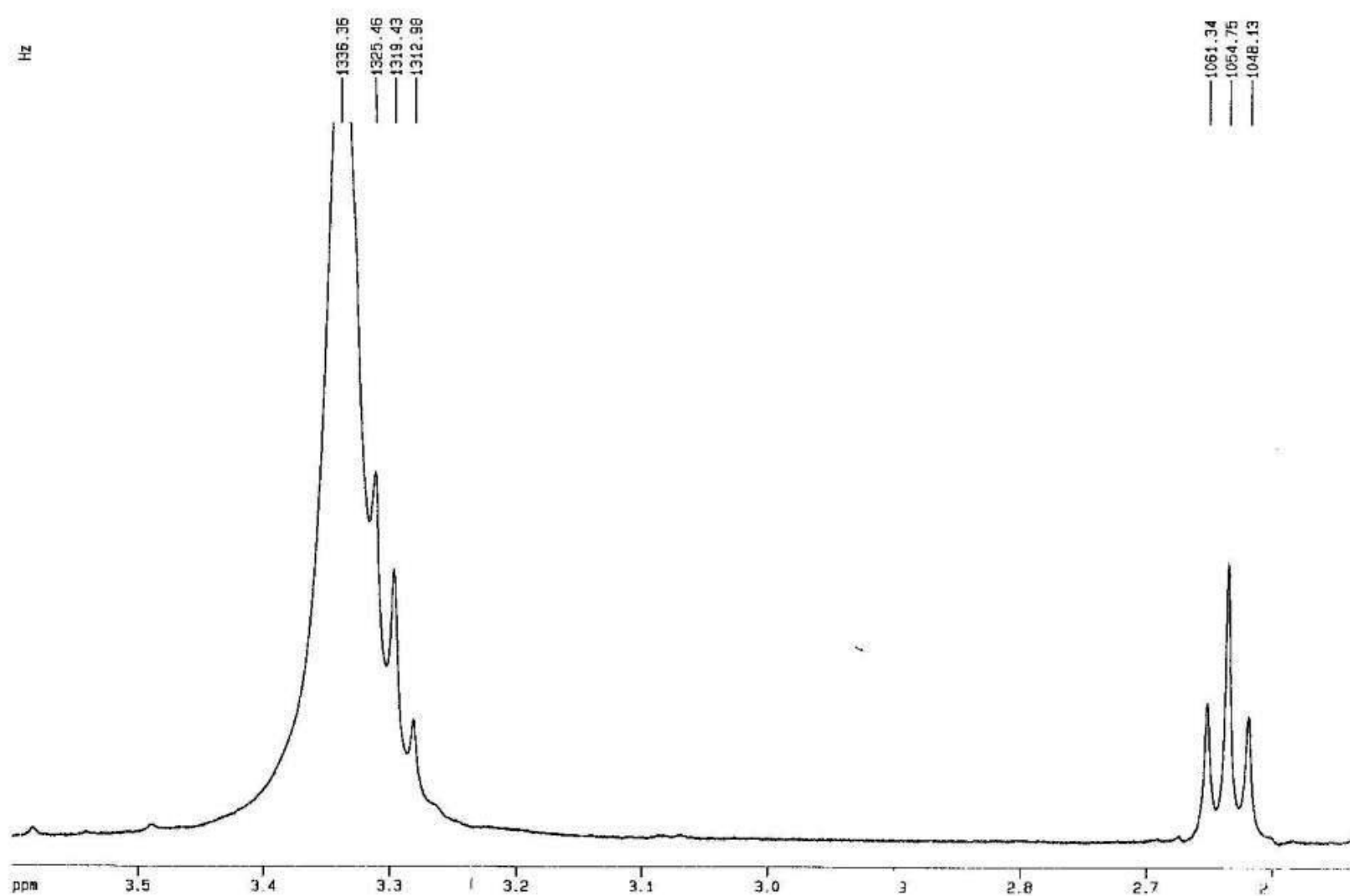
2-Amino-N-[2-(benzylamino)ethyl]benzamide (**12h**) ^1H NMR (400 MHz, DMSO-d_6)

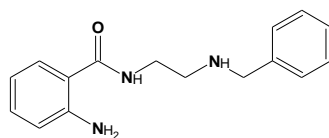
5429



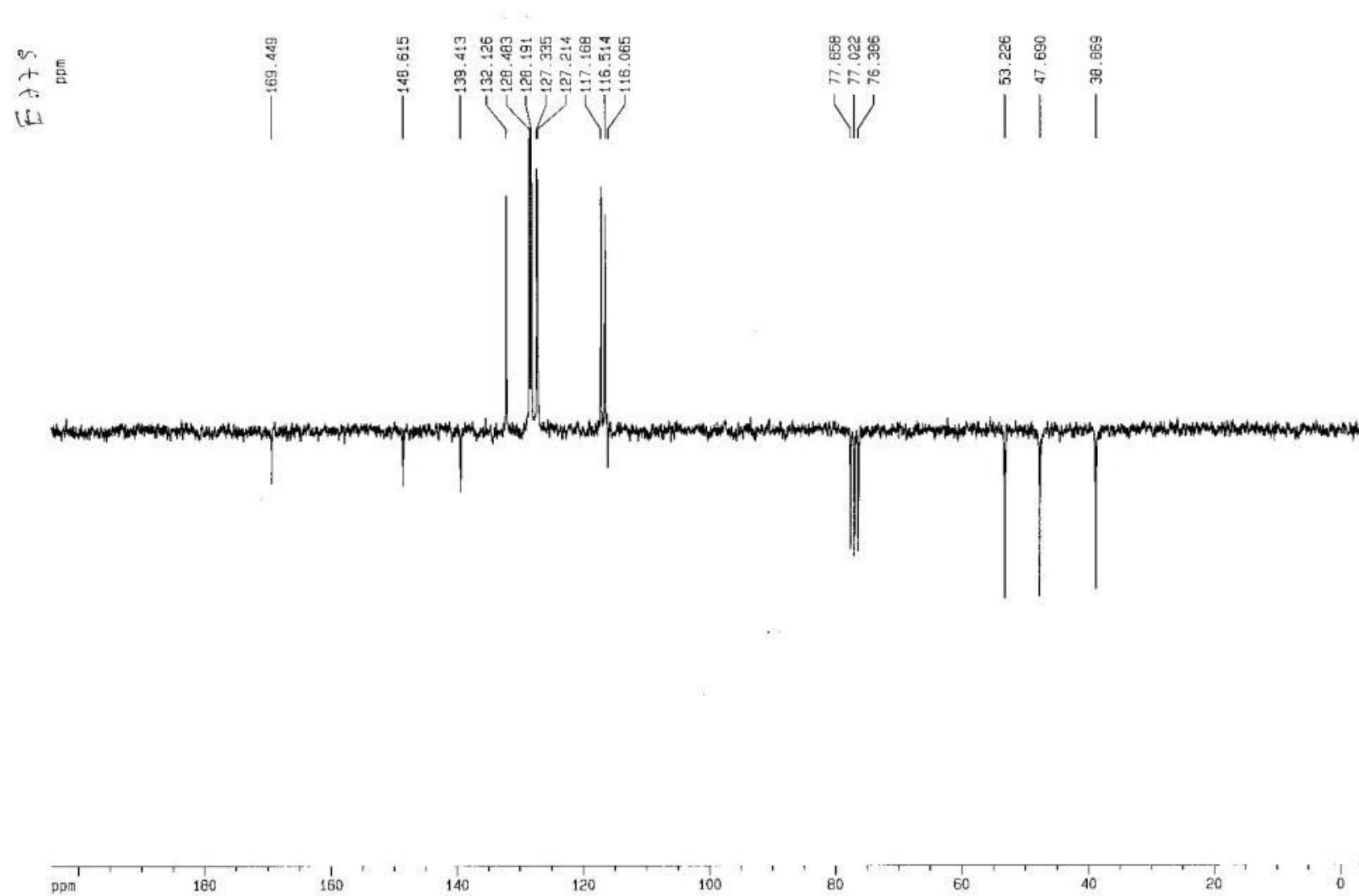


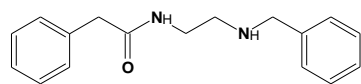
2-Amino-*N*-[2-(benzylamino)ethyl]benzamide (**12h**) ^1H NMR (400 MHz, DMSO-d_6)



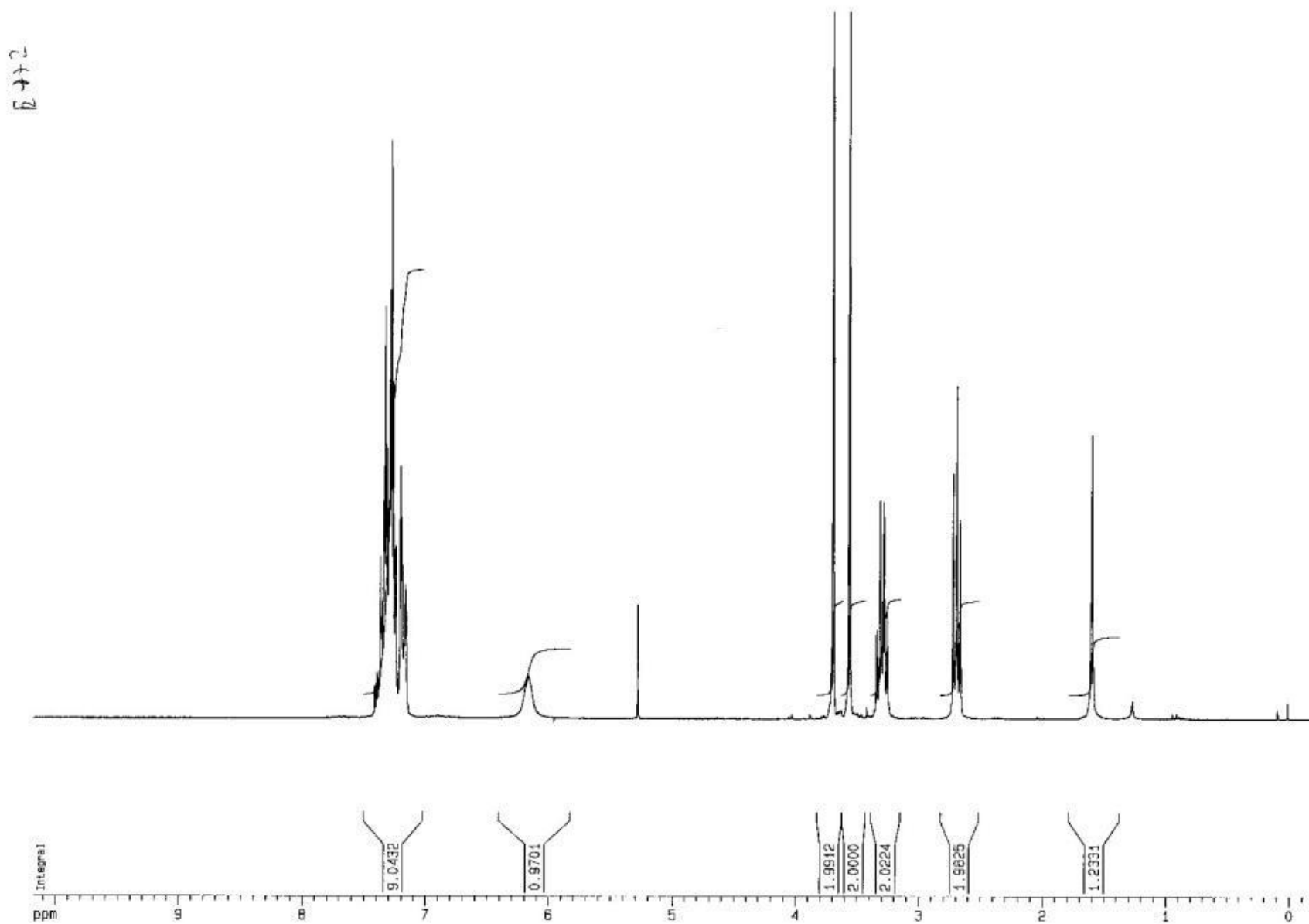


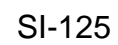
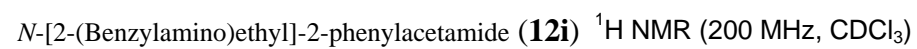
2-Amino-N-[2-(benzylamino)ethyl]benzamide (**12h**) ^{13}C NMR (50 MHz, CDCl_3)

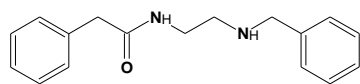




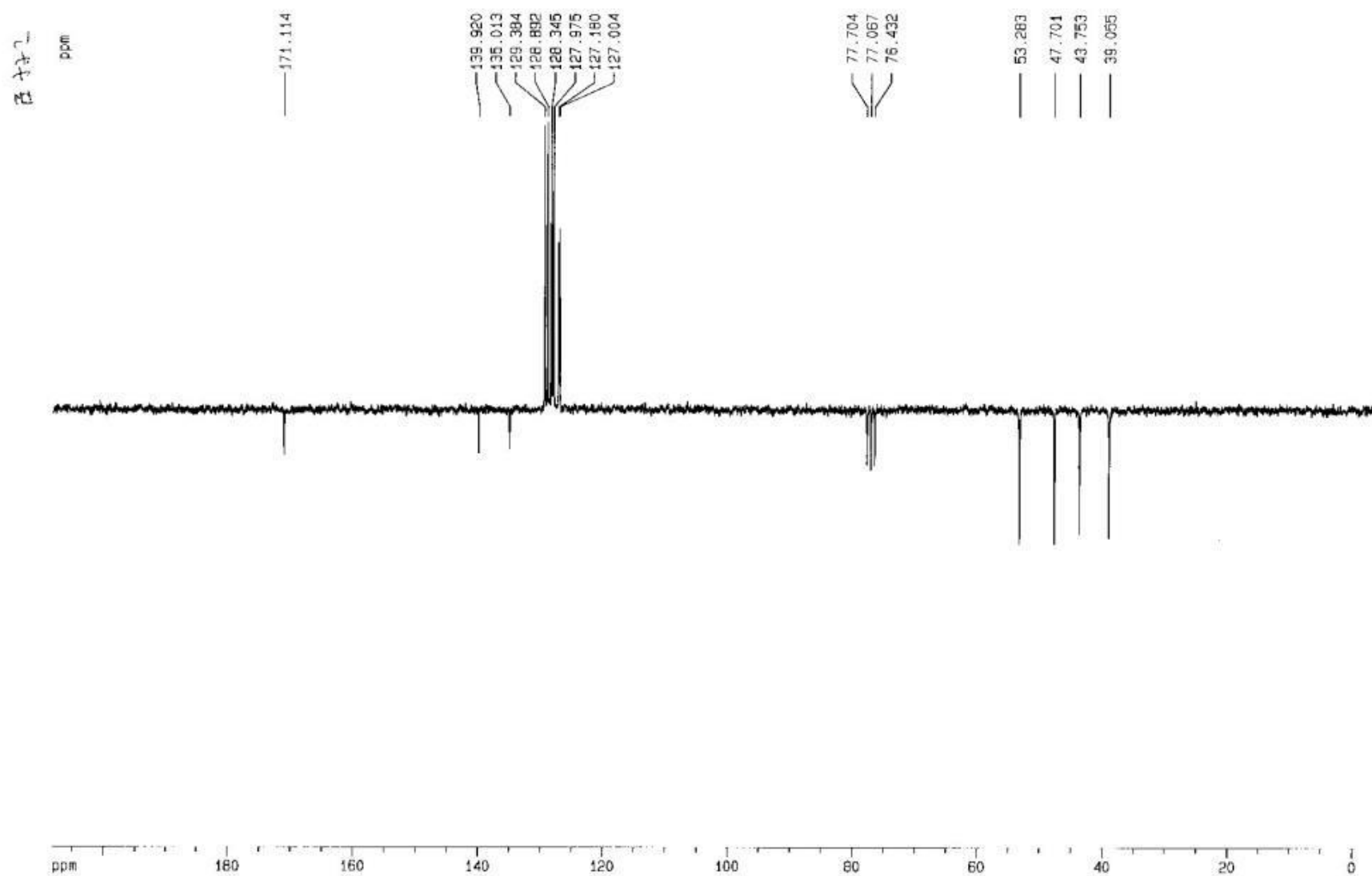
N-[2-(Benzylamino)ethyl]-2-phenylacetamide (**12i**) ^1H NMR (200 MHz, CDCl_3)

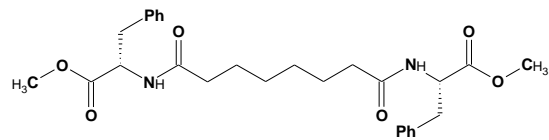




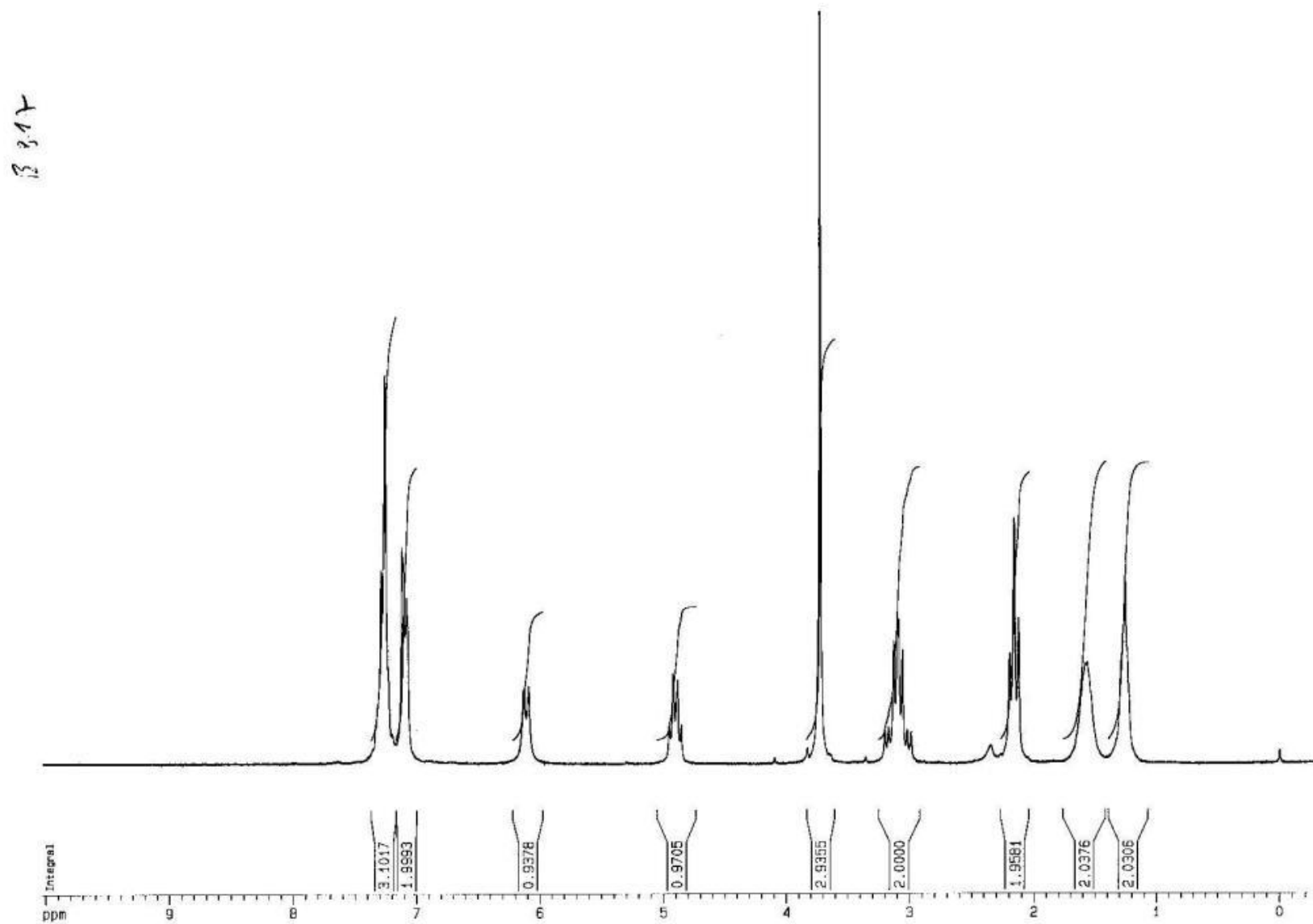


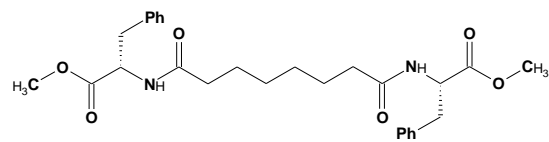
N-[2-(Benzylamino)ethyl]-2-phenylacetamide (**12i**) ^{13}C NMR (50 MHz, CDCl_3)



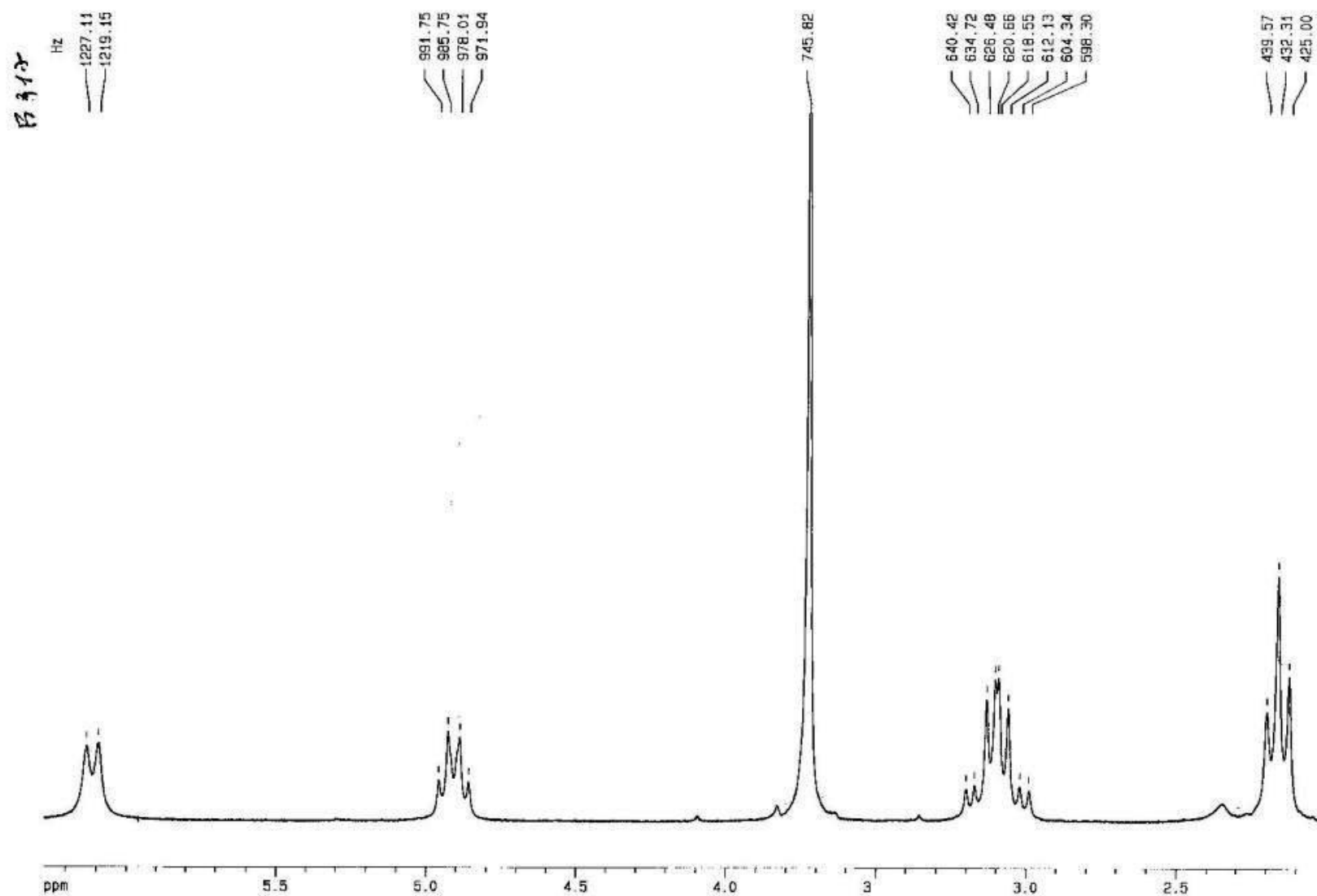


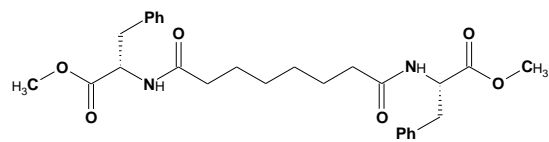
(*S*)-2-[7-((*S*)-1-Methoxycarbonyl-2-phenyl-ethylcarbamoyl)-heptanoylamino]-3-phenyl-propionic acid methyl ester (**12j**) ^1H NMR (200 MHz, CDCl_3)



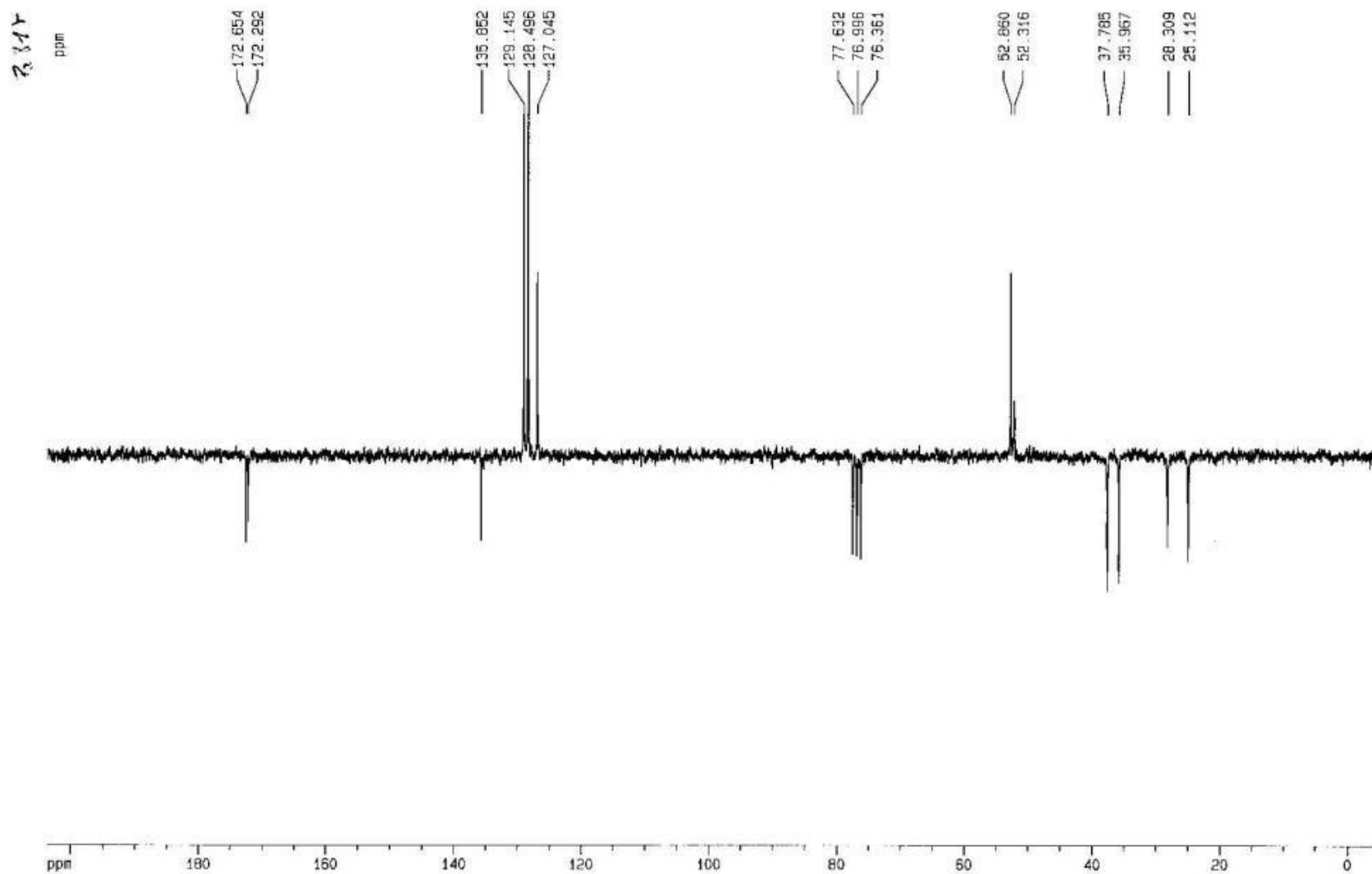


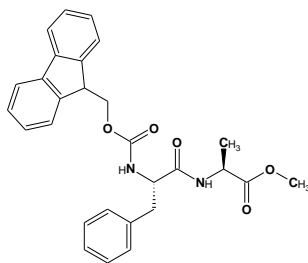
(S)-2-[7-((S)-1-Methoxycarbonyl-2-phenyl-ethylcarbamoyl)-heptanoylamino]-3-phenyl-propionic acid methyl ester (**12j**) ^1H NMR (200 MHz,



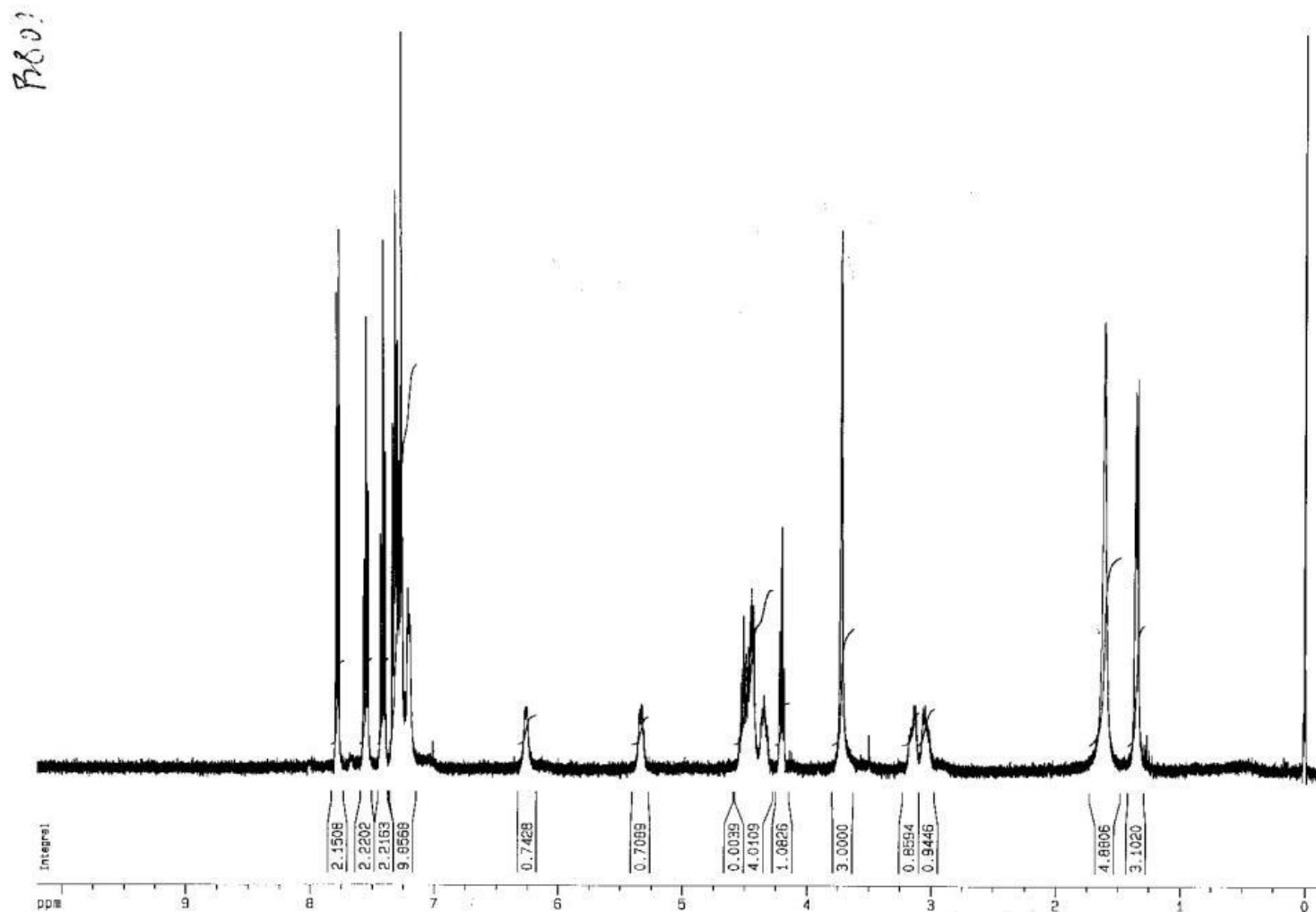


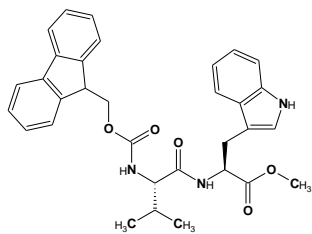
(S)-2-[7-((S)-1-Methoxycarbonyl-2-phenyl-ethylcarbamoyl)-heptanoylamino]-3-phenyl-propionic acid methyl ester (**12j**) ^{13}C NMR (50 MHz, CDCl_3)



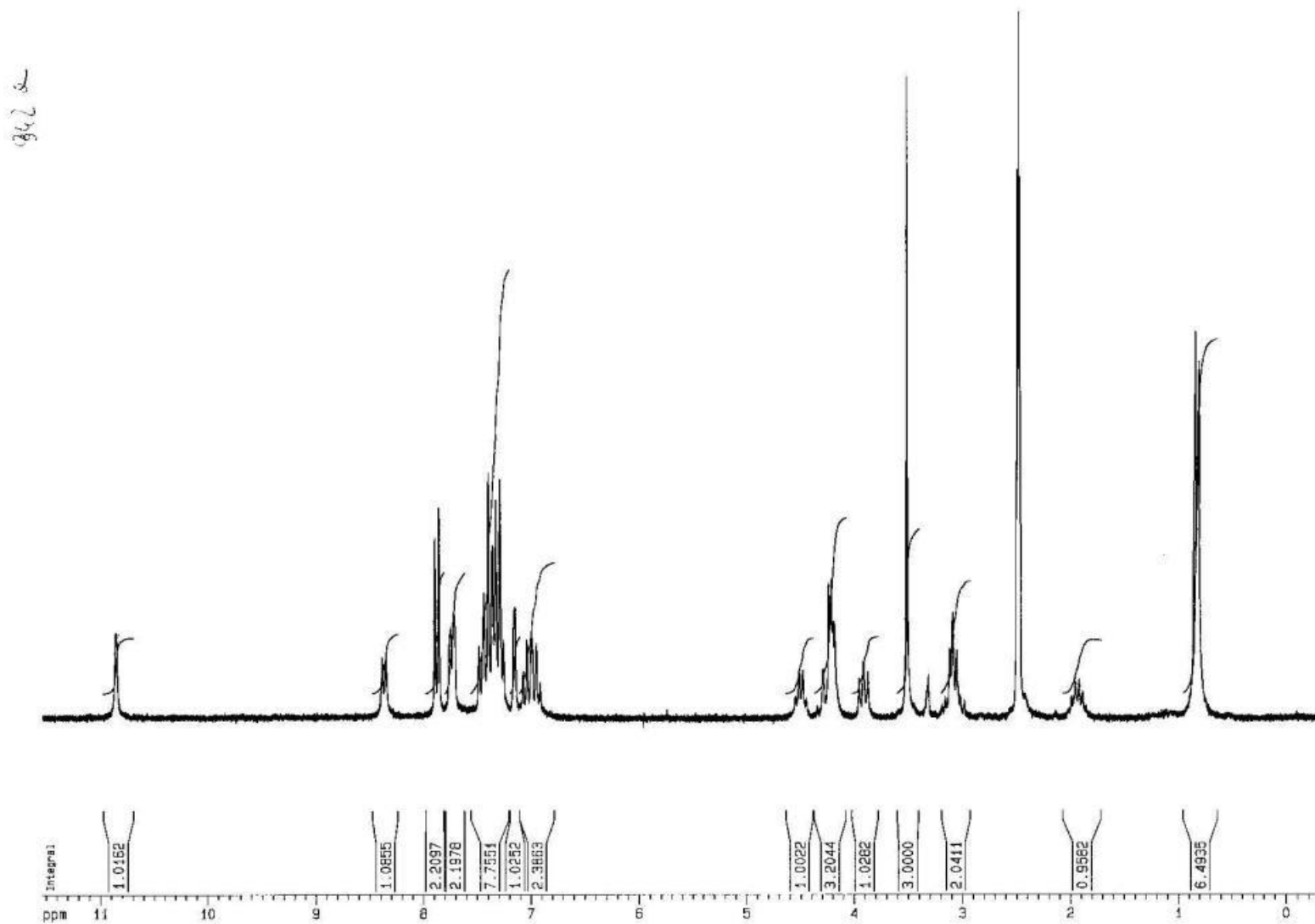


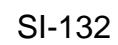
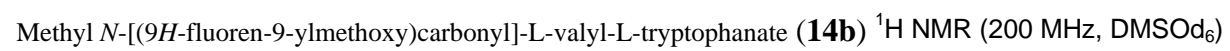
N-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-*L*-phenylalanyl-*L*-alaninate (**14a**) ^1H NMR (200 MHz, CDCl_3)

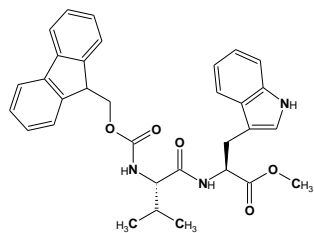




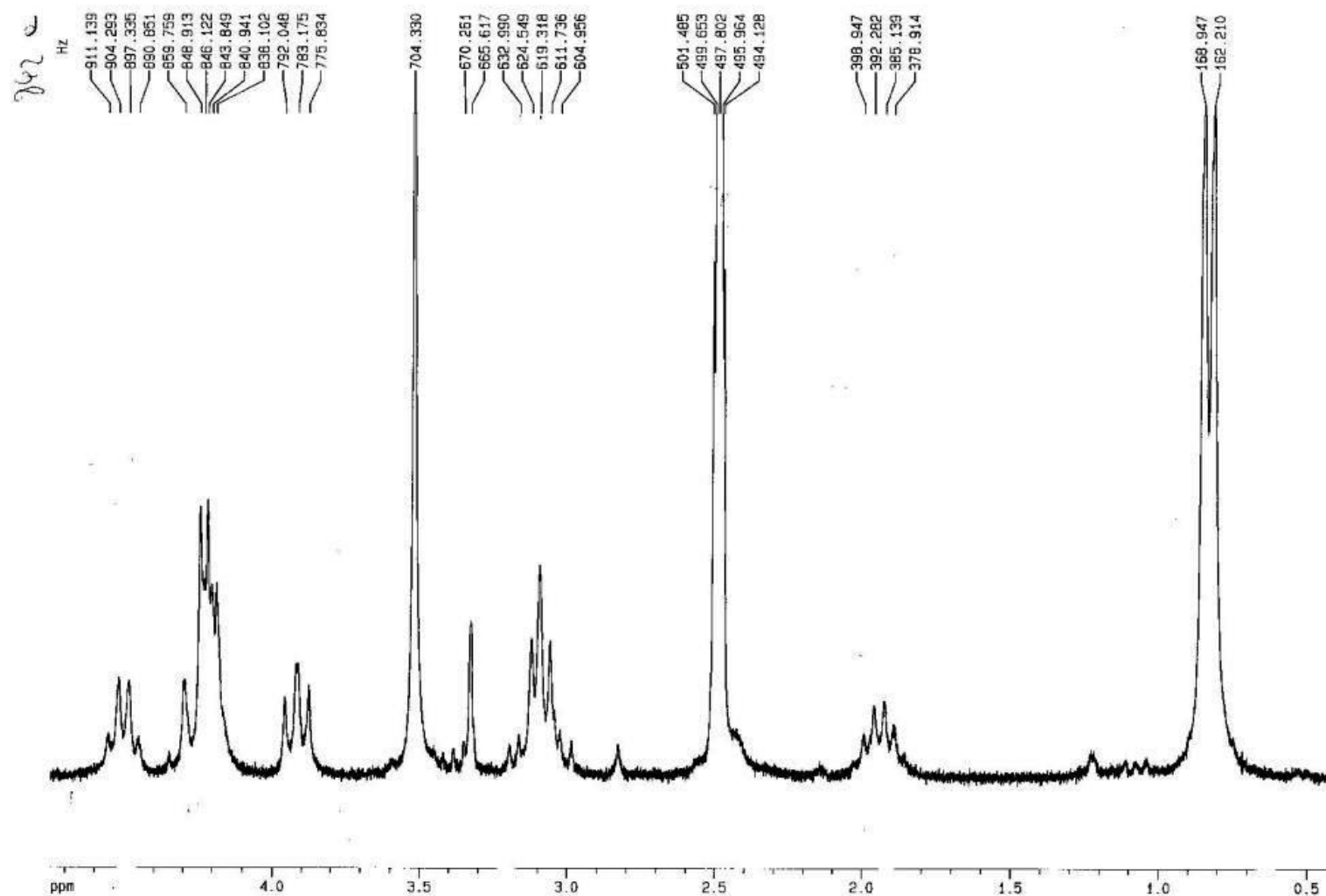
Methyl *N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-*L*-valyl-*L*-tryptophanate (**14b**) ^1H NMR (200 MHz, DMSO-d_6)

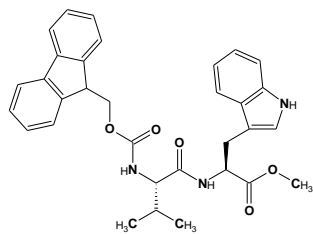




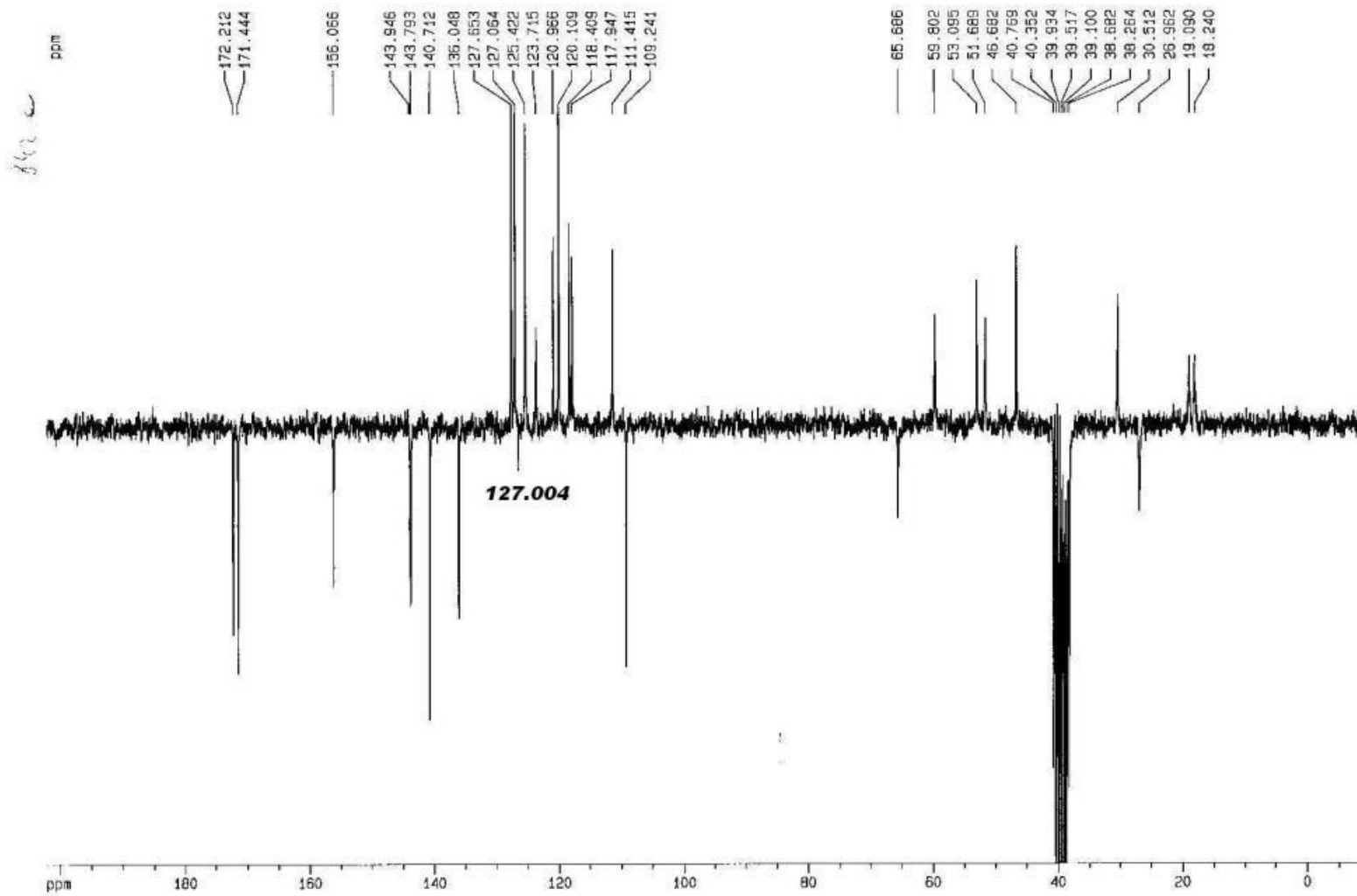


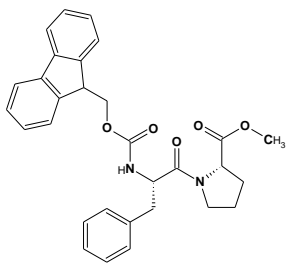
Methyl *N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-L-valyl-L-tryptophanate (**14b**) ^1H NMR (200 MHz, DMSO-d_6)





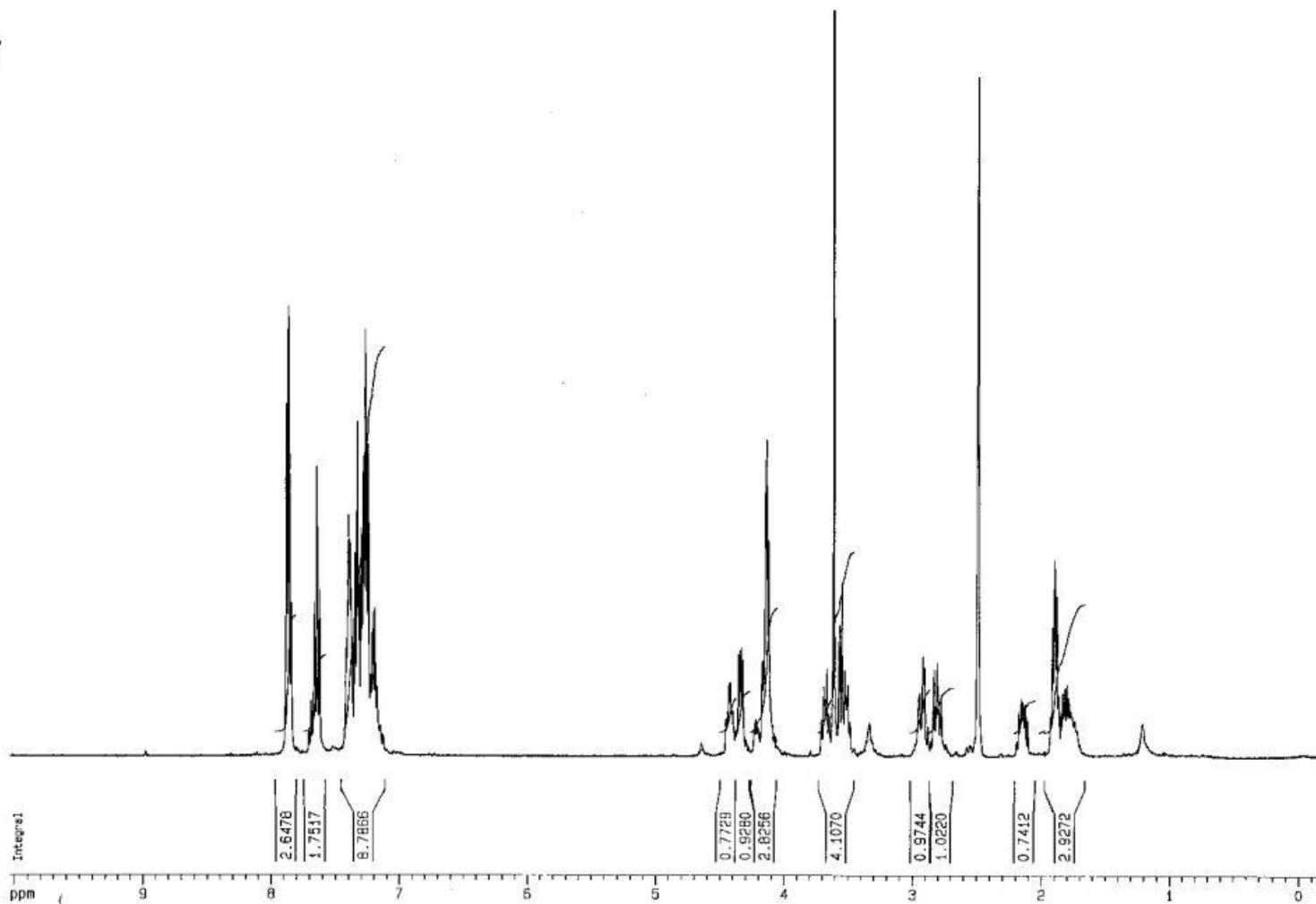
Methyl *N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-*L*-valyl-*L*-tryptophanate (**14b**) ^{13}C NMR (50 MHz, DMSO-d_6)

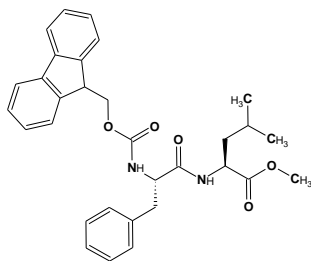




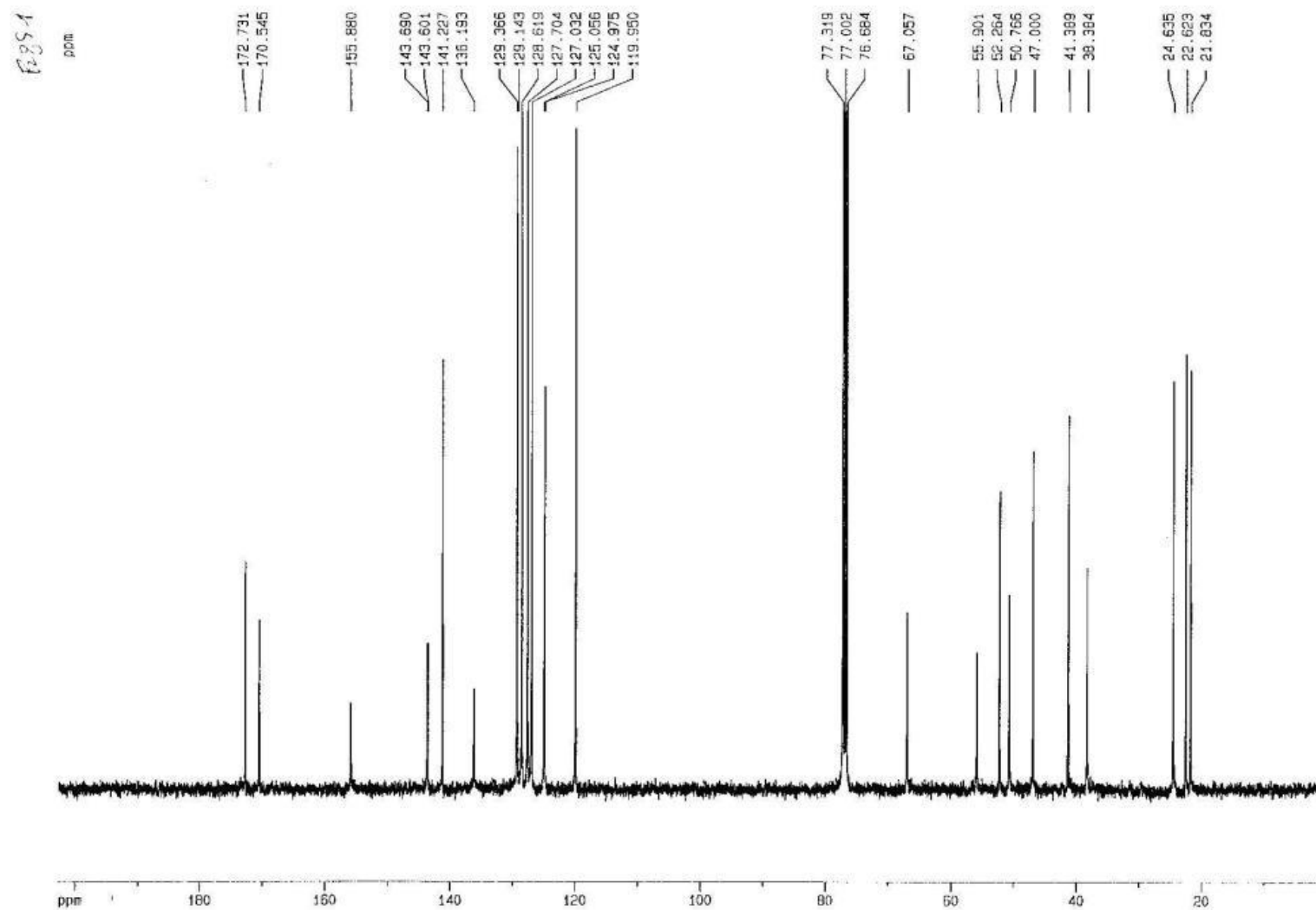
Methyl *N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-*L*-phenylalanyl-*L*-prolinate (**14c**) ^1H NMR (400 MHz, DMSO-d_6)

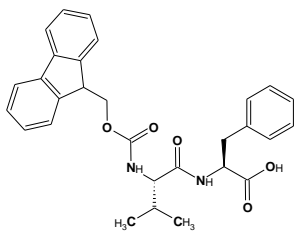
Fig 15



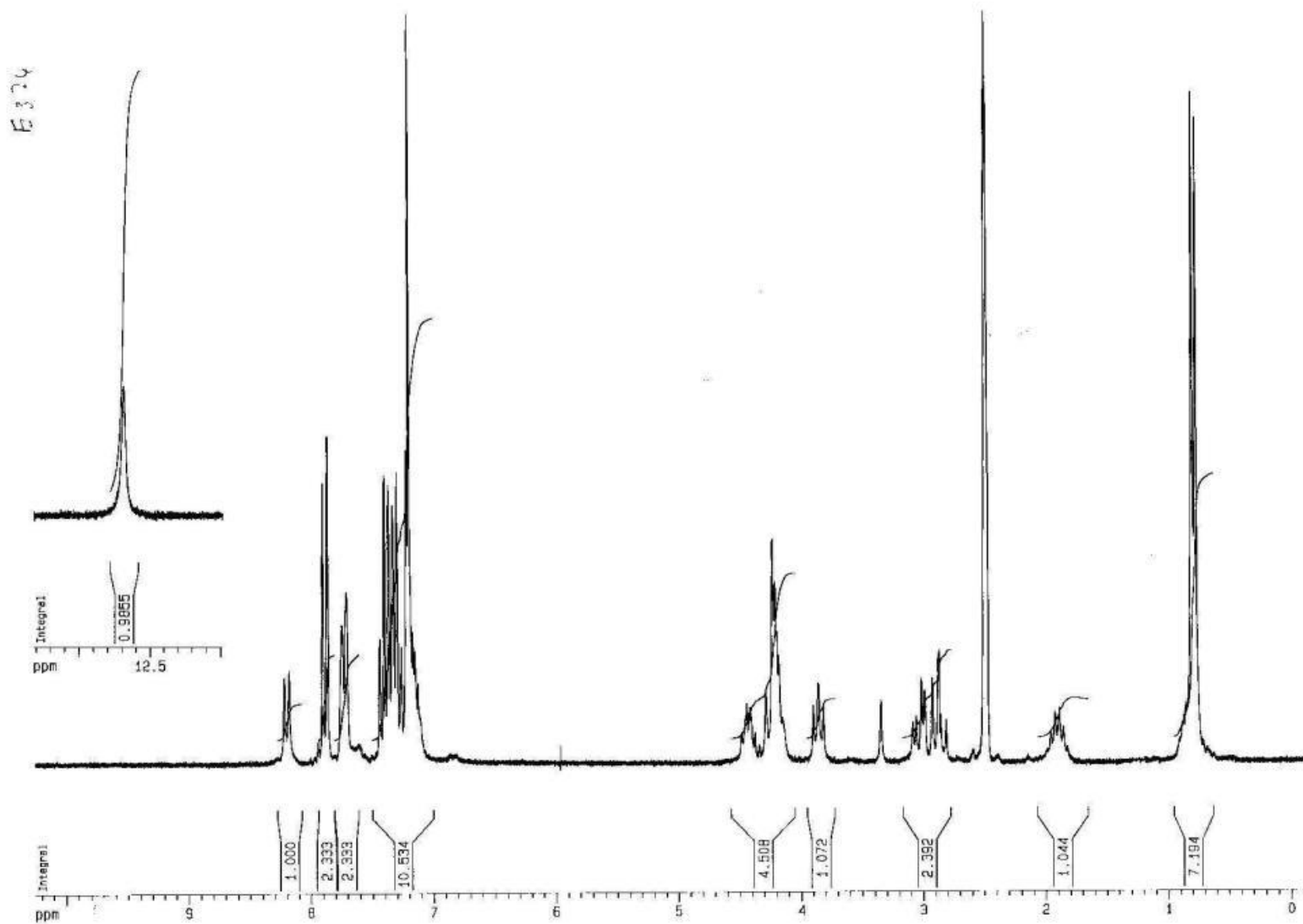


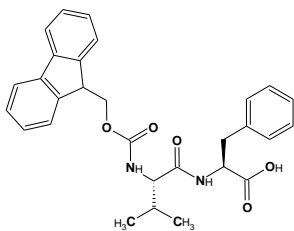
Methyl *N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-*L*-phenylalanyl-*L*-leucinate (**14d**) ^{13}C NMR (50 MHz, CDCl_3)



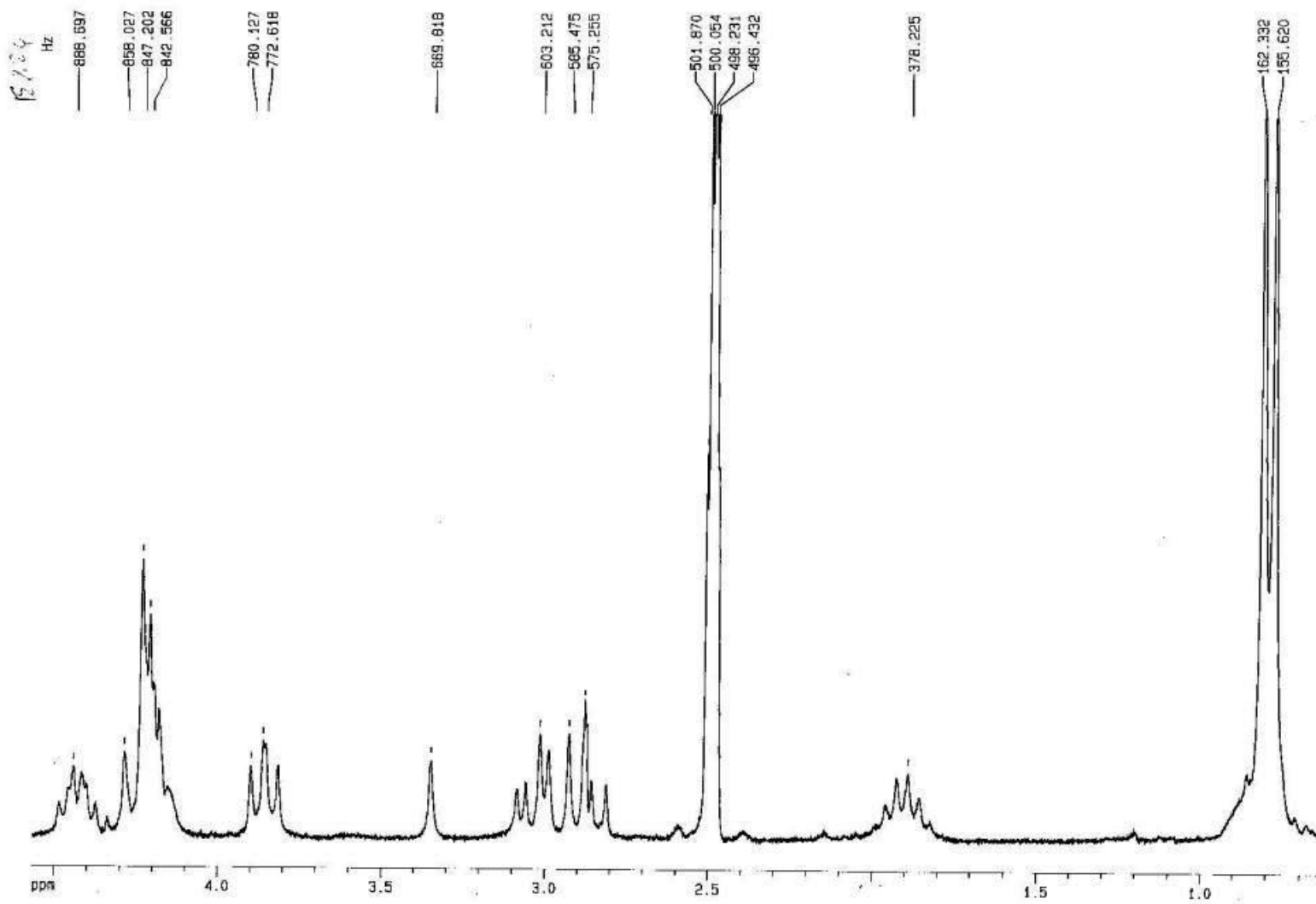


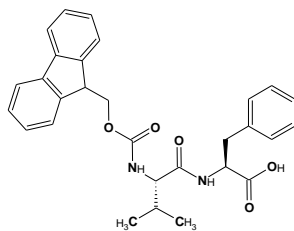
N-[(9*H*-Fluoren-9-ylmethoxy)carbonyl]-L-valyl-L-phenylalanine (**14e**) ^1H NMR (200 MHz, DMSO-d_6)



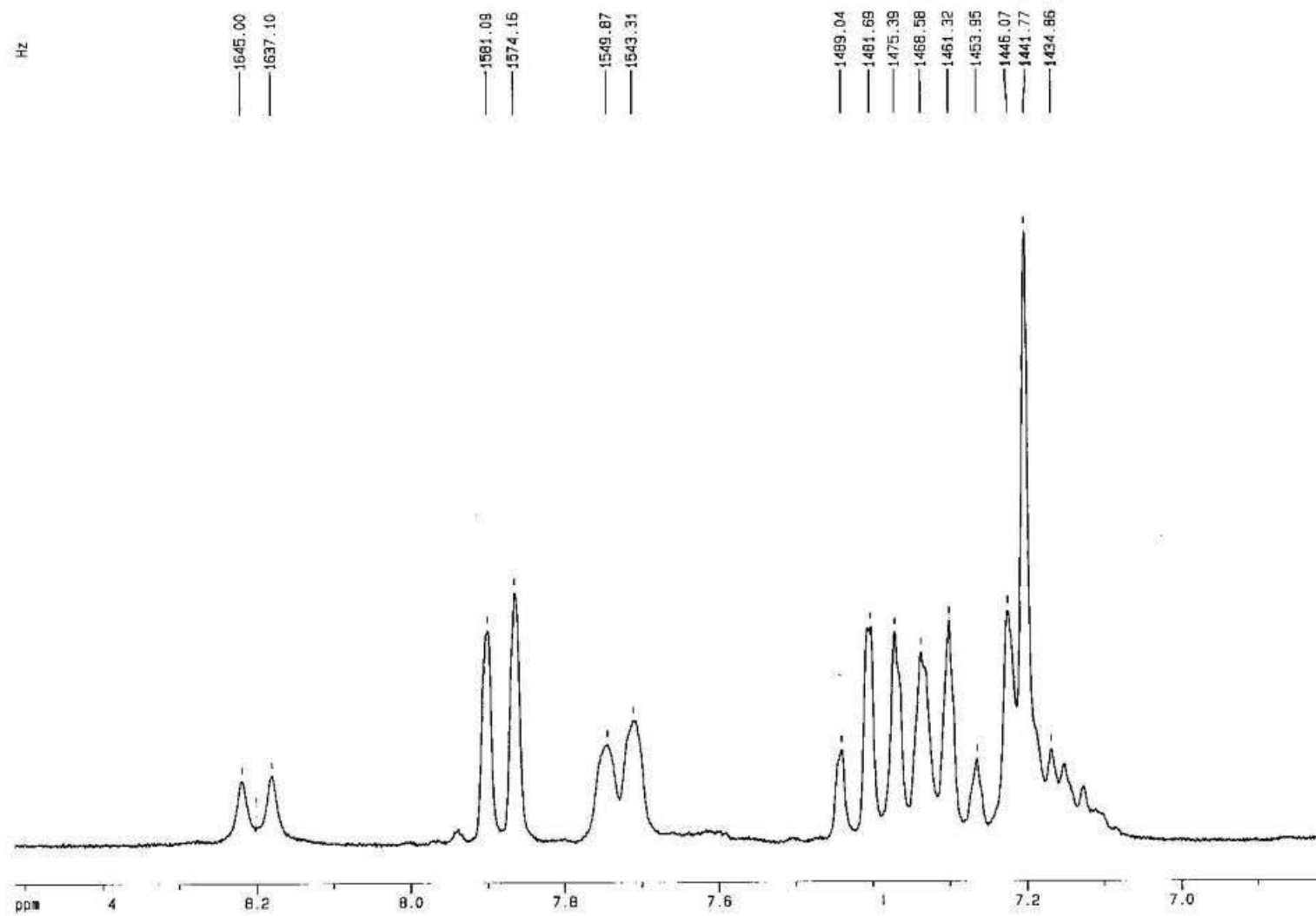


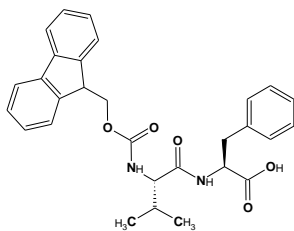
N-[(9*H*-Fluoren-9-ylmethoxy)carbonyl]-L-valyl-L-phenylalanine (**14e**) ^1H NMR (200 MHz, DMSO-d_6)



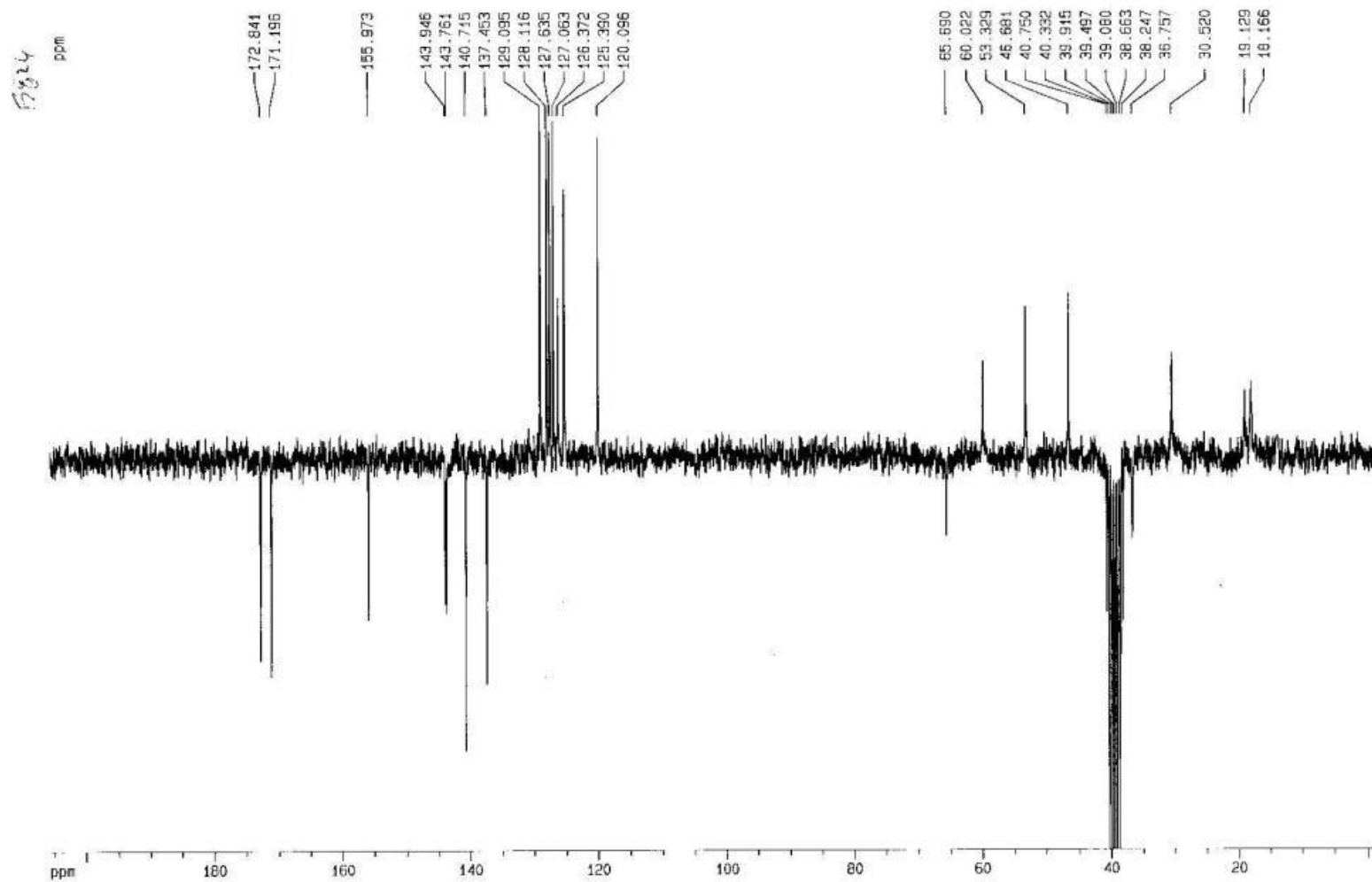


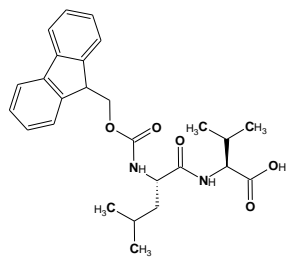
N-[(9*H*-Fluoren-9-ylmethoxy)carbonyl]-L-valyl-L-phenylalanine (**14e**) ^1H NMR (200 MHz, DMSO-d_6)



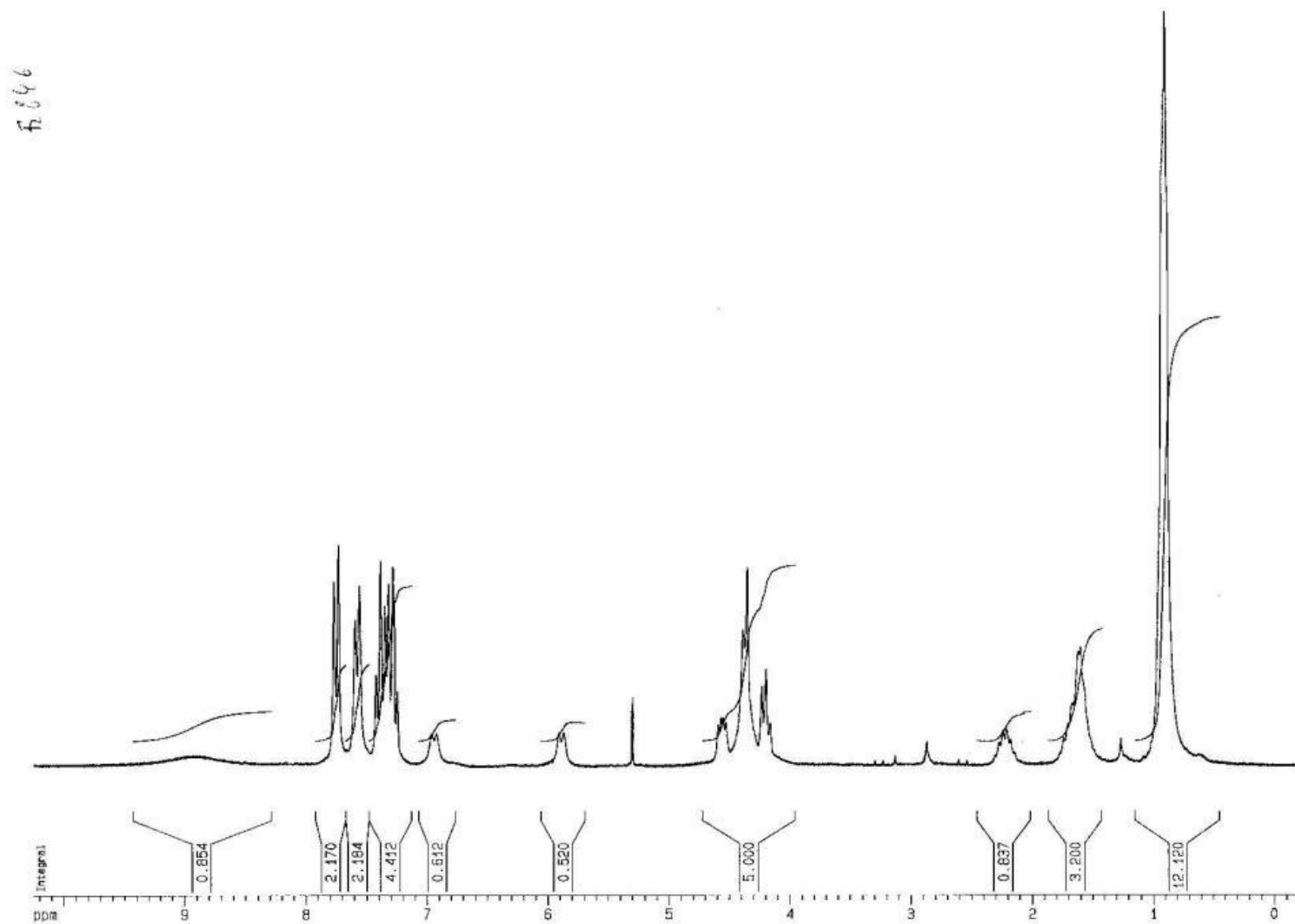


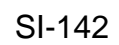
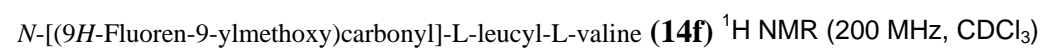
N-[(9*H*-Fluoren-9-ylmethoxy)carbonyl]-L-valyl-L-phenylalanine (**14e**) ^{13}C NMR (50 MHz, DMSO-d_6)

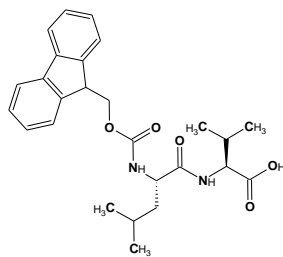




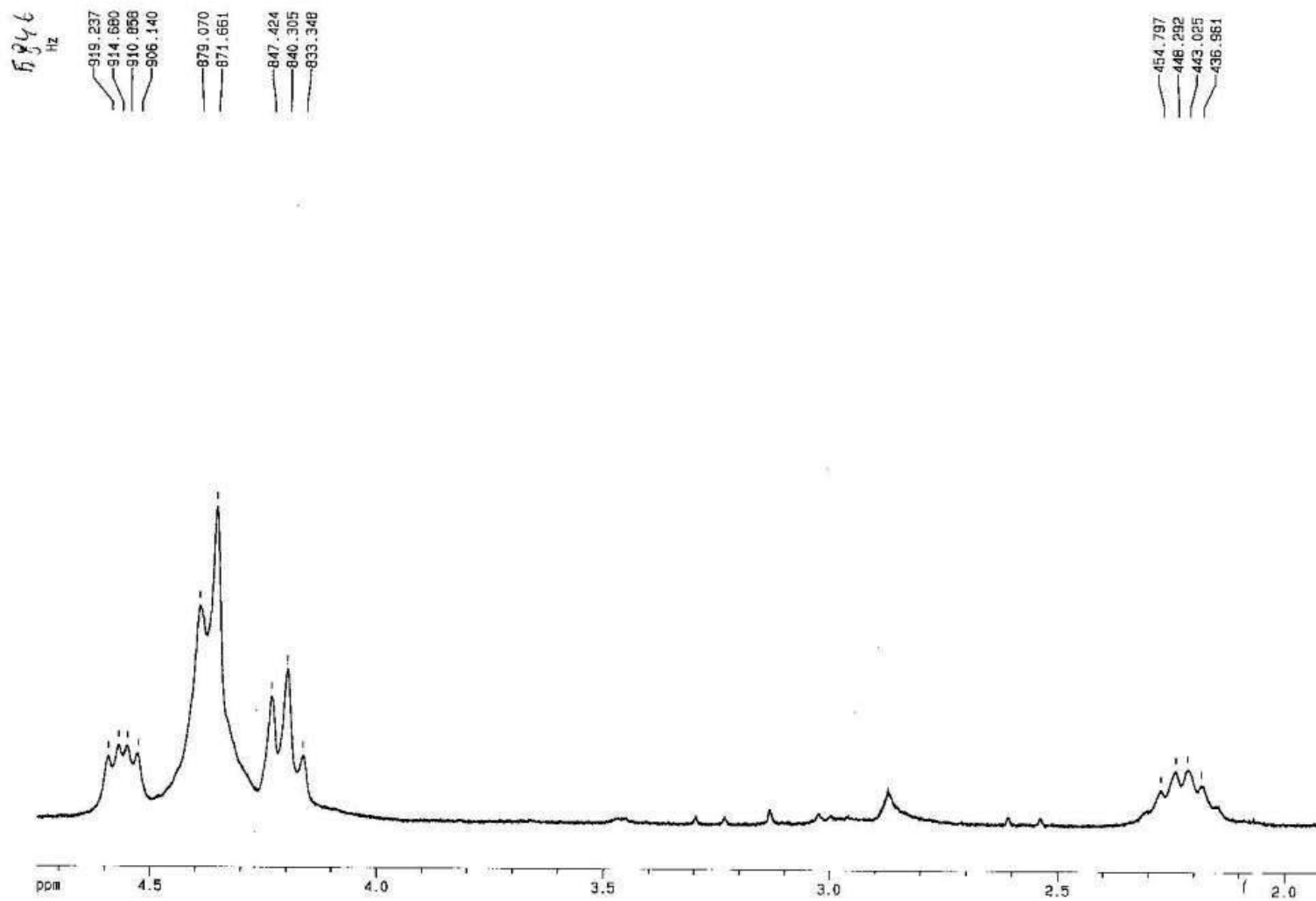
N-[(9*H*-Fluoren-9-ylmethoxy)carbonyl]-L-leucyl-L-valine (**14f**) ^1H NMR (200 MHz, CDCl_3)

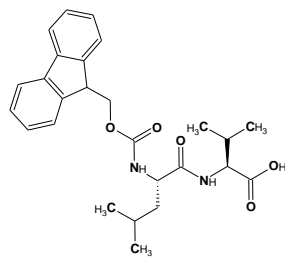




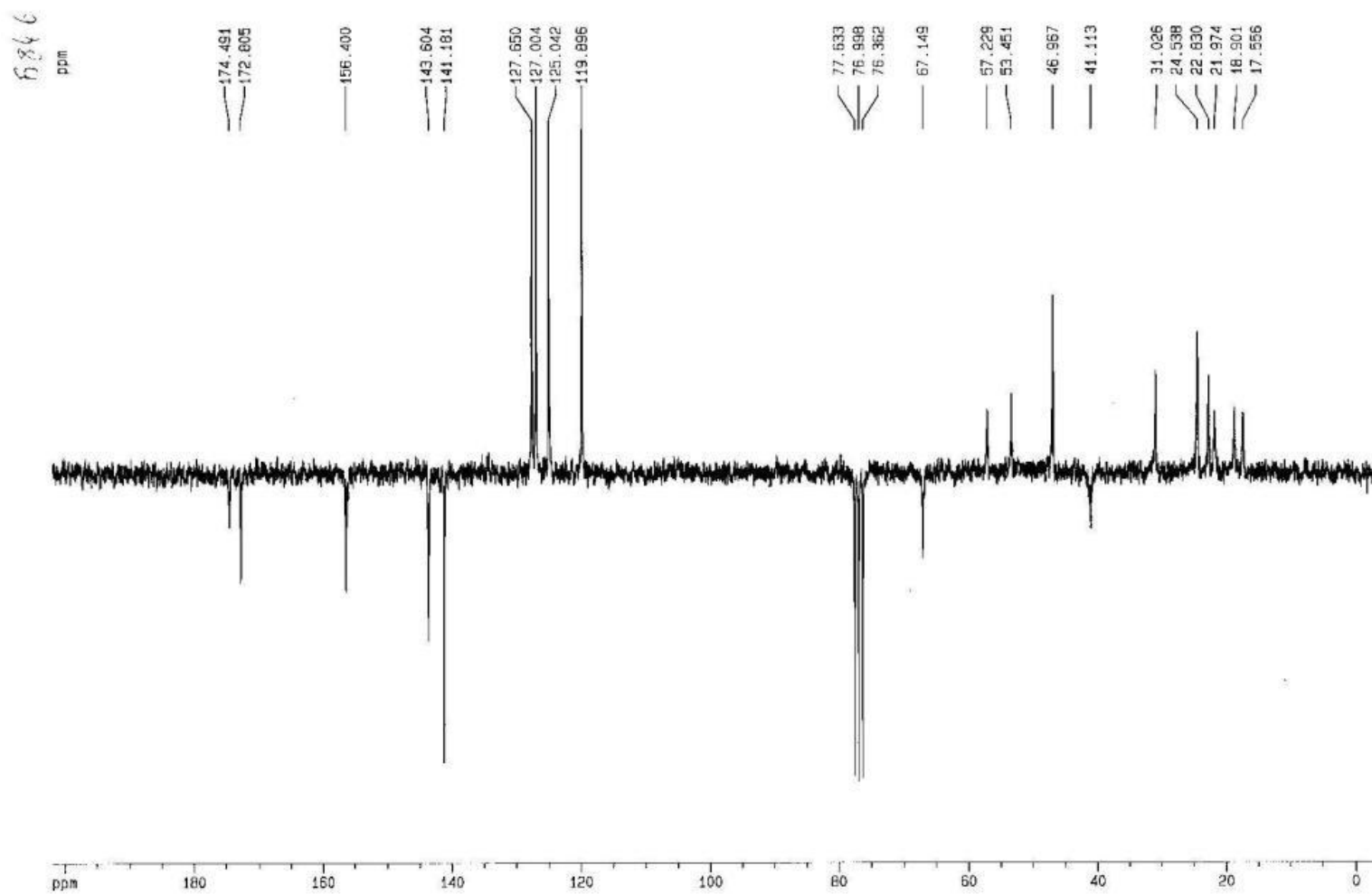


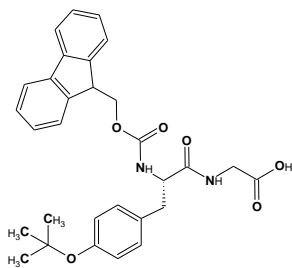
N-[(9*H*-Fluoren-9-ylmethoxy)carbonyl]-L-leucyl-L-valine (**14f**) ^1H NMR (200 MHz, CDCl_3)



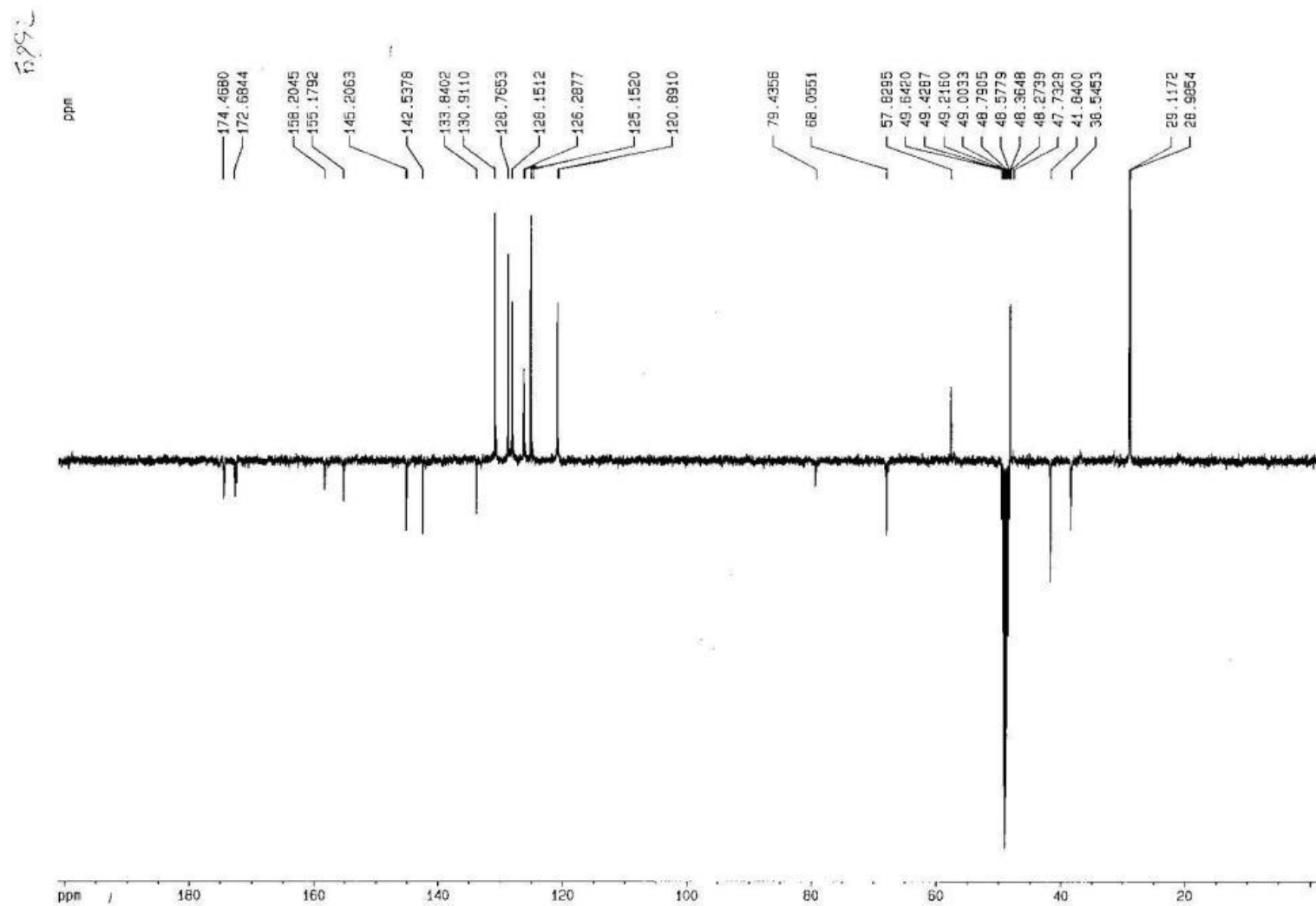


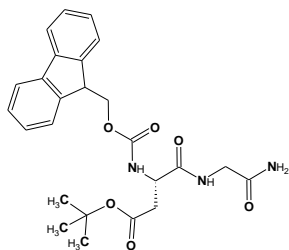
N-[(9*H*-Fluoren-9-ylmethoxy)carbonyl]-L-leucyl-L-valine (**14f**) ^{13}C NMR (50 MHz, CDCl_3)





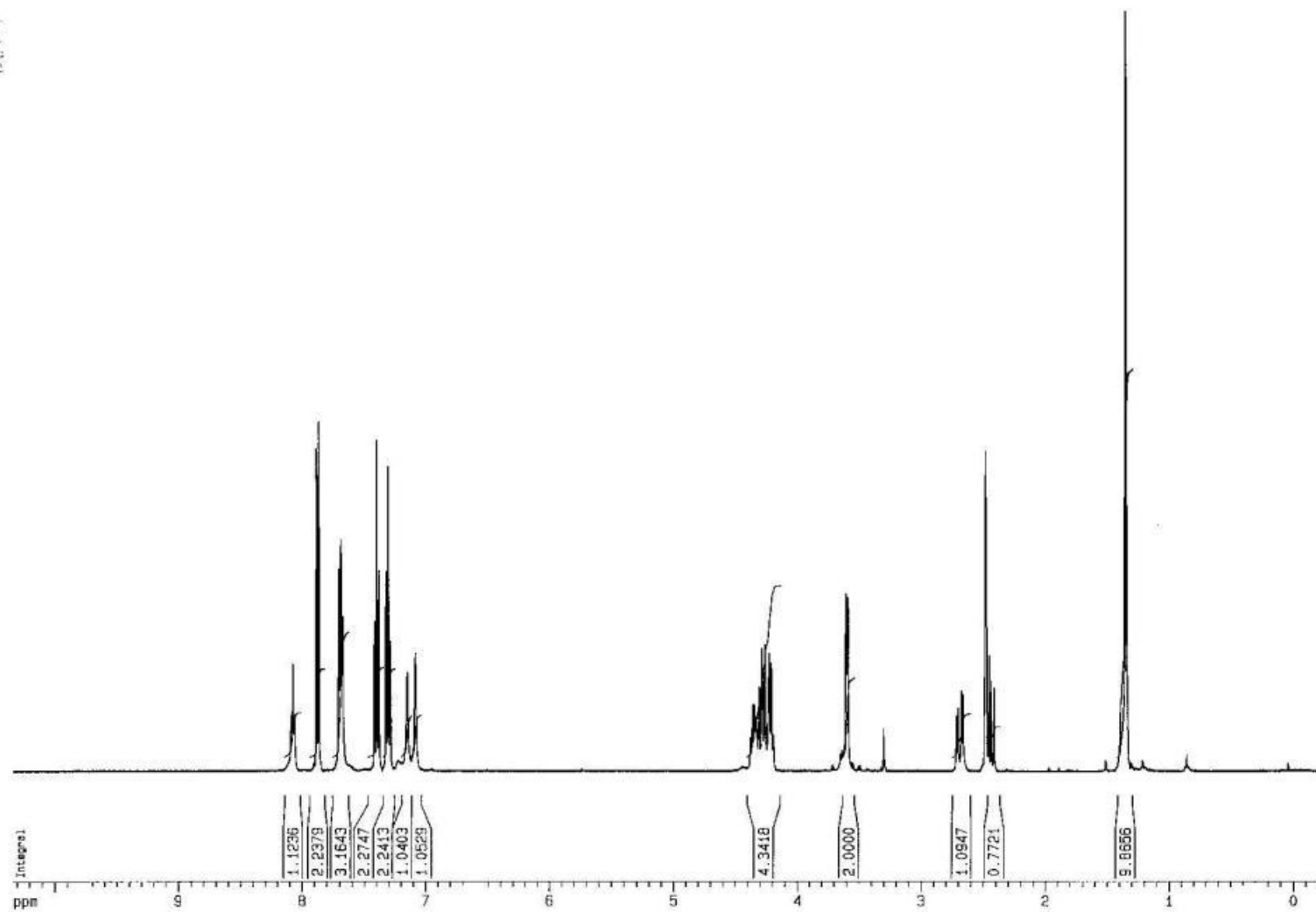
O-(*tert*-Butyl)-*N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-L-tyrosylglycine (**14g**) ^1H NMR (100 MHz, CD_3OD)

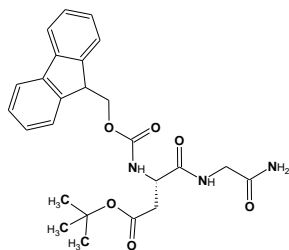




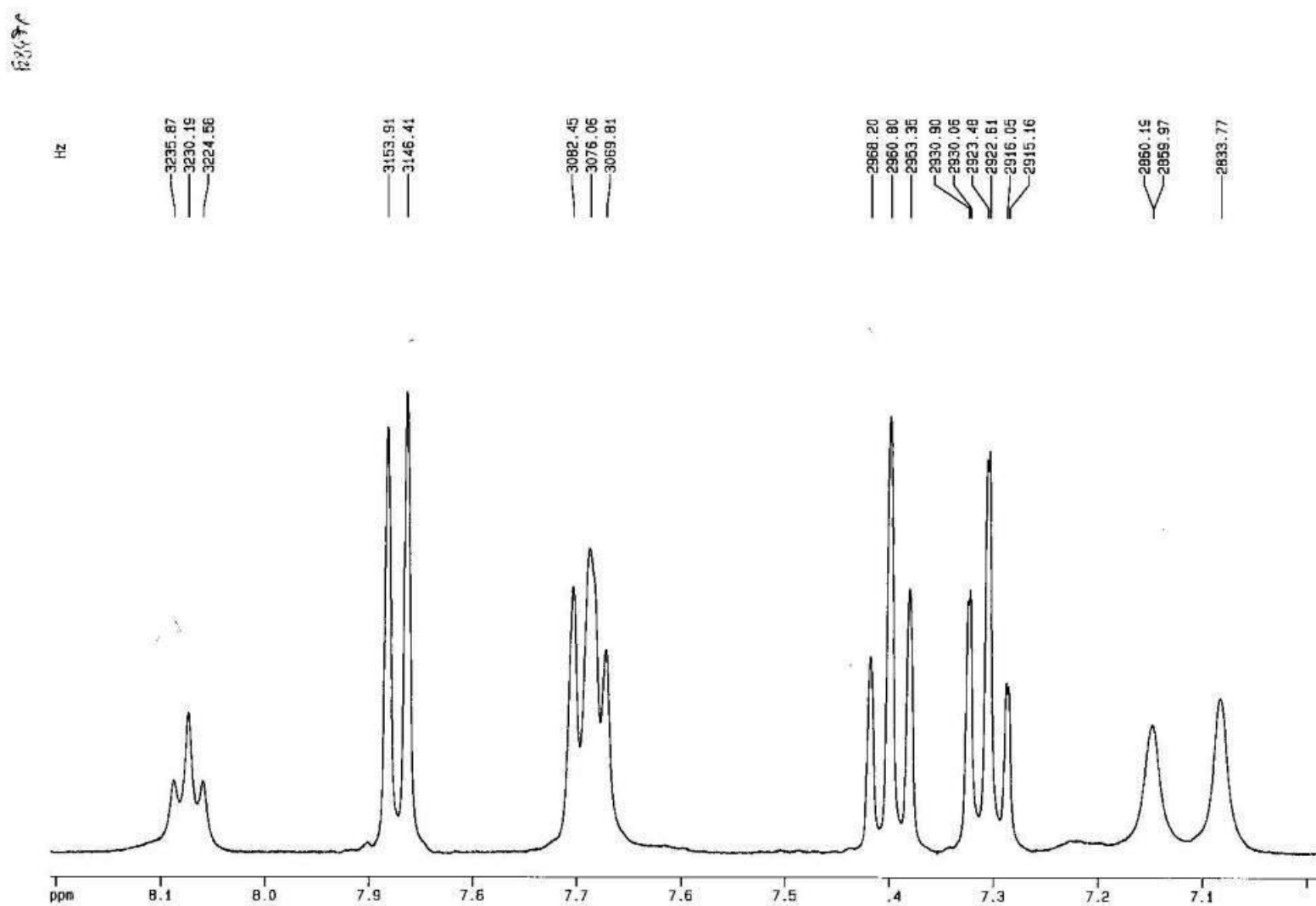
O-(*tert*-Butyl)-*N*-[(9H-fluoren-9-ylmethoxy)carbonyl]-L- α -aspartylglycinamide (**14h**) ^1H NMR (400 MHz, DMSO- d_6)

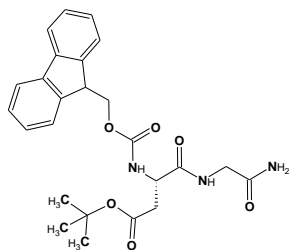
SI-146





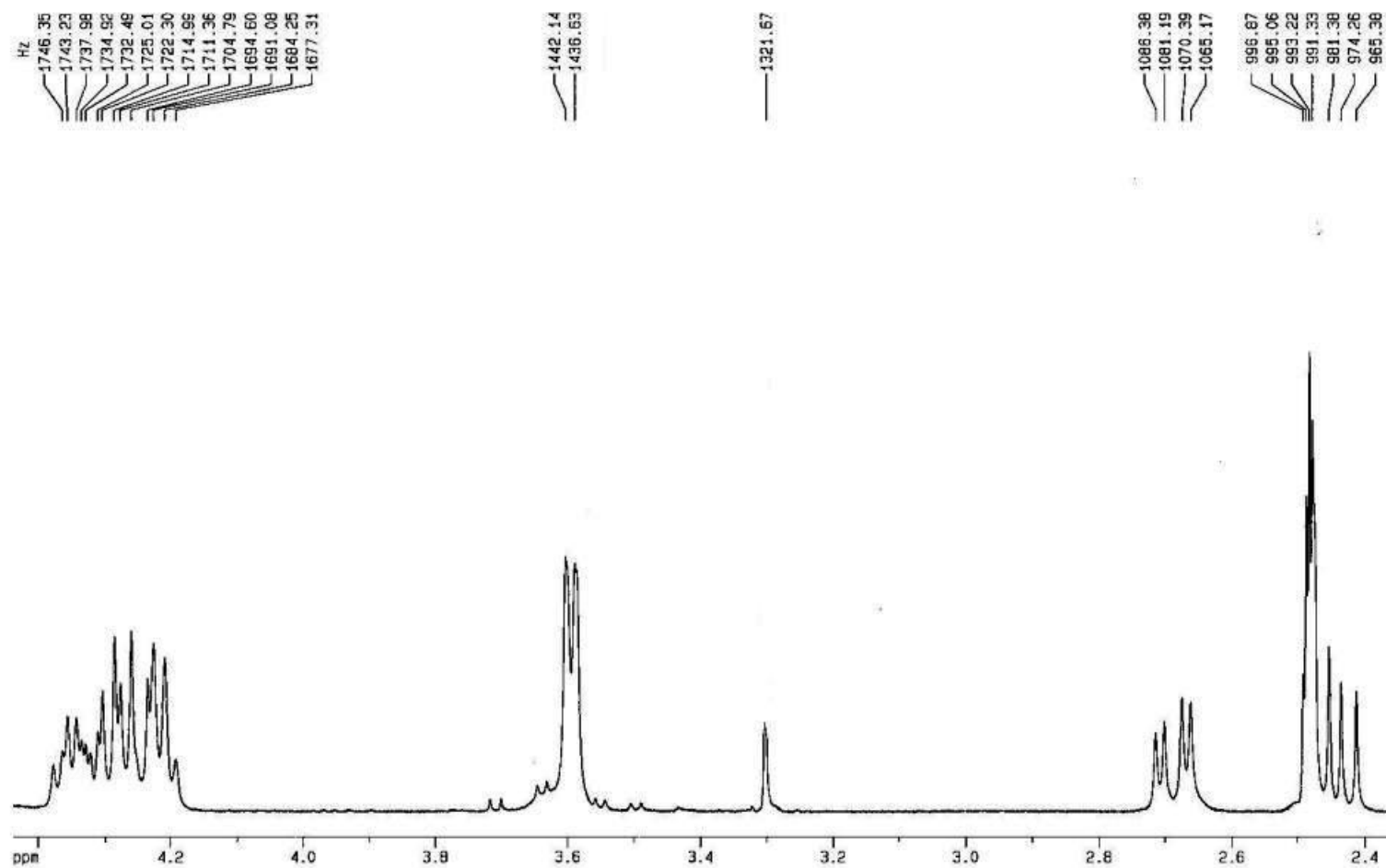
O-(*tert*-Butyl)-*N*-[(9H-fluoren-9-ylmethoxy)carbonyl]-L- α -aspartylglycinamide (**14h**) ^1H NMR (400 MHz, DMSO-d_6)

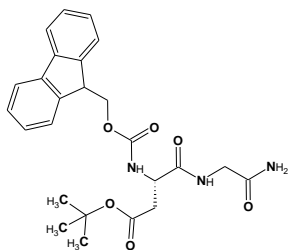




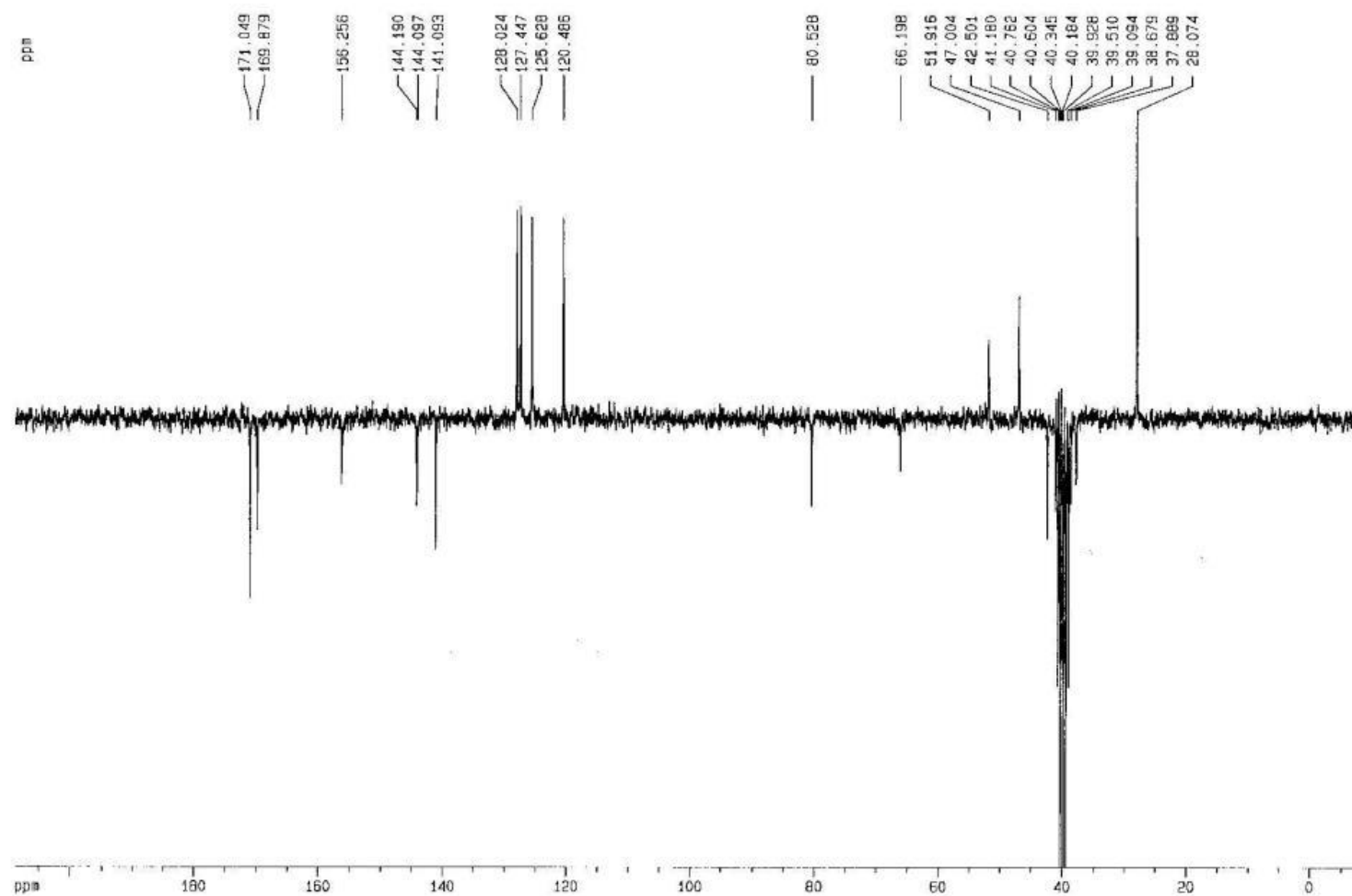
O-(*tert*-Butyl)-*N*-[(9H-fluoren-9-ylmethoxy)carbonyl]-L- α -aspartylglycinamide (**14h**) ^1H NMR (400 MHz, DMSO $_d$)

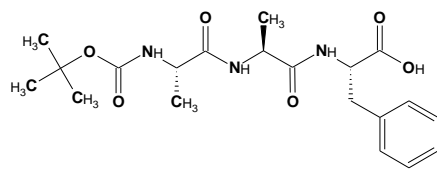
SI-148



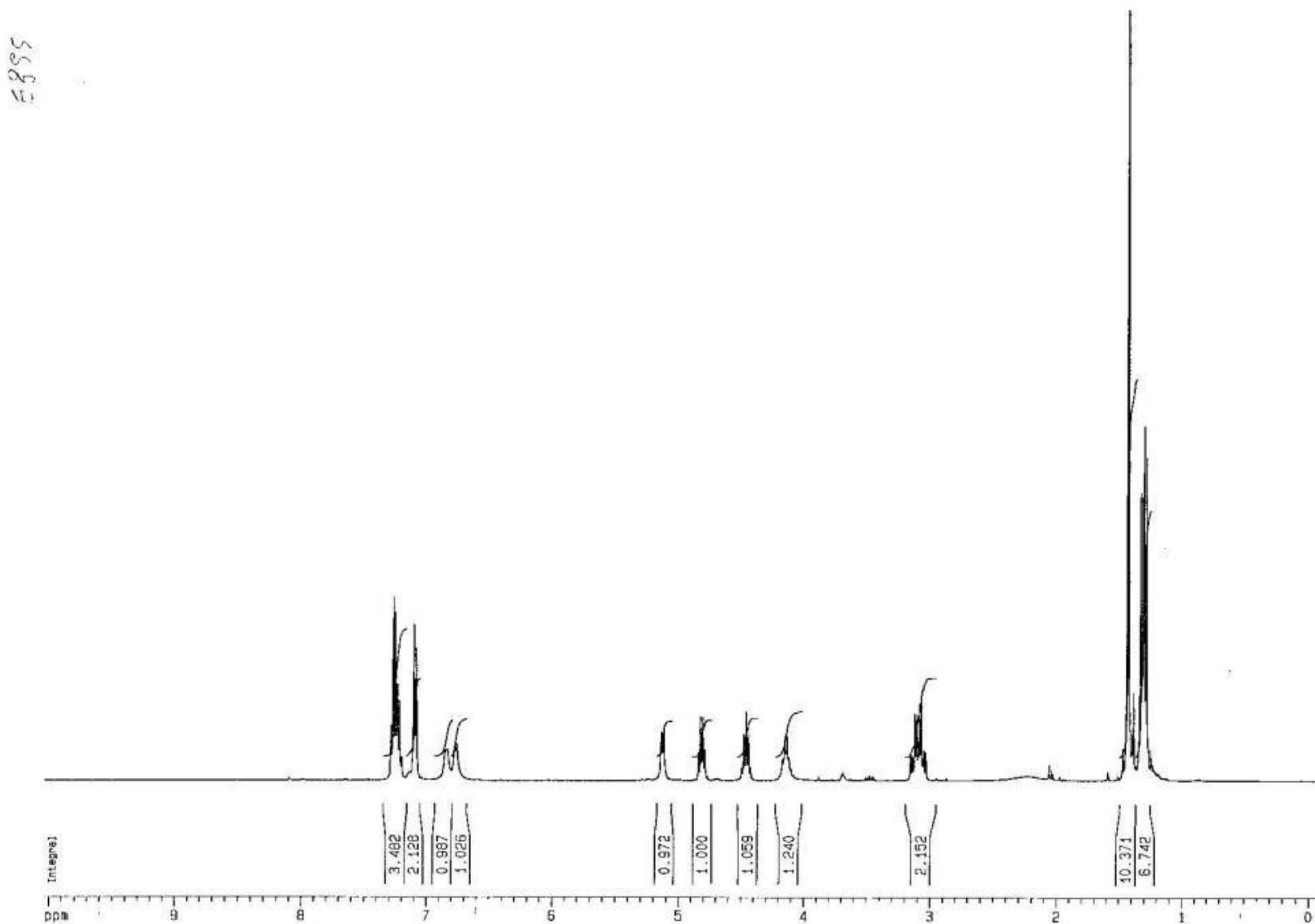


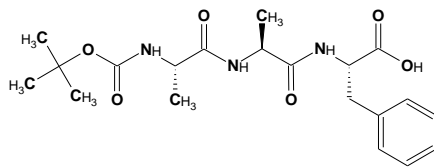
O-(*tert*-Butyl)-*N*-[(9H-fluoren-9-ylmethoxy)carbonyl]-L- α -aspartylglycinamide (**14h**) ^{13}C NMR (100 MHz, DMSO-d_6)



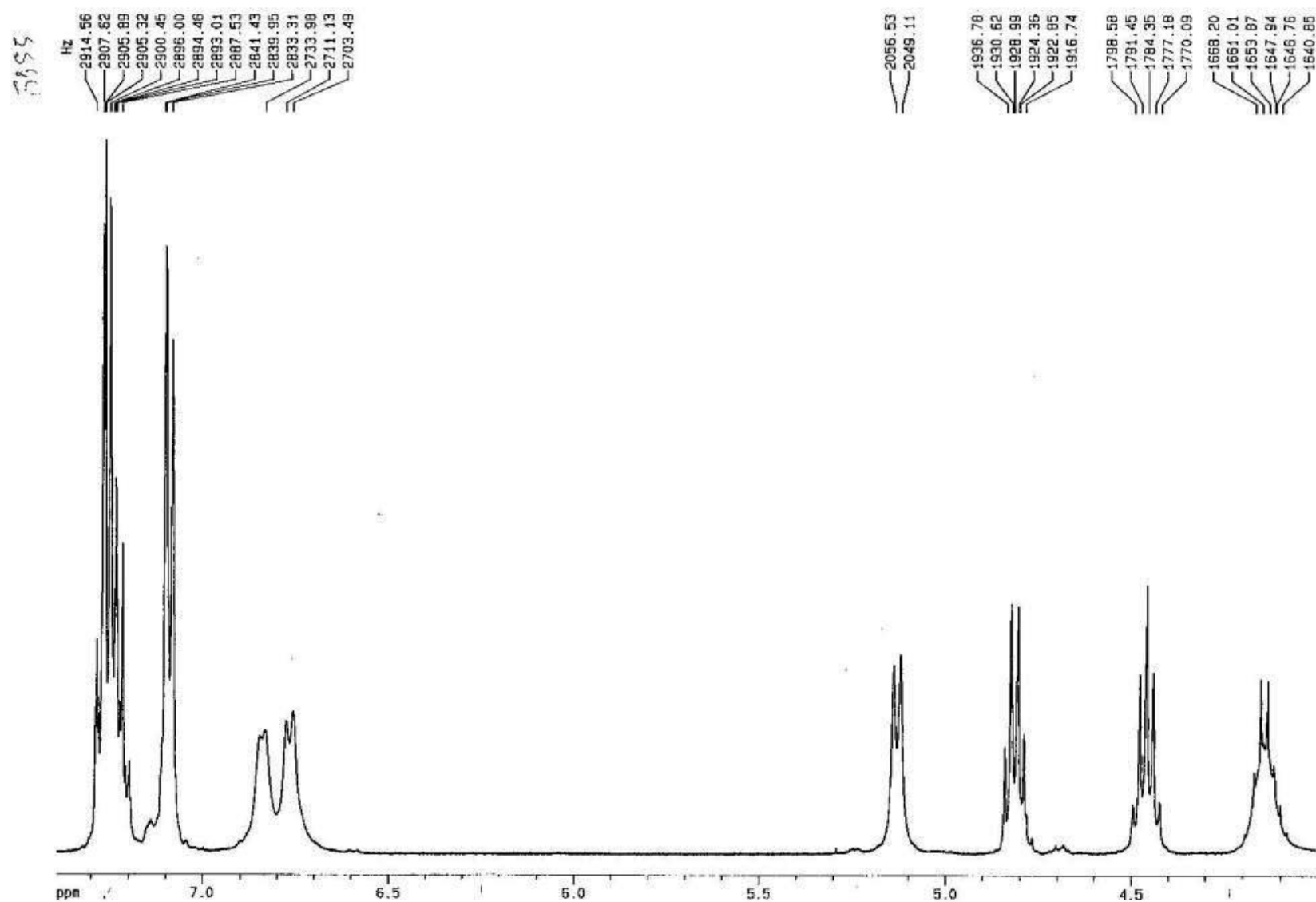


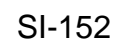
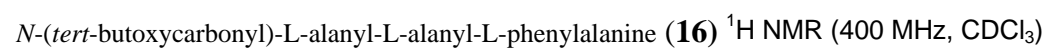
N-(*tert*-butoxycarbonyl)-L-alanyl-L-alanyl-L-phenylalanine (**16**) ^1H NMR (400 MHz, CDCl_3)

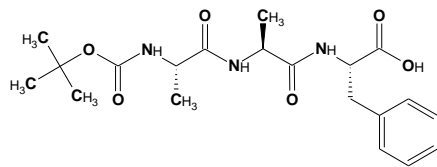




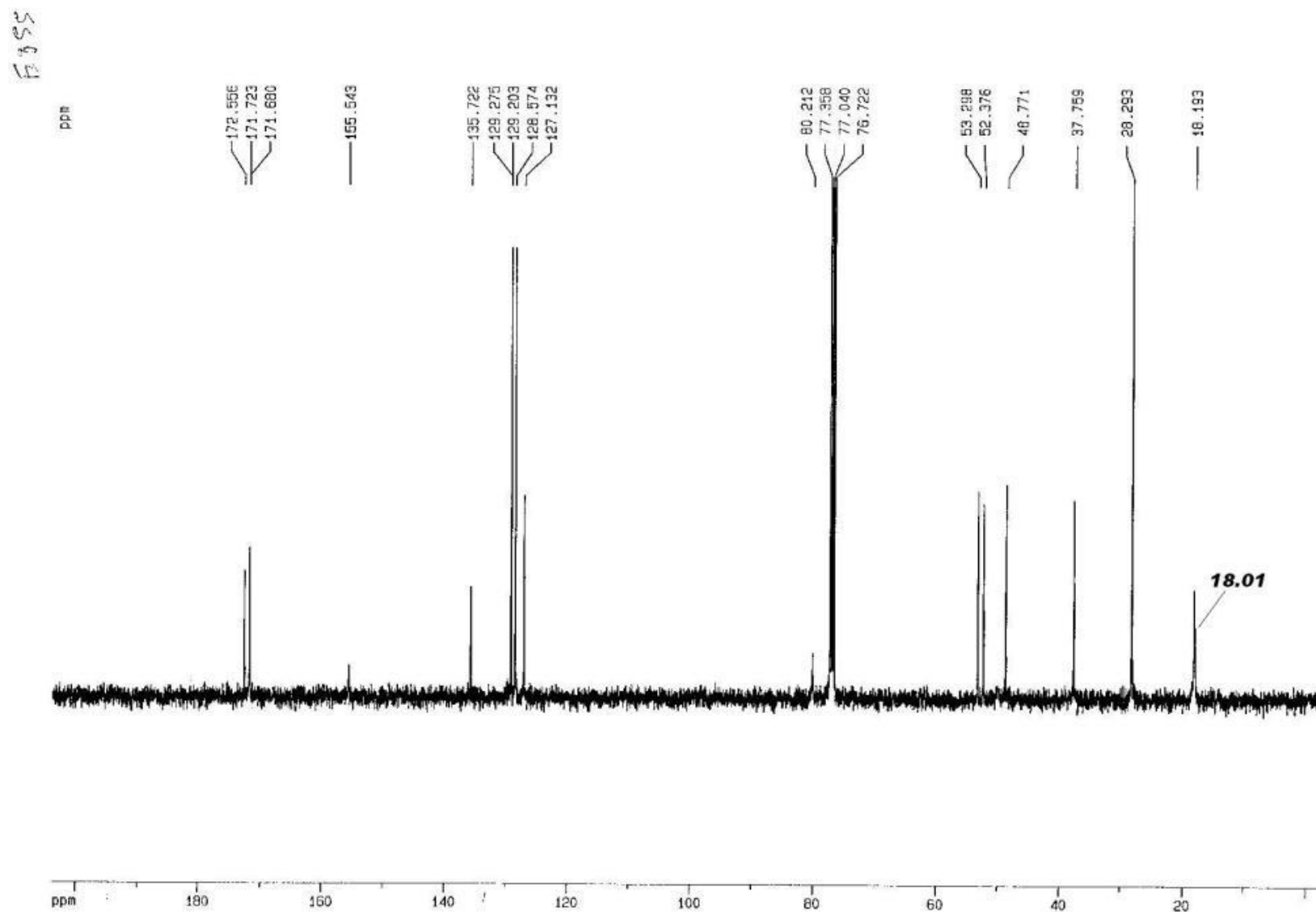
N-(*tert*-butoxycarbonyl)-L-alanyl-L-alanyl-L-phenylalanine (**16**) ^1H NMR (400 MHz, CDCl_3)

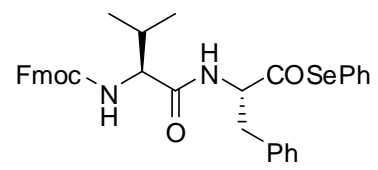




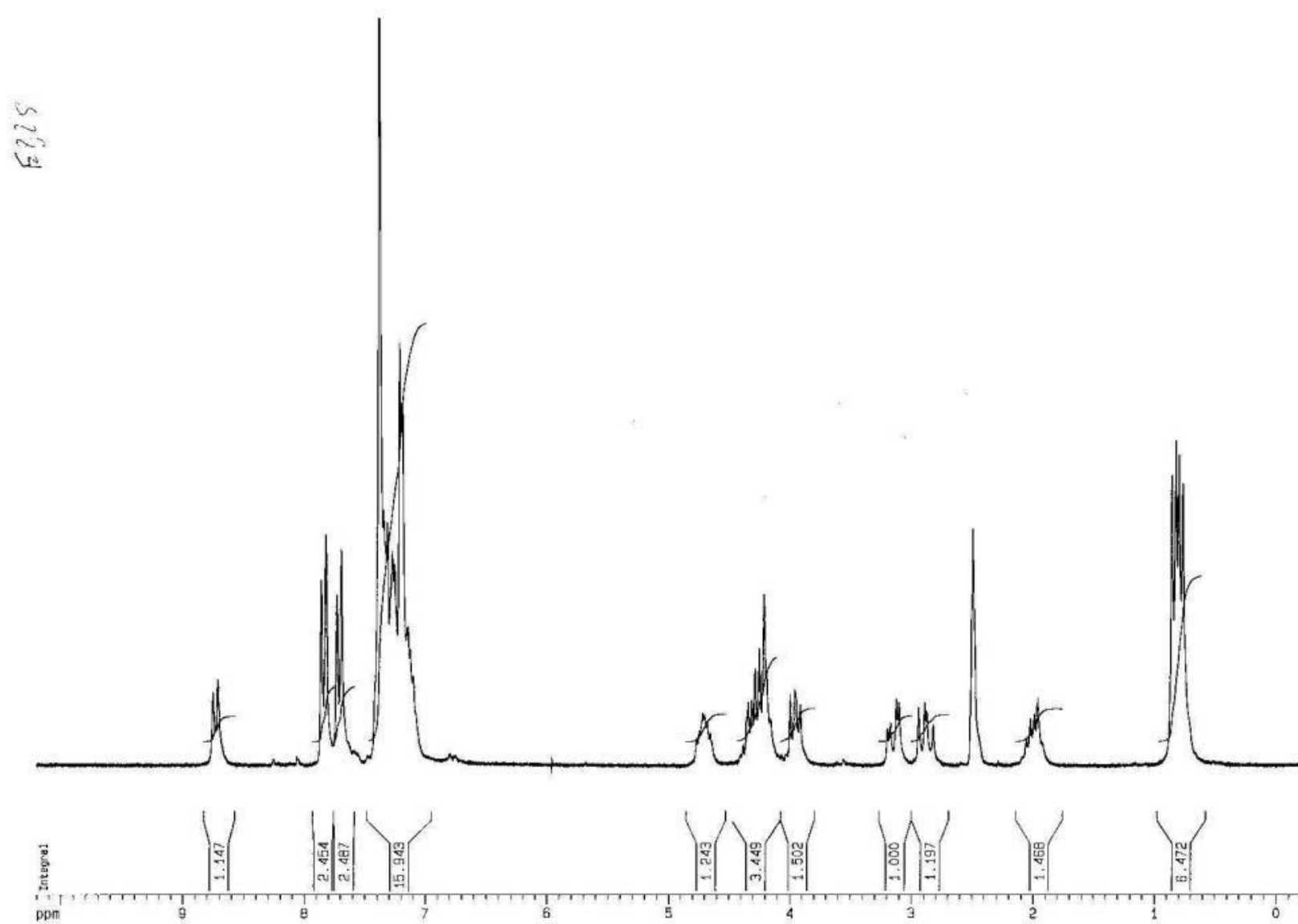


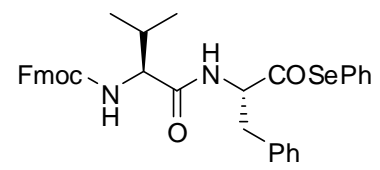
N-(*tert*-butoxycarbonyl)-L-alanyl-L-alanyl-L-phenylalanine (**16**) ^{13}C NMR (100 MHz, CDCl_3)



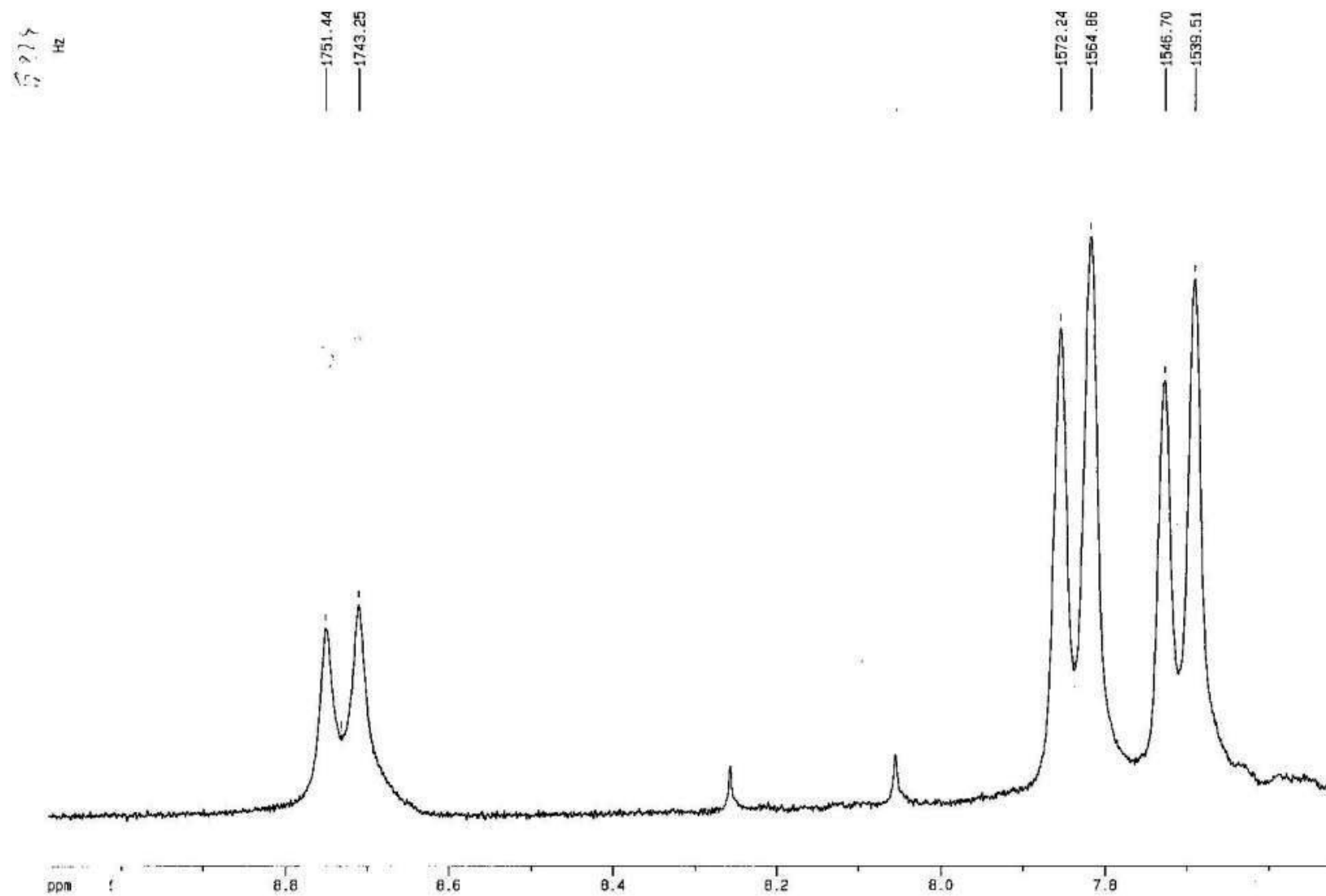


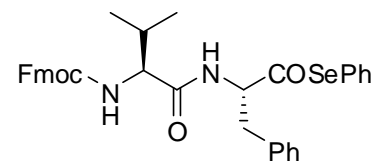
^1H NMR (200 MHz, DMSO- d_6)



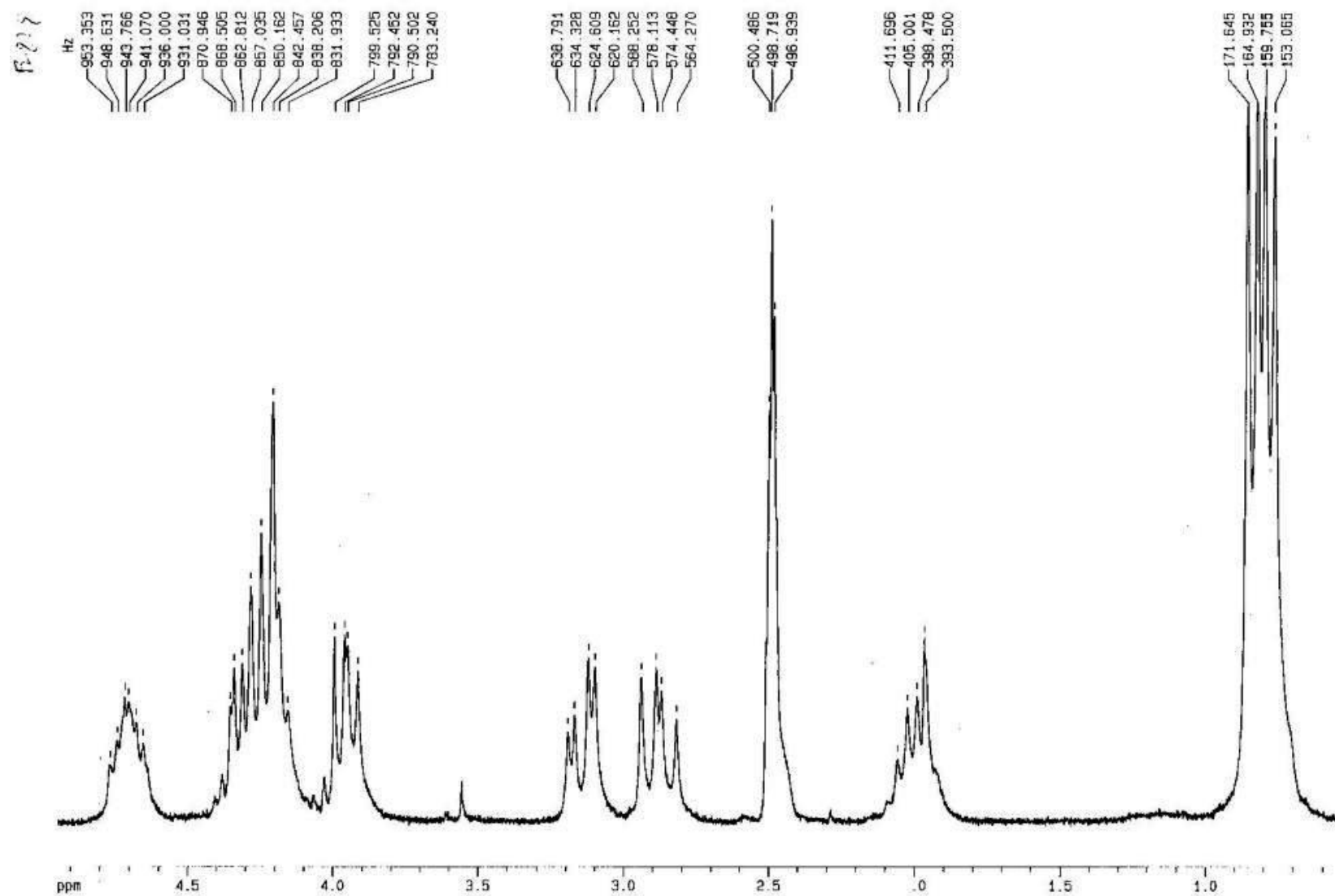


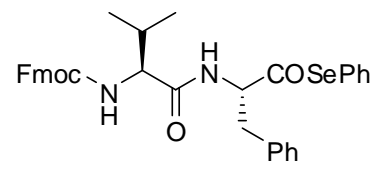
¹H NMR (200 MHz, DMSO-d₆)



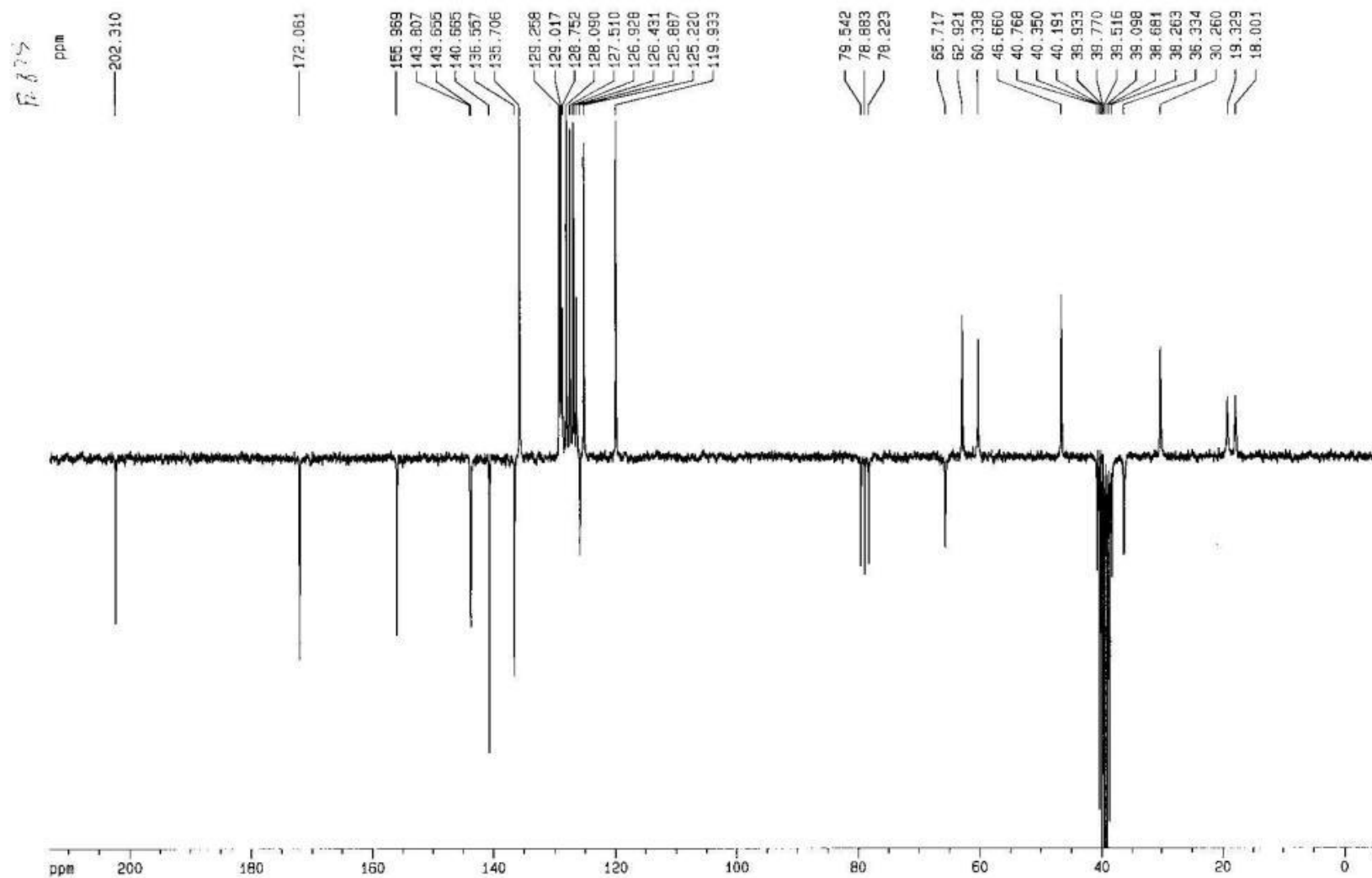


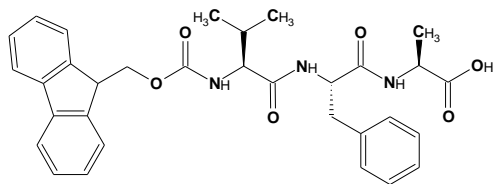
¹H NMR (200 MHz, DMSO-d₆)



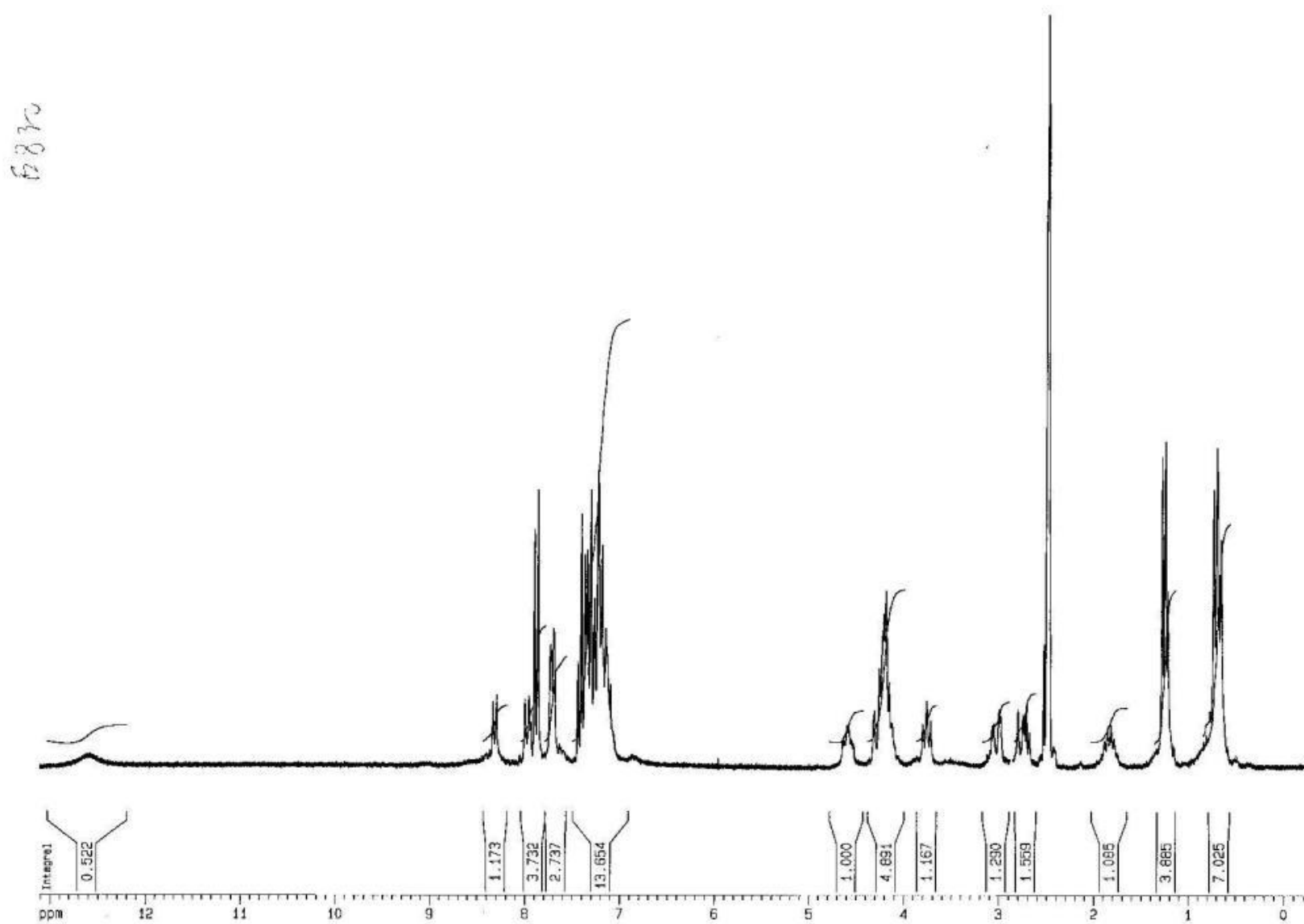


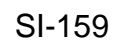
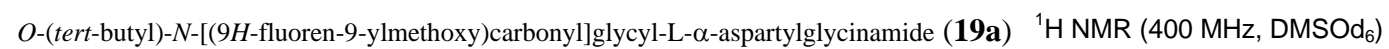
¹³C NMR (50 MHz, DMSO-d₆)

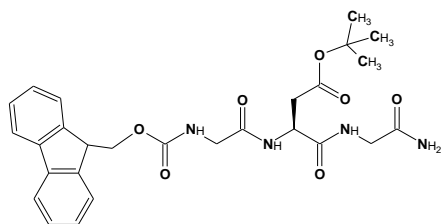




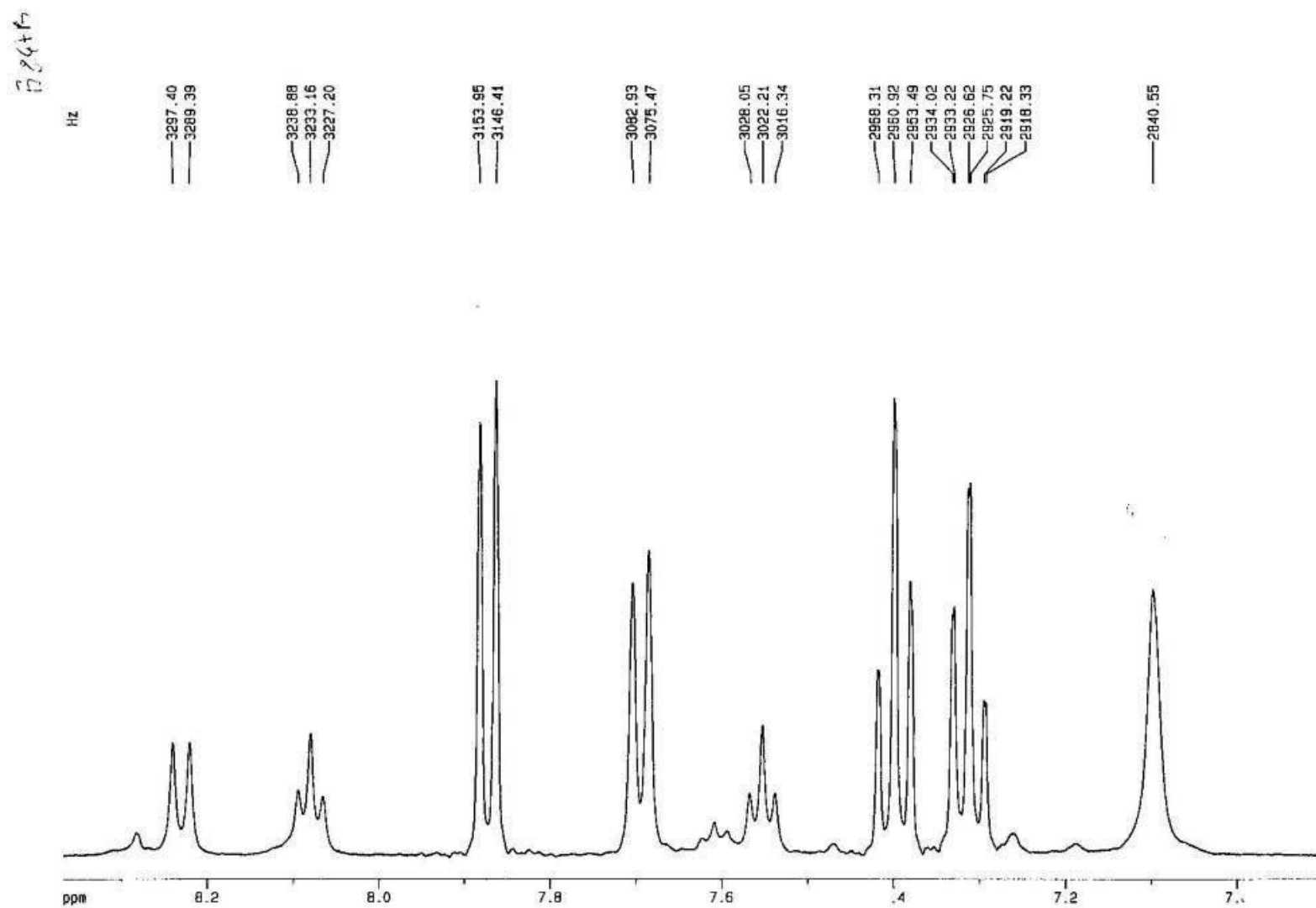
N-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-L-valyl-L-phenylalanyl-L-alanine (**18**) ^1H NMR (200 MHz, DMSO-d_6)

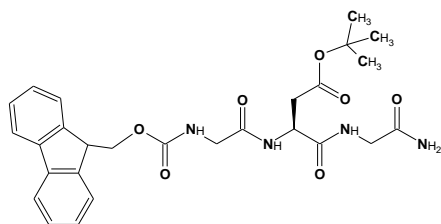






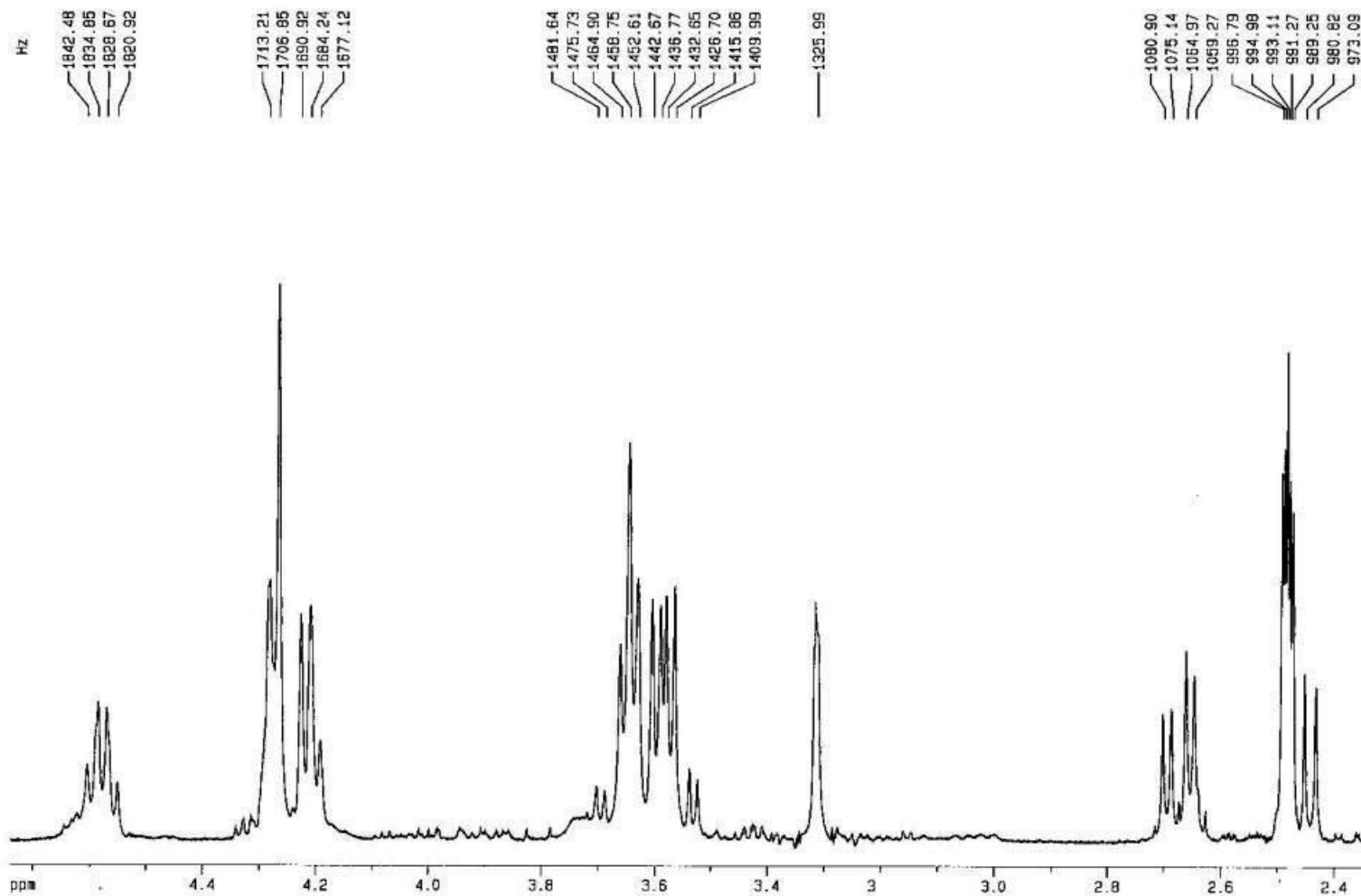
O-(*tert*-butyl)-*N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]glycyl-L- α -aspartylglycinamide (**19a**) ^1H NMR (400 MHz, DMSO-d_6)

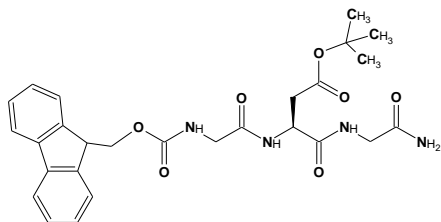




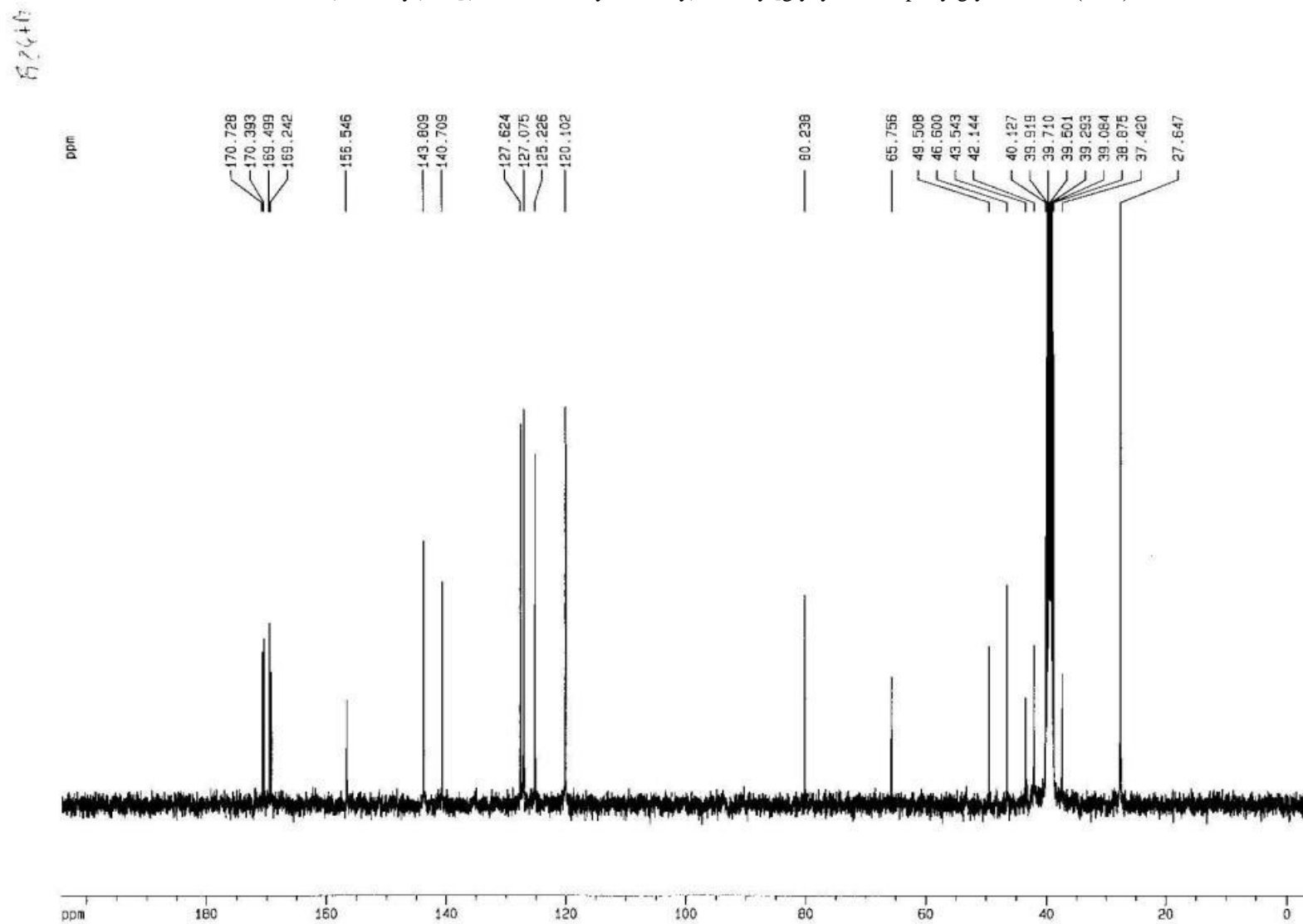
O-(*tert*-butyl)-*N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]glycyl-L- α -aspartylglycinamide (**19a**) ^1H NMR (400 MHz, DMSO-d_6)

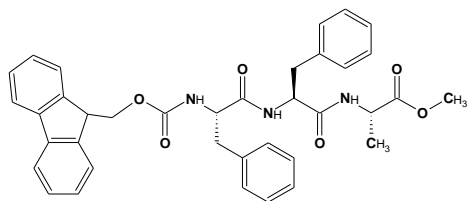
376.43



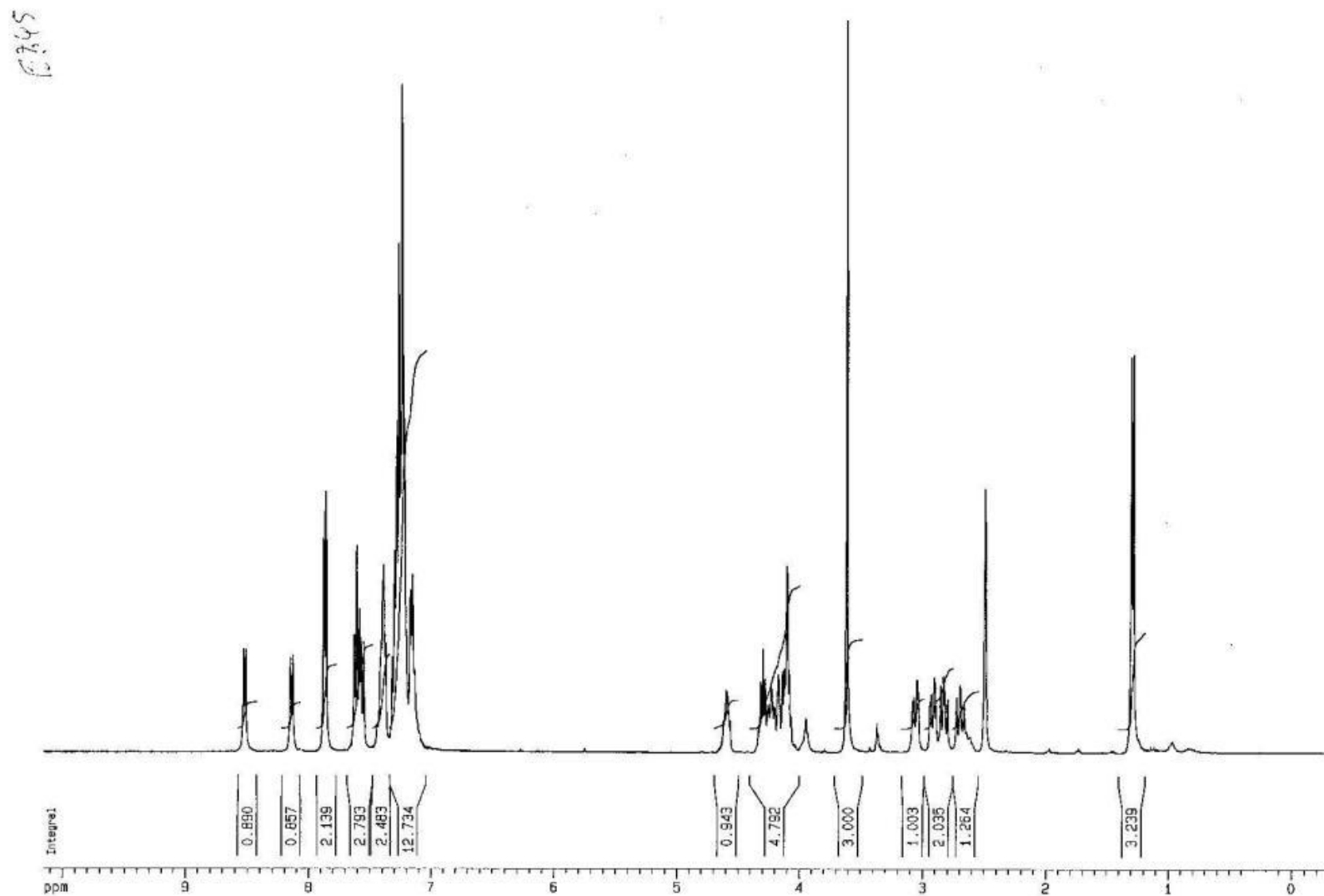


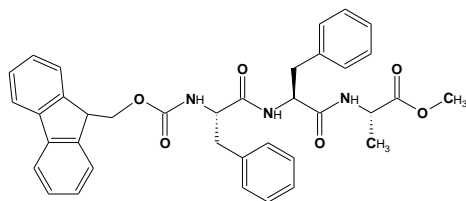
O-(*tert*-butyl)-*N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]glycyl-L- α -aspartylglycinamide (**19a**) ^{13}C NMR (100 MHz, DMSO-d_6)



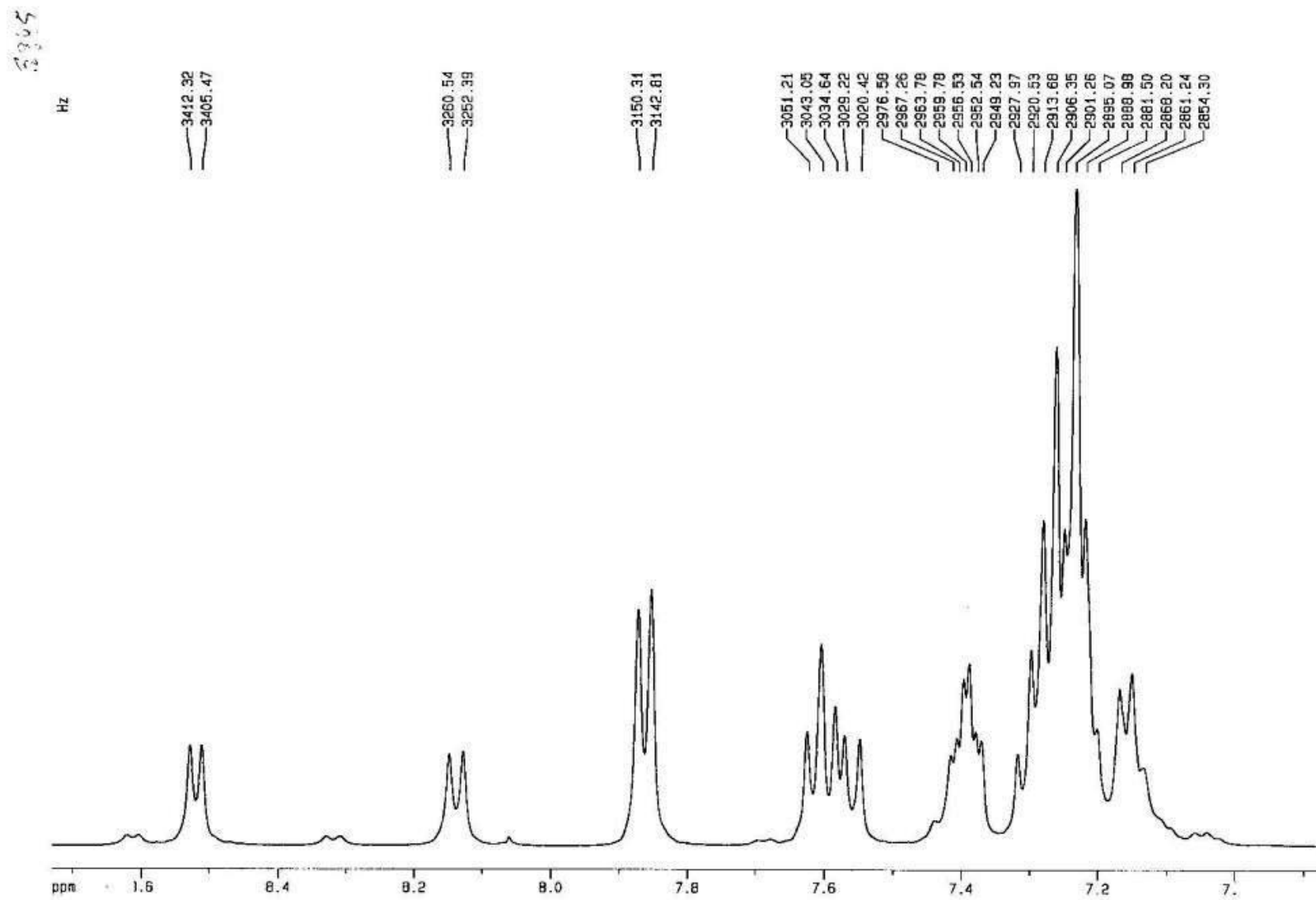


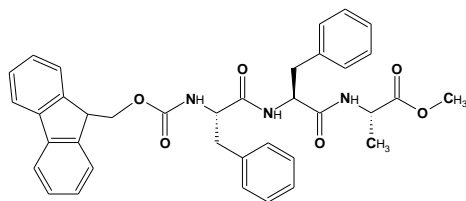
methyl *N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-L-phenylalanyl-L-phenylalanyl-L-alaninate (**19b**) ^1H NMR (400 MHz, DMSO-d_6)



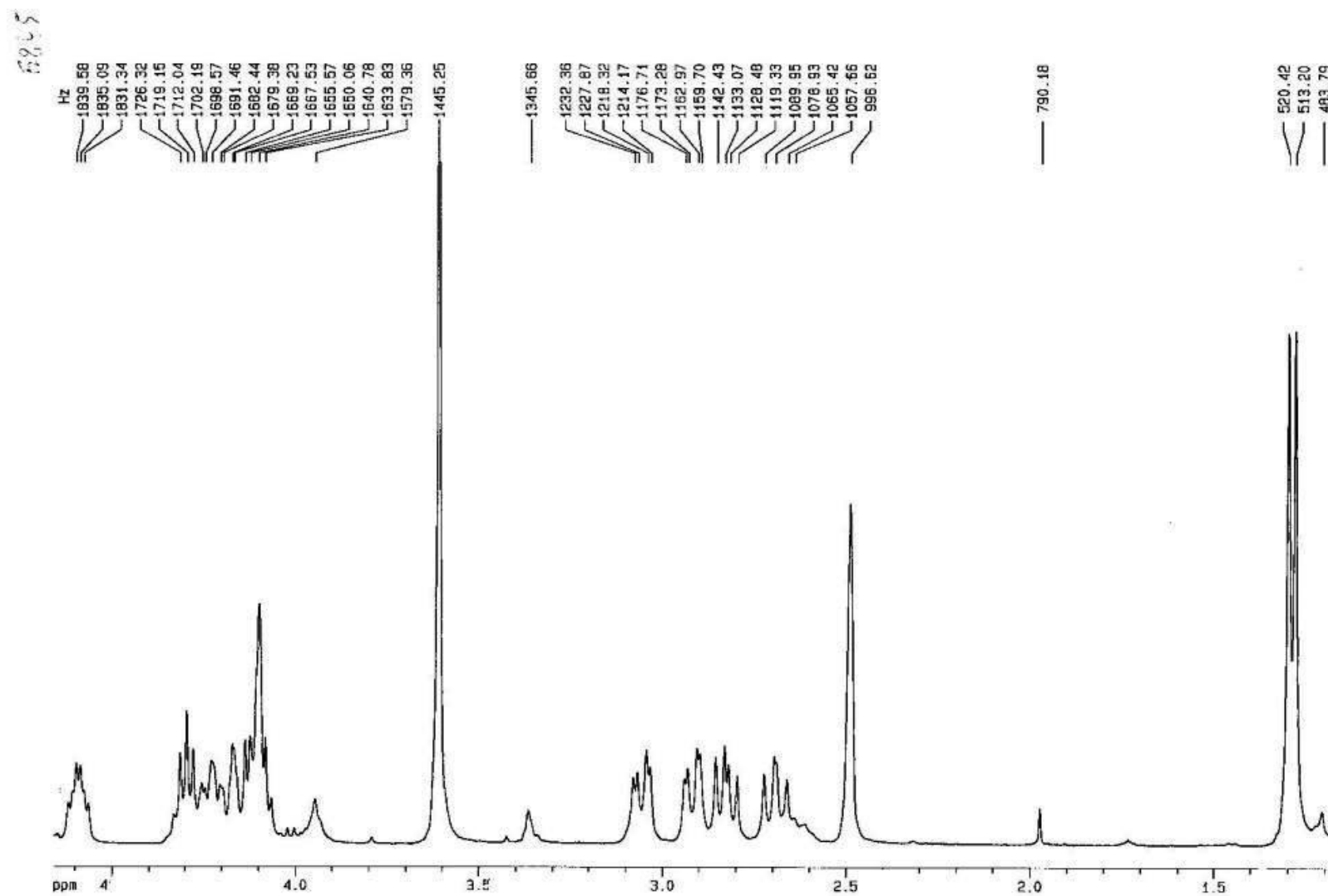


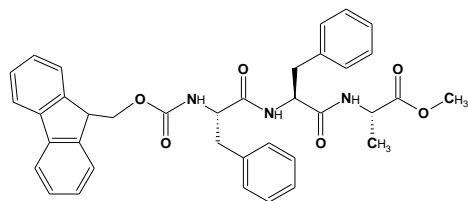
methyl *N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-L-phenylalanyl-L-phenylalanyl-L-alaninate (**19b**) ^1H NMR (400 MHz, DMSO-d_6)



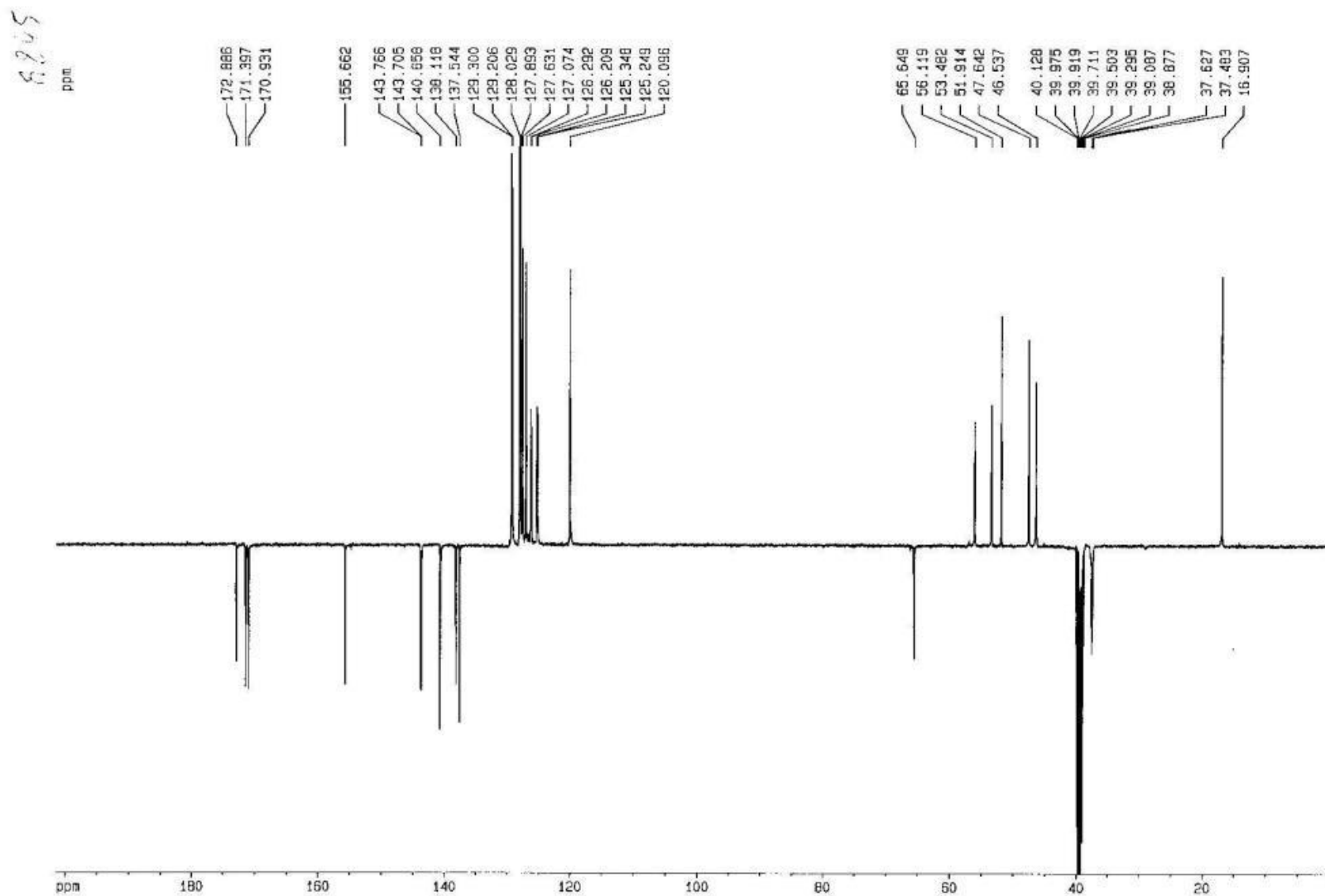


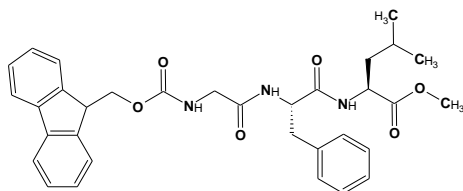
methyl *N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-*L*-phenylalanyl-*L*-phenylalanyl-*L*-alaninate (**19b**) ^1H NMR (400 MHz, DMSO-d_6)



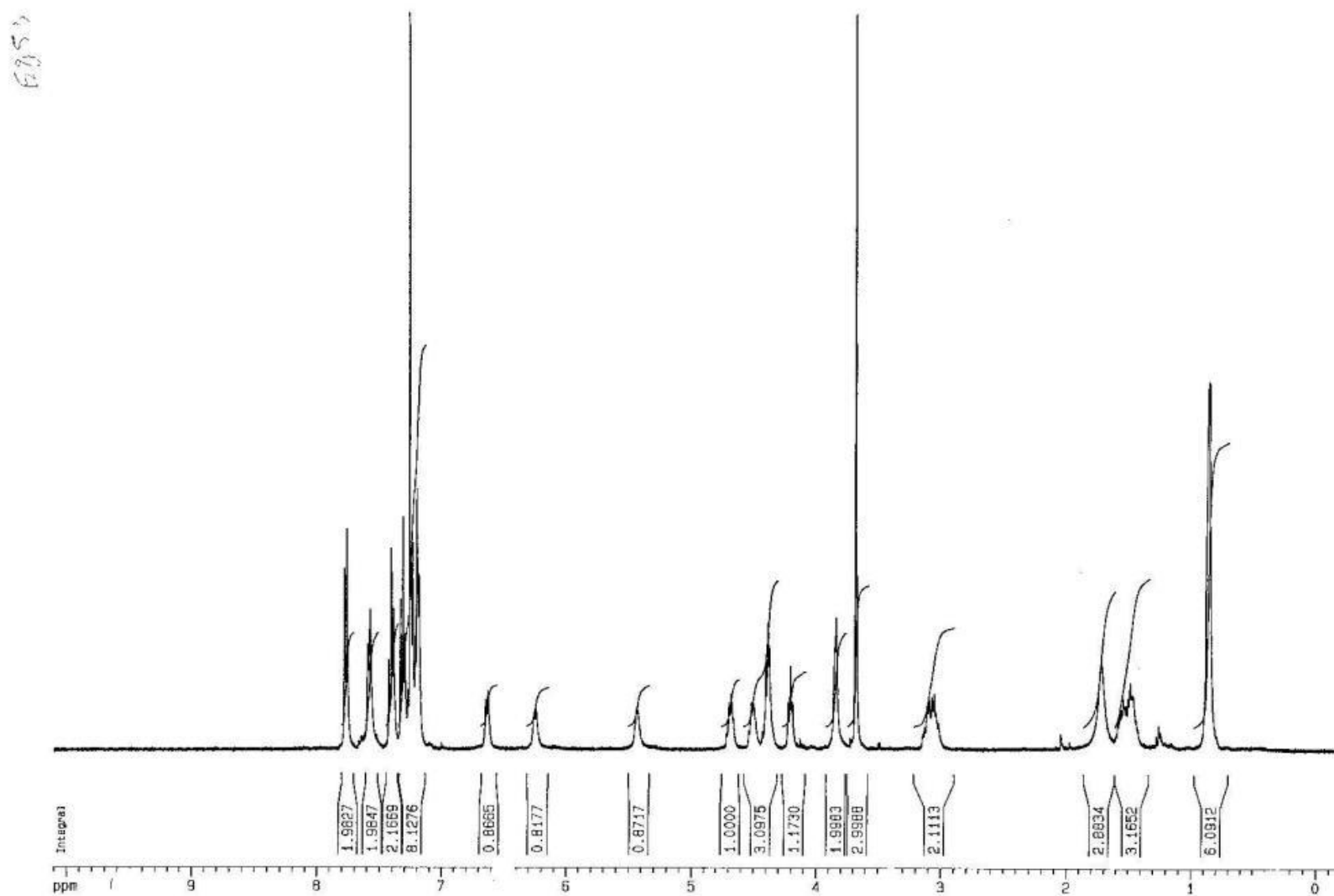


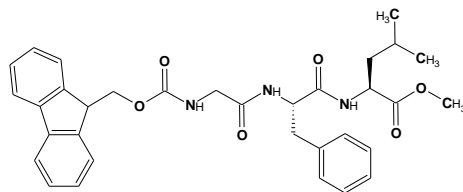
methyl *N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-L-phenylalanyl-L-phenylalanyl-L-alaninate (**19b**) ^{13}C NMR (100 MHz, DMSO-d_6)





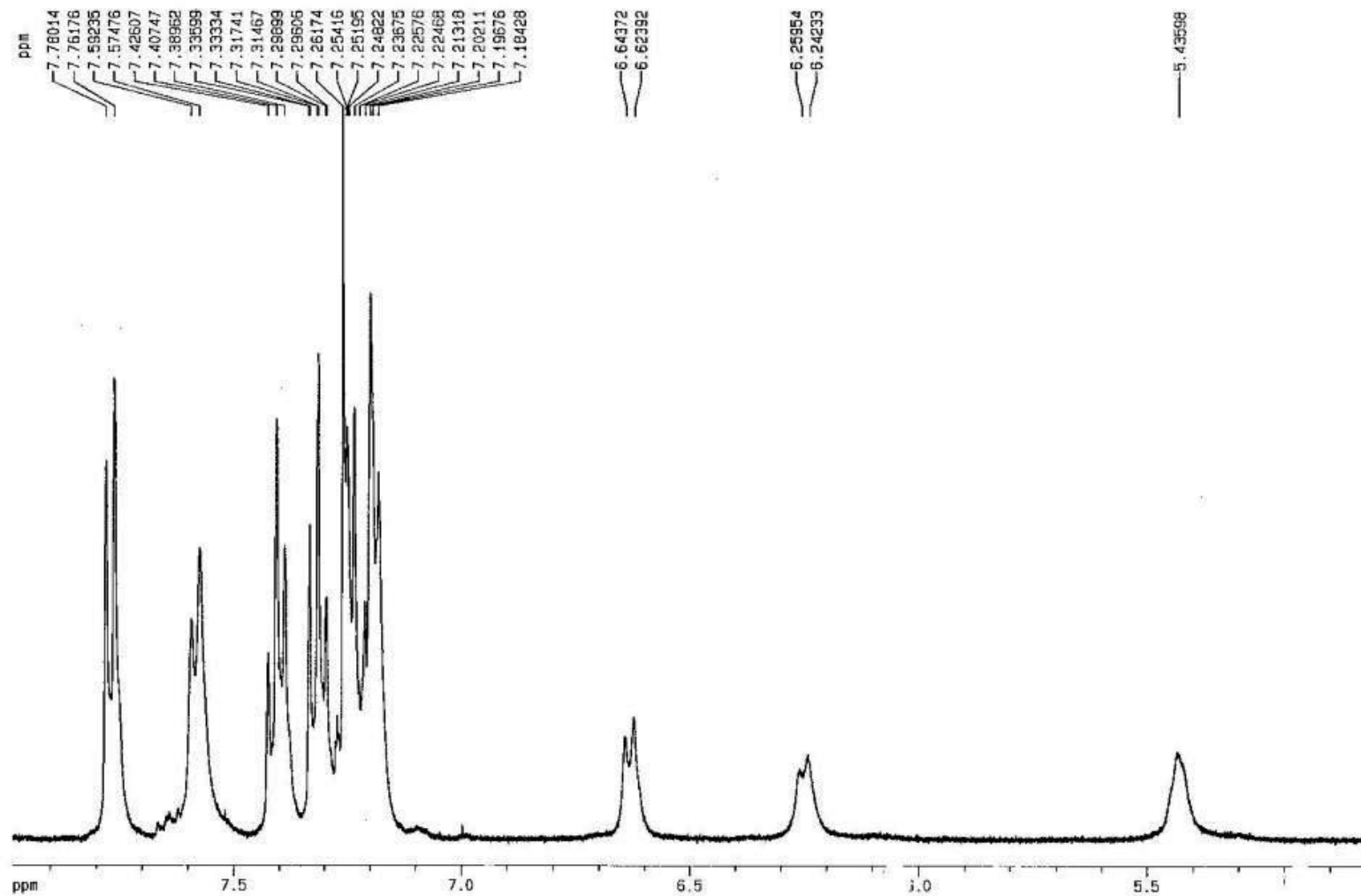
methyl *N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]glycyl-L-phenylalanyl-L-leucinate (**19c**) ^1H NMR (400 MHz, CDCl_3)

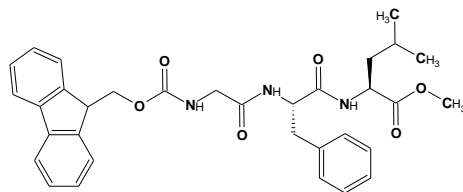




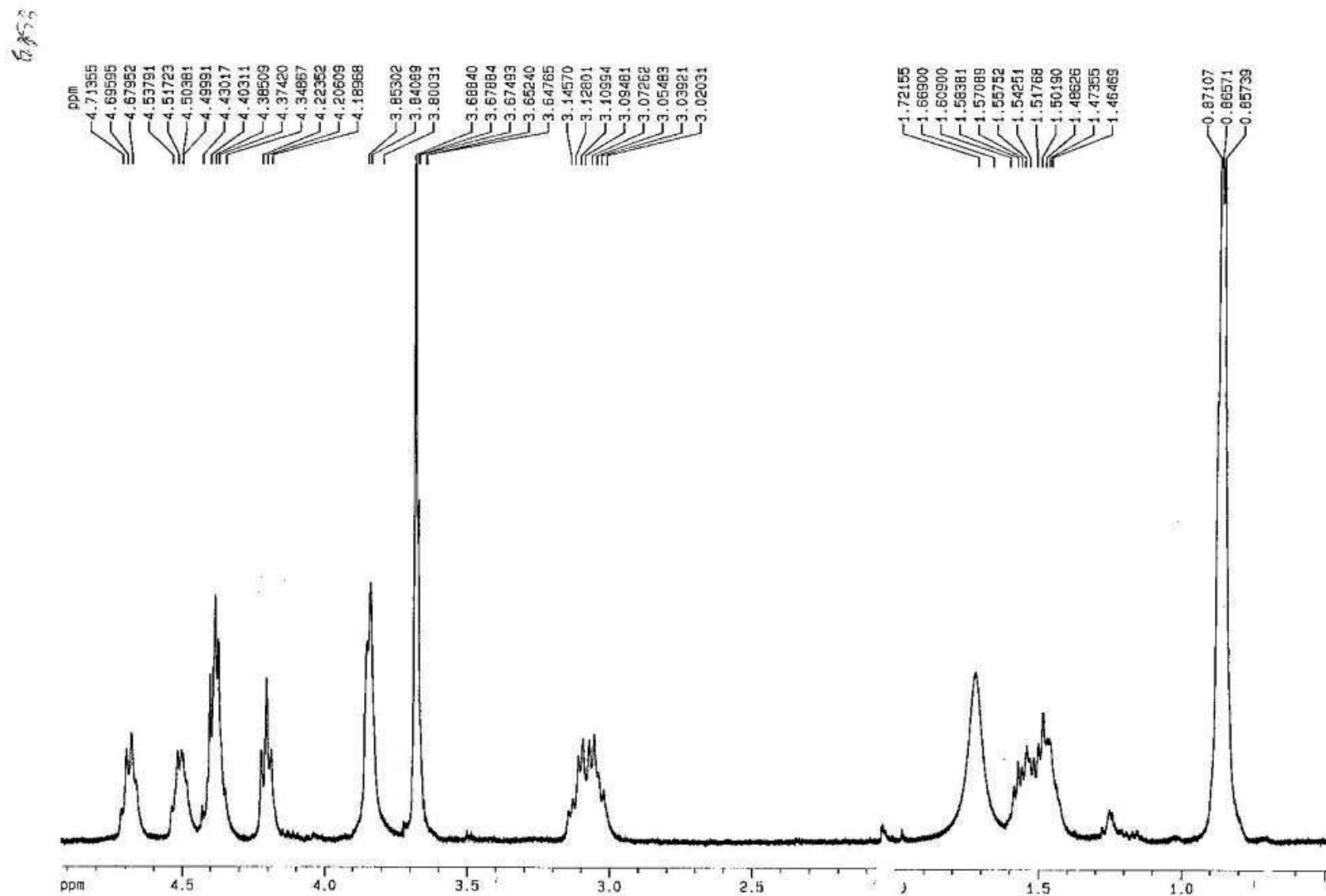
methyl *N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]glycyl-L-phenylalanyl-L-leucinate (**19c**) ^1H NMR (400 MHz, CDCl_3)

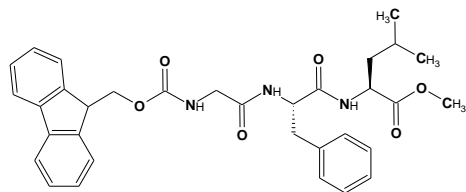
7.853



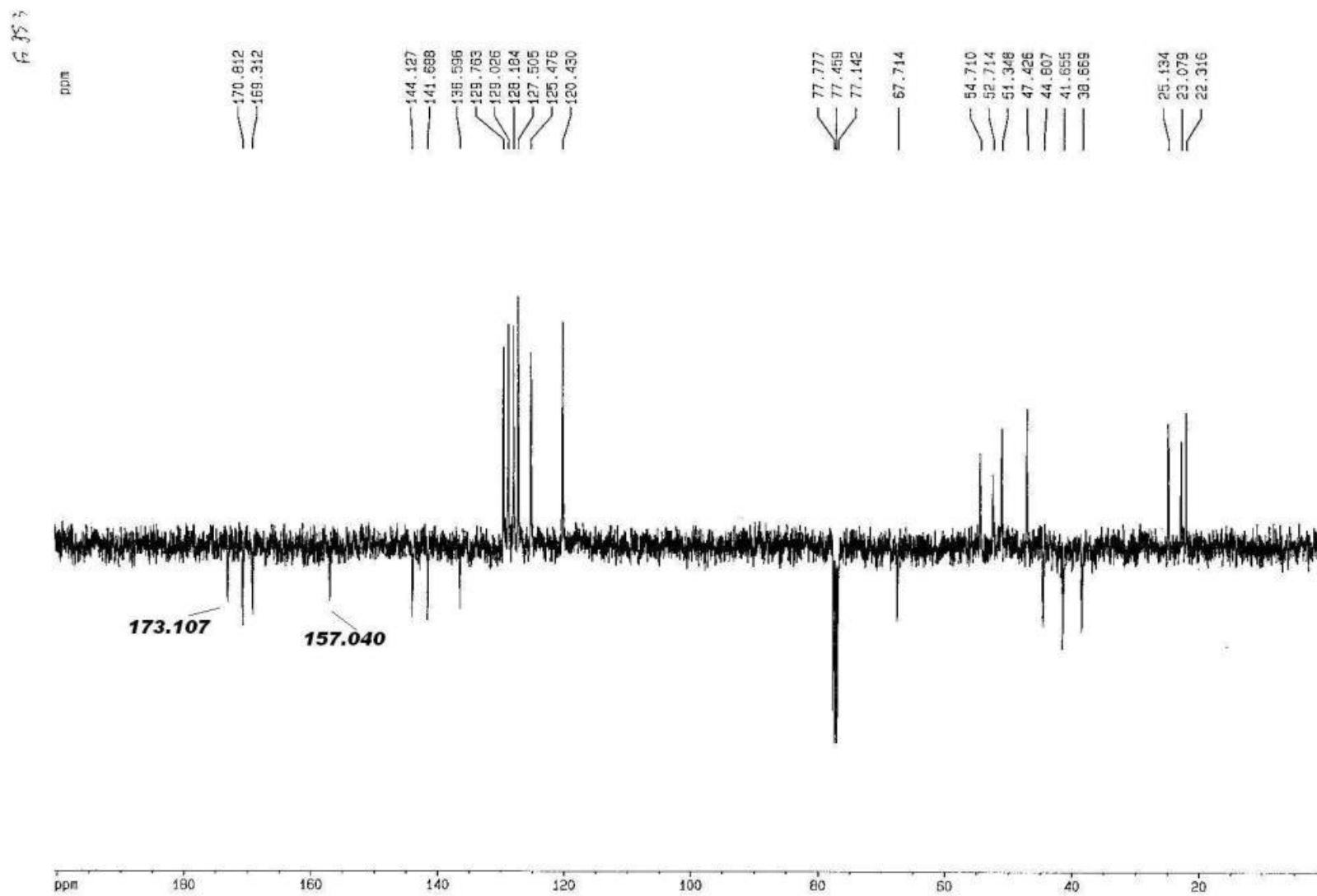


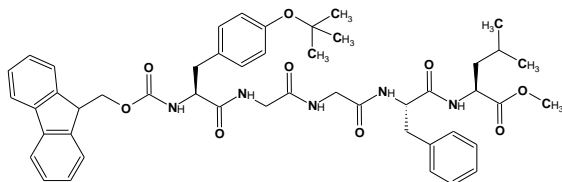
methyl *N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]glycyl-L-phenylalanyl-L-leucinate (**19c**) ^1H NMR (400 MHz, CDCl_3)





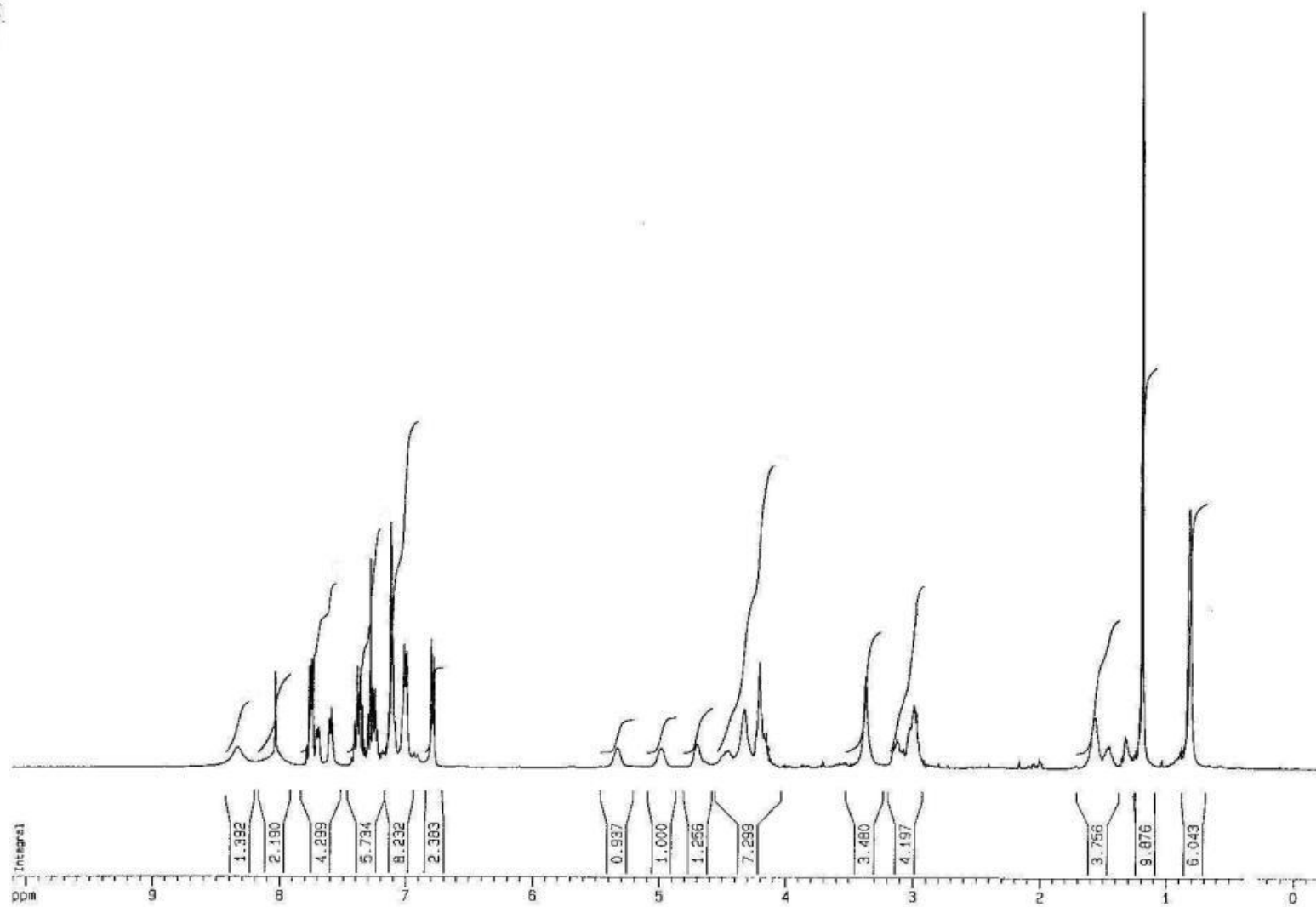
methyl *N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]glycyl-L-phenylalanyl-L-leucinate (**19c**) ^{13}C NMR (100 MHz, CDCl_3)

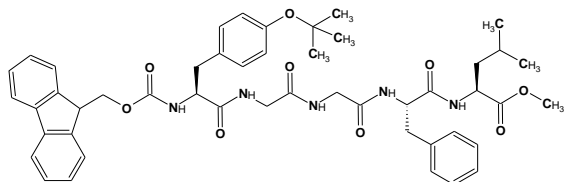




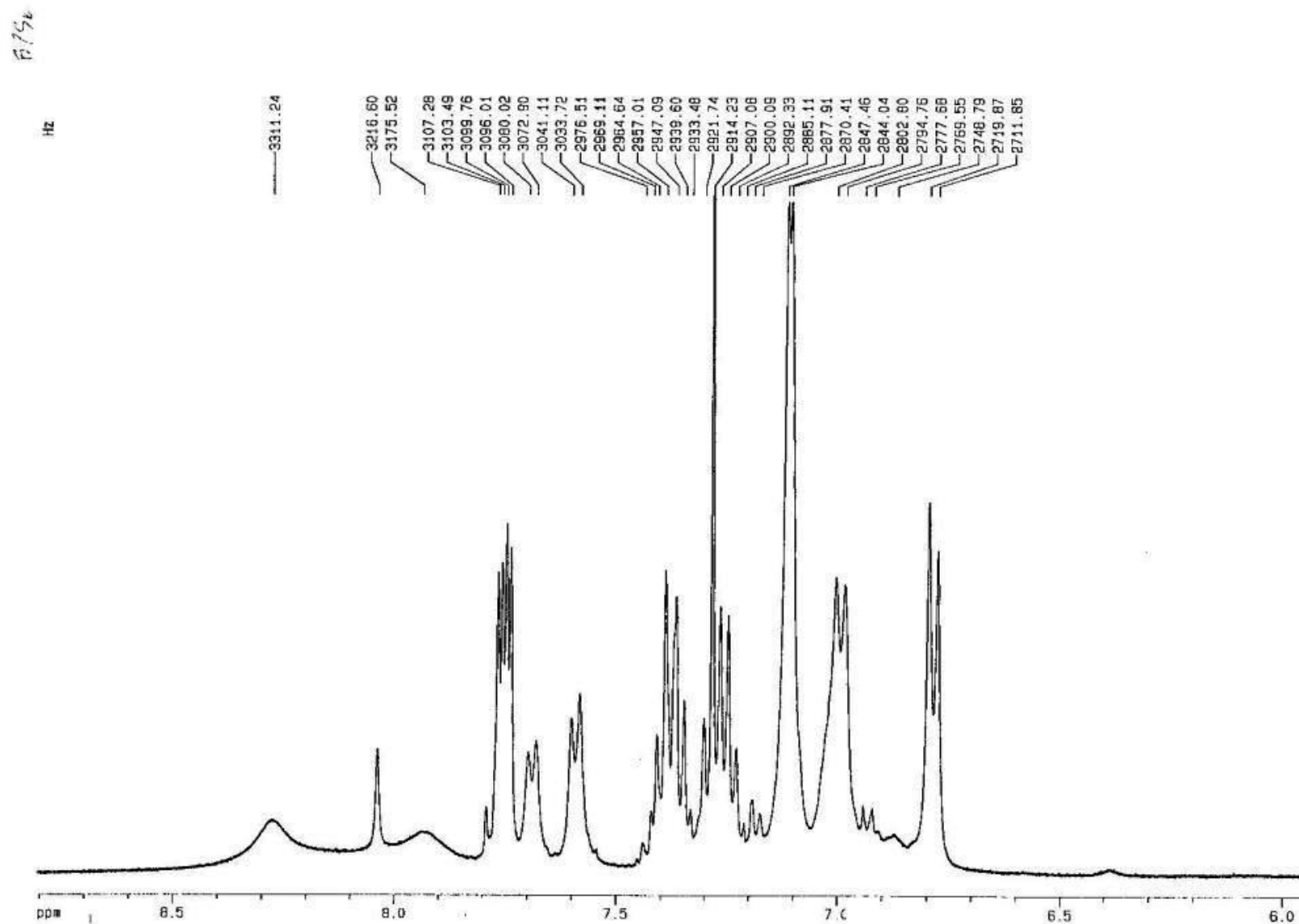
O-(*tert*-butyl)-*N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-L-tyrosylglycylglycyl-L-phenylalanyl-L-leucinate (**21**) ^1H NMR (400 MHz, CDCl_3)

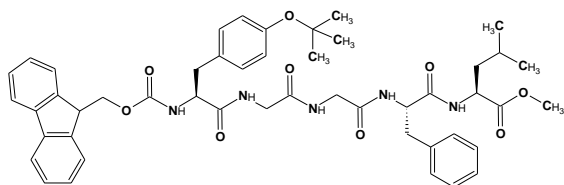
0756



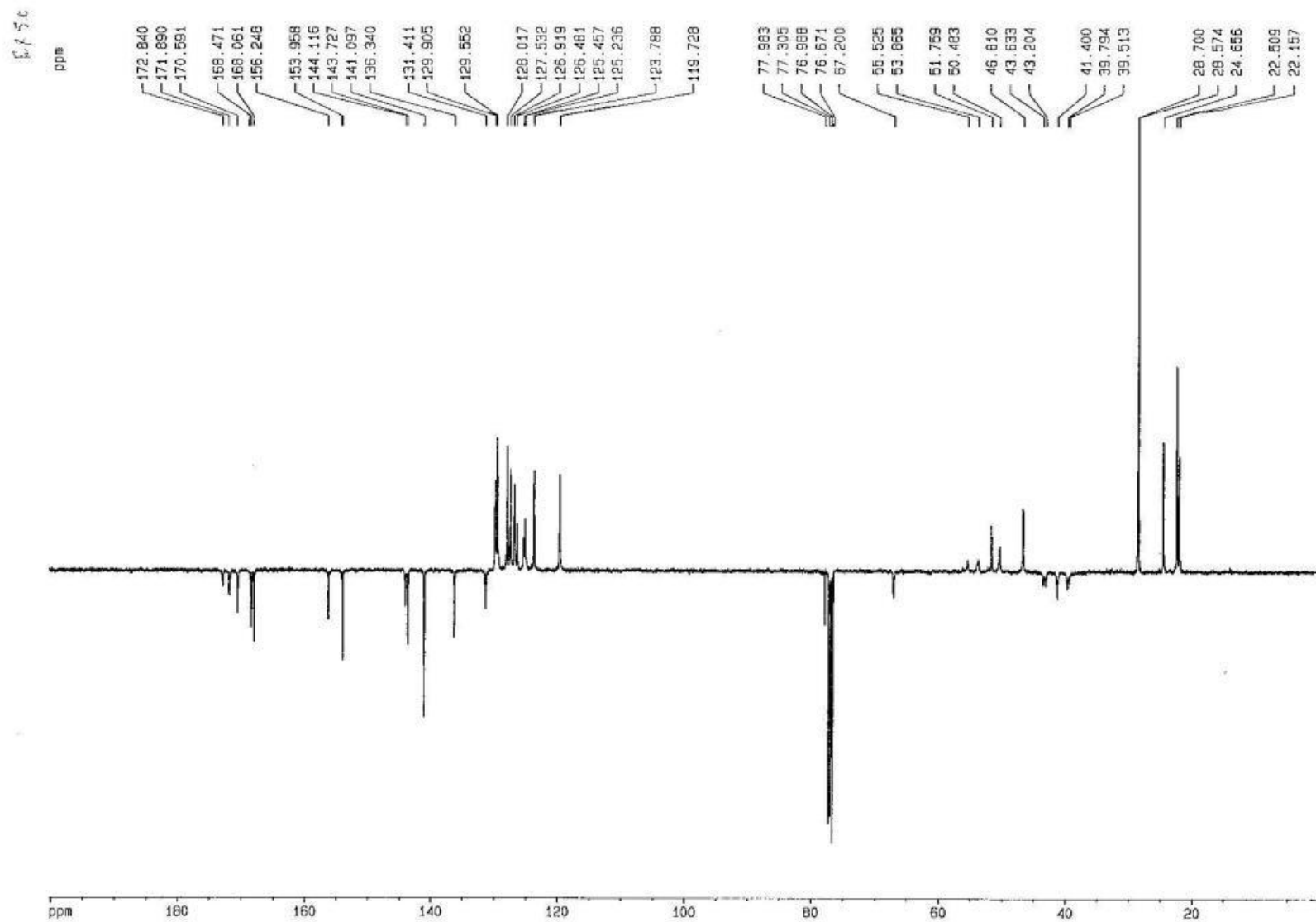


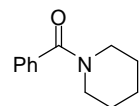
O-(*tert*-butyl)-*N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-L-tyrosylglycylglycyl-L-phenylalanyl-L-leucinate (**21**) ^1H NMR (400 MHz, CDCl_3)





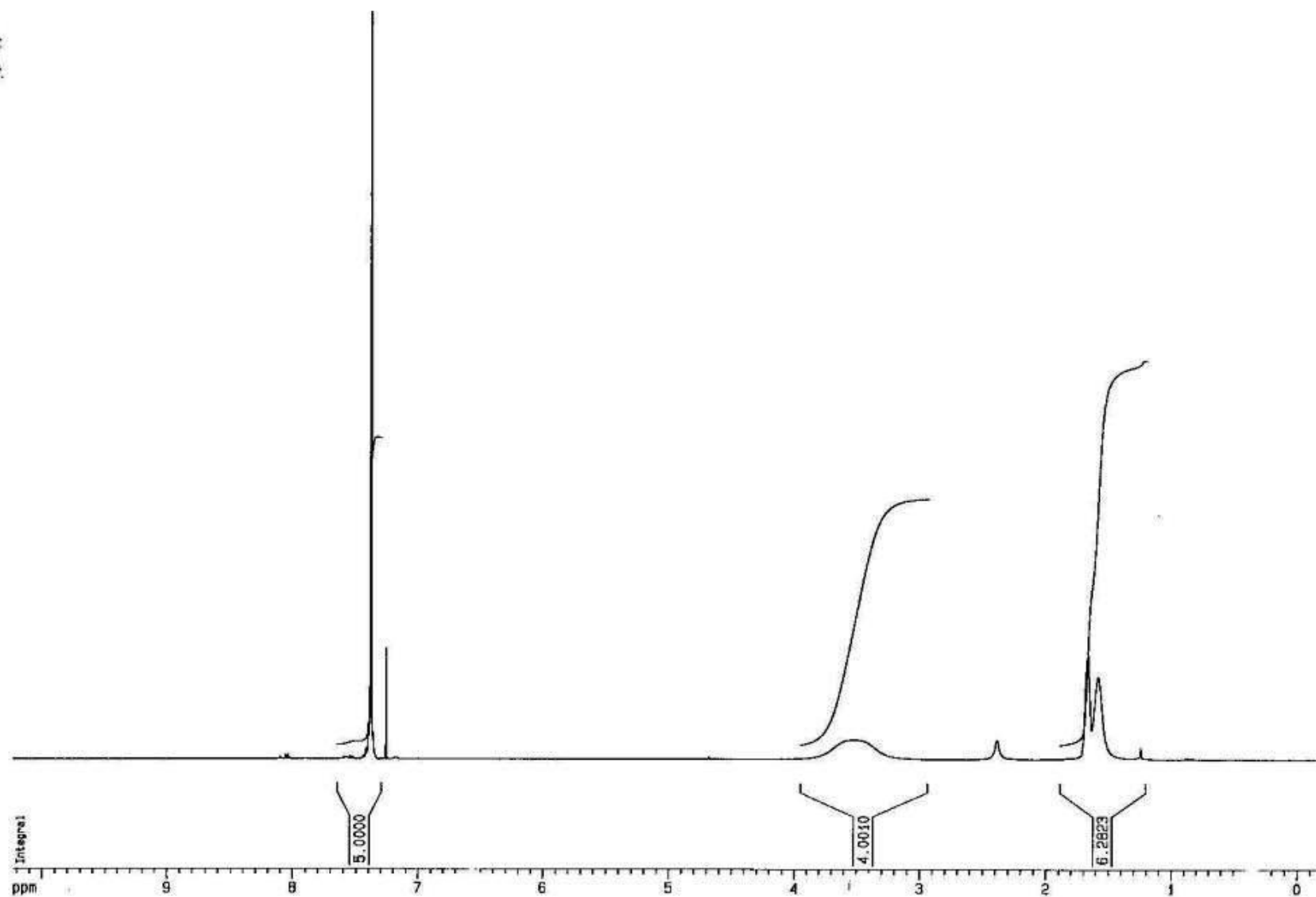
O-(*tert*-butyl)-*N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-*L*-tyrosylglycylglycyl-*L*-phenylalanyl-*L*-leucinate (**21**) ^{13}C NMR (100 MHz, CDCl_3)

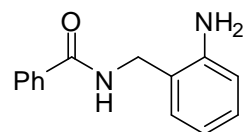




1- benzoylpiperidine (**22**) ^1H NMR (200 MHz, CDCl_3)

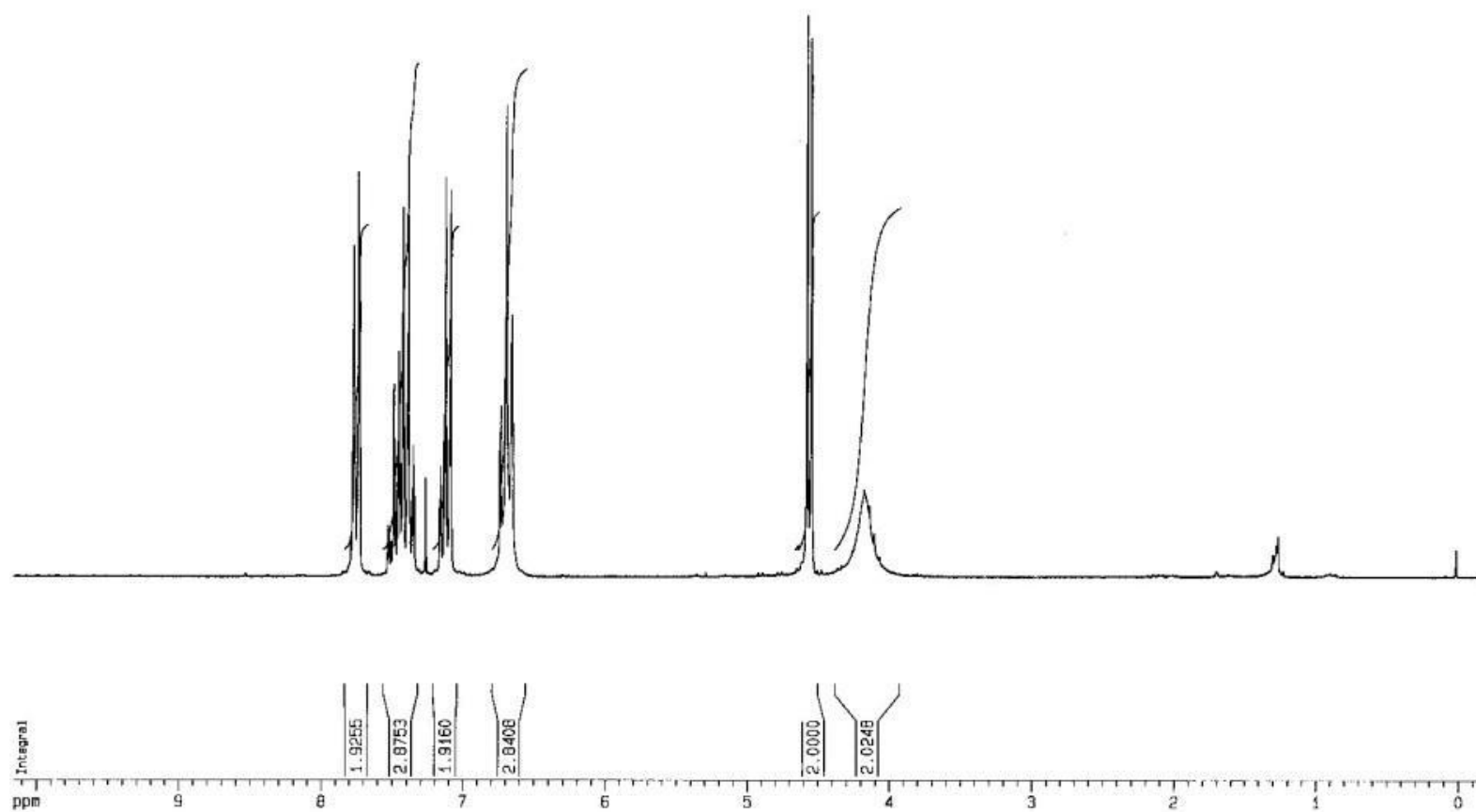
5805

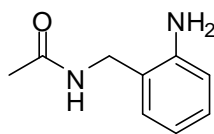




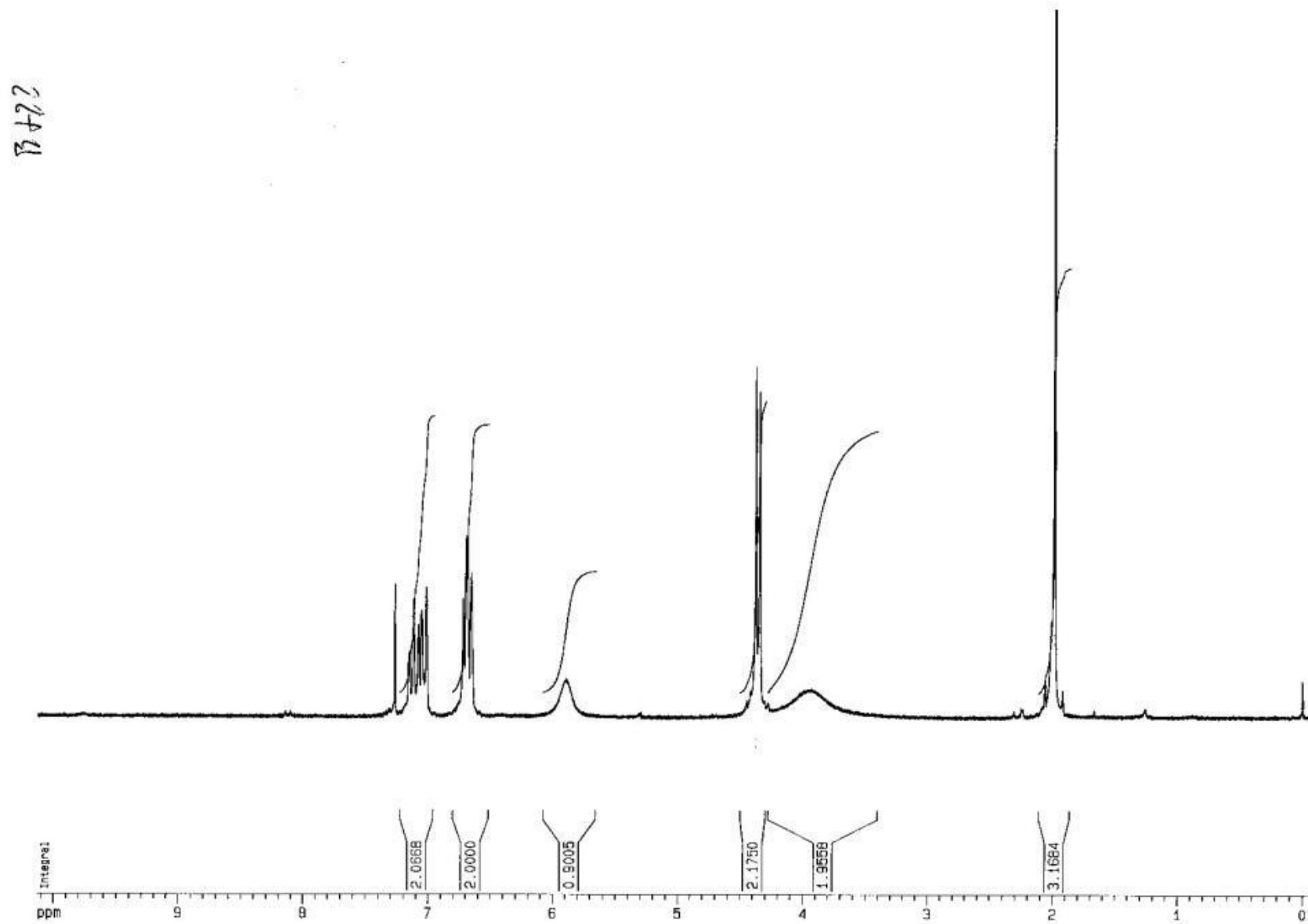
Amide **23** ^1H NMR (200 MHz, CDCl_3)

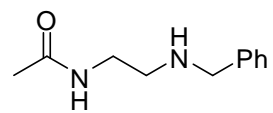
6845
5789



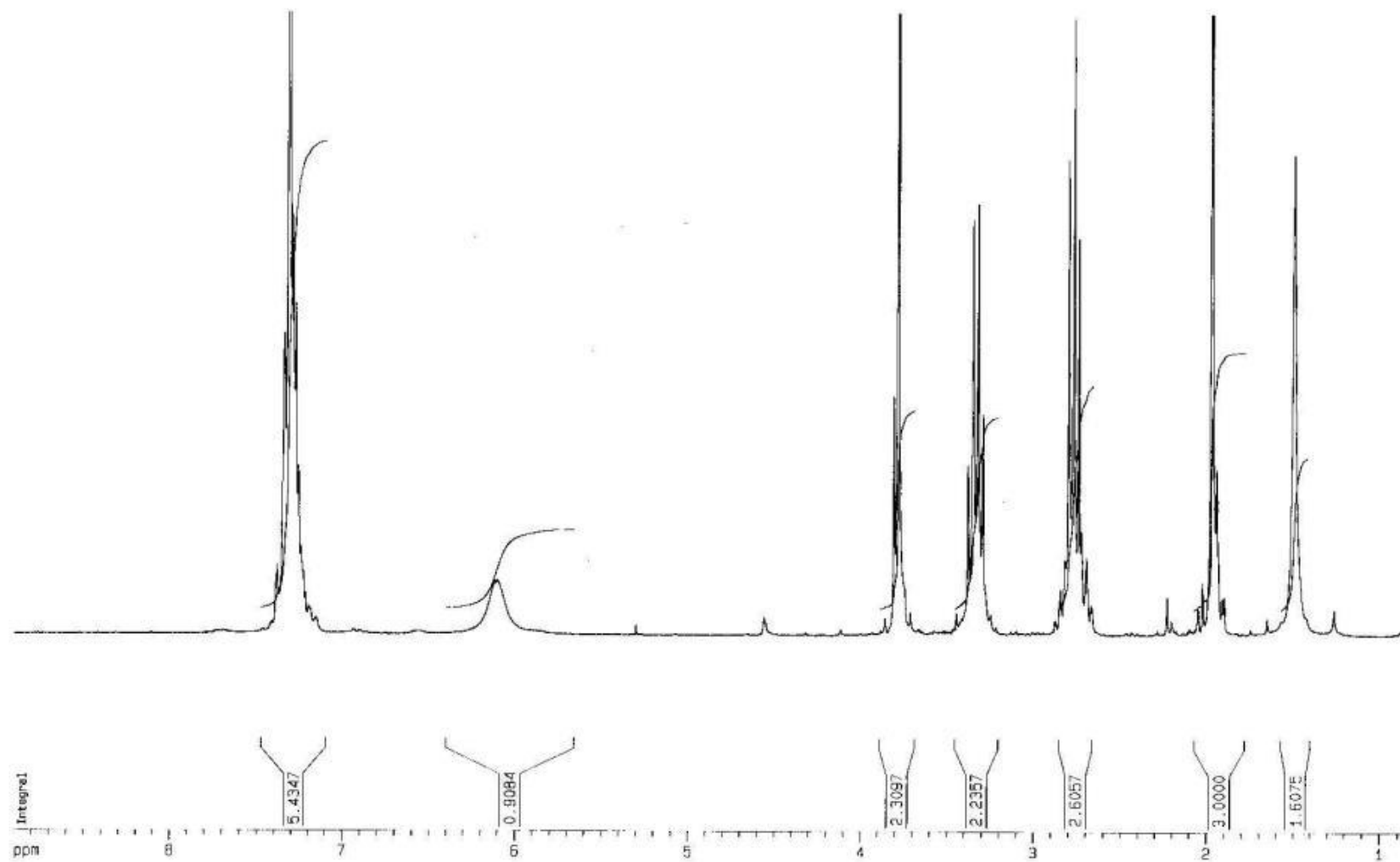


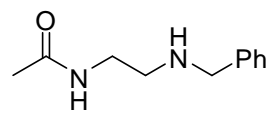
Amide **24** ^1H NMR (200 MHz, CDCl_3)



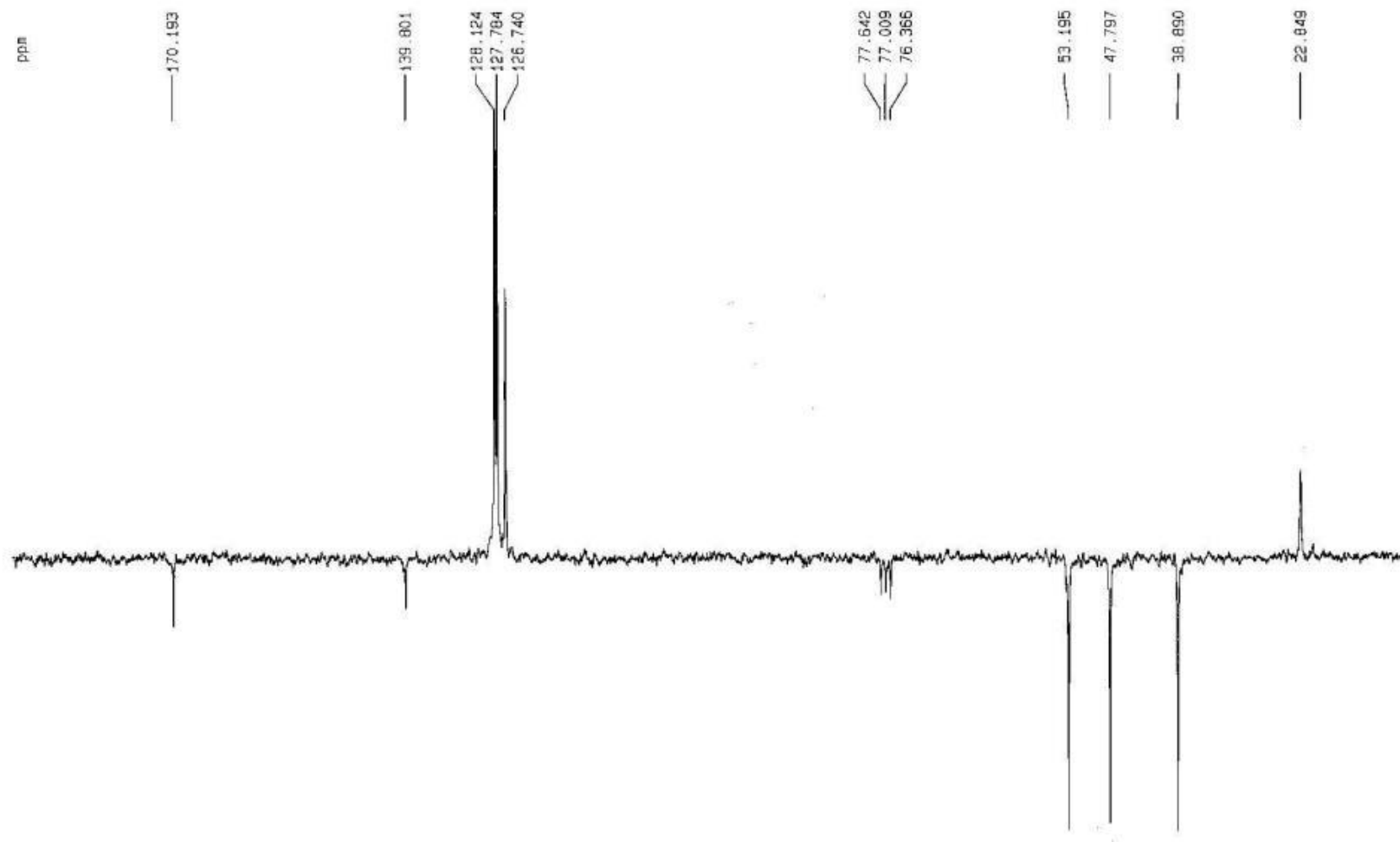


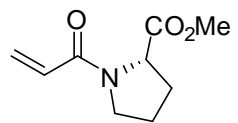
Amide **25** ^1H NMR (200 MHz, CDCl_3)



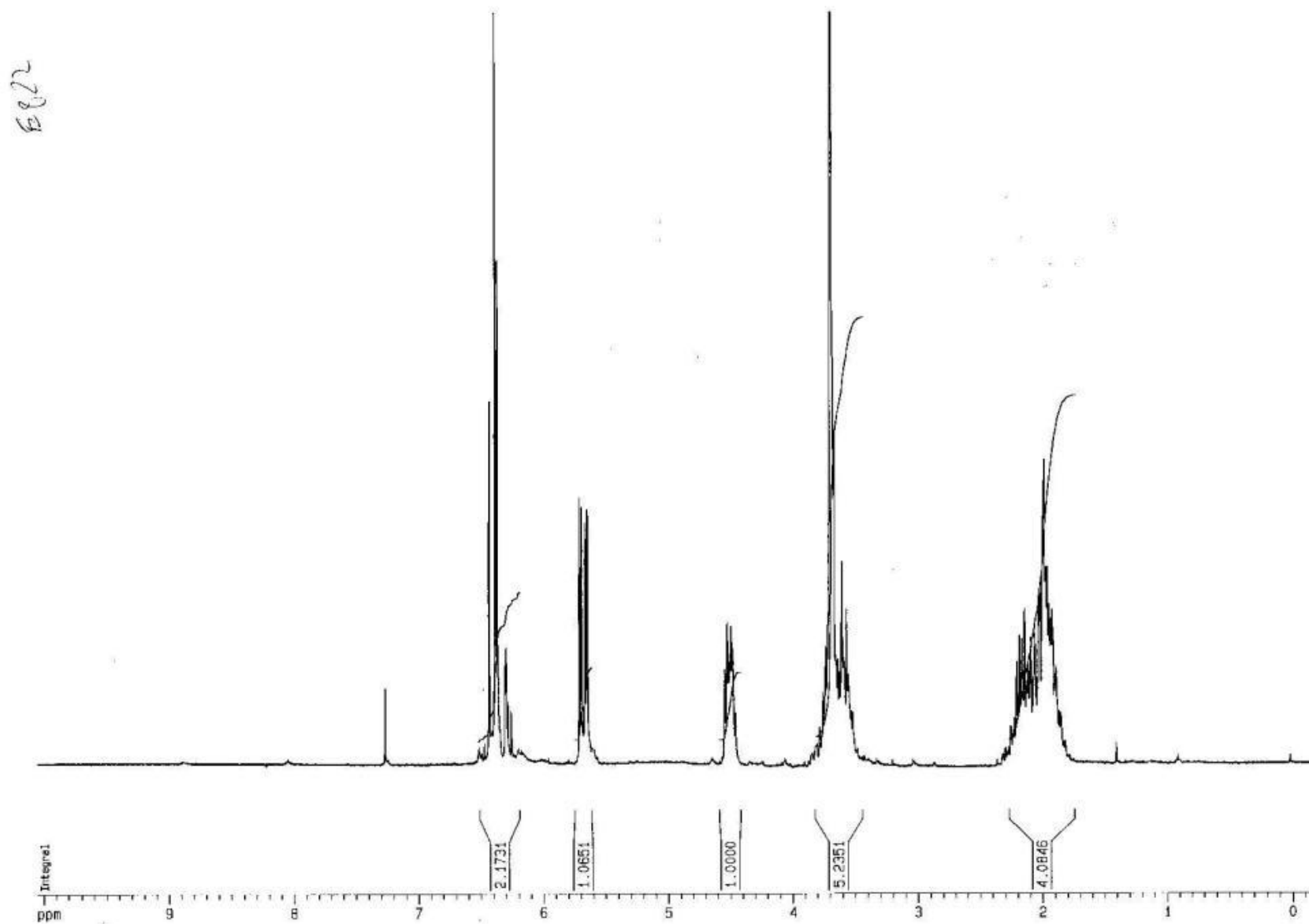


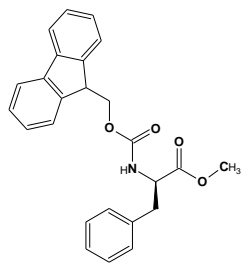
Amide **25** ^{13}C NMR (50 MHz, CDCl_3)





N-acryloyl-proline methyl ester **26** ^1H NMR (200 MHz, CDCl_3)





(*R*) Methyl N-[(9H-fluoren-9-ylmethoxy)carbonyl]-phenylalaninate ^1H NMR (200 MHz, CDCl_3)

