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Supporting Information

for the article

First principles design of derivatizing agent for direct determination of enantiomeric purity of chiral alcohols and amines by NMR spectroscopy

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CONTENTS

1. Theoretical calculations

The calculations were performed with B3LYP hybrid density functional method [1] using standard 6-31G and 6-311G basis sets [2]. No symmetry restrictions were applied in the calculations. NMR chemical shifts were calculated within GIAO (Gauge-Independent Atomic Orbital) approach [3] as implemented in the Gaussian 03 program [4]. Geometry optimization was carried out at the B3LYP/6-31G(d) level; GIAO calculations of the NMR chemical shifts were carried out at the B3LYP/6-311+G(2d,p) level. In the previous studies it was established that density functional level reasonably well describes NMR chemical shifts [5].

The $\Delta\delta_x$ values were calculated as a difference between the chemical shifts of the pure CDA and corresponding complex with analyzed substrate. Schematic representation of the complex is shown in Table 1 of the article. The $X(CH_3)_4$ and H_3C-Z-R were used as models of the CDA and substrate (R=CH_3). Distance (d) was fixed for all complexes for the purpose of comparison; all other geometry parameters were fully optimized.

The aim of these model calculations was not to give exact description of the diastereomers structures, but to provide an estimation of the upper limit of the $\Delta\delta_x$ values.

[1] (a) A. D. Becke, *Phys.Rev. A*, **1988**, *38*, 3098-3100. (b) C. Lee, W. Yang, R. G. Parr, *Phys.Rev. B,* **1988**, *37*, 785-789. (c) A. D. Becke, *J.Chem.Phys.,* **1993**, 98, 5648-5652.
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[3] (a) K. Wolinski, J. F. Hilton, P. Pulay, *J. Am. Chem. Soc.*, **1990**, *112*, 8251-8260. (b) R. Ditchfield, *Mol. Phys.,* **1974**, *27*, 789-807. (c) J. R. Cheeseman, G. W. Trucks, T. A. Keith, M. J. Frisch, *J.Chem.Phys.,* **1996**, *104*, 5497-5509. (d) G. Rauhut, S. Puyear, K. Wolinski, P. Pulay, *J.Phys.Chem.,* **1996**, *100*, 6310-6316.
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[5] Selected recent examples: (a) S. G. Smith, R. S. Paton, J. W. Burton, J. M. Goodman, *J. Org. Chem.,* **2008**, *73*, 4053-4062. (b) G. Bifulco, P. Dambruoso, L. Gomez-Paloma, R. Riccio, *Chem. Rev.,* **2007**, *107*, 3744-3779. (c) J. Vaara, *Phys. Chem. Chem. Phys.,* **2007**, *9*, 5399-5418. (d) A. Bagno, F. Rastrelli, G. Saielli, *Chem.-Eur. J.,* **2006**, *12*, 5514-5525. (e) A. M. Sarotti, S. C. Pellegrinet, *J. Org. Chem.,* **2009**, *74*, 7254-7260. (f) S. G. Smith, J. M. Goodman, *J. Org. Chem.,* **2009**, *74*, 4597-4607. (g) V. P. Ananikov, *Centr. Eur. J. Chem.* (*CEJC),* **2004**, *2*, 196-213. (h) A. V. Afonin, D. V. Pavlov, I. A. Ushakov, E. Yu. Schmidt, A. I. Mikhaleva, *Magn. Reson. Chem.,* **2009**, *47*, 879-884.

2. NMR properties

Relative NMR sensitivity was estimated based on fundamental physical properties of the nuclei (summarized in Table S1) using previously described approach [1,2].

Table S1. Main NMR characteristics of the nuclei listed in Table 1 of the article [3].

X	Spin	Quadrupole moment, m^2	Magnetogyric Ratio, rad/s*T	Natural Abundance, %	Larmor Frequencies, MHz (at 11.7467 Tesla)	Relaxation properties
^{19}F	1/2	-	25.1623 x 10^7	100	470.592	[4]
^{1}H	1/2	-	26.7522 x 10^7	99.9885	500.13	[5]
^{77}Se	1/2	-	5.1254 x 10^7	7.63	95.382	[6]
^{31}P	1/2	-	10.8394 x 10^7	100	202.456	[7]

^{11}B	3/2	4.059 x 10^{-30}	8.5847 x 10^{7}	80.1	160.462	[8]
^{15}N	1/2	-	-2.7126 x 10^{7}	0.364	50.697	[9]
^{13}C	1/2	-	6.7283 x 10^{7}	1.07	125.758	[5]
^{29}Si	1/2	-	-5.3190 x 10^{7}	4.685	99.362	[10]
^{79}Br	3/2	30.5 x 10^{-30}	6.7256 x 10^{7}	50.69	125.302	[11]
^{35}Cl	3/2	-8.165 x 10^{-30}	2.6242 x 10^{7}	75.76	49.002	[11]
^{33}S	3/2	-5.0 x 10^{-30}	2.0534 x 10^{7}	0.75	38.390	[6]

[1] D. I. Hoult, *Sensitivity of the NMR Experiment*, in Encyclopedia of Nuclear Magnetic Resonance, D. M. Grant and R. K. Harris (Eds.), John Wiley & Sons Ltd, Chichester, England, 1996, vol. 3, p. 2063.
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[9] J. Mason, *Nitrogen NMR,* ibid, vol. 5, p.3222.
[10] H. C. Marsmann, *Silicon-29 NMR*, ibid, vol. 7, p. 4386.
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3. Synthetic procedures

3.1 General

Reagents were obtained from Acros and Aldrich and used as supplied (checked by NMR and GC before use). Solvents were purified according to published methods. The samples for reactions with developed CDA were prepared using chiral compounds of known enantiomeric content.

3.2 Preparation of (R)-ethyl 2-(phenylselanyl)propanoate (2)

Ester **2** was prepared according to the modified literature procedure [1, 2]:

Mixture of 0.675 ml (5.5 mmol) of PhSeCN and 1.499 ml (6.0 mmol) of PBu_3 were placed in a 25 ml round-bottomed flask under argon atmosphere followed by addition of 2.0 ml of toluene (orange solution was formed). Mixture was cooled to -5^{o}C and 0.571 ml (5.0 mmol) of L-ethyllactate was added dropwise over 30 min under stirring. The mixture was stirred for additional 10 min and the colour of the solution changed to yellow. Solvent

was removed under reduced pressure. *Caution! Due to hazardous nature of HCN evaporation should be carried out in an efficient fume hood and a proper attention should be paid to wastes disposal*.

Crude product **2** was purified by flash chromatography on silica (eluent – hexane). Isolated yield 93% (1.969 g). Light-yellow oil. The product was identified according to the published data [3].

[1] Grieco, P. A.; Gilman, S.; Nishizawa, M.; *J. Org. Chem.* **1976**, *41*, 1485.
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[3] Shea, R. G.; Fitzner, J. N.; Fankhauser, J. E.; Spaltenstein, A.; Carpino, P. A.; Peevey, R. M.; Pratt, D. V.; Tenge, B. J.; Hopkins, P. B.; *J. Org. Chem.* **1986**, *51*, 5243.

3.3 Preparation of (R)-2-phenylselenopropanoic acid (3)

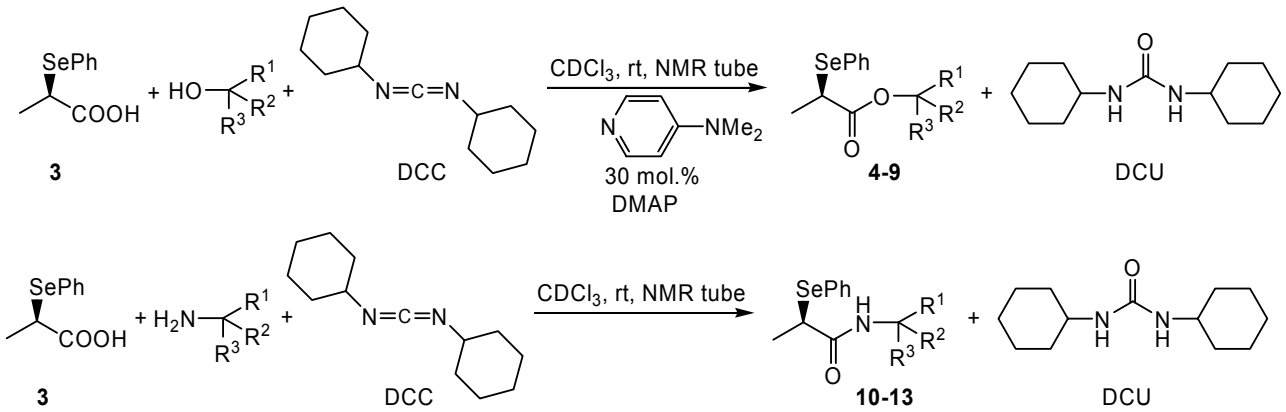
To a 25 ml round-bottomed flask, equipped with magnetic stirring, ester **2** and a mixture of 3.0 ml of glacial acetic acid and 6.0 ml of concentrated hydrochloric acid were added. Mixture was stirred at 100^{o}C for 3 hours [4]. Reaction mixture was cooled to rt, diluted by water and the product was extracted with Et_2O. Organic layer was washed with water (4x20 ml) to reach pH 5-6, dried over $MgSO_4$ followed by filtration and solvent removal under reduced pressure. Crude product **3** was purified by flash chromatography on silica (eluent – hexane/ethylacetate). Isolated yield 86% (0.916 g), 93 % e.e. Light-yellow oil. The product was identified according to the published data [1].

[1] Michelsen, P.; Annby, U.; Gronowitz, S.; *Chemica Scripta* **1984**, *24*, 251.

4. Typical procedure of derivatization of the samples of chiral alcohols and amines

0.020 g (8.7 x 10^{-5} mol) of **3** was placed in a NMR tube followed by addition of 0.6 ml of $CDCl_3$. About 8 x 10^{-5} mol of corresponding alcohol or amine, 1.0 x 10^{-4} mol of DCC and 2.6 x 10^{-5} mol of DMAP (in the case of alcohols) were subsequently added to the NMR tube followed by additional 0.2 ml of $CDCl_3$. Corresponding reactions involving alcohols and amines are shown on Scheme S1.

Mixture was shaken for 1 min and kept at rt until solid particles floated to the top of the liquid layer (0.5-3 h). A series of pictures monitoring the complete procedure are shown of Figure S1. The ^{1}H, ^{13}C and ^{77}Se NMR spectra were recorded directly in the NMR tube.



Scheme S1. The reaction of CDA **3** with alcohols and amines (DCC - N,N'-dicyclohexyl-carbodiimide; DCU - N,N'-dicyclohexylurea; DMAP - 4-dimethylaminopyridine)

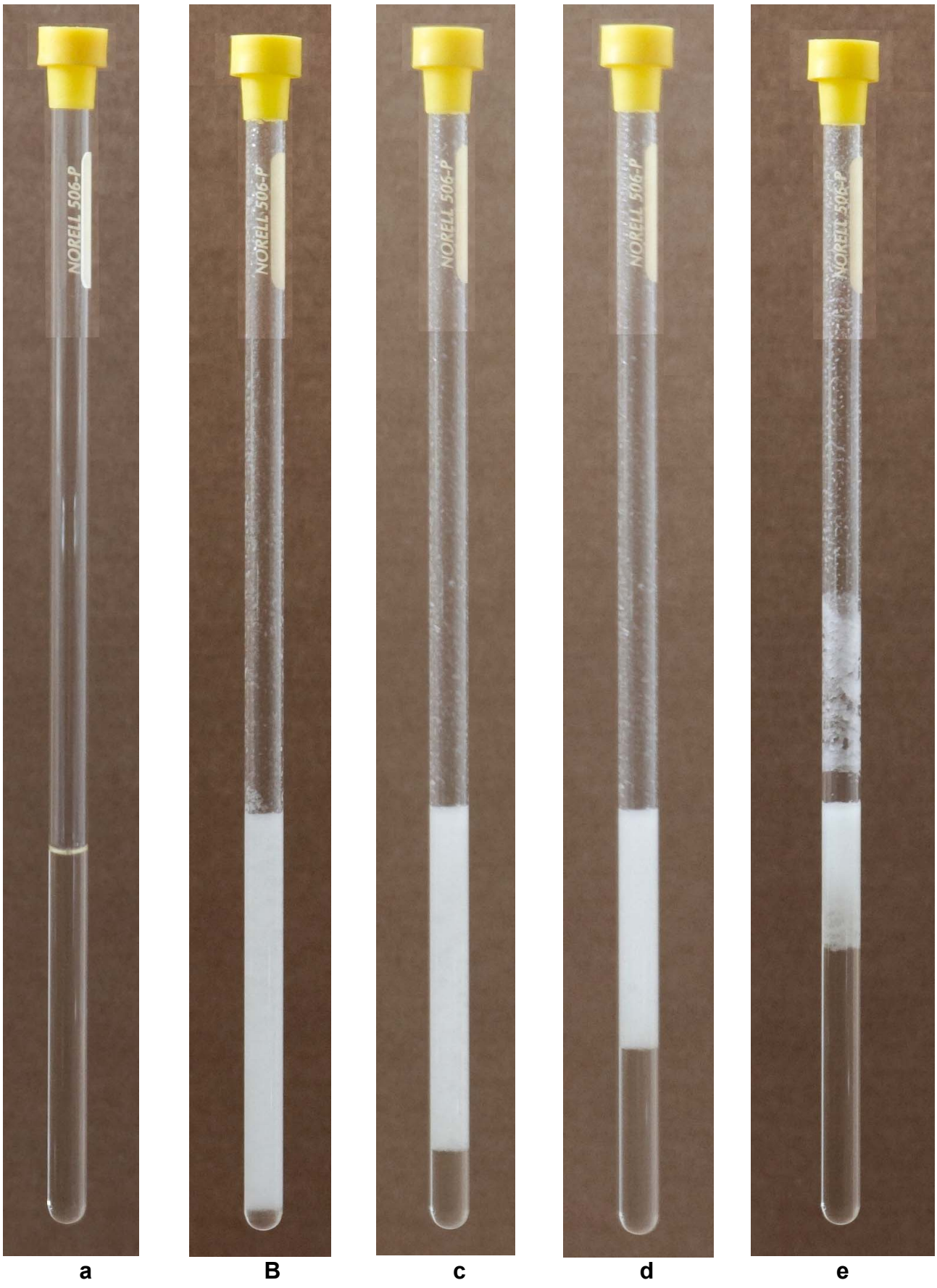


Figure S1. Pictures of the NMR tube: **a** – solution of **3** in $CDCl_3$; **b** – after addition of analyzed sample, DCC/DMAP and shaking for 1 min; **c** – after standing for 10 min; **d** – after standing for 20 min; **e** – after standing for 30 min.

5. Description of the NMR experiments

5.1 General

The NMR measurements were performed using Bruker Avance NMR spectrometers operating at 600, 500 and 300 MHz (^{1}H). The spectra were processed on a Linux workstation using TopSpin 2.1 software package. All 2D spectra were recorded using inverse triple resonance probehead with active shielded Z-gradient coil. ^{1}H and ^{13}C chemical shifts are reported relative to the corresponding solvent signals used as internal reference; external reference $Ph_2Se_2/CDCl_3$ δ=463.0 ppm (capillary insert) was used for ^{77}Se spectra.

Full assignment of signals of all studied compounds was made using 2D LR-COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC and ^{1}H-^{77}Se HMQC NMR experiments. The complete NMR data are given in Section 8 of the supporting information

5.2 Experimental setup and processing of 1D ^{77}Se NMR data

The spectrum was collected in the ^{77}Se observation and ^{1}H decoupling mode. A standard waltz16 decoupling was applied in this ^{77}Se{^{1}H} experiment. Spectral parameters: ^{77}Se 30° pulses of 4.2 μs, a relaxation delay of 1 - 2 s, a 1.0 s acquisition time, 256 – 1024 transients and 45000 Hz spectral window. The data was zero filled to 32k matrix and processed with exponential multiplication (LB=2-5).

For the samples analyzed in the present study experimental time for recording 1D ^{77}Se spectra with good signal to noise ratio was 10-40 min.

5.3 Experimental setup and processing of 2D ^{1}H- ^{77}Se HMQC NMR data

The spectrum was collected with ^{1}H and ^{77}Se 90° pulses of 12.5 μs and 16.0 μs respectively, a relaxation delay of 2s, $\Delta=(2* J_{H\text{-}Se})^{-1}$=250 ms (optimized for long range coupling constant of 2 Hz), a 0.3 s acquisition time and 4500 and 50000 Hz spectral windows for the ^{1}H(F2) and ^{77}Se(F1) dimensions correspondingly. Typically 2 - 8 transients were averaged for each of 256 increments on t_1. The data was zero filled to 2048x2048 matrix and processed with QSINE(SSB=2) window function for both F2 and F1 dimensions. The 1 ms sine shaped pulse field gradient pulses with the ratio 50.0 : 30.0 : 35.3 (%) followed with 100 μs recovery delay were applied.

For the samples analyzed in the present study experimental time for recording 2D spectra was 5-15 min.

5.4 Signal assignment utilizing 2D ^{1}H- ^{77}Se HMQC NMR

Since the signals in the ^{77}Se NMR are well separated, two dimensional correlation with the proton chemical shifts provides the key-points for the signal assignment. An example of the 2D HMQC spectrum is shown on Figure S2. After identification of the key signals of both diastereomers in the aromatic and aliphatic parts of the spectrum (Figure S3), the routine line assignment with standard NMR protocols was applied [1, 2].

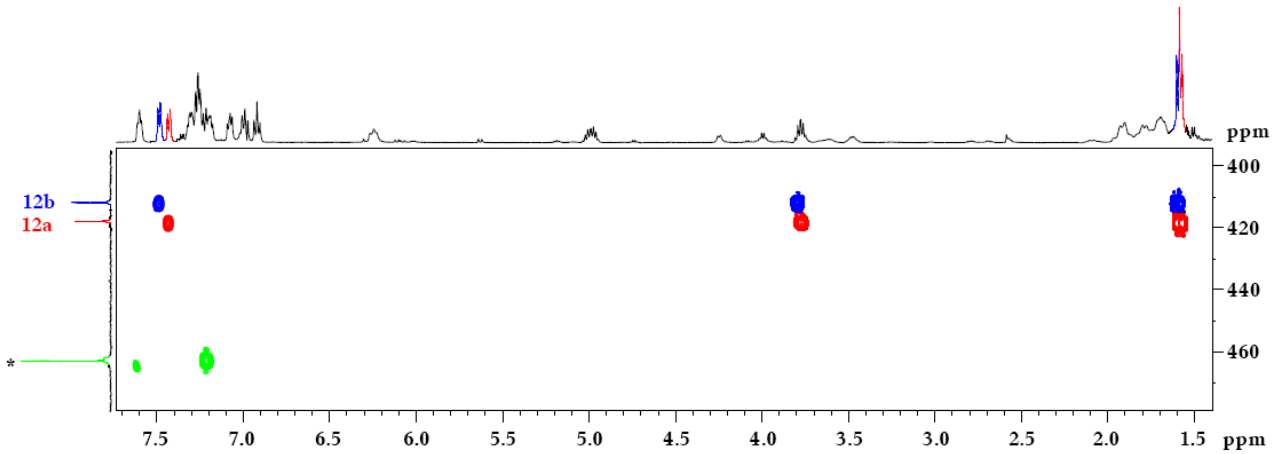


Figure S2. Two-dimensional ^{1}H – ^{77}Se HMQC NMR spectrum of the diastereomers **12a** and **12b** (vertical axis – ^{77}Se, horizontal axis – ^{1}H); green color – Ph_2Se_2 chemical shifts standard (capillary).

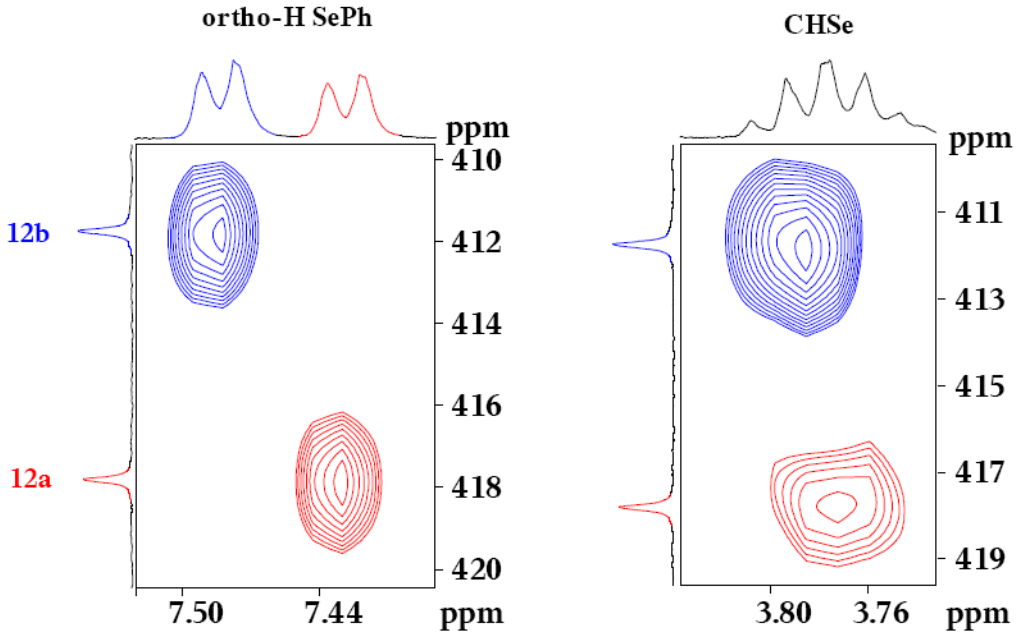


Figure S3. Two regions of the ^{1}H – ^{77}Se HMQC NMR spectrum of the diastereomers **12a** and **12b** showing cross-peaks in the aromatic and aliphatic parts of the spectrum (vertical axis – ^{77}Se, horizontal axis – ^{1}H).

[1] Kwan, E. E.; Huang, S. G.; *Eur. J. Org. Chem.* **2008**, 2671 – 2688.
[2] Friebolin H., *Basic One- and Two-Dimensional NMR Spectroscopy*, Wiley-VCH, 2005.

6. General procedure for determination of enantiomeric purity

To determine the enantiomeric purity of the samples complete line assignment was not required. The 1D ^{77}Se NMR spectra were recorded as described in Section 5.2 and the signals of the diastereomers were integrated (*I1* and *I2* denote the integral values in the formulas below). Integration of the external standard Ph_2Se_2 was not required, since it was used for chemical shifts calibration only.

For enantiomerically pure samples only one signal was observed in the ^{77}Se NMR spectrum, for a racemate two signals of equal intensity (i.e. 1 : 1) were measured. Using

the measured integral values *I1* and *I2* the following parameters were calculated for the mixtures:

- diastereomers ratio: *I1* : *I2*
- the content of the mixture (%): (*I1* / (*I1* + *I2*)) * 100 and (*I2* / (*I1* + *I2*)) * 100
- diastereomeric excess (*de, %*): *de* = ((*I1* - *I2*) / (*I1* + *I2*)) * 100

In all studied cases the measured ratios of diastereomers were found equal to the corresponding ratios of enantiomers in the initial samples (chiral compounds of known enantiomeric content were utilized to prepare the initial samples for such measurements). The series of measurements have shown neither kinetic resolution (different rate of reaction of enantiomeric pair of alcohols or amines with acid **3**) nor incomplete reaction with the acid **3** (no signals of free alcohols or amines was observed in ^{1}H and ^{13}C NMR spectra after derivatization procedure). Therefore, the above calculated parameters reflect the ratio of enantiomers, enantiomeric content of the mixture and enantiomeric excess in the chiral sample. In all studied cases the accuracy of the measurements was very high with the average error <2%.

7. The measured Δδ values in ^{1}H, ^{13}C and ^{77}Se NMR spectra of diastereomers 4 – 13

The summary of measured Δδ values is presented in Table S2. For comparative purpose the corresponding Δδ values measured using the Mosher's acid are shown in Table S3. Signals separation in ^{77}Se NMR was superior in all studied samples. In addition, the developed reagent showed very good signals separation in the ^{1}H and ^{13}C NMR as well.

Table S2. The differences in the chemical shifts of diastereomers **4-13** in ^{1}H, ^{13}C and ^{77}Se NMR spectra (See Chart 1 in the article for structural summary).[a]

Compound	Δδ ^{1}H, ppm	Δδ ^{13}C, ppm	Δδ ^{77}Se, ppm
4	0.158 (*o*-H SePh) 0.064 (CHSe) 0.015 (OMe)	0.268 (CHSe) 0.113 (CHO)	2.645
5	0.152 (*o*-H SePh) 0.069 (CHSe)	0.254 (CHSe) 0.119 (CHO)	2.280
6	0.016 (MeCHO)	0.753 (CHSe)	0.459
7	0.059 (MeCHO)	0.359 (CHSe) 0.213 (MeCHO) 0.071 (MeCHSe)	2.156
8	0.107 (MeCHO) 0.092 (MeCHSe) 0.075 (CHO)	0.365 (MeCHSe) 0.287 (CHSe) 0.147 (MeCHO) 0.079 (CHO)	0.144

9	0.106 (MeCHO) 0.092 (CHSe) 0.070 (CHO) 0.022 (OMe)	0.340 (MeCHSe) 0.318 (CHSe) 0.146 (MeCHO) 0.099 (CHO)	0.429
10	0.022 (MeCHN)	0.097 (*o*-C SePh) 0.092 (MeCHSe) 0.056 (CHSe)	2.653
11	0.112 (NH) 0.075 (*o*-H SePh)	0.141 (MeCHN) 0.099 (MeCHSe)	1.601
12	0.056 (*o*-H SePh)	0.196 (*o*-C SePh) 0.165 (CHSe) 0.085 (MeCHSe)	6.064
13	0.088 (*m*-H SePh) 0.057 (*o*-H SePh)	0.196 (*o*-C SePh)	2.313

[a] Only completely resolved signals are listed (overlapping signals between the diastereomers or overlapping with other components of the mixture are excluded, see Section 9 for complete data).

Table S3. The differences in the chemical shifts of diastereomers **4'-13'** obtained with the Mosher's acid (α-methoxy-α-trifluoromethylphenylacetic acid, MTPA) instead of acid **3**.[a,b]

Compound	Δδ ^{1}H, ppm	Δδ ^{13}C, ppm	Δδ ^{19}F, ppm
4'	0.02 (CHO in MTPA) 0.145 (COOMe) 0.16 (OMe in MTPA)	-	0.30
5'	0.024 (CHO) 0.146 (OMe in MTPA)	0.054 (CHO) 0.03 (MeCH_2) 0.058 (MeCH_2)	0.29
6'	0.13 (OMe in MTPA) 0.08 (CHOCF_3)	-	0.26
7'	0.13 (MeCH_2) 0.09 (MeCHO)	0.3 (MeCH_2) 0.4 (MeCHO) 0.1 (OMe in MTPA)	-
8'	0.079 (MeCHO) 0.110 (MeCH_2)	-	0.45
9'	0.08 (OMe in MTPA)	-	-
11'	0.01 (CHN) 0.08 (NH) 0.12 (OMe) 0.08 (MeCHN)	-	0.18
13'	-	-	0.29

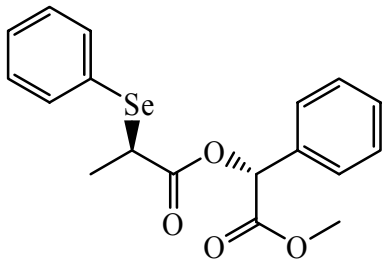
[a] For derivatization with the Mosher's acid see: (a) Y. Takeuchi, N. Itoh, T. Satoh, T. Koizumi, K. Yamaguchi, *J. Org. Chem.*, **1993**, 58, 1812. (b) F. Yasuhara, S. Yamaguchi, *Tetrahedron Lett.*, **1980**, 21, 2827. (c) A. Ohno, J.-i. Nakai, K. Nakamura,

T. Goto, S. Oka, *Bull. Chem. Soc. Jpn.*, **1981**, 54, 3486. (d) Y. Takeuchi, N. Itoh, S.-i. Kawahara, T. Koizumi, *Tetrahedron*, **1993**, 49, 1861. (e) S. K. Latypov, J. M. Seco, E. Quinoa, R. Riguera, *J. Org. Chem.*, **1996**, 61, 8569. (f) G.R. Sullivan, J.A. Dale, H.S. Mosher, *J. Org. Chem.*, **1973**, 38, 2143. (g) D.R.J. Hose, M.F. Mahon, K.C. Molloy, T. Raynham, M. Wills, *J. Chem. Soc., Perkin Trans. 1*, **1996**, 691.

[b] The experimental protocol developed in the present study (Section 4 of Supporting Information) was also applicable in this case.

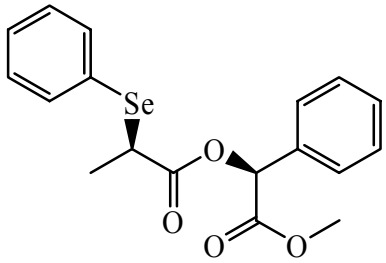
8. Spectral data for the studied compounds

(R)-((R)-2-methoxy-2-oxo-1-phenylethyl) 2-(phenylselanyl)propanoate (**4a**)



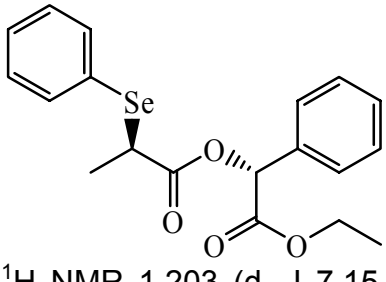
^{1}H NMR 1.583 (d, J 7.32, MeCHSe, 3H); 3.706 (s, OMe, 3H); 3.922 (q, J 7.32, CHSe, 1H); 5.880 (s, CHO, 1H); 7.147-7.188 (m, 2H, meta-H SePh); 7.229-7.283 (m, 1H, para-H SePh); 7.363 (br. s, 5H, Ph); 7.471-7.504 (m, 2H, ortho-H SePh). ^{13}C NMR 17.624 (MeCHSe); 36.602 (CHSe); 52.710 (OMe); 74.866 (CHO); 127.691 (meta-C Ph); 128.690 (para-C SePh); 128.802 (ortho-C Ph); 129.042 (meta-C SePh); 129.309 (para-C Ph); 133.684 (ipso-C Ph); 136.019 (ortho-C SePh); 169.263 (COOMe); 173.002 (COO). ^{77}Se NMR 458.148.

(R)-((S)-2-methoxy-2-oxo-1-phenylethyl) 2-(phenylselanyl)propanoate (**4b**)



^{1}H NMR 1.600 (d, J 7.32, MeCHSe, 3H); 3.721 (s, OMe, 3H); 3.858 (q, J 7.32, CHSe, 1H); 5.880 (s, CHO, 1H); 7.229-7.283 (m, 3H, meta-, para-H SePh); 7.353 (br. s, 5H, Ph); 7.632-7.659 (m, 2H, ortho-H SePh). ^{13}C NMR 17.653 (MeCHSe); 36.870 (CHSe); 52.682 (OMe); 74.979 (CHO); 127.691 (meta-C Ph); 128.605 (para-C SePh); 128.830 (ortho-C Ph); 129.106 (meta-C SePh); 129.309 (para-C Ph); 133.752 (ipso-C Ph); 135.964 (ortho-C SePh); 169.063 (COOMe); 172.895 (COO). ^{77}Se NMR 455.503.

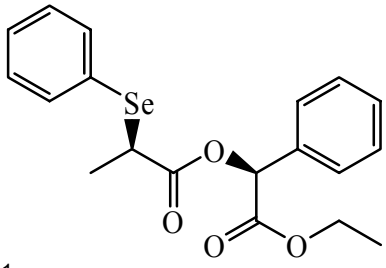
(R)-((R)-2-ethoxy-2-oxo-1-phenylethyl) 2-(phenylselanyl)propanoate (**5a**)



^{1}H NMR 1.203 (d, J 7.15, Me, 3H); 1.585 (d, J 7.16, MeCHSe, 3H); 3.924 (q, J 7.16, CHSe, 1H); 4.108-4.255 (m, CH_2O, 2H); 5.857 (s, CHO, 1H); 7.242-7.278 (m, 2H, meta-H

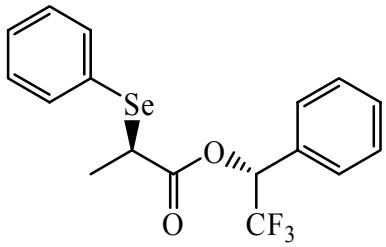
SePh); 7.284-7.337 (m, 1H, para-H SePh); 7.336-7.387 (m, Ph, 5H); 7.479-7.512 (m, 2H, ortho-H SePh). ^{13}C NMR 14.094 (Me); 17.696 (MeCHSe); 36.645 (CHSe); 61.798 (CH_2O); 74.994 (CHO); 127.642 (meta-C Ph); 128.663 (para-C SePh); 128.734 (ortho-C Ph); 129.085 (meta-C SePh); 129.127 (para-C Ph); 133.867 (ipso-C Ph); 135.992 (ortho-C SePh); 168.740 (COOEt); 173.002 (COO). ^{77}Se NMR 457.349.

(R)-((S)-2-ethoxy-2-oxo-1-phenylethyl) 2-(phenylselanyl)propanoate (**5b**)



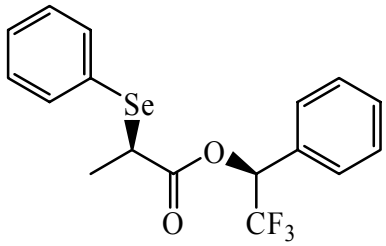
^{1}H NMR 1.222 (d, J 7.15, Me, 3H); 1.601 (d, J 7.16, MeCHSe, 3H); 3.855 (q, J 7.16, CHSe, 1H); 4.108-4.255 (m, CH_2O, 2H); 5.857 (s, CHO, 1H); 7.149-7.190 (m, 2H, meta-H SePh); 7.284-7.337 (m, 1H, para-H SePh); 7.336-7.387 (m, Ph, 5H); 7.630-7.665 (m, 2H, ortho-H SePh). ^{13}C NMR 14.123 (Me); 17.654 (MeCHSe); 36.899 (CHSe); 61.798 (CH_2O); 75.113 (CHO); 127.642 (meta-C Ph); 128.564 (para-C SePh); 128. 763 (ortho-C Ph); 129.028 (meta-C SePh); 129.127 (para-C Ph); 133.797 (ipso-C Ph); 135.936 (ortho-C SePh); 168.572 (COOEt); 172.887 (COO). ^{77}Se NMR 455.069.

(R)-((R)-2,2,2-trifluoro-1-phenylethyl) 2-(phenylselanyl)propanoate (**6a**)



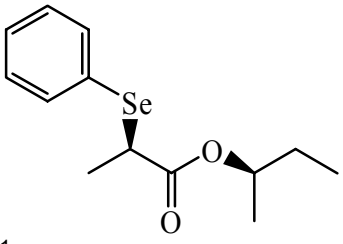
^{1}H NMR 1.549 (d, J 6.96, MeCHSe, 3H); 3.855 (q, J 6.96, CHSe, 1H); 6.085 (q, J 6.89, CHO, 1H); 7.240-7.277 (m, meta-H SePh, 2H); 7.277-7.302 (m, para-H SePh, 1H); 7.302-7.348 (m, 2H, ortho-H SePh); 7.374-7.448 (m, Ph, 5H). ^{13}C NMR 17.513 (MeCHSe); 36.759 (CHSe); 72.415 (qu, J_F 33.94, CHO); 128.257 (meta-C Ph); 128.733 (meta-C SePh); 128.873 (para-C SePh); 129.127 (ortho-C Ph); 130.013 (para-C Ph); 135.964 (ortho-C SePh); 171.344 (COO). ^{77}Se NMR 459.755.

(R)-((S)-2,2,2-trifluoro-1-phenylethyl) 2-(phenylselanyl)propanoate (**6b**)



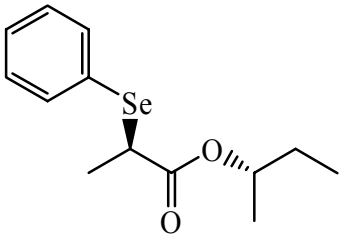
^{1}H NMR 1.565 (d, J 6.96, MeCHSe, 3H); 3.819 (q, J 6.96, CHSe, 1H); 6.122 (q, J 6.89, CHO, 1H); 7.166-7.200 (m, meta-H SePh, 2H); 7.302-7.348 (m, para-H SePh, 1H); 7.374-7.448 (m, Ph, 5H); 7.508-7.536 (m, 2H, ortho-H SePh). ^{13}C NMR 17.513 (MeCHSe); 36.006 (CHSe); 72.614 (qu, J_F 33.94, CHO); 128.386 (meta-C SePh); 128.784 (meta-C Ph); 128.873 (para-C SePh); 129.204 (ortho-C Ph); 129.970 (para-C Ph); 136.006 (ortho-C SePh); 171.415 (COO). ^{77}Se NMR 459.296.

(R)-((R)-sec-butyl) 2-(phenylselanyl)propanoate (**7a**)



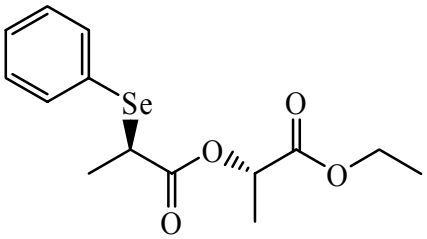
^{1}H NMR 0.863 (t, J 7.35, Me, 3H); 1.115 (d, J 6.27, MeCHO, 3H); 1.449-1.524 (m, CH_2O, 2H); 1.544 (d, J 7.07, MeCHSe, 3H); 3.765 (q, J 7.07, CHSe, 1H); 4.776-4.851 (m, CHO, 1H); 7.260-7.337 (m, meta-, para-H, 3H); 7.580-7.615 (m, ortho-H, 2H). ^{13}C NMR 9.698 (Me); 17.866 (MeCHSe); 19.158 (MeCHO); 28.799 (CH_2); 37.892 (CHSe); 73.082 (CHO); 128.397 (para-C); 129.086 (meta-C); 135.488 (ortho-C); 173.315 (COO). ^{77}Se NMR 448.407.

(R)-((S)-sec-butyl) 2-(phenylselanyl)propanoate (**7b**)



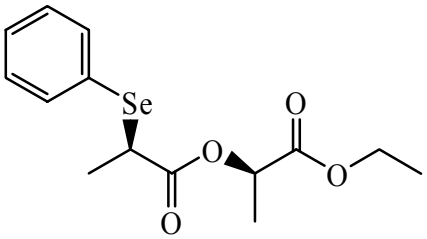
^{1}H NMR 0.869 (t, J 7.35, Me, 3H); 1,174 (d, J 6.27, MeCHO, 3H); 1.449-1.524 (m, CH_2O, 2H); 1.539 (d, J 7.07, MeCHSe, 3H); 3.756 (q, J 7.07, CHSe, 1H); 4.776-4.851 (m, CHO, 1H); 7.260-7.337 (m, meta-, para-H, 3H); 7.580-7.615 (m, ortho-H, 2H). ^{13}C NMR 9.698 (Me); 17.937 (MeCHSe); 19.371 (MeCHO); 28.799 (CH_2); 38.251 (CHSe); 73.082 (CHO); 128.397 (para-C); 129.086 (meta-C); 135.488 (ortho-C); 173.287 (COO). ^{77}Se NMR 450.563.

(R)-((S)-1-ethoxy-1-oxopropan-2-yl) 2-(phenylselanyl)propanoate (8a)



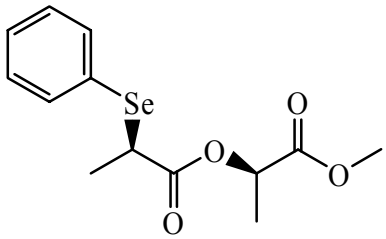
^{1}H NMR 1.254 (t, J 7.36, Me, 3H); 1.339 (d, J 7.39, MeCHO, 3H); 1.553 (d, J 7.14, MeCHSe, 3H); 3.879 (q, J 7.14, CHSe, 1H); 4.179 (q, J 7.36, CH_2O, 2H); 4.966 (q, J 7.39, CHO, 1H); 7.269-7.363 (m, meta-, para-H, 3H); 7.597-7.629 (m, ortho-H, 2H). ^{13}C NMR 14.220 (Me); 16.751 (MeCHO); 17.461 (MeCHSe); 36.640 (CHSe); 61.474 (CH_2O); 69.176 (CHO); 128.662 (para-C SePh); 129.097 (meta-C SePh); 135.935 (ortho-C SePh). ^{77}Se NMR 455.165.

(R)-((R)-1-ethoxy-1-oxopropan-2-yl) 2-(phenylselanyl)propanoate (8b)



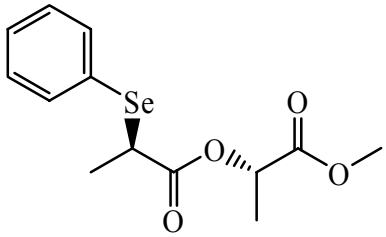
^{1}H NMR 1.279 (t, J 7.36, Me, 3H); 1.446 (d, J 7.39, MeCHO, 3H); 1.567 (d, J 7.14, MeCHSe, 3H); 3.782 (q, J 7.14, CHSe, 1H); 4.208 (q, J 7.36, CH_2O, 2H); 5.041 (q, J 7.39, CHO, 1H); 7.269-7.363 (m, meta-, para-H, 3H); 7.630-7.665 (m, ortho-H, 2H). ^{13}C NMR 14.220 (Me); 16.892 (MeCHO); 17.824 (MeCHSe); 36.927 (CHSe); 61.474 (CH_2O); 69.255 (CHO); 128.606 (para-C SePh); 129.056 (meta-C SePh); 135.935 (ortho-C SePh); 170.596 (COOEt); 172.791 (COO). ^{77}Se NMR 455.021.

(R)-((R)-1-methoxy-1-oxopropan-2-yl) 2-(phenylselanyl)propanoate (9a)



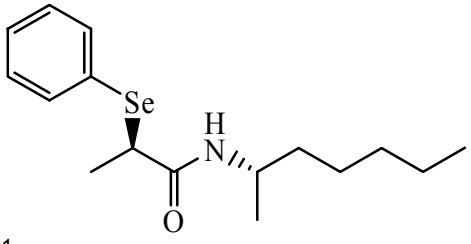
^{1}H NMR 1.341 (d, J 6.97, MeCHO, 3H); 1.555 (d, J 6.97, MeCHSe, 3H); 3.725 (s, OMe, 3H); 3.879 (q, J 6.97, CHSe, 1H); 4.999 (q, J 6.97, CHO, 1H); 7.265-7.314 (m, meta-H SePh, 2H) 7.315-7.355 (m, para-H, 1H); 7.595-7.627 (m, ortho-H SePh, 2H). ^{13}C NMR 16.782 (MeCHO); 17.448 (MeCHSe); 36.621 (CHSe); 52.407 (OMe); 69.077 (CHO); 128.677 (para-C SePh); 129.113 (meta-C SePh); 135.867 (ortho-C SePh); 171.189 (COOMe); 173.061 (COO). ^{77}Se NMR 455.920.

(R)-((S)-1-methoxy-1-oxopropan-2-yl) 2-(phenylselanyl)propanoate (9b)



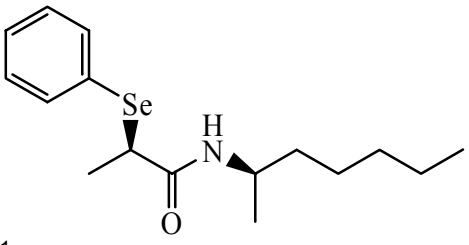
^{1}H NMR 1.447 (d, J 6.97, MeCHO, 3H); 1.570 (d, J 6.97, MeCHSe, 3H); 3.747 (s, OMe, 3H); 3.787 (q, J 6.97, CHSe, 1H); 5.069 (q, J 6.97, CHO, 1H); 7.265-7.314 (m, meta-H SePh, 2H) 7.315-7.355 (m, para-H, 1H); 7.582-7.627 (m, ortho-H SePh, 2H). ^{13}C NMR 16.928 (MeCHO); 17.816 (MeCHSe); 36.961 (CHSe); 52.407 (OMe); 69.176 (CHO); 128.621 (para-C SePh); 129.062 (meta-C SePh); 135.908 (ortho-C SePh); 171.034 (COOMe); 172.779 (COO). ^{77}Se NMR 455.491.

(R)-N-((S)-heptan-2-yl)-2-(phenylselanyl)propanamide (**10a**)



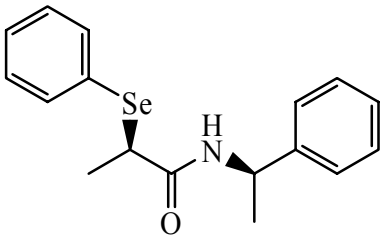
^{1}H NMR 0.879 (t, J 6.95, Me, 3H); 0.998 (d, J 6.60, MeCHN, 3H); 1.217-1.367 (m, CH_2, 8H); 1.595 (d, J 7.33, MeCHSe, 3H); 3.766 (q, J 7.33, CHSe, 1H); 3.838-3.915 (m, CHN, 1H); 5.804-5.909 (m, NH, 1H); 7.258-7.306 (m, 3H, meta-, para-H Ph); 7.516-7.555 (m, 2H, ortho-H Ph). ^{13}C NMR 14.111 (Me); 18.551 (MeCHSe); 20.805 (MeCHN); 22.648 (CH_2); 25.676 (CH_2); 31.778 (CH_2); 36.899 (CH_2CHN); 41.288 (CHSe); 45.677 (CHN); 128.198 (para-C SePh); 129.371 (meta-C SePh); 134.317 (ortho-C SePh); 171.442 (CON). ^{77}Se NMR 412.079.

(R)-N-((R)-heptan-2-yl)-2-(phenylselanyl)propanamide (**10b**)



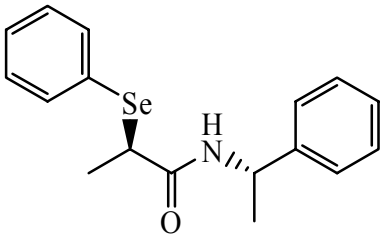
^{1}H NMR 0.844 (t, J 6.95, Me, 3H); 1.020 (d, J 6.60, MeCHN, 3H); 1.217-1.367 (m, CH_2, 8H); 1.583 (d, J 7.33, MeCHSe, 3H); 3.771 (q, J 7.33, CHSe, 1H); 3.838-3.915 (m, CHN, 1H); 5.804-5.909 (m, NH, 1H); 7.258-7.306 (m, 3H, meta-, para-H Ph); 7.516-7.555 (m, 2H, ortho-H Ph). ^{13}C NMR 14.111 (Me); 18.459 (MeCHSe); 20.805 (MeCHN); 22.606 (CH_2); 25.676 (CH_2); 32.073 (CH_2); 36.842 (CH_2CHN); 41.232 (CHSe); 45.706 (CHN); 128.198 (para-C SePh); 129.371 (meta-C SePh); 134.220 (ortho-C SePh); 171.442 (CON). ^{77}Se NMR 409.426.

(R)-N-((R)-1-phenylethyl)-2-(phenylselanyl)propanamide (**11a**)



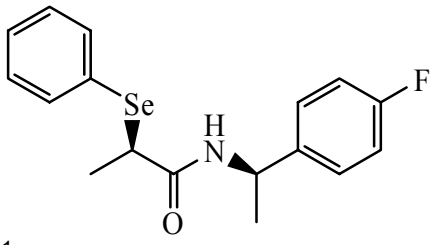
^{1}H NMR 1.356 (d, J 6.64, MeCHN, 3H); 1.577 (d, J 7.35, MeCHSe, 3H); 3.770 (q, J 7.35, CHSe, 1H); 4.972-5.076 (m, CHN, 1H); 6.241 (br. s, NH, 1H); 7.112-7.151 (m, 2H meta-H Ph); 7.182-7.217 (m, para-H Ph, 1H); 7.219-7.288 (m, ortho-H Ph, para-H SePh, 3H); 7.288-7.342 (m, meta-H SePh, 2H); 7.488-7.522 (m, ortho-H SePh, 2H). ^{13}C NMR 18.201 (MeCHN); 21.619 (MeCHSe); 40. 892 (CHSe); 49.220 (CHN); 126.207 (meta-C Ph); 127.409 (para-C Ph); 128.310 (para-C SePh); 128.715 (ortho-C Ph); 129.436 (meta-C SePh); 134.584 (ortho-C SePh); 171.371 (CON). ^{77}Se NMR 414.485.

(R)-N-((S)-1-phenylethyl)-2-(phenylselanyl)propanamide (**11b**)



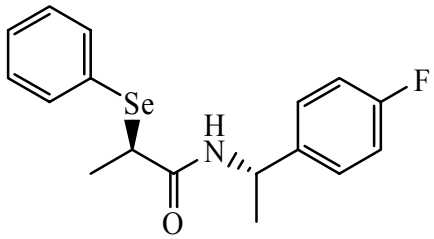
^{1}H NMR 1.367 (d, J 6.64, MeCHN, 3H); 1.572 (d, J 7.35, MeCHSe, 3H); 3.780 (q, J 7.35, CHSe, 1H); 4.972-5.076 (m, CHN, 1H); 6.338 (br. s, NH, 1H); 7.219-7.288 (m, Ph, para-H SePh, 6H); 7.288-7.342 (m, meta-H SePh, 2H); 7.411-7.449 (m, ortho-H SePh, 2H). ^{13}C NMR 18.342 (MeCHN); 21.718 (MeCHSe); 40.837 (CHSe); 49.164 (CHN); 126.242 (meta-C Ph); 127.409 (para-C Ph); 128.282 (para-C SePh); 128.749 (ortho-C Ph); 129.351 (meta-C SePh); 134.584 (ortho-C SePh); 171.371 (CON). ^{77}Se NMR 416.086.

(R)-N-((R)-1-(4-fluorophenyl)ethyl)-2-(phenylselanyl)propanamide (**12a**)



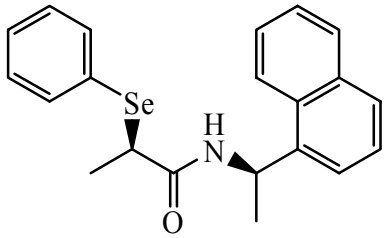
^{1}H NMR 1.354 (d, J 6.98, MeCHN, 3H); 1.581 (d, J 7.33, MeCHSe, 3H); 3.768 (q, J 7.33, CHSe, 1H); 4.950-5.039 (m, CHN, 1H); 6.198-6.302 (br. t, NH, 1H); 6.899-6.947 (m, meta-H *p*-F-C_6H_4, 2H); 7.171-7.331 (m, meta-, para-H SePh, ortho-H *p*-F-C_6H_4, 5H); 7.418-7.440 (m, ortho-H SePh, 2H). ^{13}C NMR 18.233 (MeCHN); 21.747 (MeCHSe); 40.641 (CHSe); 48.494 (CHN); 115.444 (d, J_F 21.08, meta-C *p*-F-C_6H_4); 127.880 (d, J_F 7.85, ortho-C *p*-F-C_6H_4); 128.325 (para-C SePh); 129.369 (meta -C SePh); 134.528 (ortho-C SePh); 138.946 (d, J_F 3.58, ipso-C *p*-F-C_6H_4); 171.387 (COO). ^{77}Se NMR 417.806.

(R)-N-((S)-1-(4-fluorophenyl)ethyl)-2-(phenylselanyl)propanamide (**12b**)



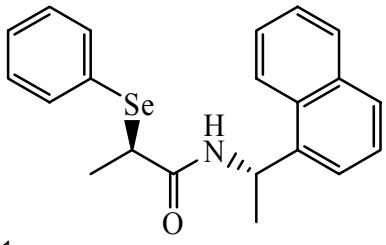
^{1}H NMR 1.359 (d, J 6.98, MeCHN, 3H); 1.579 (d, J 7.33, MeCHSe, 3H); 3.786 (q, J 7.33, CHSe, 1H); 4.950-5.039 (m, CHN, 1H); 6.198-6.302 (br. t, NH, 1H); 6.969-7.011 (m, meta-H *p*-F-C_6H_4, 2H); 7.171-7.331 (m, meta-, para-H SePh, ortho-H *p*-F-C_6H_4, 5H); 7.474-7.497 (m, ortho-H SePh, 2H). ^{13}C NMR 18.188 (MeCHN); 21.662 (MeCHSe); 40.806 (CHSe); 48.558 (CHN); 115.496 (d, J_F 21.08, meta-C *p*-F-C_6H_4); 127.818 (d, J_F 7.85, ortho-C *p*-F-C_6H_4); 128.282 (para-C SePh); 129.479 (meta-C SePh); 134.332 (ortho-C SePh); 138.875 (d, J_F 3.58, ipso-C *p*-F-C_6H_4); 171.358 (COO). ^{77}Se NMR 411.742.

(R)-N-((R)-1-(naphthalen-1-yl)ethyl)-2-(phenylselanyl)propanamide (**13a**)



^{1}H NMR 1.549 (d, J 6.67, MeCHN, 3H); 1.597 (d, J 7.34, MeCHSe, 3H); 3.713 (q, J 7.34, CHSe, 1H); 5.808-5.875 (m, CHN, 1H); 6.222 (br. d, NH, 1H); 7.133-7.176 (m, meta-H SePh, 2H); 7.221-7.263 (m, para-H SePh, 1H); 7.283-7.334 (m, 1H, Ar); 7.341-7.391 (m, 1H, Ar); 7.416-7.444 (m, ortho-H SePh, 2H); 7.446-7.486 (m, 2H, Ar); 7.748-7.775 (m, 1H, Ar); 7.822-7.856 (m, 1H, Ar); 7.983-8.020 (m, 1H, Ar). ^{13}C NMR 18.327 (MeCHSe); 20.736 (MeCHN); 40.937 (CHSe); 45.072 (CHN); 122.599 (Ar); 123.488 (Ar); 125.273 (Ar); 125.934 (Ar); 126.641 (Ar); 128.283 (para-C SePh); 128.414 (Ar); 128.858 (Ar); 129.324 (meta-C SePh); 131.139 (Ar); 134.036 (Ar); 134.653 (ortho-C SePh); 136.090 (Ar); 138.243 (Ar); 171.246 (CON). ^{77}Se NMR 415.411.

(R)-N-((S)-1-(naphthalen-1-yl)ethyl)-2-(phenylselanyl)propanamide (**13b**)



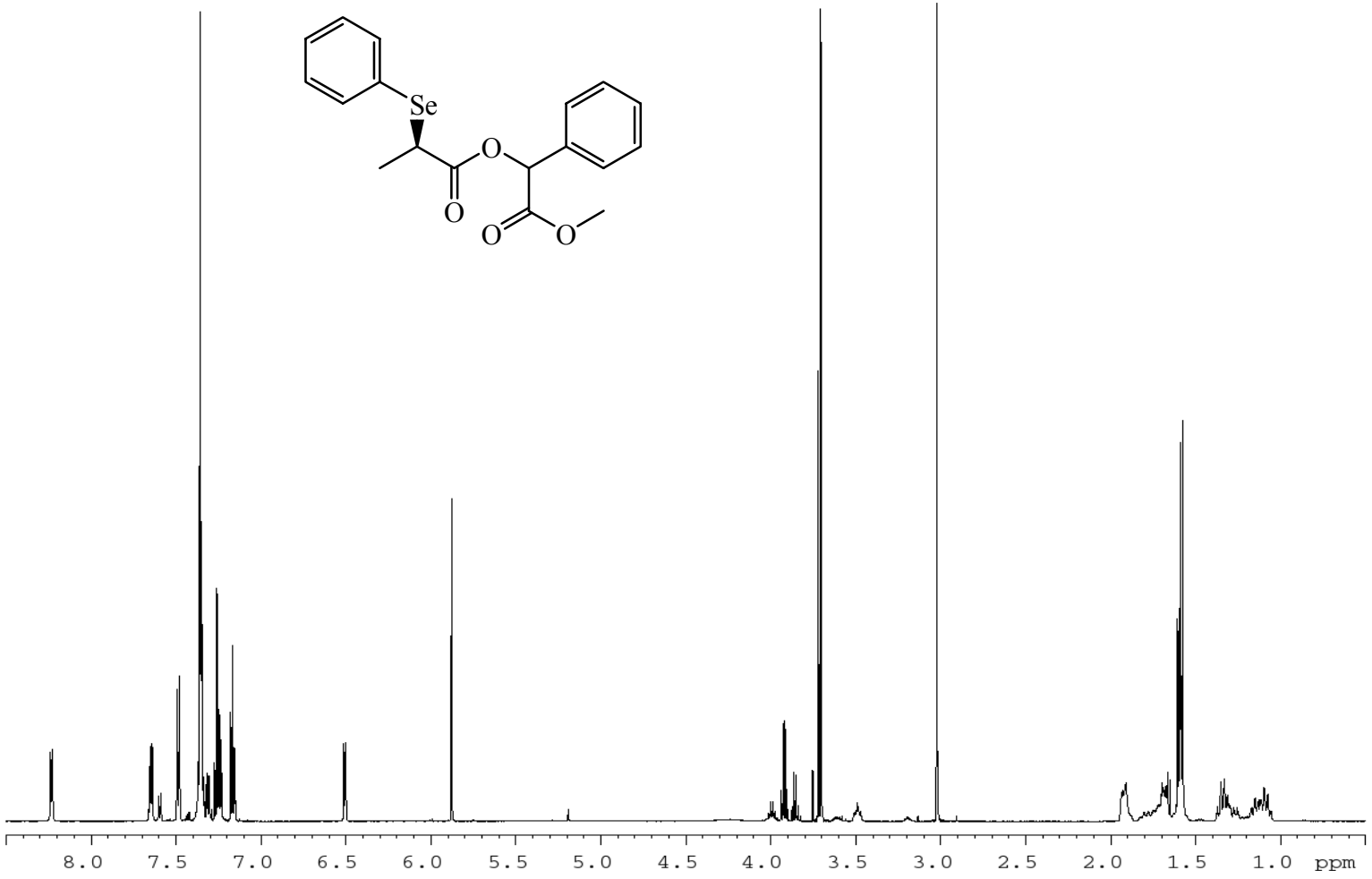
^{1}H NMR 1.533 (d, J 6.67, MeCHN, 3H); 1.597 (d, J 7.34, MeCHSe, 3H); 3.769 (q, J 7.34, CHSe, 1H); 5.808-5.875 (m, CHN, 1H); 6.298 (br. d, NH, 1H); 7.047-7.084 (m, meta-H SePh, 2H); 7.221-7.263 (m, para-H SePh, 1H); 7.283-7.334 (m, 1H, Ar); 7.341-7.391 (m, 1H, Ar); 7.416-7.444 (m, ortho-H SePh, 2H); 7.446-7.486 (m, 2H, Ar); 7.782-7.808 (m, 1H, Ar); 7.859-7.882 (m, 1H, Ar); 8.062-8.089 (m, 1H, Ar). ^{13}C NMR 18.327 (MeCHSe); 20.861 (MeCHN); 40.937 (CHSe); 45.072 (CHN); 122.599 (Ar); 123.692 (Ar); 125.273 (Ar); 126.003 (Ar); 126.524 (Ar); 128.142 (para-C SePh); 128.414 (Ar); 128.858 (Ar); 129.268 (meta-C SePh); 131.139 (Ar); 134.077 (Ar); 134.375 (ortho-C SePh); 136.090 (Ar); 138.243 (Ar); 171.246 (CON). ^{77}Se NMR 413.098.

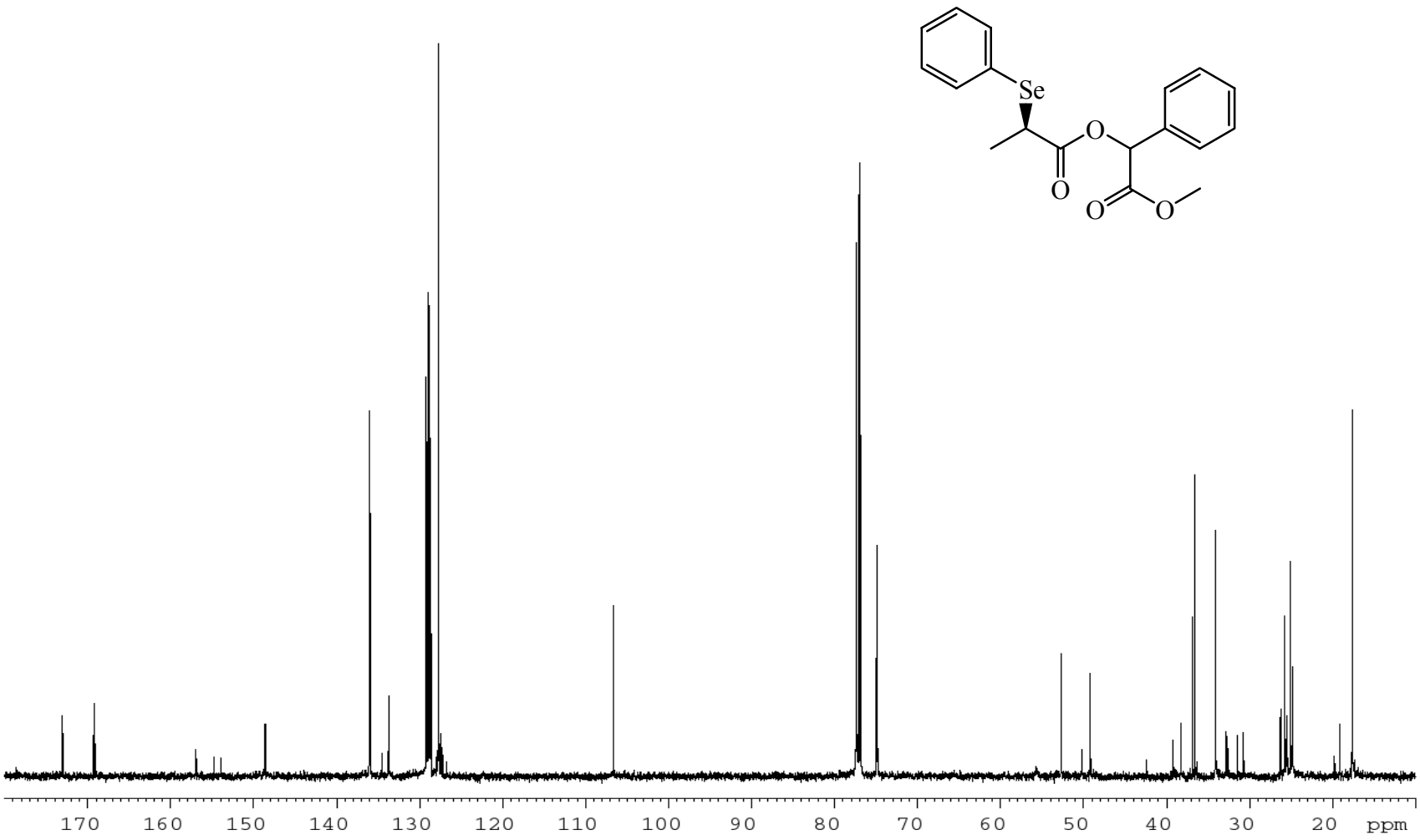
Acknowledgement

The research work was supported by Research Grant MK-1085.2008.3.

9. ^{1}H, ^{13}C and ^{77}Se NMR spectra of the studied compounds

(R)-((R)-2-methoxy-2-oxo-1-phenylethyl) 2-(phenylselanyl)propanoate **4a** and (R)-((S)-2-methoxy-2-oxo-1-phenylethyl) 2-(phenylselanyl)propanoate **4b** (ratio 66 : 34)




Se
O
O
O
O
170
160
150
140
130
120
110
100
90
80
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40
30
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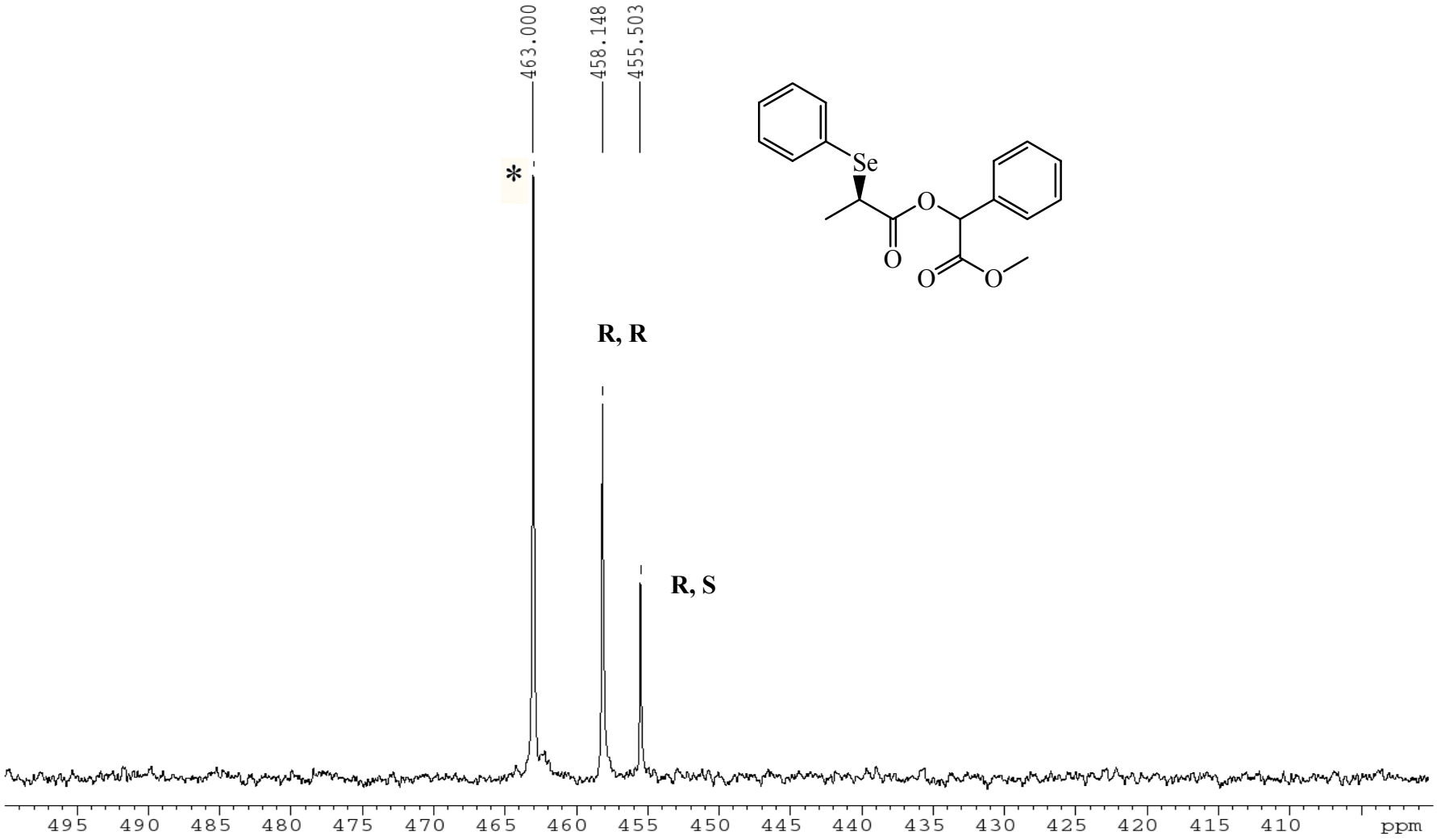
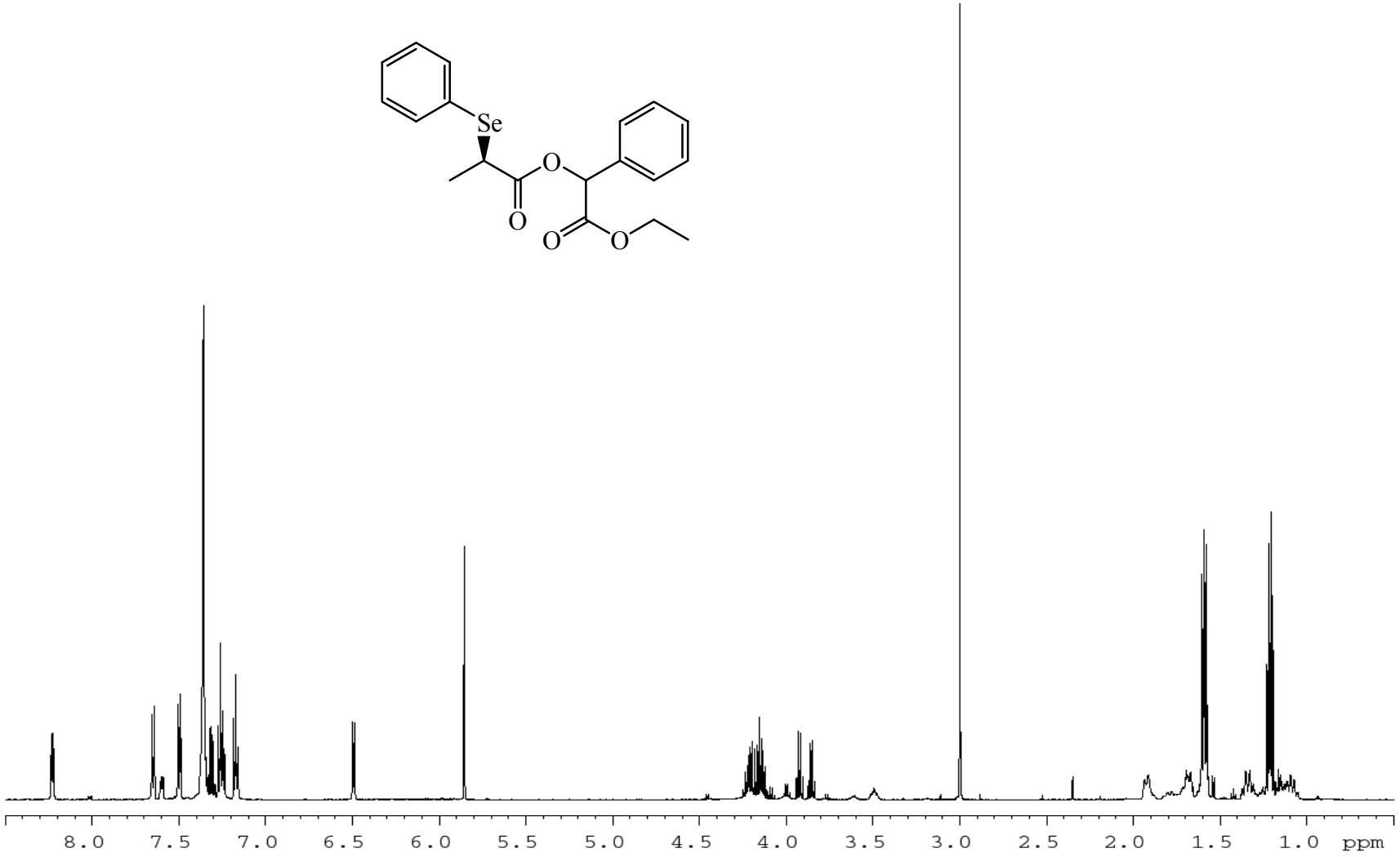
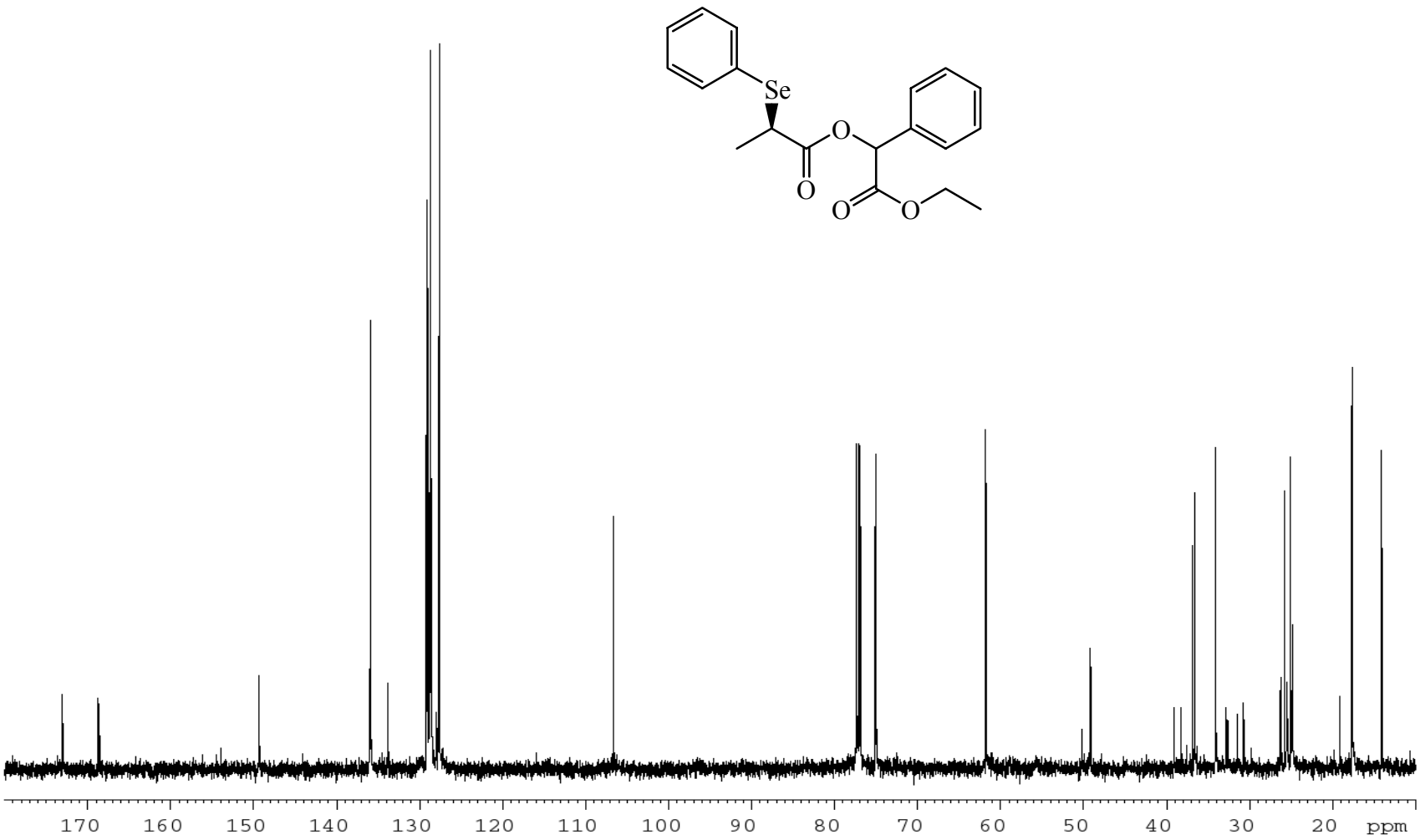
ppm



* Ph_2Se_2 standard (capillary insert)

(R)-((R)-2-ethoxy-2-oxo-1-phenylethyl) 2-(phenylselanyl)propanoate and **5a** (R)-((S)-2-ethoxy-2-oxo-1-phenylethyl) 2-(phenylselanyl)propanoate **5b** (ratio 50 : 50)

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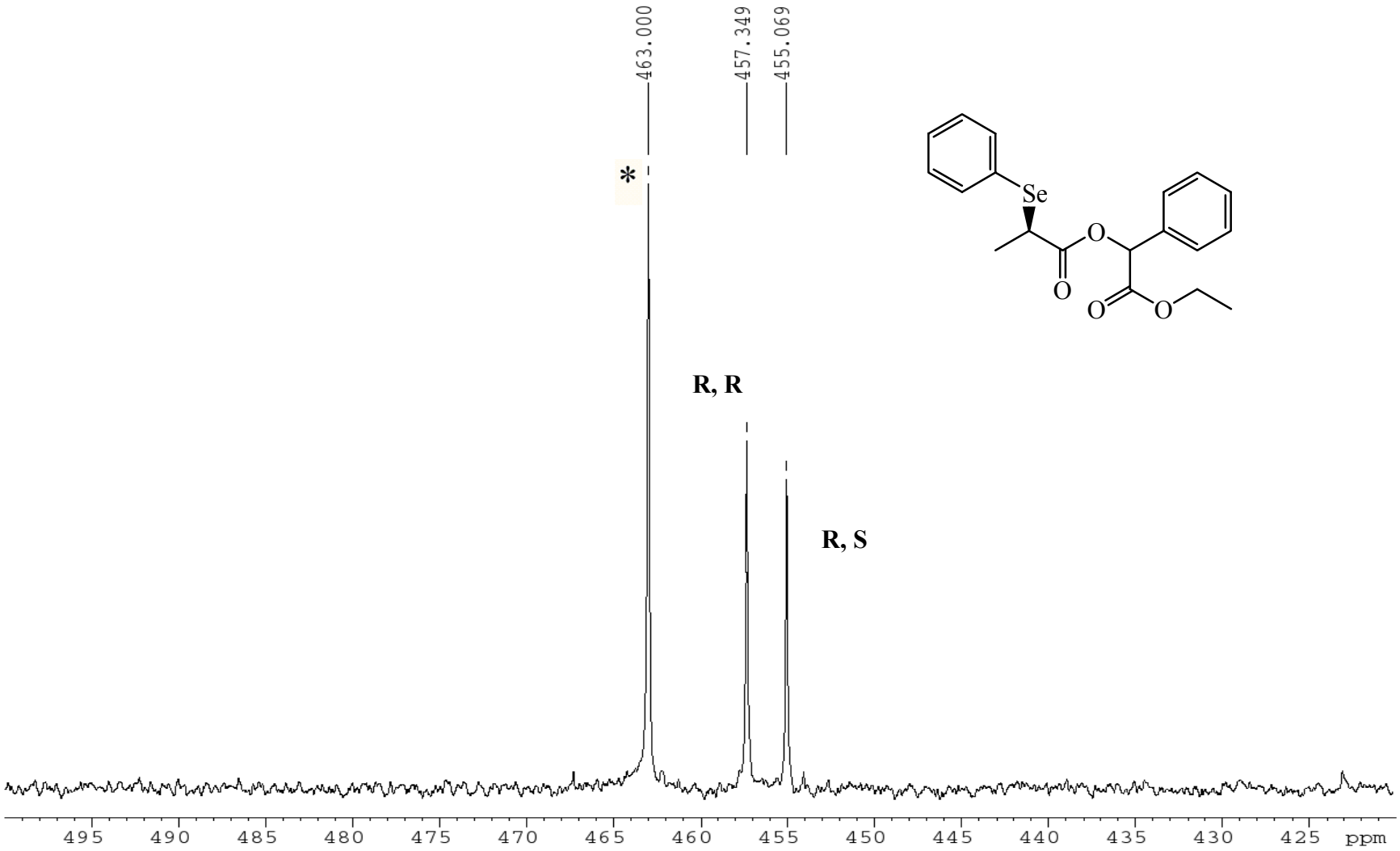
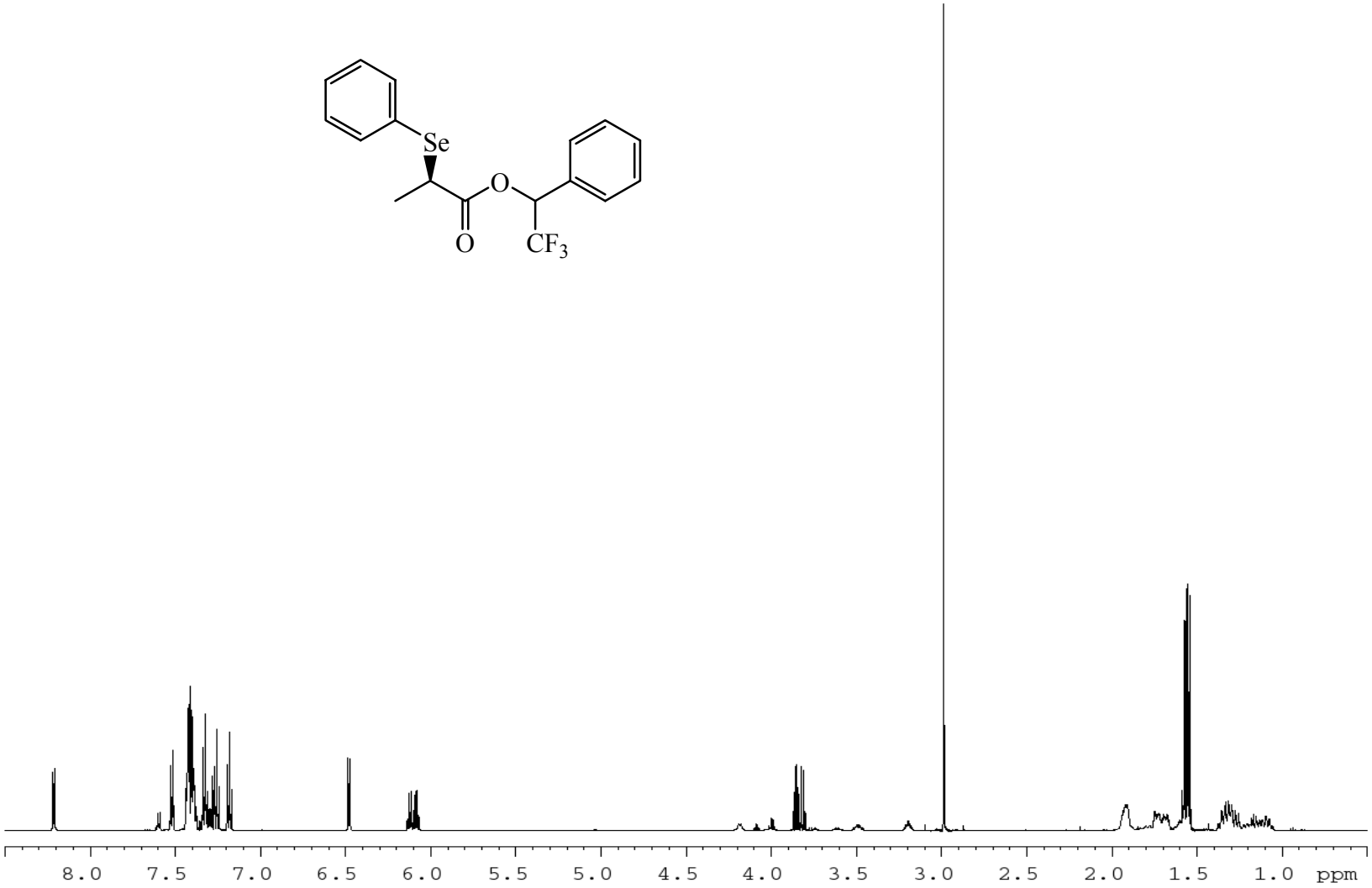
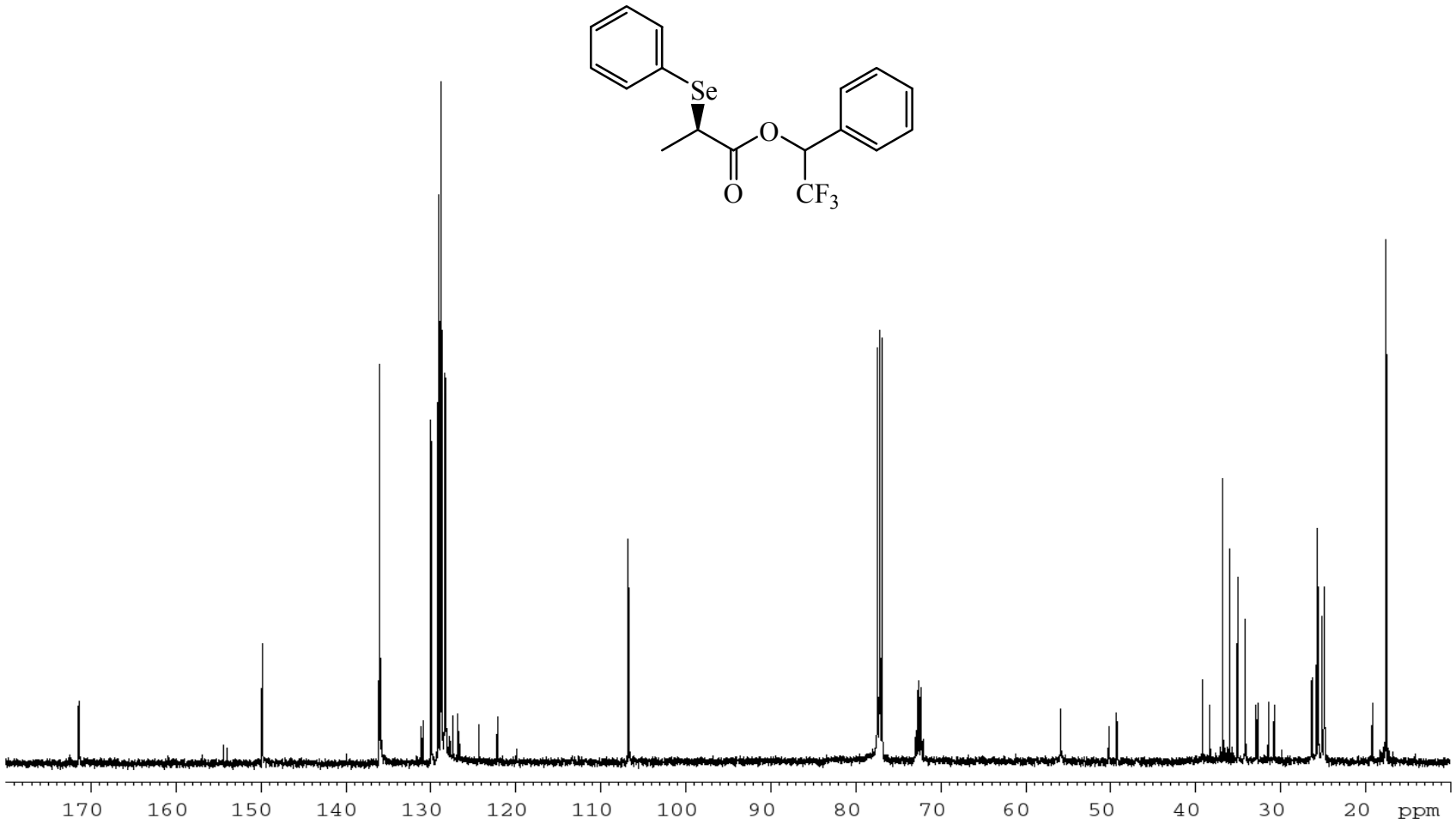


* Ph_2Se_2 standard (capillary insert)

(R)-((R)-2,2,2-trifluoro-1-phenylethyl) 2-(phenylselanyl)propanoate **6a** and (R)-((S)-2,2,2-trifluoro-1-phenylethyl) 2-(phenylselanyl)propanoate **6b** (ratio 50 : 50)

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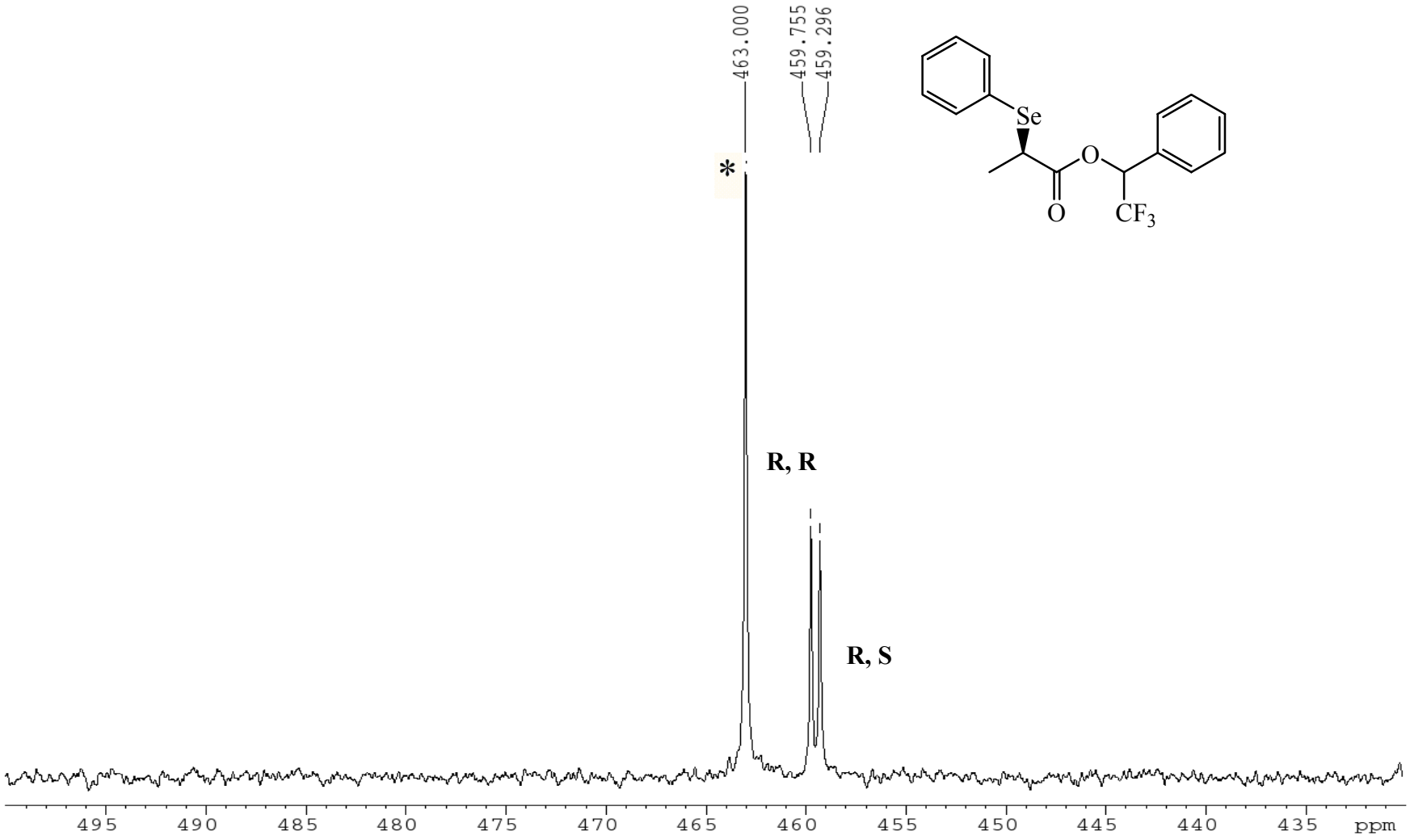
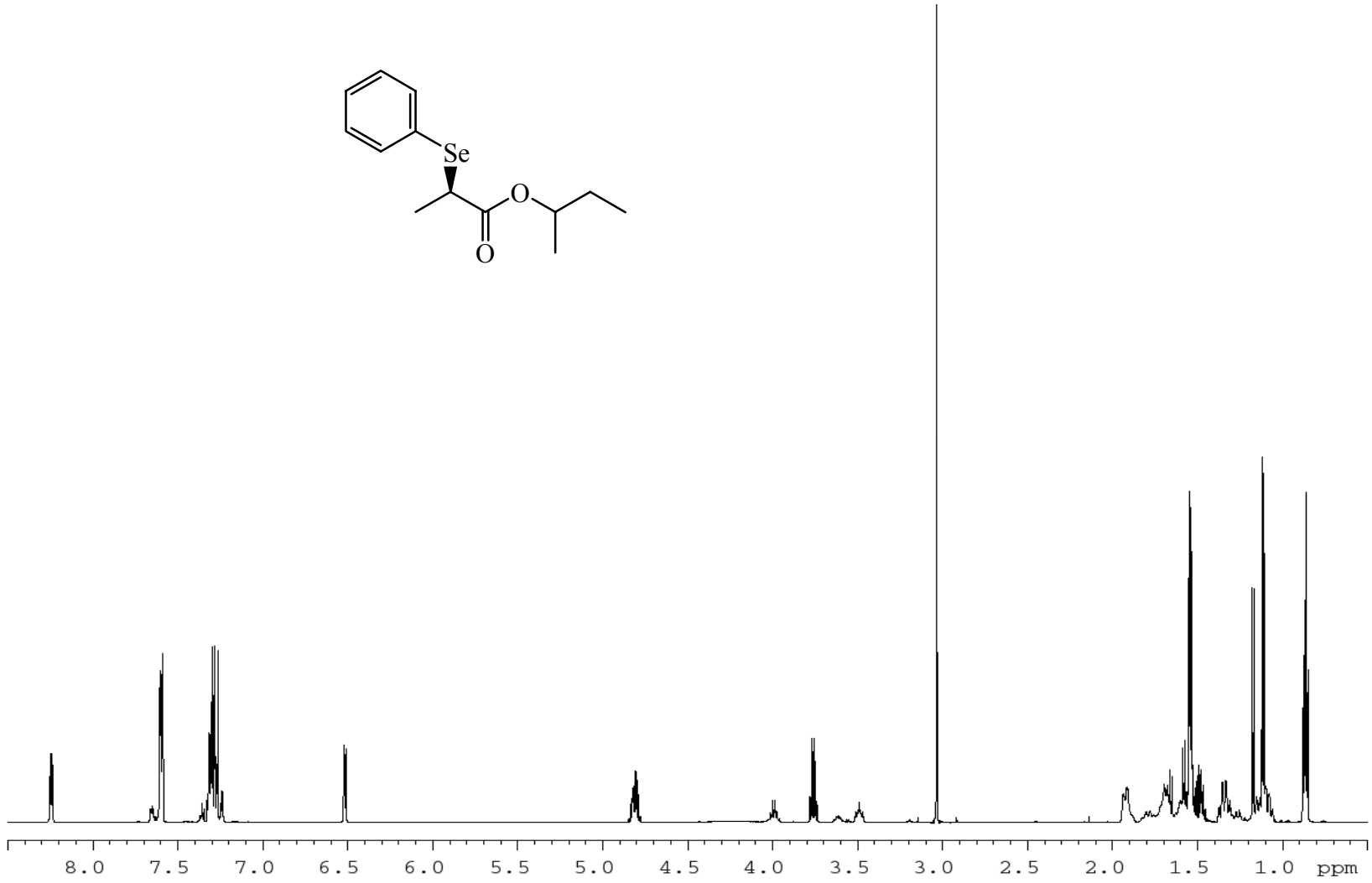
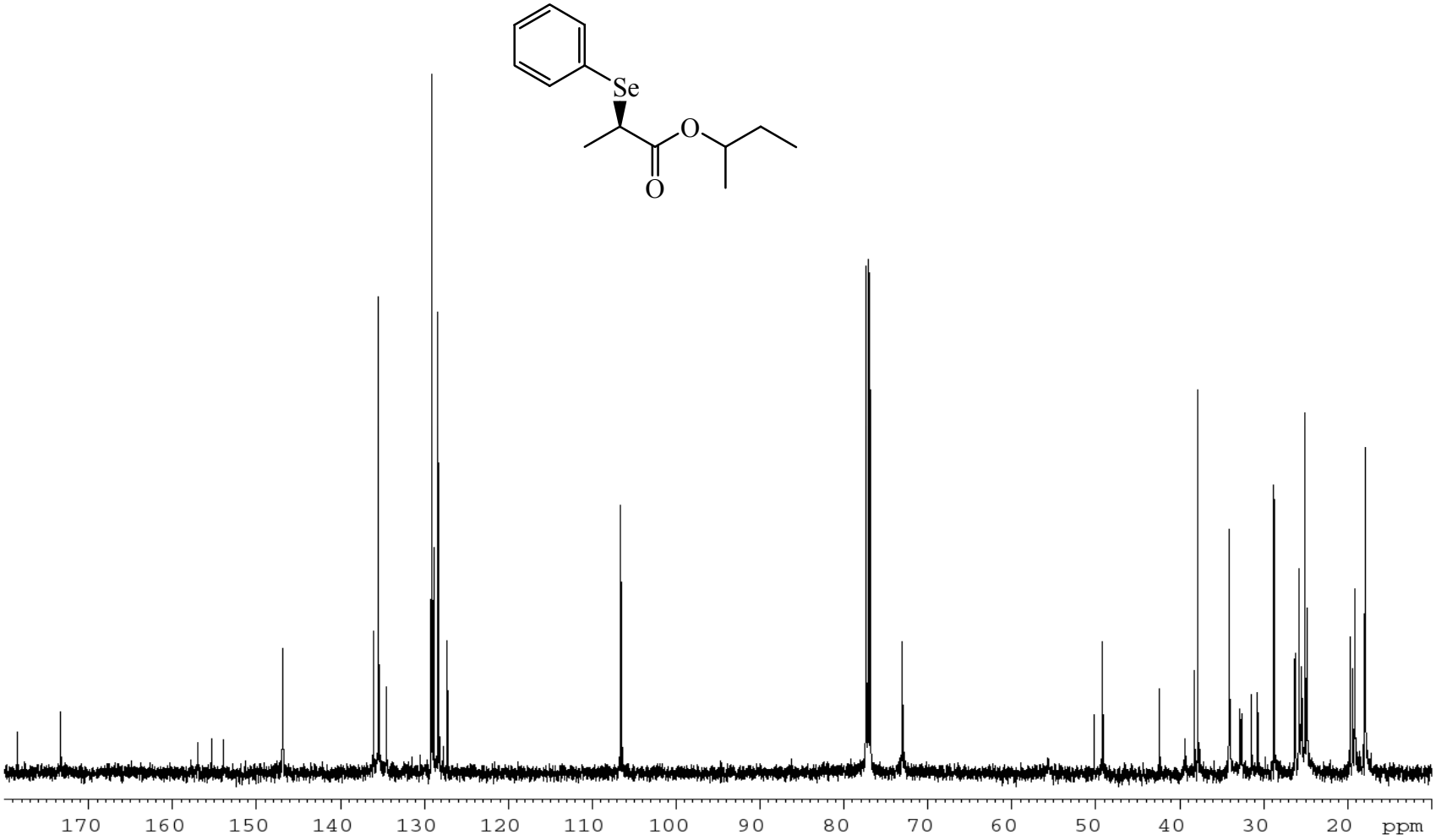


* Ph_2Se_2 standard (capillary insert)

(R)-((R)-sec-butyl) 2-(phenylselanyl)propanoate **7a** and (R)-((S)-sec-butyl) 2-(phenylselanyl)propanoate **7b** (ratio 64 : 36)

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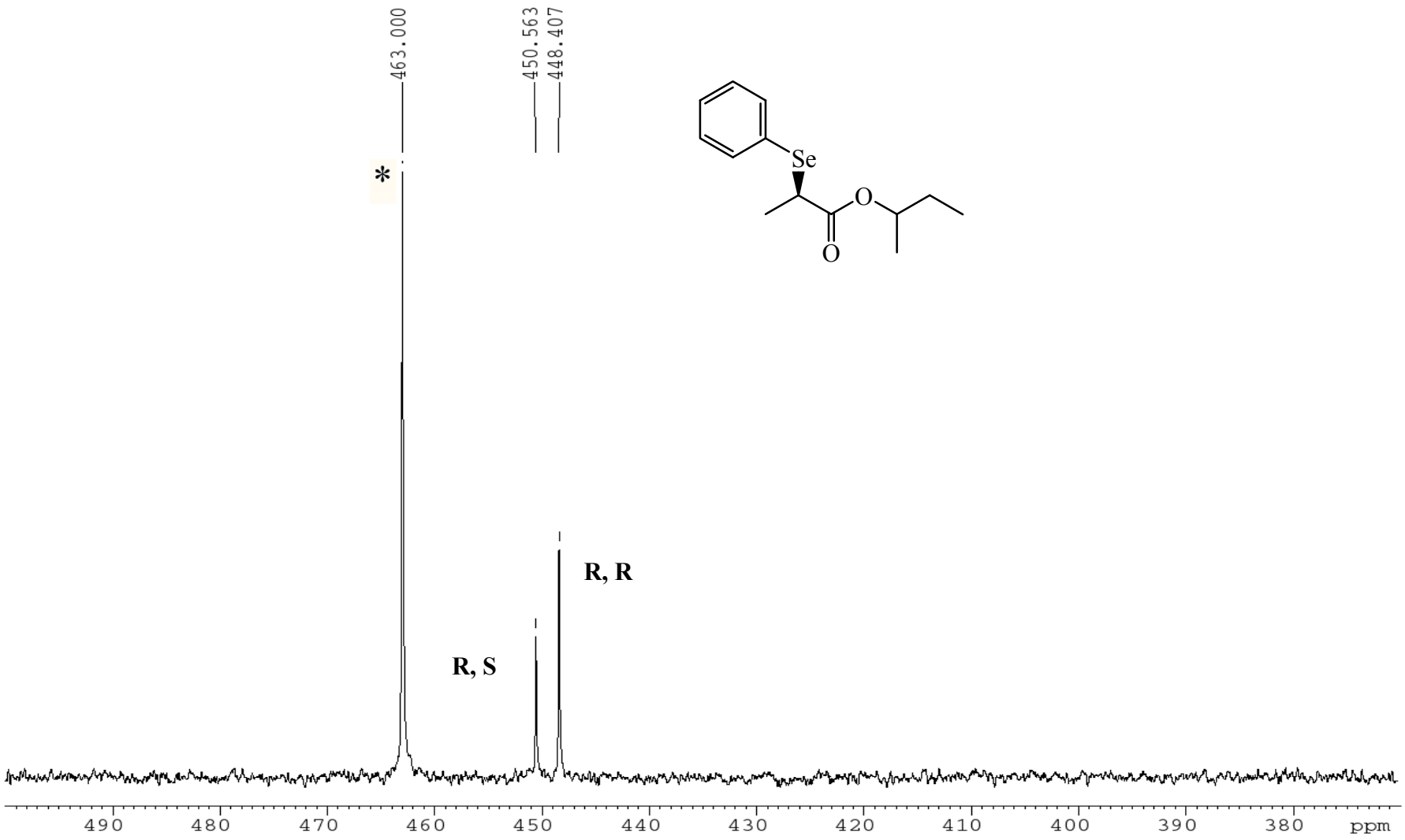
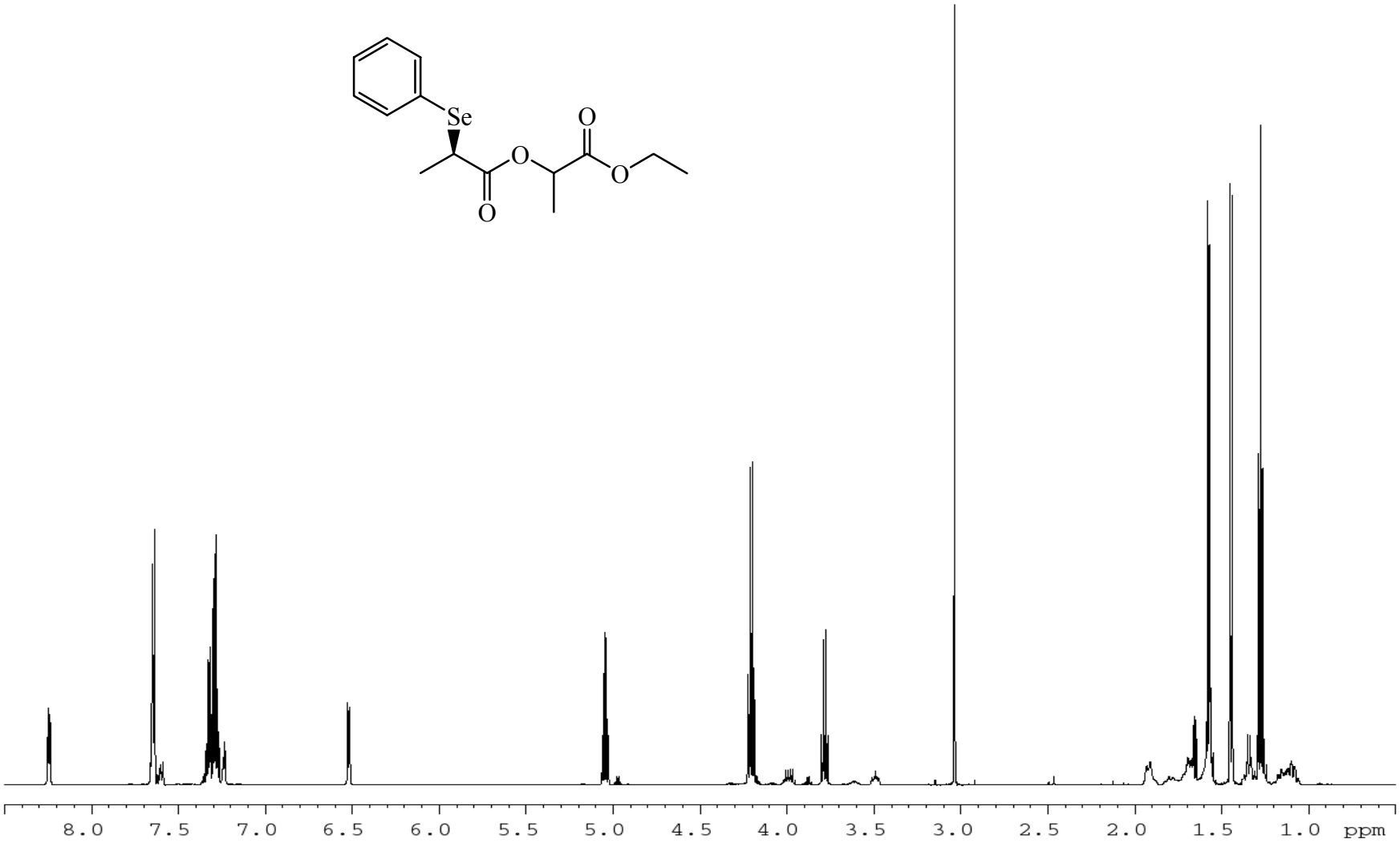
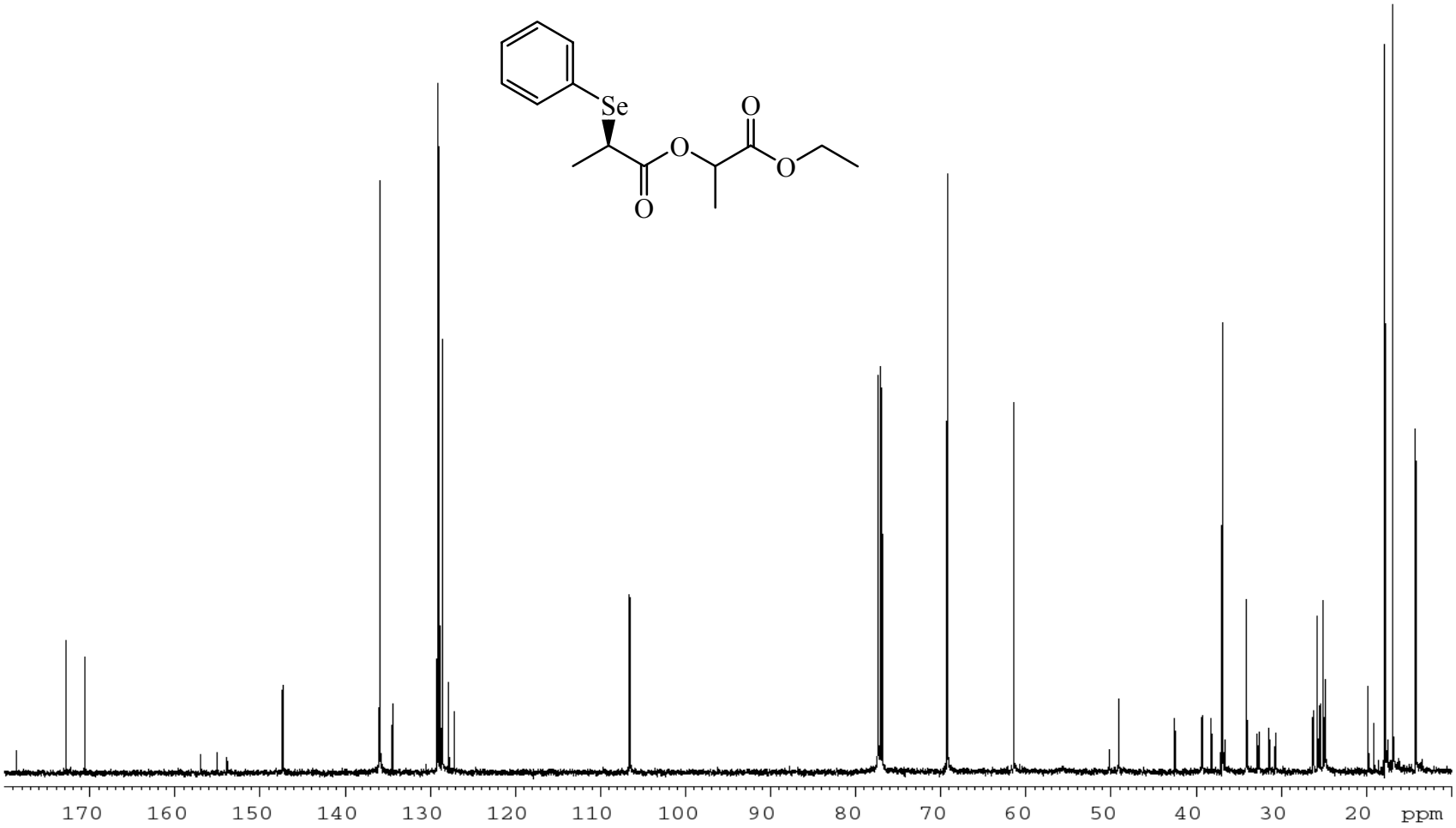


* Ph_2Se_2 standard (capillary insert)

(R)-((S)-1-ethoxy-1-oxopropan-2-yl) 2-(phenylselanyl)propanoate **8a** and (R)-((R)-1-ethoxy-1-oxopropan-2-yl) 2-(phenylselanyl)propanoate **8b** (ratio 96 : 4)

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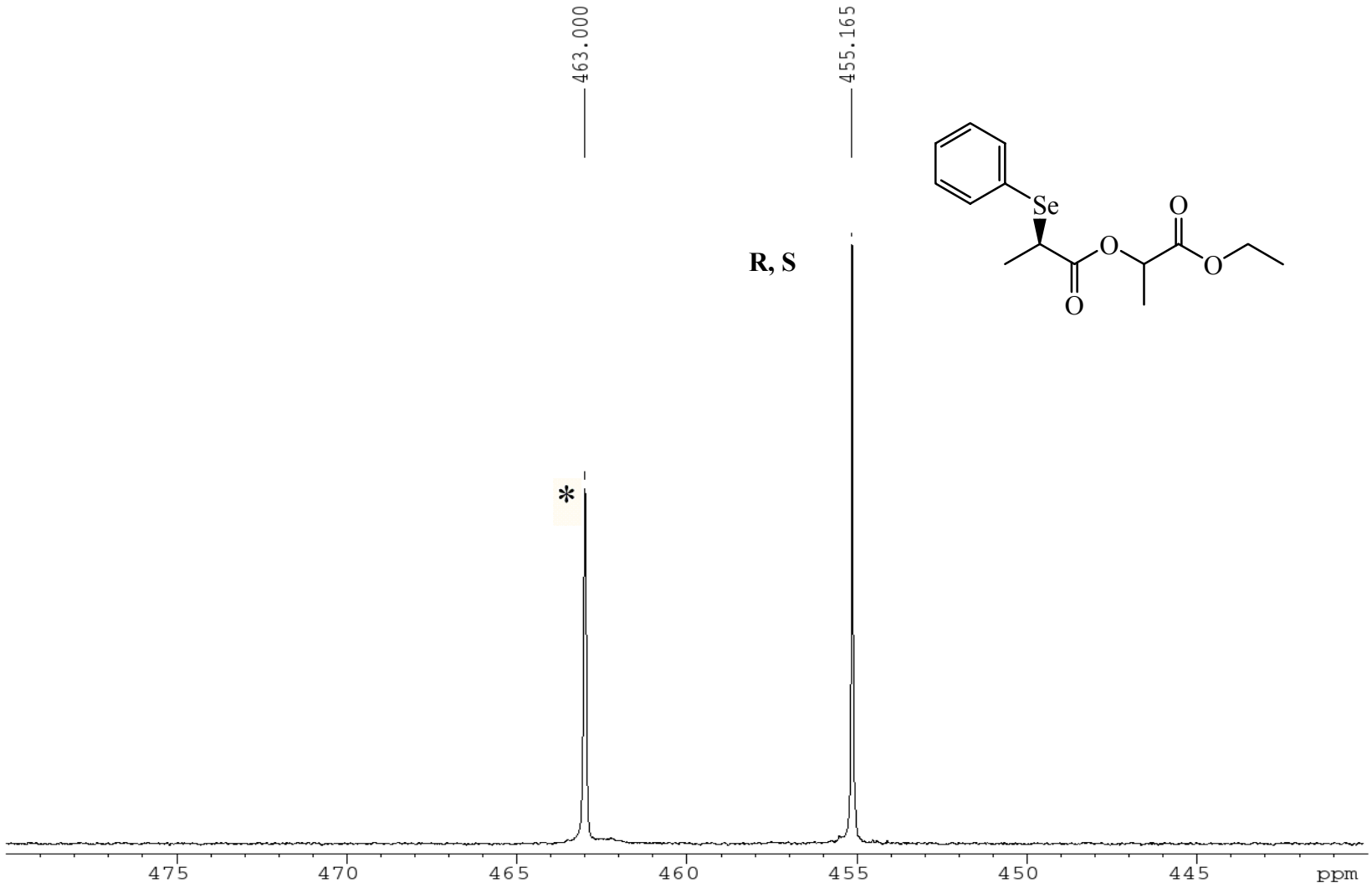
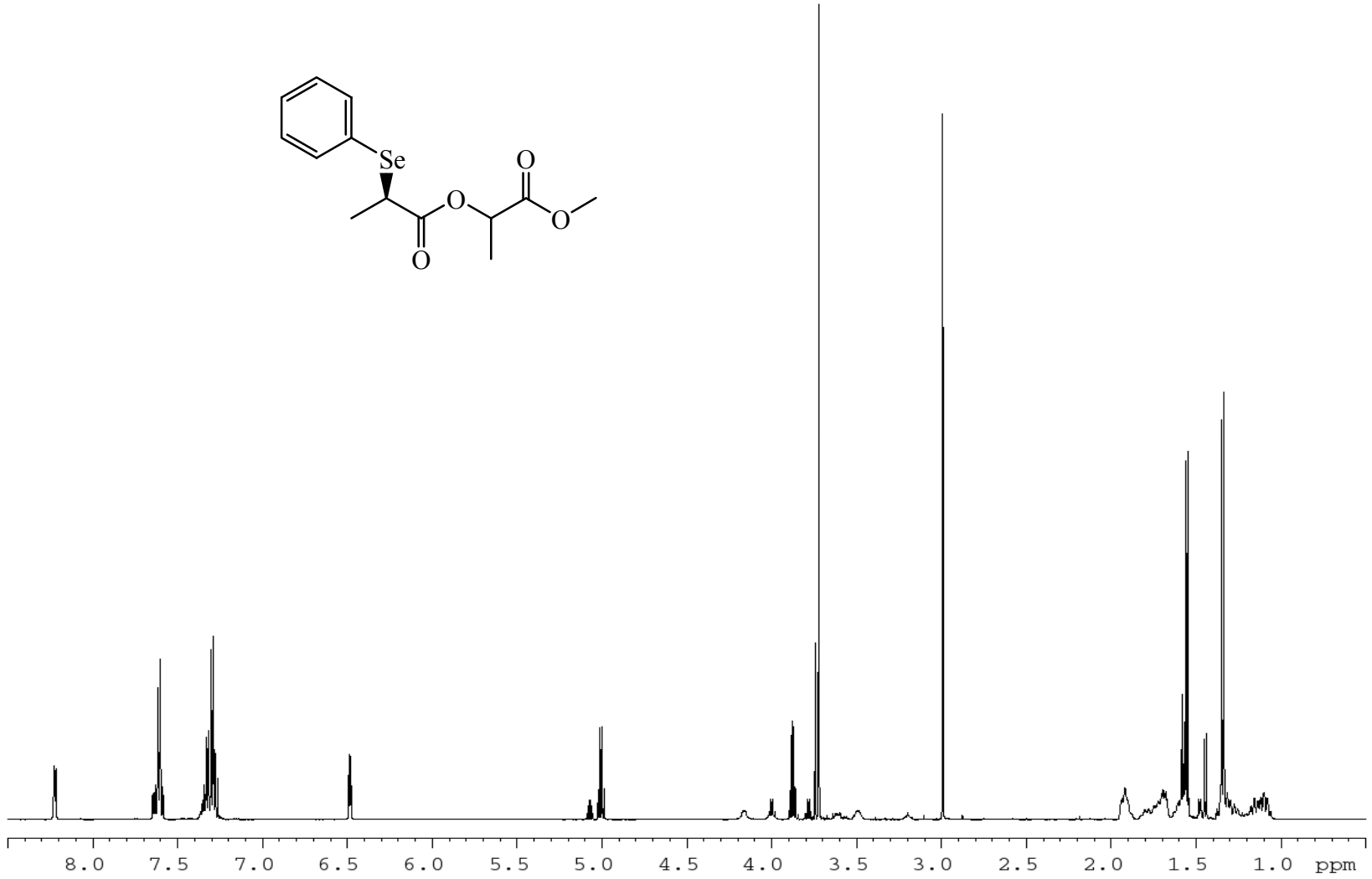
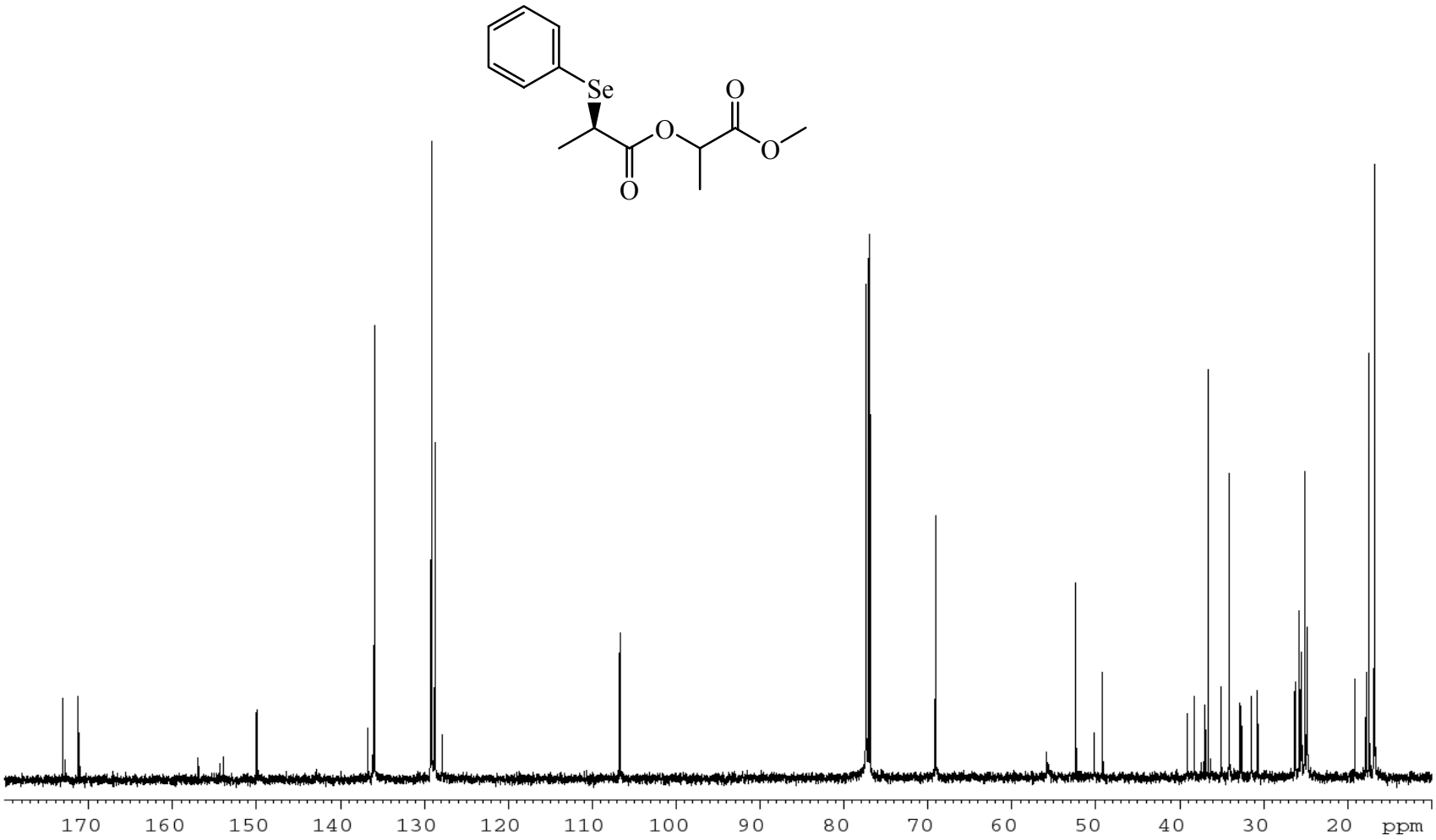


* Ph_2Se_2 standard (capillary insert). The minor diastereomer **8b** was not resolved in this spectrum.

(R)-((R)-1-methoxy-1-oxopropan-2-yl) 2-(phenylselanyl)propanoate **9a** (R)-((S)-1-methoxy-1-oxopropan-2-yl) 2-(phenylselanyl)propanoate **9b** (ratio 84 : 16)

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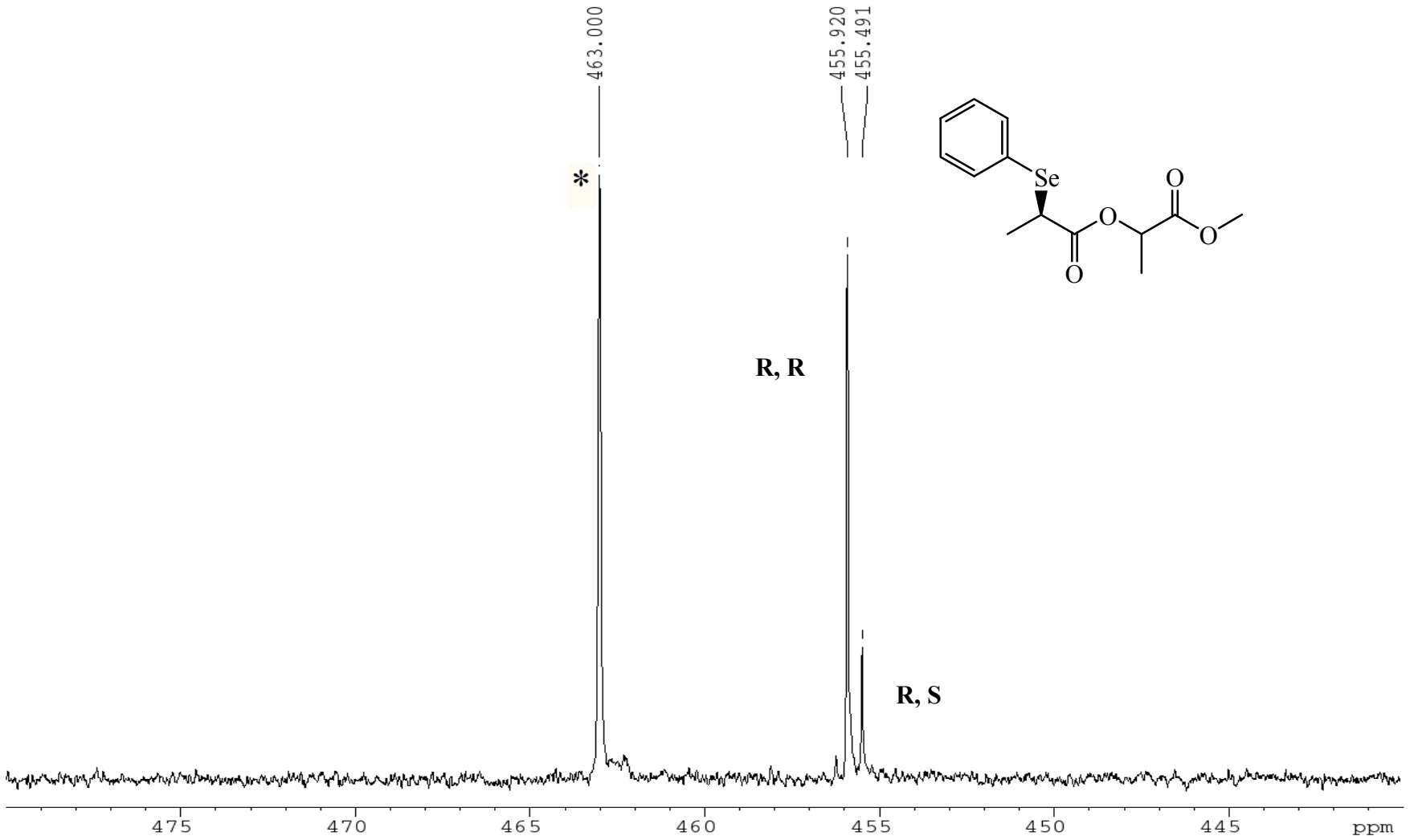
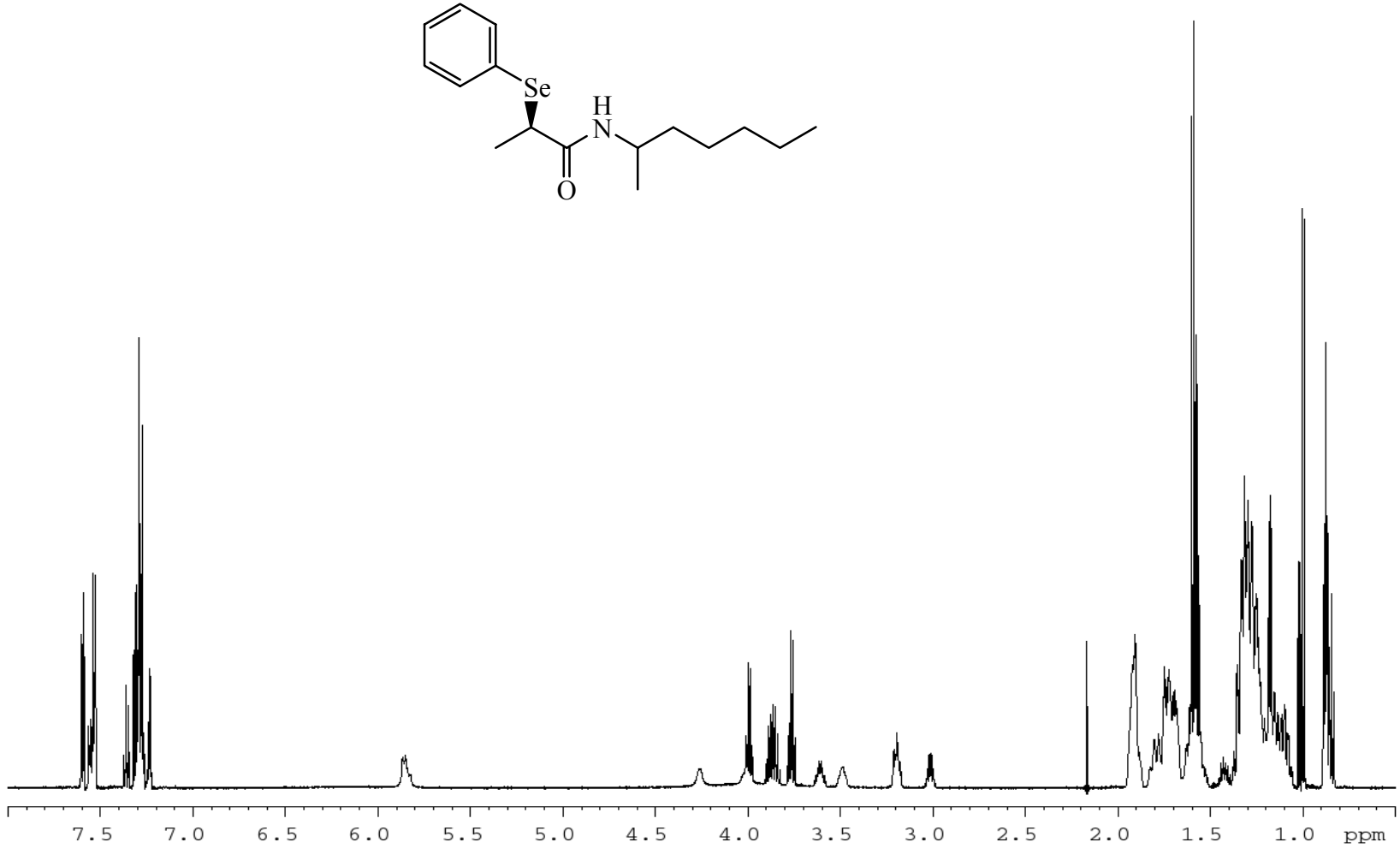
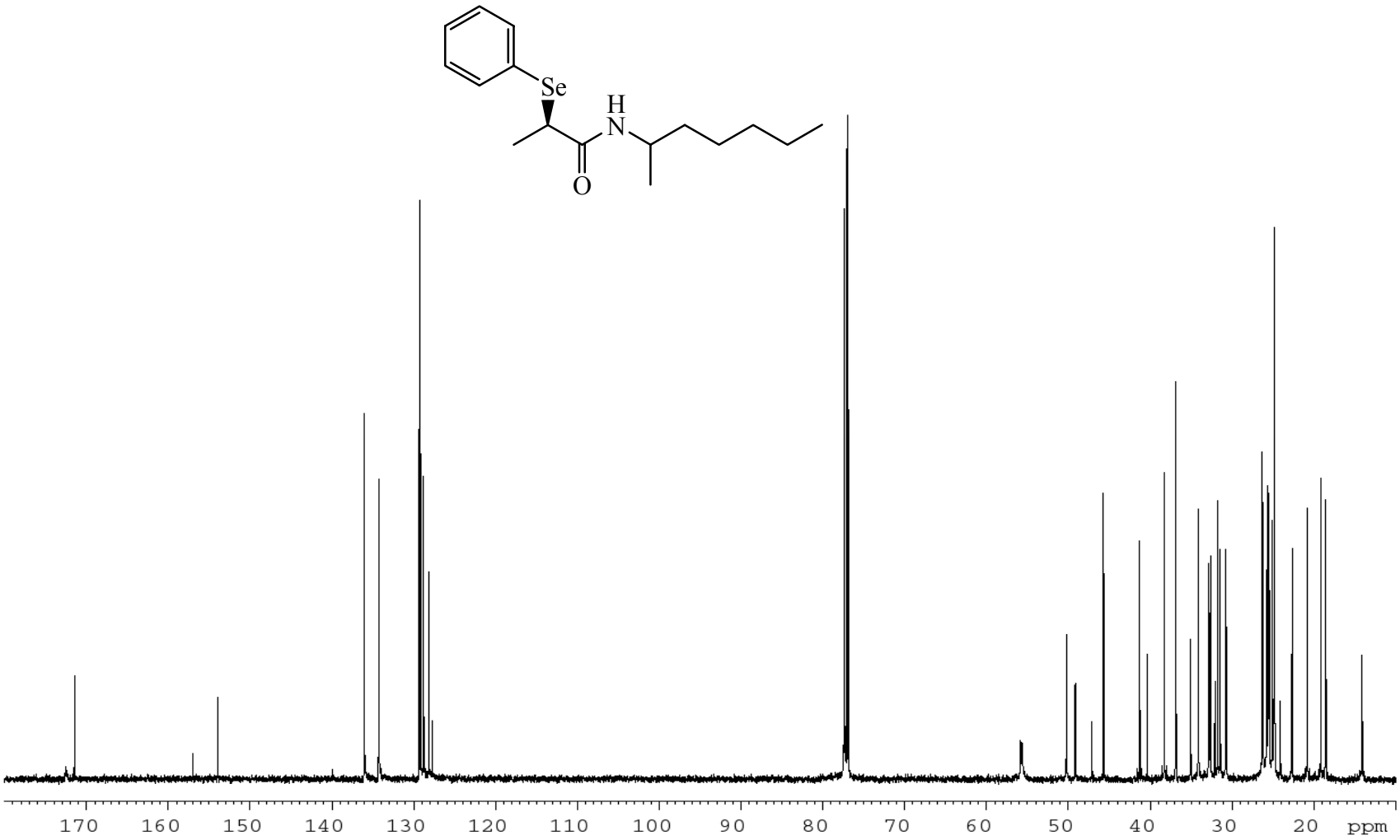


* Ph_2Se_2 standard (capillary insert)

(R)-N-((S)-heptan-2-yl)-2-(phenylselanyl)propanamide **10a** and (R)-N-((R)-heptan-2-yl)-2-(phenylselanyl)propanamide **10b** (ratio 70 : 30)

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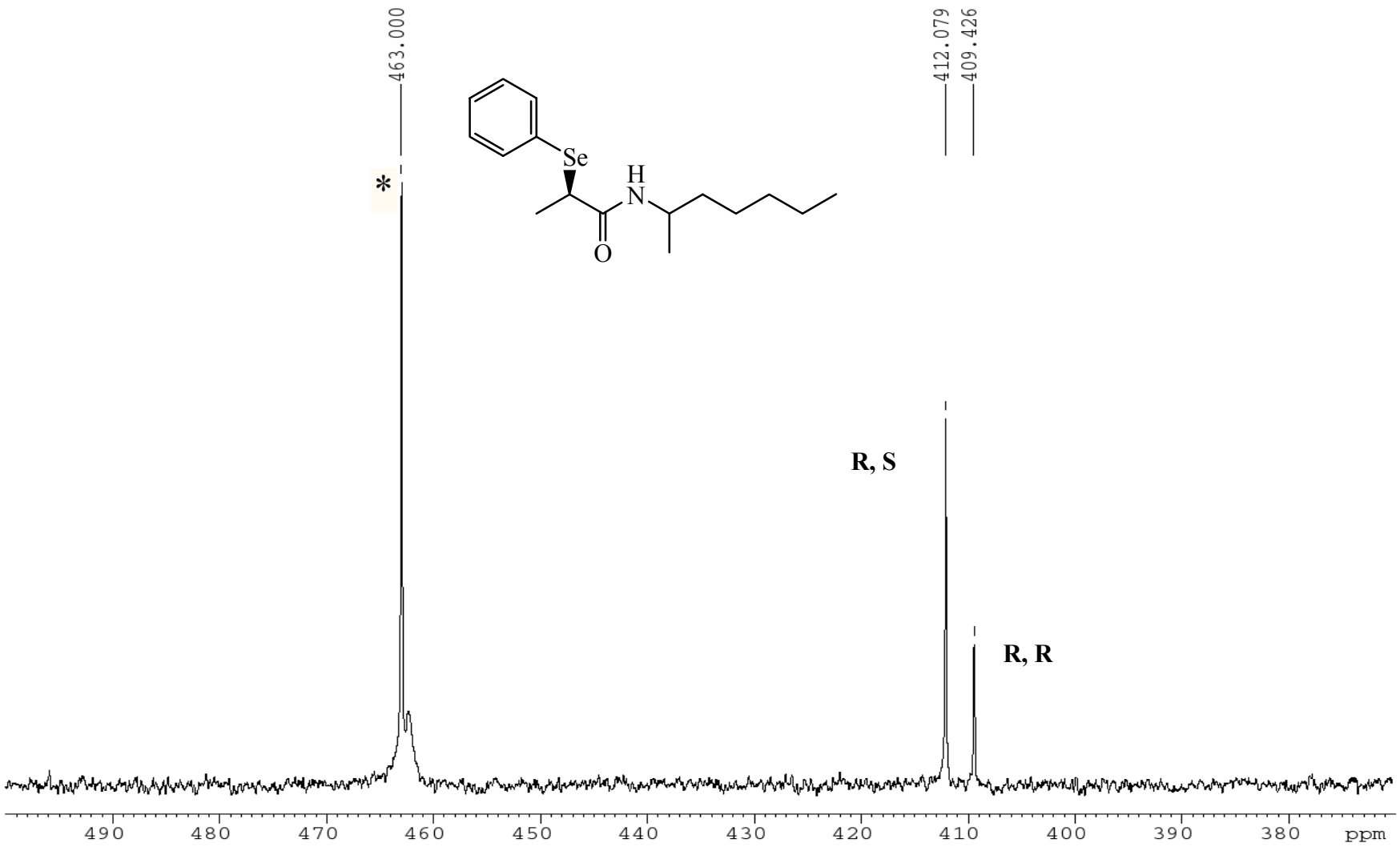
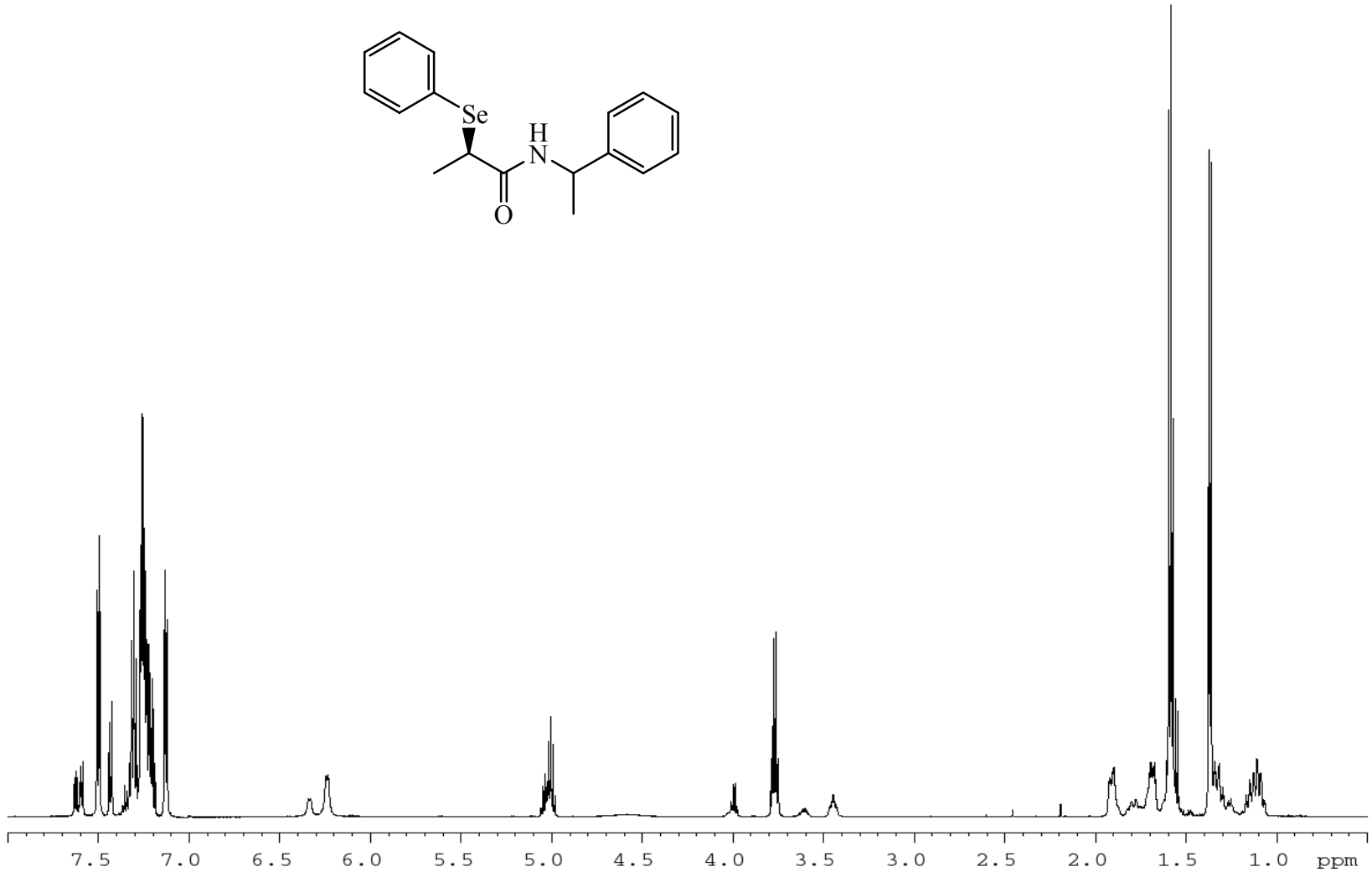
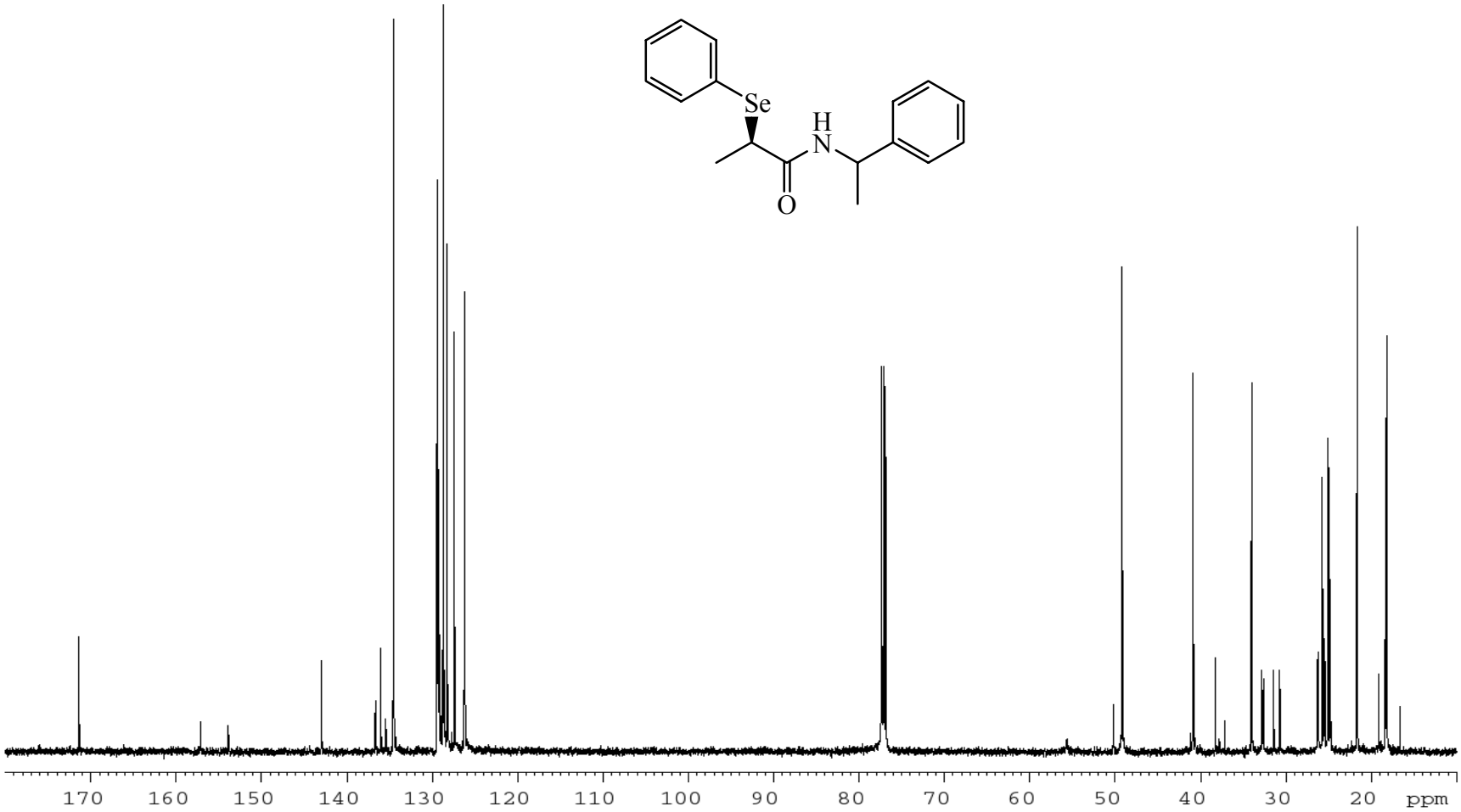


* Ph_2Se_2 standard (capillary insert)

(R)-N-((R)-1-phenylethyl)-2-(phenylselanyl)propanamide **11a** and (R)-N-((S)-1-phenylethyl)-2-(phenylselanyl)propanamide **11b** (ratio 64 : 36)

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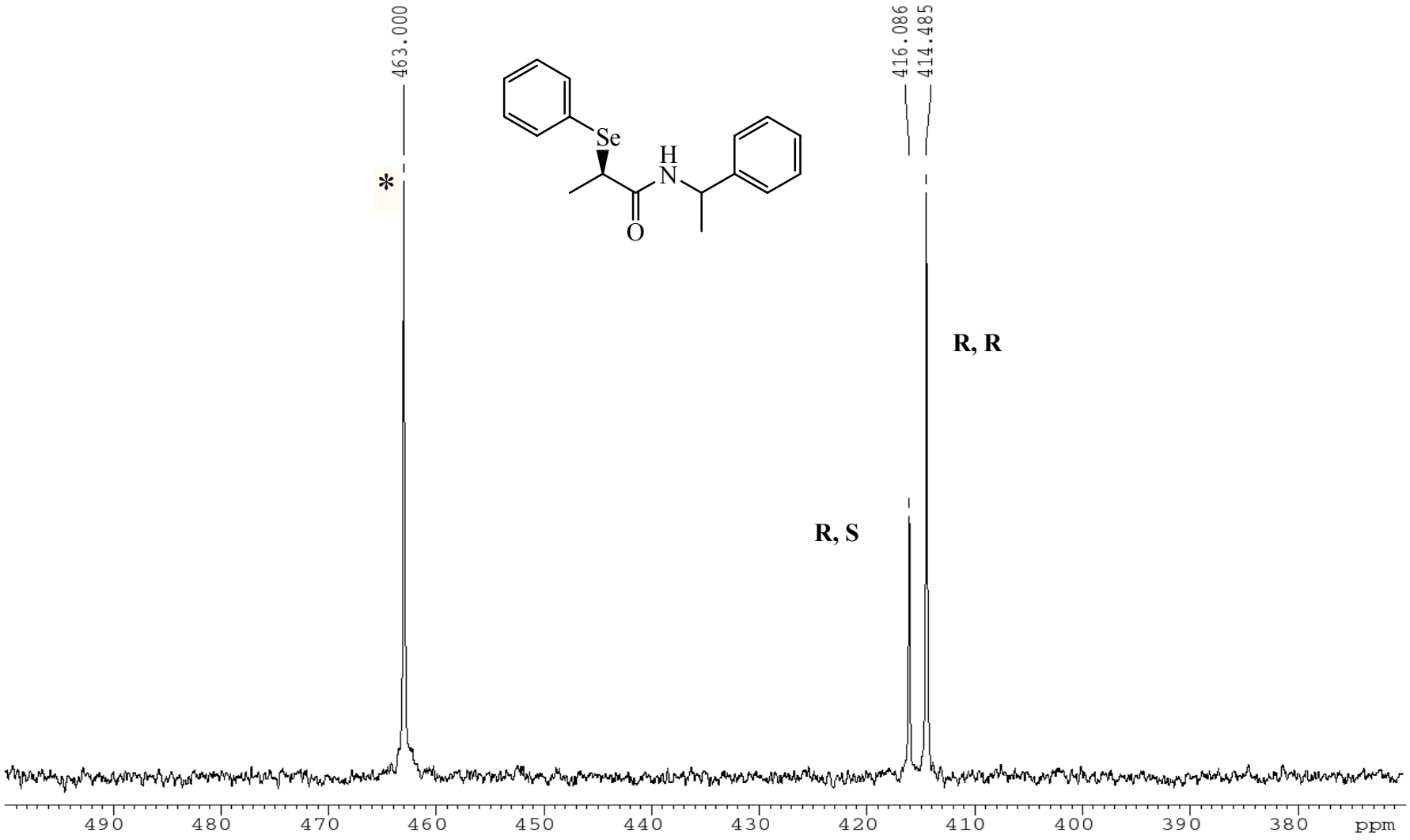
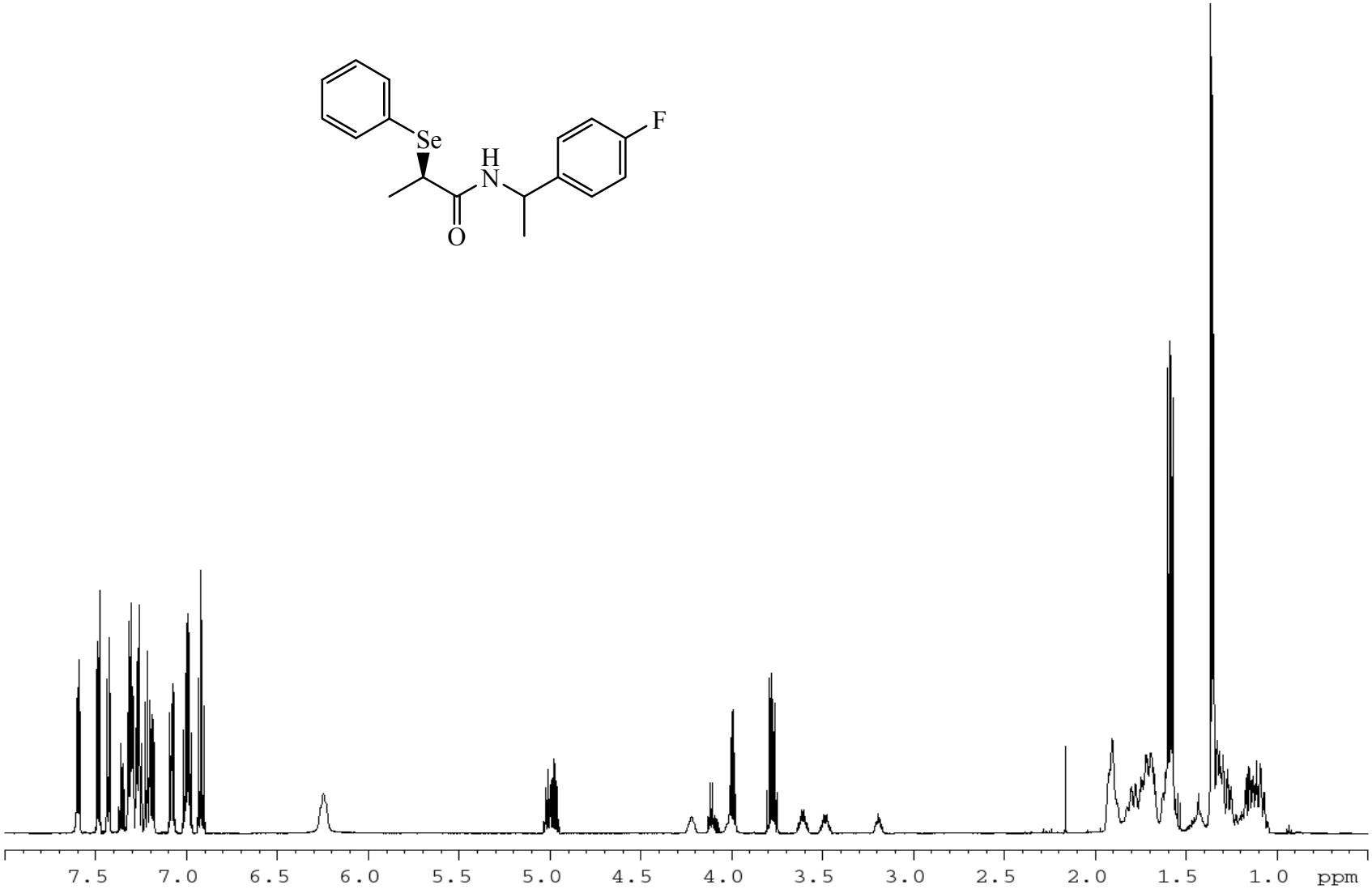
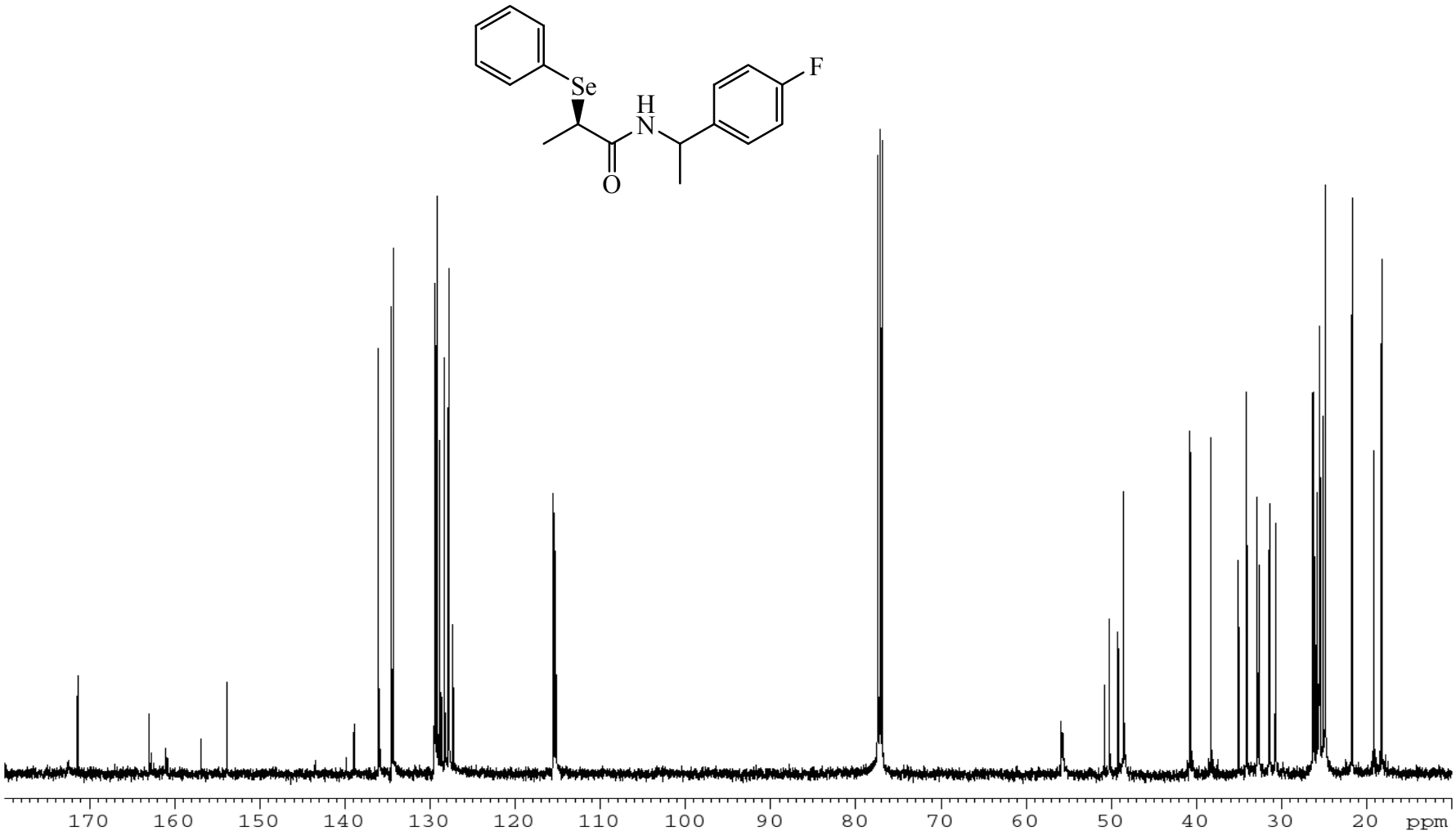


* Ph_2Se_2 standard (capillary insert)

(R)-N-((R)-1-(4-fluorophenyl)ethyl)-2-(phenylselanyl)propanamide **12a** (R)-N-((S)-1-(4-fluorophenyl)ethyl)-2-(phenylselanyl)propanamide **12b** (ratio 50 : 50)

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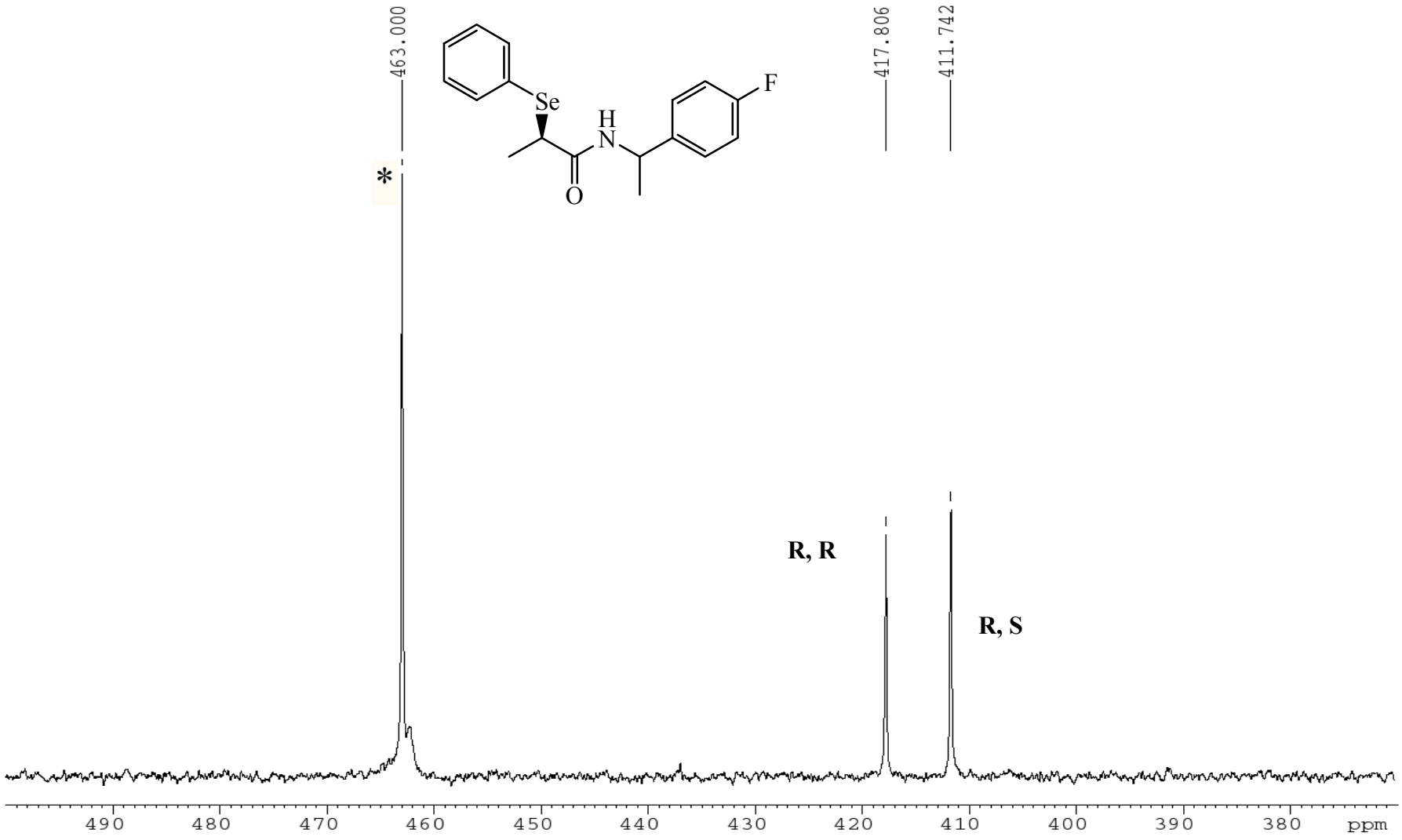
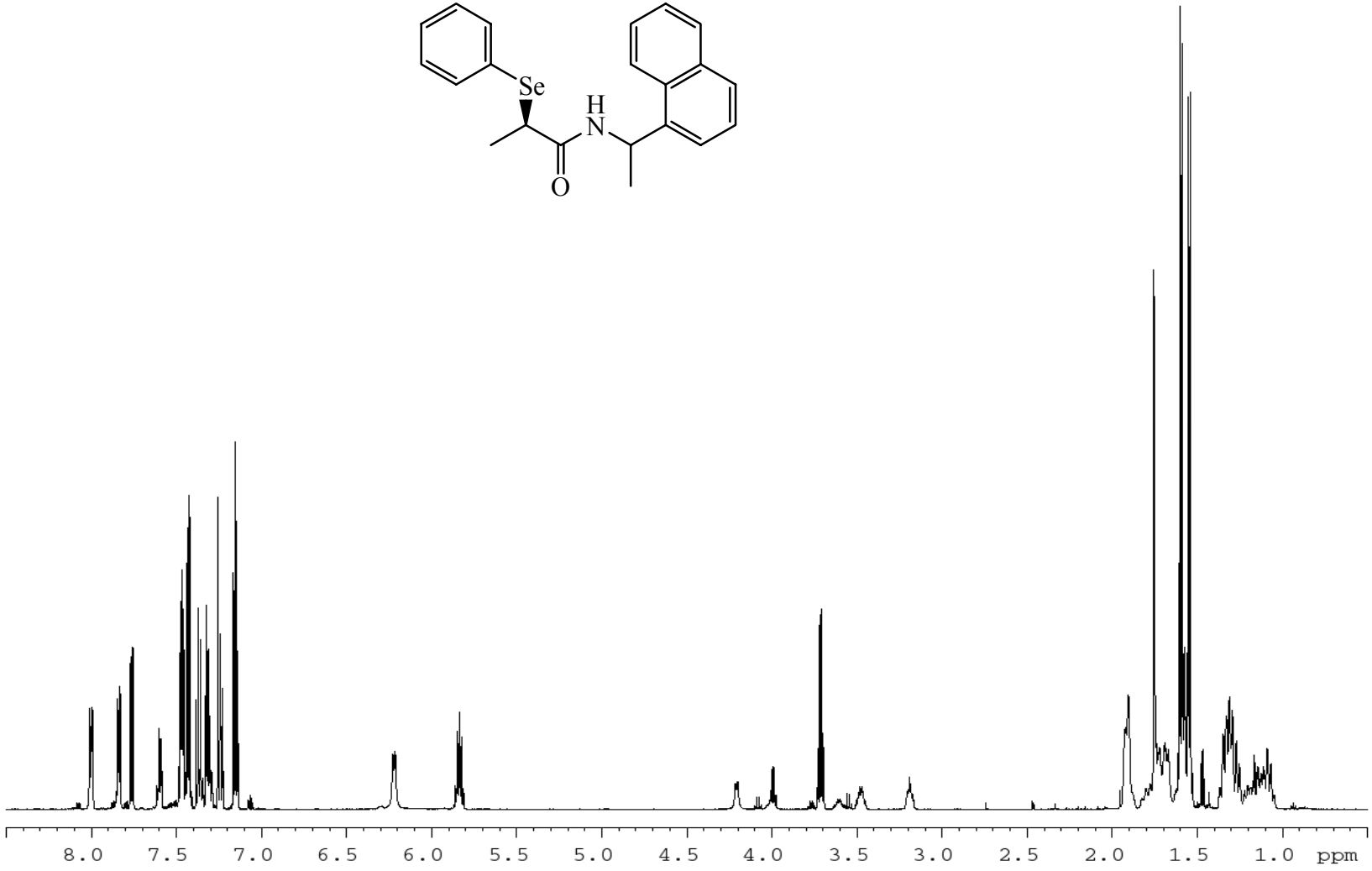
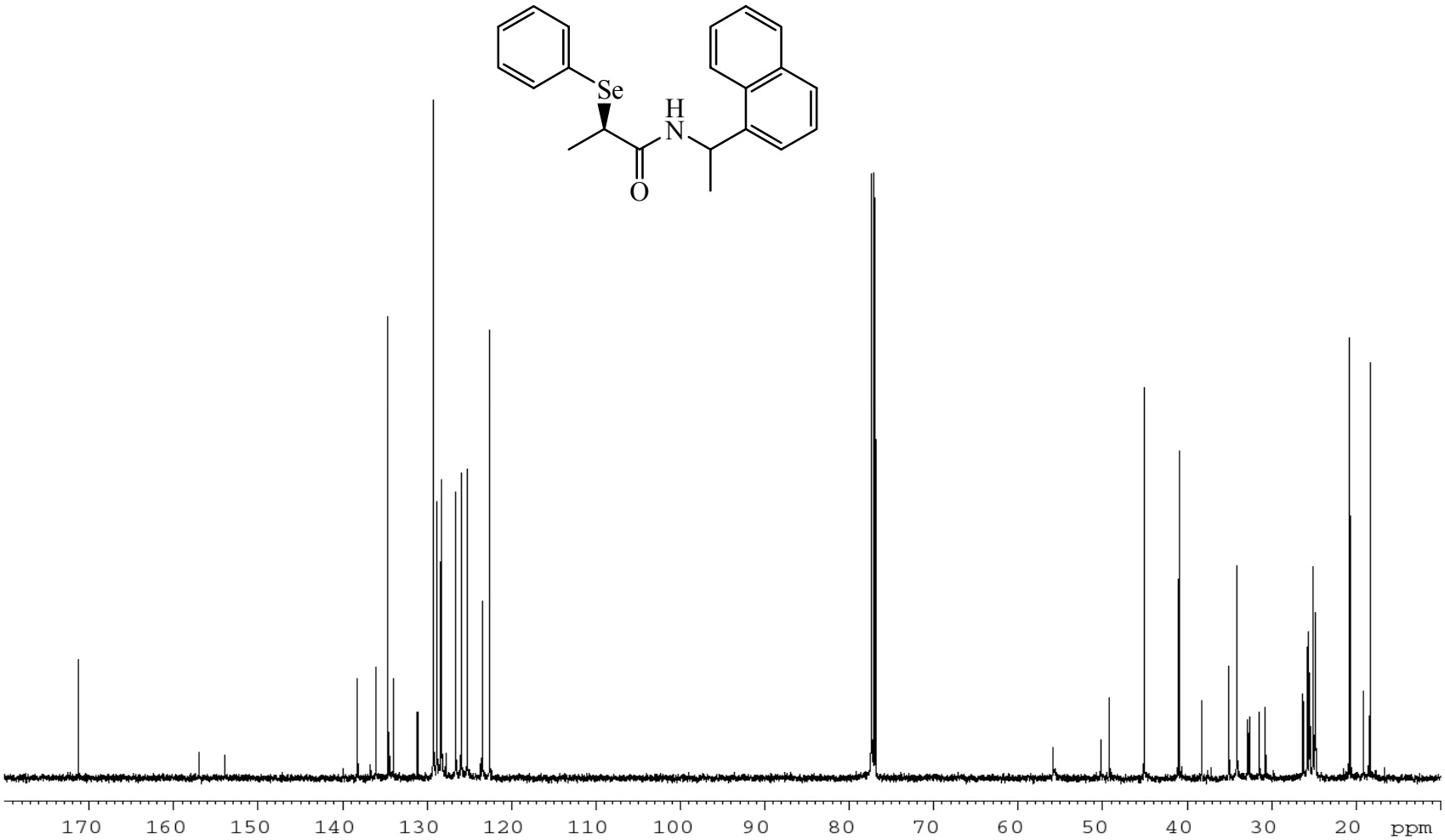


* Ph_2Se_2 standard (capillary insert)

(R)-N-((R)-1-(naphthalen-1-yl)ethyl)-2-(phenylselanyl)propanamide **13a** and (R)-N-((S)-1-(naphthalen-1-yl)ethyl)-2-(phenylselanyl)propanamide **13b** (ratio 96 : 4)

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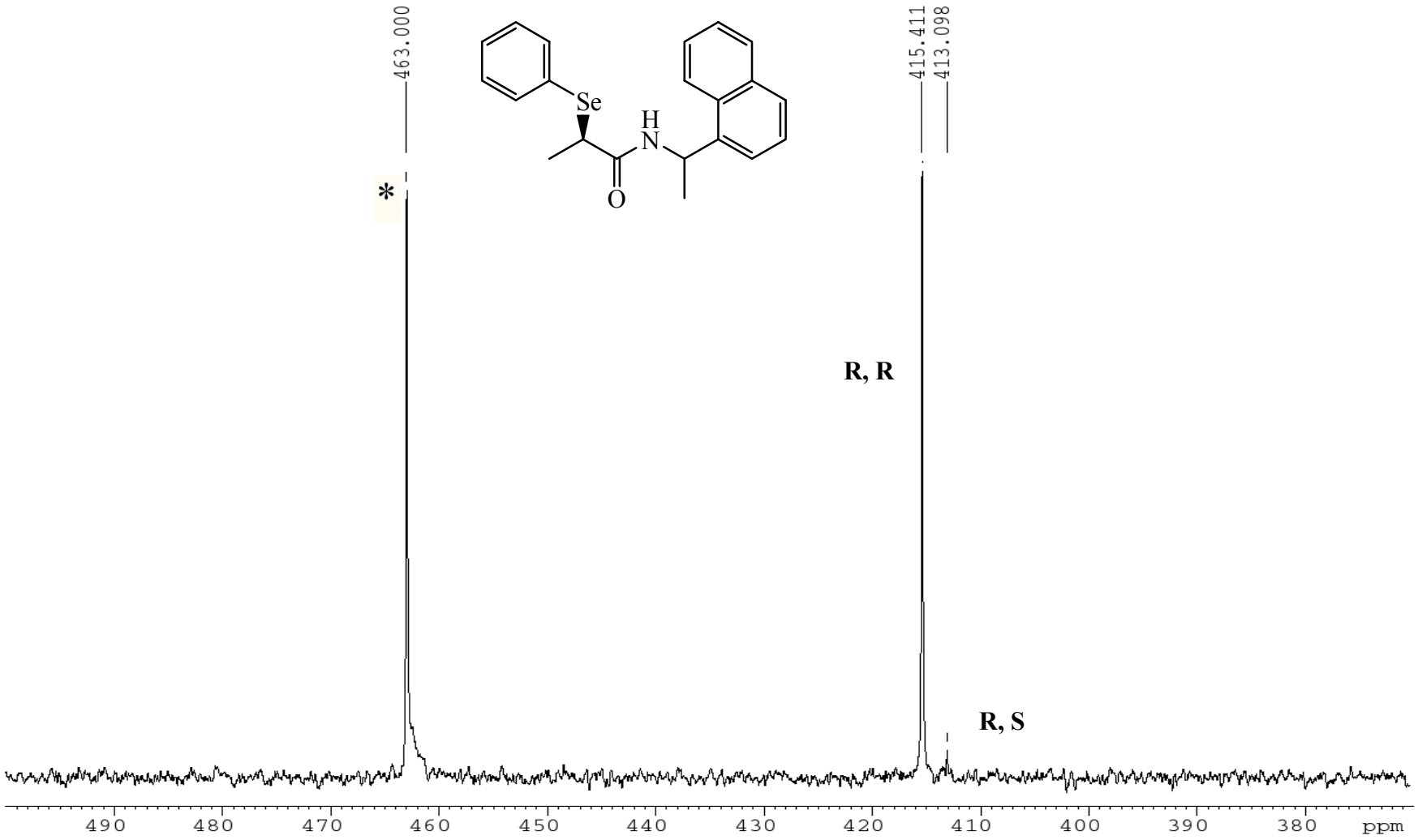

* Ph_2Se_2 standard (capillary insert)