

Synthesis of New Chiral Aliphatic Amino Diselenides and their Application as Catalysts for the Enantioselective Addition of Diethylzinc to Aldehydes

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SUPPORTING INFORMATION

Materials and Methods

Proton nuclear magnetic resonance spectra (^1H NMR) were obtained at 400 MHz on a Bruker DPX-400 NMR spectrometer. Spectra were recorded in CDCl_3 solutions. Chemical shifts are reported in ppm, referenced to the solvent peak of CDCl_3 . Data are reported as follows: chemical shift (δ), multiplicity, coupling constant (J) in Hertz and integrated intensity. Carbon-13 nuclear magnetic resonance spectra (^{13}C NMR) were obtained either at 100 MHz. ^{77}Se NMR are reported relative to diphenyl diselenide (δ 475 ppm) on the Bruker DPX-400 NMR. Spectra were recorded in CDCl_3 solutions. Chemical shifts are reported in ppm, referenced to the solvent peak of CDCl_3 . High-resolution mass spectra (ESI) were measured at the Institut of Plant Biochemistry, Halle-Saale, Germany, using a Bruker BioApex 70eV spectrometer. Gas chromatography (GC) was performed using a Varian 3800 gas chromatograph with Hydrodex *b*-3P column. HPLC analyses were carried out on a Shimadzu SCL – 10 Avp chromatograph using a Diacel Chiralcel OD column; solvent, 99:1 hexane/isopropanol; flow rate 0.5 $\text{ml}\cdot\text{min}^{-1}$; 254 nm detection. Column chromatography was performed using Merck Silica Gel (230-400 mesh) following the methods described by Still.¹ Thin layer chromatography (TLC) was performed using Merck Silica Gel GF₂₅₄, 0.25 mm thickness. For visualization, TLC plates were either placed under ultraviolet light, or stained with iodine vapor, or acidic vanillin. Most reactions were monitored by TLC for disappearance of starting material. The following

¹ Still, W.C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1975**, *43*, 2923-2925

solvents were dried and purified by distillation from the reagents indicated: tetrahydrofuran from sodium with a benzophenone ketyl indicator; dichloromethane from calcium hydride. All other solvents were ACS or HPLC grade unless otherwise noted. Air- and moisture-sensitive reactions were conducted in flame-dried or oven dried glassware equipped with tightly fitted rubber septa and under a positive atmosphere of dry nitrogen or argon. Reagents and solvents were handled using standard syringe techniques. Temperatures above room temperature were maintained by use of a mineral oil bath with an electrically heated coil connected to a Variac controller.

General Procedure for the Ring-Opening Reaction of Aziridines 2 with Li₂Se₂. Synthesis of Amino Diselenides 3. Lithium Diselenide was generated by reaction of gray elemental selenium (0.0947 g, 1.2 mmol) with Lithium Triethylborohydride (1.2 mL, 1.2 mmol) in dry THF (5 mL). The suspension was allowed to stir for at least 20 min, and a THF (10 mL) solution of aziridine 2 (1.0 mmol) was dropwise added within 20 min. The resulting solution was stirred for 12h at room temperature. The mixture was quenched with a saturated NH₄Cl solution (20 mL), extracted with CH₂Cl₂ and the combined organic fractions were collected, dried over magnesium sulphate and filtered, the solvent was removed *in vacuo* yielding a yellow solid which was purified by flash chromatography (Hexane:ethyl acetate 90:10). Drying *in vacuo* afforded the amino diselenide 3.

Selected spectral and analytical data for 3a: The enantiomeric purity was determined by HPLC analysis (column, Chiralcel-OD; eluent, hexane/2-propanol 98:02; flow rate, 1 mL/min; *R* isomer, *t_R* 16.3 min, *S* isomer, *t_R* 17.2 min) and found to be >99.9%. yield 0.235g (75%); mp 96 – 98 °C; [α]_D²⁰ = -8 (c = 1.0, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz) δ 7.24-7.11 (m, 5H); 4.89-4.87 (m, 1H); 4.09-4.05 (m, 1H); 3.11-2.99 (m, 2H); 2.83-2.80 (m, 2H); 1.33 (s, 9H); ¹³C NMR (CDCl₃, 100 MHz) δ 155.06; 137.46; 129.22; 128.95; 126.35; 79.14; 51.99; 39.75; 34.77; 28.25; ⁷⁷Se NMR (CDCl₃) δ 314.421; HRMS-ESI *m/z* calcd for C₂₈H₄₀N₂O₄Se₂ + Na⁺ 651.1209980, found 651.1210725

Selected spectral and analytical data for 3b: yield 0.194g (73%); mp 117°C; [α]_D²⁰ = +25 (c = 1.0, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz) δ 4.90-4.87 (m, 1H); 3.67-3.64 (m, 1H); 3.16-3.14 (m, 2H); 1.91-1.85 (m, 1H); 1.44 (s, 9H); 0.96 (d, 3H, *J* = 8.2); 0.92 (d, 3H, *J* = 8.2); ¹³C NMR (CDCl₃, 100 MHz) δ 155.59; 78.87; 56.28; 34.80; 34.03; 28.08; 19.36; 17.59; HRMS-ESI *m/z* calcd for C₂₀H₄₀N₂O₄Se₂ + Na⁺ 555.1194630, found 555.1210725.

Selected spectral and analytical data for 3c: yield 0.198g (71%); mp 86°C; [α]_D²⁰ = -19 (c = 1.0, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz) δ 4.97-4.95 (m, 1H); 3.88-3.86 (m, 1H); 3.25-3.23 (m, 1H); 3.11-3.07 (m, 2H); 1.70-1.65 (m, 2H); 1.44 (s, 9H); 0.94 (d, 6H, *J* = 9.4); ¹³C NMR (CDCl₃, 100 MHz) δ 155.35; 79.08; 49.22; 42.33; 28.37; 26.00; 24.94; 23.01; 22.10; HRMS-ESI *m/z* calcd for C₂₂H₄₄N₂O₄Se₂ + Na⁺ 583.1527540, found 583.15233727.

Selected spectral and analytical data for 3d: yield 0.201g (72%); mp 88°C; $[\alpha]_D^{20} = +53$ (c = 1.0, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz) δ 4.74-4.72 (m, 1H); 3.66-3.64 (m, 1H); 3.13-3.09 (m, 2H); 1.59-1.57 (m, 1H); 1.37 (s, 9H); 1.08-1.03 (m, 2H); 0.86-0.82 (m, 6H); ¹³C NMR (CDCl₃, 100 MHz) δ 155.57; 79.02; 55.51; 38.01; 34.11; 28.38; 24.91; 15.41; 11.49; HRMS-ESI *m/z* calcd for C₂₂H₄₄N₂O₄Se₂ + Na⁺ 583.1527540, found 583.15233727.

General Procedure for the Diethylzinc Addition to Aldehydes

In a 25 mL flask, a solution of toluene (7 mL), aldehyde (1.0 mmol), and the catalyst (0.5 mol%, 12.5 μmol) was stirred for 30 min at room temperature. Diethylzinc (1M in hexane, 2.5 mmol) was slowly injected under constant stirring and was continued for 24h at room temperature. Cooling (0°C) of the reaction mixture was followed by the slow addition of HCl (aq, 1M, 5mL). The organic layer was separated and washed with HCl (aq, 1M, 3 mL). Drying over magnesium sulphate, filtration, and evaporation of the solvent *in vacuo* yielded the crude alcohol. Purification was performed by bulb-to-bulb distillation under reduced pressure (ca. 0.1mbar).

Conditions for the Analysis of Chiral Secondary Alcohols

Chiral Capillary GC: Hydrodex *b*-3P column 25 m x 0.25 mm. Carrier Gas: H₂ (5 mL/min). Detector: FID, 280 °C. Injector: 220 °C.

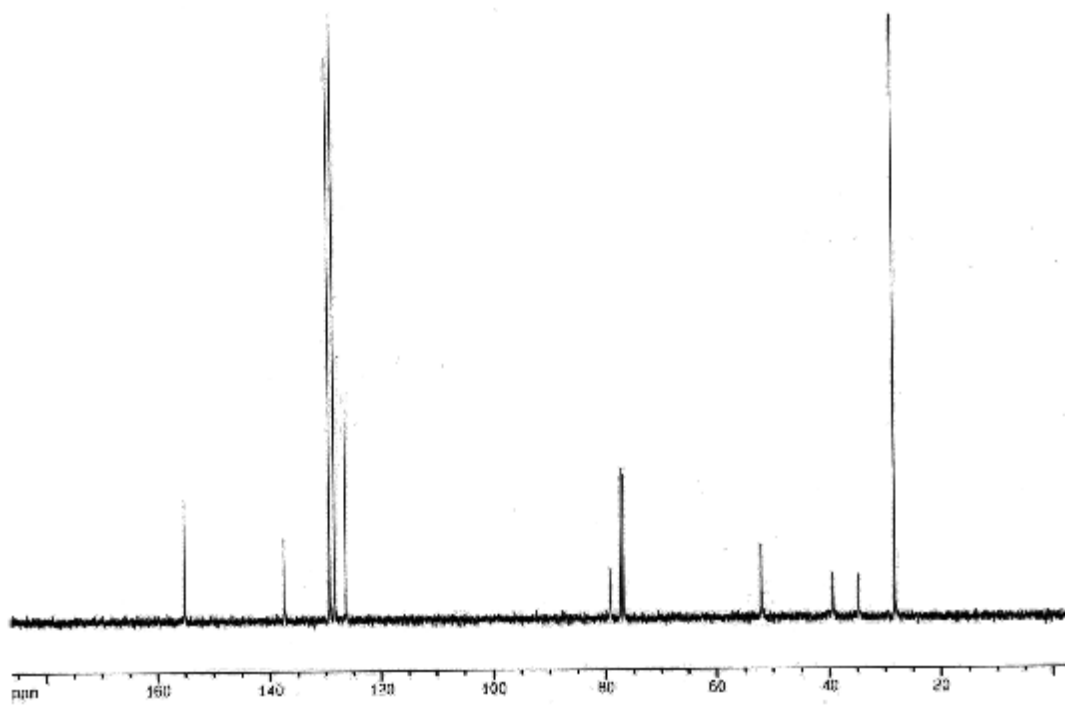
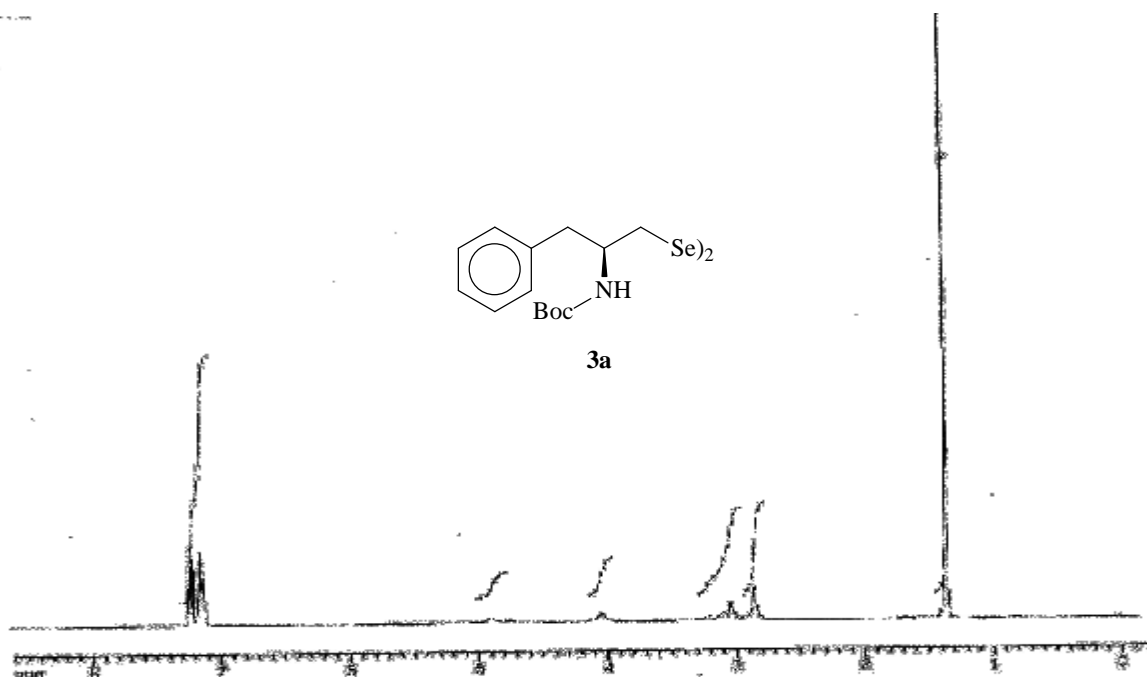
Chiral HPLC: Chiralcel OD column; 254 nm UV detector.

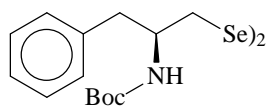
The racemic alcohols products were obtained by addition of EtMgBr to aldehydes. The conditions of analysis and retention times of the *R* and *S* isomers have been reported elsewhere.²

² (a) Huang, W. -S.; Hu, Q. -S.; Pu, L. *J. Org. Chem.* **1998**, *63*, 1364-1365 (see also supporting information)

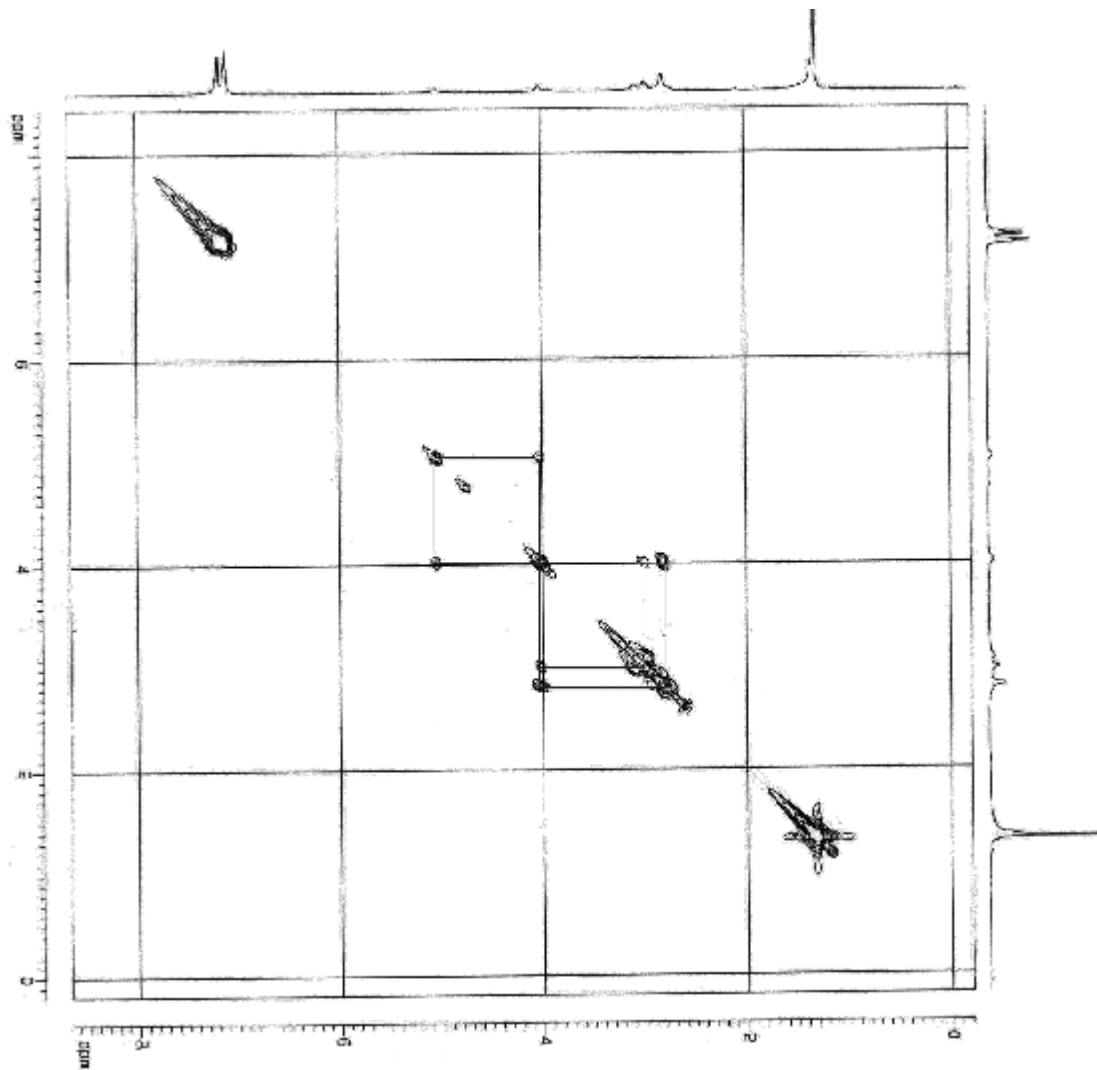
(b) Huang, W. -S.; Pu, L. *J. Org. Chem.* **1999**, *64*, 4222-4223.

SELECTED SPECTRA:

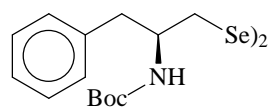




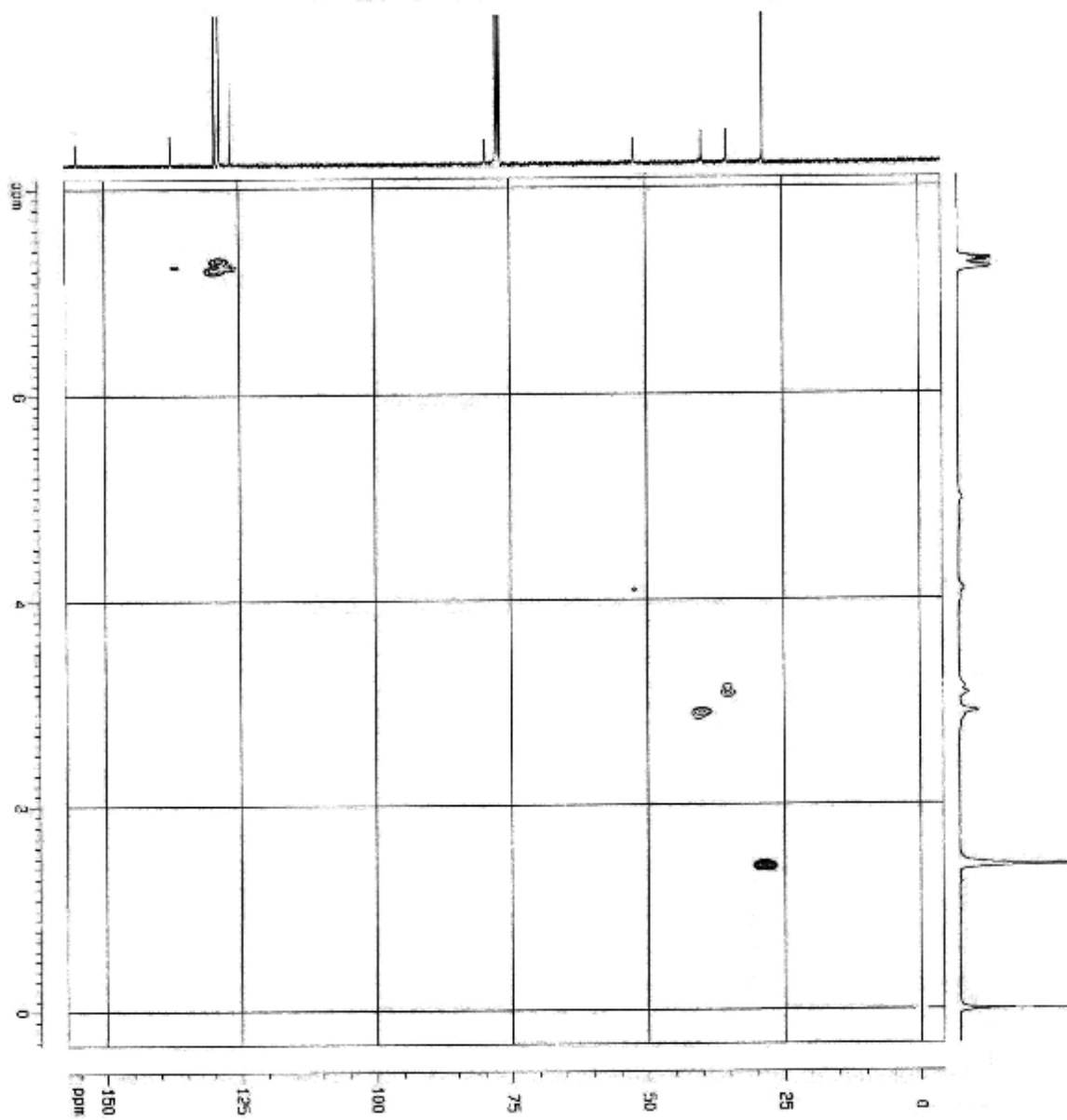
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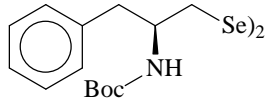


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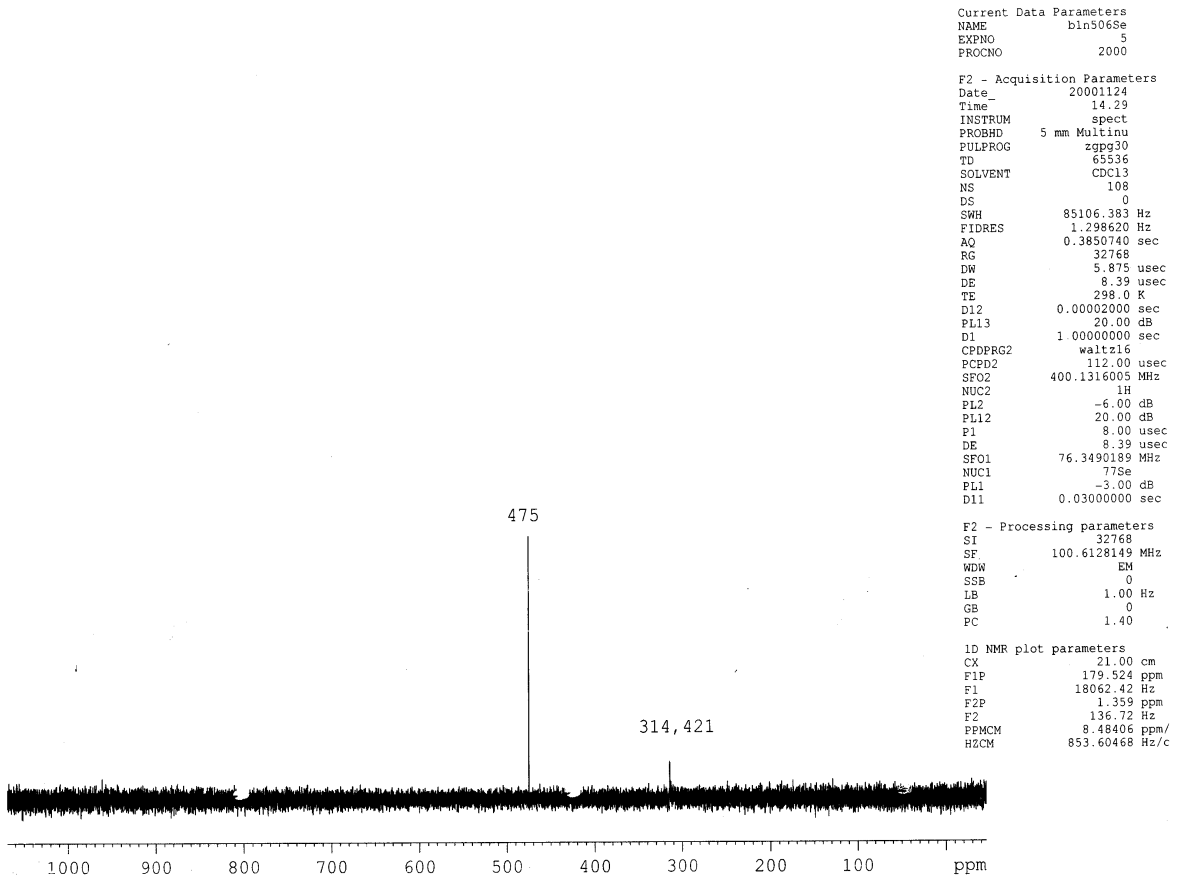


3a





3a



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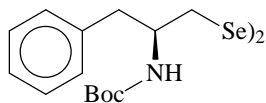
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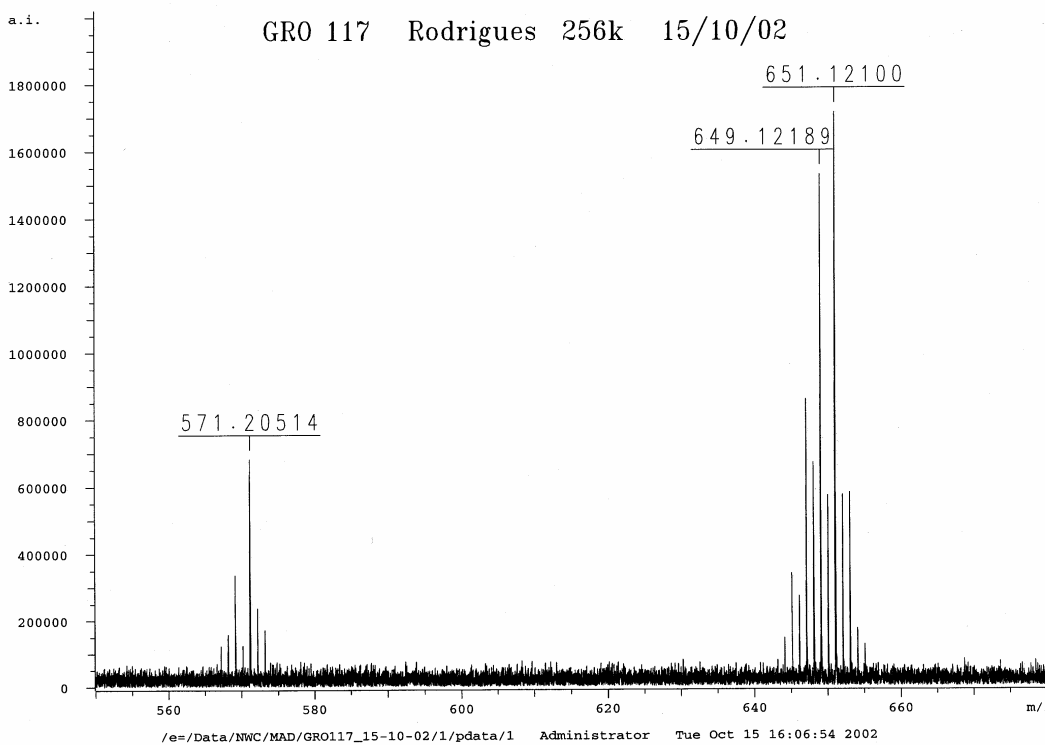
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NMR ⁷⁷Se



3a



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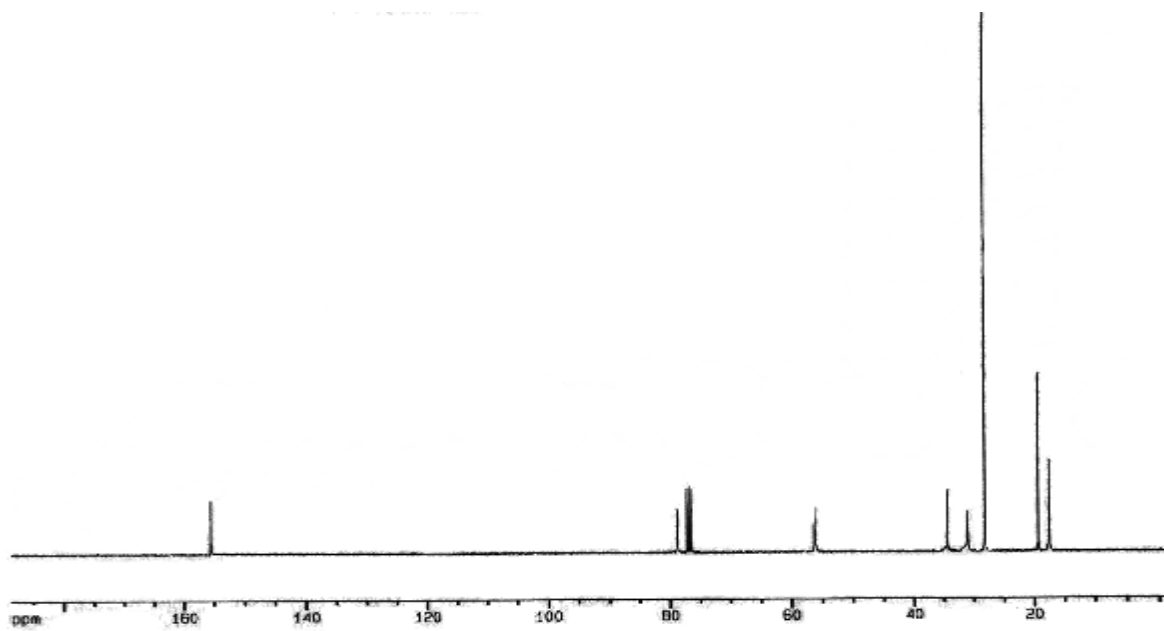
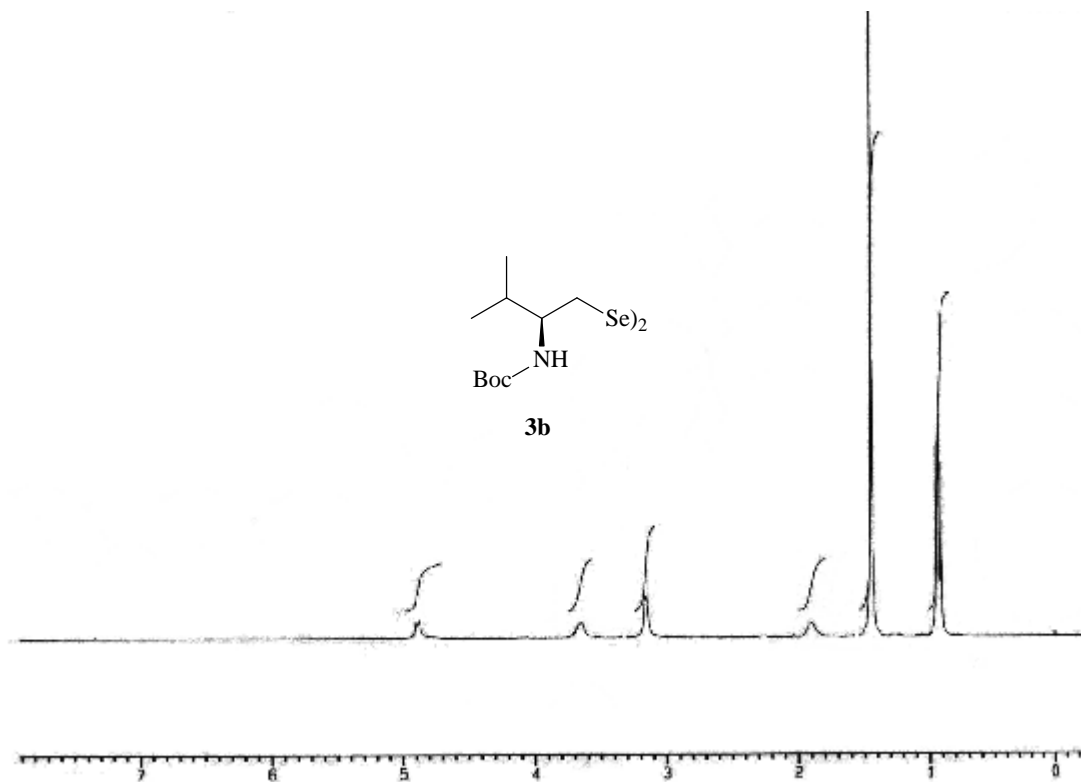
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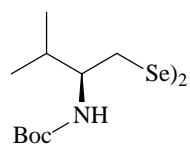
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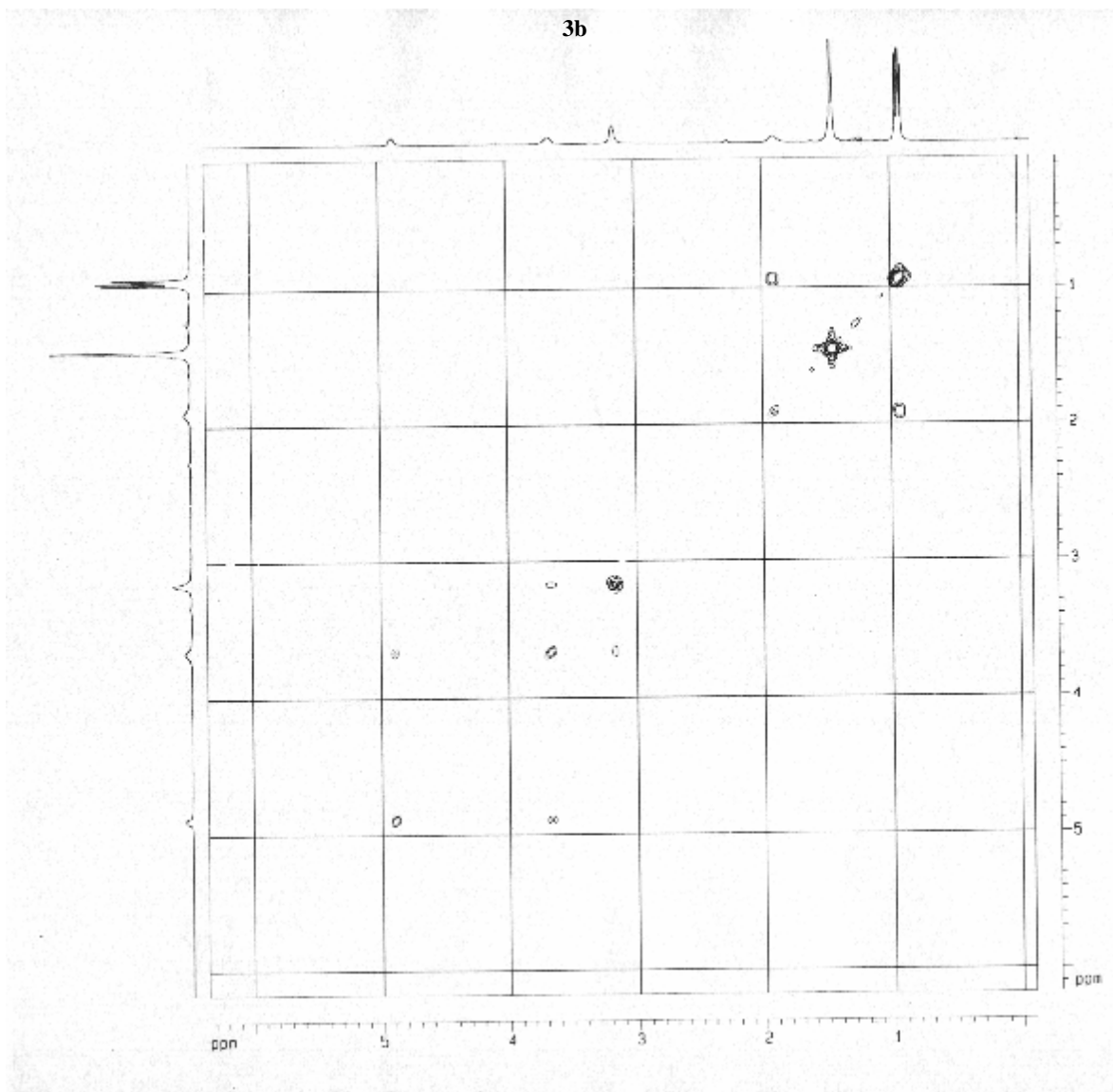
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80Se	0 2	0.00 100.00
14N	0 2	0.00 100.00
23Na	0 1	0.00 100.00

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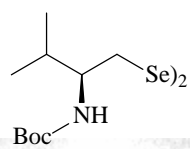




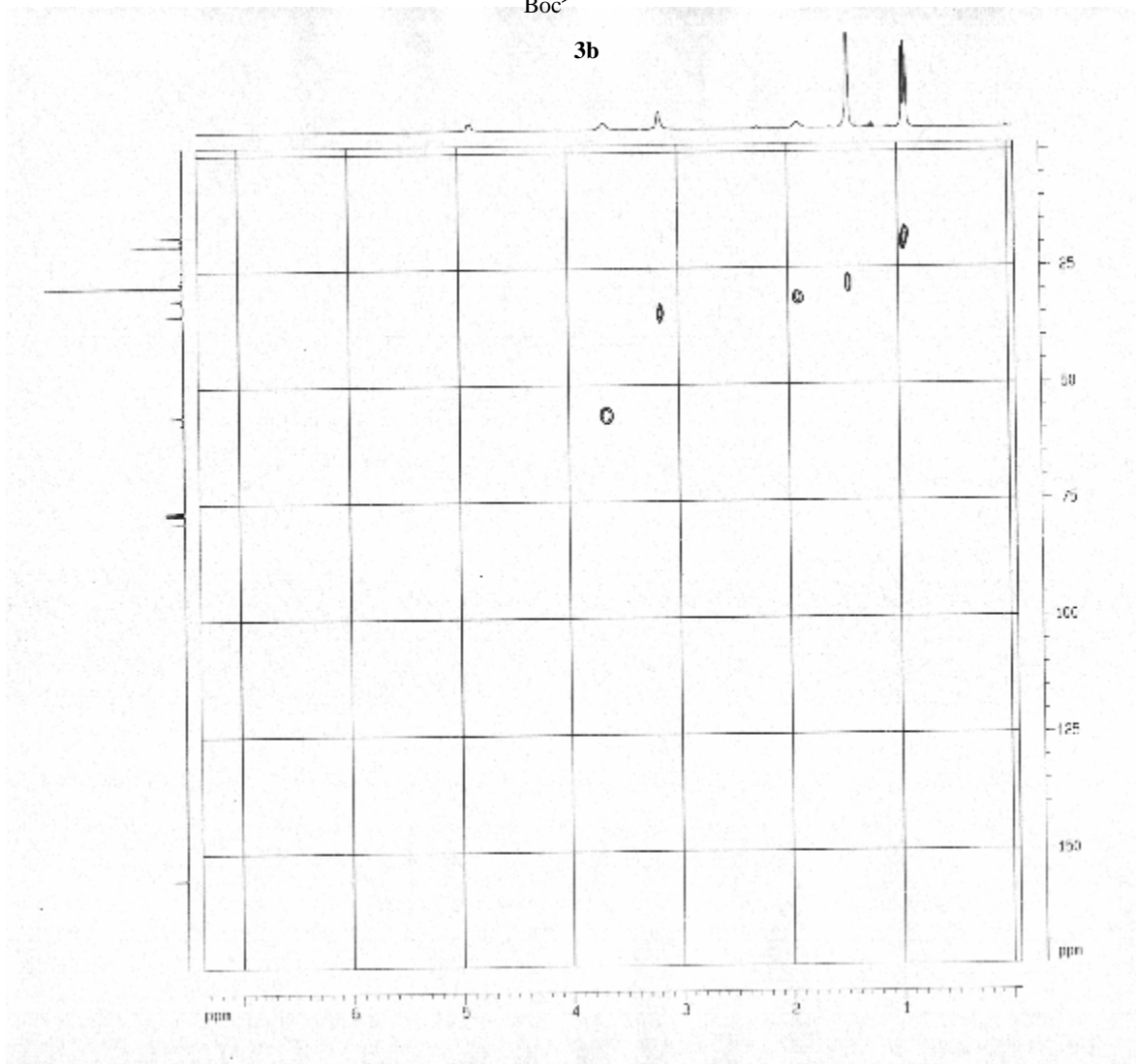
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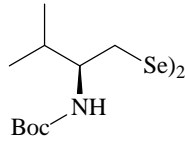
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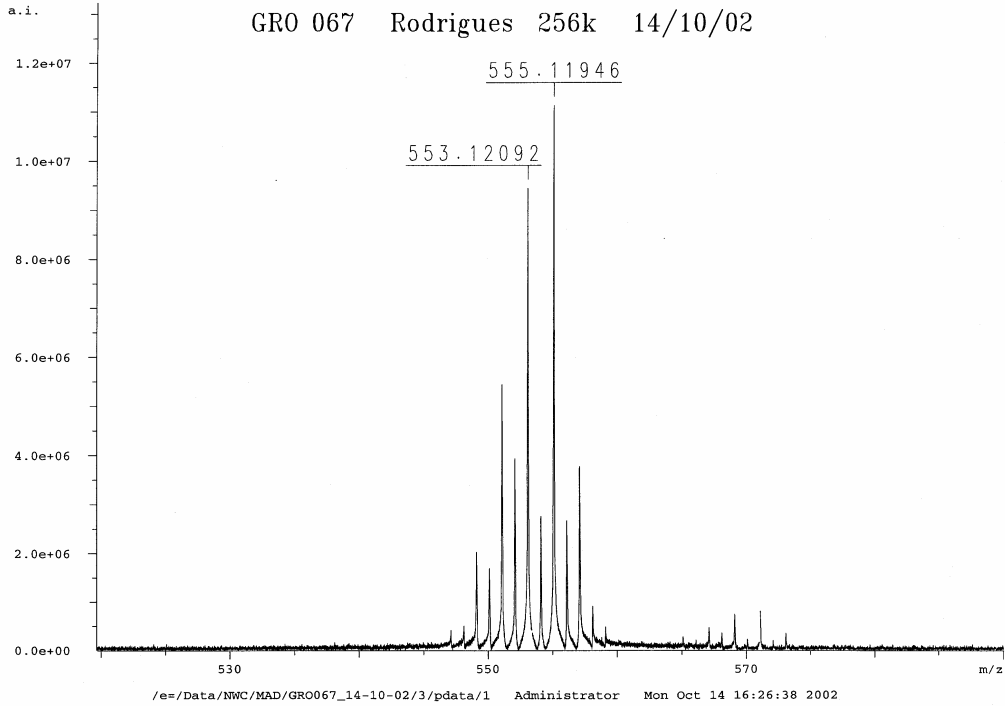
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2D-NMR HMQC $^1\text{H} - ^{13}\text{C}$



3b



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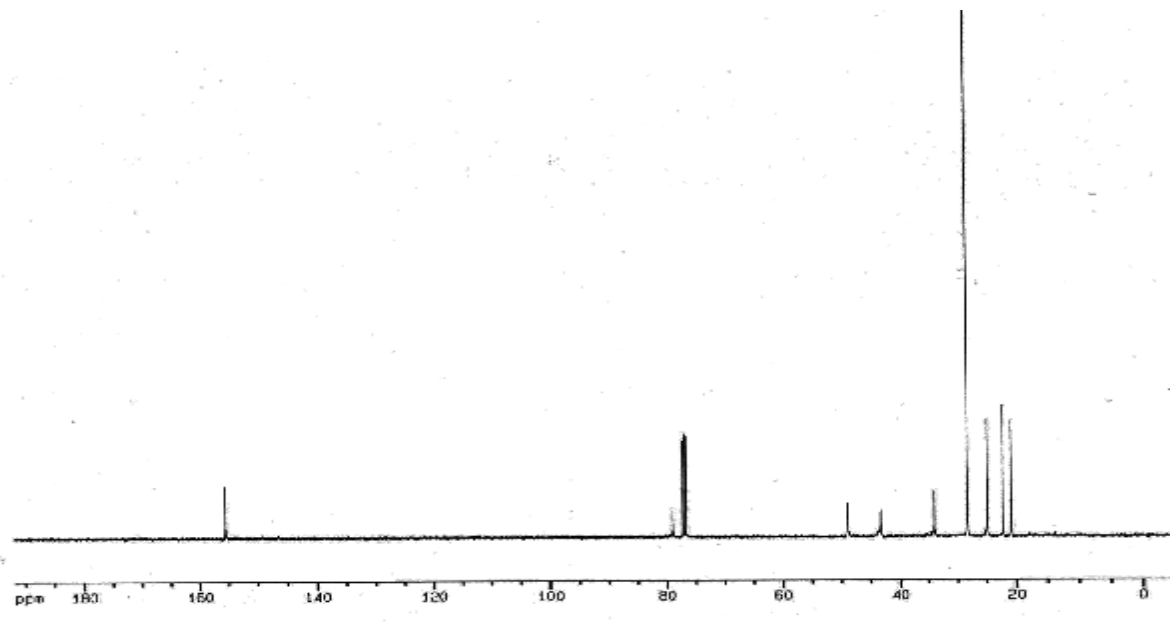
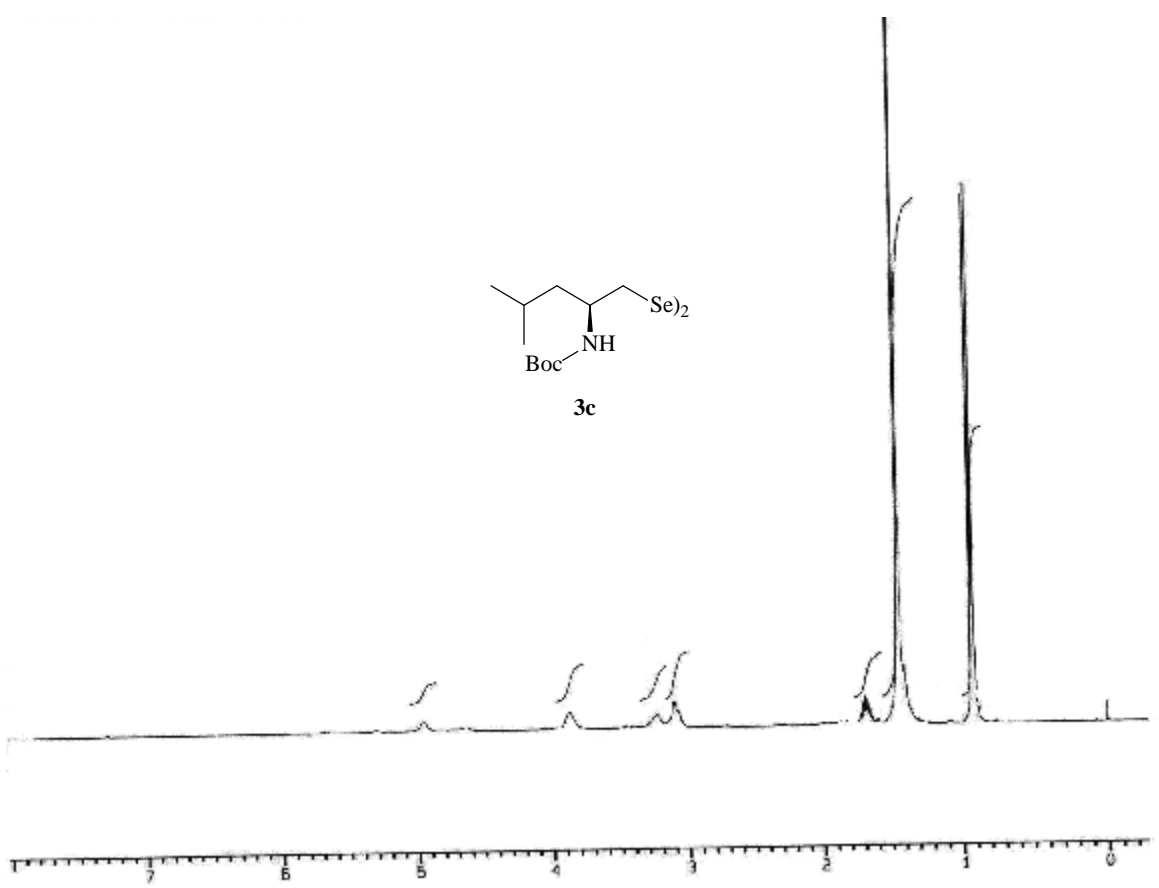
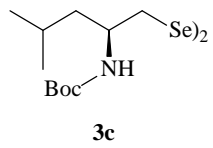
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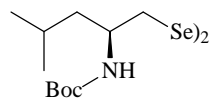
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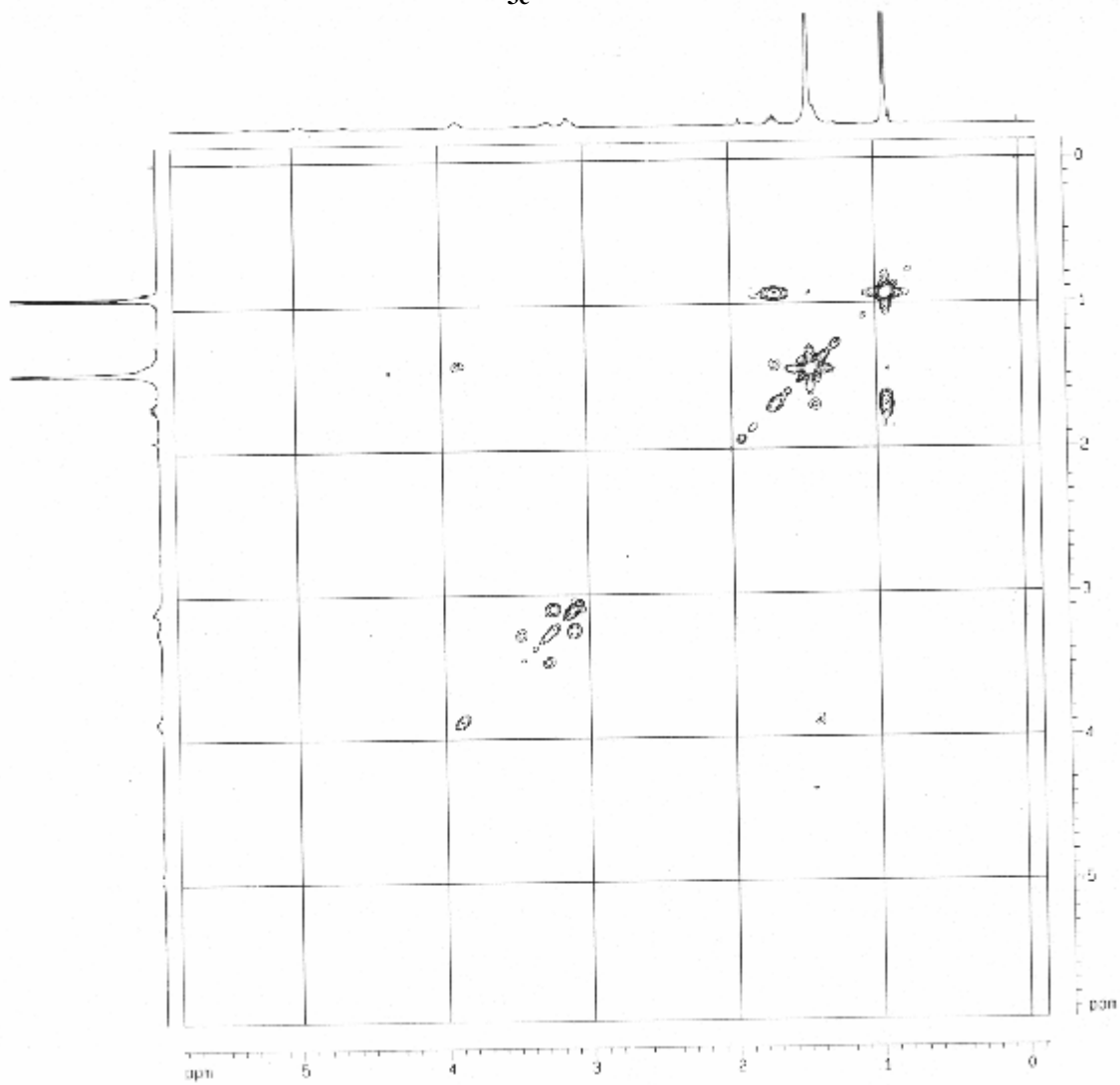
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16O	0 10	0.00 100.00
80Se	0 2	0.00 100.00
14N	0 4	0.00 100.00
23Na	1 1	0.00 100.00

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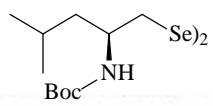




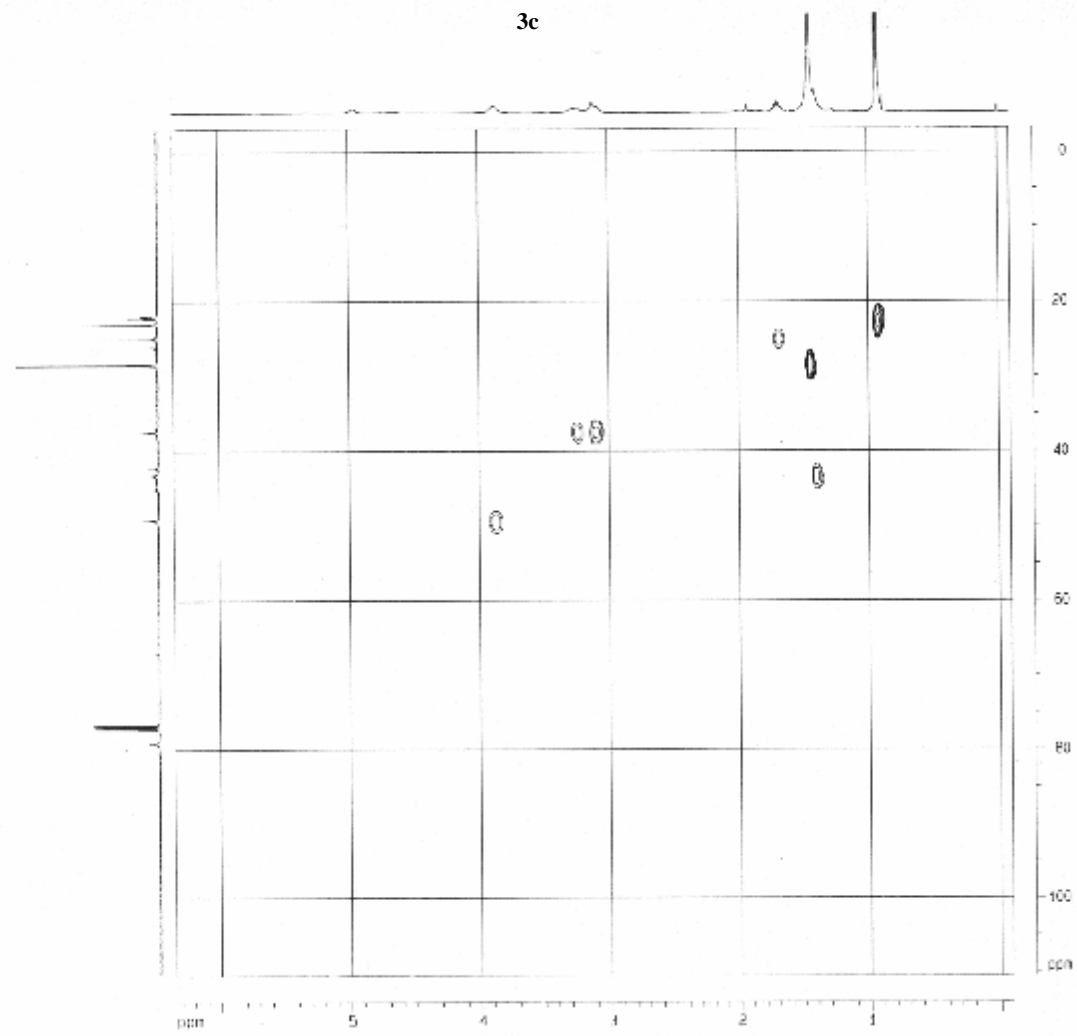
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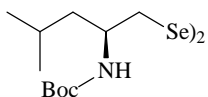
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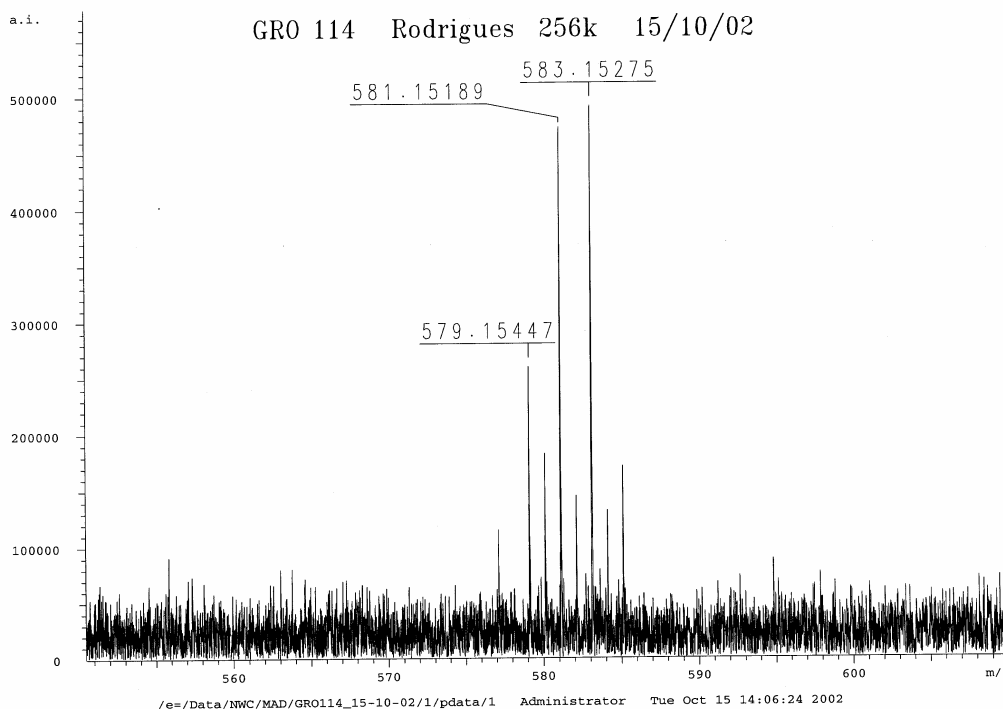
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2D-NMR HMQC ^1H - ^{13}C



3c



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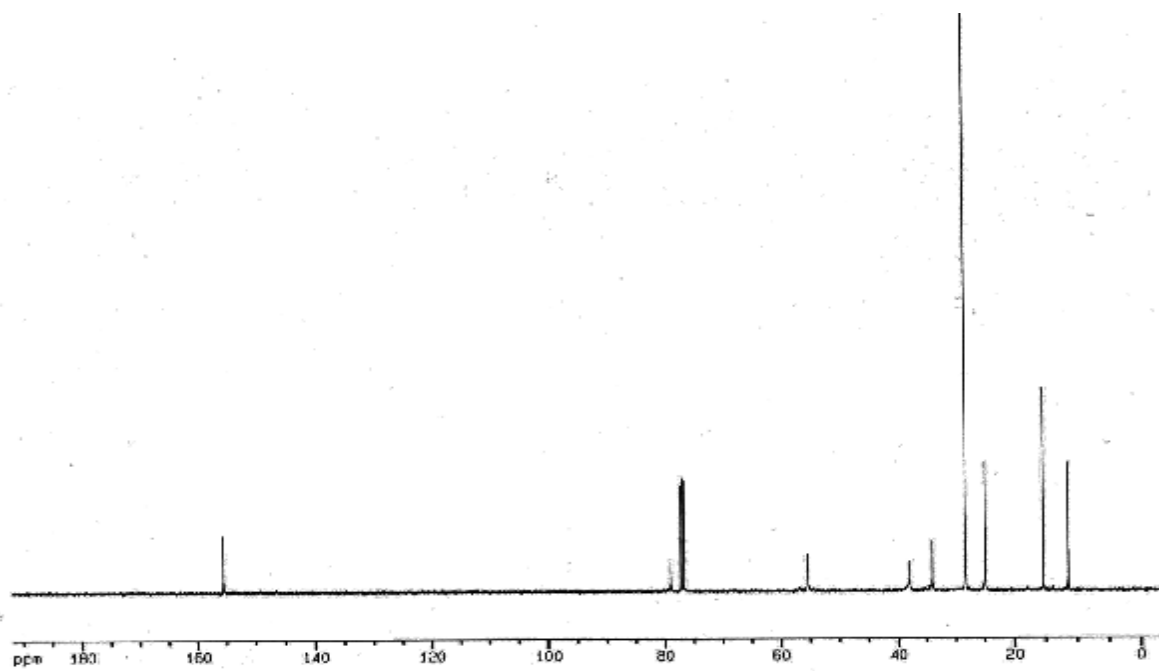
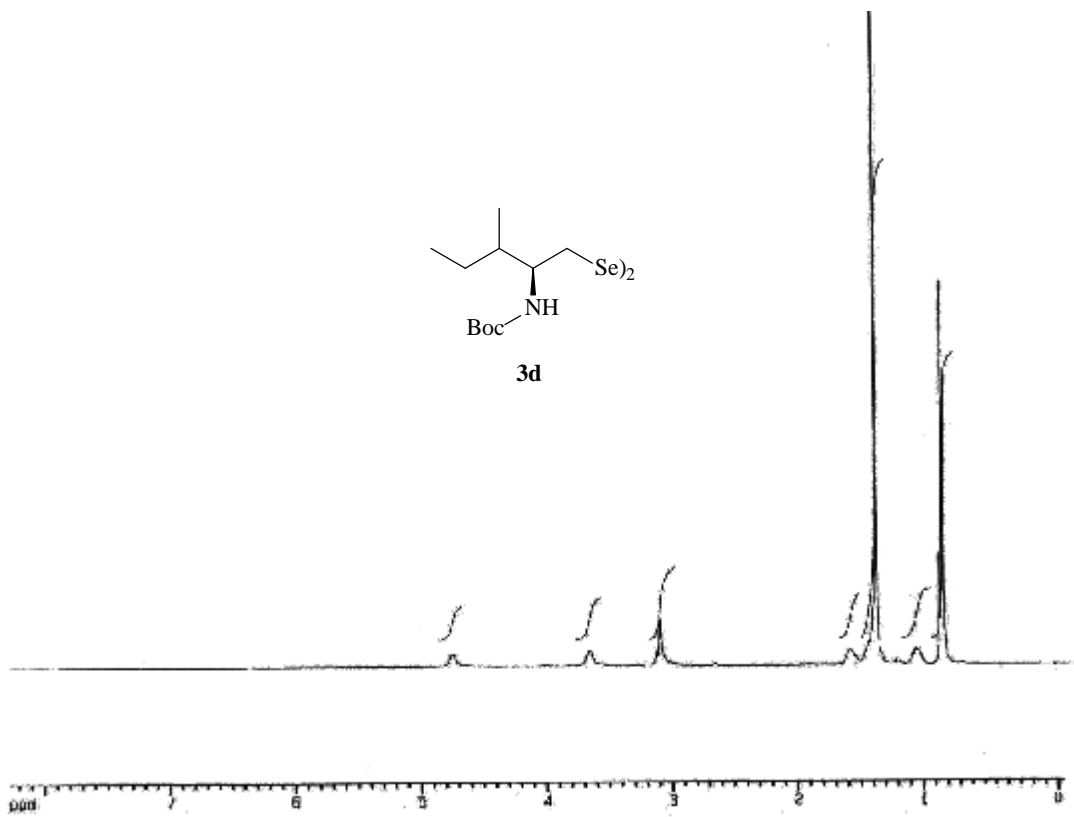
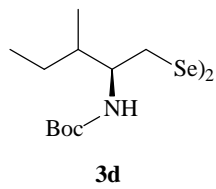
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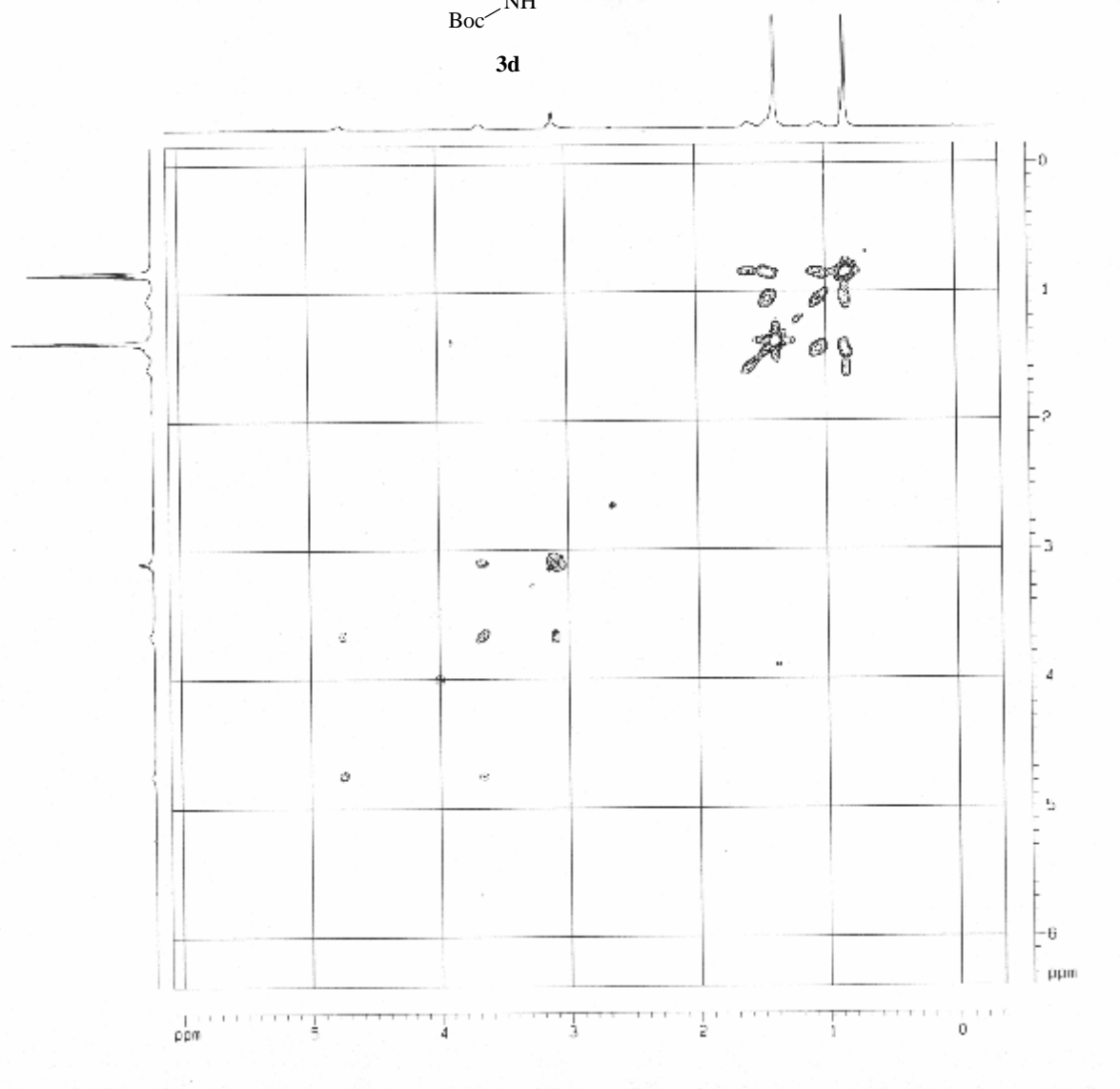
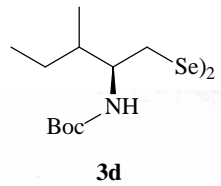
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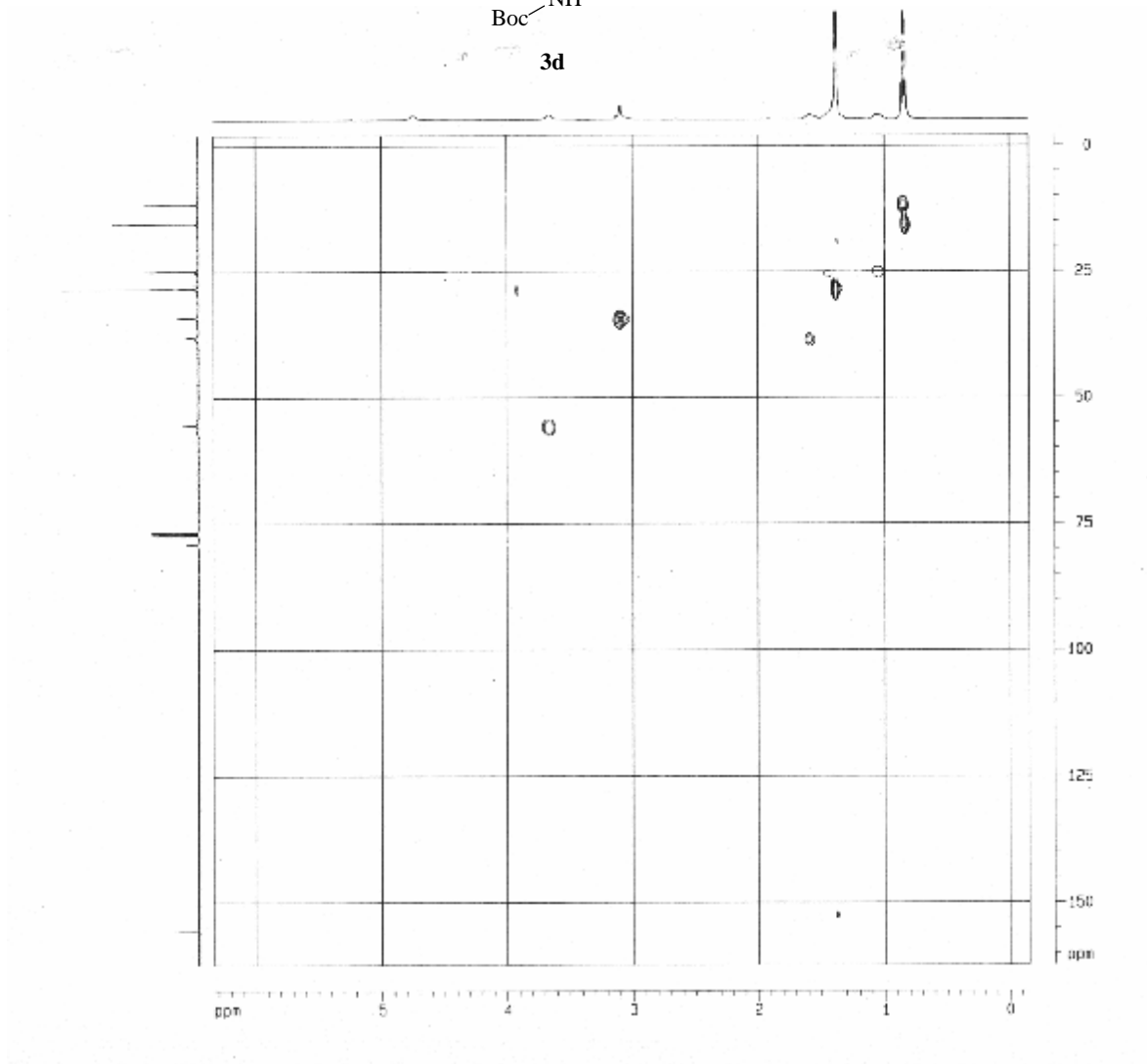
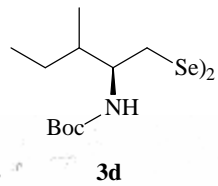
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23Na	1 1	0.00 100.00

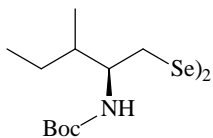
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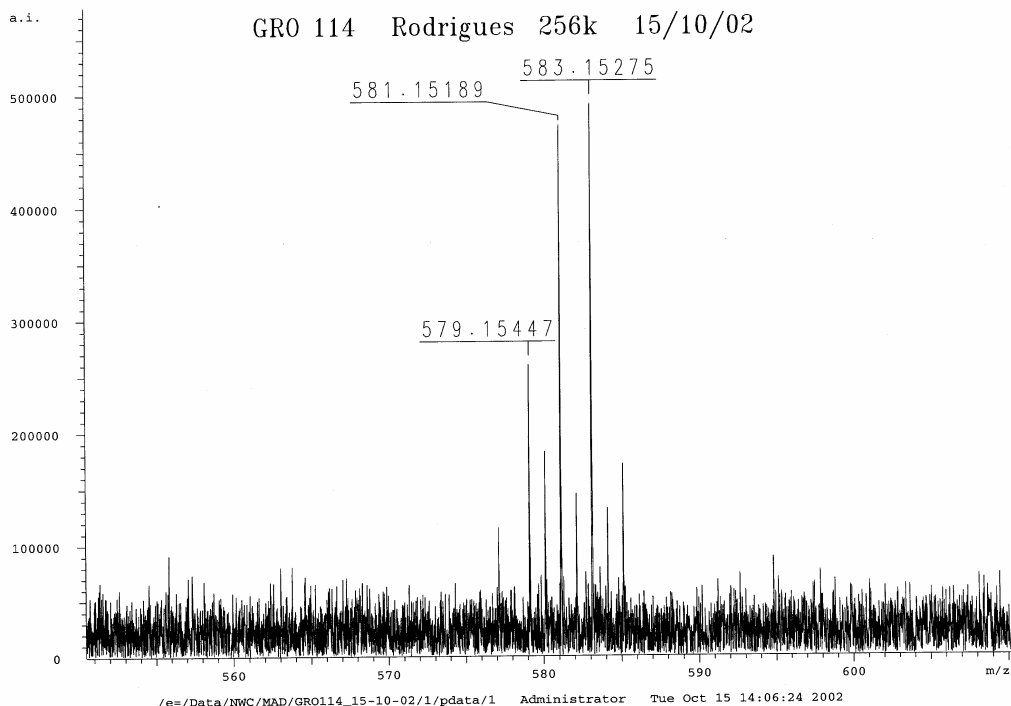


2D-NMR COSY $^1\text{H} - ^1\text{H}$





3d



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16O	0 10	0.00 100.00
80Se	0 2	0.00 100.00
14N	0 2	0.00 100.00
23Na	1 1	0.00 100.00

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3	36	32	1	1	0	1	583.1510586	20.5 2.907e-06

