SUPPORTING INFORMATION FOR

Diselenides and Allyl Selenides as Glutathione Peroxidase Mimetics. Remarkable Activity of Cyclic Seleninates Produced In Situ by the Oxidation of Allyl ω-Hydroxyalkyl Selenides

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Experimental Procedures

NMR spectra were recorded in $CDCl_3$ unless otherwise noted; ^{77}Se NMR spectra were obtained in $CDCl_3$ with diphenyl diselenide used as an external standard. Chemical shifts are reported relative to dimethyl selenide (δ 0.0) by assuming that the resonance of diphenyl diselenide is at δ 461.0.[1] Mass spectra were obtained by EI unless otherwise noted. The following compounds were prepared by literature methods: Ebselen (**1**),[2] selenenamide **2**,[3] and the selenocystine derivative **16**.[4] Selenocystamine (**11**) was commercially available as the hydrochloride salt. Chromatography refers to flash chromatography over silica gel unless otherwise indicated.

Preparation of diselenides: di(3-hydroxypropyl) diselenide (9),[5] typical procedure. Sodium borohydride (5.60 g, 148 mmol) and selenium (5.60 g, 70.9 mmol) were placed in an ice-cooled 3-necked flask fitted with a condenser, gas inlet adapter and dropping funnel under a nitrogen atmosphere. Water (300 mL) was added in one portion, with stirring. (**Caution: Vigorous reaction with hydrogen evolution!).** After the initial vigorous reaction had subsided (ca. 10 min), the ice-bath was removed and a second portion of elemental selenium (5.60 g, 70.9 mmol) was added to the colorless mixture. The mixture was then warmed briefly using a hot air gun to complete the dissolution of the selenium (ca. 15 min). The brownish-red aqueous solution of Na_2Se_2 was cooled to room temperature and 3-bromopropanol (20.0 g, 144 mmol) in 100 mL of H_2O was added. The resulting yellow solution was stirred for a further 3 h. The aqueous layer was extracted with several portions of ether and ethyl acetate and the organic extracts were combined, dried (Na_2SO_4) and the solvent was concentrated *in vacuo*. The residue was chromatographed (elution with 50% ethyl acetate-hexanes) to afford 8.70 g (44%) of **9**

as a yellow oil; ^{1}H NMR (200 MHz) δ 3.78 (t, *J* = 6.2 Hz, 4 H), 3.04 (t, *J* = 7.2 Hz, 4 H), 2.24 (br s, 2 H), 2.02 (quintet, *J* = 6.6 Hz, 4 H); ^{13}C NMR (50 MHz) δ 61.5, 33.5, 26.1; mass spectrum, *m/z* (relative intensity) 278 (9, M^+), 202 (63), 160 (51), 107 (55), 59 (100), 41 (84). Exact mass calcd for $C_6H_{14}O_2Se_2$: 277.9324. Found: 277.9313.

The following known diselenides were prepared similarly from Na_2Se_2 and the corresponding bromo compounds in the indicated yields. Water was employed as the solvent, except in the case of **7**, where ethanol was used. The products were isolated by flash chromatography or direct recrystallization from the crude mixtures. Diselenide **4**: white solid, 25% yield, mp 102-105 °C (lit.[6] mp 104.5-105.5 °C); **5**: pale yellow solid, 52% yield, mp 130-132 °C (lit.[7] mp 134.5-135.5 °C); **6**: pale yellow solid, 46% yield, mp 85-86 °C (from carbon tetrachloride), (lit.[8] mp 88 °C); **7**:[6] yellow oil, 46% yield; **8**:[9] yellow oil, 57% yield; **10**:[5] yellow oil, 51% yield; **12**:[10] yellow oil obtained as an inseparable mixture of the diselenide and selenide in the ratio of 79:21 (^{1}H NMR integration) and used without further purification.

***N,N'*-Dibenzoyl di(3-aminopropyl) diselenide (13).** From *N*-(3-bromopropyl)-benzamide[11] and Na_2Se_2 by the same procedure as used in the preparation of **9**: pale yellow solid, 98% yield; mp 134-136 °C (from methanol); IR (film) 3316, 1631 cm^{-1}; ^{1}H-NMR (200 MHz) δ 7.87 (m, 4 H), 7.56-7.31 (m, 6 H), 6.66 (br s, 2 H), 3.58 (crude q, J = 6.6 Hz, 4 H), 3.03 (t, *J* = 7.2 Hz, 4 H), 1.09 (quintet, *J* = 7.1 Hz, 4 H); mass spectrum, *m/z* (relative intensity) 484 (1, M^+), 160 (93), 134 (100). Anal. calcd for $C_{20}H_{24}N_2O_2Se_2$: C, 49.80; H, 5.02; N, 5.81. Found: C, 49.91; H, 4.86; N, 5.75.

***N,N'*-Di(methoxycarbonyl) di(3-aminopropyl) diselenide (14).** Methyl *N*-(3-bromopropyl)carbamate was obtained from 3-bromopropylamine and methyl

chloroformate by the same method as employed previously for the preparation of the corresponding 2-bromoethyl homolog.[12] It was then treated with Na_2Se_2 by the same procedure as used in the preparation of **9**: pale yellow solid, 63% yield; mp 54-56 ^oC (from ethyl acetate-hexanes); IR (film) 3335, 1697 cm^{-1}; ^1H-NMR (200 MHz) δ 4.92 (br s, 2 H), 3.69 (s, 6 H), 3.30 (crude q, *J* = 6.6 Hz, 4 H), 2.95 (t, *J* = 7.3 Hz, 4 H), 1.98 (quintet, *J* = 7.1 Hz, 4 H); mass spectrum, *m/z* (relative intensity) 392 (1, M^+), 116 (100). Anal. calcd for $C_{10}H_{20}N_2O_4Se_2$: C, 30.78; H, 5.17; N, 7.18. Found: C, 30.88; H, 4.90; N, 7.15.

***N,N'*-Diacetyl di(3-aminopropyl) diselenide (15).** Diselenide **12** (8.76 g of the inseparable 79:21 mixture with the corresponding selenide, vide supra) was treated with acetic anhydride (6 mL) in pyridine (14 mL) for 24 h at room temperature. Volatile material was removed under reduced pressure and the residue was flash chromatographed over silica gel (10% methanol-ethyl acetate) to afford 8.68 g of a 79:21 mixture of the corresponding *N,N'*-diacetylated diselenide **15** and its selenide derivative. The mixture was then converted into the corresponding allyl selenide **20** (vide infra), from which the pure diselenide **15** was regenerated by the following procedure, based on a similar method used earlier for deprotection of allyl selenides.[13]

Allyl selenide **20** (114 mg, 0.52 mmol) and *m*-CPBA (299 mg of ca. 77% purity; 1.3 mmol) were stirred in 3 mL of dichloromethane at –78 ^oC. The mixture was warmed to -40 ^oC over 35 min and diethylamine was added until the mixture became homogeneous (~ 0.4 mL), followed by 0.26 mL of ethyl vinyl ether, and the mixture was stored at –28 ^oC for 3 h, with occasional stirring. Hydrazine (82 μL, 2.6 mmol) was added and the mixture warmed to room temperature and stirred for 40 min. The mixture

was then concentrated in vacuo and the residue was chromatographed (elution with 5% methanol-ethyl acetate) to afford 24 mg (26%) of the pure diselenide **15** as a yellow powder, mp 68-69 ^{o}C, IR (film) 3394, 1635, 1558 cm^{-1}; ^{1}H NMR (200 MHz) δ 6.34 (br s, 2 H), 3.33 (crude q, *J* = 6.6 Hz, 4 H), 2.92 (t, *J* = 7.3 Hz, 4 H), 2.07-1.83 (s at δ 1.97 superimposed on quintet, 10 H); ^{13}C NMR (50 MHz) δ 170.6, 39.3, 30.7, 27.0, 23.2; mass spectrum, *m/z* (relative intensity) 360 (<1, M^{+}), 180 (12), 138 (50), 100 (100), 72 (99). Anal. calcd for $C_{10}H_{20}N_2O_2Se_2$: C, 33.53; H, 5.63; N, 7.82. Found: C, 34.03; H, 5.62; N, 7.75.

Oxidation of selenocystine 16 with TBHP. Selenocystine **16** (102 mg, 0.180 mmol) and 90% TBHP (386 μL, 3.47 mmol) were stirred in 2 mL of deuteriochloroform at room temperature for 50 h, until the yellow color of **16** had completely faded. ^{1}H NMR analysis indicated that dehydroalanine was formed as the sole product. The solvent was removed in vacuo and the crude product was chromatographed (elution 30% ethyl acetate-hexanes) to afford 72 mg (100%) of *N*-(*t*-Boc)dehydroalanine methyl ester as a colorless oil with ^{1}H and ^{13}C NMR spectra identical to those reported in the literature.[14]

Oxidation of selenocystine 16 with TBHP in the presence of BnSH. A solution containing benzyl thiol (182 mg, 1.47 mmol), selenocystine **16** (79 mg, 0.14 mmol) and 90% TBHP (222 μL, 2.00 mmol) was stirred for 95 h in 50 mL of dichloromethane-methanol (95:5). After removal of the solvent in vacuo, NMR analysis of the crude product indicated the presence of a small amount (ca. 15%) of *N*-(*t*-Boc)dehydroalanine methyl ester. Chromatography (20% ethyl acetate-hexanes) afforded the corresponding selenenyl sulfide as a pale yellow oil (50 mg, 44%): IR (film) 1733, 1647, 1161 cm^{-1}; ^{1}H NMR (200 MHz) δ 7.38-7.28 (m, 5 H), 5.27 (br d, 1 H), 4.62-4.44 (m, 1 H), 4.01 (s, 2

H), 3.73 (s, 3 H), 3.05-2.75 (m, 2 H), 1.46 (s, 9 H); ^{13}C NMR (50 MHz) δ 171.2, 154.9, 138.0, 129.1, 128.4, 127.4, 80.1, 53.2, 52.4, 42.3, 32.9, 28.3; mass spectrum, *m/z* (relative intensity) 405 (27, M^+), 146 (96), 91 (100). Exact mass calcd for $C_{16}H_{23}NO_4SSe$: 405.0513. Found: 405.0501.

Preparation of allyl selenides: allyl 3-hydroxypropyl selenide (25), typical procedure. Sodium borohydride (2.19 g, 57.9 mmol) was added to an ice-cooled solution of di(3-hydroxypropyl) diselenide (**9**) (3.17 g, 11.4 mmol) in 100 mL of absolute ethanol. Once the addition was complete, the ice-bath was removed and the reaction was stirred at room temperature for 15 min. Allyl bromide (3.91 mL, 45.2 mmol) was added, and stirring was continued for 45 min. The mixture was poured into ether (200 mL), washed with saturated solutions of NH_4Cl and NaCl, and with water. It was dried and concentrated *in vacuo*. The residue was flash chromatographed over silica gel (elution with 10% ethyl acetate-hexanes) to afford 3.53 g (86%) of the product as a colorless oil; IR (neat) 3359, 1632, 1052 cm^{-1}; ^{1}H NMR (200 MHz) δ 5.89 (ddt, *J* = 16.9, 10.1, 7.6 Hz, 1 H), 5.11-4.94 (m, 2 H), 3.74 (t, *J* = 6.0 Hz, 2 H), 3.20 (d, *J* = 7.5 Hz, 2 H), 2.63 (t, *J* = 7.2 Hz, 2 H), 1.92 (quintet, *J* = 6.6 Hz, 2 H), 1.64 (br s, 1 H); ^{13}C NMR (50 MHz) δ 134.9, 116.1, 62.2, 32.6, 25.9, 19.5; mass spectrum, *m/z* (relative intensity) 180 (57, M^+), 133 (21), 122 (26), 57 (71), 41 (100), 39 (49). Exact mass calcd for $C_6H_{12}OSe$: 180.0053. Found: 180.0065.

The following allyl selenides were prepared from the corresponding diselenides and allyl bromide, using a similar procedure to that used in the preparation of selenide **25**.

Methyl (allylseleno)acetate (17). Diselenide **7** was converted to **17**, as in the typical procedure for **25**, in 59% yield; pale yellow oil, IR (neat) 1736 cm^{-1}; ^{1}H-NMR

(200 MHz) δ 5.87 (ddt, *J* = 16.9, 9.9, 7.7 Hz, 1 H), 5.11 (ddt, *J* = 16.9, 1.7, 1.1 Hz, 1 H), 5.08 (ddt, *J* = 9.9, 1.7, 0.7 Hz, 1 H), 3.73 (s, 3 H), 3.35 (ddd, *J* = 6.6, 1.1, 0.6 Hz, 2 H), 3.14 (s, 2 H); ^{13}C-NMR (50 MHz) δ 171.9, 133.5, 117.4, 52.1, 27.2, 21.1; mass spectrum, *m/z* (relative intensity) 194 (16, M^+), 133 (56), 121 (44), 107 (67), 41 (100). Exact mass calcd for $C_6H_{10}O_2Se$: 193.9846. Found: 193.9863.

Methyl 3-(allylseleno)propanoate (18). The dimethyl ester[15] of diselenide **5** was first prepared in 52% yield from methyl 3-bromopropanoate and Na_2Se_2 as in the typical procedure for the preparation of diselenide **9**. The diselenide was then converted to **18**, as in the typical procedure for **25**, in 52% yield; colorless oil, IR (neat) 1738 cm^{-1}; ^{1}H-NMR (200 MHz) δ 5.88 (ddt, *J* = 16.9, 9.2, 7.7 Hz, 1 H), 5.13-4.96 (m, 2 H), 3.74 (s, 3 H), 3.22 (dt, *J* = 7.7, 0.7 Hz, 2 H), 2.81-2.68 (m, 4 H); ^{13}C-NMR (50 MHz) δ 172.5, 134.7, 116.3, 51.6, 35.2, 26.1, 16.8; mass spectrum, *m/z* (relative intensity) 208 (44, M^+), 167 (50), 133 (37), 107 (100). Exact mass calcd for $C_7H_{12}O_2Se$: 208.0003. Found:208.0001.

***N*-[2-(Allylseleno)ethyl]acetamide (19).** *N,N'*-diacetyl di(2-aminoethyl) diselenide[16] was first prepared from the reaction of 2-bromoethylamine hydrobromide and Na_2Se_2 as in the typical procedure for diselenide **9**, followed by treatment with acetic anhydride in pyridine for 24 h at room temperature. The diselenide was obtained as an inseparable 73:27 mixture with *N,N'*-diacetyl di(2-aminoethyl) selenide and was used directly in the next step. The crude mixture was converted to **19**, as in the typical procedure for **25**, in 89% yield (based on the amount of diselenide in the preceding 73:27 mixture); colorless oil, IR (neat) 3283, 1652 cm^{-1}; ^{1}H-NMR (200 MHz) δ 5.89 (ddt, *J* = 16.7, 9.9, 7.7 Hz, 1 H), 5.13-4.96 (m, 2 H), 3.47 (q, *J* = 6.4 Hz, 2 H), 3.19 (d, *J* = 7.5 Hz, 2 H), 2.65 (t, *J* = 6.7 Hz, 2 H), 1.98 (s, 3 H); ^{13}C-NMR (50 MHz) δ 170.1, 134.6, 116.5,

39.2, 25.7, 23.1, 22.6; mass spectrum, *m/z* (relative intensity) 207 (4, M^+), 166 (16), 86 (100). Exact mass calcd for $C_7H_{13}NOSe$: 207.0162. Found: 207.0161.

***N*-[3-(Allylseleno)propyl]acetamide (20).** Diselenide **15** (inseparable 79:21 mixture with the corresponding selenide, vide supra) was converted to **20**, as in the typical procedure for **25**, in 99% yield (based on the amount of diselenide in the 79:21 mixture); colorless oil, IR (neat) 3279, 1651 cm^{-1}; ^{1}H-NMR (200 MHz) δ 5.88 (ddt, *J* = 17.3, 9.4, 7.7 Hz, 1 H), 5.63 (br s, 1 H), 5.09-4.94 (m, 2 H), 3.33 (q, *J* = 6.6 Hz, 2 H), 3.16 (d, *J* = 7.7 Hz, 2 H), 2.51 (t, *J* = 7.2 Hz, 2 H), 1.98 (s, 3 H), 1.85 (quintet, *J* = 7.1 Hz, 2 H); ^{13}C-NMR (50 MHz) δ 170.3, 134.8, 116.1, 39.5, 29.8, 25.8, 23.2, 20.2; ^{77}Se NMR δ 185.1; mass spectrum, *m/z* (relative intensity) 221 (1, M^+), 100 (100). Exact mass calcd for $C_8H_{15}NOSe$: 221.0319. Found: 221.0306.

***N*-[3-(Allylseleno)propyl]benzamide (21).** Diselenide **13** was converted to **21**, as in the typical procedure for **25**, in 58% yield; colorless oil, IR (neat) 3313, 1634 cm^{-1}; ^{1}H-NMR (200 MHz) δ 7.86-7.70 (m, 2 H), 7.50-7.27 (m, 3 H), 7.01 (br s, 1 H), 5.82 (ddt, *J* = 16.8, 9.9, 7.7 Hz, 1 H), 5.06-4.89 (m, 2 H), 3.48 (q, *J* = 6.6 Hz, 2 H), 3.14 (d, *J* = 7.5 Hz, 2 H), 2.52 (t, *J* = 7.2 Hz, 2 H), 1.91 (quintet, *J* = 7.1 Hz, 2 H); ^{13}C-NMR (50 MHz) δ 167.7, 134.8, 134.5, 131.3, 128.4, 126.9, 116.2, 40.1, 29.9, 25.9, 20.4; mass spectrum, *m/z* (relative intensity) 283 (3, M^+), 242 (8), 162 (84), 134 (100), 105 (70), 77 (55), 51 (29). Exact mass calcd for $C_{13}H_{17}NOSe - C_3H_5$: 242.0084. Found: 242.0104.

Methyl *N*-[3-(allylseleno)propyl]carbamate (22). Diselenide **14** was was converted to **22**, as in the typical procedure for **25**, in 76% yield; colorless oil, IR (neat) 3330, 1701 cm^{-1}; ^{1}H-NMR (200 MHz) δ 5.87 (ddt, *J* = 17.1, 9.5, 7.6 Hz, 1 H), 5.13-4.93 (m, 2 H), 4.81 (br s, 1 H), 3.69 (s, 3 H), 3.25 (q, *J* = 6.6 Hz, 2 H), 3.16 (d, *J* = 7.7, 2 H),

2.51 (t, J = 7.4 Hz, 2 H), 1.83 (quintet, J = 7.1 Hz, 2 H); ^{13}C-NMR (50 MHz) δ 157.0, 134.8, 116.1, 51.9, 40.9, 30.3, 25.8, 19.9; mass spectrum, *m/z* (relative intensity) 237 (3, M^+), 116 (100), 88 (71). Exact mass calcd for $C_8H_{15}NO_2Se$: 237.0268. Found: 237.0264.

***N*-[3-(Allylseleno)propyl]trifluoroacetamide (23).** Diselenide **12** (inseparable 79:21 mixture with the corresponding selenide; vide supra) was treated with trifluoroacetic anhydride in pyridine for 20 h at room temperature. The resulting mixture of *N,N'*-bis(trifluoroacetyl) di(2-aminopropyl) diselenide and the corresponding selenide was used directly in the next step. The crude mixture was converted into **23**, as in the typical procedure for **25**, in 86% yield (based on the amount of diselenide in the preceding mixture); yellow oil, IR (neat) 3307, 1707 cm^{-1}; ^{1}H-NMR (200 MHz) δ 7.22 (br s, 1 H), 5.82 (ddt, J = 17.1, 9.6, 7.5 Hz, 1 H), 5.10-4.88 (m, 2 H), 3.43 (q, J = 6.5 Hz, 2 H), 3.15 (d, J = 7.5 Hz, 2 H), 2.51 (t, J = 7.2 Hz, 2 H), 1.90 (quintet, J = 7.1 Hz, 2 H); ^{13}C-NMR (50 MHz) δ 157.4 (q), 134.6, 116.3, 115.8 (q), 39.9, 28.9, 25.9, 19.6; mass spectrum, *m/z* (relative intensity) 275 (67, M^+), 234 (34), 154 (100). Exact mass calcd for $C_8H_{12}F_3NOSe$: 275.0036. Found: 275.0047.

Allyl 2-hydroxyethyl selenide (24).[17] Diselenide **8** was converted to **24**, as in the typical procedure for **25**, in 70% yield; pale yellow oil, ^{1}H-NMR (200 MHz) δ 5.89 (ddt, J = 17.1, 9.5, 7.5 Hz, 1 H), 5.17-4.93 (m, 2 H), 3.77 (q, J = 6.2 Hz, 2 H), 3.22 (dd, J = 7.8, 0.8 Hz, 2 H), 2.77 (t, J = 6.2 Hz, 2 H), 2.02 (t, J = 6.2 Hz, 1 H); mass spectrum, *m/z* (relative intensity) 166 (18, M^+), 133 (52), 122 (51), 107 (96), 41 (100).

Allyl 4-hydroxybutyl selenide (26). Diselenide **10** was converted to **26**, as in the typical procedure for **25**, in 71% yield; pale yellow oil, IR (neat) 3349, 1631 cm^{-1}; ^{1}H NMR (200 MHz) δ 5.87 (ddt, J = 16.4, 10.2, 7.6 Hz, 1 H), 5.11-4.93 (m, 2 H), 3.67 (t, J

= 6.1 Hz, 2 H), 3.20 (d, *J* = 7.7 Hz, 2 H), 2.56 (t, *J* = 7.1 Hz, 2 H), 1.85-1.58 (m, 4 H), 1.46 (br s, 1 H); ^{13}C NMR (50 MHz) δ 135.0, 115.9, 62.1, 32.8, 26.5, 25.8, 23.0; mass spectrum, *m/z* (relative intensity) 194 (4, M^+), 133 (100), 107 (24), 73 (43), 55 (77), 41 (60). Exact mass calcd for $C_7H_{14}OSe$: 194.0210. Found: 194.0206.

1,2-Oxaselenolane *Se*-oxide (31). TBHP (7.37 mL of a 90% aqueous solution, 66.3 mmol) and di(3-hydroxypropyl) diselenide (**25**) (1.43 g, 5.15 mmol) in 40 mL of dichloromethane was stirred at room temperature for 18 h. The mixture was concentrated in vacuo and the residue was chromatographed (elution with 10% methanol-ethyl acetate) to afford 1.55 g (98%) of the cyclic seleninate ester **31** as a white powder, mp 54-56 ^{o}C (from methanol-ethyl acetate); IR (film) 1039, 955, 857 cm^{-1}; ^{1}H NMR (400 MHz, CD_3NO_2) δ 4.46 (ddd, *J* = 9.1, 7.6, 5.3 Hz, 1 H), 4.38 (dt, *J* = 9.1, 5.7 Hz, 1 H), 3.60 (ddd, *J* = 11.8, 7.7, 6.7 Hz, 1 H), 2.85 (dt, *J* = 11.8, 7.1 Hz, 1 H), 2.52 (m, 1 H), 2.22 (m, 1 H); ^{13}C NMR (50 MHz) δ 74.5, 59.3, 28.9; ^{77}Se-NMR δ 1340.9; mass spectrum, *m/z* (relative intensity) 154 (27, M^+), 126 (44), 107 (75), 80 (26), 58 (100). Anal. calcd for $C_3H_6O_2Se$: C, 23.55; H, 3.95. Found: C, 23.51; H, 3.63.

The same product was obtained in 96% yield from the similar oxidation of allyl 3-hydroxypropyl selenide (1.36 g, 7.59 mmol) with TBHP (4.33 mL of a 90% aqueous solution, 39.0 mmol) in dichloromethane at room temperature for 3 h.

Selenenyl sulfide 34. Benzyl thiol (204 μL, 1.74 mmol) and oxaselenolane **31** (90 mg, 0.58 mmol) in 6 mL of dichloromethane were stirred at room temperature for 5 min. The solvent was removed in vacuo and the residue was chromatographed (elution with 20% ethyl acetate-hexanes) to afford 150 mg (99%) of the product as a pale yellow oil, IR (neat) 3434, 1653 cm^{-1}; ^{1}H NMR (200 MHz) δ 7.49-7.25 (m, 5 H), 4.00 (s, 2 H), 3.63

(t, *J* = 6.0 Hz, 2 H), 2.60 (t, *J* = 7.0 Hz, 2 H), 1.86 (m, 2 H), 1.51 (br s, 1 H); ^{13}C NMR (50 MHz) δ 138.5, 129.1, 128.4, 127.3, 61.8, 42.3, 32.3, 27.2; mass spectrum, *m/z* (relative intensity) 262 (2, M^+), 121 (28), 91 (100), 89 (53), 45 (15). Exact mass calcd for $C_{10}H_{14}OSSe$: 261.9931. Found: 261.9929. Anal. calcd for $C_{10}H_{14}OSSe$: C, 45.98; H, 5.40. Found: C, 46.27; H, 4.97.

1,2-Oxaselenane *Se*-oxide (37). TBHP (0.28 mL of a 90% aqueous solution, 2.5 mmol) and allyl 4-hydroxybutyl selenide (87 mg, 0.45 mmol) in 3 mL of dichloromethane were stirred at room temperature for 18 h. The mixture was then concentrated in vacuo and the residue was chromatographed (elution with 10% methanol-ethyl acetate) to afford 65 mg (86%) of the product as a white powder, mp 55-58 ^{o}C (from methanol); IR (film) 1005, 914, 855 cm^{-1}; ^{1}H NMR (200 MHz) δ 4.38 (td, *J* = 12.1, 2.4 Hz, 1 H), 3.66-3.49 (m, 1 H), 3.04-2.81 (m, 1 H), 2.67-2.36 (m, 2 H), 1.97-1.49 (m, 3 H); ^{13}C NMR (50 MHz) δ 58.8, 47.7, 26.2, 15.0; ^{77}Se-NMR δ 1213.4; mass spectrum, *m/z* (relative intensity) 168 (3, M^+), 138 (33), 107 (32), 71 (56), 57 (100), 41 (78). Anal. calcd for $C_4H_8O_2Se$: C, 28.76; H, 4.83. Found: C, 29.10; H, 5.12.

2-Hyroxyethaneseleninic acid (39). TBHP (0.50 mL of a 70% aqueous solution, 3.6 mmol) and allyl 2-hydroxyethyl selenide (**24**) (157 mg, 0.95 mmol) were stirred in 5 mL of dichloromethane at room temperature for 18 h. The mixture was then concentrated in vacuo and the residue was chromatographed (elution with 30% methanol-ethyl acetate) to afford 128 mg (86%) of **39** as a white powder, mp 82-84 ^{0}C (from methanol); IR (film) 3224, 1647, 1421, 1066 cm^{-1}; ^{1}H NMR (200 MHz, CD_3OD) δ 4.08-3.90 (m, 2 H), 3.33-3.15 (m, 1 H), 3.08-2.91 (m, 1 H); ^{13}C-NMR (50 MHz, CD_3OD) δ 60.2, 56.5; ^{77}Se-NMR

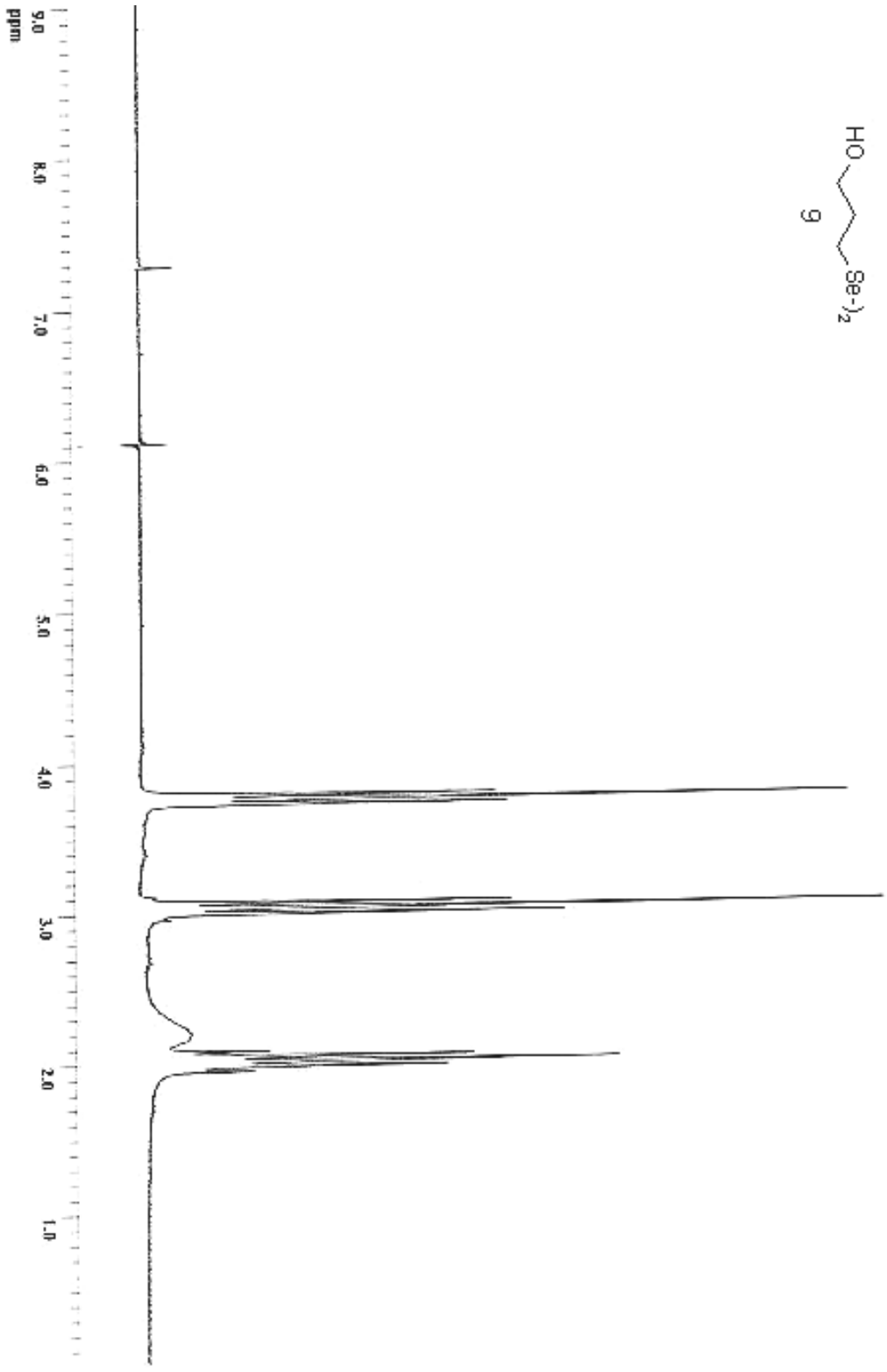
(CD_3OD) δ 1298.2; mass spectrum (ESI), *m/z* (relative intensity) 157 (78, M^+ - H), 113 (100). Anal. calcd for $C_2H_6O_3Se$: C, 15.30; H, 3.85. Found: C, 15.63; H, 3.84.

Oxidation of benzyl thiol with TBHP in the presence of 10 mol % of selenide 25. A solution containing benzyl thiol (41 mg, 0.33 mmol), naphthalene (10.4 mg, 0.081 mmol) as an internal standard and 10 mol % of allyl 3-hydroxypropyl selenide (**25**) (5.9 mg, 0.033 mmol) in 10.5 mL of dichloromethane-methanol (95:5) was treated with 90% aqueous TBHP (50 μL, 0.45 mmol). The reaction mixture was stirred in a water bath at 18 ^oC and the progress of reaction was monitored by HPLC, using a 3.9 x 150 mm Nova Pak C_{18} reverse phase column, a UV detector (λ 254 nm) and water/acetonitrile (40:60) as the solvent at a flow rate of 0.9 mL/min. See Figure 1 for a plot of yield (%) of BnSSBn vs. time (h). The reaction half-life ($t_{1/2}$) was determined when 50% of the thiol was converted into its disulfide. After 11 h, the solvent was removed in vacuo and the crude product was analyzed by ^1H NMR spectroscopy, which indicated that the cyclic seleninate ester **31** and the selenenyl sulfide **34** were present in the molar ratio of 1.3:1. A small amount of allyl benzyl sulfide (**35**)[18] was also detected, but could not be separated from BnSSBn. When the reaction was repeated at room temperature on a larger scale (147 mg, 0.817 mmol of **25**) for 24 h, further oxidation of **35** was observed, affording 47 mg (32%, based on **25**) of allyl benzyl sulfoxide (**36**), which was isolated by flash chromatography (ethyl acetate-hexanes, 1:4; then pure ethyl acetate) and identified by comparison with an authentic sample (vide infra).

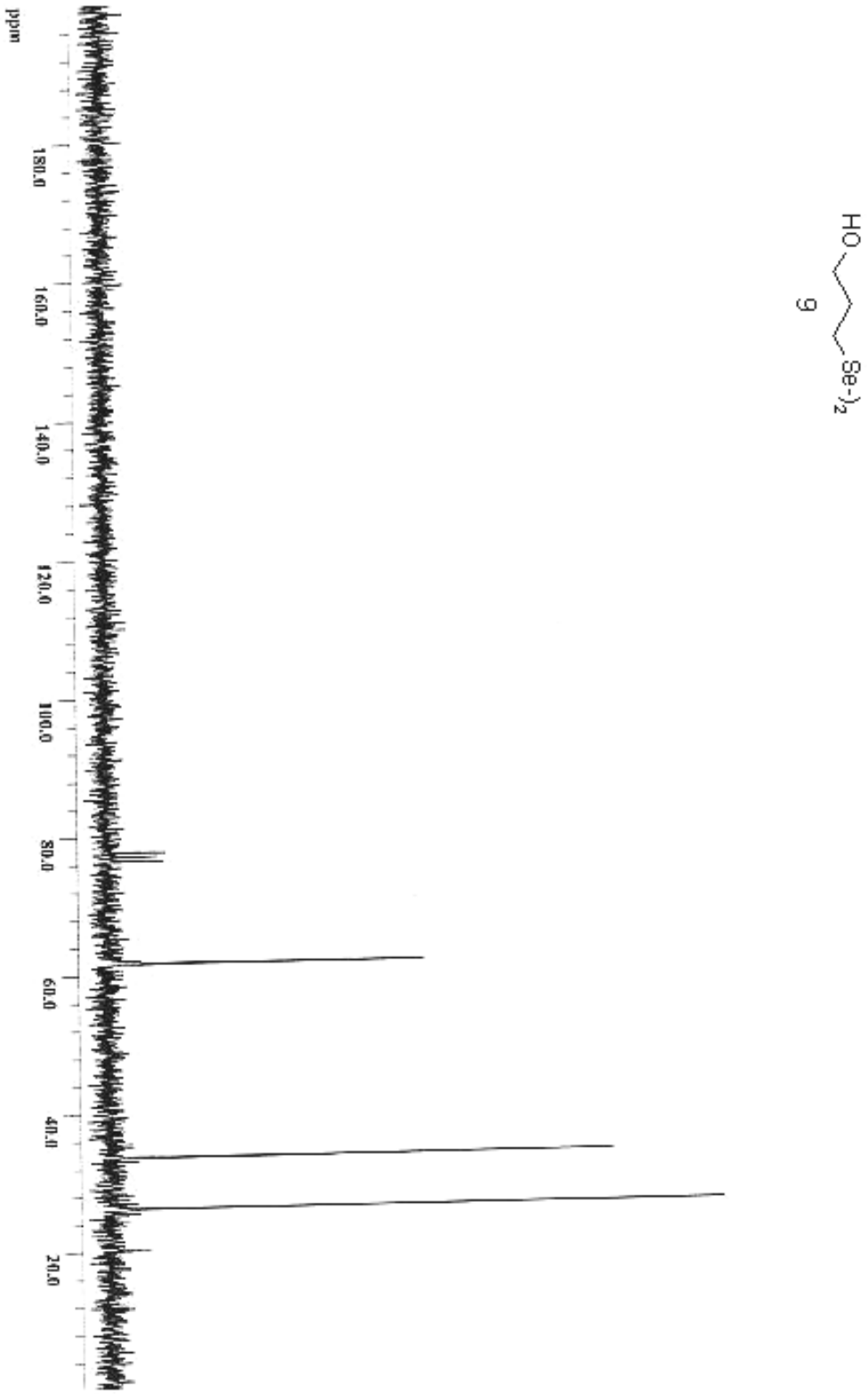
All other half-lives ($t_{1/2}$) listed in Tables 1 and 2, as well as that measured in the presence of **31** and all of the reactions indicated in Figures 2-11 below were determined under identical conditions.

Allyl benzyl sulfoxide (36). A solution of allyl benzyl sulfide[18] (**35**) (320 mg, 1.95 mmol) and 3.52 mL (31.7 mmol) of 90% TBHP in 20 mL of dichloromethane was stirred at room temperature for 20 h. The solvent was removed in vacuo and the residue was chromatographed (elution with 90% ethyl acetate-hexanes) to afford 230 mg (66%) of the corresponding sulfoxide **36**.[19]

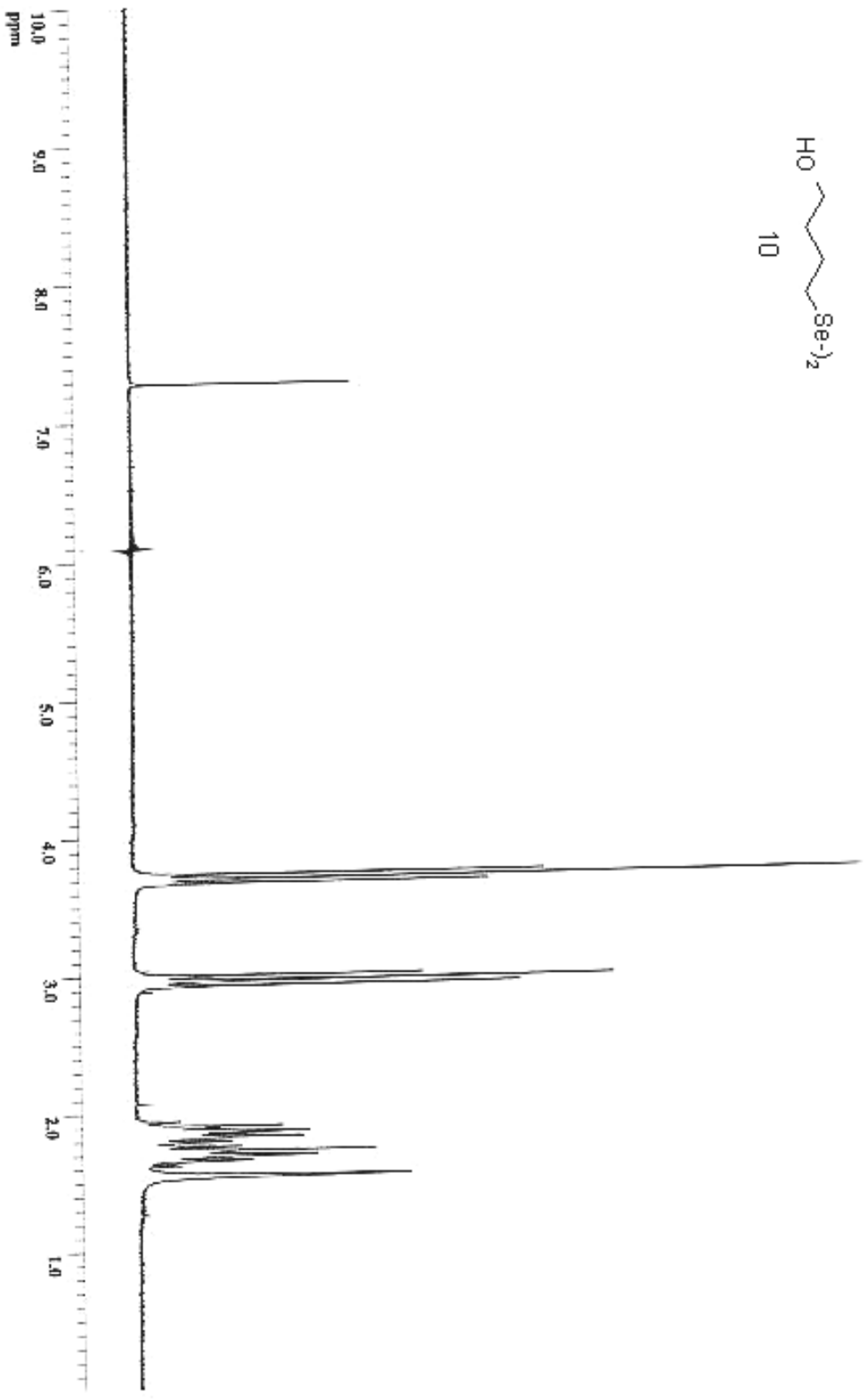
^{1}H NMR Spectrum of Diselenide 9



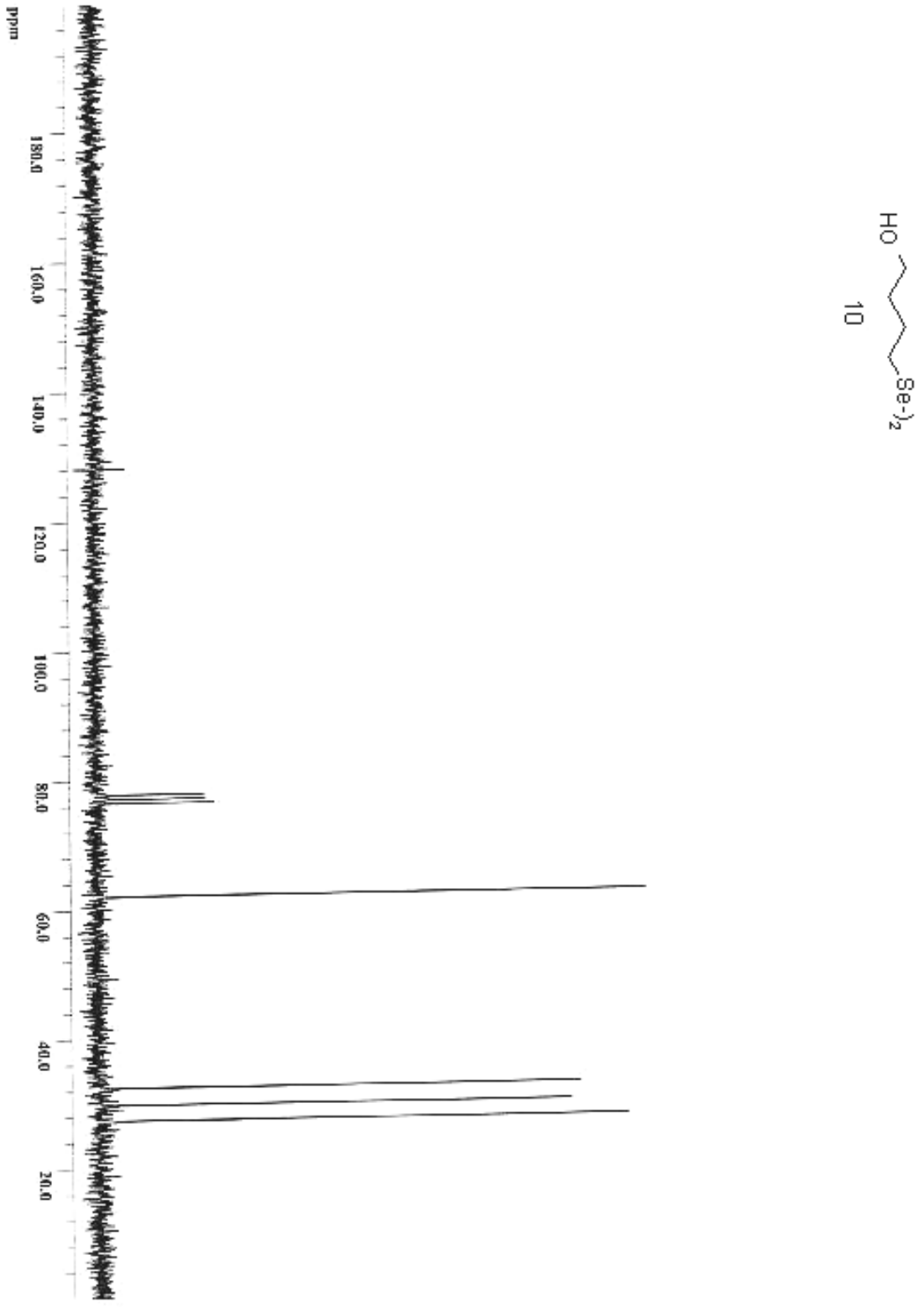
^{13}C NMR Spectrum of Diselenide 9



^{1}H NMR Spectrum of Diselenide 10

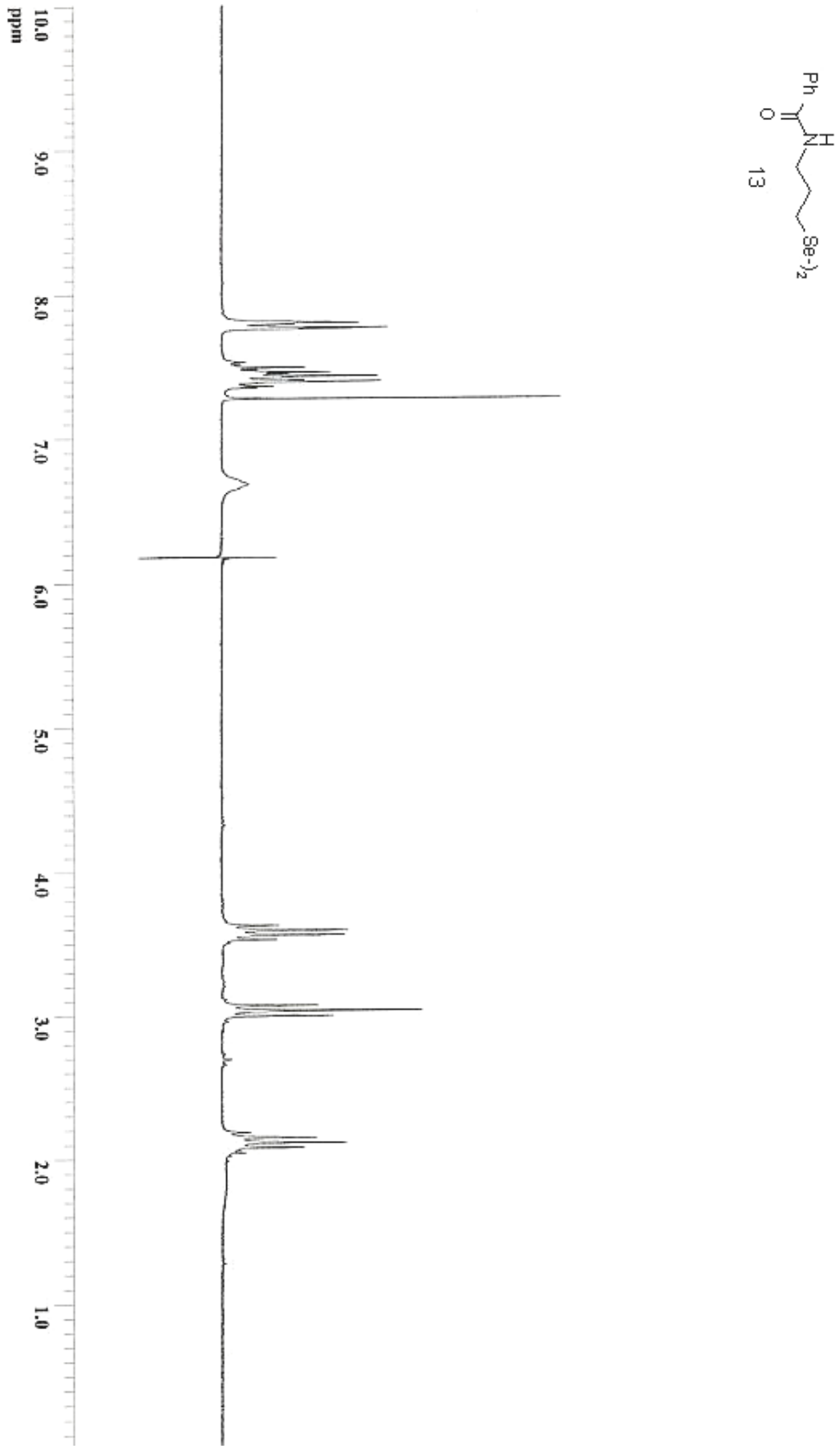


^{13}C NMR Spectrum of Diselenide 10

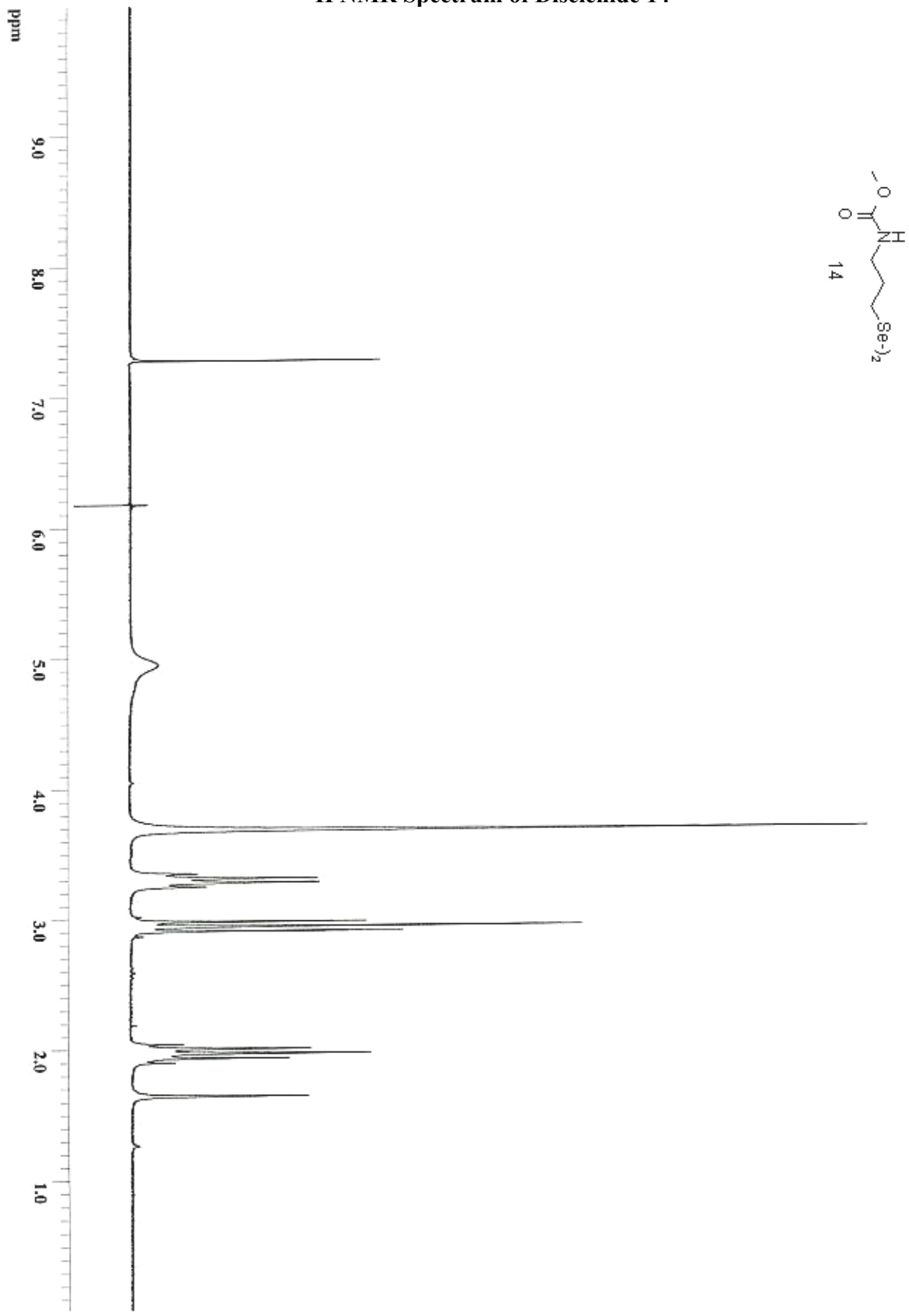


10

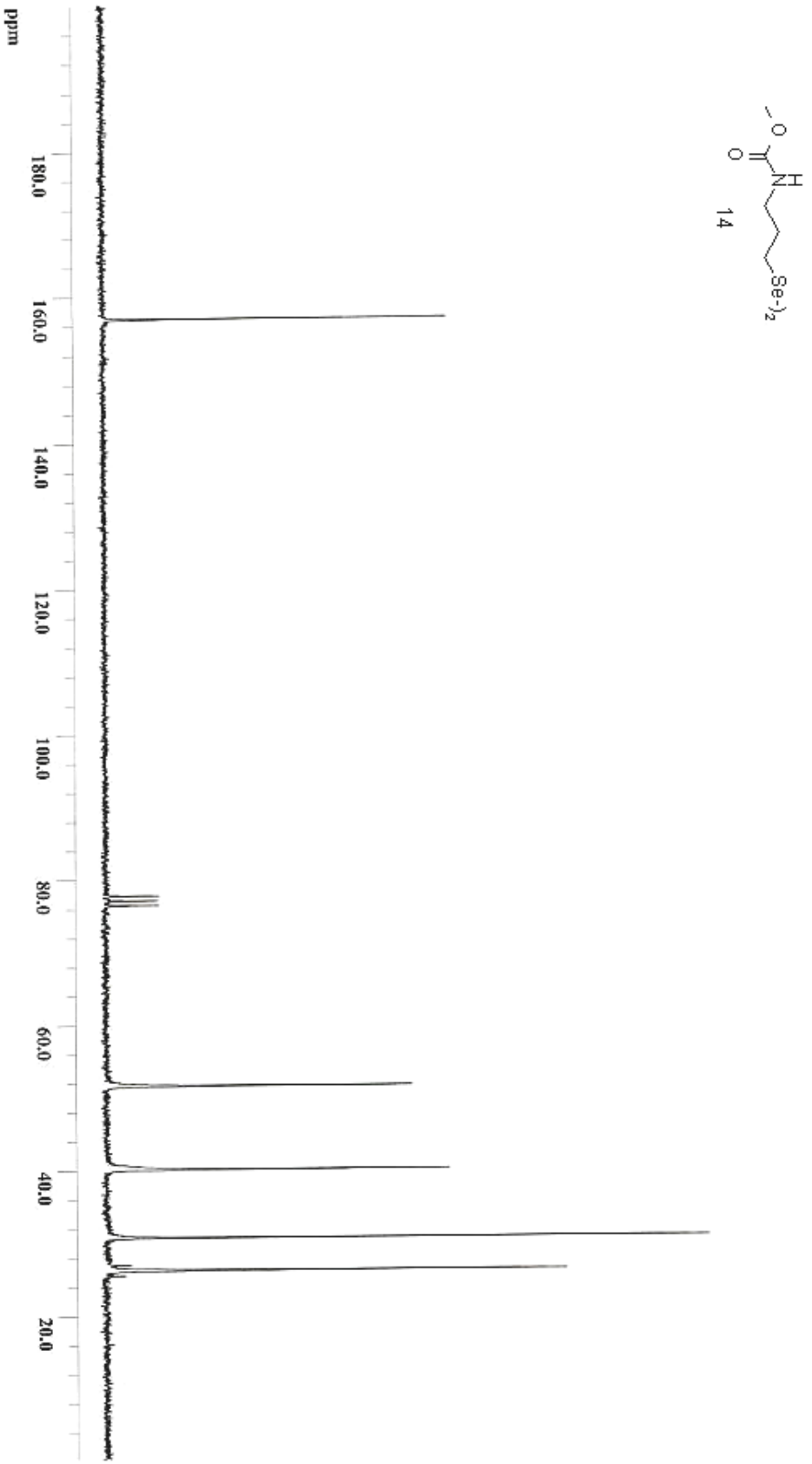
^{1}H NMR Spectrum of Diselenide 13



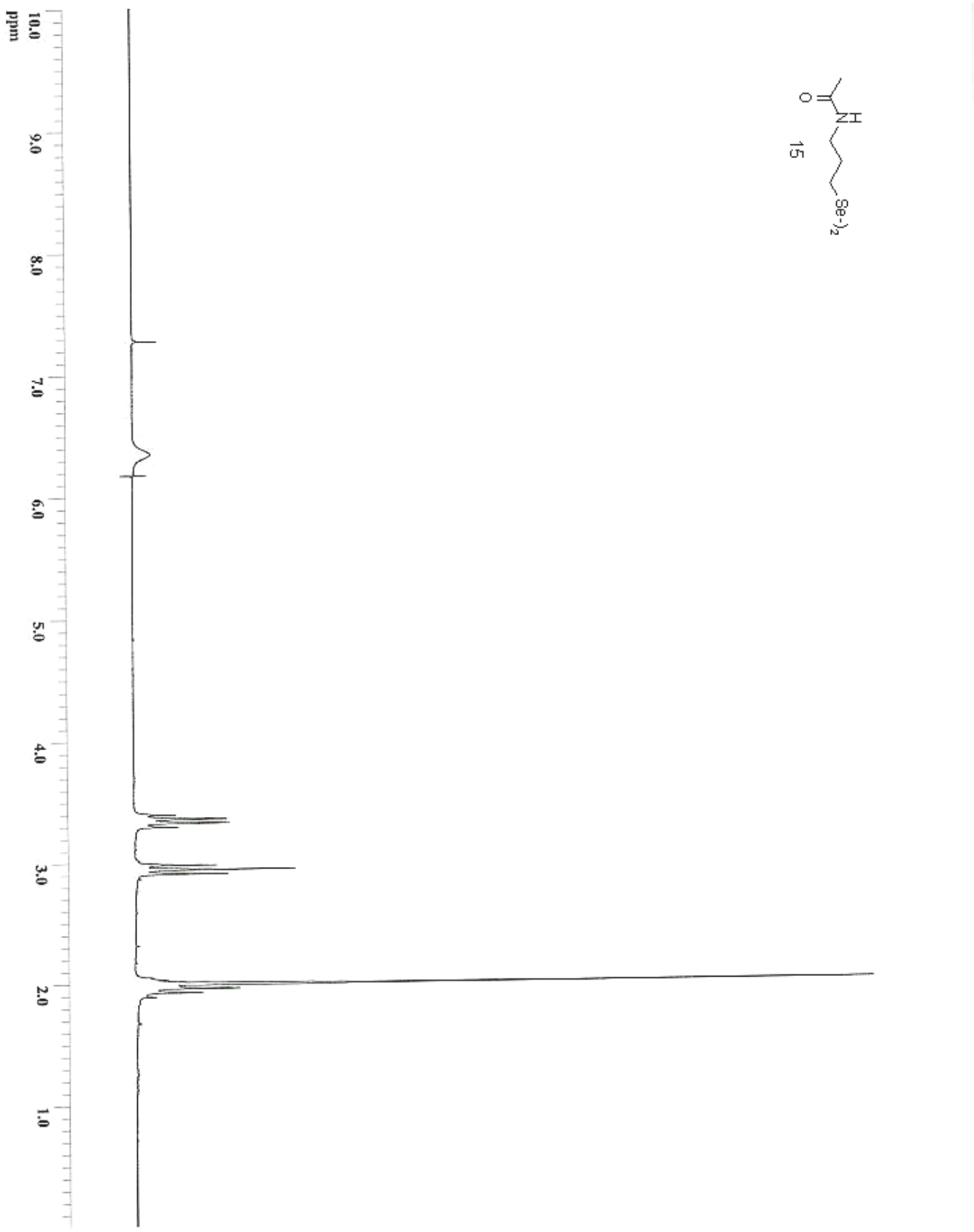
^{1}H NMR Spectrum of Diselenide 14



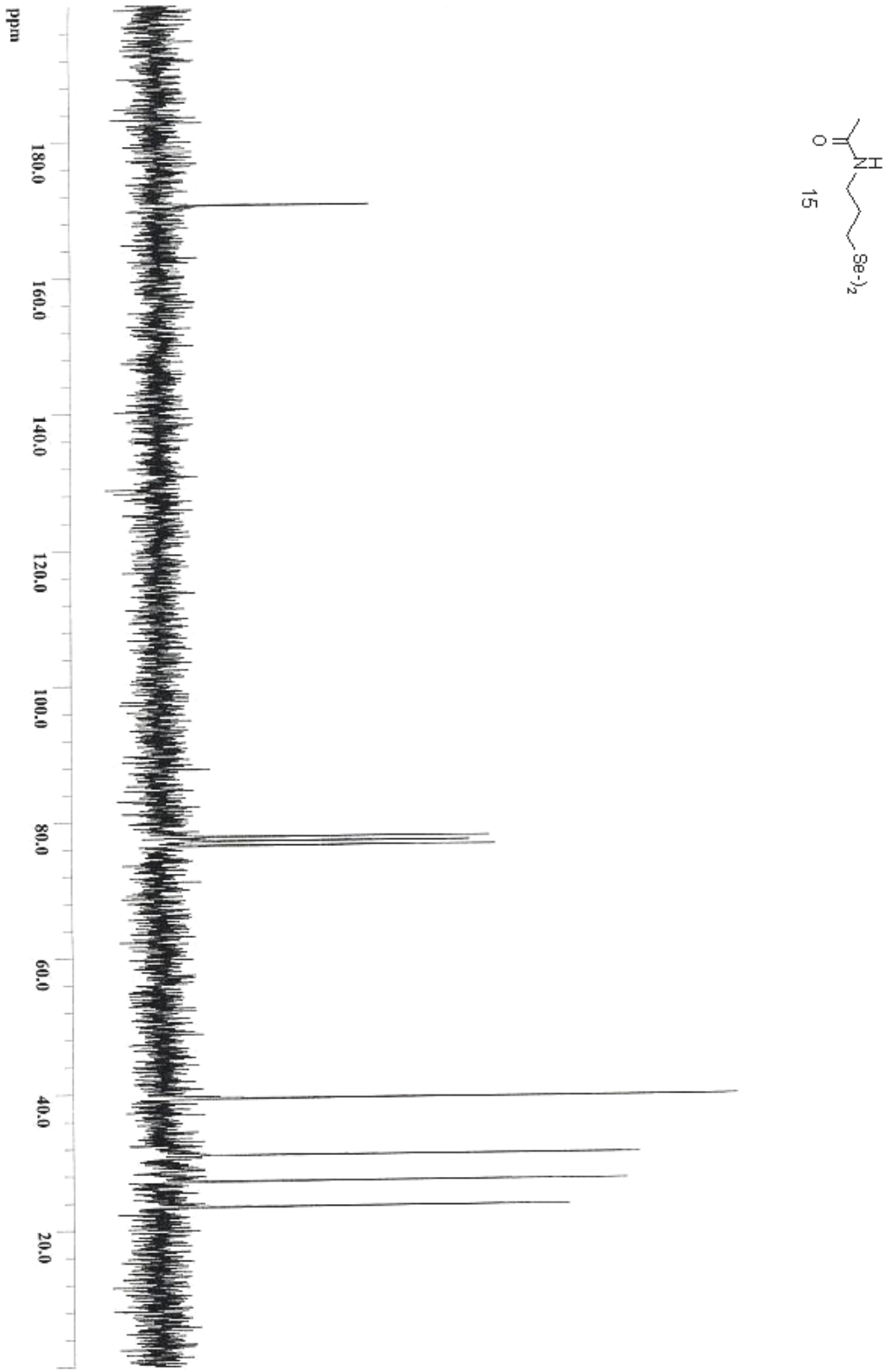
^{13}C NMR Spectrum of Diselenide 14



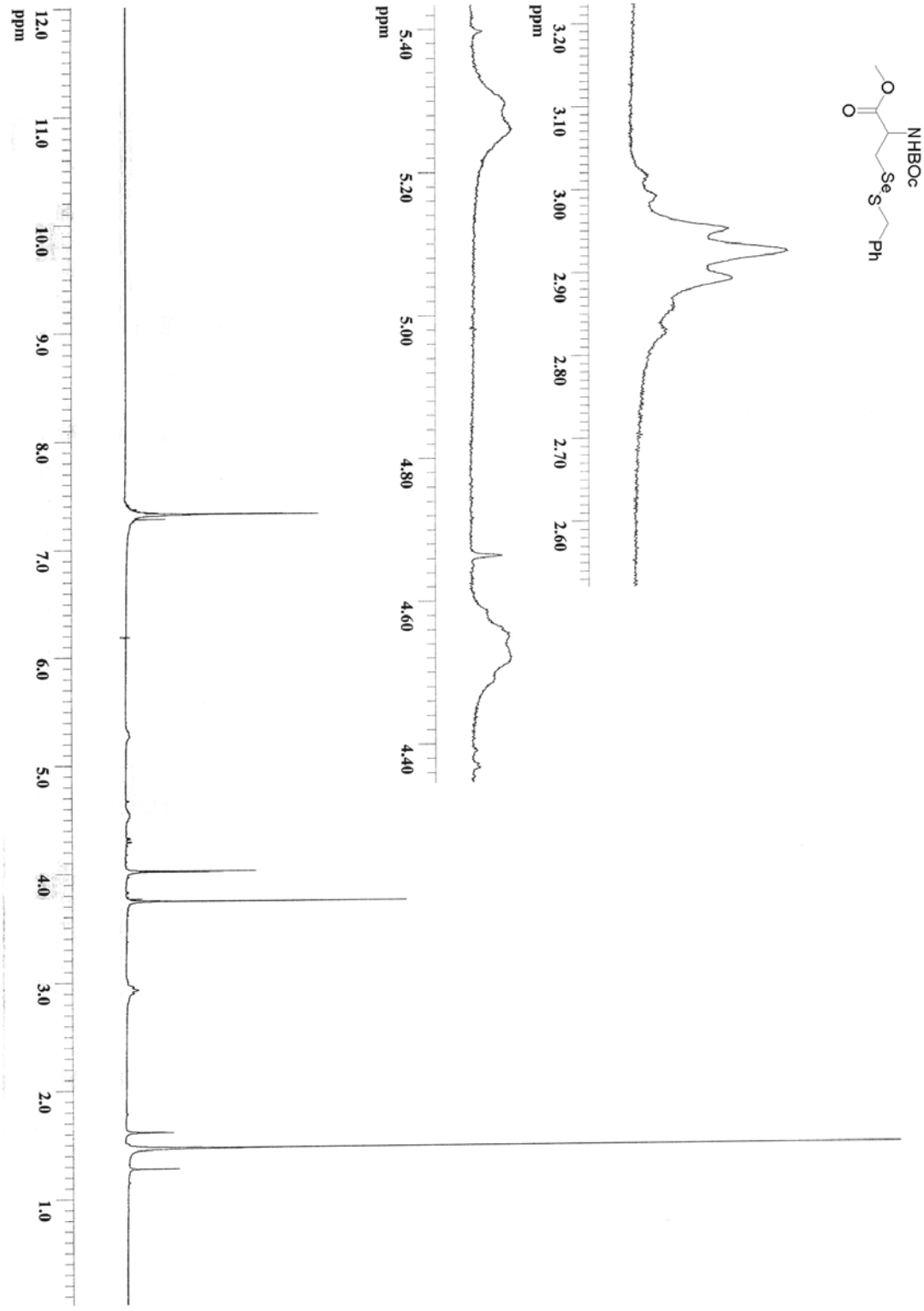
^{1}H NMR Spectrum of Diselenide 15



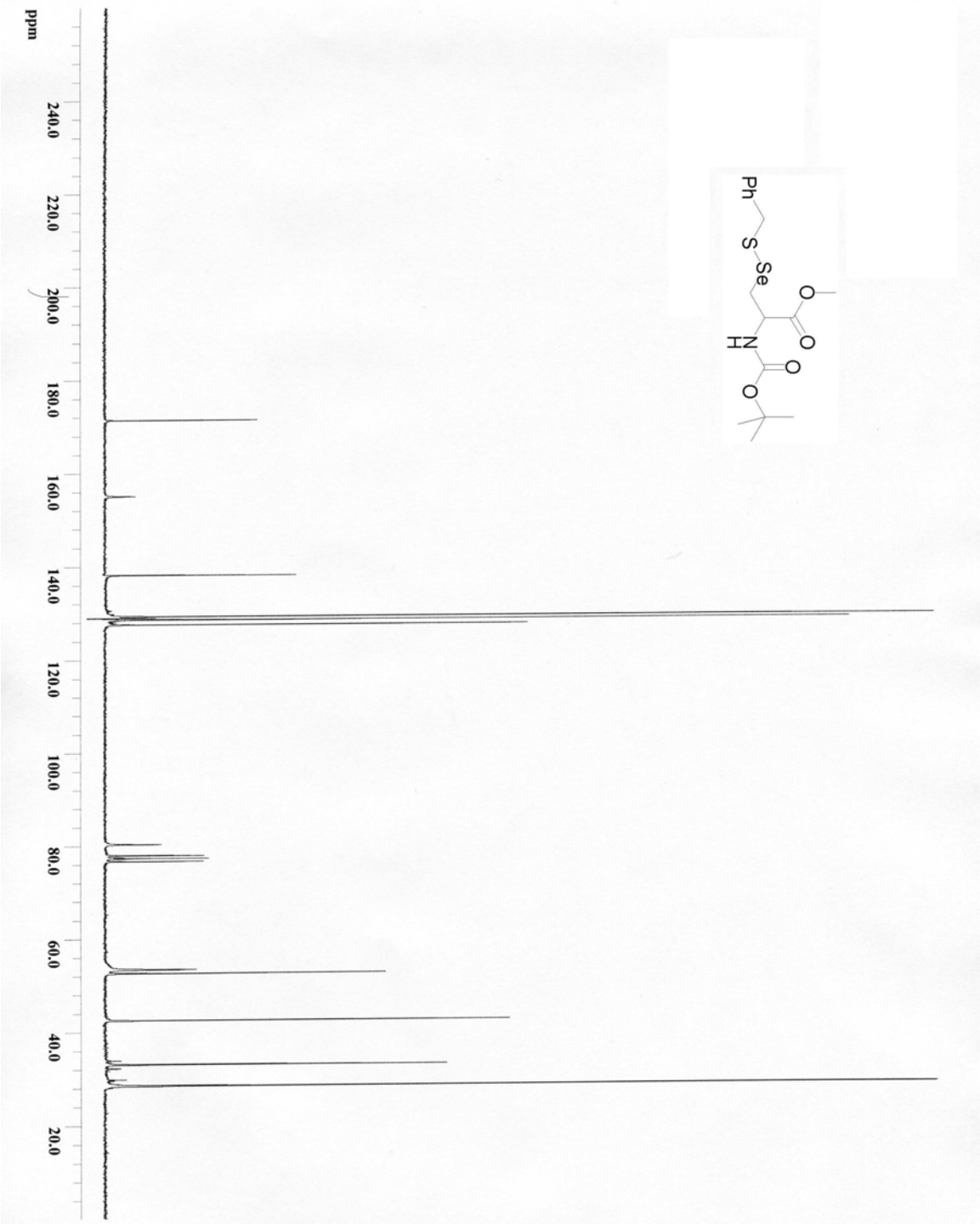
^{13}C NMR Spectrum of Diselenide 15



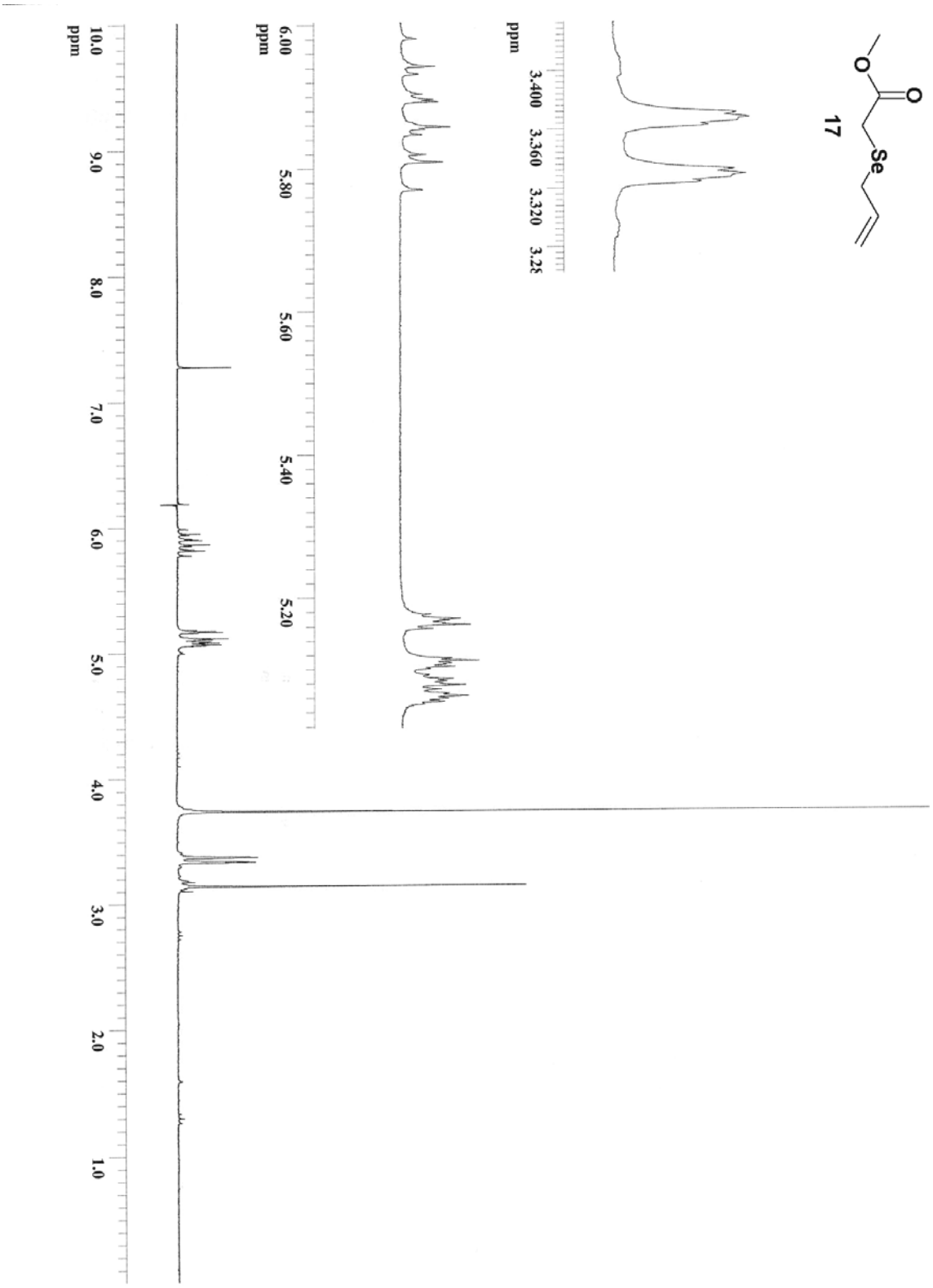
^{1}H NMR Spectrum of the Selenenyl Sulfide Derived from 16



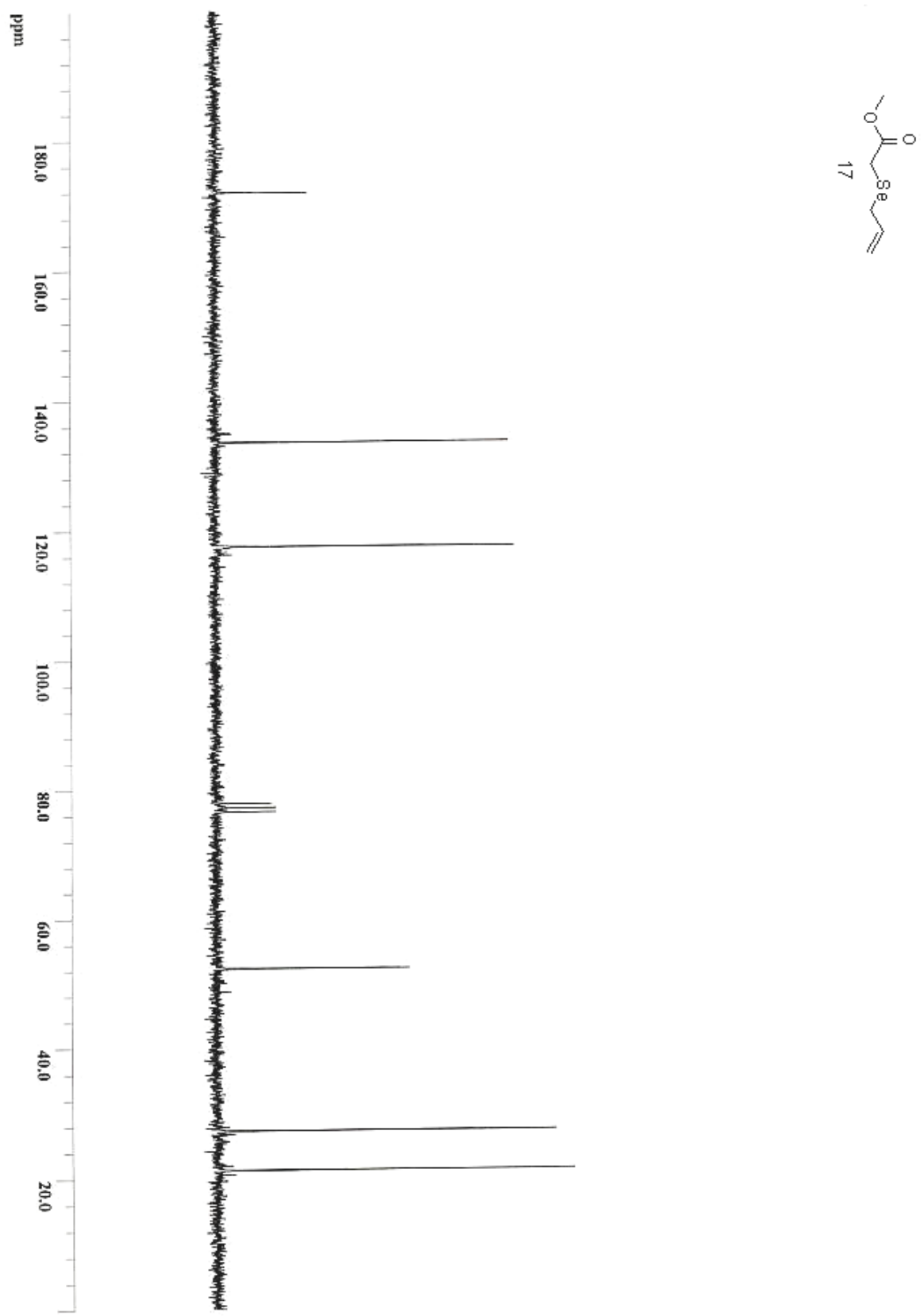
^{13}C NMR Spectrum of the Selenenyl Sulfide Derived from 16



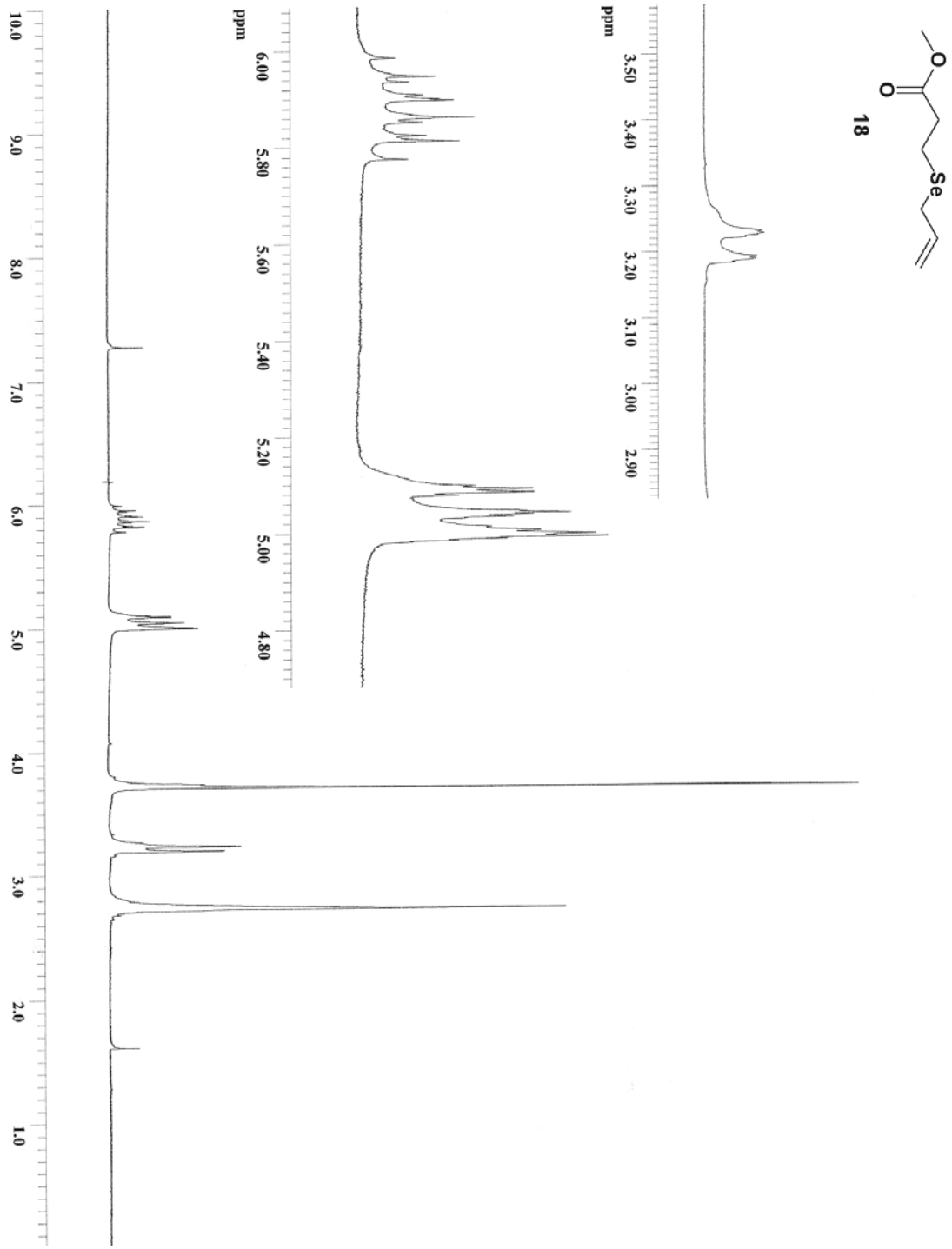
^{1}H NMR Spectrum of Selenide 17



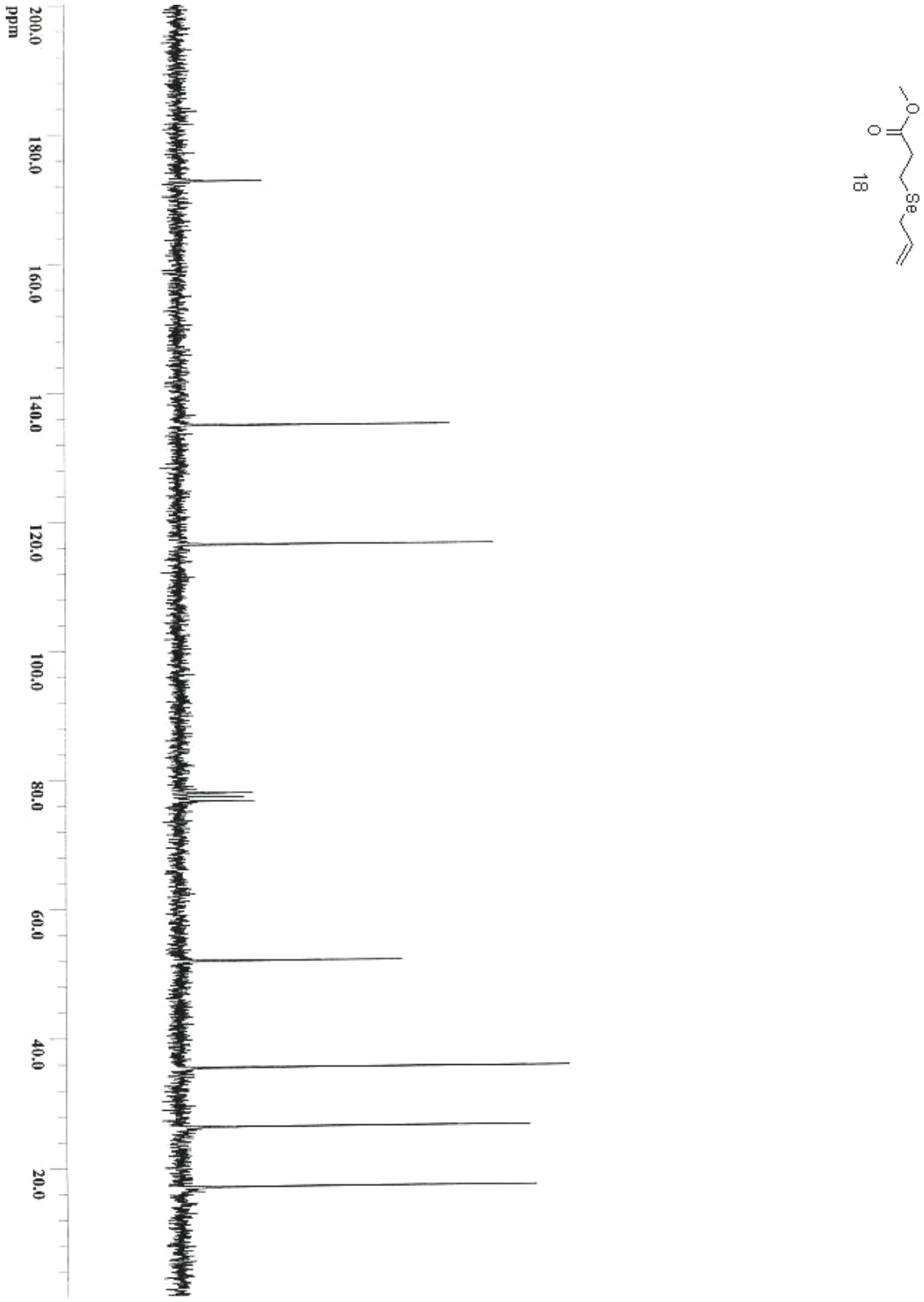
^{13}C NMR Spectrum of Selenide 17



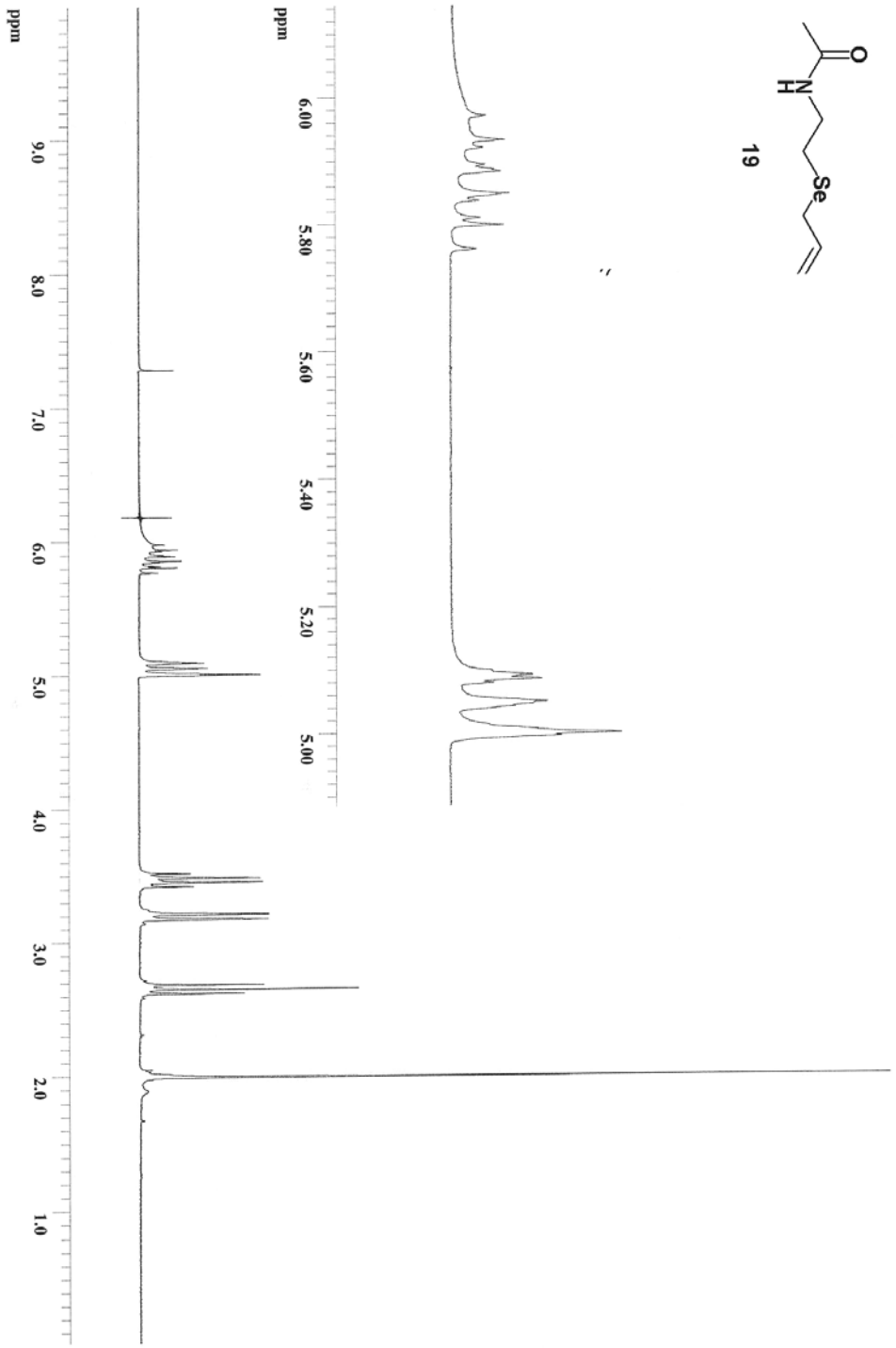
^{1}H NMR Spectrum of Selenide 18



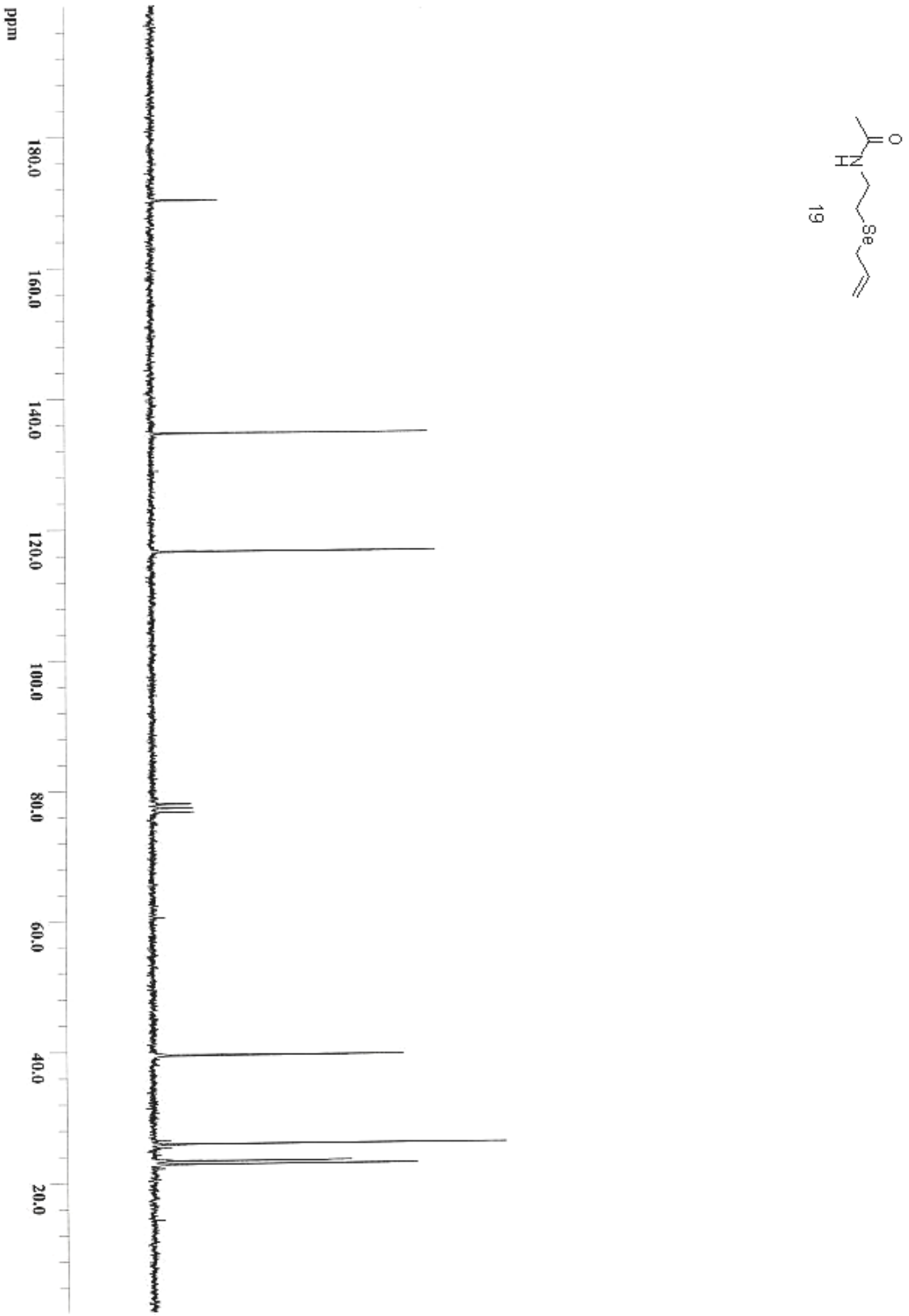
^{13}C NMR Spectrum of Selenide 18



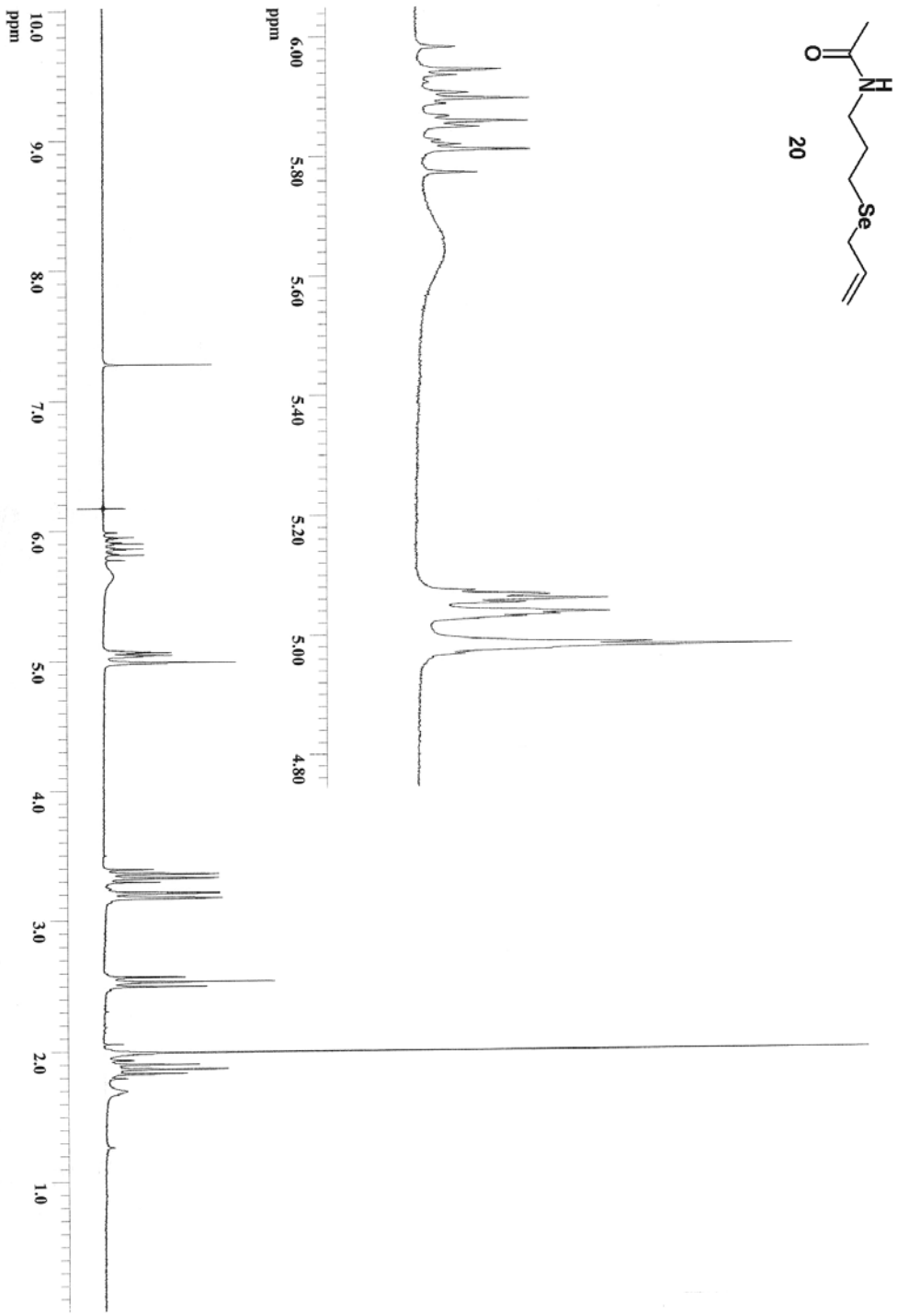
^{1}H NMR Spectrum of Selenide 19



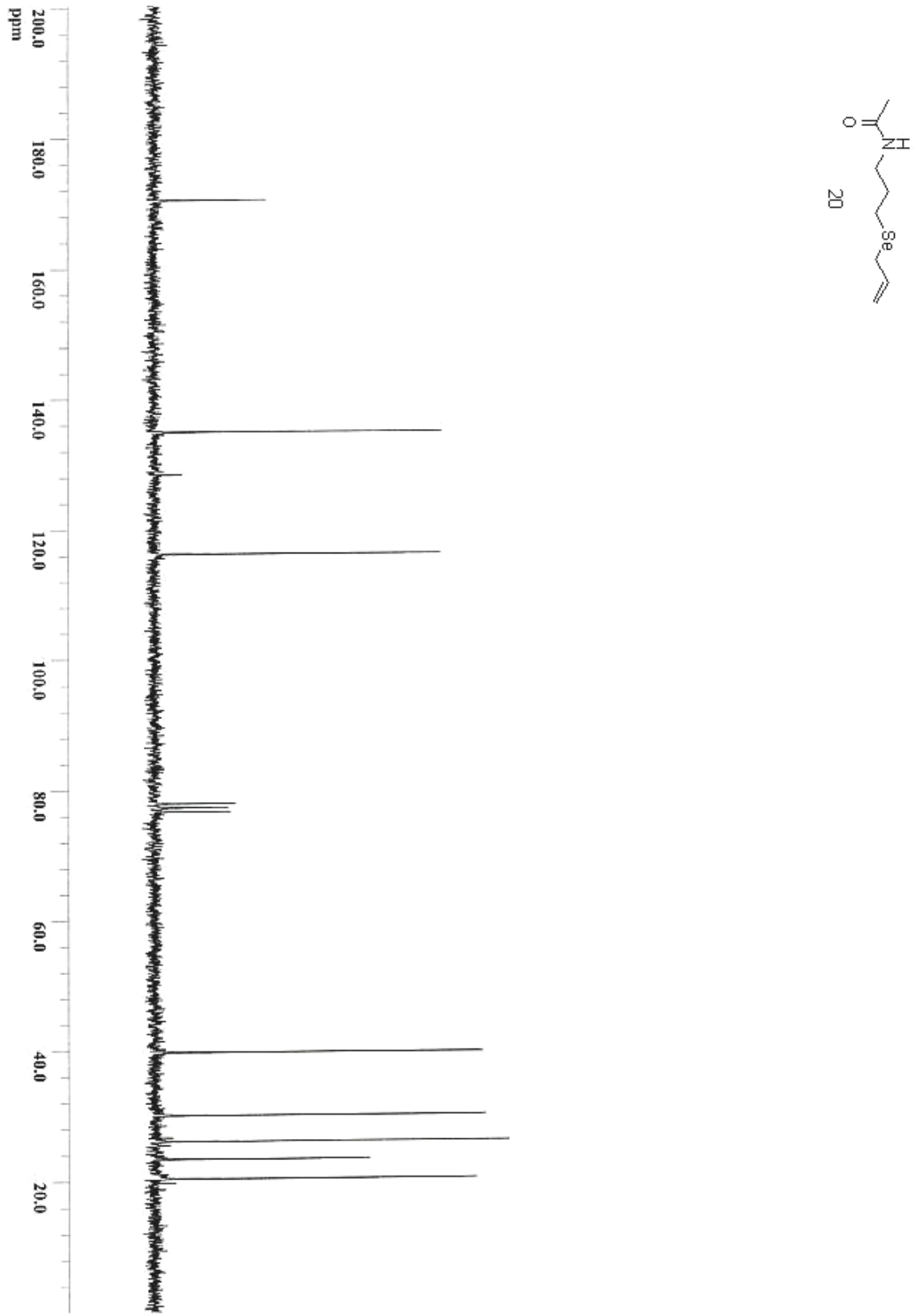
^{13}C NMR Spectrum of Selenide 19



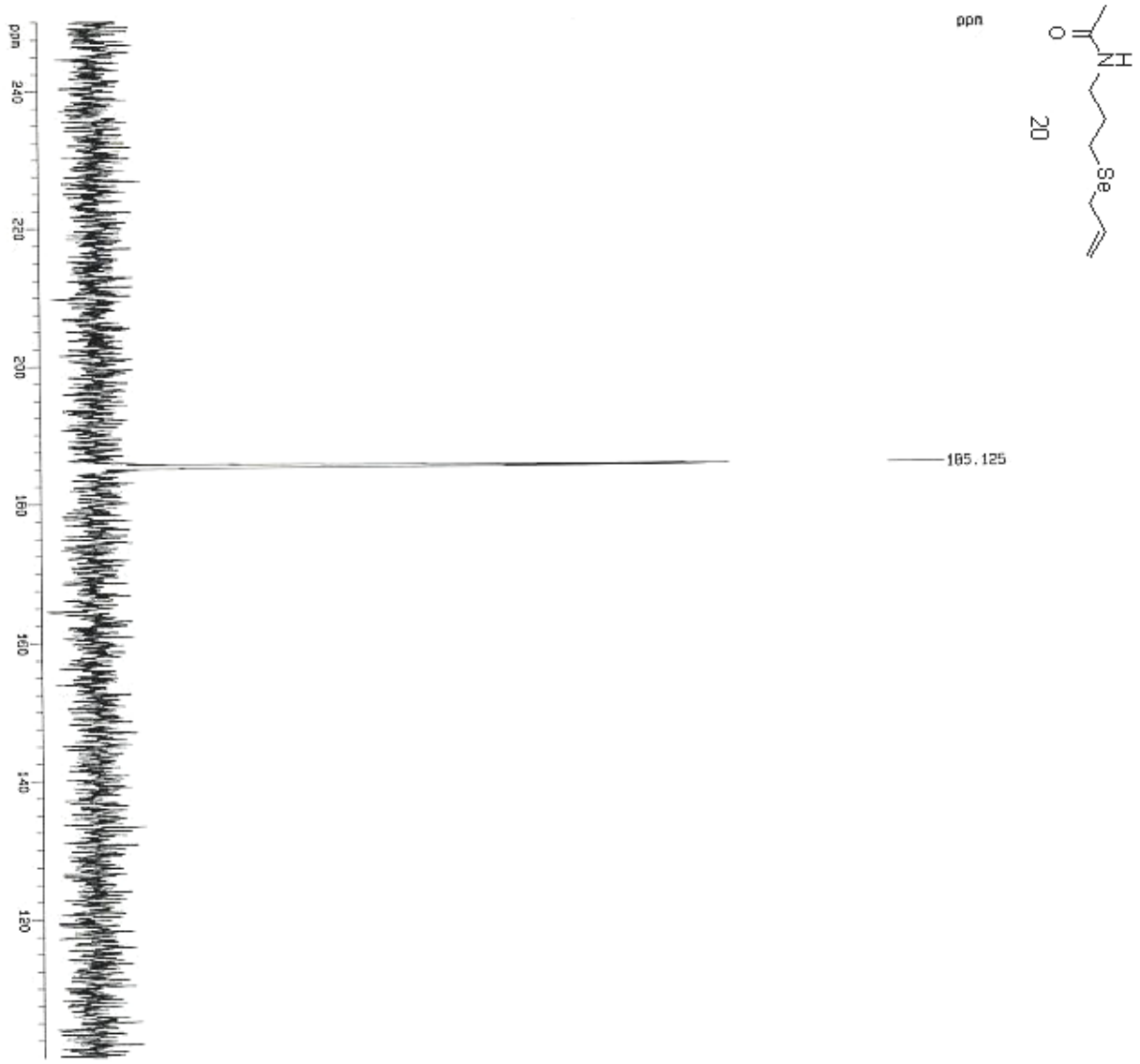
^{1}H NMR Spectrum of Selenide 20



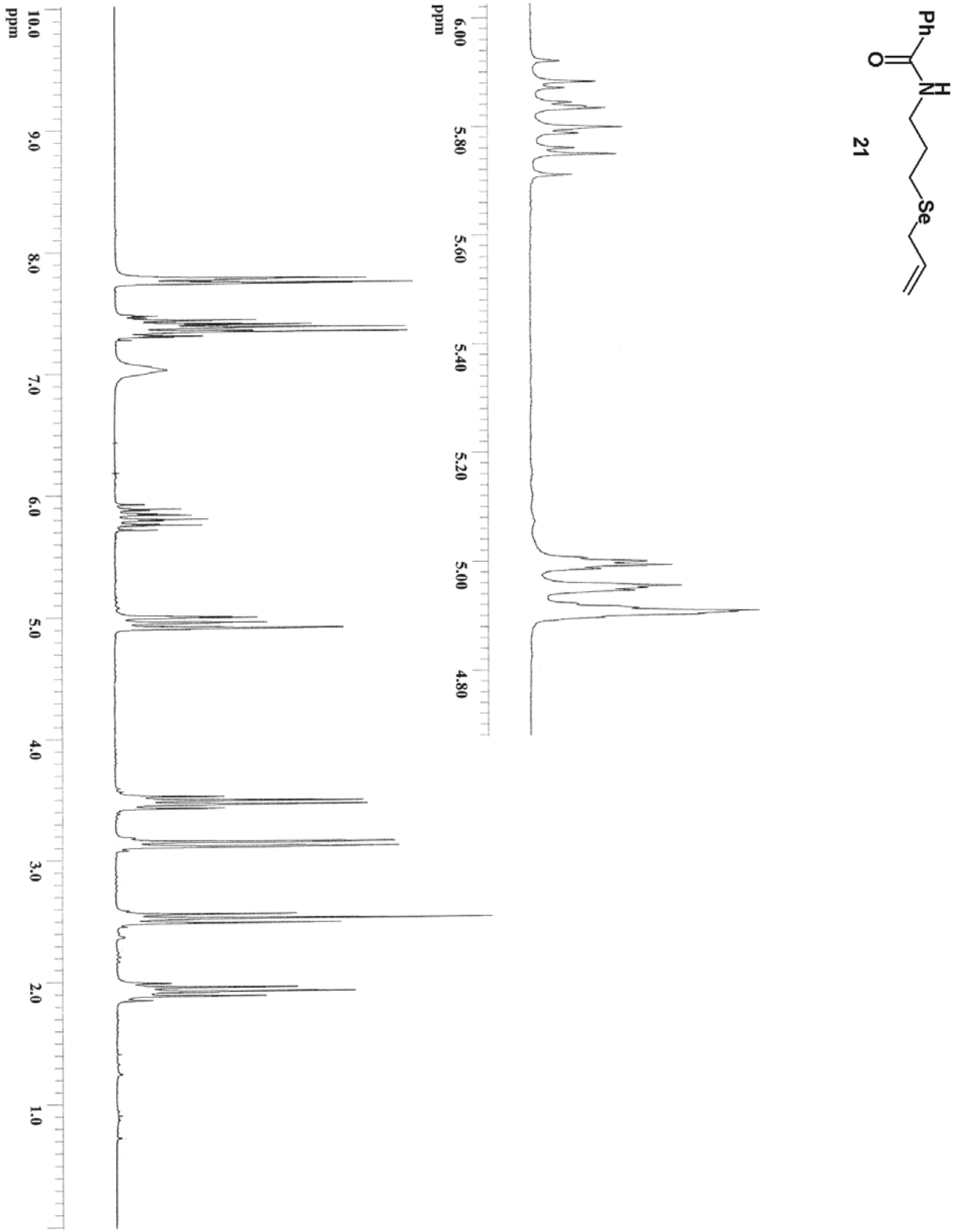
^{13}C NMR Spectrum of Selenide 20



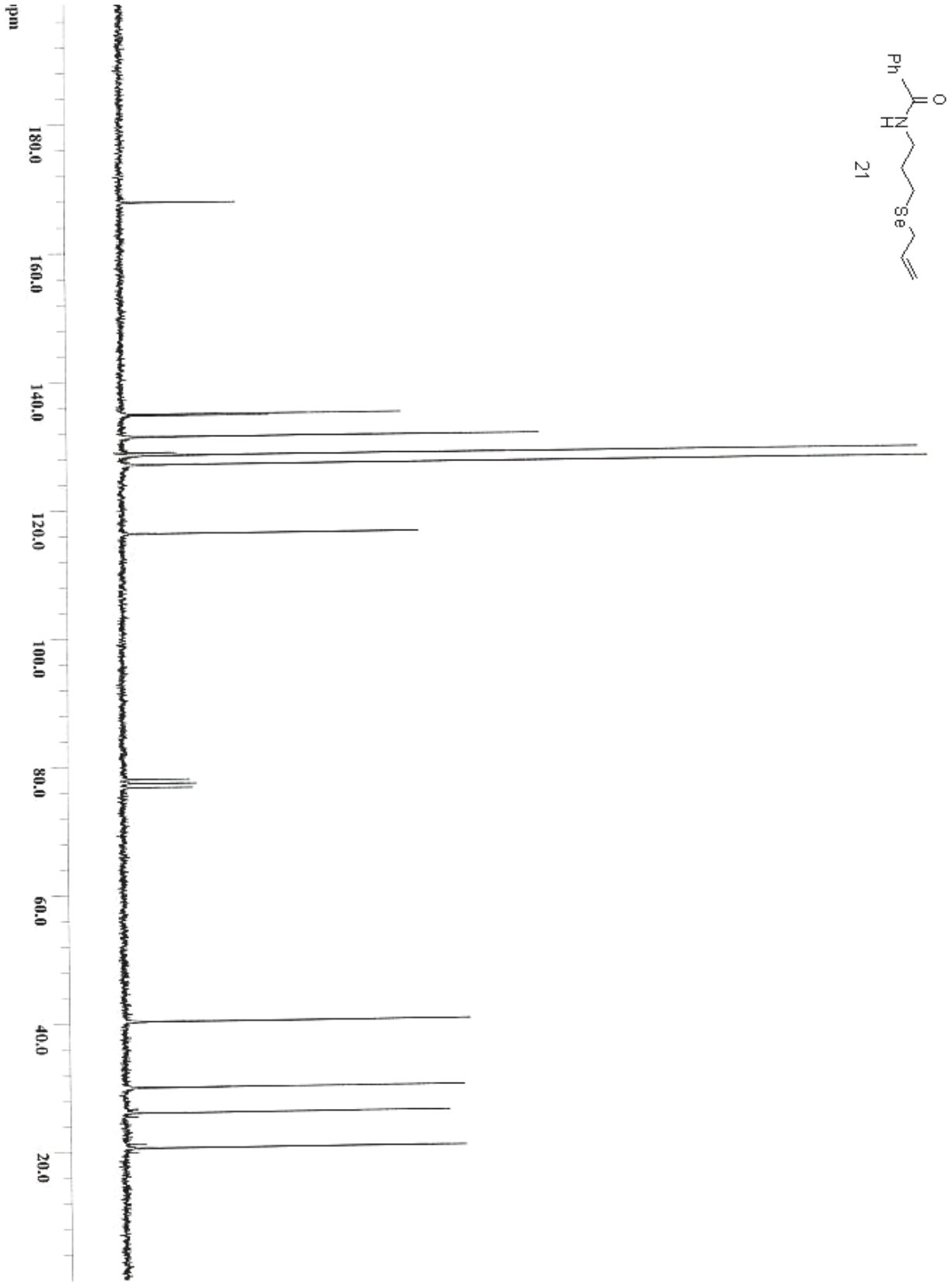
^{77}Se NMR Spectrum of Selenide 20



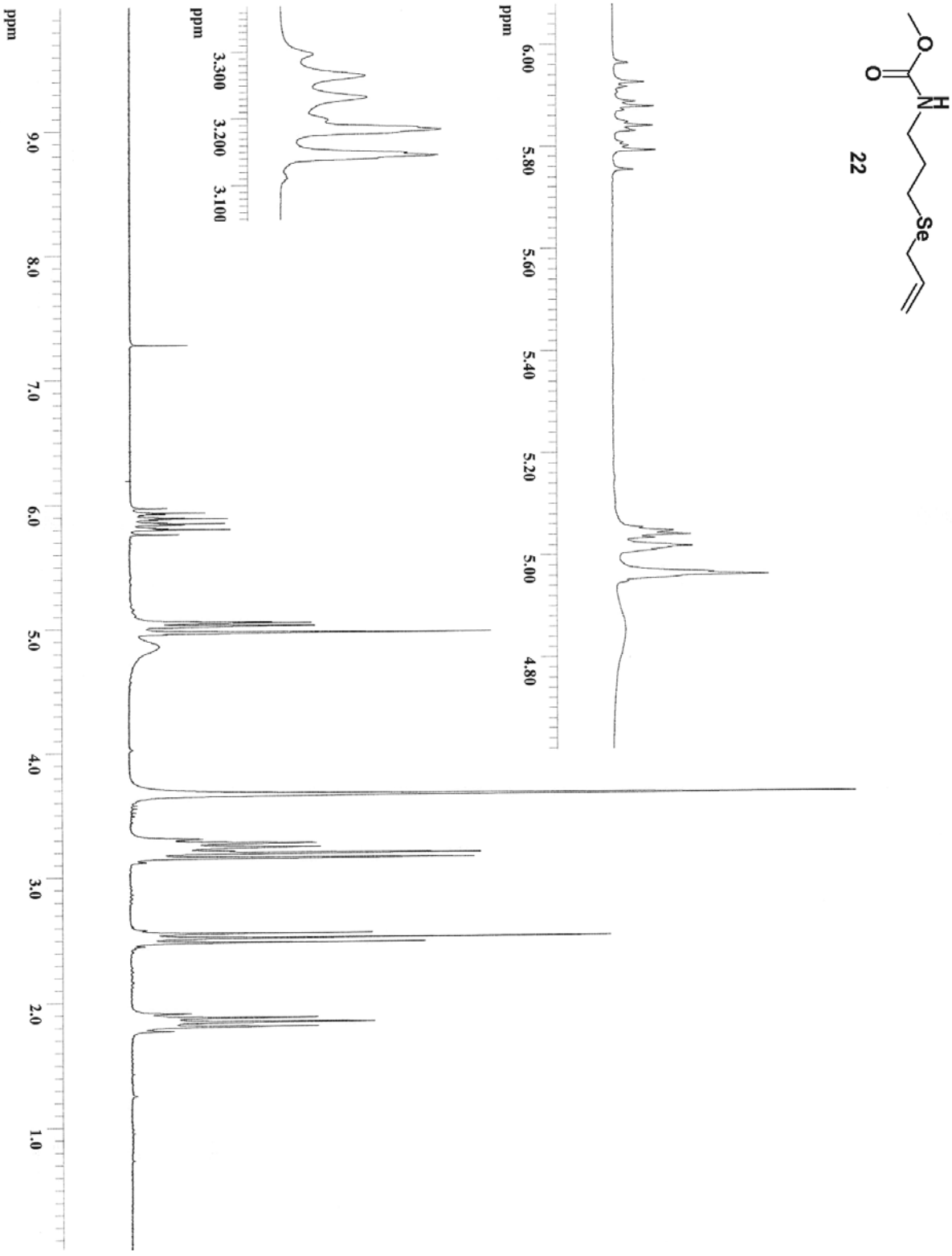
^{1}H NMR Spectrum of Selenide 21



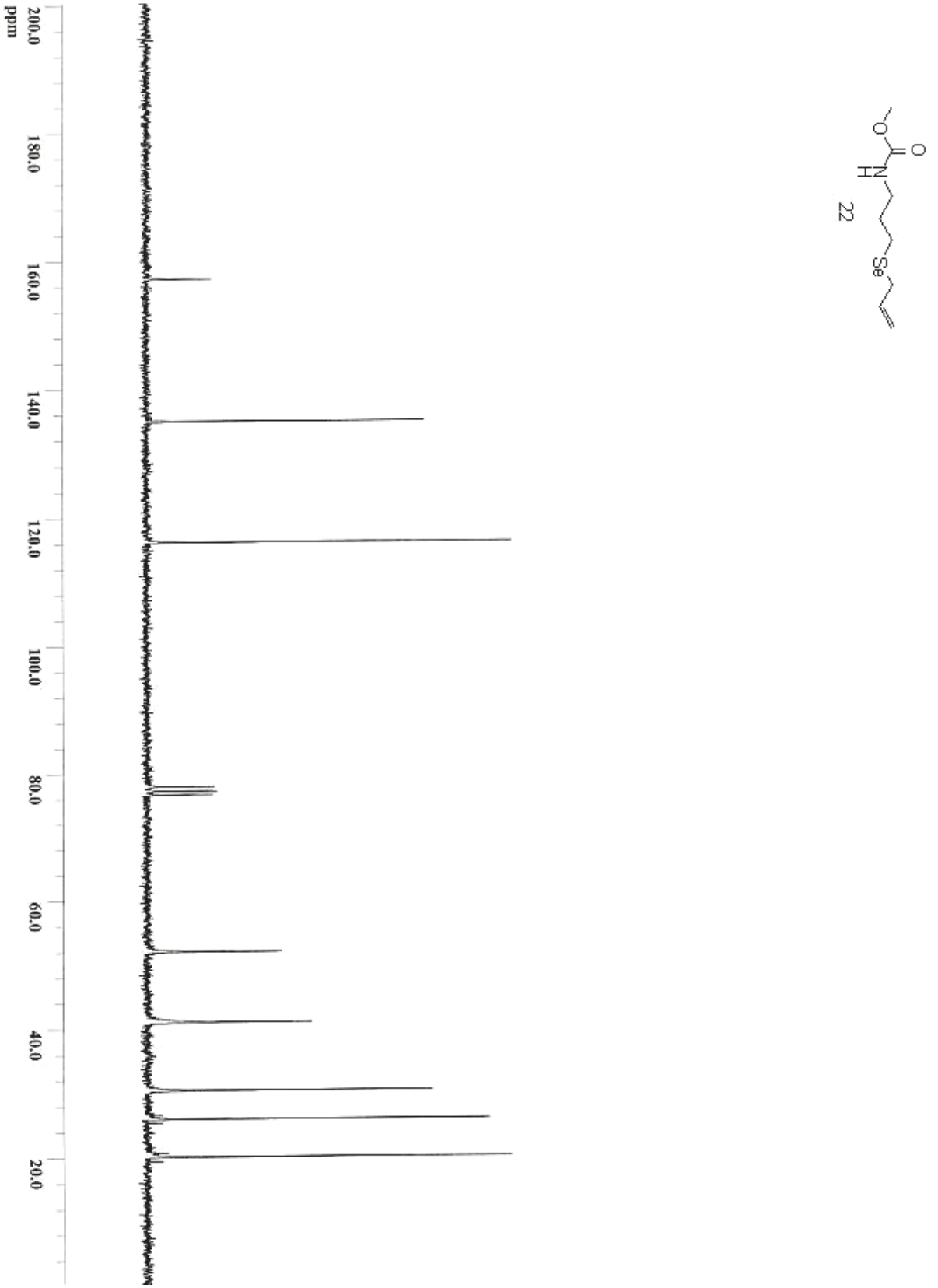
^{13}C NMR Spectrum of Selenide 21



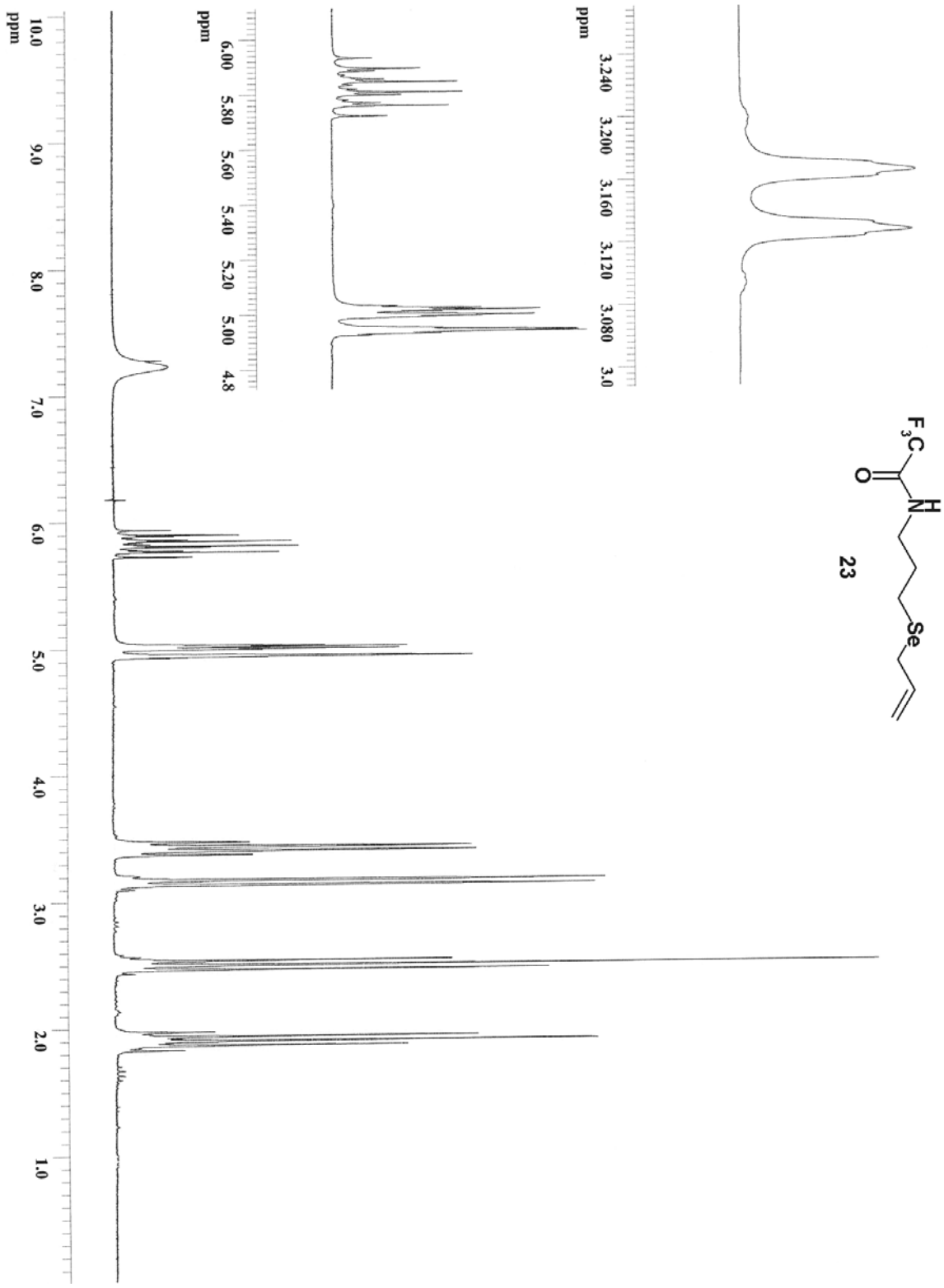
^{1}H NMR Spectrum of Selenide 22



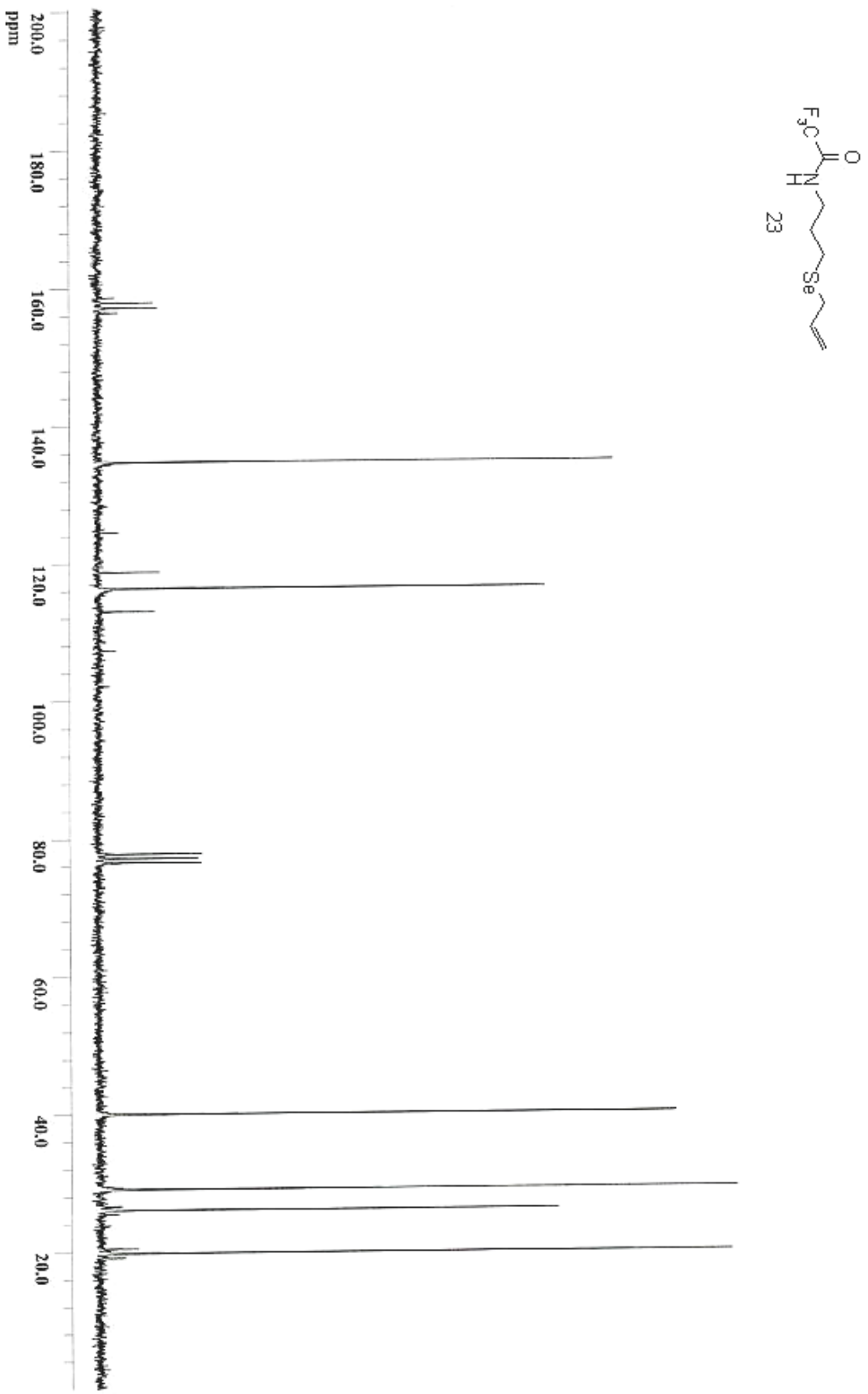
^{13}C NMR Spectrum of Selenide 22



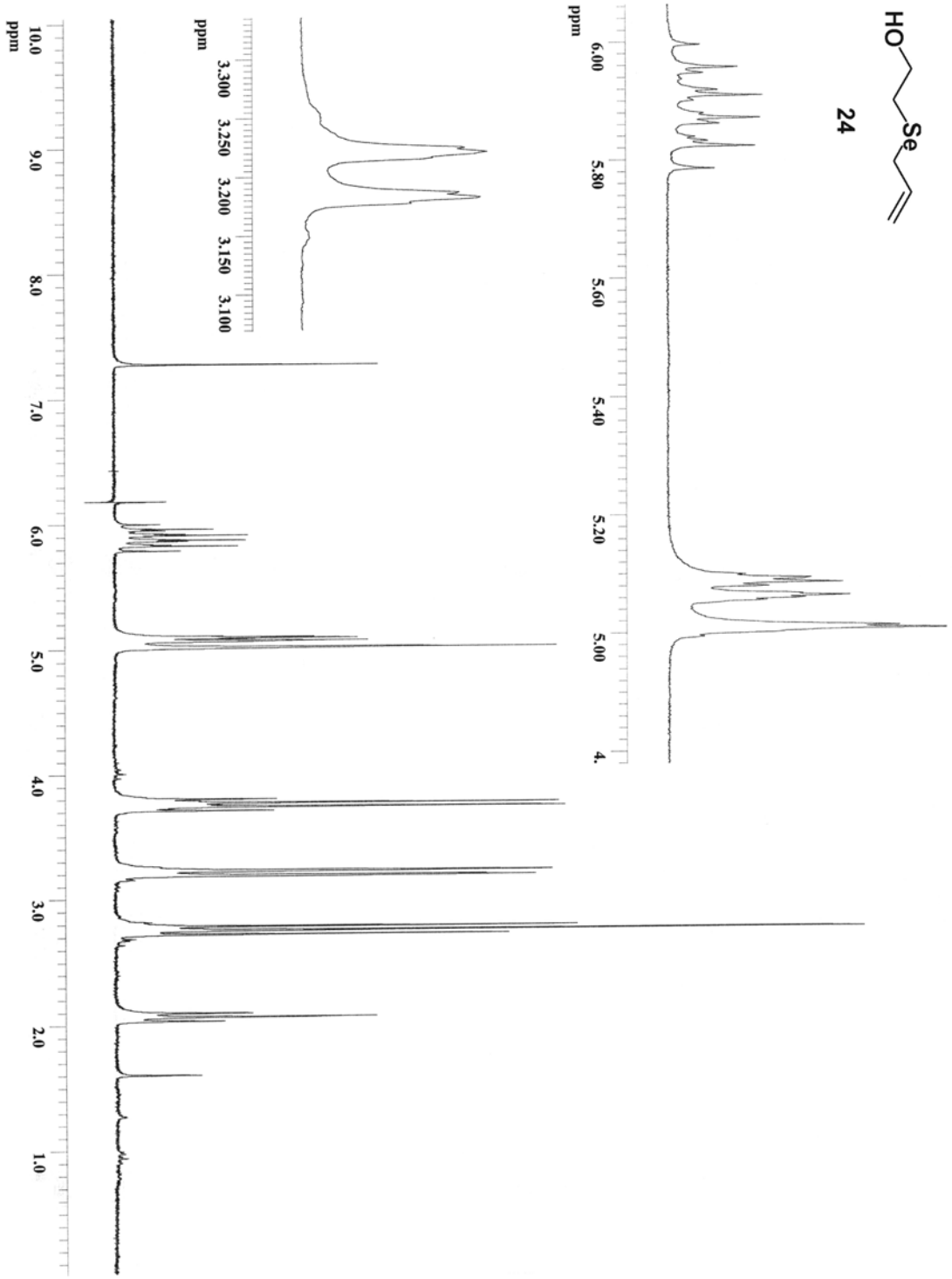
^{1}H NMR Spectrum of Selenide 23



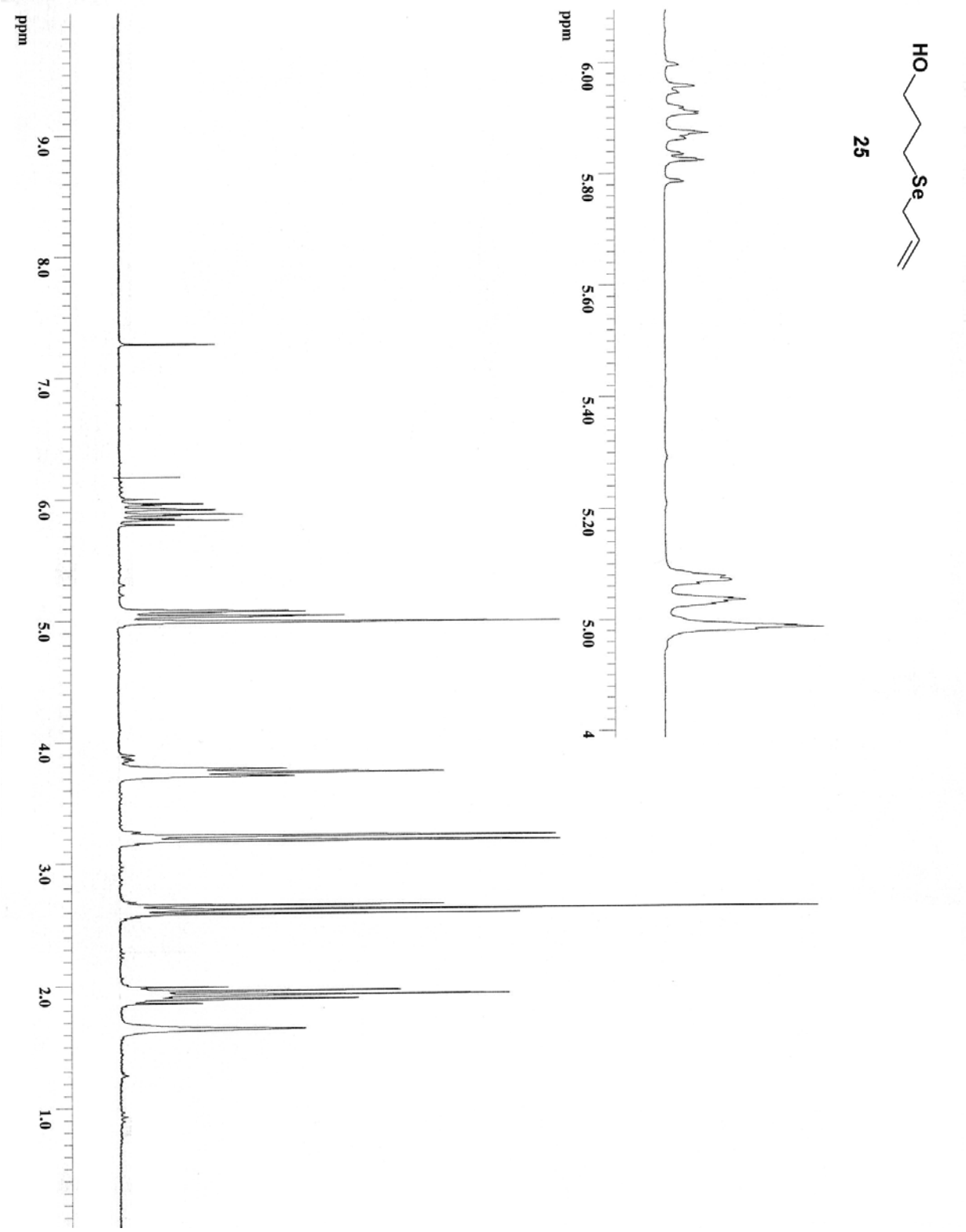
^{13}C NMR Spectrum of Selenide 23



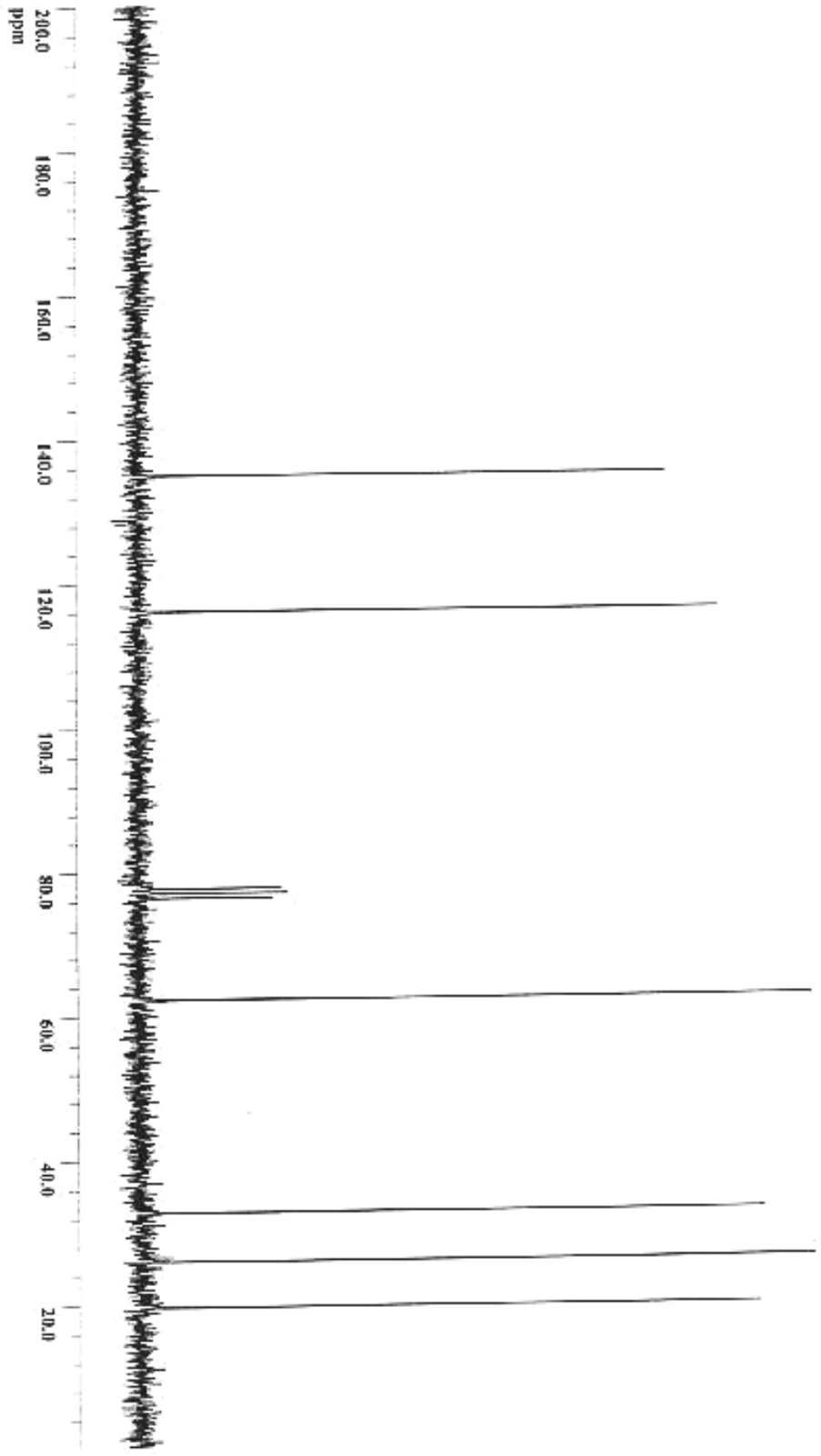
^{1}H NMR Spectrum of Selenide 24

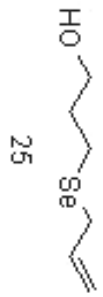


^{1}H NMR Spectrum of Selenide 25



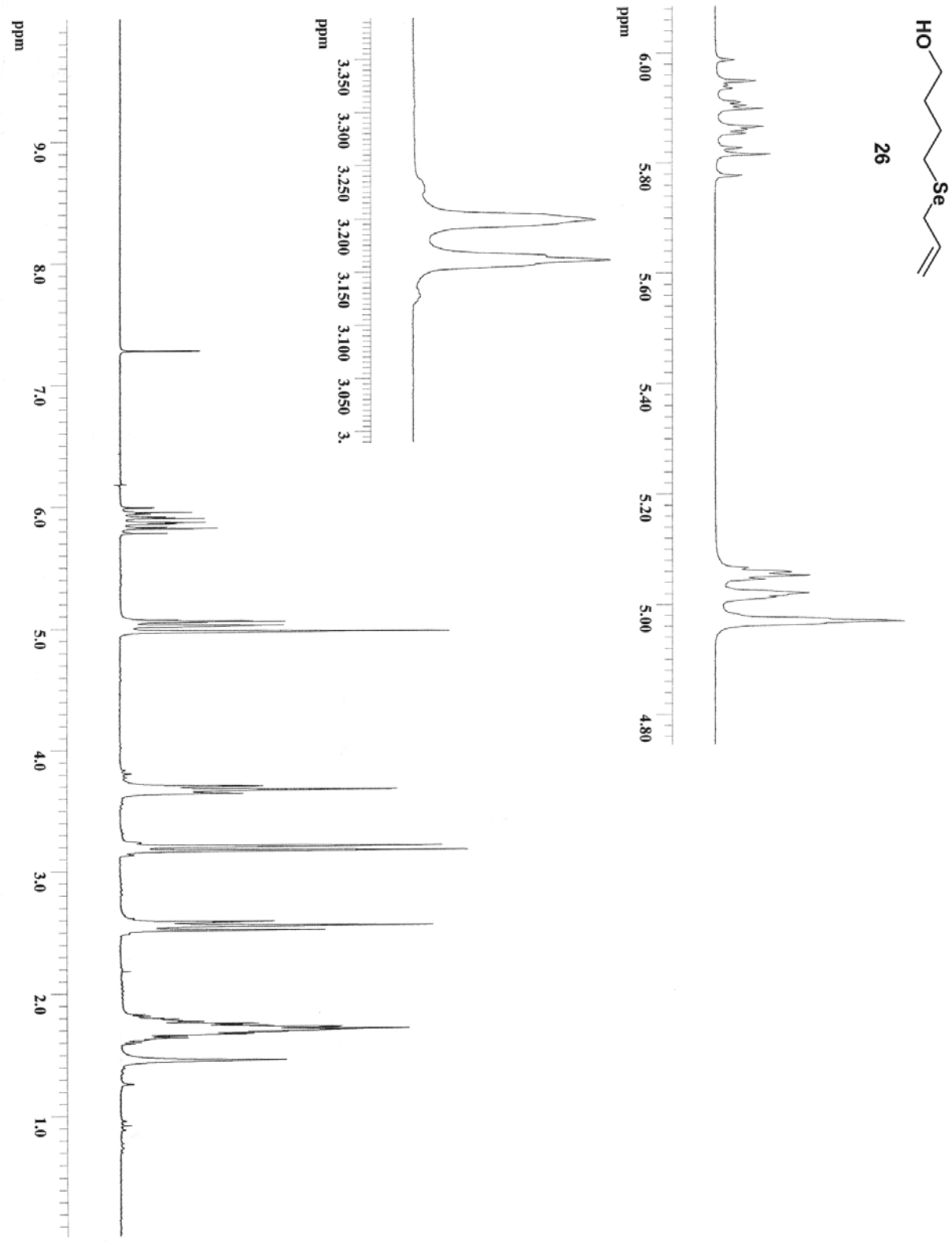
^{13}C NMR Spectrum of Selenide 25



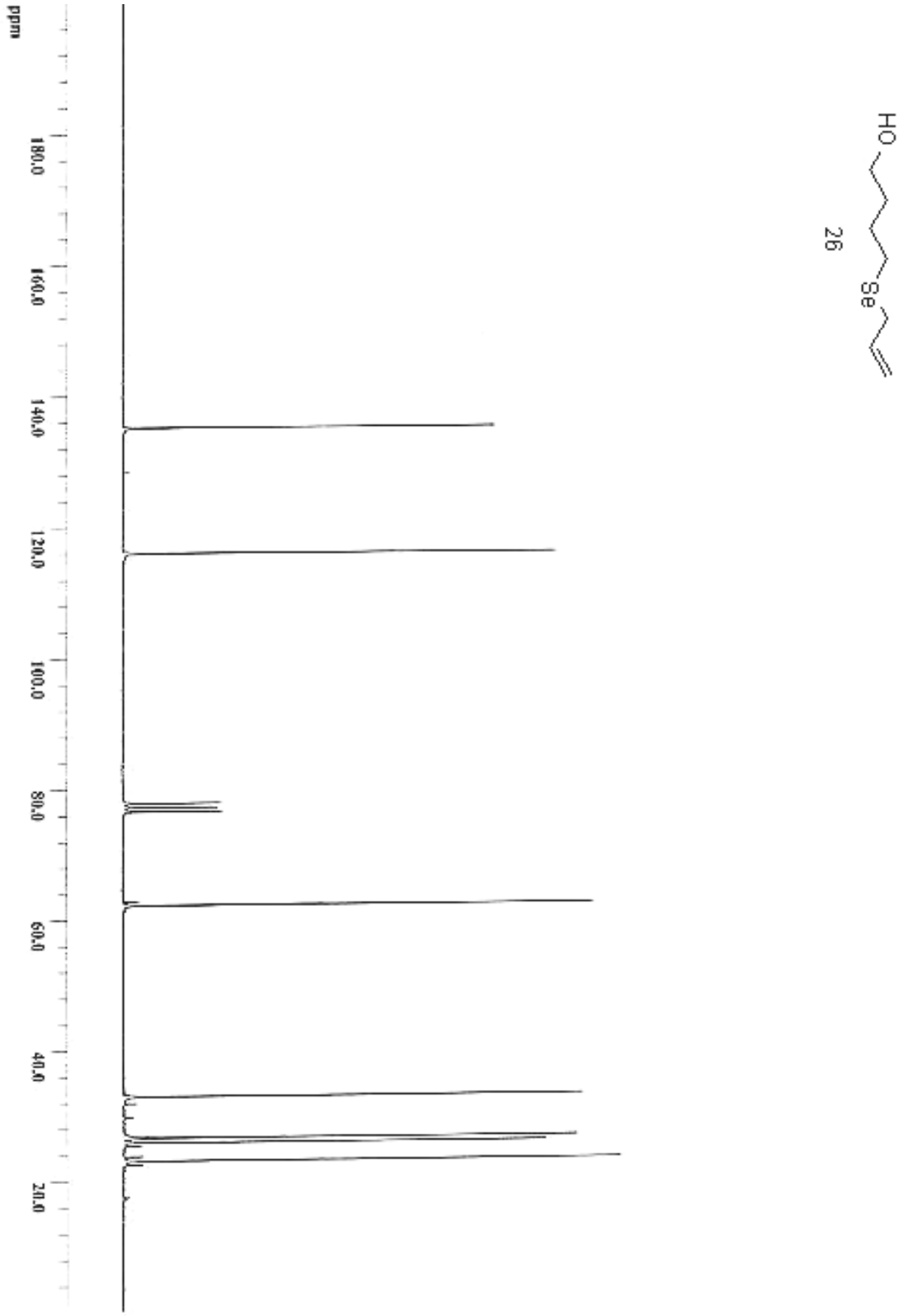


25

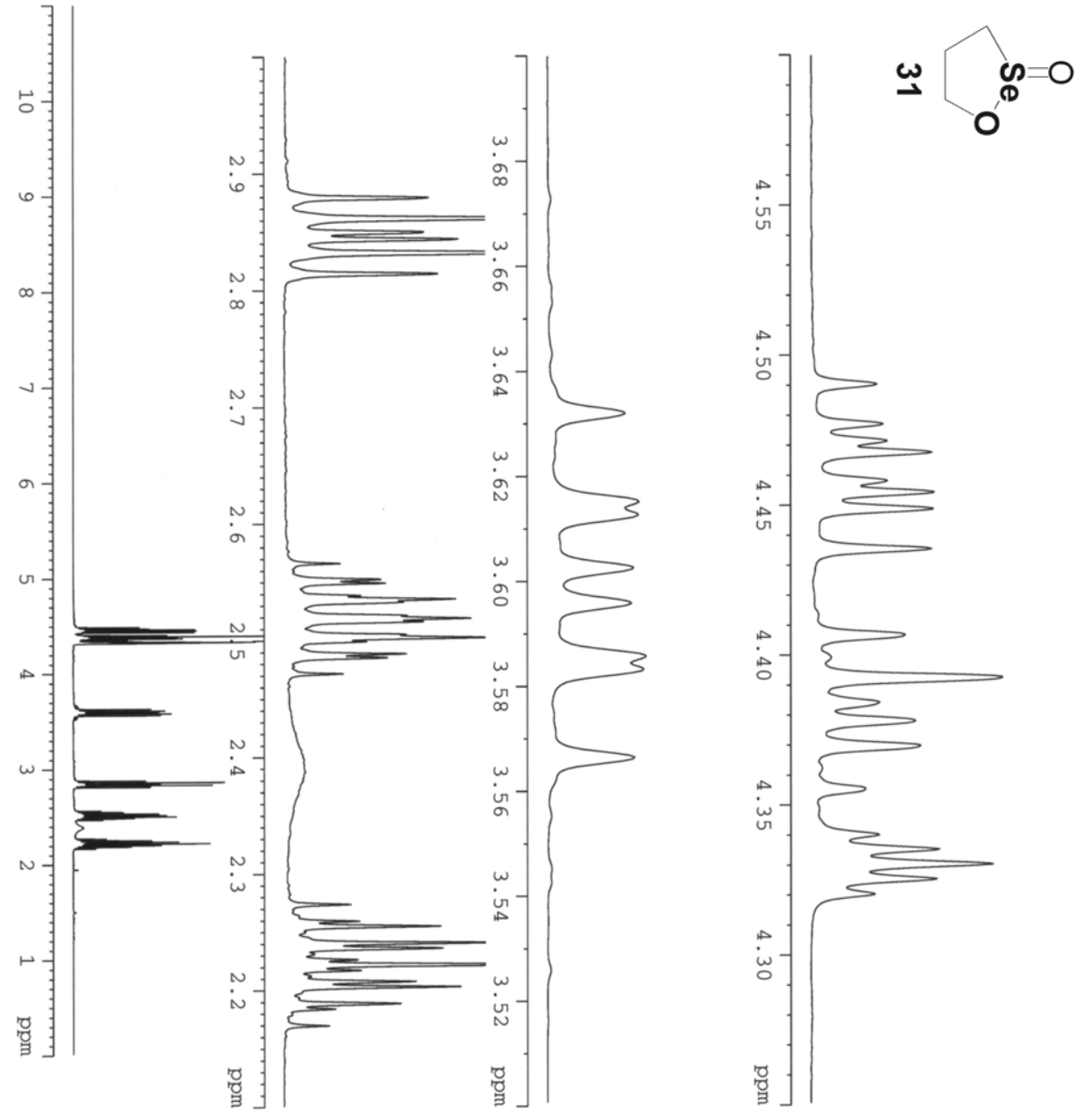
^{1}H NMR Spectrum of Selenide 26



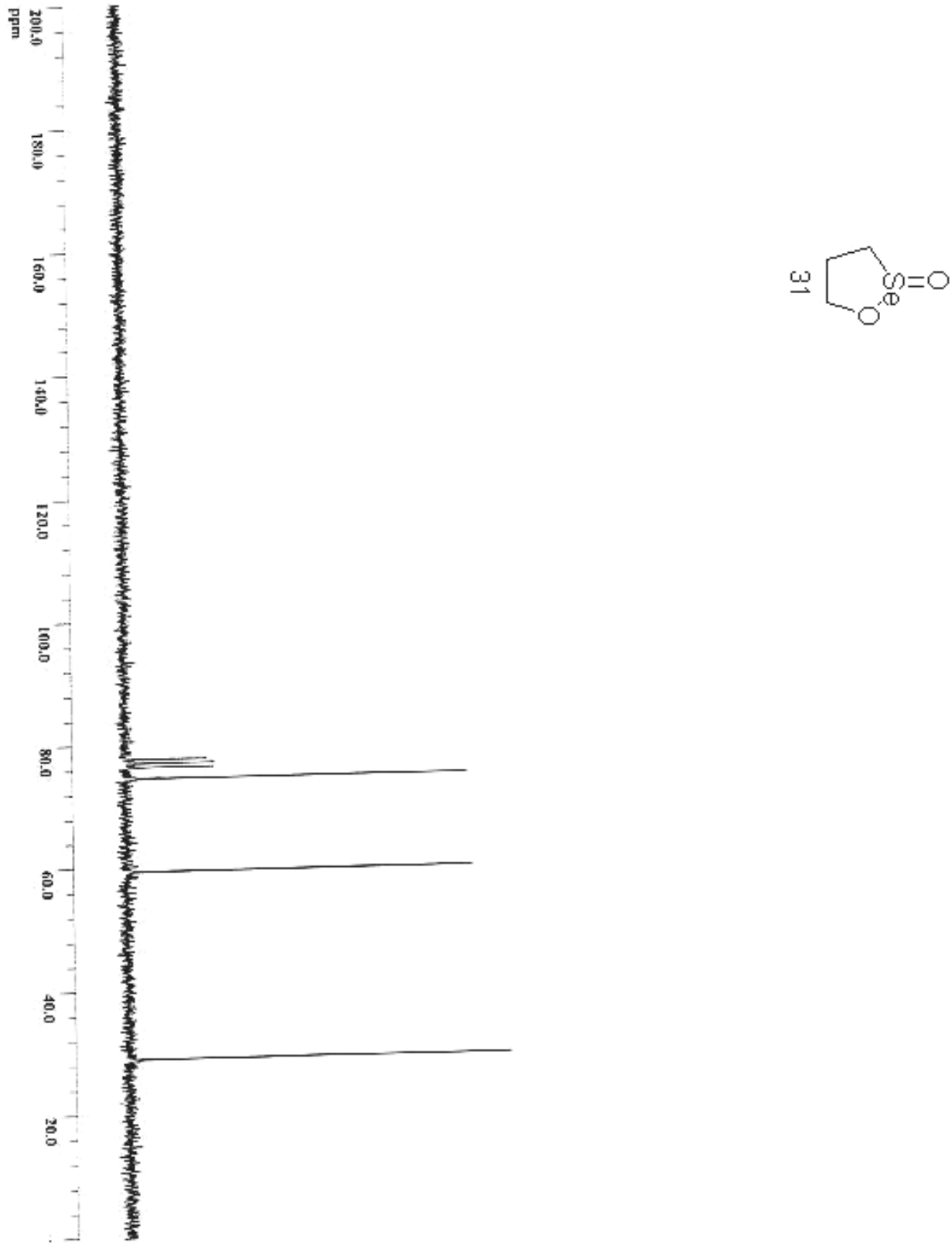
^{13}C NMR Spectrum of Diselenide 26



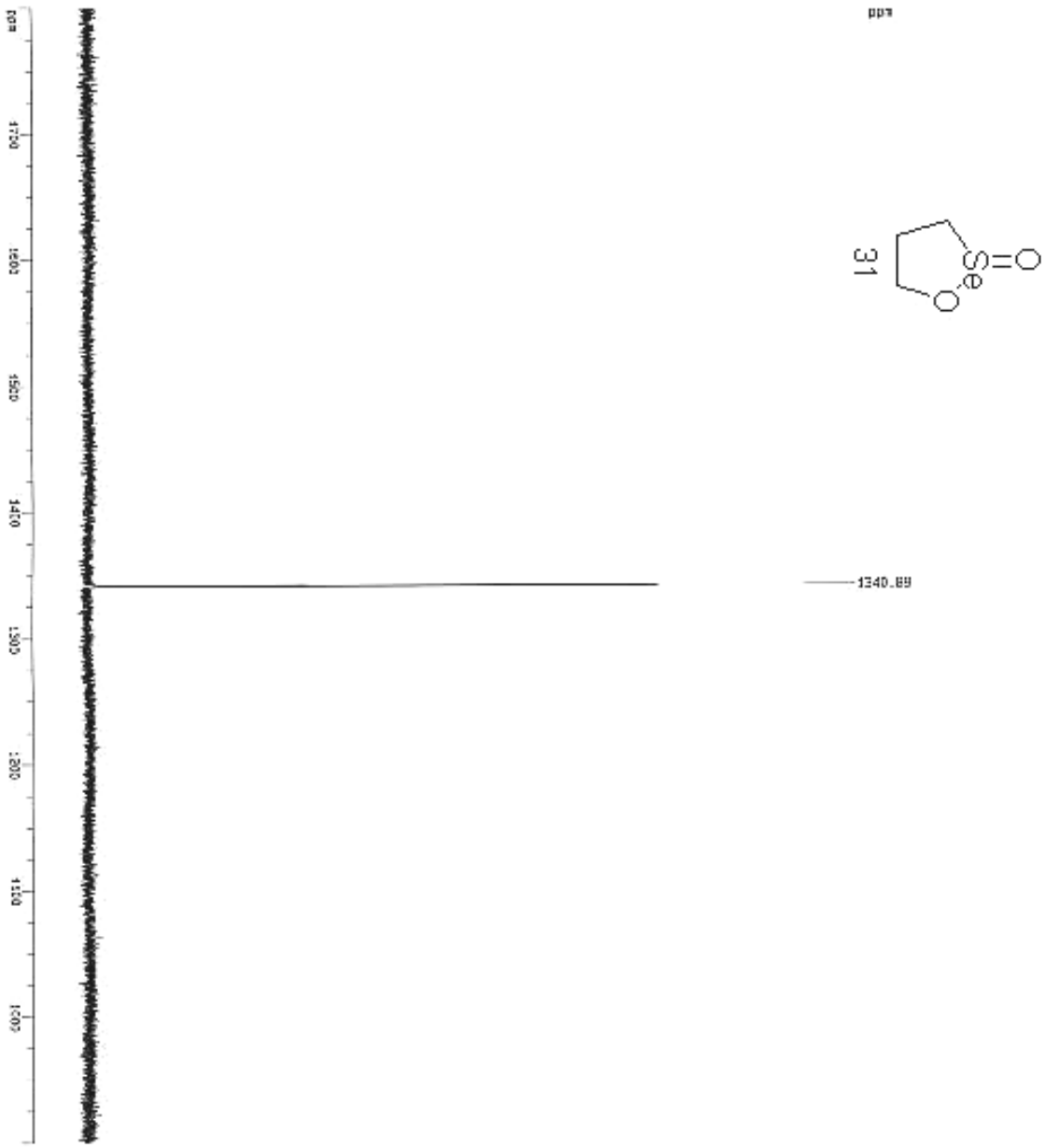
^{1}H NMR Spectrum of 1,2-Oxaselenolane *Se*-Oxide (31) in CD_3NO_2



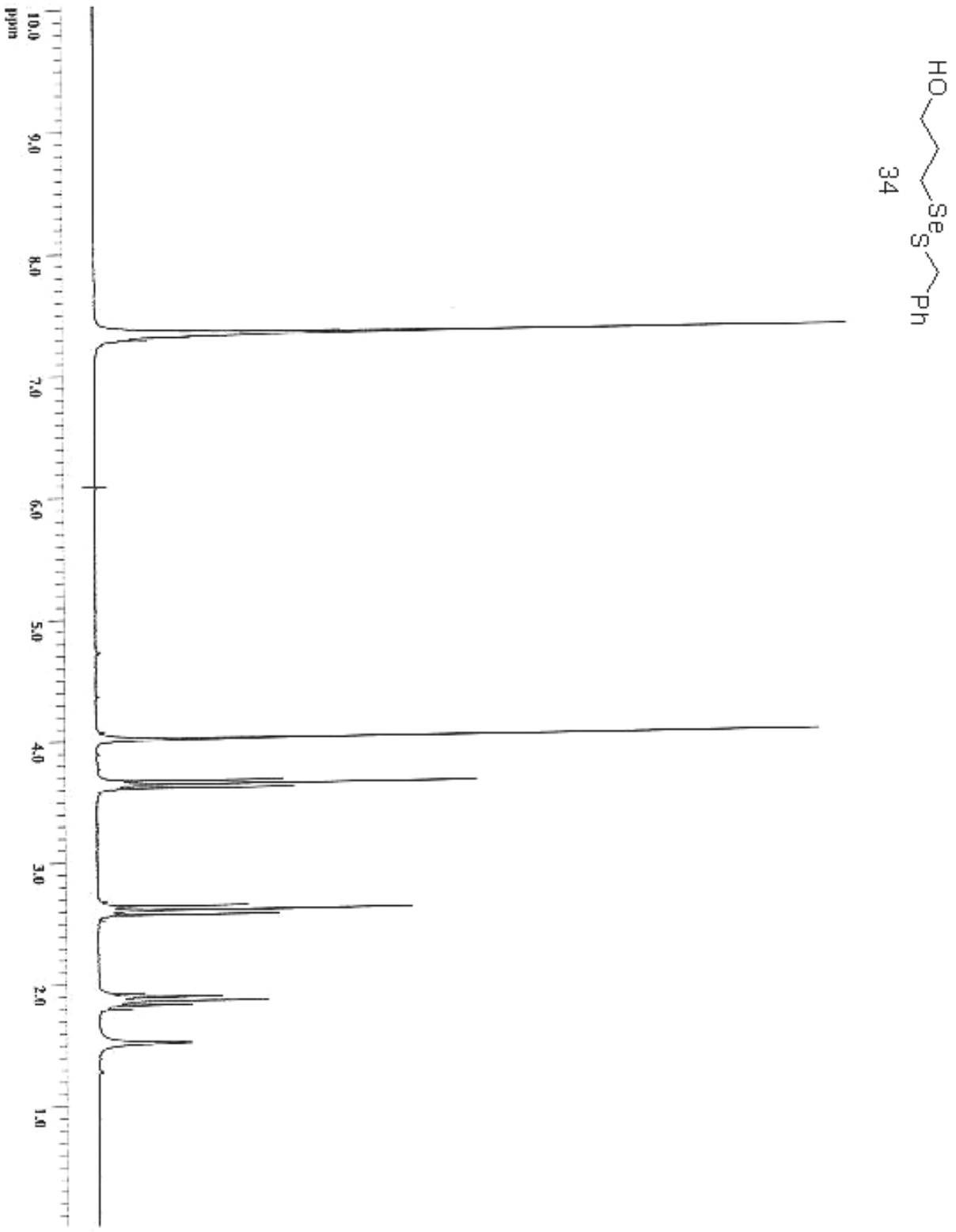
^{13}C NMR Spectrum of 1,2-Oxaselenolane *Se*-Oxide (31)



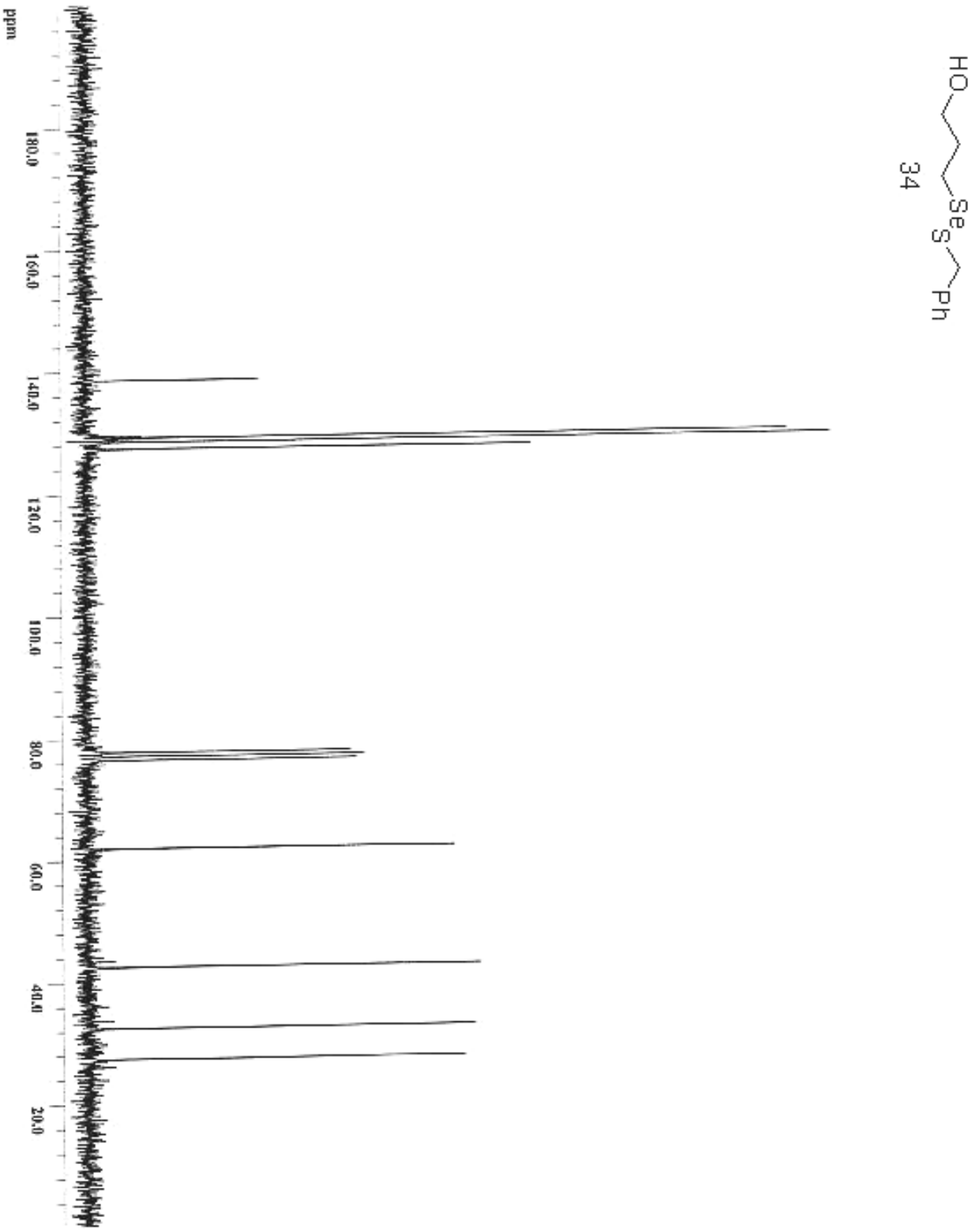
^{77}Se NMR Spectrum of 1,2-Oxaselenolane *Se*-Oxide (31)



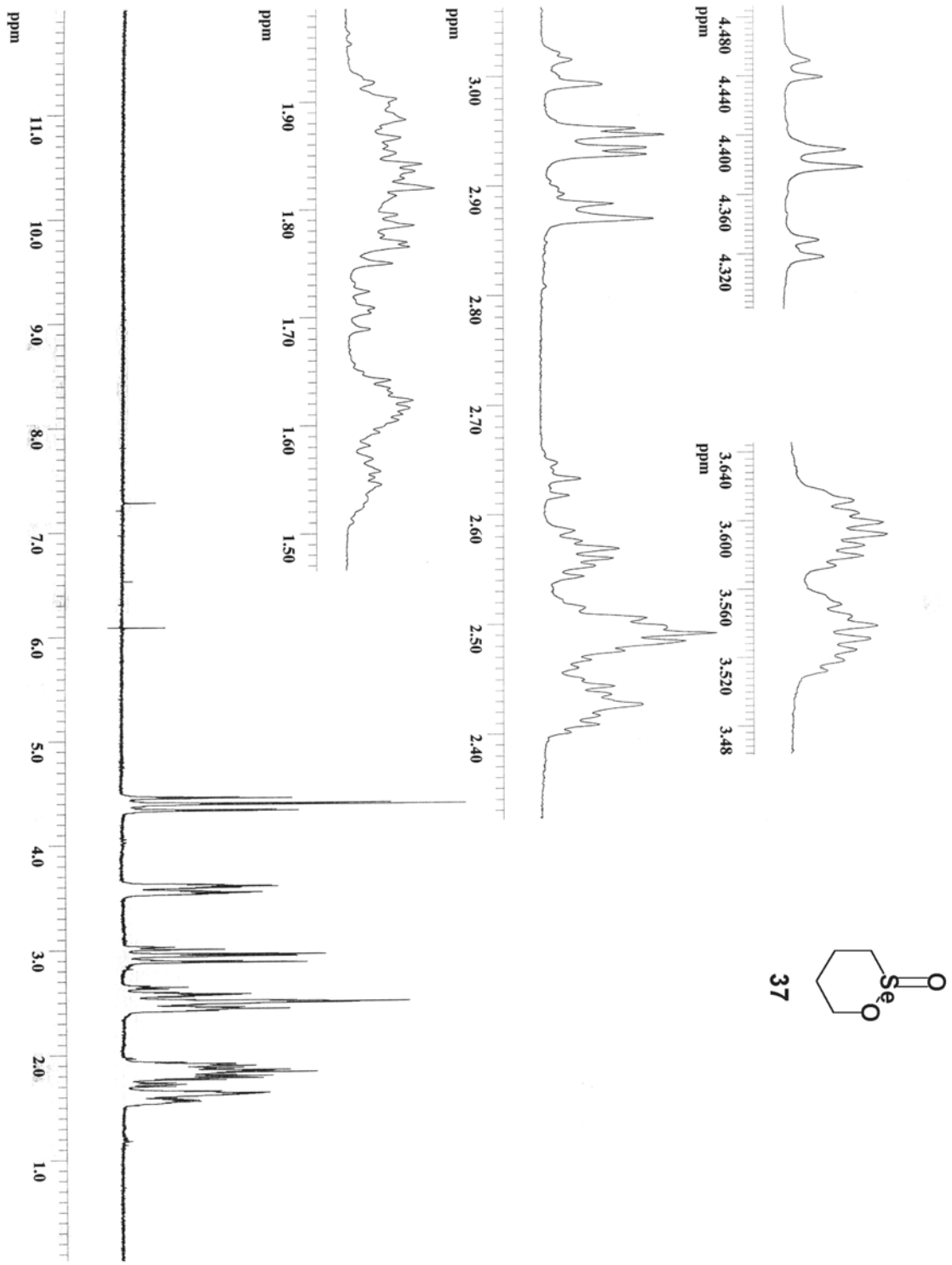
^{1}H NMR Spectrum of Selenenyl Sulfide 34



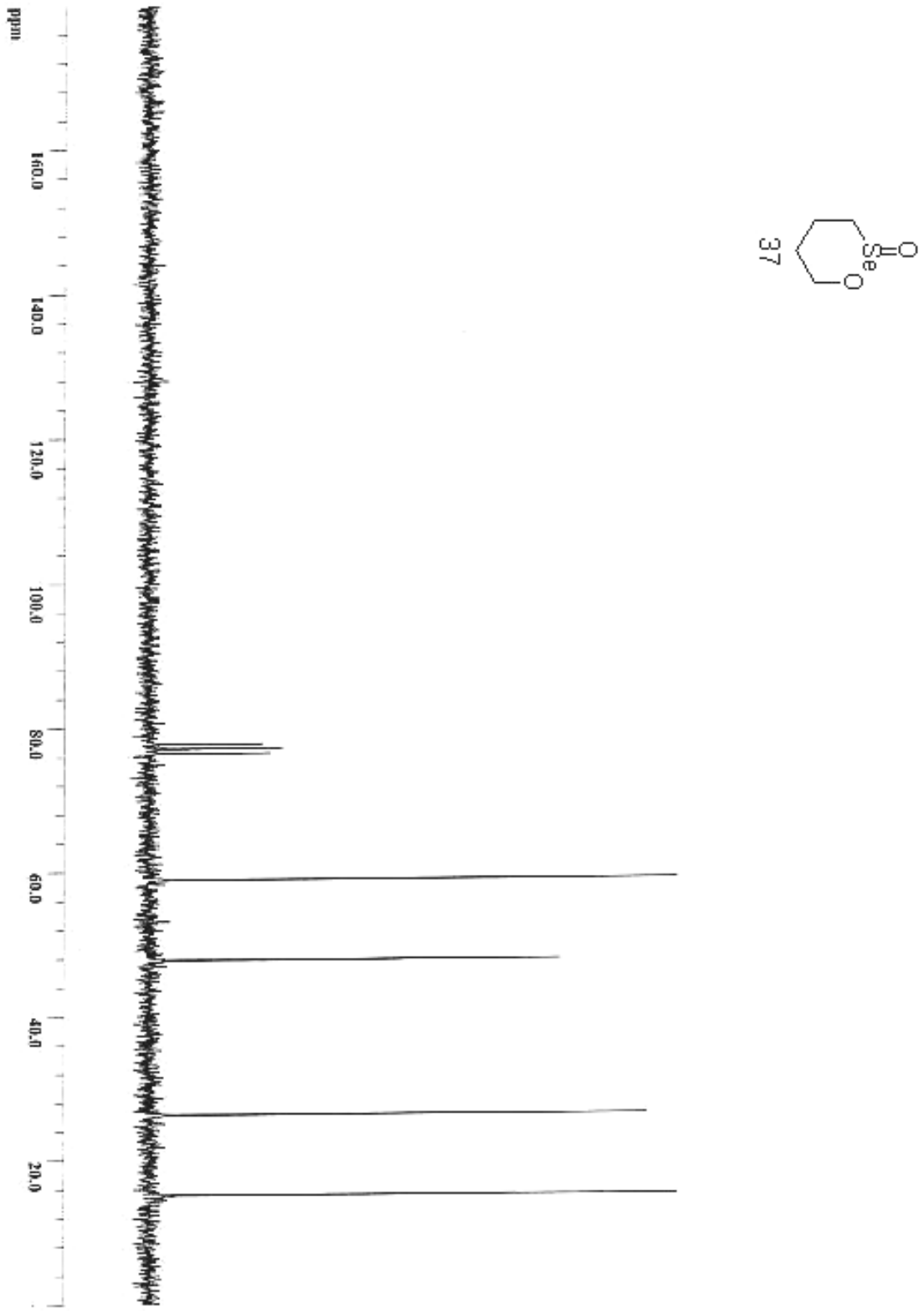
^{13}C NMR Spectrum of Selenenyl Sulfide 34



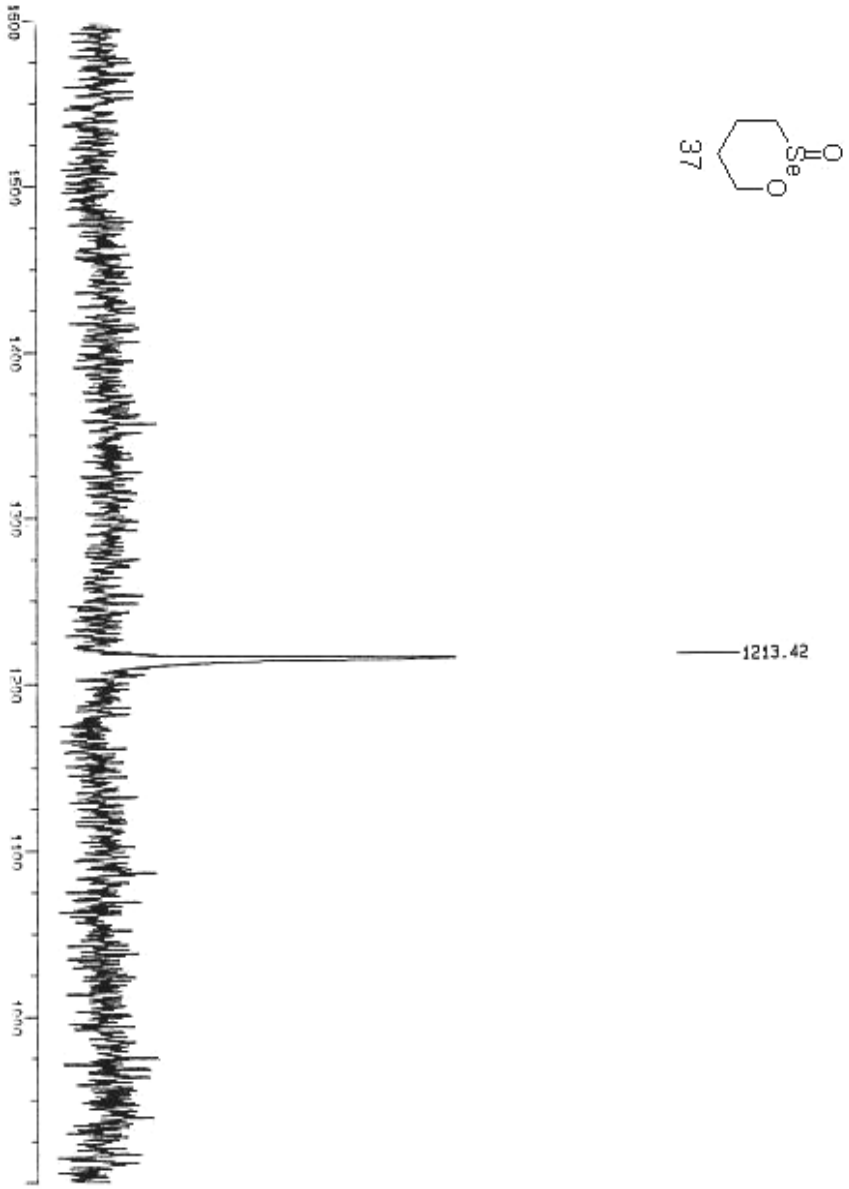
^{1}H NMR Spectrum of 1,2-Oxaselenane *Se*-Oxide (37)



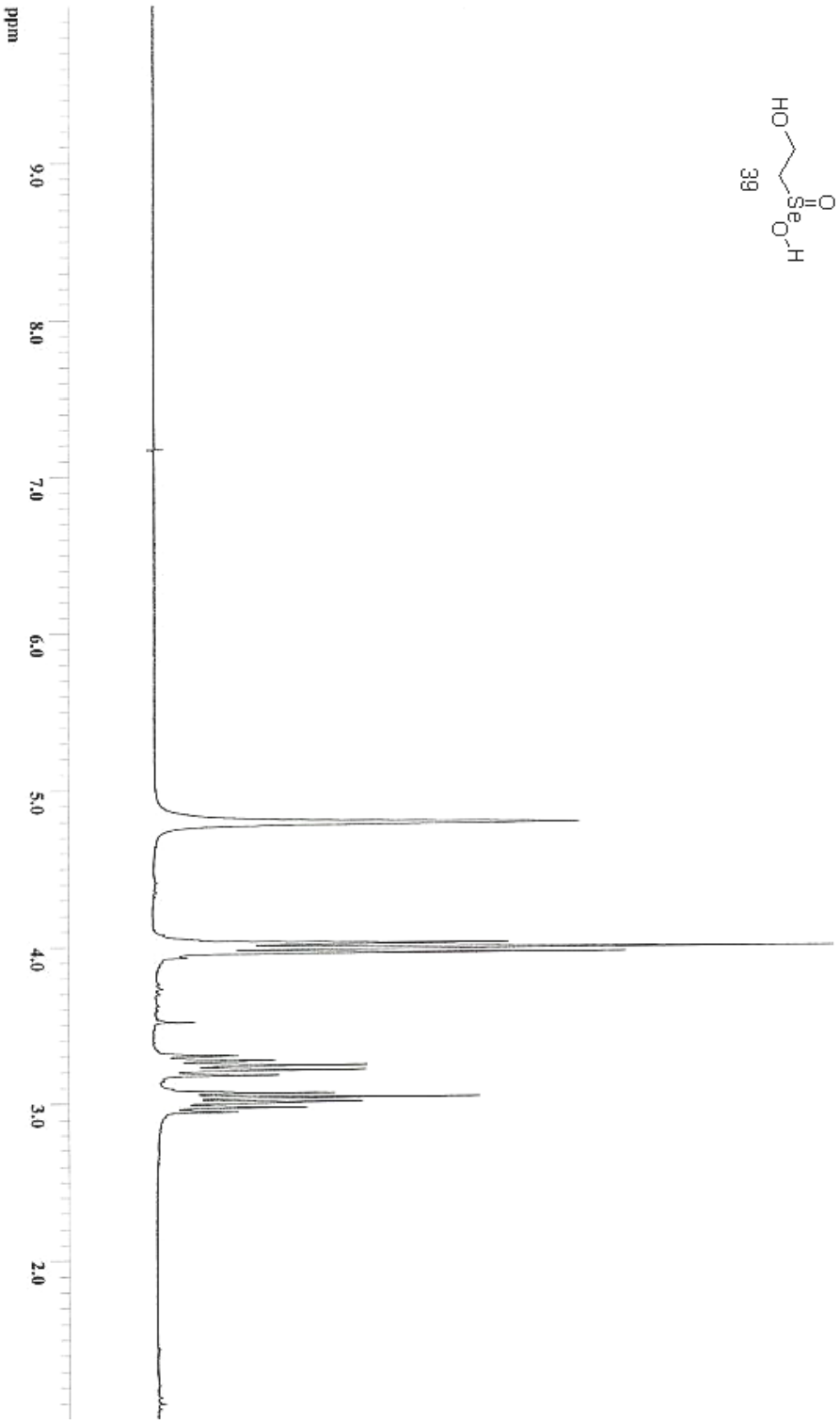
^{13}C NMR Spectrum of 1,2-Oxaselenane *Se*-Oxide (37)



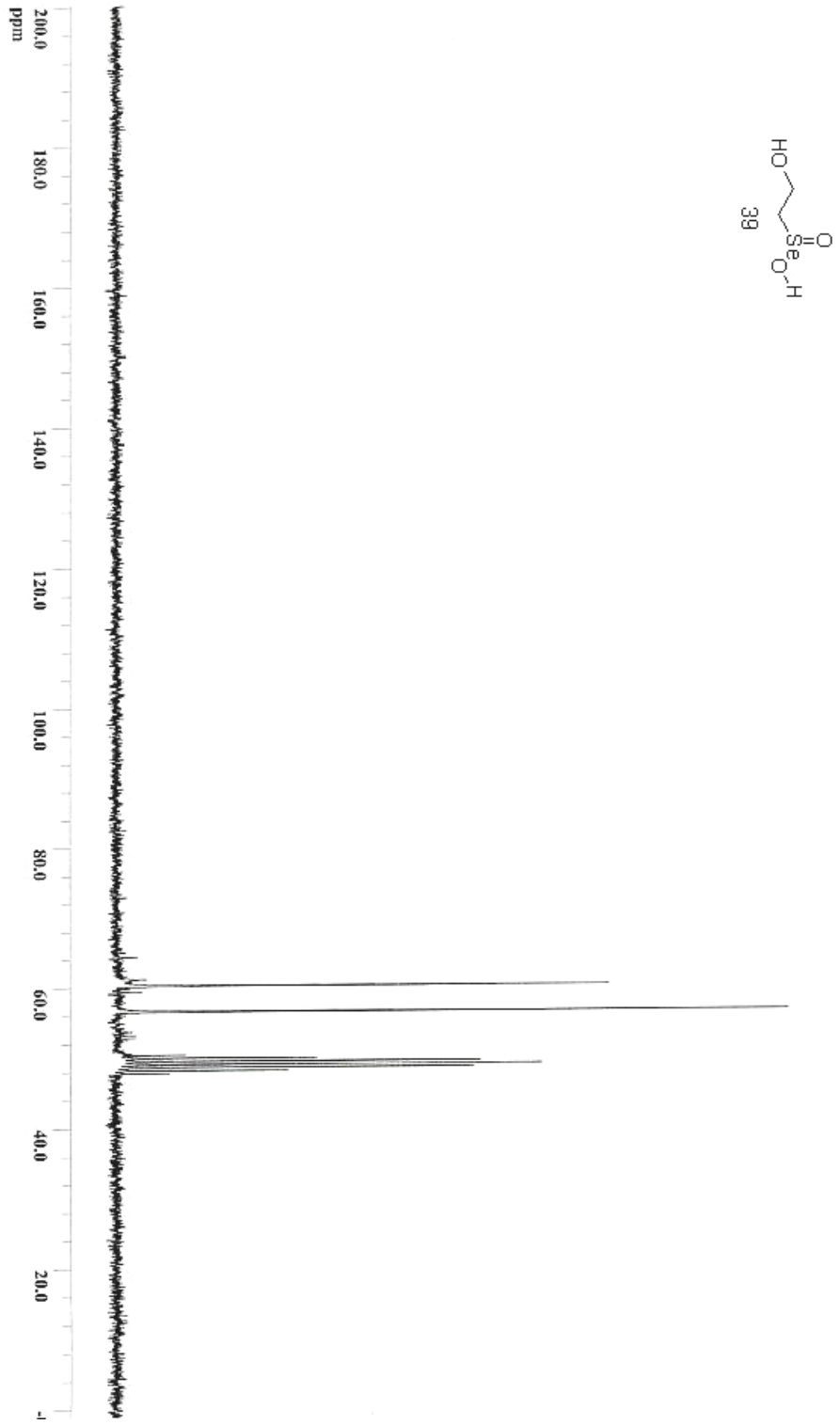
^{77}Se NMR Spectrum of 1,2-Oxaselenane *Se*-Oxide (37)



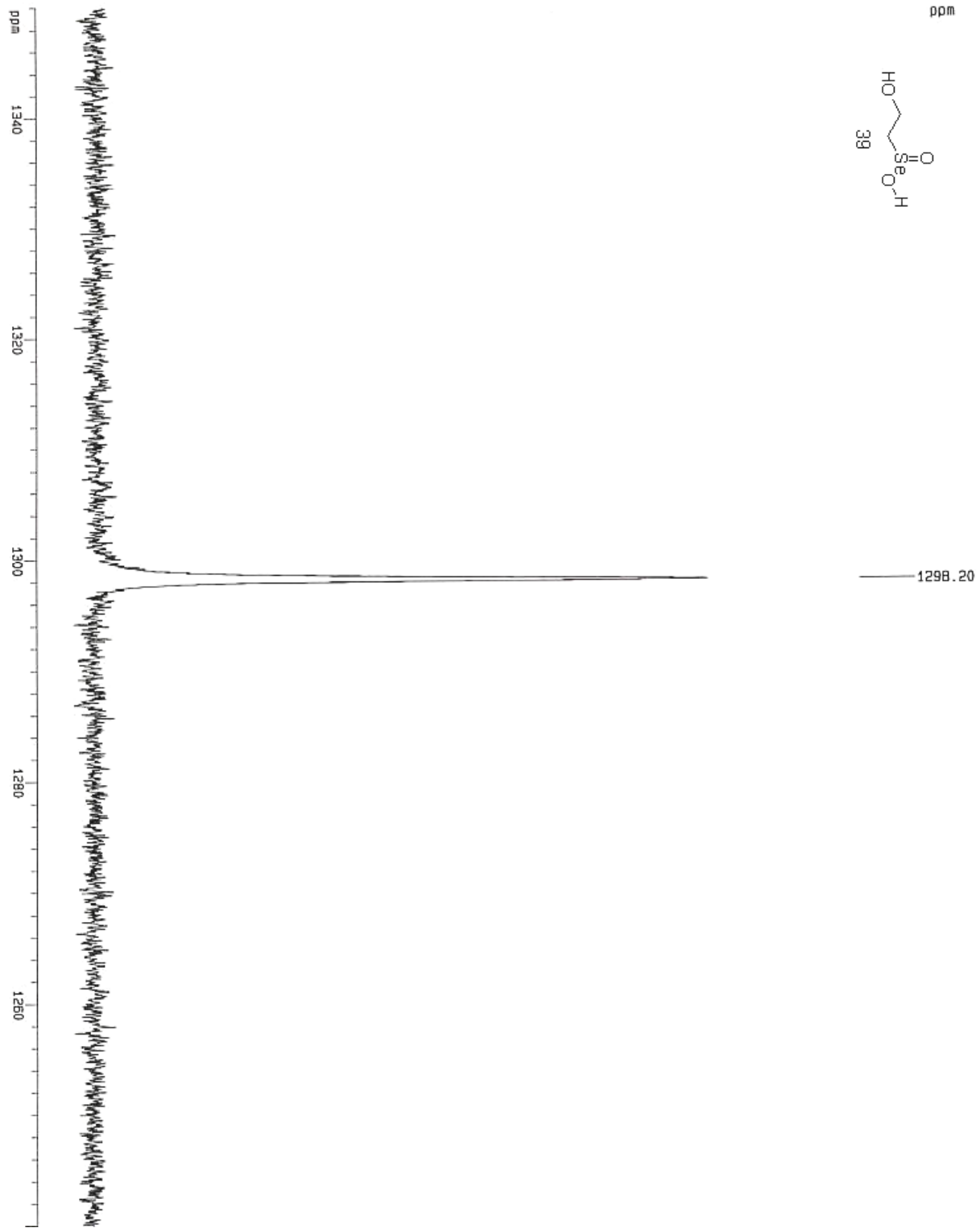
^{1}H NMR Spectrum of 2-Hydroxyethaneseleninic Acid (39) in CD_3OD



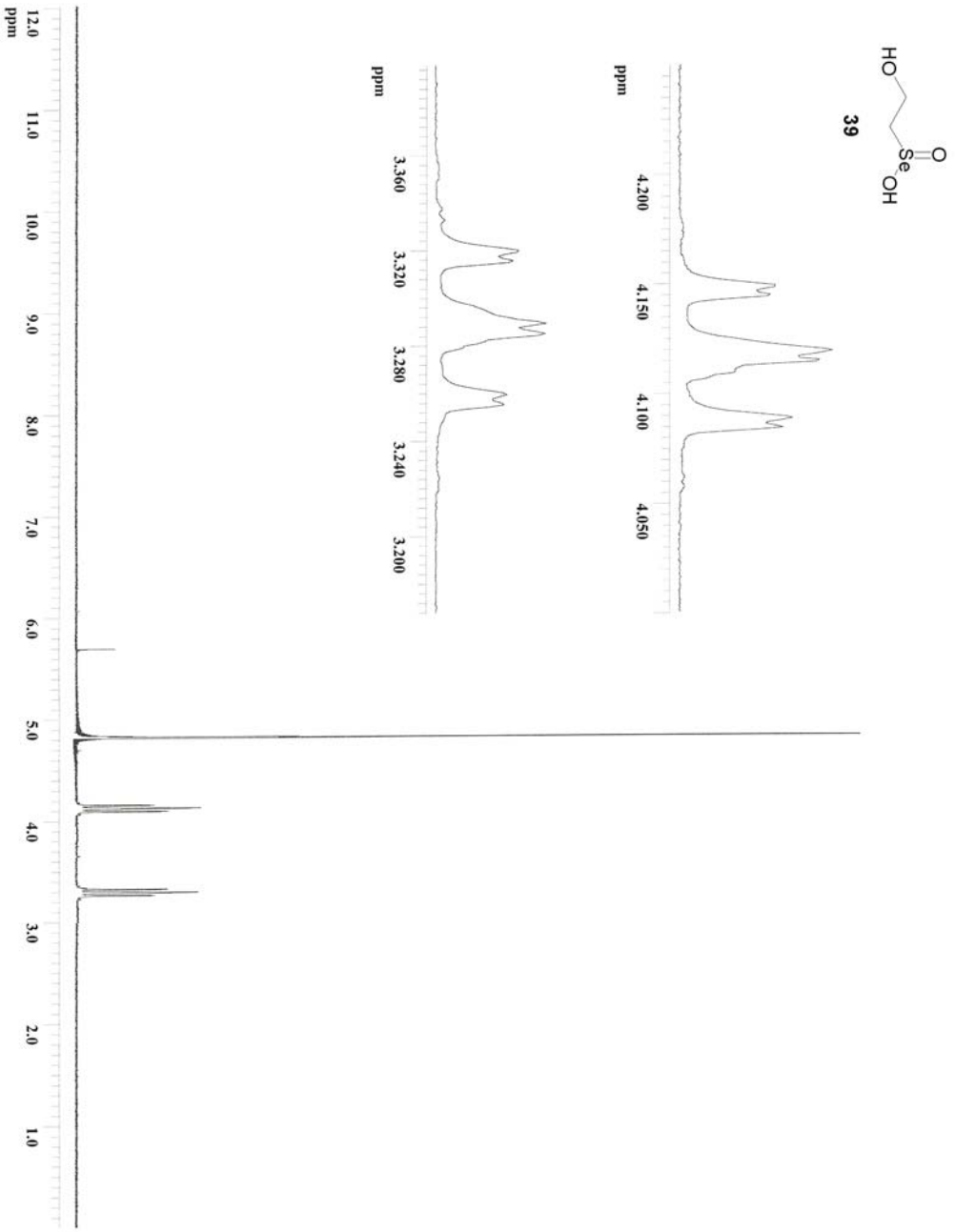
^{13}C NMR Spectrum of 2-Hydroxyethaneseleninic Acid (39) in CD_3OD



^{77}Se NMR Spectrum of 2-Hydroxyethaneseleninic Acid (39) in CD_3OD



^{1}H NMR Spectrum of 2-Hydroxyethaneselenenic Acid (39) in D_2O



For Figure 1 (comparison of rates of compounds **1**, **2**, **9**, **25** and control), see the Article.

Figure 2. Rates of formation of BnSSBn from oxidation of BnSH (0.031 M) with 90% aqueous TBHP (0.043 M) in the presence of catalysts **4, 5**, and **6** (0.0031 M) in CH_2Cl_2-MeOH (95:5) at 18°C.

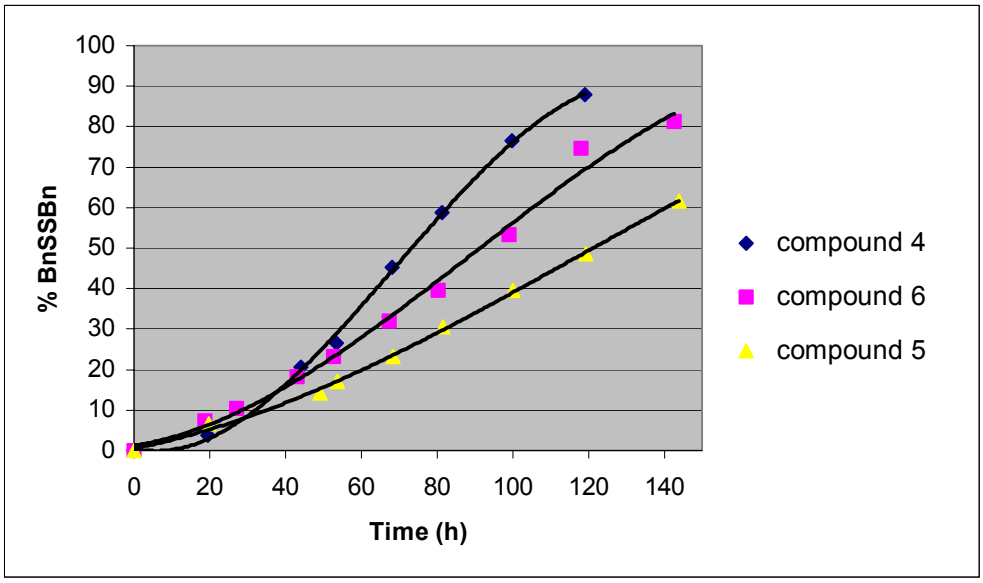


Figure 3. Rate of formation of BnSSBn from oxidation of BnSH (0.031 M) with 90% aqueous TBHP (0.043 M) in the presence of catalyst **7** (0.0031 M) in CH_2Cl_2-MeOH (95:5) at 18°C.

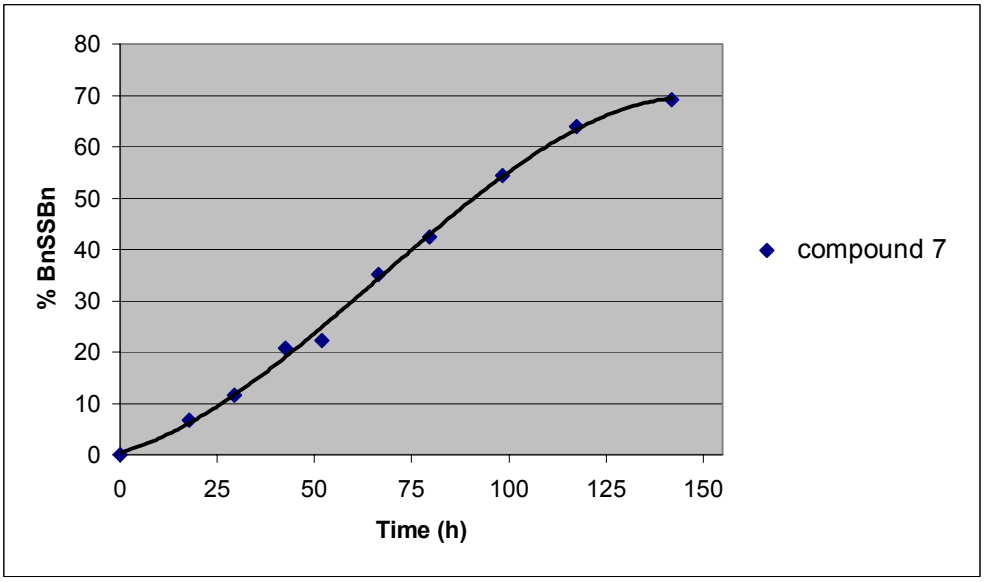


Figure 4. Rate of formation of BnSSBn from oxidation of BnSH (0.031 M) with 90% aqueous TBHP (0.043 M) in the presence of catalyst **8** (0.0031 M) in CH_2Cl_2-MeOH (95:5) at 18°C.

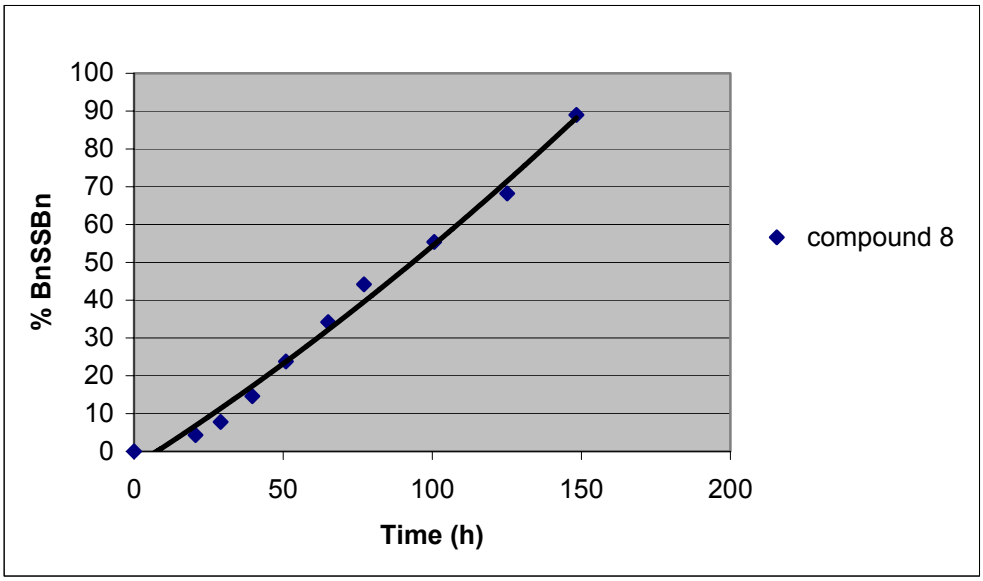


Figure 5. Rate of formation of BnSSBn from oxidation of BnSH (0.031 M) with 90% aqueous TBHP (0.043 M) in the presence of catalyst **9** (0.0031 M) in CH_2Cl_2-MeOH (95:5) at 18°C.

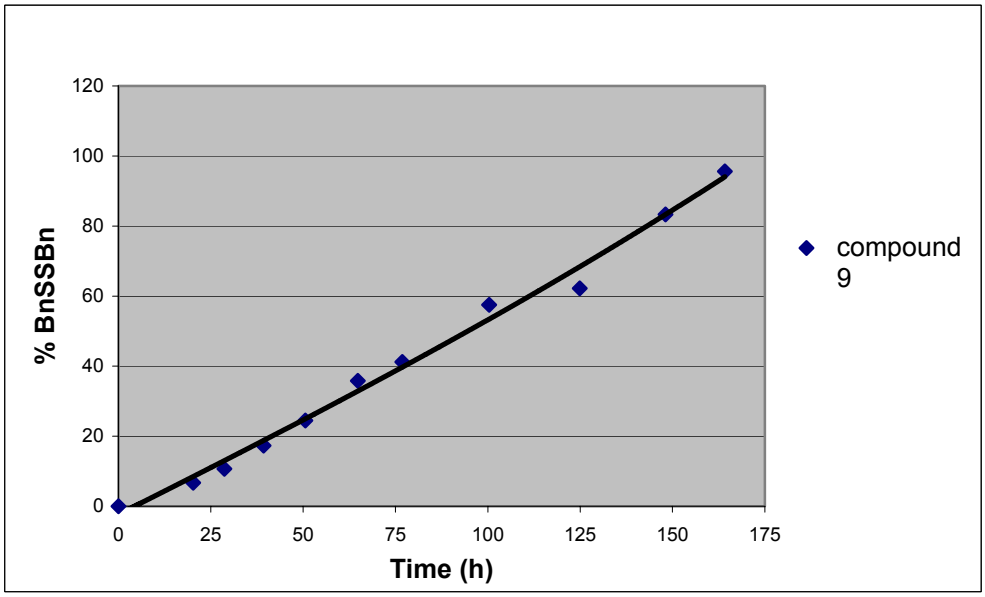


Figure 6. Rates of formation of BnSSBn from oxidation of BnSH (0.031 M) with 90% aqueous TBHP (0.043 M) in the presence of catalysts **10** and **13** (0.0031 M) in CH_2Cl_2-MeOH (95:5) at 18°C.

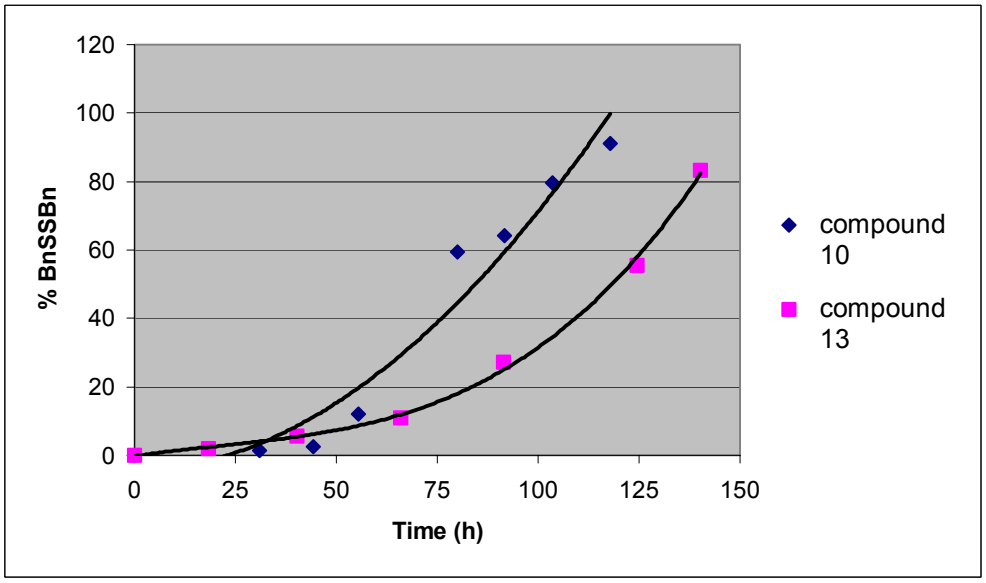


Figure 7. Rates of formation of BnSSBn from oxidation of BnSH (0.031 M) with 90% aqueous TBHP (0.043 M) in the presence of catalysts **11, 12**, **14** and **15** (0.0031 M) in CH_2Cl_2-MeOH (95:5) at 18°C.

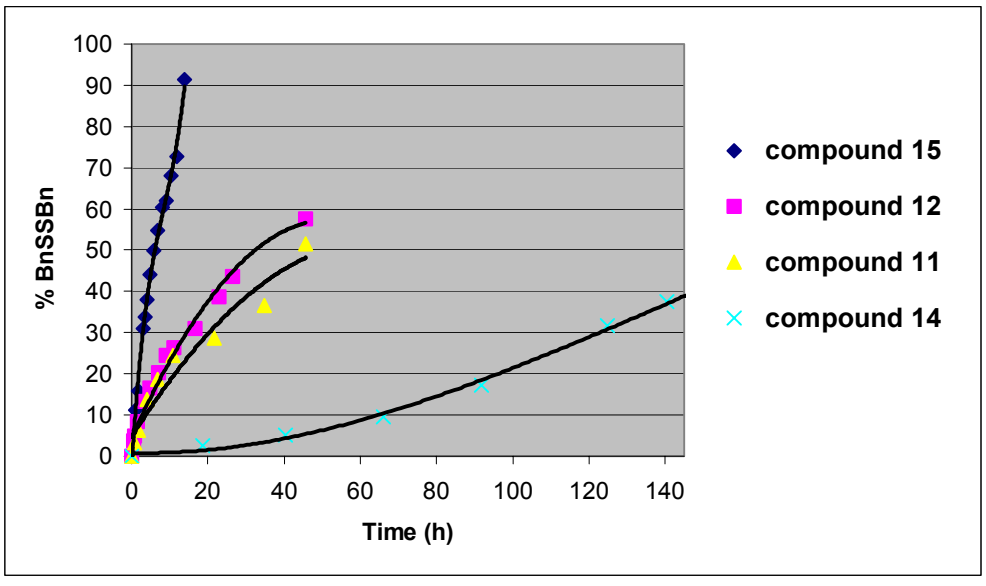


Figure 8. Rate of formation of BnSSBn from oxidation of BnSH (0.031 M) with 90% aqueous TBHP (0.043 M) in the presence of catalysts **16** (0.0031 M) in CH_2Cl_2-MeOH (95:5) at 18°C.

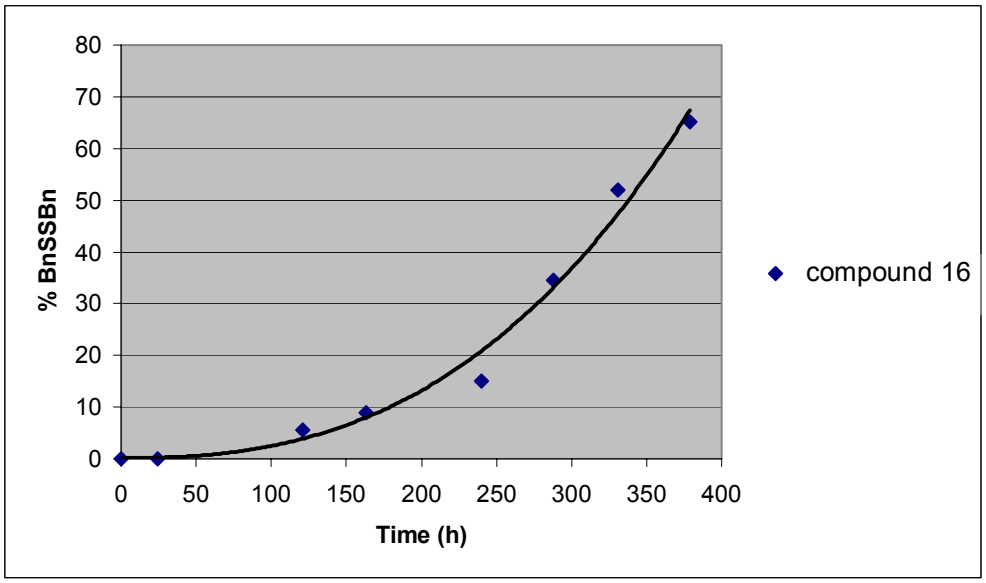


Figure 9. Rates of formation of BnSSBn from oxidation of BnSH (0.031 M) with 90% aqueous TBHP (0.043 M) in the presence of catalysts **17** and **20** (0.0031 M) in CH_2Cl_2-MeOH (95:5) at 18°C.

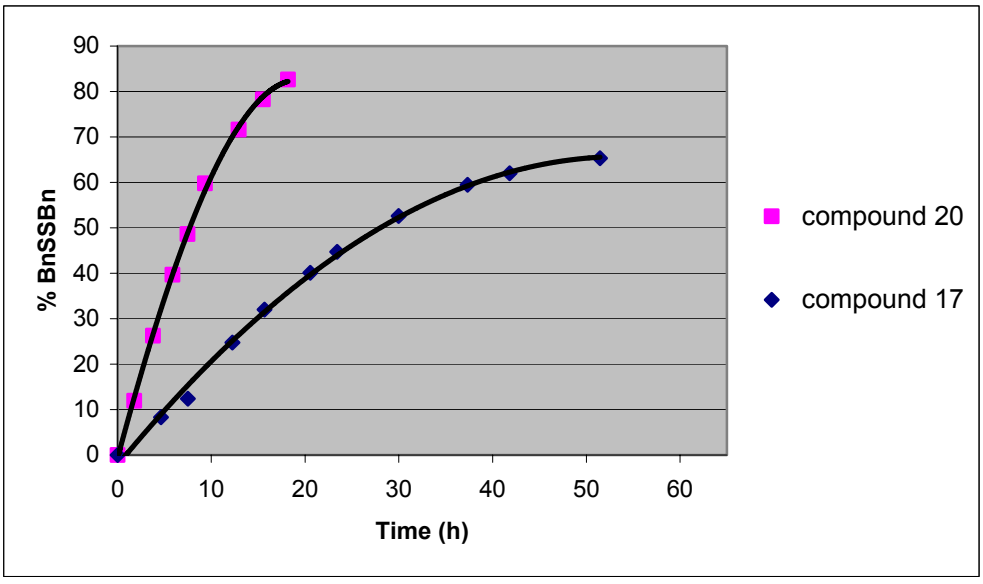


Figure 10. Rates of formation of BnSSBn from oxidation of BnSH (0.031 M) with 90% aqueous TBHP (0.043 M) in the presence of catalysts **18, 21** and **22** (0.0031 M) in CH_2Cl_2-MeOH (95:5) at 18°C.

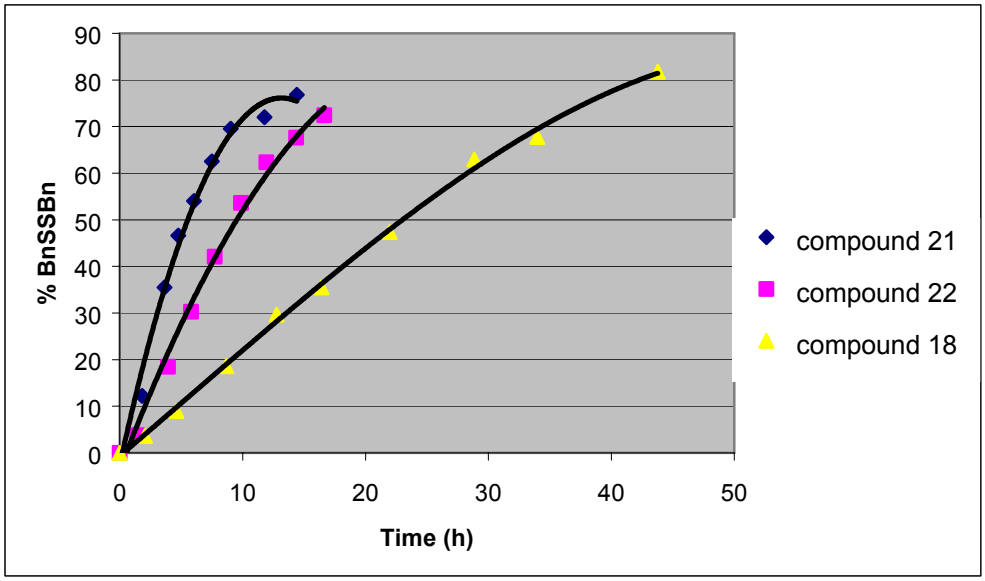


Figure 11. Rates of formation of BnSSBn from oxidation of BnSH (0.031 M) with 90% aqueous TBHP (0.043 M) in the presence of catalysts **19** and **23** (0.0031 M) in CH_2Cl_2-MeOH (95:5) at 18°C.

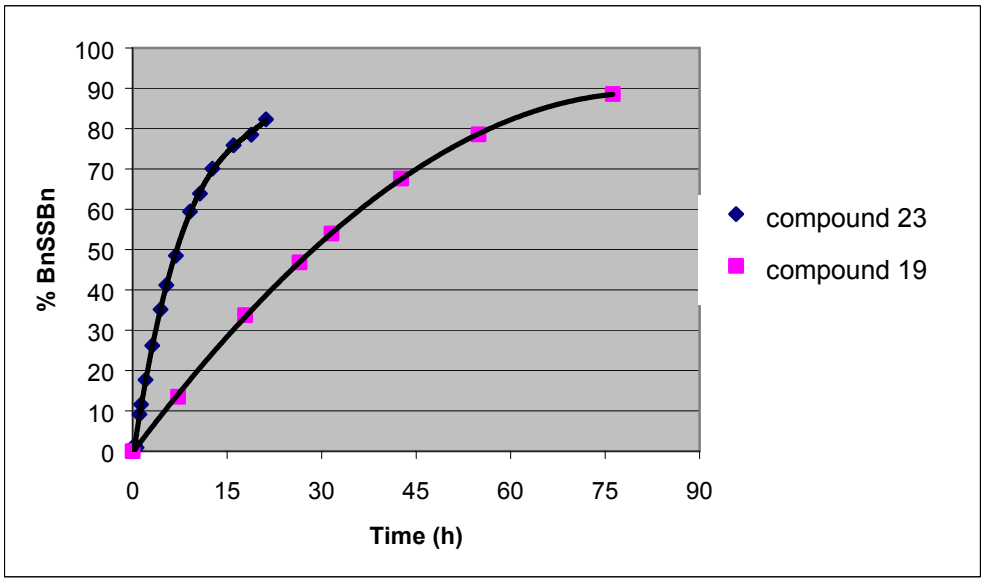


Figure 12. Rates of formation of BnSSBn from oxidation of BnSH (0.031 M) with 90% aqueous TBHP (0.043 M) in the presence of catalysts **24**, **25**, **26** and **34** (0.0031 M) in CH_2Cl_2-MeOH (95:5) at 18°C.

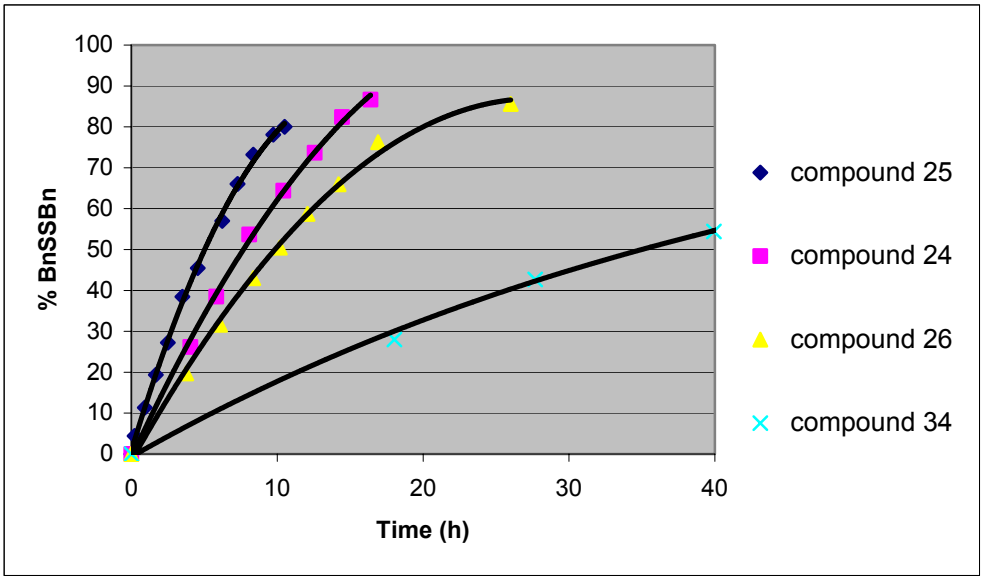


Figure 13. Rates of formation of BnSSBn from oxidation of BnSH (0.031 M) with 90% aqueous TBHP (0.043 M) in the presence of catalysts **1**, **2** and **31** (0.0031 M) in CH_2Cl_2-MeOH (95:5) at 18°C.

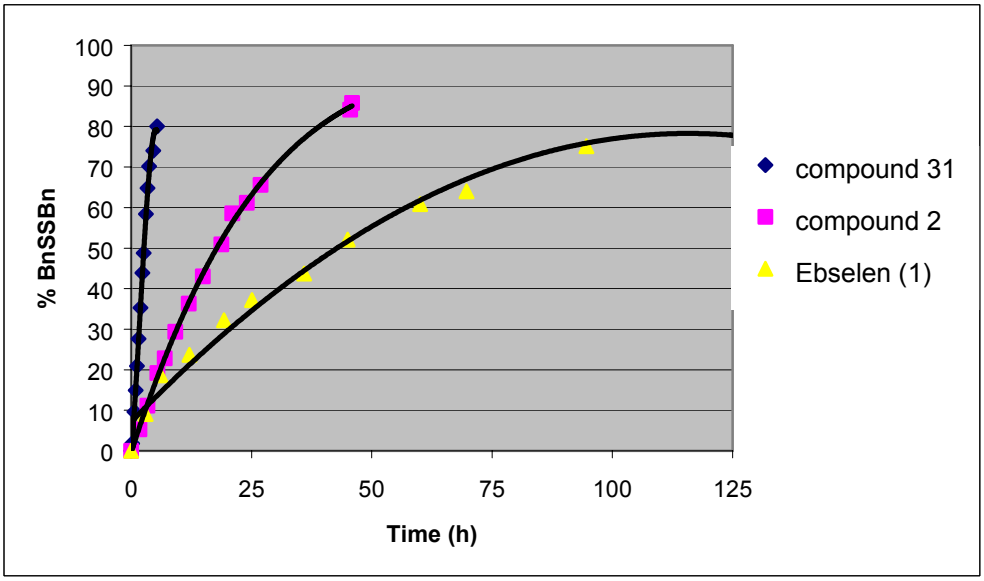
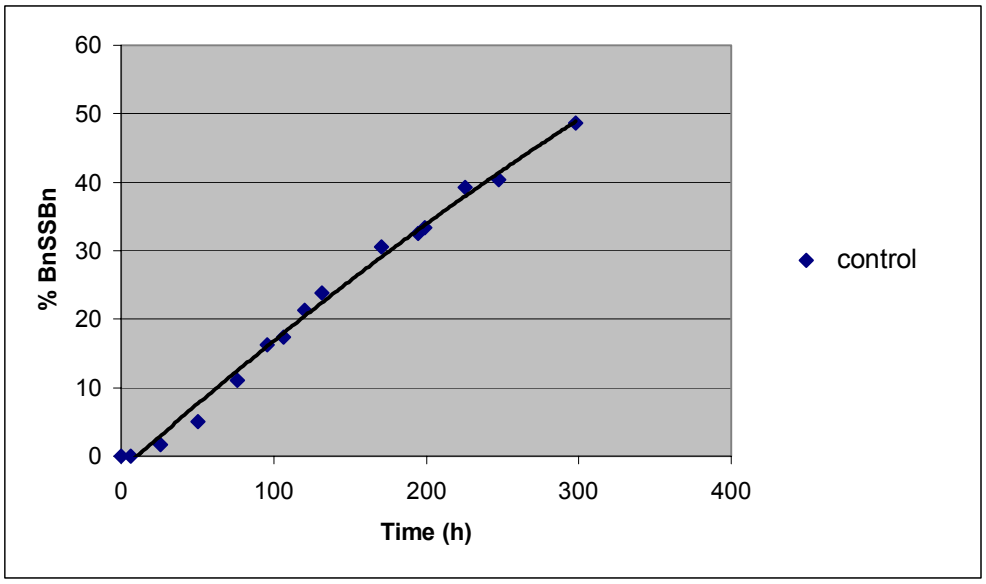


Figure 14. Rate of formation of BnSSBn from oxidation of BnSH (0.031 M) with 90% aqueous TBHP (0.043 M)in the absence of a catalyst in CH_2Cl_2-MeOH (95:5) at 18°C.



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