Diastereoselective Vinyl Addition to Chiral Hydrazones via Tandem Thiyl Radical Addition and Silicon-Tethered Cyclization

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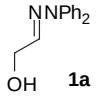
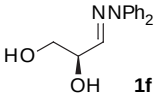
Supporting Information

Materials and Methods. Reactions employed oven- or flame-dried glassware under nitrogen unless otherwise noted. Tetrahydrofuran (THF) and toluene were distilled from sodium/benzophenone ketyl under argon. CH_2Cl_2 was distilled from CaH_2 under argon or nitrogen. Nitrogen was passed successively through columns of anhydrous $CaSO_4$ and R3-11 catalyst (Schweizer-Hall, South Plainfield, NJ) for removal of water and oxygen, respectively. All other materials were used as received from Aldrich or purified by standard procedures. Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates with UV indicator. Flash chromatography columns were packed with 230-400 mesh silica gel as a slurry in the initial elution solvent. Gradient flash chromatography was conducted by adsorption of product mixtures on silica gel, packing over a short pad of clean silica gel as a slurry in hexane, and eluting with a continuous gradient from hexane to the indicated solvent. Radial chromatography refers to centrifugally accelerated thin-layer chromatography performed using a Chromatotron (Harrison Research, Palo Alto, CA) with precast rotors supplied by Analtech (Newark, DE). Melting points were determined on a Meltemp apparatus and are uncorrected. Proton and carbon NMR data were obtained with a Bruker ARX 500 spectrometer. Infrared spectra were recorded with a Perkin-Elmer 2000 FT-IR spectrophotometer. Optical rotations were determined using a Rudolph Research Autopol IV polarimeter. Low resolution mass spectra were obtained with a Finnegan 4610 quadrupole spectrometer or a Hewlett Packard 5988 GCMS. Combustion analyses were performed by Atlantic Microlab (Norcross, GA) or Robertson Laboratories (Madison, NJ).



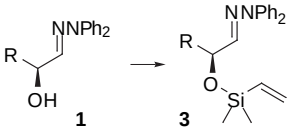
1a

Glycolaldehyde *N*,*N*-Diphenylhydrazone (1a). A solution of glycolaldehyde (dimeric form, 304 mg, 2.53 mmol) in toluene (ca. 50 mL) at room temperature was treated with *N*,*N*-diphenylhydrazine (931 mg, 5.06 mmol) and Na_2SO_4 (15 g). After 24 h, filtration, concentration, and flash chromatography (5:1 → 1:1 hexane/ethyl acetate) furnished **1a** (894 mg, 78% yield) as a colorless oil: IR (film) 3400 (br, s), 1591, 1496 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.40-7.37 (m, 4H), 7.16-7.10 (m, 2H), 7.11-7.09 (m, 4H), 6.63 (t, J = 3.3 Hz, 1H), 4.32 (d, J = 3.3 Hz, 2H), 2.7 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.6, 135.8, 129.7, 124.4, 122.3, 62.5; MS (CI) m/z (relative intensity) 227 ($[M+H]^+$, 100%), 168 (25%); Anal. Calcd for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.23; N, 12.38. Found: C, 74.50; H, 6.36; N, 12.27.

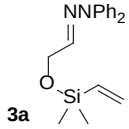


D-Glyceraldehyde *N*,*N*-Diphenylhydrazone (1f). A solution of D-glyceraldehyde (70% aqueous solution, 34 mg, 0.26 mmol) in toluene (ca. 7.60 mL) was treated with *N*,*N*-diphenylhydrazine hydrochloride (57 mg, 0.26 mmol) and Na_2SO_4 (2.4 g) at room temperature. After 2 d, filtration, concentration, and flash chromatography (10:1 hexane/ethyl acetate) afforded **1f** (29 mg, 43% yield) as a yellow oil: $[\alpha]_D^{28}$ -3.3° (*c* 3.23, $CHCl_3$); IR (film) 3391 (br, s), 1590, 1495, 1297, 1213, 1053, 749, 699 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.40-7.37 (m, 4H), 7.18-7.17 (m, 2H), 7.10-7.08 (m, 4H), 6.54 (d, *J* = 3.2 Hz, 1H), 4.40 (ddd, *J* = 5.5, 3.3, 3.3 Hz, 1H), 3.79 (dd, *J* = 11.4, 3.6 Hz, 1H), 3.65 (dd, *J* = 11.5, 5.6 Hz, 1H), 3.40 (br s, 1H), 2.50 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.3, 135.6, 129.8, 124.6, 122.2, 71.6, 65.0; MS (CI) *m*/*z* (relative intensity) 257 ($[M+H]^+$, 81%), 168 (100%); Anal. Calcd for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 70.22; H, 6.23; N, 10.74.

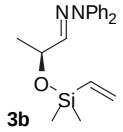
General Procedure A: Preparation of Dimethylvinylsilyl Ethers



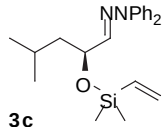
A solution of 1[1] in dry CH_2Cl_2 (ca. 1M) at 0 °C was treated sequentially with triethylamine (1.3 equiv) and chlorodimethylvinylsilane (**2**, 1.3 equiv). White precipitate formed immediately. After warming to room temperature over 5 h, the mixture was diluted with ether (ca. 4 mL/mmol triethylamine) and filtered through a short plug of silica gel (elution with ether). Flash chromatography (10:1 hexane/ethyl acetate) gave silyl ether **3** as colorless oil.



Dimethylvinylsilyl Ether 3a. From **1a** (300 mg, 1.32 mmol), **2** (0.23 mL, 1.71 mmol) and Et_3N (0.24 mL, 1.71 mmol) by General Procedure A was obtained **3a** (381 mg, 93% yield) as a colorless oil: IR (film) 3067, 2958, 1595, 1495, 1295, 1252, 1213, 838 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.39-7.36 (m, 4H), 7.14-7.11 (m, 2H), 7.11-7.09 (m, 4H), 6.51 (t, *J* = 5.1 Hz, 1H), 6.11 (dd, *J* = 20.0, 14.7 Hz, 1H), 6.03 (dd, *J* = 14.7, 4.1 Hz, 1H), 5.79 (dd, *J* = 20.0, 4.1 Hz, 1H), 4.34 (d, *J* = 5.1 Hz, 2H), 0.19 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.6, 137.1, 136.4, 133.4, 129.6, 124.2, 122.3, 63.5, -2.0; MS (CI) *m*/*z* (relative intensity) 311 ($[M+H]^+$, 100%), 168 (50%); Anal. Calcd for $C_{18}H_{22}SiN_2O$: C, 69.64; H, 7.14 N, 9.02. Found: C, 69.92; H, 7.26; N, 8.91.

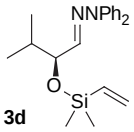


Dimethylvinylsilyl Ether 3b. From **1b** (718 mg, 3.00 mmol), **2** (0.53 mL, 3.90 mmol) and Et_3N (0.54 mL, 3.90 mmol) by General Procedure A was obtained **3b** (813 mg, 83% yield) as a colorless oil: $[\alpha]_D^{29}$ -21.8° (*c* 1.85, $CHCl_3$); IR (film) 3050, 2969, 1591, 1496, 1085, 1007, 835, 700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.48-7.45 (m, 4H), 7.24-7.21 (m, 6H), 6.55 (d, *J* = 5.9 Hz, 1H), 6.26 (dd, *J* = 20.3, 14.8 Hz, 1H), 6.11 (dd, *J* = 14.8, 3.8 Hz, 1H), 5.90 (dd, *J* = 20.3, 3.8 Hz, 1H), 4.72-4.69 (m, 1H) 1.45 (d, *J* = 6.3 Hz, 3H), 0.35 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.9, 140.9, 137.9, 133.1, 129.7, 124.3, 122.4, 69.5, 22.6, -1.1, -1.2; MS (CI) *m*/*z* (relative intensity) 325 ($[M+H]^+$, 100%), 168 (M, 20%); Anal. Calcd for $C_{19}H_{24}SiN_2O$: C, 70.33; H, 7.45; N, 8.63. Found: C, 70.37; H, 7.48; N, 8.49.



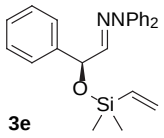
Dimethylvinylsilyl Ether 3c. From **1c** (750 mg, 2.65 mmol), **2** (0.47 mg, 3.44 mmol) and Et_3N (0.48 mL, 3.44 mmol) by General Procedure A was obtained **3c** (810 mg, 83% yield) as a colorless oil: $[\alpha]_D^{29}$ -13.2° (*c* 1.41, $CHCl_3$); IR (film) 3050, 2869, 2956, 1595, 1496, 1300, 1213, 1054, 956 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.40-7.37 (m, 4H), 7.17-7.14 (m, 2H), 7.11-7.09 (m, 4H), 6.35 (d, *J* = 6.5 Hz, 1H), 6.15 (dd, *J* = 20.2, 14.7 Hz, 1H), 6.03 (dd, *J* = 14.7, 3.7 Hz, 1H), 5.79 (dd, *J* = 20.2, 3.7 Hz, 1H) 4.49 (ddd, *J* = 8.1, 6.2, 6.2 Hz, 1H), 1.75-1.67 (m, 1H), 1.55 (ddd, *J* = 13.8, 8.1, 6.1 Hz, 1H), 1.38 (ddd, *J* = 13.5, 7.6, 5.9 Hz, 1H), 0.96 (d, *J* = 6.6 Hz, 3H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.21 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.9, 140.7, 137.9, 133.0, 129.7, 124.2, 122.4, 71.9, 45.3, 24.2, 23.1, 22.4, -1.1; MS (CI) *m*/*z*

(relative intensity) 367 ([M+H]$^+$, 100%), 168 (M, 20%); Anal. Calcd for $C_{22}H_{30}SiN_2O$: C, 72.08; H, 8.25; N, 7.64; O. Found: C, 72.35; H, 8.33; N, 7.48.



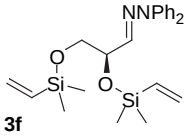
3d

Dimethylvinylsilyl Ether 3d. From **1d** (140 mg, 0.522 mmol), **2** (0.09 mL, 0.68 mmol) and Et_3N (0.09 mL, 0.68 mmol) by General Procedure A was obtained **3d** (170 mg, 92% yield) as a colorless oil: $[\alpha]_D^{29}$ +15.0° (*c* 1.38, $CHCl_3$); IR (film) 3050, 2958, 1594, 1496, 1298, 1251, 1213, 1047, 957 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.37 (m, 4H), 7.15-7.14 (m, 2H), 7.11-7.09 (m, 4H), 6.35 (d, *J* = 6.9 Hz, 1H), 6.15 (dd, *J* = 20.3, 13.8 Hz, 1H), 6.00 (dd, *J* = 13.8, 2.8 Hz, 1H), 5.80 (dd, *J* = 20.3, 2.8 Hz, 1H), 4.05-4.10 (m, 1H), 1.75-1.70 (m, 1H), 0.93 (d, *J* = 6.7 Hz, 3H), 0.84 (d, *J* = 6.7 Hz, 3H), 0.19 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.0, 140.2, 138.1, 132.9, 129.8, 124.2, 122.4, 78.6, 33.8, 18.4, -1.1, -1.2; MS (CI) *m*/*z* (relative intensity) 353 ([M+H]$^+$, 100%), 168 (11%); Anal. Calcd for $C_{21}H_{28}SiN_2O$: C, 71.54; H, 8.00; N, 7.96. Found: C, 71.67; H, 8.05; N, 8.05.



3e

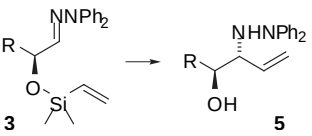
Dimethylvinylsilyl Ether 3e. From **1e** (520 mg, 1.72 mmol), **2** (0.31 mL, 2.23 mmol) and Et_3N (0.31 mL, 2.23 mmol) by General Procedure A was obtained **3e** (500 mg, 75% yield) as a colorless oil: $[\alpha]_D^{29}$ -74.4° (*c* 1.17, $CHCl_3$); IR (film) 3060, 2959, 1592, 1495, 1298, 1252, 1214, 1054, 958 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31-7.24 (m, 8H), 7.20-7.10 (m, 1H), 7.05-7.02 (m, 6H), 6.42 (d, *J* = 6.7 Hz, 1H), 6.15 (dd, *J* = 20.3, 14.9 Hz, 1H), 6.10 (dd, *J* = 14.9, 3.9 Hz, 1H), 5.75 (dd, *J* = 20.3, 3.9 Hz, 1H), 5.50 (d, *J* = 6.7 Hz, 1H), 0.20 (s, 3H), 0.18 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.8, 142.0, 139.6, 137.6, 133.4, 129.8, 128.3, 127.3, 126.0, 124.4, 122.4, 75.3, -1.1, -1.2; MS (CI) *m*/*z* (relative intensity) 387 ([M+H]$^+$, 52%), 168 (15%); Anal. Calcd for $C_{24}H_{26}SiN_2O$: C, 74.57; H, 6.78; N, 7.25. Found: C, 74.86; H, 6.85; N, 7.29.



3f

Bis(dimethylvinylsilyl) Ether 3f. A solution of 1**f** (29 mg, 0.11 mmol) in dry CH_2Cl_2 (ca. 1.10 mL) at 0 °C under nitrogen was treated sequentially with triethylamine (0.040 mL, 0.29 mmol) and chlorodimethylvinylsilane (0.048 mL, 0.29 mmol). White precipitate formed immediately. After warming to room temperature over 5 h, the mixture was diluted with ether (ca. 4 mL/mmol triethylamine) and filtered through a short plug of silica gel (elution with ether). Flash chromatography (10:1 hexane/ethyl acetate) gave **3f** (33 mg, 70% yield) as a colorless oil: $[\alpha]_D^{29}$ +31.7° (*c* 1.28, $CHCl_3$); IR (film) 3050, 2958, 1592, 1496, 1407, 1214, 1084, 838, 700 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42-7.39 (m, 4H), 7.17-7.12 (m, 6H), 6.42 (d, *J* = 6.2 Hz, 1H), 6.21-6.10 (m, 2H), 6.13-6.00 (m, 2H), 5.81-5.77 (m, 2H), 4.53-4.45 (m, 1H), 3.70 (d, *J* = 5.5 Hz, 2H), 0.24 (s, 3H), 0.23 (s, 3H), 0.20 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.6, 137.9, 137.7, 137.3, 133.1, 133.0, 129.6, 124.1, 122.3, 74.0, 66.0, -1.3, -1.4, -2.0, -2.1; MS (CI) *m*/*z* (relative intensity) 425 ([M+H]$^+$, 100%), 409 (54%); Anal. Calcd for $C_{23}H_{32}N_2O_2Si_2$: C, 65.05; H, 7.59; N, 6.59. Found: C, 65.29; H, 7.78; N, 6.44.

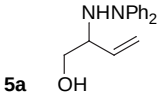
General Procedure B: Tandem Thiyl Radical Addition, Cyclization, and Elimination



3 5

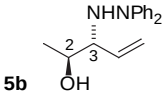
A solution of silyl ether and thiophenol (1.2 equiv) in cyclohexane (ca. 0.1M) was deoxygenated (nitrogen via needle) for ca. 10 min. 2,2'-Azobis(isobutyronitrile) (AIBN, 10 mol %) was added, and the mixture was deoxygenated for 5 min, then heated at reflux for 2-3 h. If TLC indicated incomplete reaction at this point, additional AIBN was added and heating continued for another 15 h. After concentration of the reaction mixture, a solution of the residual oil in tetrahydrofuran (ca. 0.15 M) was treated at room temperature with a saturated KF/MeOH solution (14 mL/mmol silyl ether). After 20 h the solution was diluted with hexane, washed with water, dried (Na_2SO_4), and concentrated. Diastereomer ratios were determined by integration of ^{1}H NMR spectra prior to flash chromatography (10:1 → 5:1 hexane/ ethyl acetate), which afforded the hydrazino alcohol as a mixture of diastereomers.

The pure *anti*-diastereomers of **5b**–**5d** were obtained by chromatographic separation of their 2,2-dimethyloxazolidine (acetonide) derivatives followed by hydrolysis. Only in the case of **5b** could both diastereomers be obtained in pure form. We previously showed via Mosher ester analysis that a closely related sequence maintains the enantiomeric purity originating in an α-hydroxy acid except for the isolated case of mandelic acid where a phenyl group can facilitate racemization (e.g., **6e**).[1]



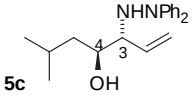
5a

***N*-Diphenylaminovinylglycinol (5a).** From **3a** (77 mg, 0.25 mmol), thiophenol (0.03 mL, 0.30 mmol) and AIBN (4 mg, 0.025 mmol) by General Procedure B was obtained racemic **5a** (34 mg, 54% yield) as a pale yellow oil: IR (film) 3391 (br, s), 3062, 2930, 2873, 1588, 1496, 1272, 1028, 749, 694 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.31-7.28 (m, 4H), 7.17-7.15 (m, 4H), 7.02-7.01 (m, 2H), 5.90 (ddd, *J* = 17.7, 10.5, 7.5 Hz, 1H), 5.30-5.15 (m, 2H), 4.22 (s, 1H), 3.80-3.71 (m, 1H), 3.70-3.58 (m, 2H), 1.95 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.0, 135.7, 129.1, 122.5, 120.4, 118.8, 63.9, 61.9; MS (CI) *m*/*z* (relative intensity) 255 ($[M+H]^+$, 42%), 165 (100%), 183 (27%); Anal. Calcd for $C_{16}H_{18}N_2O$: C, 75.56; H, 7.13; N, 11.01. Found: C, 75.31; H, 7.14; N, 10.78.



5b

(2*S*,3*R*)-3-(*N*,*N*-diphenylhydrazino)-4-penten-2-ol (5b). From **3b** (94 mg, 0.29 mmol), thiophenol (0.03 mL, 0.35 mmol) and AIBN (4 mg, 0.029 mmol) by General Procedure B was obtained **5b** as a mixture of diastereomers (60 mg, 77% yield, *anti*/*syn* = 90:10) as a pale yellow oil. For characterization, both pure diastereomers were obtained via acetonide **6b**. Major diastereomer (*anti*-**5b**): $[\alpha]_D^{31}$ +48.5° (*c* 1.98, $CHCl_3$); IR (film) 3435 (br, s), 2977, 1588, 1495, 1271, 1076, 923 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.33-7.30 (m, 4H), 7.15-7.13 (m, 4H), 7.04-7.01 (m, 2H), 5.93 (ddd, *J* = 17.3, 10.4, 8.4 Hz, 1H), 5.33 (dd, *J* = 10.4, 1.8 Hz, 1H), 5.26 (dd, *J* = 17.3, 1.8 Hz, 1H), 4.10 (dddd, *J* = 6.5, 6.5, 6.5, 2.7 Hz, 1H), 4.20-3.50 (br s, 1H), 3.43 (dd, *J* = 8.4, 2.7 Hz, 1H), 2.55 (br s, 1H), 1.18 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.1, 133.5, 129.2, 122.6, 120.4, 120.3, 66.53, 66.48, 18.1. Minor diastereomer (*syn*-**5b**): IR (film) 3401 (br, s), 1588, 1496, 1272, 1073, 924 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.30-7.26 (m, 4H), 7.16-7.15 (m, 4H), 7.11-6.95 (m, 2H), 5.73 (ddd, *J* = 17.2, 10.3, 8.7 Hz, 1H), 5.18 (dd, *J* = 10.3, 1.4 Hz, 1H), 5.15 (dd *J* = 17.2, 1.4 Hz, 1H), 4.50 (br s, 1H), 3.90-3.86 (m, 1H), 1H), 3.35 (dd, *J* = 7.9, 7.9 Hz, 1H), 2.10 (br s, 1H), 1.18 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.0, 135.9, 129.0, 122.4, 120.6, 119.5, 69.5, 67.2, 20.4. Diastereomeric mixture: MS (CI) *m*/*z* (relative intensity) 269 ($[M+H]^+$, 100%), 168 (98%), 183 (36%); Anal. Calcd for $C_{17}H_{20}N_2O$: C, 76.09; H, 7.51; N, 10.44. Found: C, 76.27; H, 7.67; N, 10.18.



5c

(3*R*,4*S*)-3-(*N*,*N*-diphenylhydrazino)-6-methyl-1-hepten-4-ol (5c). From **3c** (400 mg, 1.09 mmol) thiophenol (0.13 mL, 1.31 mmol) and AIBN (17 mg, 0.11 mmol) by General Procedure B was obtained **5c** as a mixture of diastereomers (226 mg, 67% yield, *anti*/*syn* = 94:6) as a pale yellow oil. For characterization, the pure major diastereomer was obtained via acetonide **6c**. Major diastereomer (*anti*-**5c**): $[\alpha]_D^{27}$ +26.3° (*c* 0.58, $CHCl_3$); IR (film) 3447 (br, s), 3063, 2955, 1589, 1495, 1272, 1074, 924, 749, 695 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.32-7.29 (m, 4H), 7.13-7.11 (m, 4H), 7.03-7.00 (m, 2H), 5.87 (ddd, *J* = 19.1, 10.4, 8.6 Hz, 1H), 5.30 (dd, *J* = 10.4, 1.7 Hz, 1H), 5.22 (dd, *J* = 19.1, 1.8 Hz, 1H), 4.04 (s, 1H), 4.01-3.96 (m, 1H), 3.40 (dd, *J* = 8.5, 2.3 Hz, 1H), 2.42 (dd, *J* = 2.1, 1.1 Hz, 1H), 1.79-1.71 (m, 1H), 1.44 (ddd, *J* = 13.9, 9.3, 5.5 Hz, 1H), 1.11-1.05 (m, 1H), 0.90 (d, *J* = 6.6 Hz, 1H), 0.87 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.1, 133.5, 129.2, 122.6, 120.3, 120.1, 68.2, 65.8, 41.6, 24.6, 23.4, 22.0; MS (CI) *m*/*z* (relative intensity) 311 ($[M+H]^+$, 98%), 168 (M, 100%), 183 (33%). Diastereomeric mixture: Anal. calcd for $C_{20}H_{26}N_2O$: C, 77.38; H, 8.44; N, 9.02. Found: C, 77.44; H, 8.41; N, 8.92.

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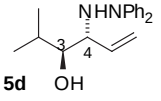
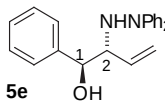


5d

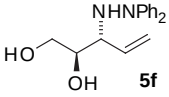
(3*S*,4*R*)-4-(*N*,*N*-diphenylhydrazino)-2-methyl-5-hexen-3-ol (5d). From **3d** (5.00 g, 14.17 mmol), thiophenol (1.74 mL, 17.00 mmol) and AIBN (232 mg, 1.42 mmol) by General Procedure B was obtained *anti*-**5d** as a single diastereomer after crystallization from hexane (3.77 g, 89% yield). In a smaller scale experiment, the crude product had a diastereomer

ratio of 98:2 (*anti*/*syn*). Major diastereomer (*anti*-**5d**): mp 94-96 °C; $[\alpha]_D^{29}$ +64.6° (*c* 1.51, $CHCl_3$); IR (film) 3554 (br, s), 2962, 2872, 1588, 1497, 1274, 991, 930, 753, 695 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.33-7.30 (m, 4H), 7.13-7.11 (m, 4H), 7.01-7.04 (m, 2H), 5.95 (ddd, *J* = 19.1, 10.4, 8.7 Hz, 1H), 5.32 (dd, *J* = 10.4, 1.5 Hz, 1H), 5.27 (dd, *J* = 19.0, 1.4 Hz, 1H), 3.93 (br s, 1H), 3.61 (dd, *J* = 8.7, 2.3 Hz, 1H), 3.50 (dd, *J* = 9.1, 1.7 Hz, 1H), 2.70 (s, 1H), 1.65 (dddd, *J* = 9.1, 6.6, 6.6, 6.6 Hz, 1H), 1.02 (d, *J* = 6.6 Hz, 3H), 0.79 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.1, 133.2, 129.2, 122.7, 120.5, 120.0, 75.2, 63.2, 30.1, 19.7, 18.3; MS (CI) *m*/*z* (relative intensity) 297 ($[M+H]^+$, 90%), 168 (100%), 183 (30%); Anal. Calcd for $C_{19}H_{24}N_2O$: C, 76.99; H, 8.16; N, 9.45. Found: C, 77.09; H, 8.20; N, 9.45.



5e

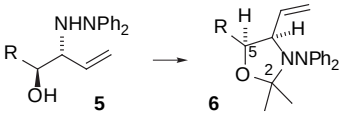
(1*S*,2*R*)-2-(*N*,*N*-diphenylhydrazino)-1-phenyl-3-buten-1-ol (5e). From **3e** (75 mg, 0.19 mmol) thiophenol (0.02 mL, 0.23 mmol) and AIBN (3 mg, 0.019 mmol) by General Procedure B was obtained **5e** as mixture of diastereomers (31 mg, 49% yield, *anti*/*syn* = >98:2) as pale yellow oil: IR (film) 3447 (br, s), 3061, 2924, 1588, 1496, 1272, 1028, 925, 749, 695 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.30-7.26 (m, 11H), 7.09-7.07 (m, 2H), 6.95-7.05 (m, 2H), 5.86 (ddd, *J* = 18.4, 10.4, 8.1 Hz, 1H), 5.23 (d, *J* = 10.4 Hz, 1H), 5.10 (d, *J* = 17.3 Hz, 1H), 4.93 (d, *J* = 4.5 Hz, 1H), 4.08 (s, 1H), 3.63 (dd, *J* = 8.1, 4.6 Hz, 1H), 2.67 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.7, 140.2, 134.0, 129.1, 128.1, 127.5, 126.4, 122.6, 120.3, 120.3, 72.7, 66.8; MS (CI) *m*/*z* (relative intensity) 331 ($[M+H]^+$, 46%), 170 (100%), 168 (60%); Anal. Calcd for $C_{22}H_{22}N_2O$: C, 79.97; H, 6.71; N, 8.48. Found: C, 80.45; H, 6.72; N, 8.76.



5f

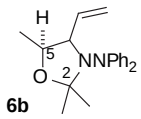
Hydrazino Diol (5f). From **3e** (75 mg, 0.19 mmol) thiophenol (0.02 mL, 0.23 mmol) and AIBN (3 mg, 0.019 mmol) by General Procedure B was obtained **5f** after flash chromatography (10:1 → 1:1 hexane/ ethyl acetate) as a mixture of diastereomers (16 mg, 64% yield, *anti*/*syn* = 91:9) as a colorless oil: IR (film) 3399 (br, s), 1588, 1494, 1271, 1072, 748, 694 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.31-7.28 (m, 4H), 7.13-7.11 (m, 4H), 7.03-7.00 (m, 2H), 5.90 (ddd, *J* = 18.8, 10.4, 8.4 Hz, 1H), 5.28 (d, *J* = 10.4 Hz, 1H), 5.22 (d, *J* = 18.2 Hz, 1H), 3.98-3.95 (m, 1H), 3.70 (dd, *J* = 11.5, 7.2 Hz, 1H), 3.63-3.60 (m, 2H), 2.70 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.8, 133.8, 129.2, 122.8, 120.4, 120.1, 71.8, 63.8, 63.2; MS (CI) *m*/*z* (relative intensity) 285 ($[M+H]^+$, 77%), 168(100%); Anal. Calcd for $C_{17}H_{20}N_2O_2$: C, 71.81; H, 7.09; N, 9.85. Found: C, 71.32; H, 7.16; N, 9.41.

General Procedure C: Preparation of 2,2-Dimethyloxazolidines (Acetonides)



5 **6**

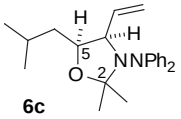
A solution of **5** in $CHCl_3$ (ca. 0.2M) was treated with 2,2-dimethoxypropane (ca. 1 mL/mmol **5**) and pyridinium *p*-toluenesulfonate (1 equiv). After 1 d at room temperature, the reaction mixture was partitioned between $CHCl_3$ and saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated. Radial chromatography (10:1 hexane/ethyl acetate) furnished the major diastereomer *cis*-**6**. Only from **5b** was the minor diastereomer *trans*-**6b** obtained in pure form.



6b

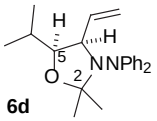
5-Methyl oxazolidine 6b. From **5b** (89 mg, 0.33 mmol), 2,2-dimethoxypropane (0.33 mL, 2.68 mmol), and pyridinium *p*-toluenesulfonate (83 mg, 0.33 mmol) by General Procedure C was obtained acetonide as a mixture of diastereomers (82 mg, 81% yield) as a colorless oil. Major diastereomer (*cis*-**6b**): $[\alpha]_D^{28}$ -19.5° (*c* 0.38, ether); IR (film) 2978, 1589, 1491, 1376, 1260, 1178, 1070, 925, 747 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.30-7.20 (m, 4H), 7.15-7.10 (m, 4H), 7.05-6.90 (m, 2H), 5.98 (ddd, *J* = 19.5, 10.5, 9.0 Hz, 1H), 5.21 (d, *J* = 19.0 Hz, 1H), 5.19 (d, *J* = 10.5 Hz, 1H), 4.25 (ddd, 7.7, 6.5, 6.5, 6.5), 1H), 4.08 (dd, *J* = 8.8, 7.9 Hz, 1H), 1.47 (s, 3H), 1.27 (d, *J* = 6.5 Hz, 3H), 1.05 (s, 3H) ; ^{13}C NMR (125 MHz, C_6D_6) δ 136.9, 128.8, 118.4, 94.1, 72.8, 63.6, 27.7, 23.3, 18.3; MS (CI) *m*/*z* (relative intensity) 309 ($[M+H]^+$, 47%), 170 (100%). Minor diastereomer (*trans*-**6b**): $[\alpha]_D^{25}$ +27.6° (*c* 0.51 ether); IR (film) 2979, 1589, 1491, 1376,

1260, 1070, 856, 747, 695 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.25-7.20 (m, 4H), 7.20-7.15 (m, 4H), 6.90-7.00 (m, 2H), 5.90 (ddd, *J* = 18.4, 10.0, 8.4 Hz, 1H), 5.14 (d, *J* = 10.0 Hz, 1H), 5.06 (d, *J* = 18.1 Hz, 1H), 3.99 (dddd, *J* = 8.3, 6.1, 6.1, 6.1 Hz, 1H), 3.59 (dd, *J* = 8.3, 8.3 Hz, 1H), 1.40 (s, 3H), 1.33 (s, 3H), 1.30 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 138.5, 128.7, 118.0, 96.6, 74.7, 67.5, 28.2, 24.2, 17.2; MS (CI) *m*/*z* (relative intensity) 309 ($[M+H]^+$, 73%), 168 (100%). Diastereomeric mixture: Anal. Calcd for $C_{20}H_{24}N_2O$: C, 77.89; H, 7.84; N, 9.08. Found: C, 77.95; H, 8.06; N, 8.81.



6c

5-Isobutyl oxazolidine 6c. From **5c** (98 mg, 0.31 mmol), 2,2-dimethoxypropane (0.31 mL, 2.52 mmol), and pyridinium *p*-toluenesulfonate (78 mg, 0.31 mmol) by General Procedure C was obtained **6c** as a mixture of diastereomers (73 mg, 67% yield) as a colorless oil. Major diastereomer (*cis*-**6c**): $[\alpha]_D^{28}$ -23.07° (*c* 0.88, ether); IR (film) 2955, 1589, 1491, 1376, 1259, 1176, 1028, 746 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.24-7.22 (m, 4H), 7.13-7.11 (m, 4H), 6.88-6.80 (m, 2H), 6.00 (ddd, *J* = 19.5, 10.4, 9.2 Hz, 1H), 4.93 (d, *J* = 19.1 Hz, 1H), 4.91 (d, *J* = 10.0 Hz, 1H), 4.11 (ddd, *J* = 10.9, 7.9, 3.3 Hz, 1H), 4.00 (dd, *J* = 8.9, 8.0 Hz, 1H), 2.05-1.95 (m, 1H), 1.78 (ddd, *J* = 13.5, 10.5, 4.9 Hz, 1H), 1.52 (s, 3H), 1.25 (ddd, *J* = 13.5, 8.8, 3.3 Hz, 1H), 1.10 (s, 3H), 0.98 (d, *J* = 6.7 Hz, 3H), 0.90 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 137.3, 128.9, 118.3, 94.2, 74.9, 63.7, 41.4, 27.9, 24.8, 23.7, 23.4, 21.5; MS (CI) *m*/*z* (relative intensity) 351 ($[M+H]^+$, 80%), 170 (100%). Diastereomeric mixture: Anal. Calcd for $C_{23}H_{30}N_2O$: C, 78.82; H, 8.63; N, 7.99. Found: C, 78.81; H, 8.68; N, 7.98.

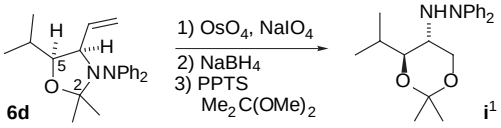


6d

5-Isopropyl oxazolidine 6d. From **5d** (100 mg, 0.33 mmol), 2,2-dimethoxypropane (0.33 mL, 2.68 mmol), and pyridinium *p*-toluenesulfonate (83 mg, 0.33 mmol) by General Procedure C was obtained *cis*-**6d** (92 mg, 82% yield) after recrystallization from hexane as a colorless solid: mp 97-99 °C; $[\alpha]_D^{29}$ +52.8°, (*c* 0.69, $CHCl_3$); IR (film) 2980, 1589, 1491, 1258, 1176, 1029, 746 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.28-7.26 (m, 4H), 7.26-7.25 (m, 4H), 7.18-7.16 (m, 2H), 6.11 (ddd, *J* = 17.3, 10.0, 10.0 Hz, 1H), 5.20 (d, *J* = 10.0 Hz, 1H), 5.15 (d, *J* = 17.3 Hz, 1H), 4.05 (dd, *J* = 8.8, 7.9 Hz, 1H), 3.77 (dd, *J* = 7.8, 7.8 Hz, 1H), 1.94-1.86 (m, 1H), 1.42 (s, 3H), 1.23 (s, 3H), 1.11 (d, *J* = 6.6 Hz, 3H), 0.92 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CHCl_3$) δ 137.0, 128.7, 118.6, 94.3, 82.0, 62.7, 28.7, 28.1, 23.3, 19.7, 19.0; MS (CI) *m*/*z* (relative intensity) 337($[M+H]^+$, 100%), 168 (33%); Anal. Calcd for $C_{22}H_{28}N_2O$: C, 78.53; H, 8.39; N, 8.33. Found: C, 78.95; H, 8.51; N, 8.12.

Configurational Assignments

Oxazolidine **6d** was converted by Lemieux-Johnson oxidation, reduction and acetonide equilibration to known *anti*-2-hydrazino-1,3-diol acetonide **i**.[1] Configurations of the other products **5** and **6** were assigned by analogy to **5d** and **6d**, in accord with related reactions[1] and with generally accepted predictive models for 5-hexenyl cyclizations based on theoretical analyses and extensive experimental results.[2]



6d **i**[1]

A solution of diastereomerically pure **6d** (186.6 mg, 0.56 mmol) in dioxane/water (3:1, 18 mL) and OsO_4 (84 mg, 0.33 mmol) was stirred at room temperature for 1 h, and sodium periodate (230.0 mg, 1.12 mmol) was added. After 1 d the solution was diluted with ethyl acetate, washed with water, then brine, dried (Na_2SO_4), and concentrated. A solution of the crude aldehyde in MeOH (2.03 mL) was treated with $NaBH_4$ (53.4 mg, 1.40 mmol) at 0 °C. After 12 h the solution was diluted with ether, washed with water, dried (Na_2SO_4) and concentrated. Flash chromatography (10:1 hexane/ethyl acetate) furnished an oxazolidine (acetonide) derivative of the 2-hydrazino-1,3-diol (20 mg, 10% yield) as a colorless oil; $[\alpha]_D^{26}$ +20.4° (*c* 0.51, ether); IR (film) 3481, 2960, 1588, 1490, 1270, 1029, 747 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.30-7.29 (m, 4H), 7.10-7.06 (m, 4H), 6.81-6.79 (m, 2H), 4.00 (d, *J* = 9.0 Hz, 2H), 3.72 (ddd, *J* = 8.3, 8.3, 5.4 Hz, 1H), 3.50 (dd, *J* = 9.3, 5.4 Hz, 1H), 1.72-1.69 (m, 1H), 1.61 (d, *J* = 3.9 Hz, 1H), 1.37 (s, 6H), 0.73 (d, *J* = 6.8 Hz,

3H), 0.67 (d, J = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 128.9, 97.8, 76.6, 64.0, 59.1, 30.5, 27.4, 23.4, 19.1, 16.9; MS (CI) m/z (relative intensity) 341 ($[M+H]^+$, 60%), 170 (100%); Anal. Calcd for $C_{21}H_{28}N_2O_2$: C, 74.08; H, 8.29; N, 8.23. Found: C, 73.90; H, 8.42; N, 8.27.

A solution of the oxazolidine (10 mg, 0.03 mmol) obtained above, 2,2-dimethoxypropane (0.035 mL, 0.28 mmol), and pyridinium *p*-toluenesulfonate (7.3 mg, 0.029 mmol) in $CHCl_3$ (0.15 mL) was stirred for 1 d at room temperature, then partitioned between $CHCl_3$ and saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated. Flash chromatography with 10:1 hexane/ethyl acetate furnished **i** (7.2 mg, 70% yield) as a colorless oil, identical to a fully characterized sample prepared by a different method.[1]

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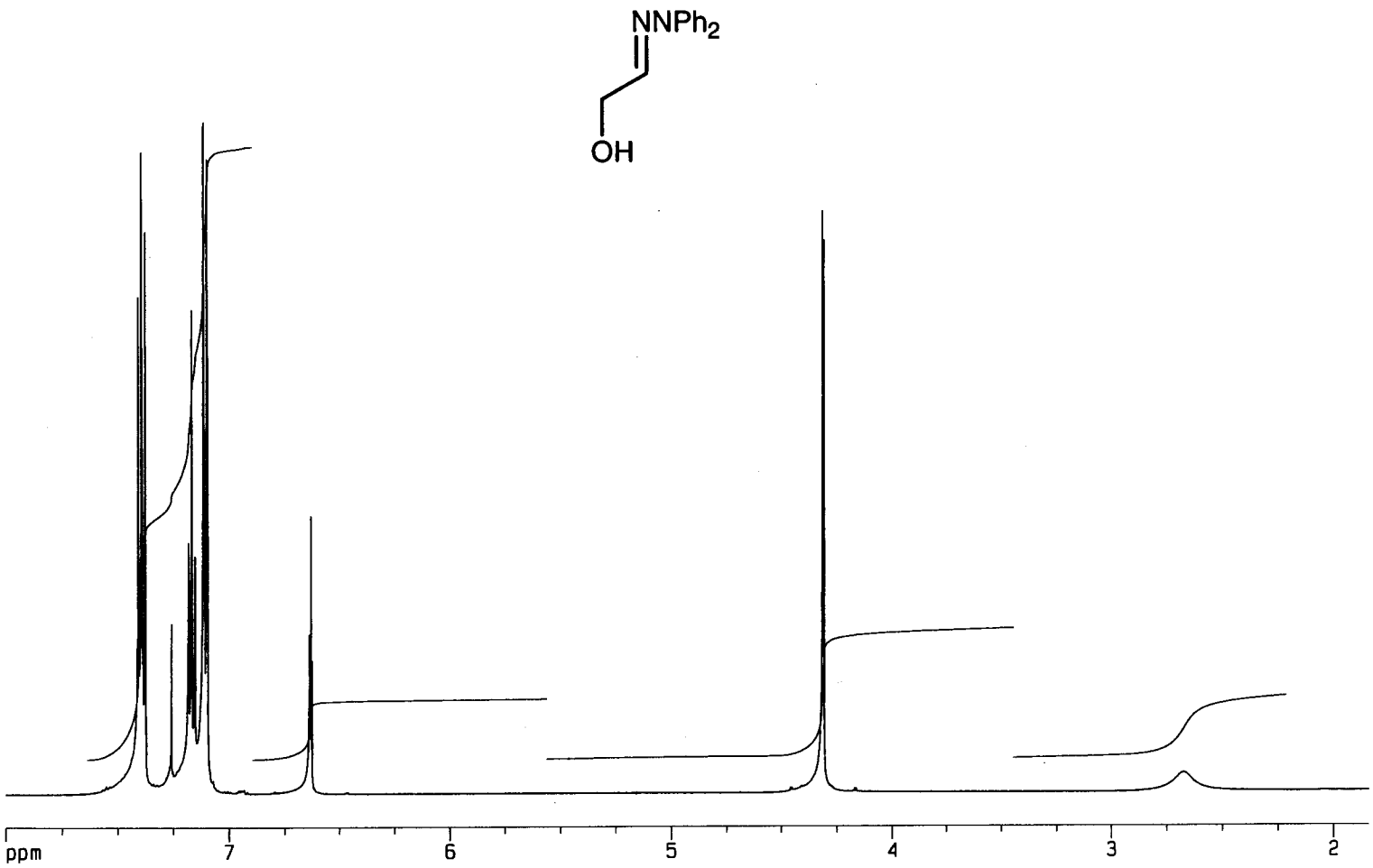
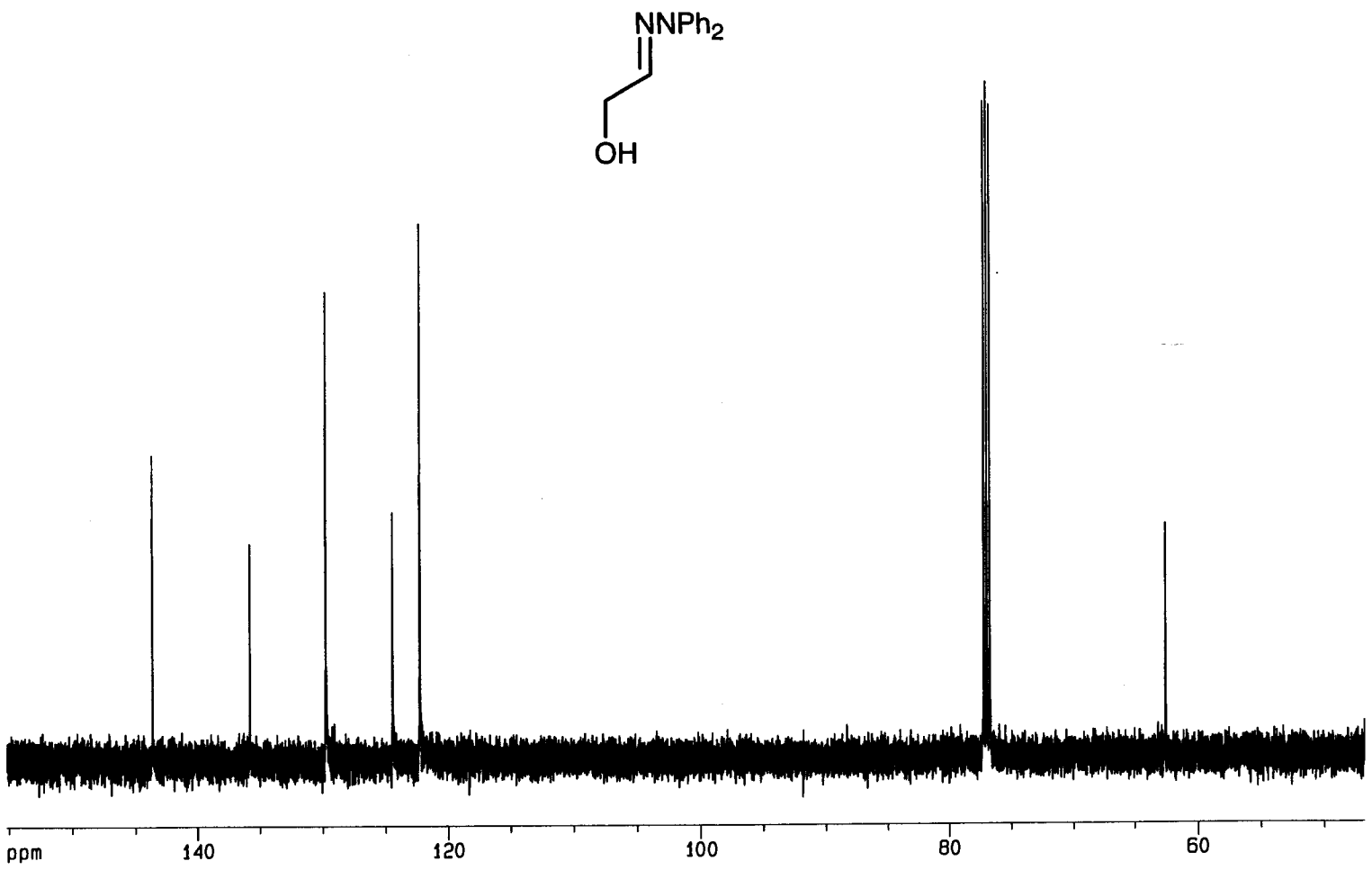
(1) Friestad, G. K. *Org. Lett.* **1999**, *1*, 1499.
(2) Beckwith, A. L. J.; Schiesser, C. H. *Tetrahedron* **1985**, *41*, 3925. Spellmeyer, D. C.; Houk, K. N. *J. Org. Chem.* **1987**, *52*, 959. Curran, D. P.; Porter, N. A.; Giese, B. *Stereochemistry of Radical Reactions: Concepts, Guidelines, and Synthetic Applications*; VCH: New York; 1995.

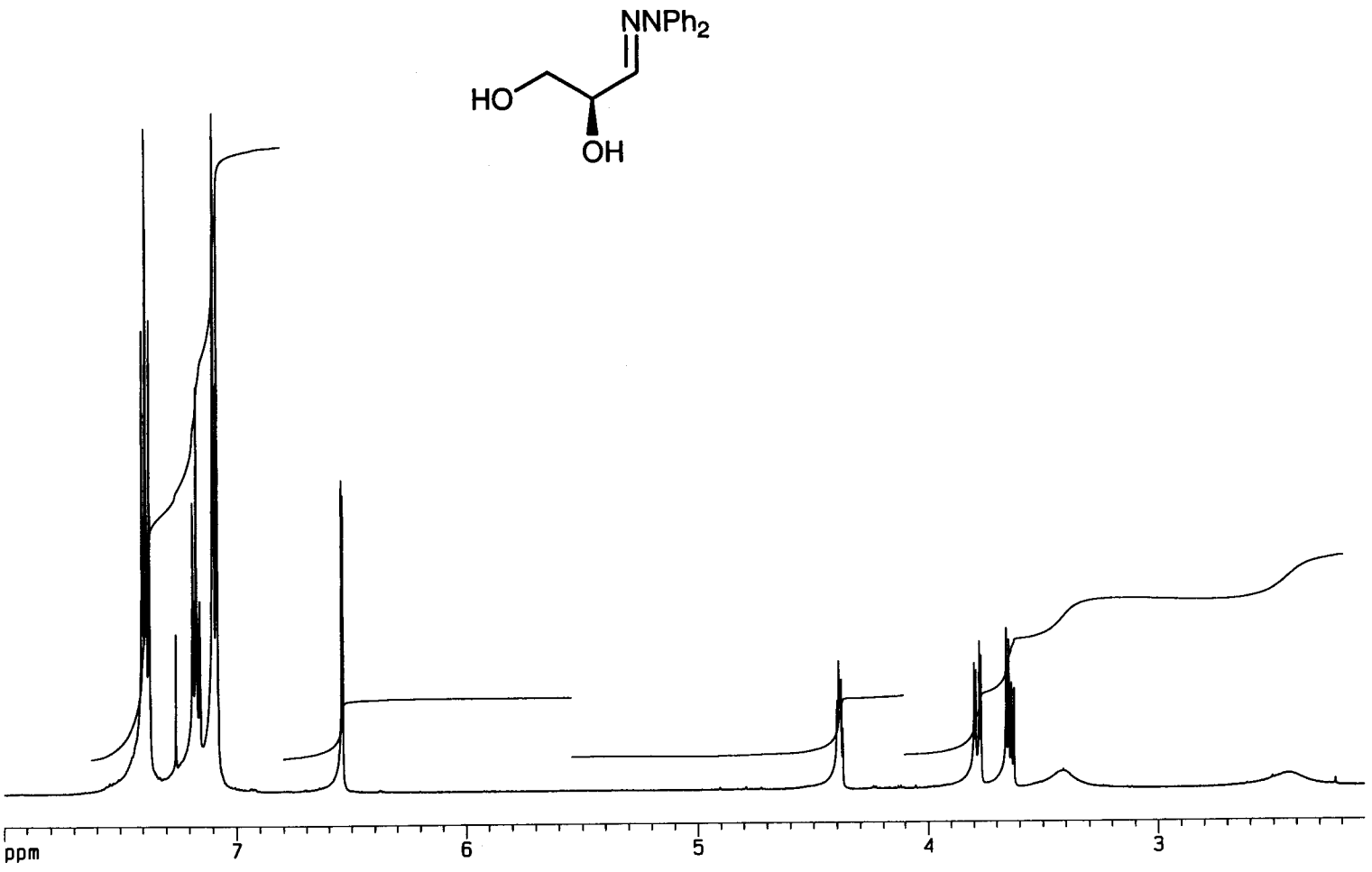
^{1}HNMR 1a



^{13}C NMR 1a



^{1}H NMR 1f



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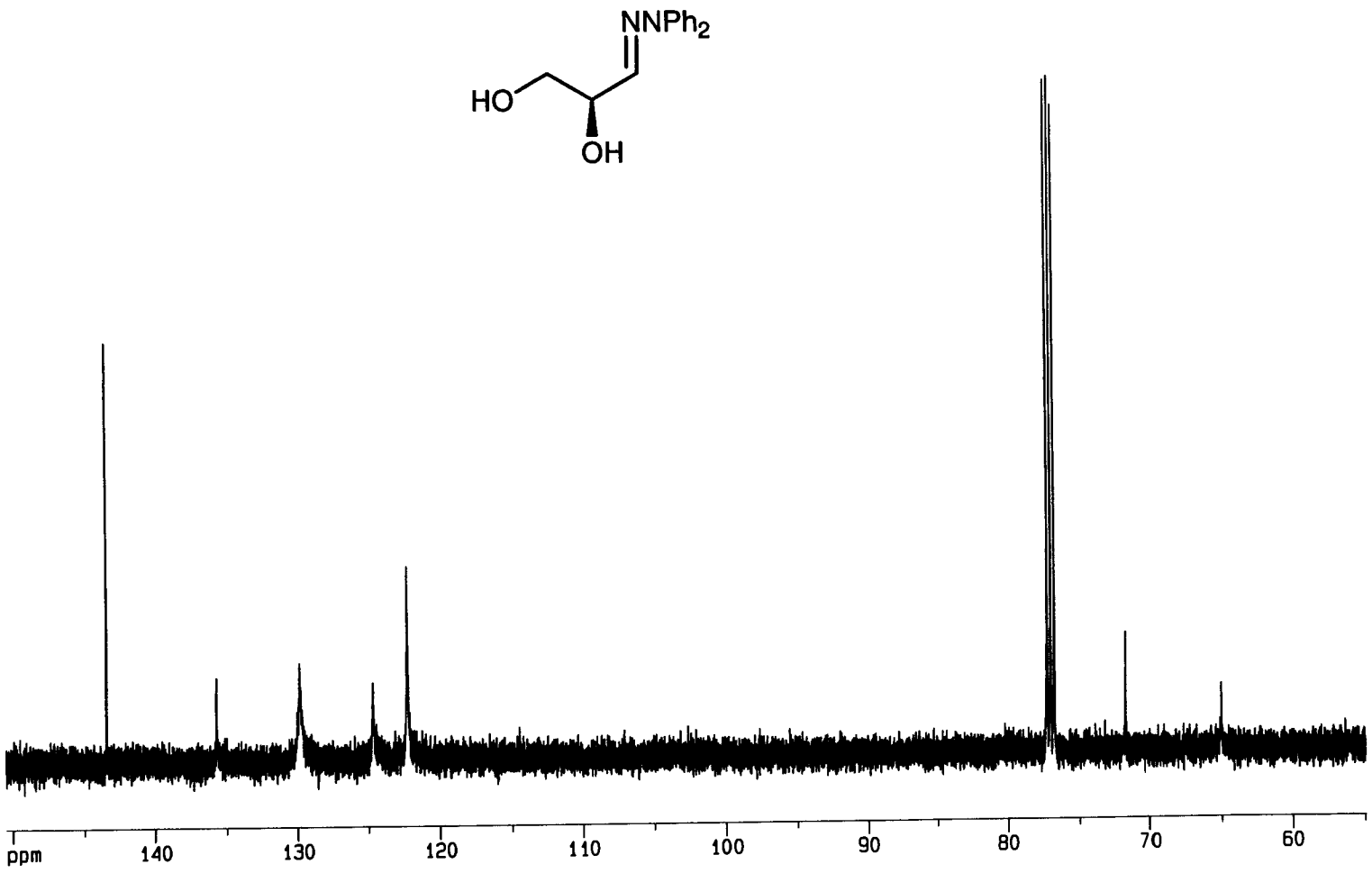

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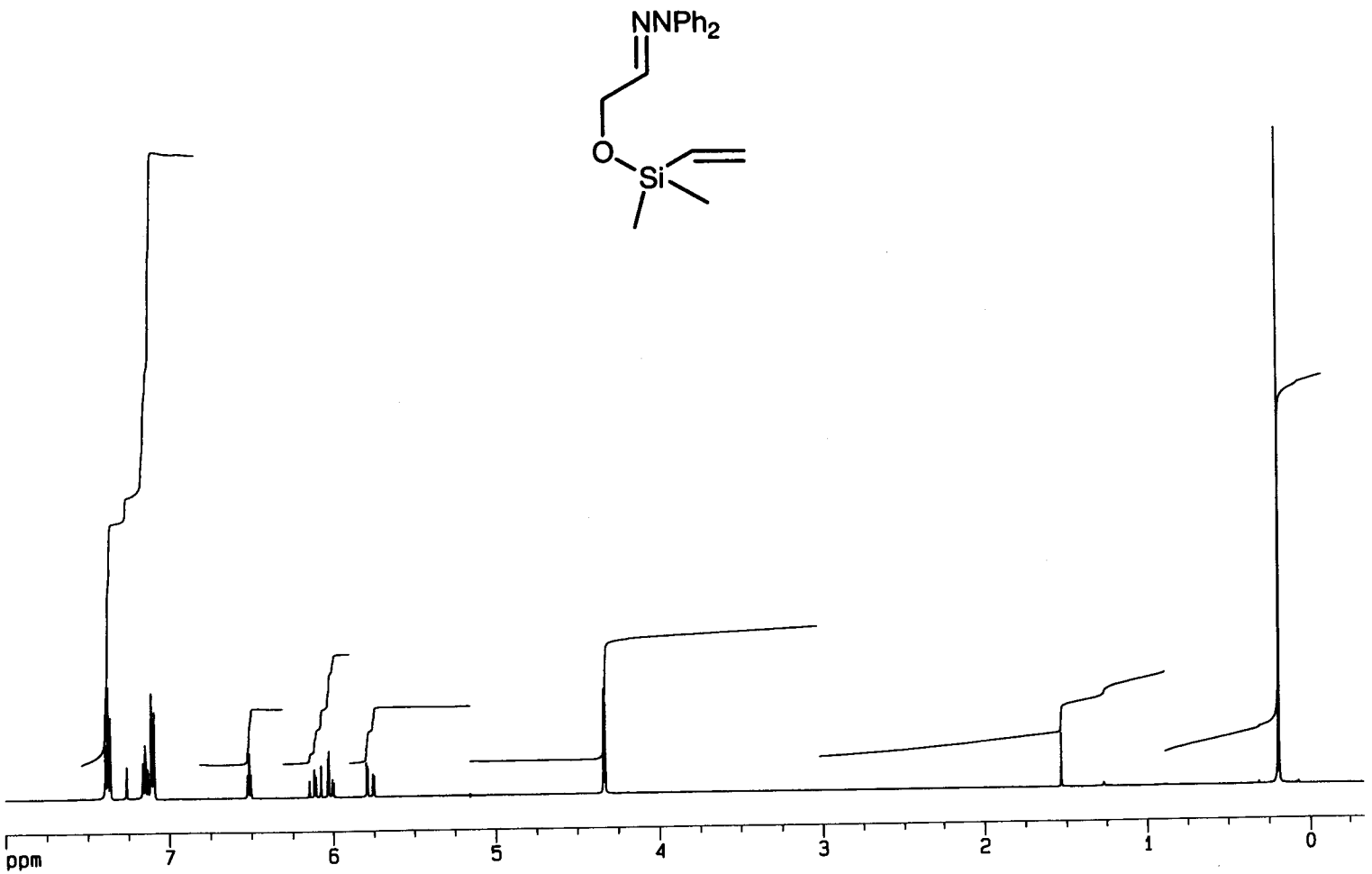

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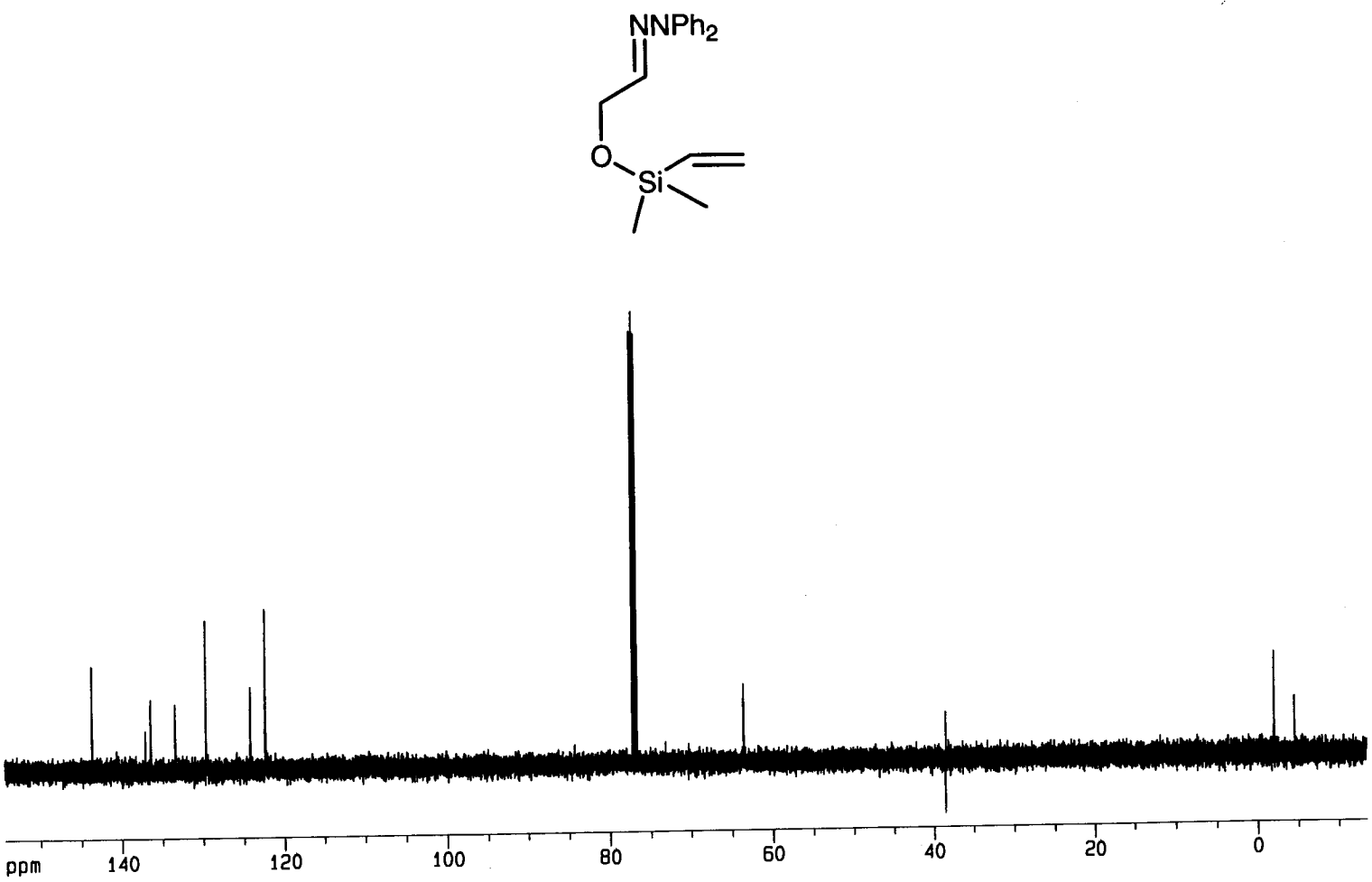
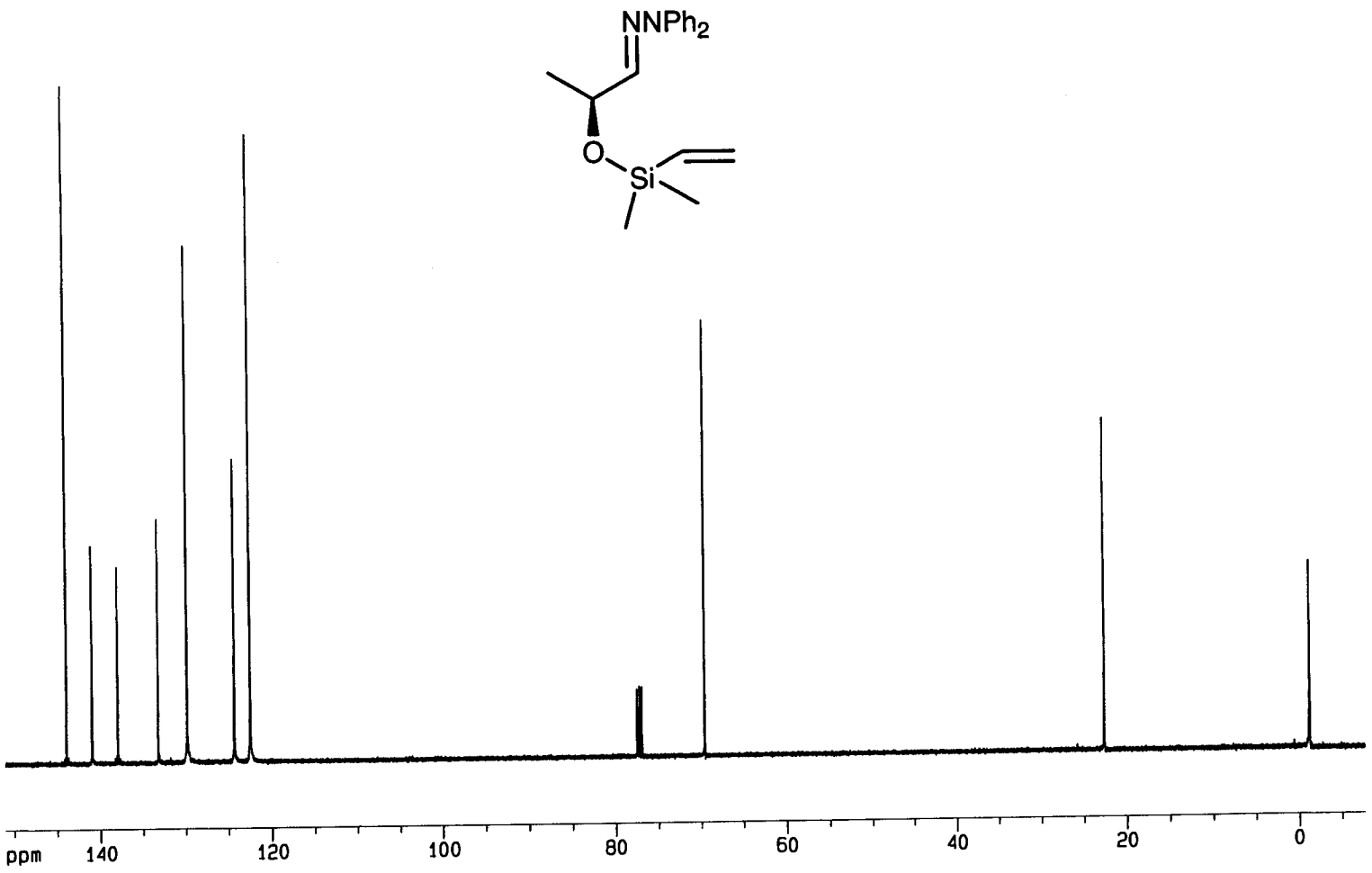


^{1}H NMR 3b

^{13}C NMR 3b



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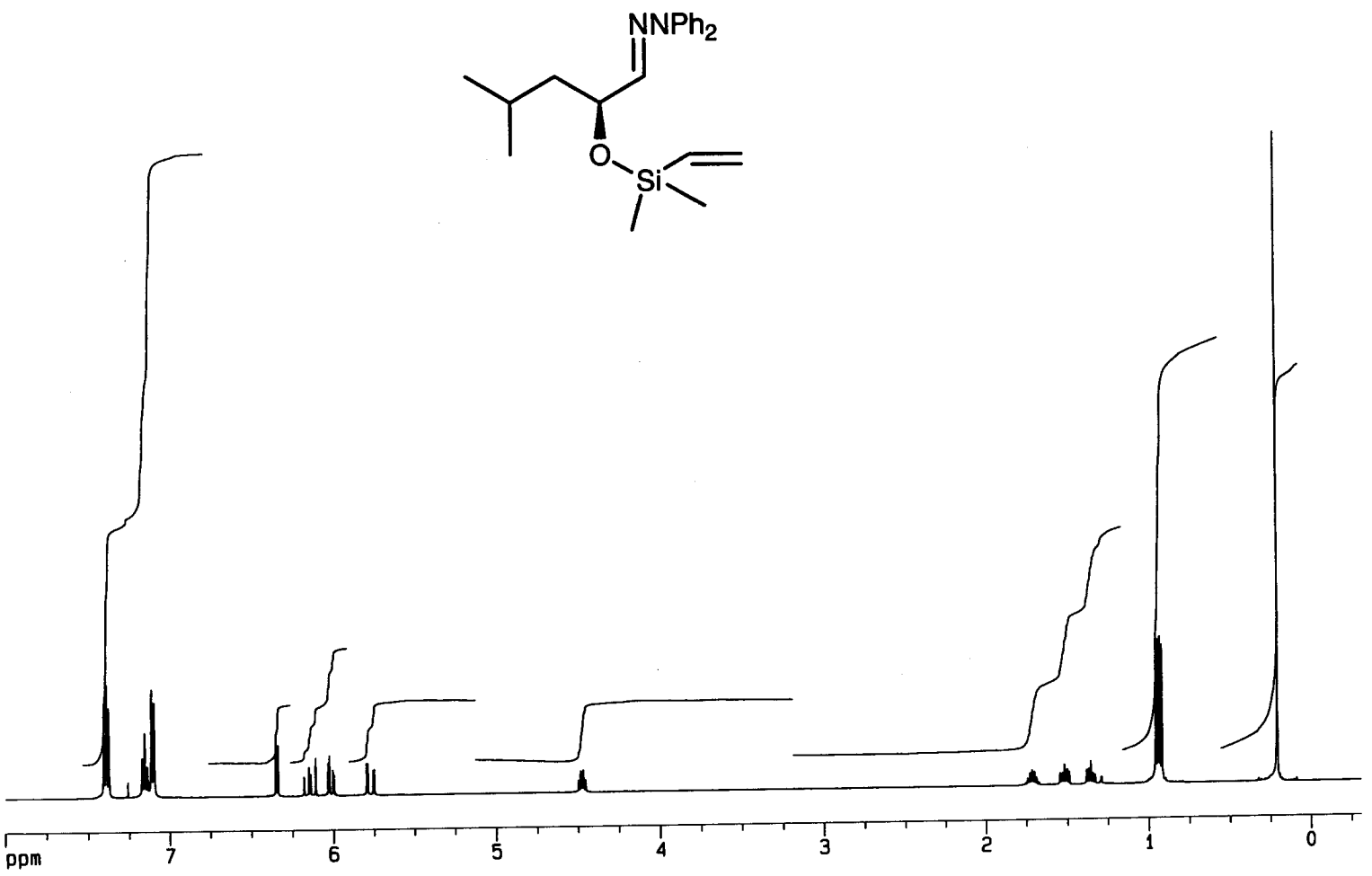

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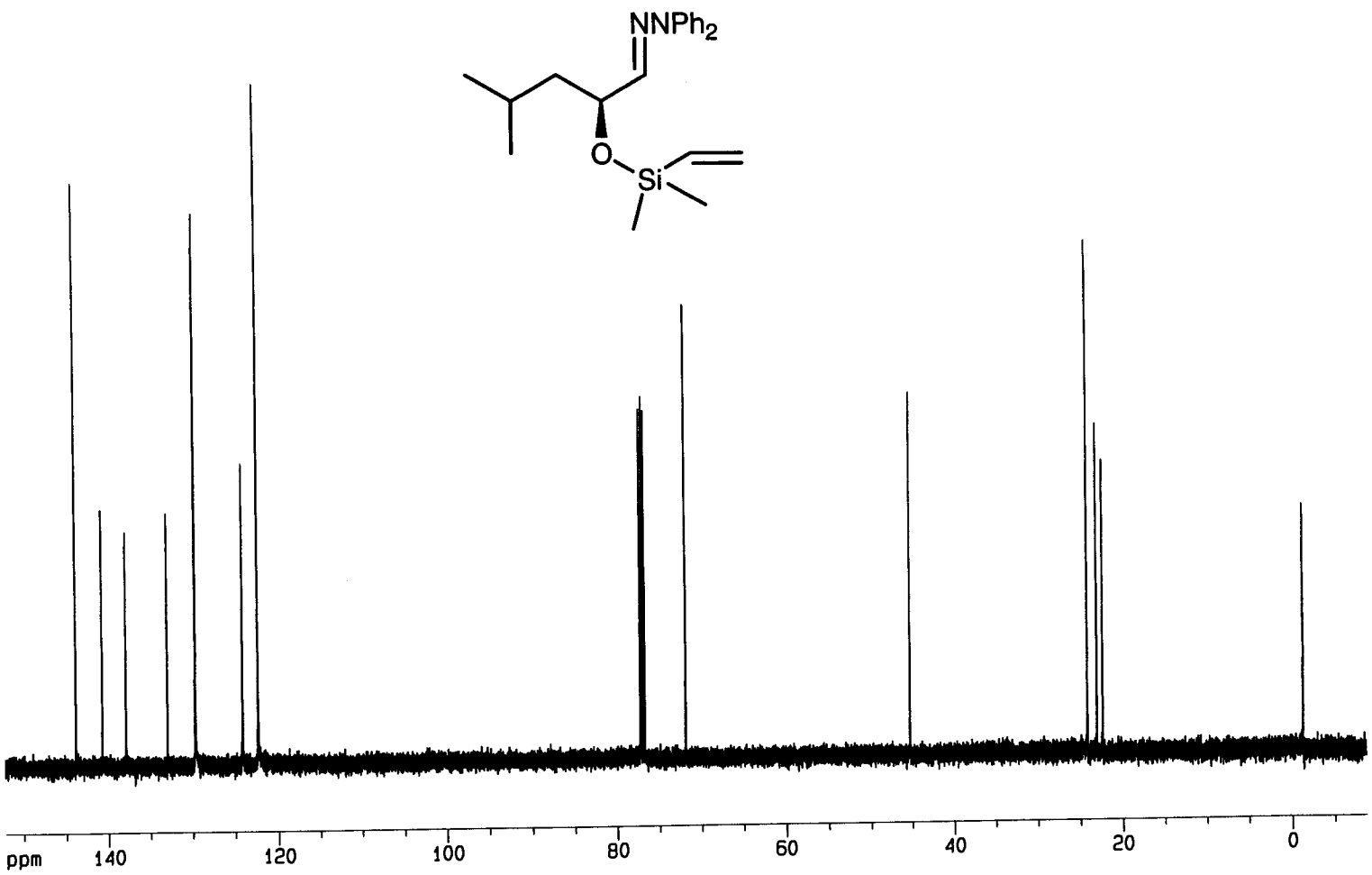

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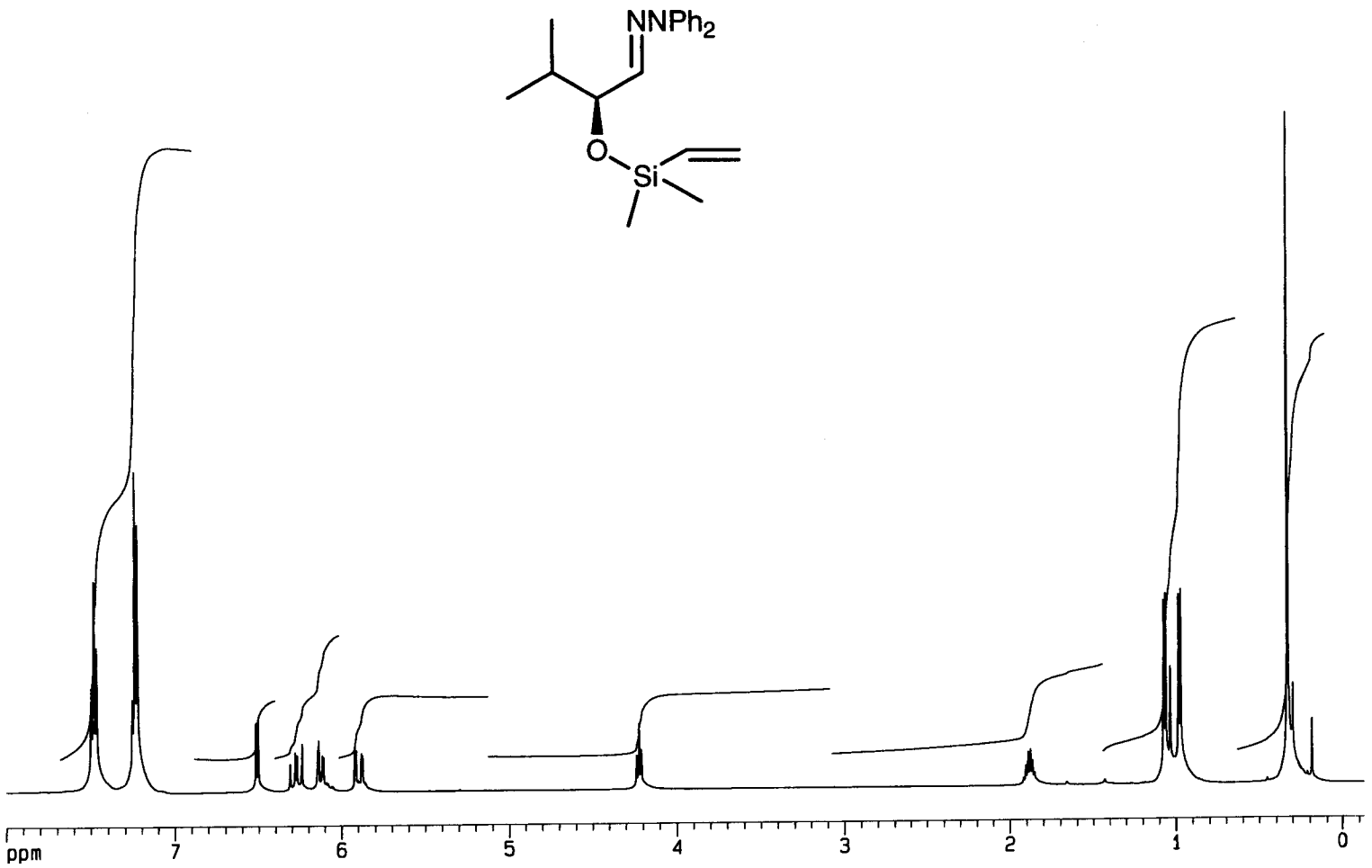
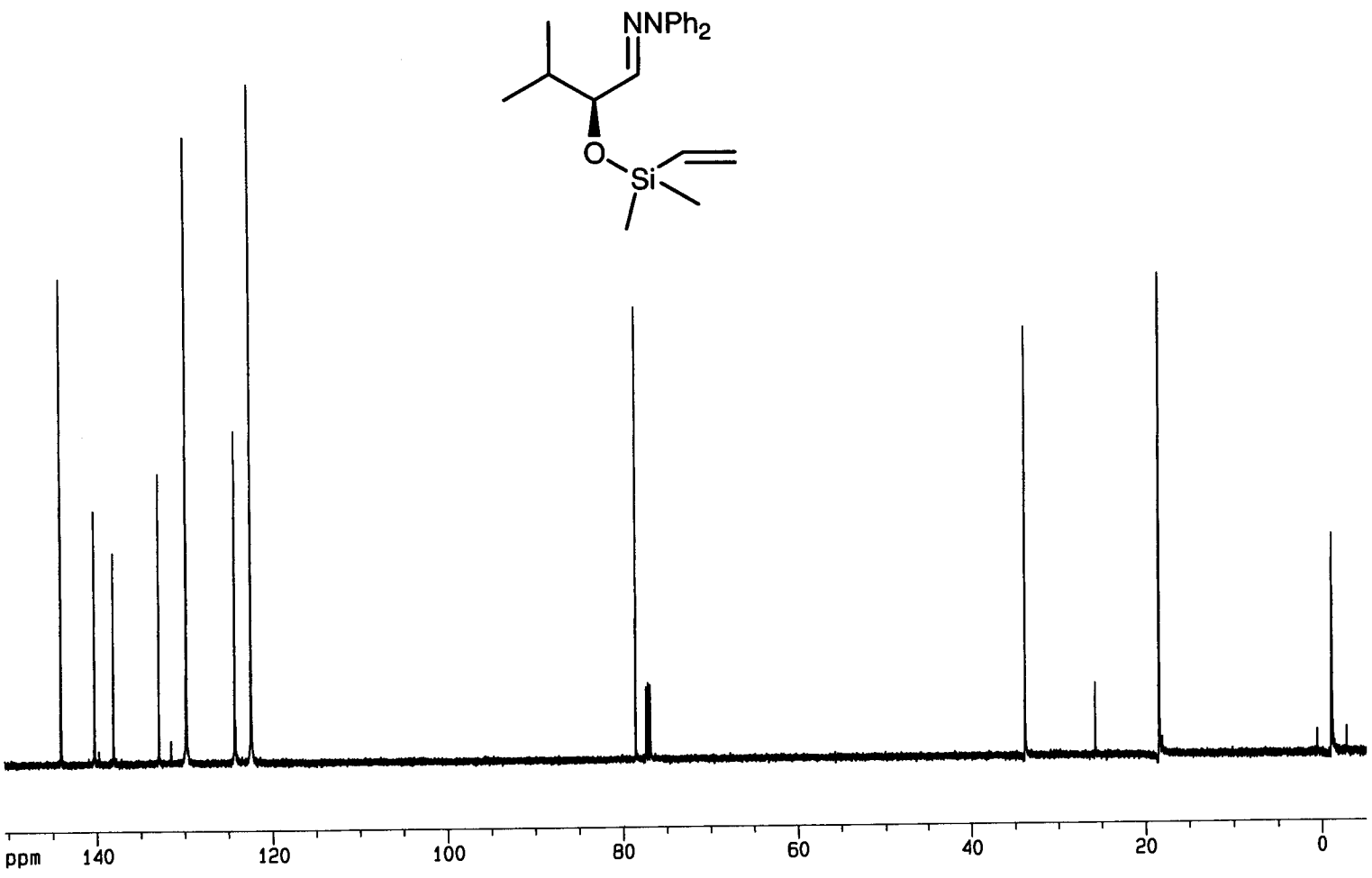
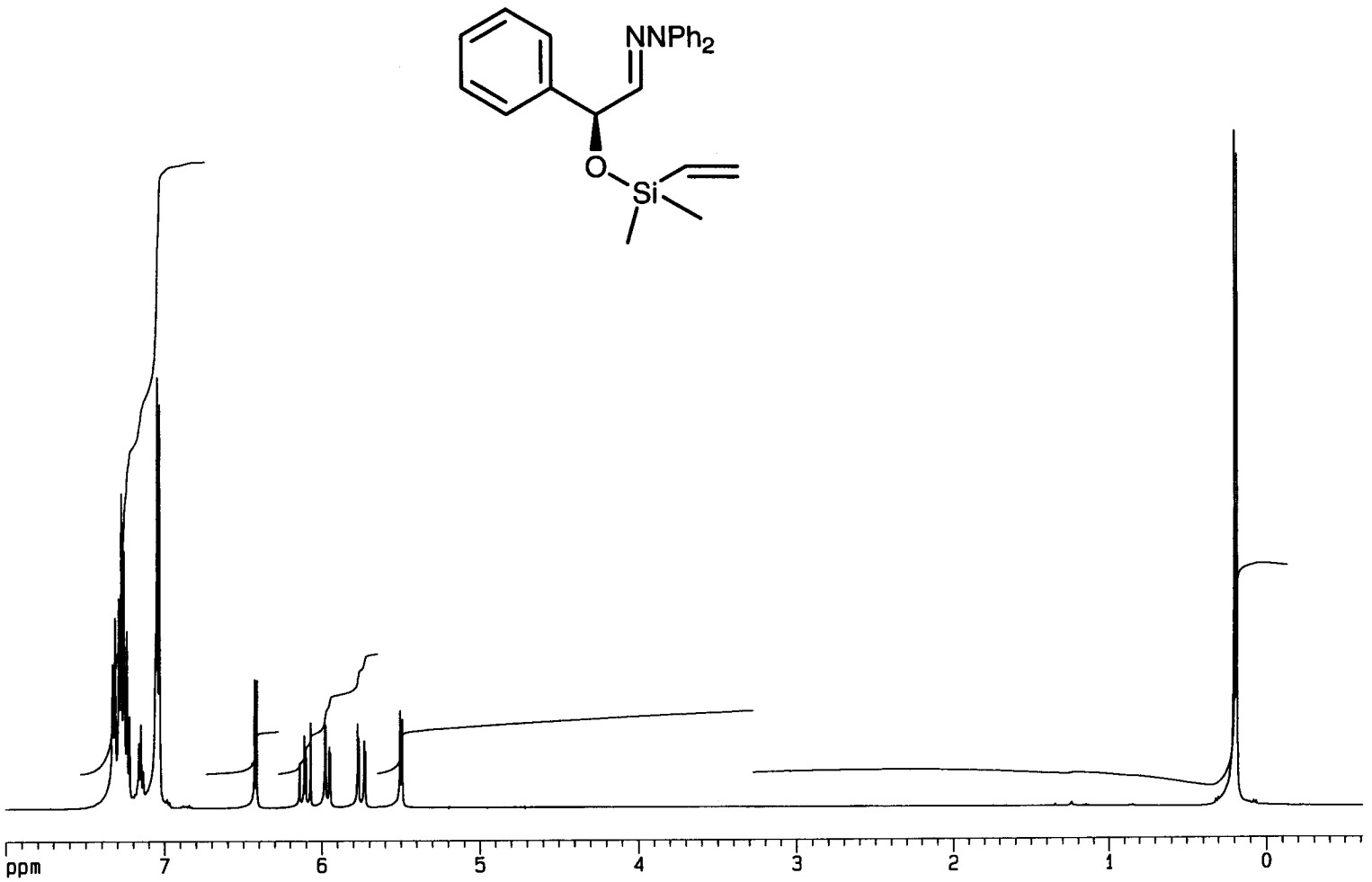


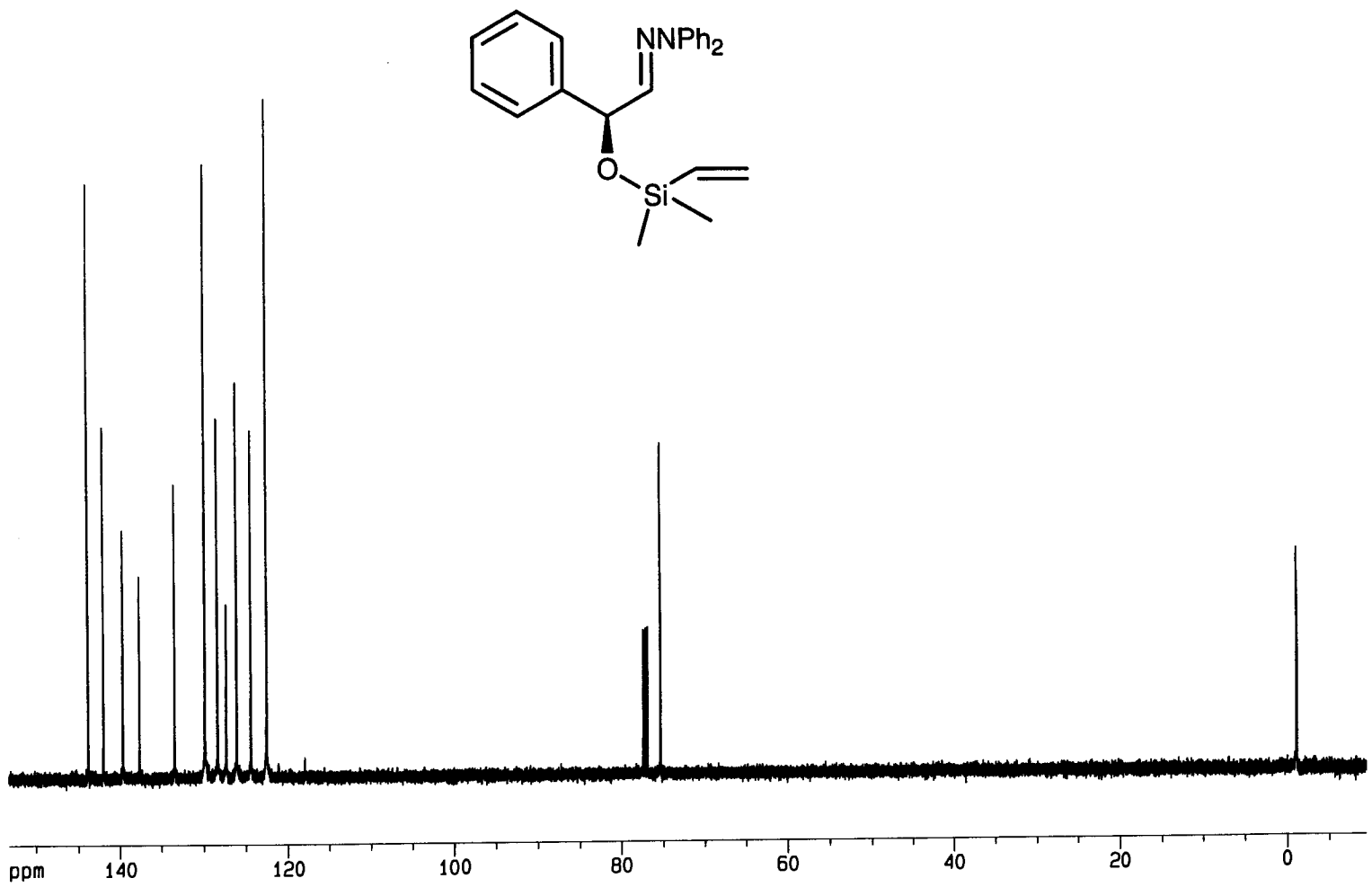
^{13}C NMR 3d



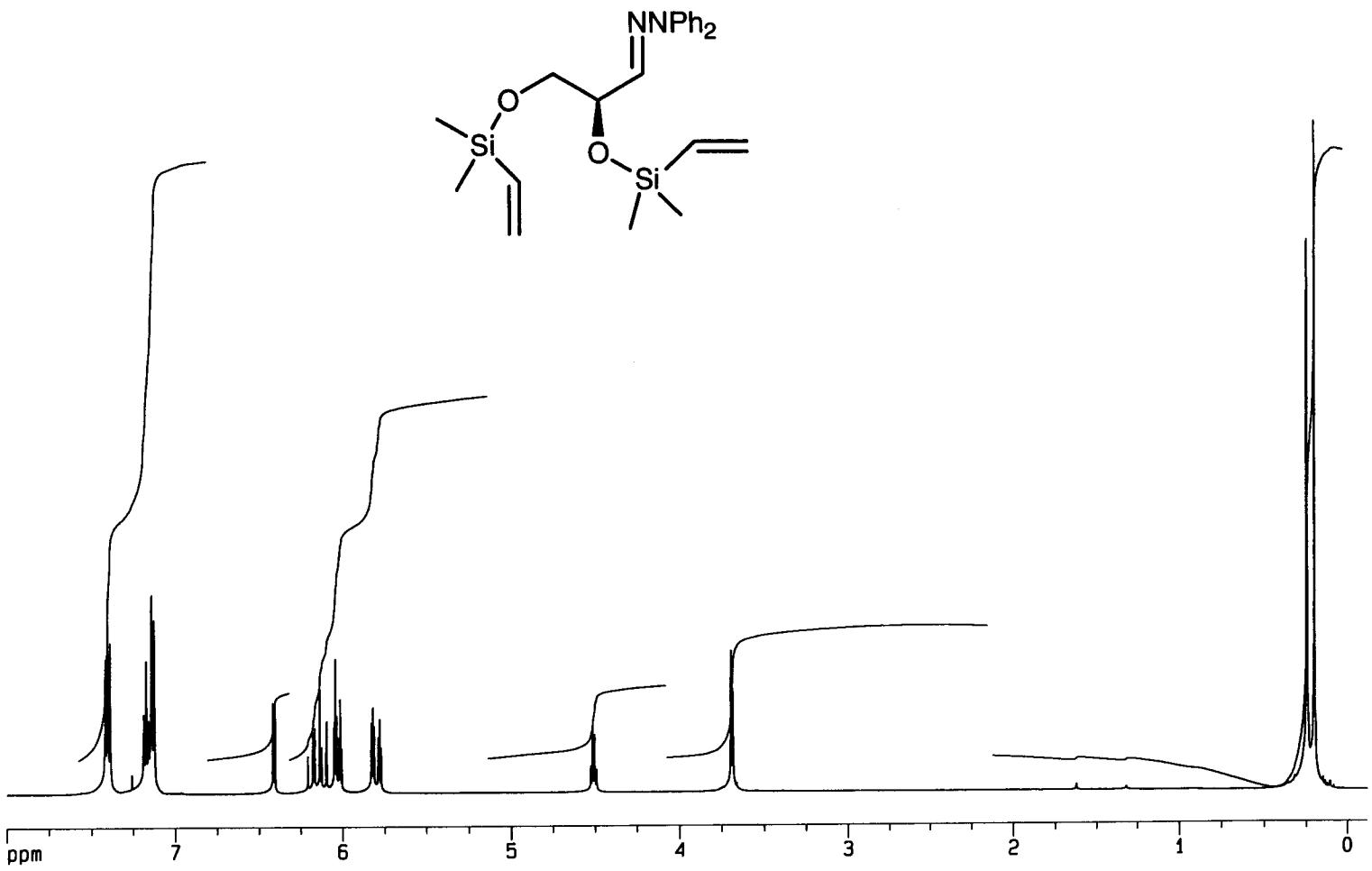
^{1}H NMR 3e



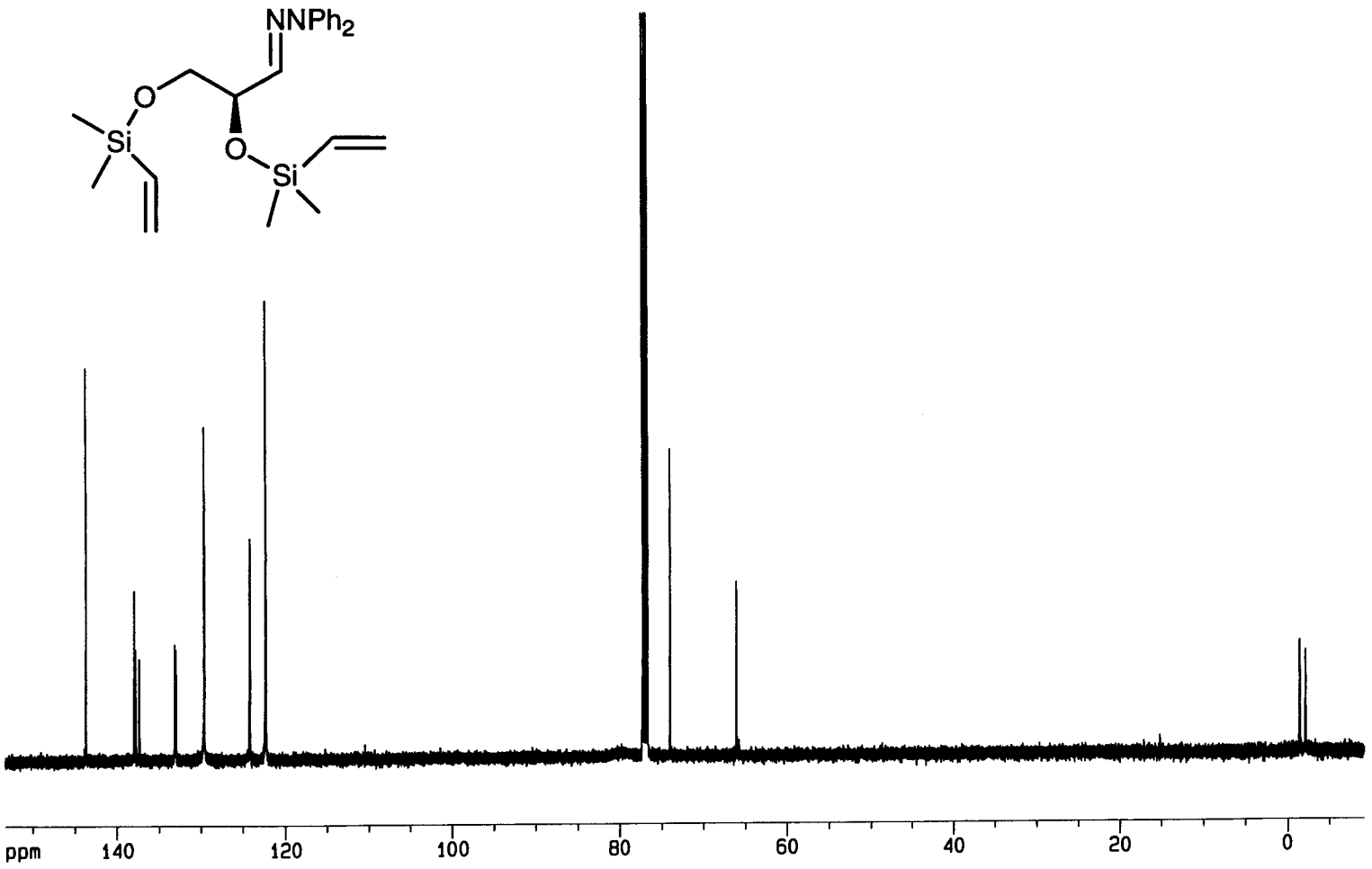
^{13}C NMR 3e



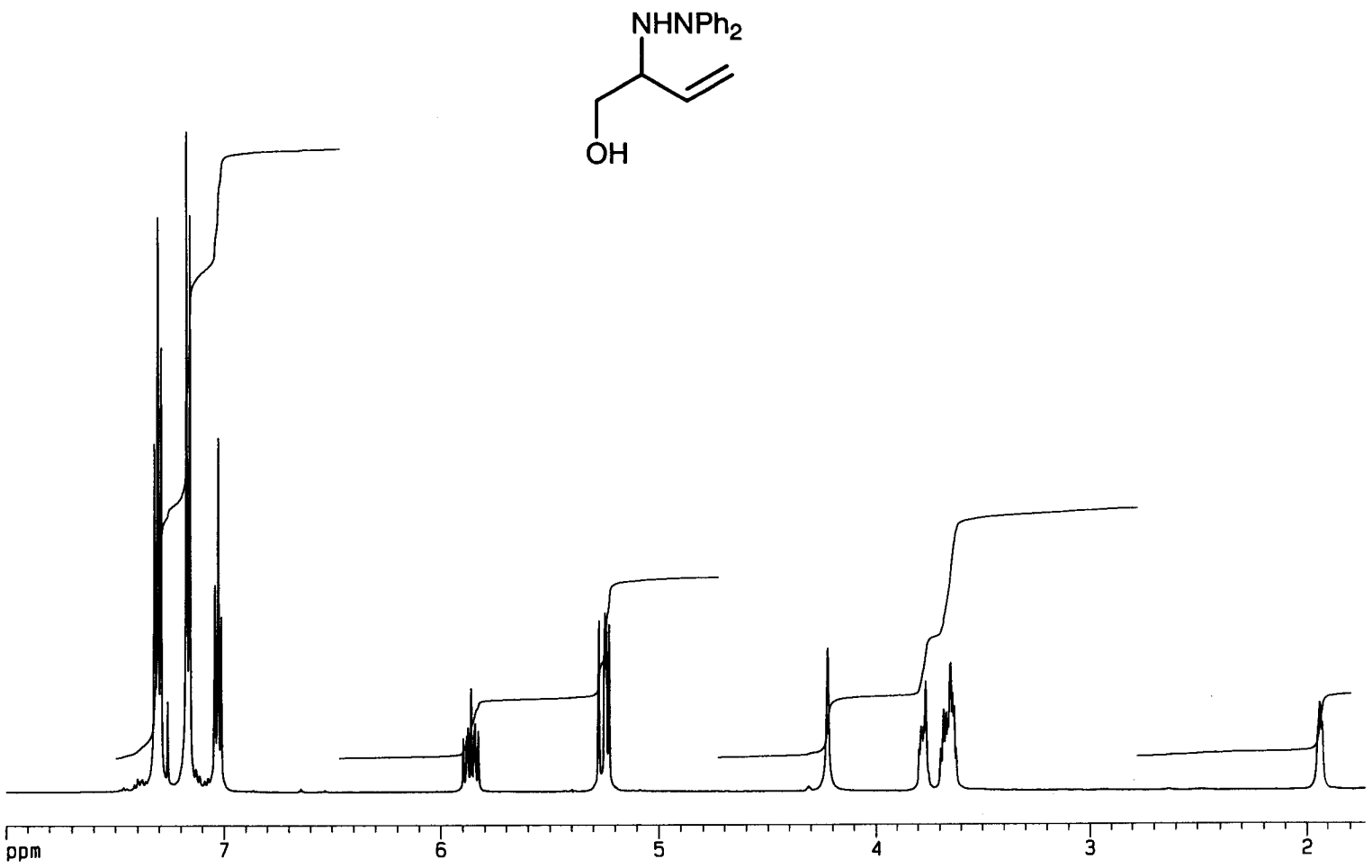
^{1}H NMR 3f



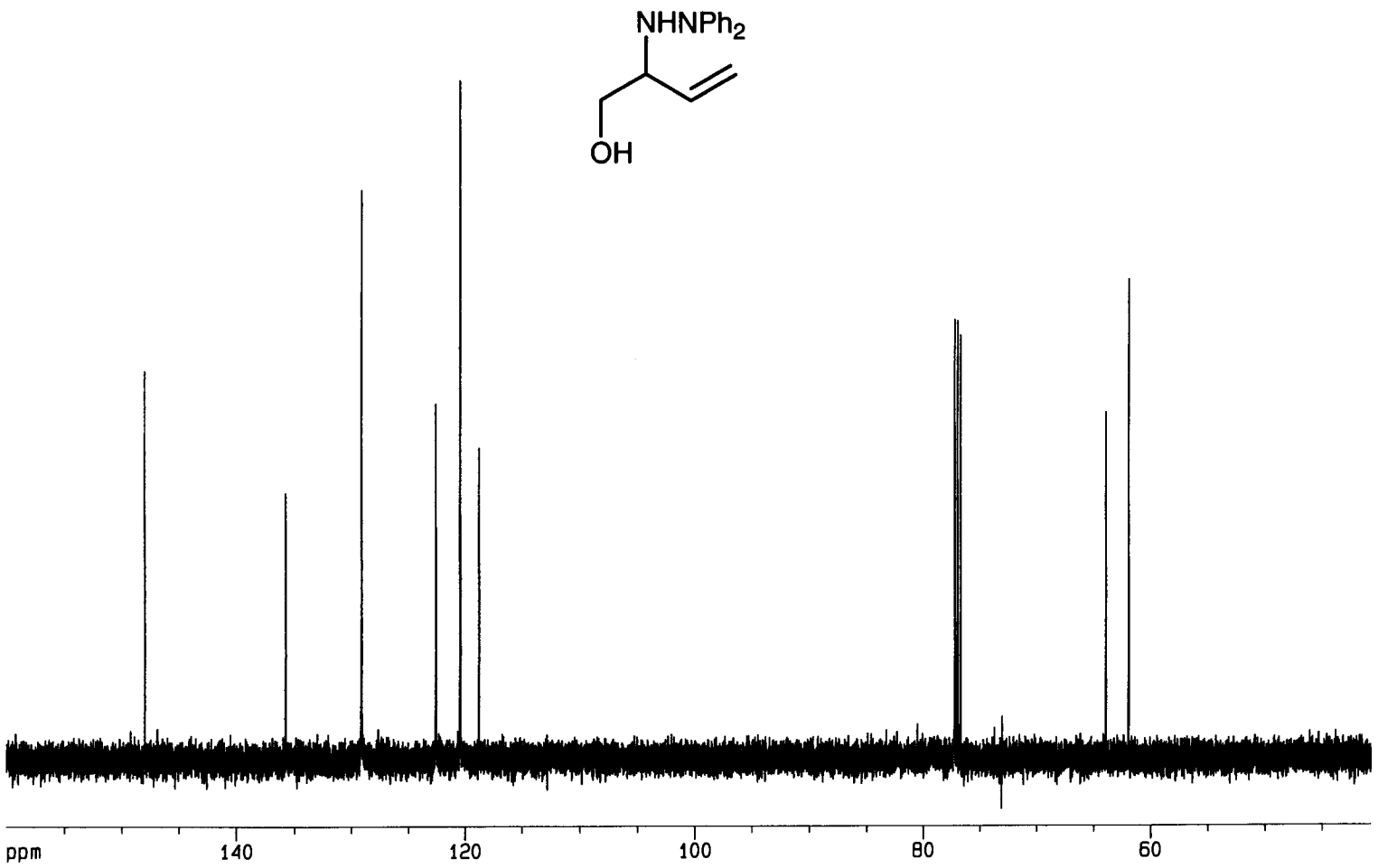
^{13}C NMR 3f



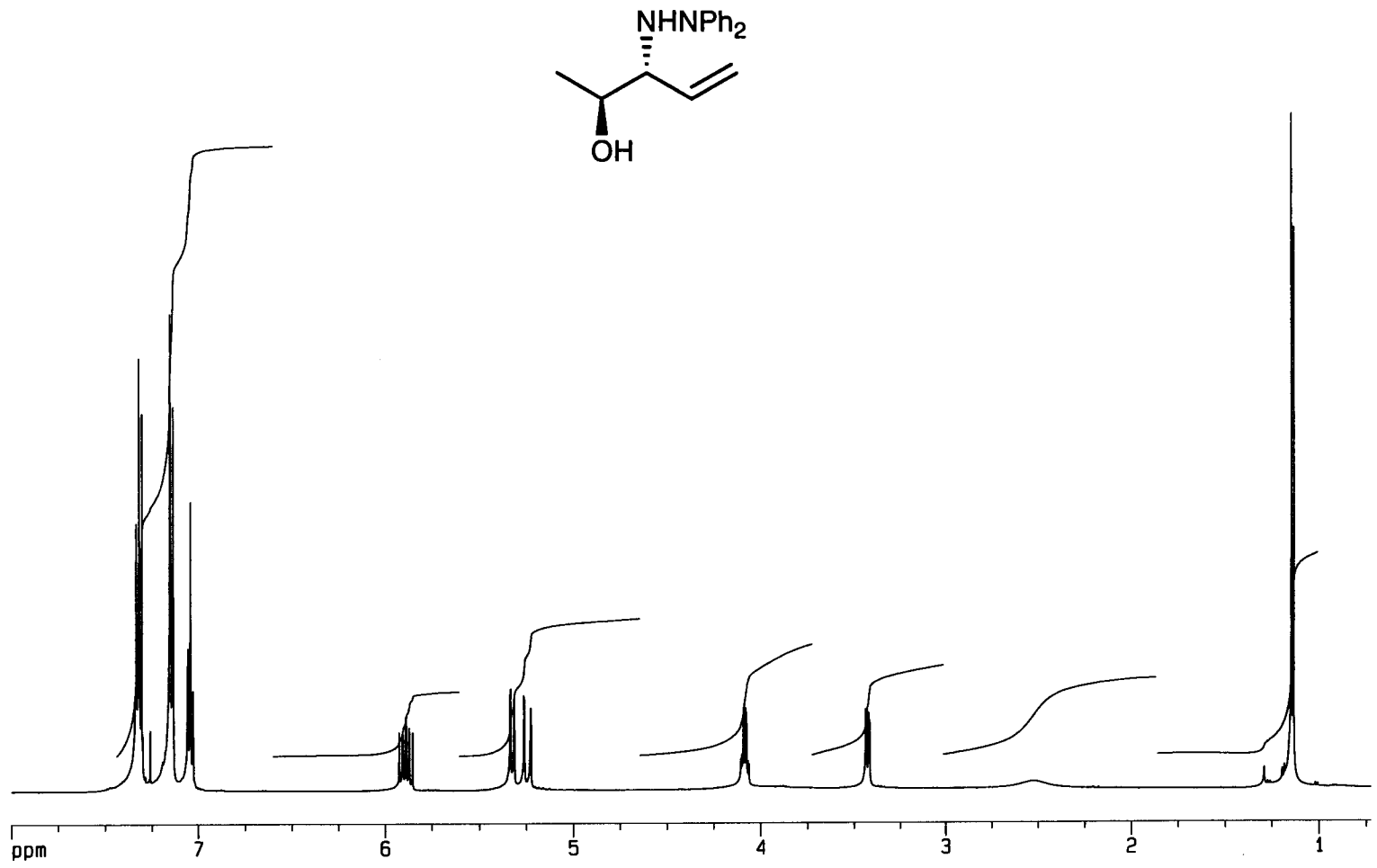
^1H NMR 5a



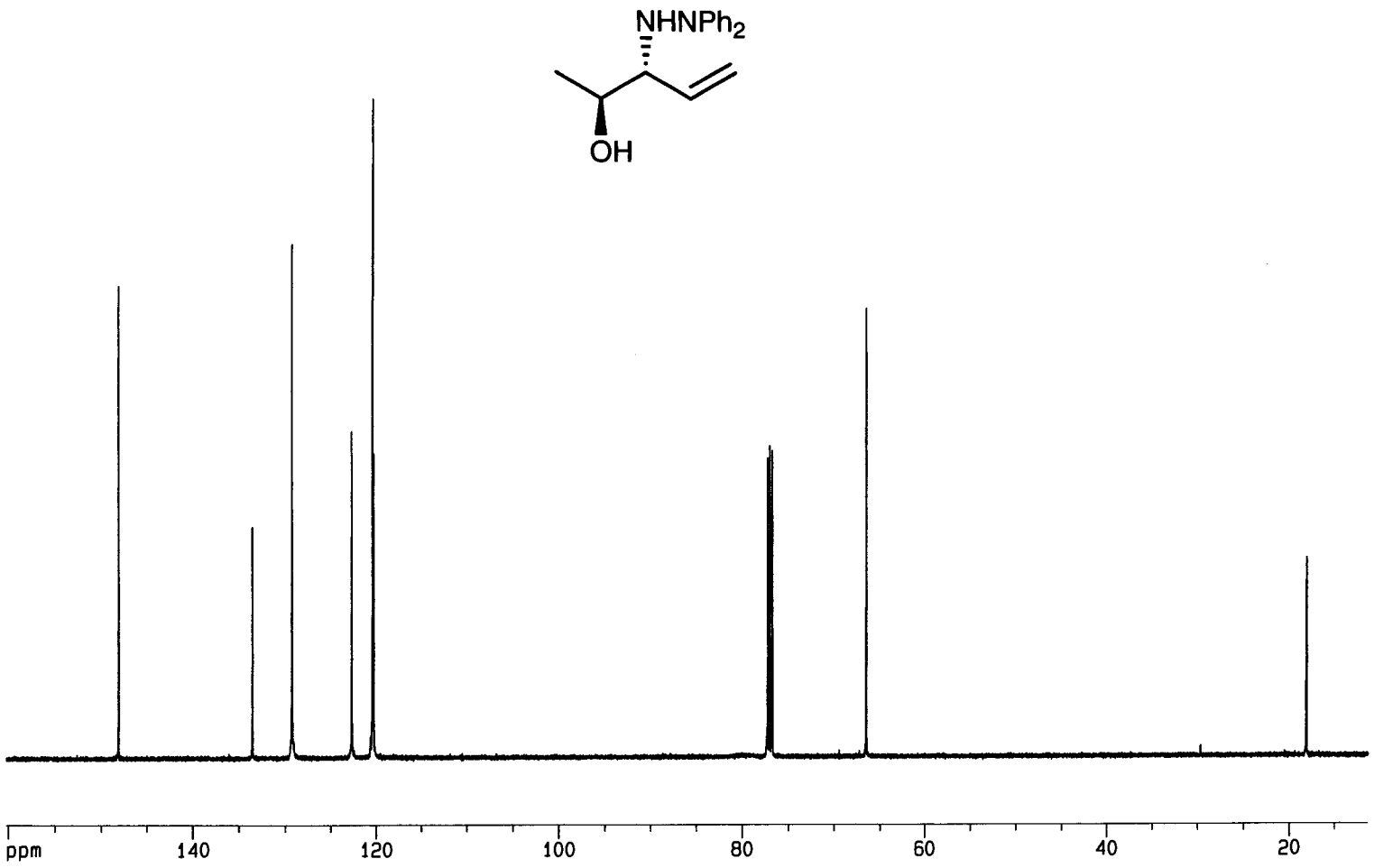
^{13}C NMR 5a



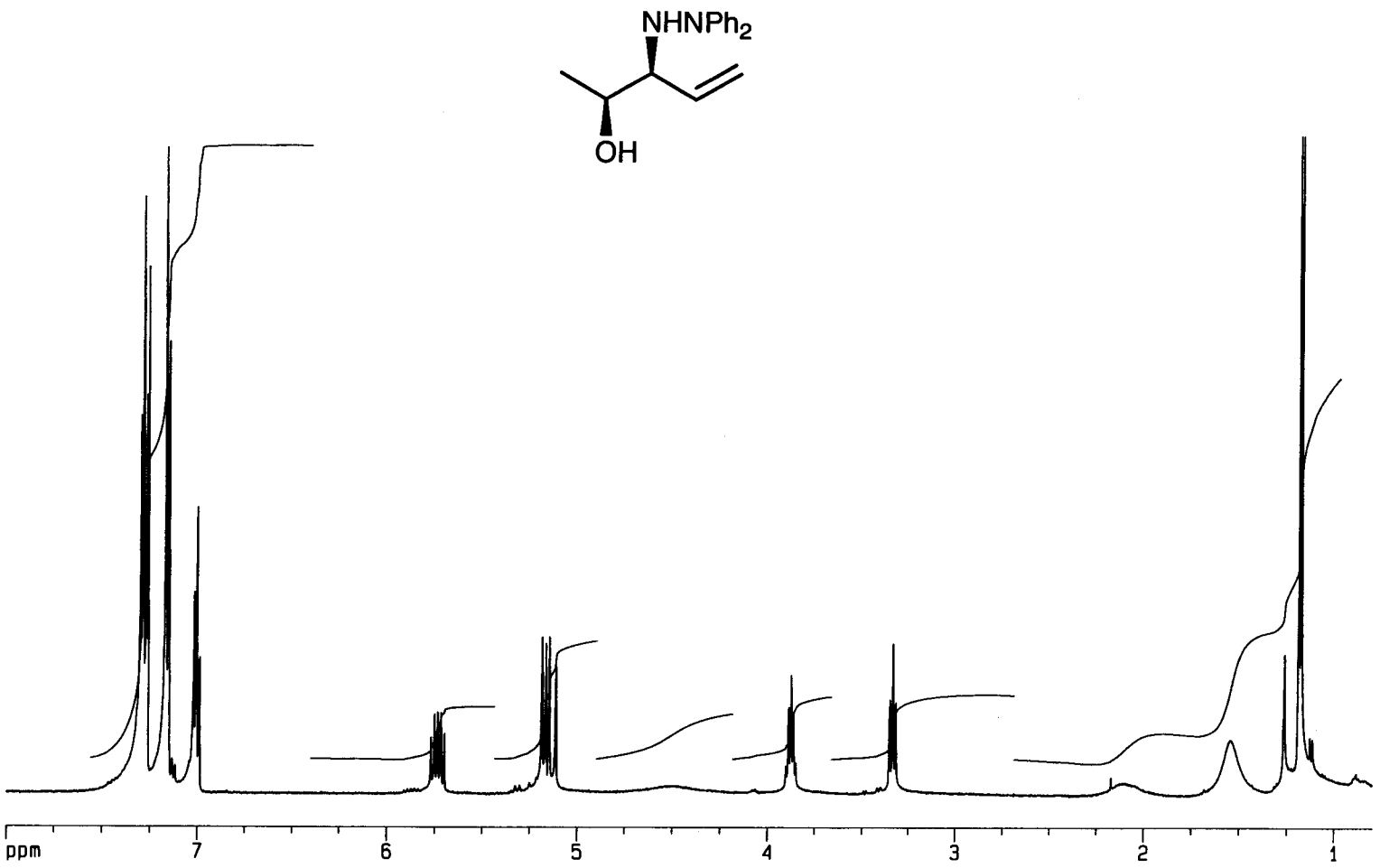
^{1}H NMR 5b (anti)



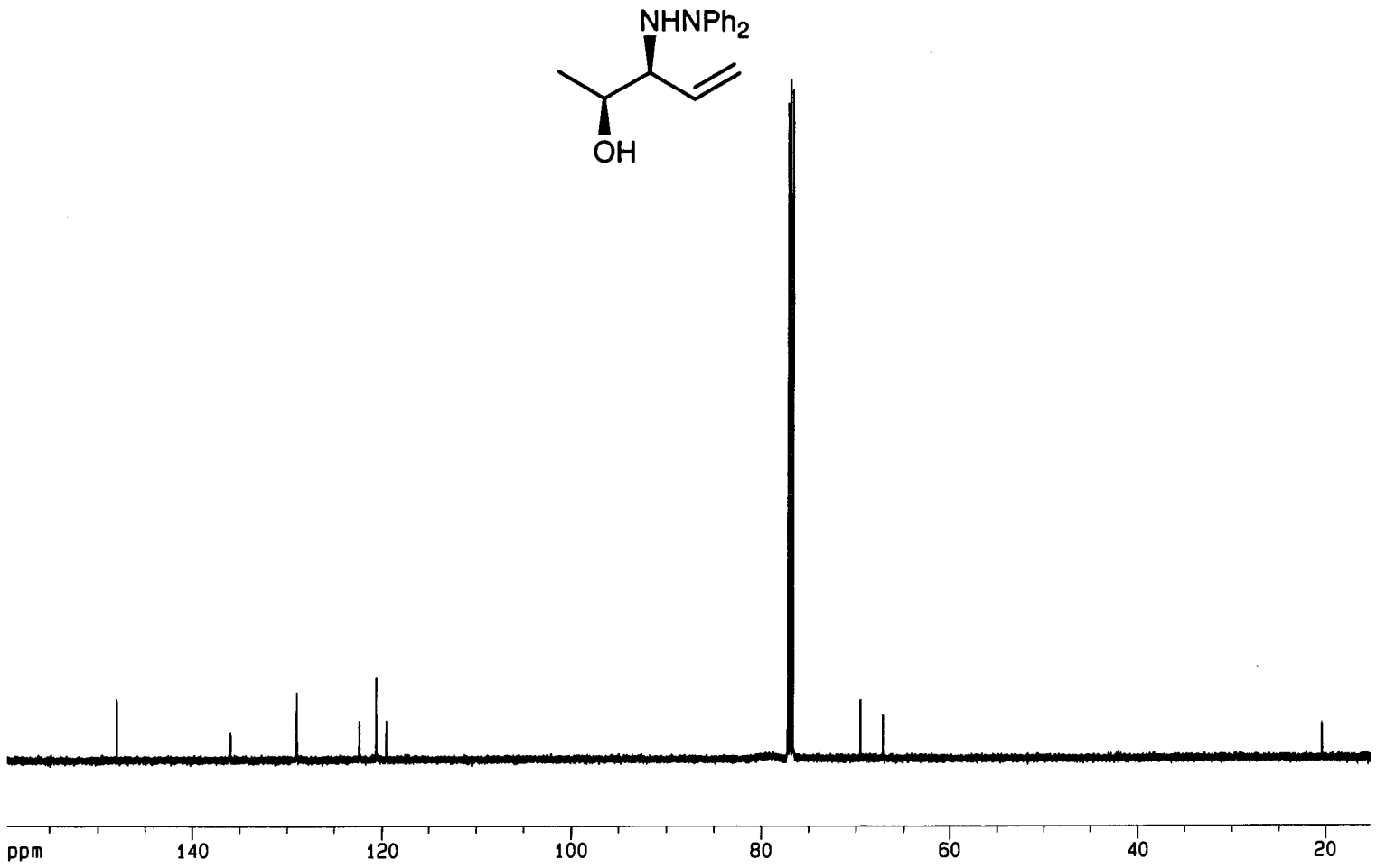
^{13}C NMR 5b (anti)



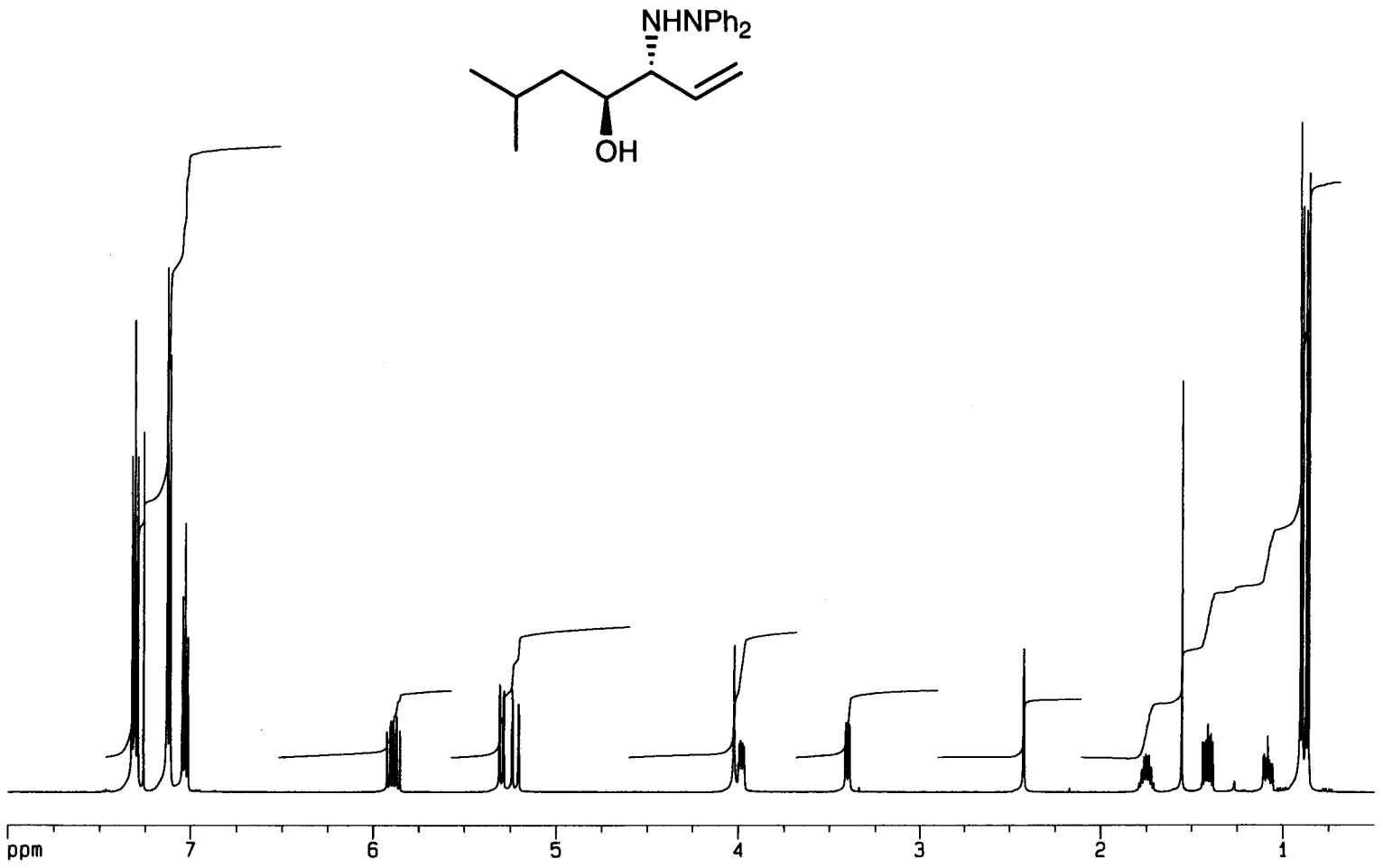
^{1}HNMR 5b (syn)



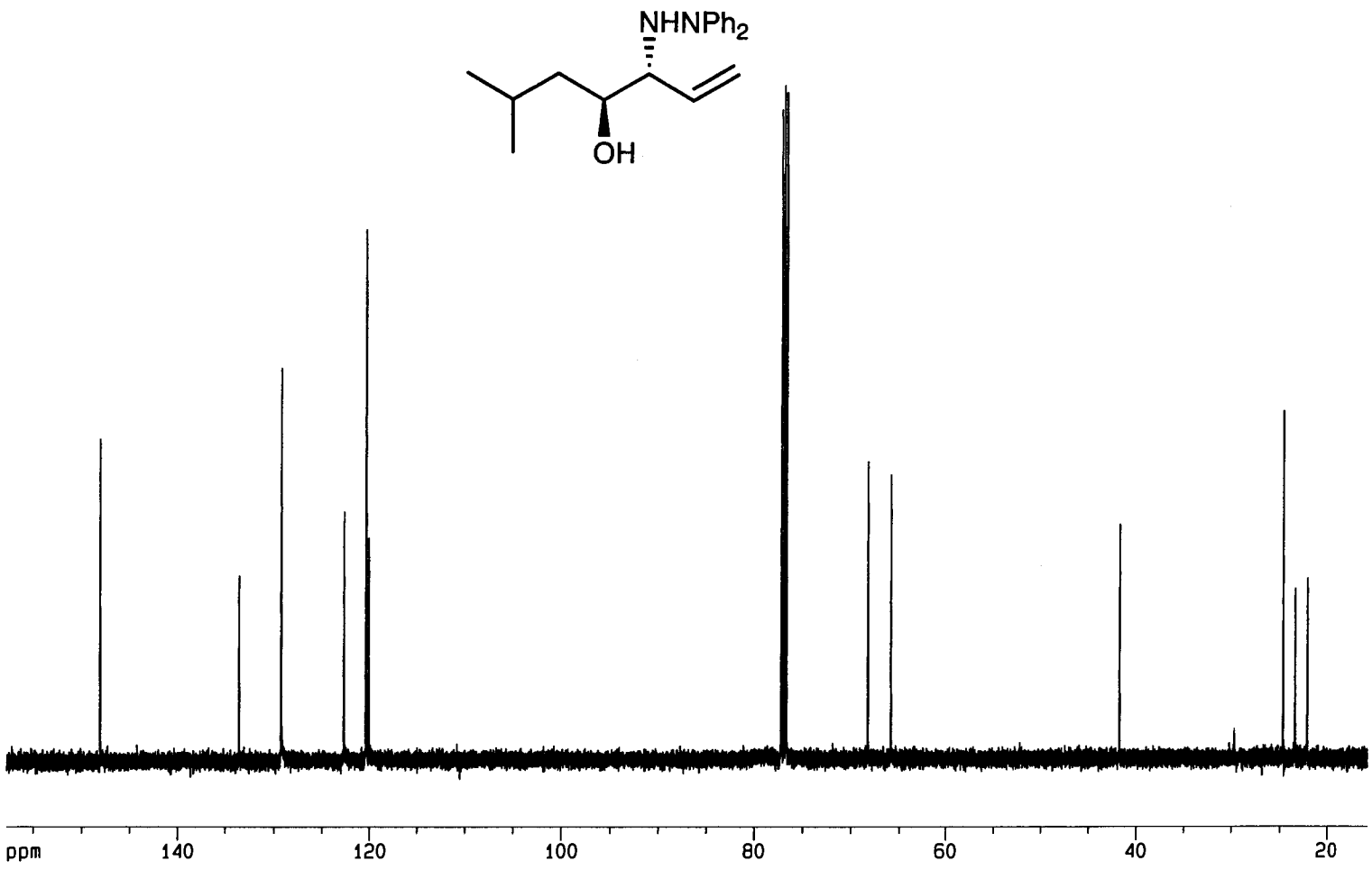
^{13}C NMR 5b (syn)



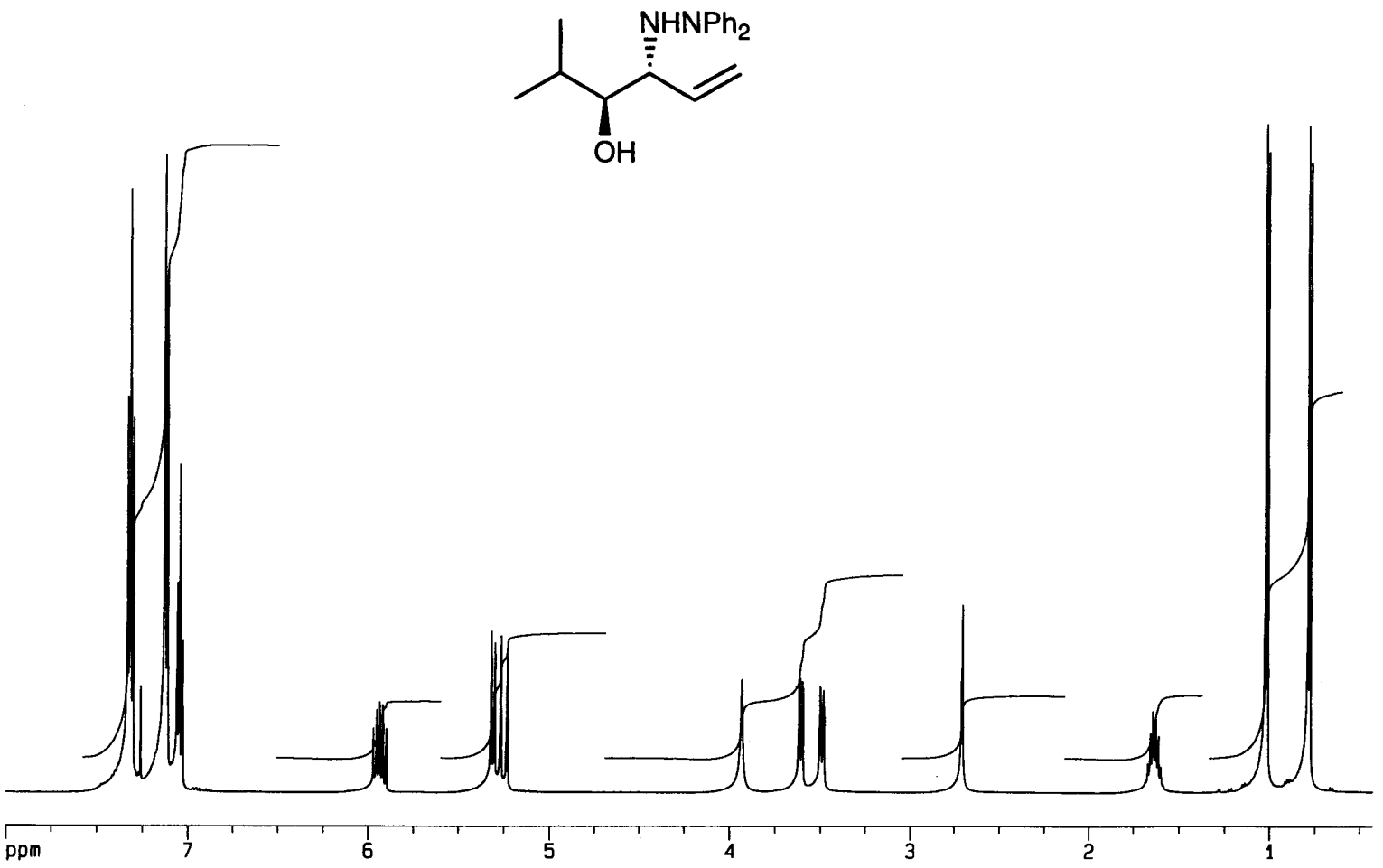
^{1}H NMR 5c



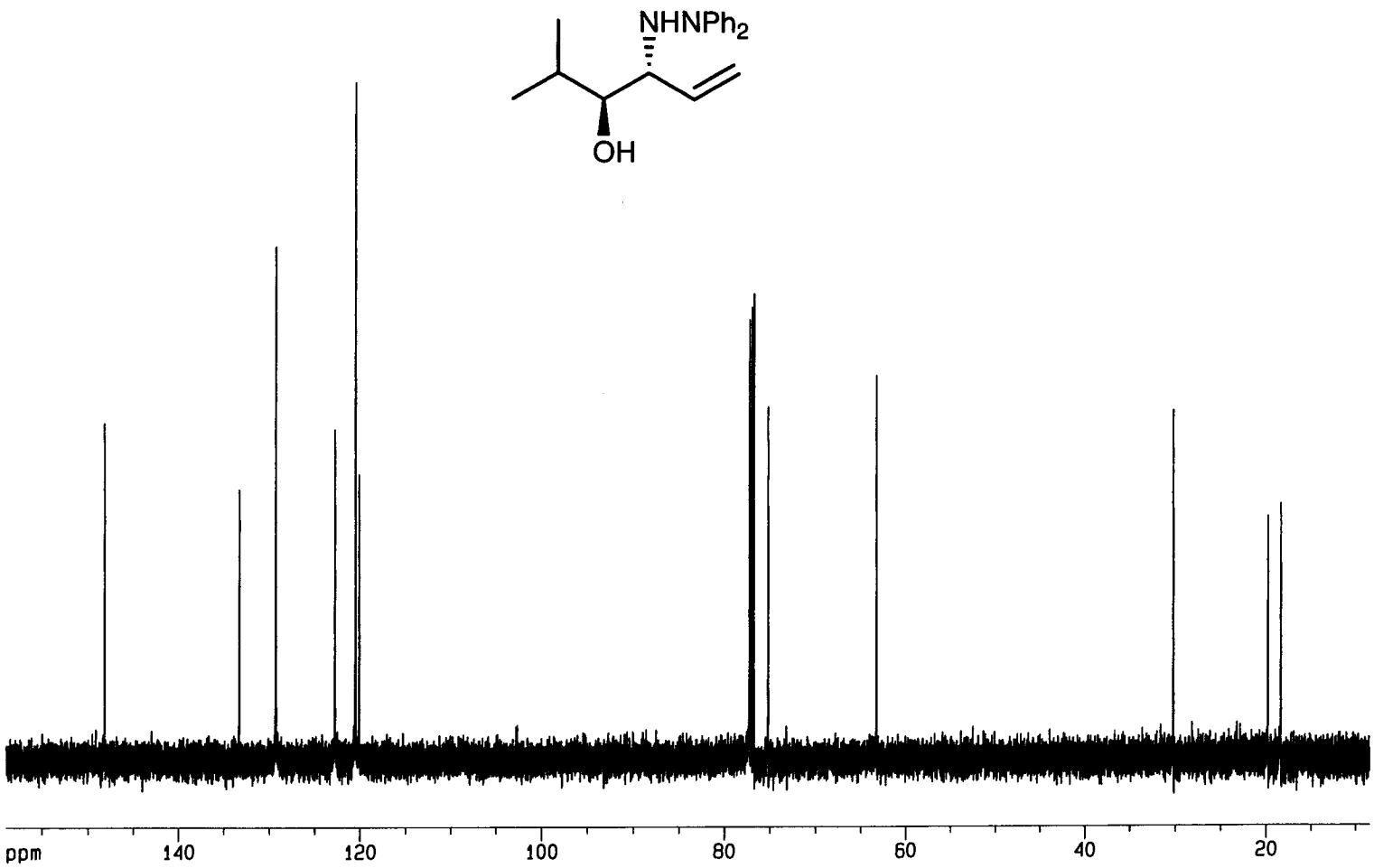
^{13}C NMR 5c



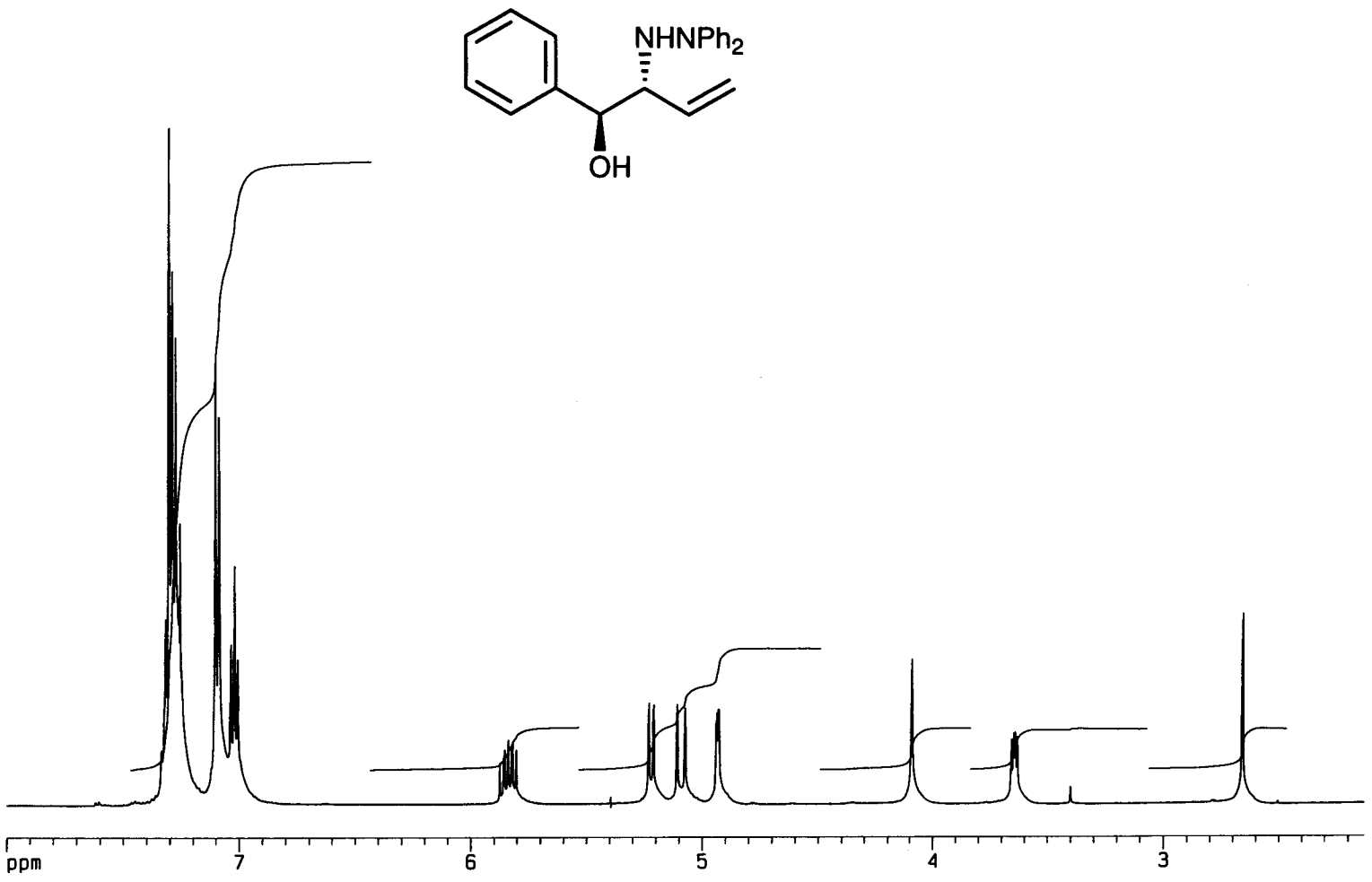
^{1}H NMR 5d



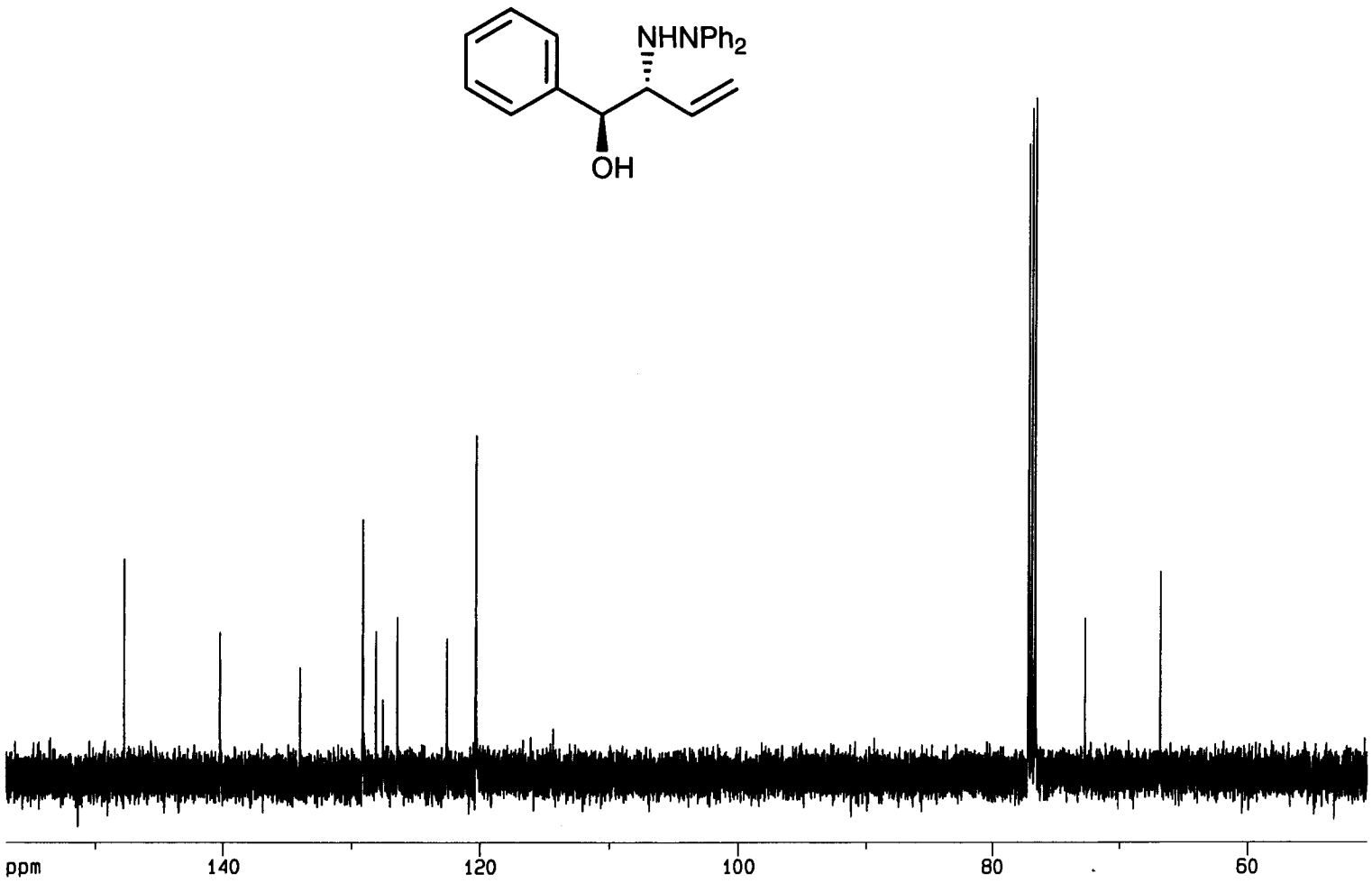
^{13}C NMR 5d



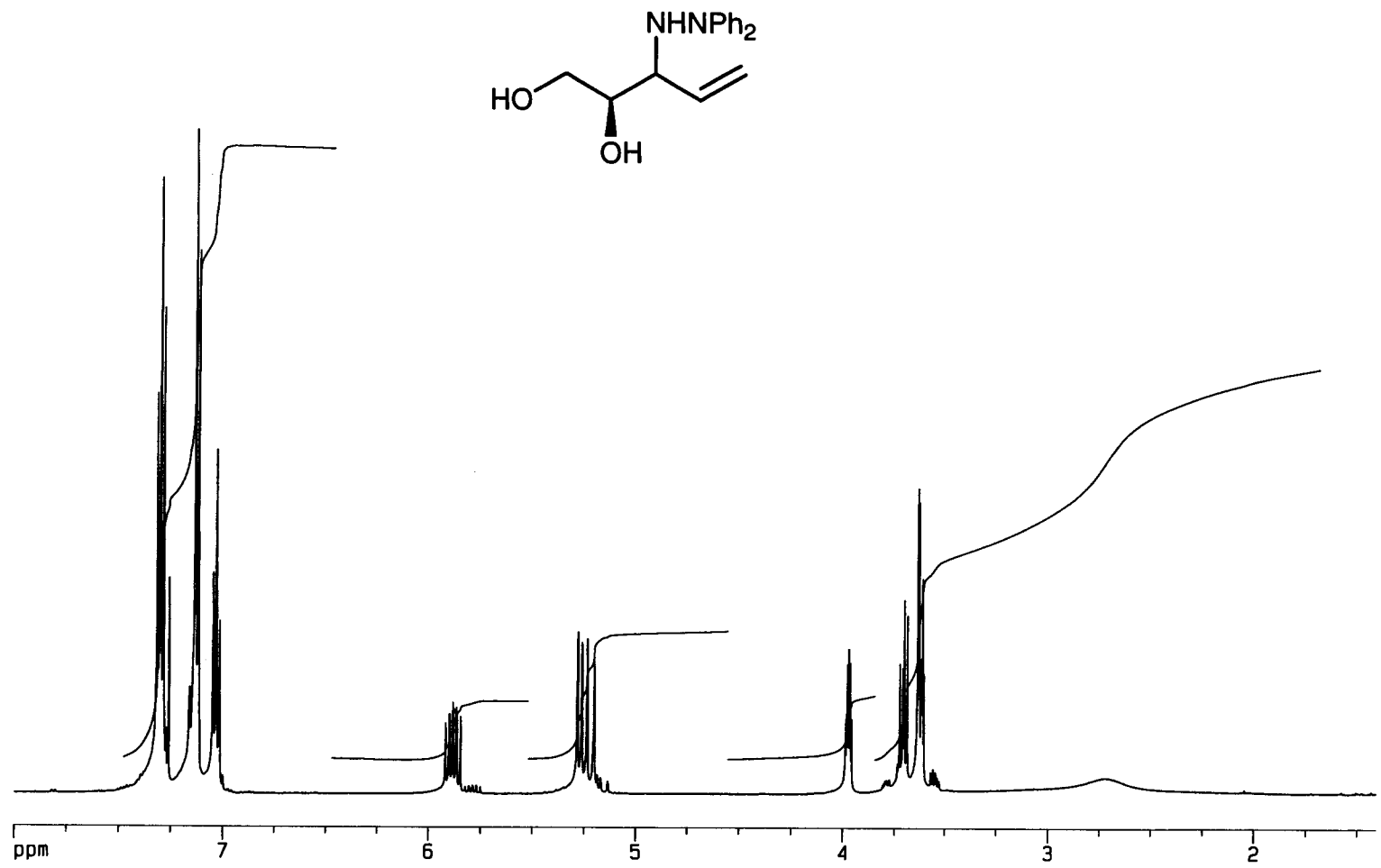
^{1}H NMR 5e



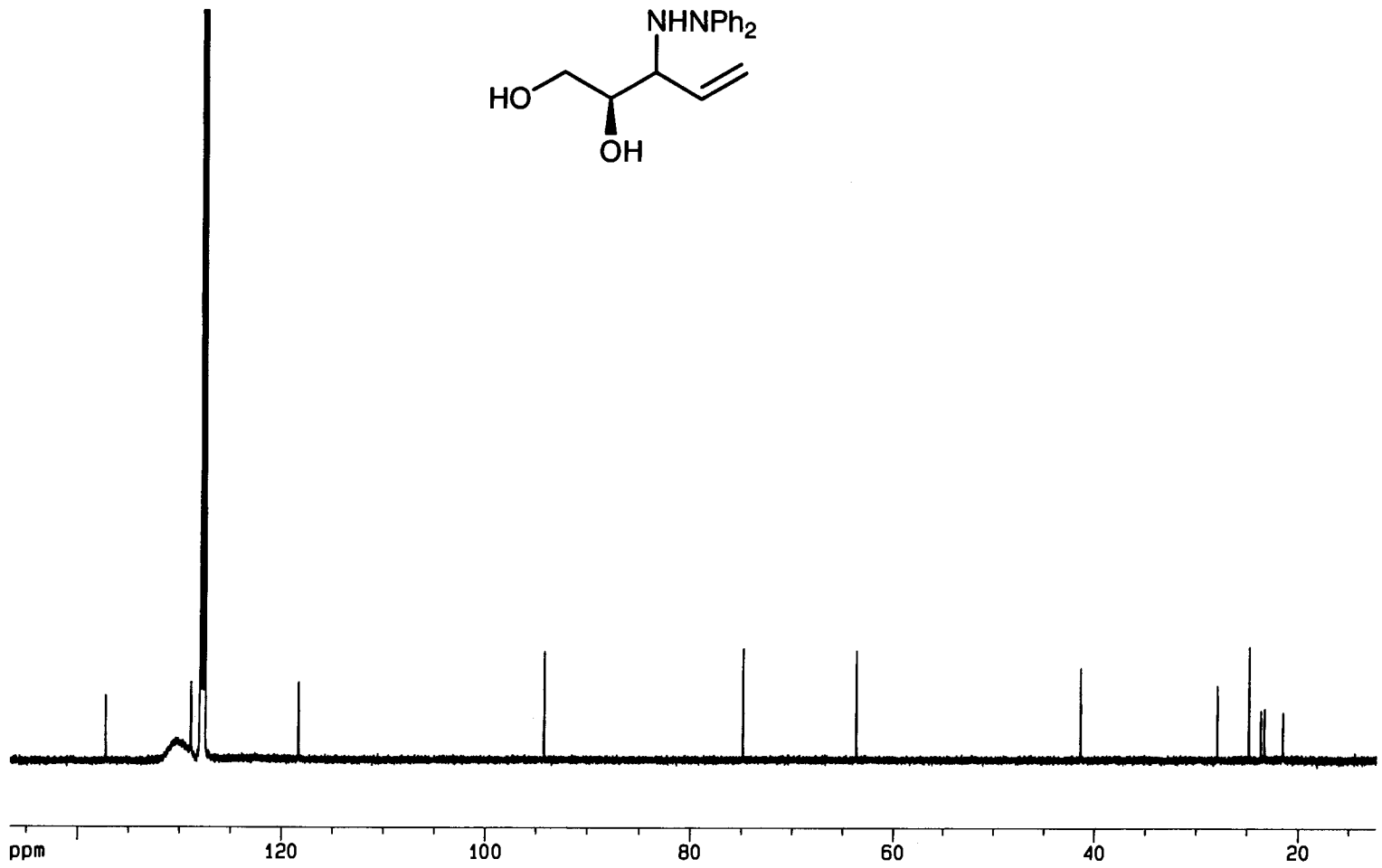
^{13}C NMR 5e



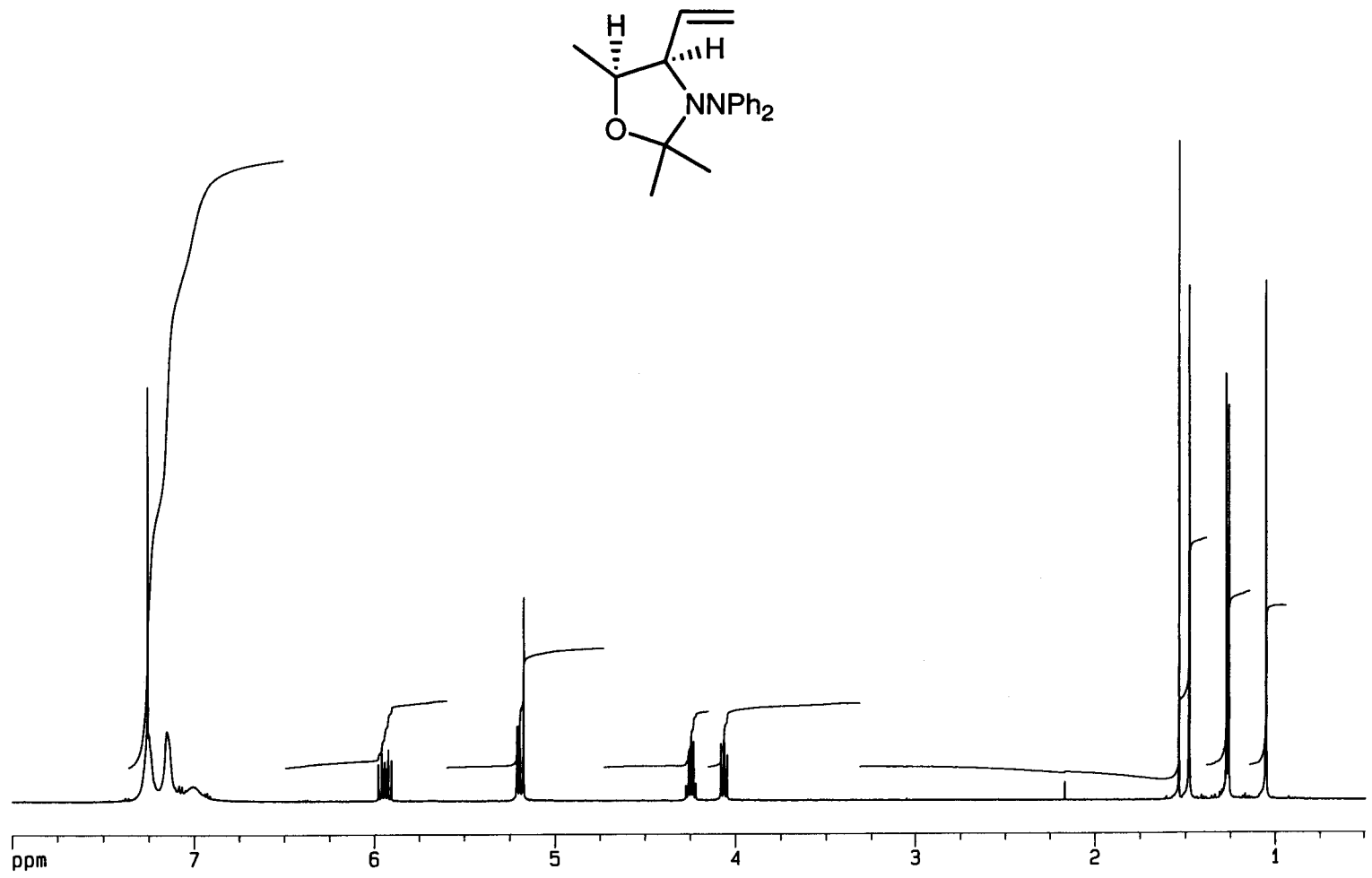
^{1}H NMR 5f (anti/syn 91:9)



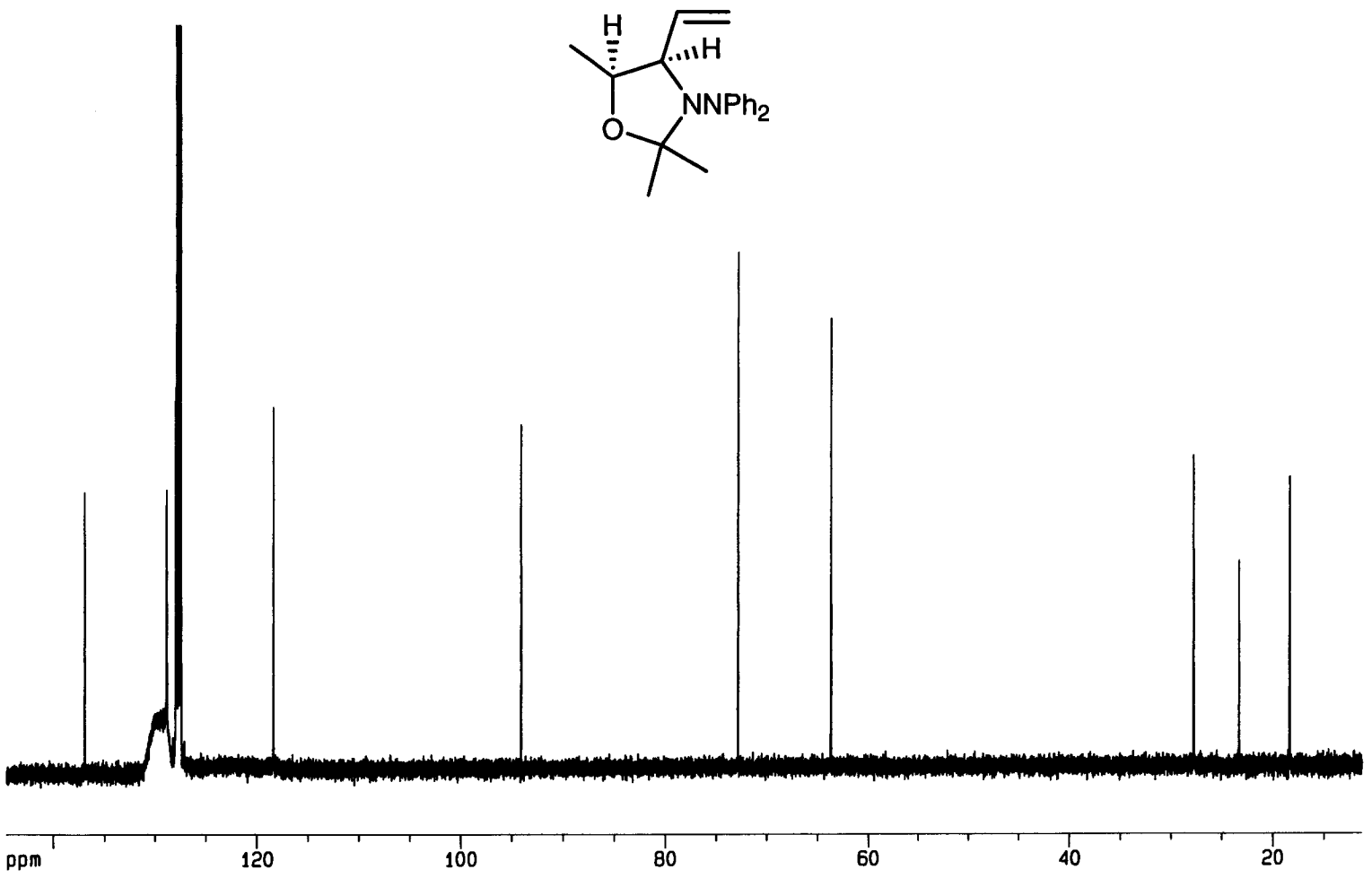
^{13}C NMR 5f (anti/syn 91:9)



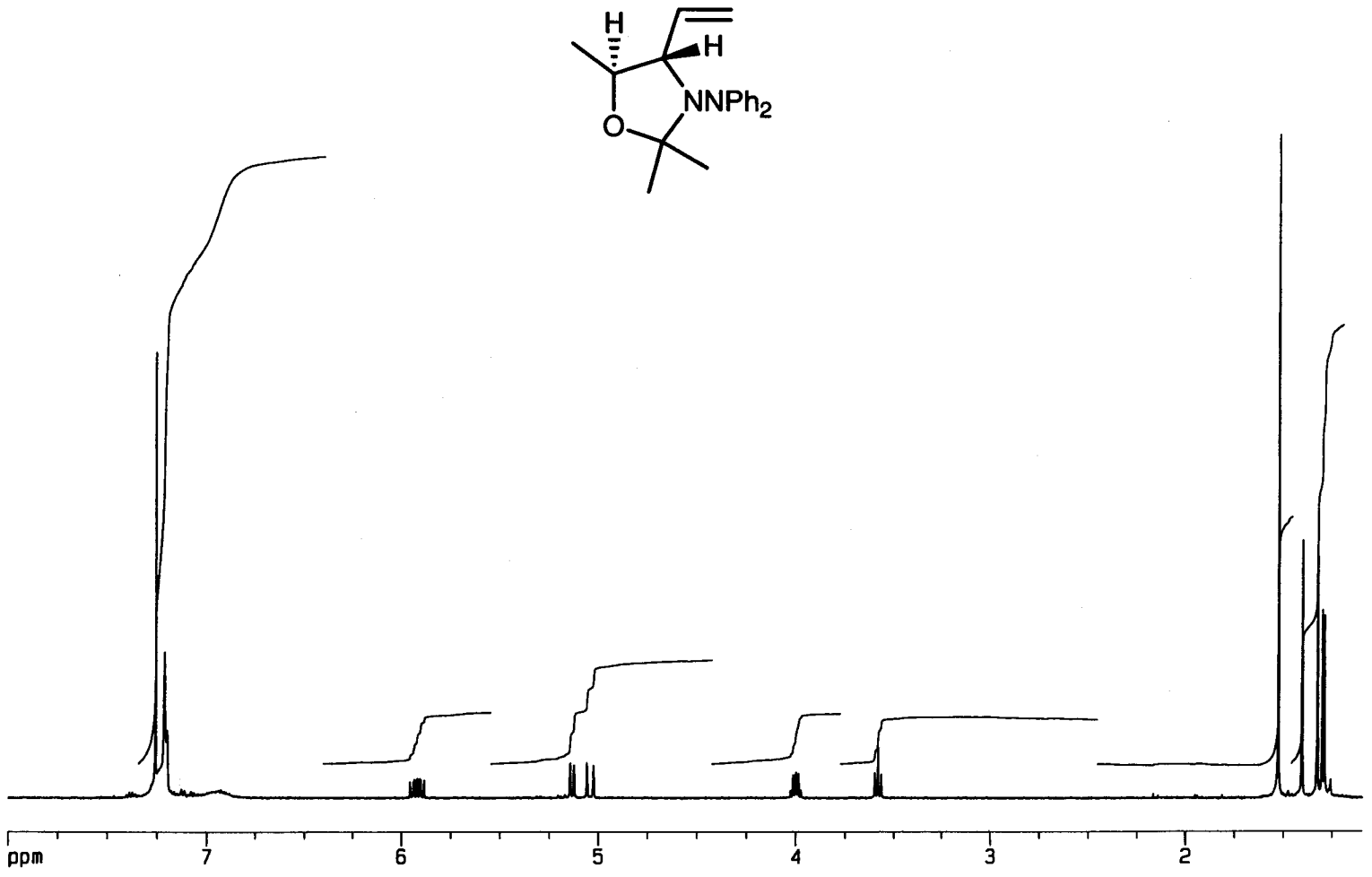
^{1}H NMR 6b (cis)



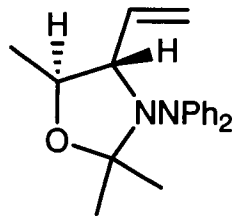
^{13}C NMR **6b** (cis)



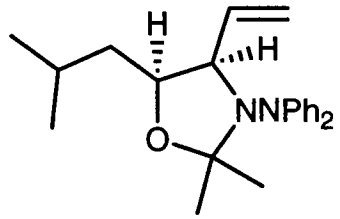
^{1}HNMR 6b (trans)

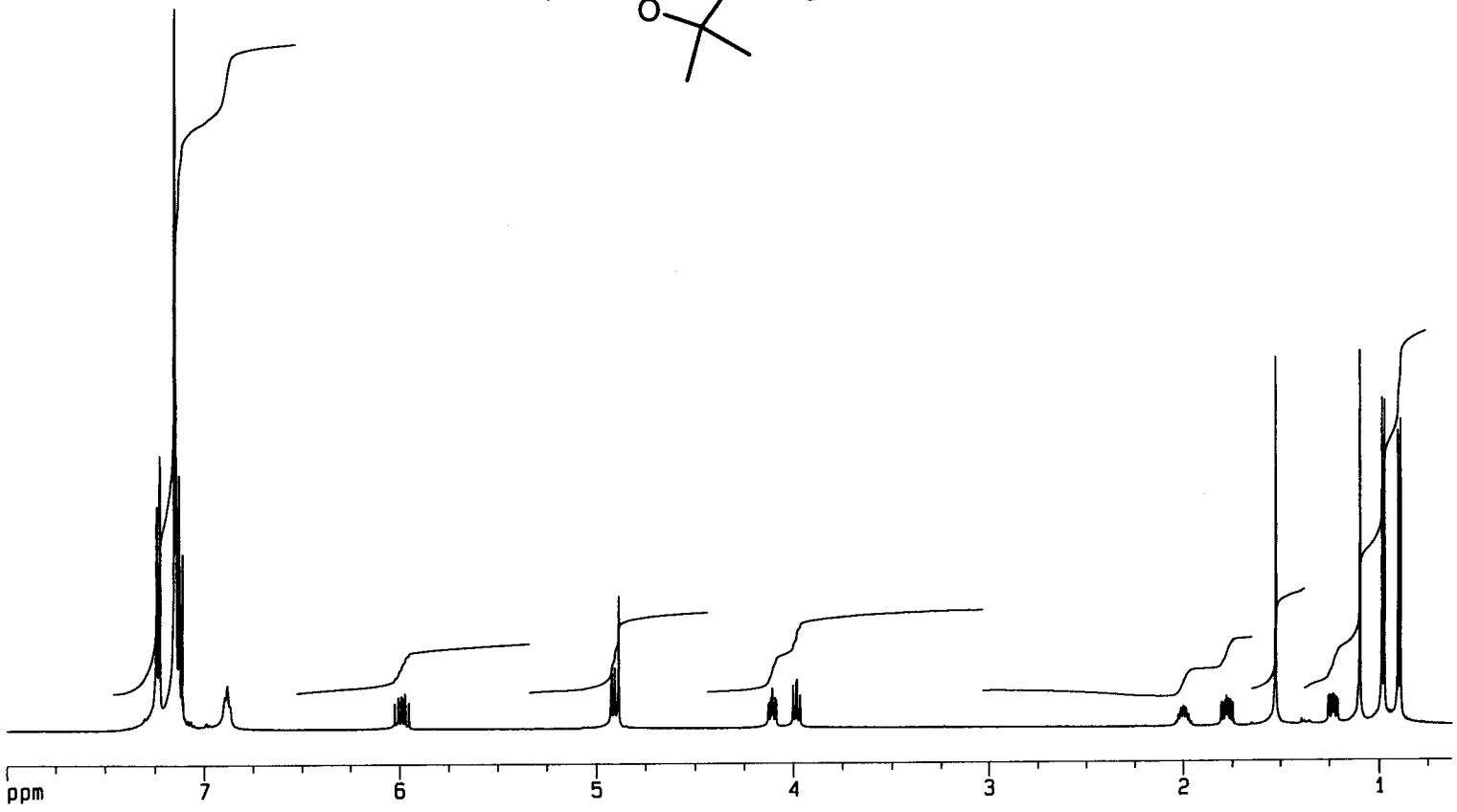


^{13}C NMR 6b (trans)

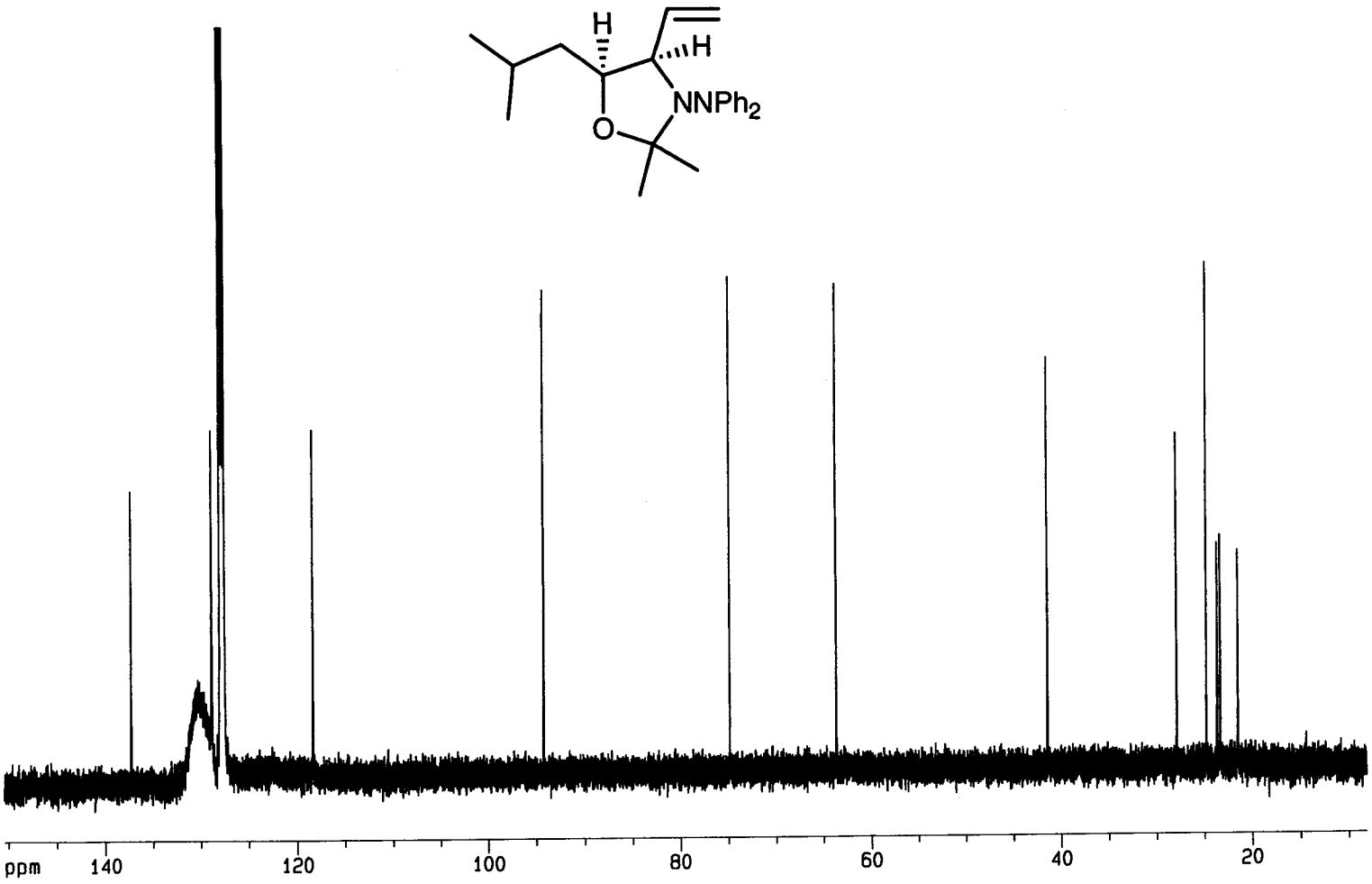


^{1}HNMR 6c

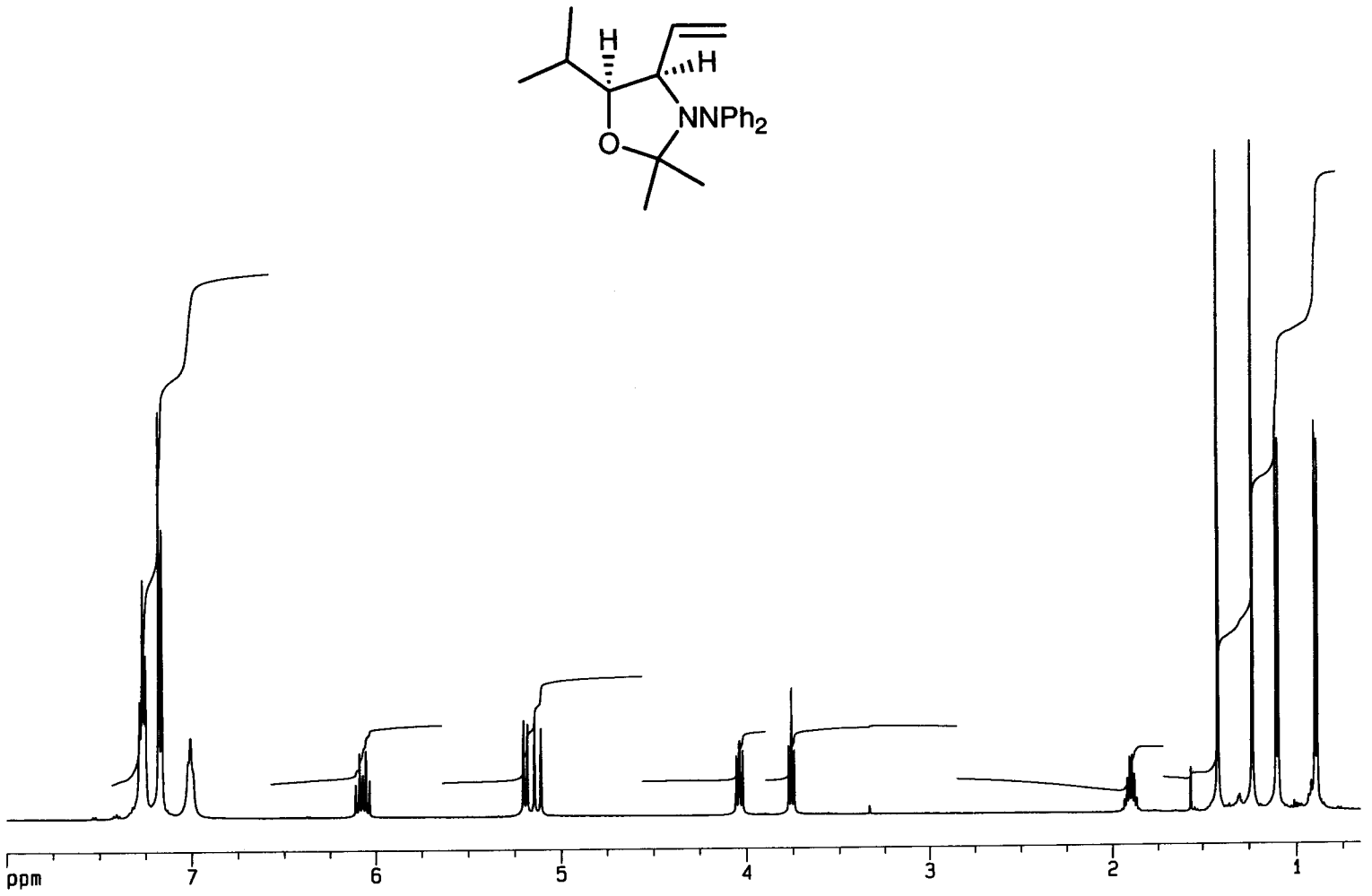




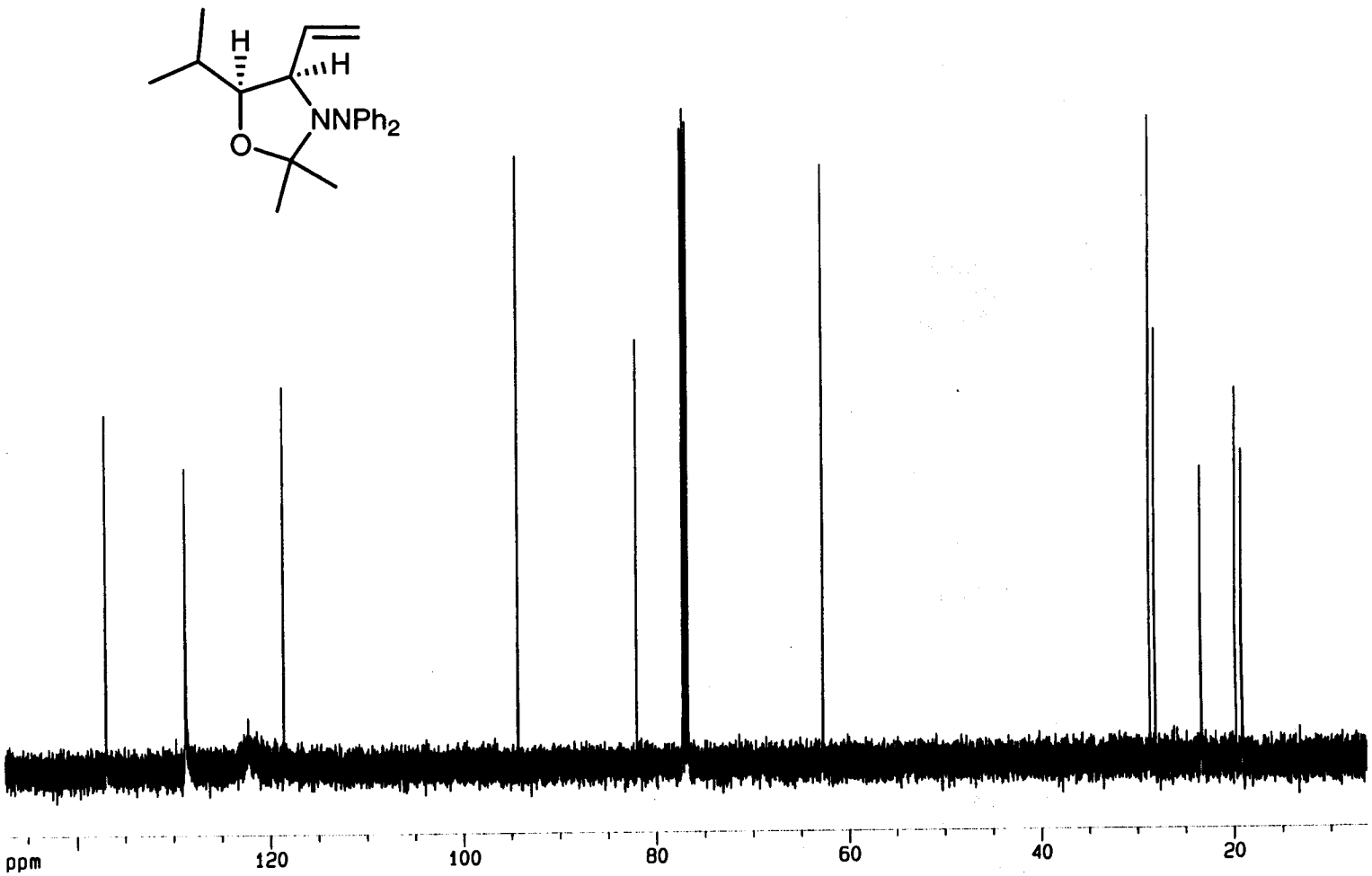
^{13}C NMR 6c



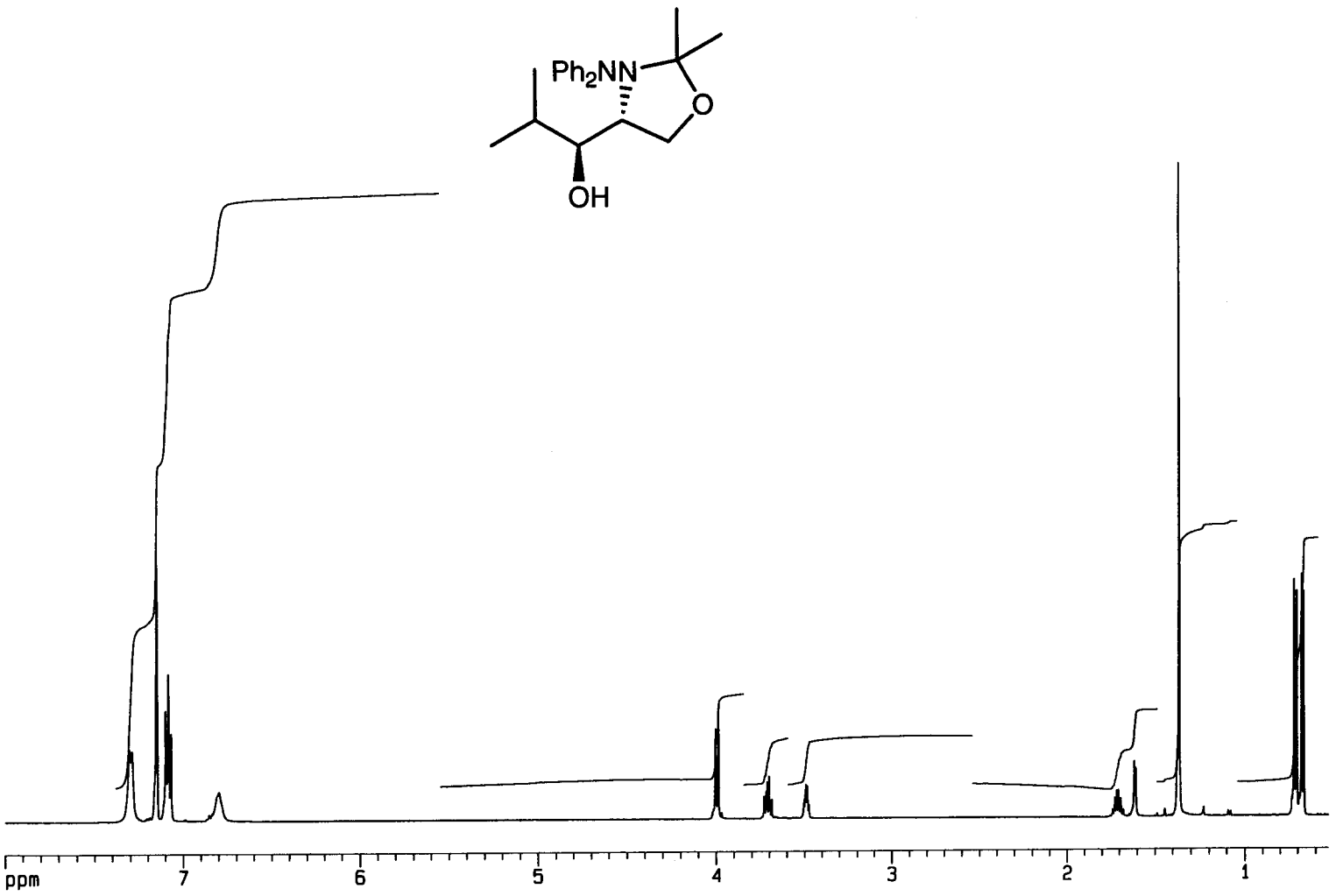
^{1}H NMR 6d



^{13}C NMR 6d



^{1}HNMR isomer of acetonide i



^{13}C NMR isomer of acetonide i