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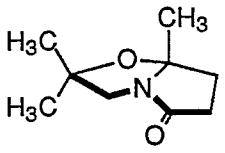
Experimental Section

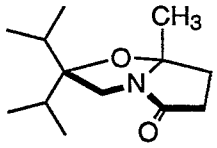
General Experimental: All reactions were carried out under argon in septum stoppered flasks. Unless otherwise noted, reagents were added by syringe, organic extracts were dried over anhydrous Na_2SO_4, filtered through a fritted glass funnel and concentrated with a rotary evaporator at aspirator pressure (20-40 mm). Flash chromatography was performed with Amicon (200-400 mesh) silica gel. Thin layer chromatography (TLC) was performed with Merck F-254 silica gel plates.

Unless otherwise noted, starting materials were obtained from commercial suppliers and used without further purification. Tetrahydrofuran (THF) and ether were distilled under N_2 from sodium/benzophenone immediately prior to use. Dichloromethane (CH_2Cl_2) and toluene were distilled from CaH_2 immediately prior to use.

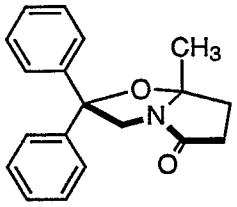
^1H NMR spectra were recorded with a Bruker AC-300 spectrometer. ^{13}C NMR spectra were recorded with the same instrument at 75 MHz. All NMR spectra were recorded in $CDCl_3$ and chemical shifts are expressed in ppm relative to internal $CHCl_3$ (7.27 ppm). Significant NMR data are tabulated in order: multiplicity (s, singlet; d, doublet; t, triplet; m, multiplet), coupling constants in hertz, and number of protons. Infrared spectra were recorded on a Perkin-Elmer 1600 Fourier Transform Infrared Spectrometer. Microanalyses were performed by Atlantic Microlab, Inc., Norcross, Georgia.



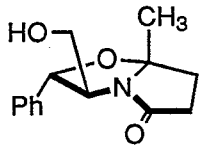
General Procedure for Bicyclic Lactam Formation: Lactam (5a, R = Me). 2-Amino-1-hydroxy-1-methyl propane (2.45 g, 27.0 mmol) and levulinic acid (**7**) (3.13 g, 27.0 mmol) were dissolved in toluene (50 mL). The flask was equipped with Dean-Stark trap and the solution was heated to reflux. After 16h the solution was cooled, washed with saturated aqueous $NaHCO_3$, dried and concentrated. Chromatography on silica gel with ethyl acetate afforded 4.06 g (89%) of lactam (**5a**) as a light yellow oil. IR (neat) 2974, 1713 cm^{-1}. ^1H NMR (300 MHz) δ 0.98 (s, 3H), 1.24 (s, 3H), 1.30 (s, 3H), 2.06 (m, 2H), 2.37 (m, 1H), 2.53 (m, 1H), 2.81 (d, J = 11.6, 1H), 3.74 (d, J = 11.6, 1H). ^{13}C NMR (75 MHz) δ 26.6, 27.7, 28.0, 32.3, 34.8, 52.8, 81.3, 99.4, 177.4. Anal. Calcd for $C_9H_{15}NO_2$: C, 63.88; H, 8.93. Found: C, 63.95; H, 8.97.



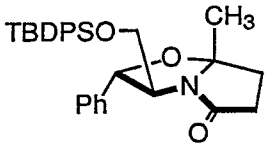
Lactam (5b, R = i-Pr). Light yellow oil. IR (neat) 2974, 1713 cm^{-1}. ^1H NMR (300 MHz) δ 0.79 (d, J = 6.7, 3H), 0.83 (d, J = 6.7, 3H), 0.90 (d, J = 6.7, 3H), 0.95 (d, J = 6.7, 3H), 1.42 (s, 3H), 1.76 (m, 1H), 2.03 (m, 1H), 2.15 (m, 2H), 2.36 (m, 1H), 2.61 (m, 1H), 2.95 (d, J = 12.2, 1H), 3.72 (d, J = 12.2, 1H). ^{13}C NMR (75 MHz) δ 17.9, 18.0, 18.4, 18.6, 27.0, 32.7, 33.3, 33.8, 35.8, 44.0, 92.2, 99.4, 175.0.



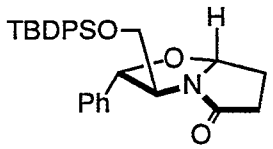
Lactam (5c, R = Ph). White solid, mp. 95-96 °C (hexane/EtOAc). IR (neat) 2977, 1716 cm^{-1}. ^1H NMR (300 MHz) δ 1.47 (s, 3H), 2.09 (m, 3H), 2.48 (m, 1H), 3.41 (d, *J* = 12.3, 1H), 4.90 (d, *J* = 12.3, 1H), 7.11-7.33 (m, 10H). ^{13}C NMR (75 MHz) δ 27.1, 32.8, 34.6, 53.0, 89.0, 101.0, 126.1, 126.8, 127.7, 128.0, 128.80, 128.82, 144.1, 145.3, 177.7. Anal. Calcd for $C_{19}H_{19}NO_2$: C, 77.79; H, 6.53. Found: C, 77.66; H, 6.61.



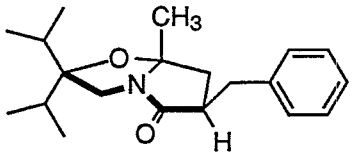
Lactam (9). Colorless crystals. mp. 89-90 °C (hexanes/EtOAc). $[\alpha]_D^{23}$ +65.3° (c 1.4, EtOH). IR (neat) 3407, 2978, 1686 cm^{-1}. ^1H NMR (300 MHz) δ 1.65 (s, 3H), 2.39 (m, 2H), 2.60 (m, 1H), 2.85 (m, 2H), 3.70 (m, 1H), 3.76 (m, 2H), 5.14 (d, J = 7.6, 1H), 7.35 (m, 5H). ^{13}C NMR (75 MHz) δ 24.8, 33.4, 35.3, 63.1, 65.0, 82.9, 100.1, 126.3, 128.7, 128.8, 178.6.



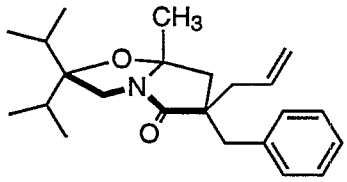
General Silylation Procedure: Lactam (10). To a CH_2Cl_2 solution (100 mL) of lactam **9** (8.0 g, 33.7 mmol) and TBDPS-Cl (11.1 g, 40.5 mmol) was added neat imidazole (2.8 g, 41.0 mmol). After stirring for 24h at 25 °C the slurry was filtered through celite and concentrated. Recrystallization from hexanes/ethyl acetate afforded lactam **10** (13.9 g, 28.6 mmol) in 85% yield as colorless crystals. Mp. 127-128 °C (hexanes/EtOAc). $[\alpha]_D^{23}$ +38.7° (c 2.0, EtOH). IR (neat) 3409, 2976, 1687 cm^{-1}. ^1H NMR (300 MHz) δ 1.00 (s, 9H), 1.53 (s, 3H), 2.23 (m, 2H), 2.49 (m, 1H), 2.74 (m, 1H), 3.75 (m, 1H), 3.87 (m, 2H), 5.30 (d, J = 6.7, 1H), 7.30 (m, 9H), 7.61 (m, 6H). ^{13}C NMR (75 MHz) δ 19.5, 25.3, 26.8, 27.1, 33.6, 34.9, 63.9, 64.0, 83.1, 100.5, 126.8, 127.9, 128.0, 128.5, 128.8, 129.8, 130.0, 130.1, 133.1, 133.3, 135.0, 135.8, 135.9, 139.3, 178.3. Anal. Calcd for $C_{19}H_{19}NO_2$: C, 74.19; H, 7.26. Found: C, 74.04; H, 7.31.



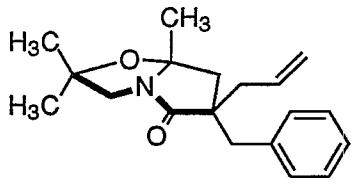
Lactam (12).[8] Colorless oil. $[\alpha]_D^{23}$ +28.2° (c 1.5, EtOH). IR (neat) 2930, 1719 cm^{-1}. ^1H NMR (300 MHz) δ 1.06 (s, 9H), 2.17 (m, 1H), 2.37 (m, 1H), 2.60 (m, 2H), 3.78 (m, 1H), 3.95 (m, 2H), 5.15 (d, *J* = 5.8, 2H), 5.36 (dd, *J* = 6.1, 2.1, 1H), 7.16-7.42 (m, 11H), 7.61 (m, 4H). ^{13}C NMR (75 MHz) δ 19.2, 24.3, 26.9, 31.3, 63.5, 63.9, 82.6, 93.1, 126.3, 127.8, 127.9, 128.3, 128.6, 129.8, 129.9, 133.0, 135.6, 135.7, 139.1, 179.3.



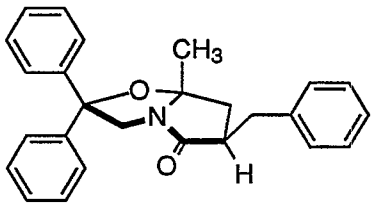
General Procedure for Bicyclic Lactam Alkylation: Lactam (6b, R=i-Pr, R^1=H, R^2=Bn). Lactam **5b** (400 mg, 1.80 mmol) was dissolved in THF (20 mL) and cooled to -78 °C. s-BuLi (1.65 mL, 1.1M in hexane) was added dropwise to the solution over 5 min. After 2h the solution was placed in a 0 °C bath for 15 min and subsequently recooled to -78 °C. To the stirring -78 °C solution was added benzyl bromide (0.34 g, 1.97 mmol) dropwise over 5 min. After 2h the solution was quenched by addition of saturated aqueous NH_4Cl solution (4 mL). Ethyl acetate (20 mL) was added to the mixture and the resulting solution was separated, dried and concentrated. Purification on silica (hexanes/EtOAc, 1:1) afforded 516 mg (91%) of **6b** as a clear oil. IR (neat) 2965, 1707 cm^{-1}. ^1H NMR (300 MHz) δ 0.88 (app t, J = 7.0, 6H), 0.99 (app t, J = 7.0, 6H), 1.23 (s, 3H), 1.81 (m, 1H), 2.05 (m, 2H), 2.43 (dd, J = 14.0, 10.1, 1H), 3.01 (m, 4H), 3.89 (d, J = 12.2, 1H), 7.27 (m, 5H). ^{13}C NMR (75 MHz) δ 17.9, 18.1, 18.5, 18.6, 28.8, 33.4, 33.6, 37.5, 38.7, 45.3, 46.9, 91.3, 98.5, 126.5, 128.4, 129.1, 138.6, 178.1.



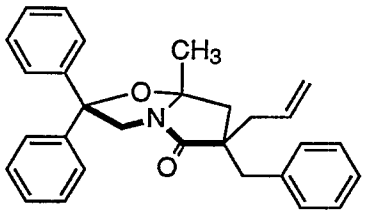
Lactam (6b, R=i-Pr, R^1=Bn, R^2=Allyl). White solid, mp. 65-66 °C (hexanes). IR (neat) 2962, 1709 cm^{-1}. ^1H NMR (300 MHz) δ 0.53 (d, J = 6.7, 3H), 0.74 (d, J = 6.7, 3H), 0.95 (m, 6H), 1.50 (s, 3H), 2.02 (m, 2H), 2.32 (d, J = 13.4, 1H), 2.47 (m, 2H), 2.74 (d, J = 13.7, 1H), 2.96 (d, J = 11.9, 1H, 3.05 (d, J = 13.7, 1H), 3.84 (d, J = 11.9, 1H), 5.20 (m, 2H), 5.93 (m, 1H), 7.25 (m, 5H). ^{13}C NMR (75 MHz) δ 17.0, 19.1, 19.2, 28.2, 31.8, 34.6, 40.3, 42.8, 44.0, 45.2, 52.9, 90.5, 96.2, 118.8, 126.4, 128.0, 131.2, 133.6, 137.3, 179.0.



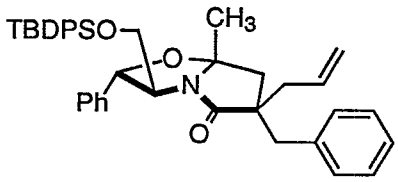
Lactam (6a, R=Me, R^1=Bn, R^2=Allyl). IR (neat) 2976, 1707 cm^{-1}. ^1H NMR (300 MHz) δ 0.61 (s, 3H), 1.30 (s, 3H), 1.44 (s, 3H), 1.98 (d, *J* = 13.7, 1H), 2.40 (m, 2H), 2.75 (d, *J* = 13.7, 1H), 2.94 (d, *J* = 11.5, 1H), 3.04 (d, *J* = 13.4, 1H), 3.81 (d, *J* = 11.7, 1H), 5.17 (m, 2H), 5.84 (m, 1H), 7.21 (m, 5H). ^{13}C NMR (75 MHz) δ 27.7, 28.6, 42.0, 42.3, 43.4, 52.8, 53.2, 80.7, 96.9, 119.2, 126.7, 128.3, 131.4, 133.8, 137.4, 180.4.



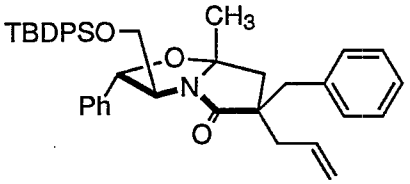
Lactam (6c, R=Ph, R^1=H, R^2=Ph). Yellow oil. IR (neat) 3026, 2978, 1714 cm^{-1}. ^1H NMR (300 MHz) δ 1.24 (s, 3H), 1.91 (dd, *J* = 14.3, 4.8, 1H), 2.40 (m, 1H), 2.62 (m, 1H), 2.79 (m, 1H), 2.95 (dd, *J* = 13.5, 4.8, 1H), 3.57 (d, *J* = 12.2, 1H), 4.98 (d, *J* = 11.9, 1H), 7.09-7.38 (m, 15H). ^{13}C NMR (75 MHz) δ 27.3, 37.0, 37.2, 44.9, 53.9, 87.7, 99.3, 125.5, 126.0, 126.4, 127.1, 127.3, 128.1, 128.3, 129.0, 138.3, 144.0, 145.0, 180.3.



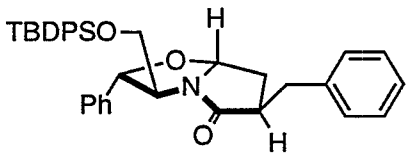
Lactam (6c, R=Ph, R^1=Bn, R^2=Allyl). Yellow oil. IR (neat) 3027, 2977, 1712 cm^{-1}. ^1H NMR (300 MHz) δ 1.54 (s, 3H), 1.79 (d, *J* = 11.8, 1H), 1.86 (d, *J* = 12.0, 1H), 2.15 (m, 1H), 2.40 (dd, *J* = 13.5, 6.4, 1H), 2.52 (d, *J* = 14.0, 1H), 2.67 (d, *J* = 13.7, 1H), 3.58 (d, *J* = 11.9, 1H), 5.11 (m, 2H), 5.76 (m, 1H), 7.03 (m, 2H), 7.19-7.48 (m, 13H). ^{13}C NMR (75 MHz) δ 27.3, 41.5, 41.8, 42.8, 51.3, 52.9, 87.8, 97.8, 118.8, 125.5, 126.4, 126.6, 127.2, 127.5, 128.0, 128.30, 128.33, 130.5, 133.9, 137.2, 143.7, 145.3, 181.4.



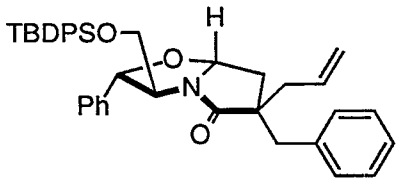
Lactam (11, R^1=Bn, R^2=Allyl). Clear oil. $[\alpha]_D^{23}$ +63.8° (c 1.9, EtOH). IR (neat) 3067, 2965, 1709 cm^{-1}. ^1H NMR (300 MHz) δ 1.12 (s, 9H), 1.60 (s, 3H), 2.09 (d, *J* = 13.8, 1H), 2.60 (m, 4H), 3.24 (d, *J* = 13.4, 1H), 3.81 (m, 2H), 3.94 (m, 1H), 5.15 (d, *J* = 6.7, 1H), 5.23 (m, 2H), 5.93 (m, 1H), 6.81 (d, *J* = 8.0, 2H), 7.19-7.44 (m, 14H), 7.71 (m, 4H). ^{13}C NMR (75 MHz) δ 19.3, 26.3, 27.0, 41.2, 41.7, 44.1, 53.5, 64.0, 64.9, 81.6, 97.3, 119.3, 126.5, 127.9, 128.0, 128.2, 128.5, 128.6, 129.9, 130.0, 131.3, 133.0, 133.2, 133.7, 135.7, 135.8, 135.9, 137.7, 139.3, 181.7.



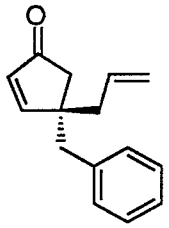
Lactam (11, R^1=Allyl, R^2=Bn). Clear oil. $[\alpha]_D^{23}$ +11.8° (c 1.3, EtOH). IR (neat) 3067, 2965, 1709 cm^{-1}. ^1H NMR (300 MHz) δ 0.87 (s, 3H), 1.05 (s, 9H), 2.06 (d, *J* = 14.4, 1H), 2.27 (m, 1H), 2.44 (d, *J* = 14.3, 1H), 2.59 (m, 1H), 2.65 (d, *J* = 13.5, 1H), 3.08 (d, *J* = 13.4, 1H), 3.71-3.98 (m, 3H), 5.05 (d, *J* = 7.0, 1H), 5.15 (m, 2H), 5.73 (m, 1H), 7.19 (m, 10H), 7.35 (m, 6H), 7.68 (m, 4H). ^{13}C NMR (75 MHz) δ 19.1, 24.8, 26.7, 40.7, 43.2, 44.0, 53.2, 63.8, 64.9, 80.9, 97.3, 119.3, 126.2, 126.7, 127.7, 128.0, 128.1, 128.3, 129.7, 130.4, 132.8, 133.9, 135.5, 137.0, 139.3, 182.1.



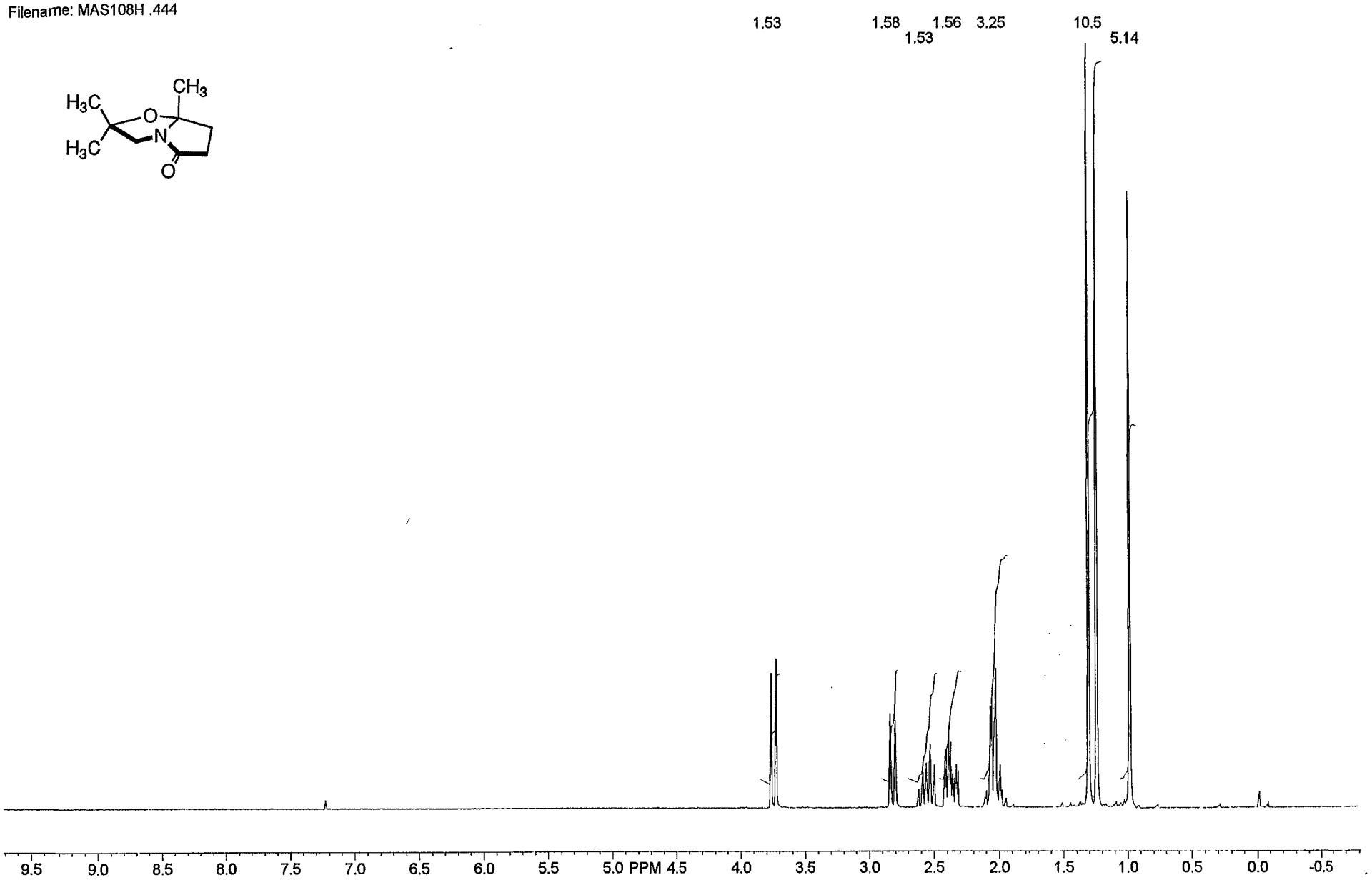
Lactam (13, R=H, R'=Bn). White solid, mp. 109-110 °C. $[\alpha]_D^{23}$ = +8.2° (c 0.8, EtOH). IR (neat) 3029, 2930, 1716 cm^{-1}. ^1H NMR (300 MHz) δ 1.06 (s, 9H), 2.07 (m, 1H), 2.25 (m, 1H), 2.80 (dd, *J* = 13.7, 9.1, 1H), 3.04 (m, 1H), 3.19 (dd, *J* = 13.7, 4.5, 1H), 3.78 (m, 1H), 3.90 (m, 1H), 4.05 (m, 1H), 5.06 (d, *J* = 6.1, 1H), 5.14 (dd, *J* = 4.6, 1.2, 1H), 7.20 (m, 10H), 7.34 (m, 6H), 7.64 (d, J = 6.5, 4H). ^{13}C NMR (75 MHz) δ 19.1, 26.8, 29.3, 37.7, 44.2, 63.5, 64.5, 82.3, 91.5, 126.2, 126.5, 127.7, 128.1, 128.4, 128.5, 128.9, 129.7, 129.8, 132.8, 135.5, 138.3, 139.1, 181.4.



Lactam (13, R=Bn, R'=Allyl). Yellow oil. $[\alpha]_D^{23}$ = +60.0° (c 1.0, EtOH). IR (neat) 3069, 2929, 1706 cm^{-1}. ^1H NMR (300 MHz) δ 1.02 (s, 9H), 2.20 (m, 3H), 2.50 (dd, *J* = 13.4, 6.4, 1H), 2.63 (d, *J* = 13.4, 1H), 3.15 (d, *J* = 13.4, 1H), 3.65 (m, 2H), 3.91 (dd, *J* = 10.7, 3.6, 1H), 5.05 (d, *J* = 6.5, 1H), 5.11 (m, 2H), 5.81 (m, 1H), 6.73 (dd, J = 7.9, 2.1), 7.10-7.38 (m, 16H), 7.60 (m, 4H). ^{13}C NMR (75 MHz) δ 19.3, 26.9, 33.9, 42.5, 44.0, 53.7, 62.9, 63.7, 82.5, 90.3, 119.1, 126.3, 126.5, 127.8, 127.9, 128.2, 128.4, 128.5, 129.9, 130.0, 131.1, 132.9, 133.4, 135.6, 135.7, 137.6, 139.0, 179.9.



Cyclopentenone (4, R^1=Allyl, R^2=Bn). Clear oil. $[\alpha]_D^{23}$ -62.6° (c 1.7, EtOH), (lit.[5] $[\alpha]_D^{23}$ -64.1°). IR (neat) 3028, 2916, 1714 cm^{-1}. ^1H NMR (300 MHz) δ 2.27 (d, *J* = 1.5, 2H), 2.30 (m, 2H), 2.77 (d, *J* = 3.4, 1H), 2.90 (d, *J* = 3.4, 1H), 5.06 (m, 2H), 5.65 (m, 1H), 6.04 (d, *J* = 5.8, 1H), 7.07 (m, 2H), 7.25 (m, 3H), 7.44 (d, *J* = 5.8, 3H). ^{13}C NMR (75 MHz) δ 42.8, 44.6, 45.3, 49.1, 119.3, 126.7, 128.2, 130.3, 133.2, 133.4, 136.7, 170.2, 213.0.



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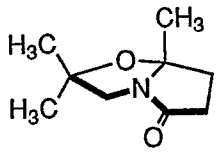

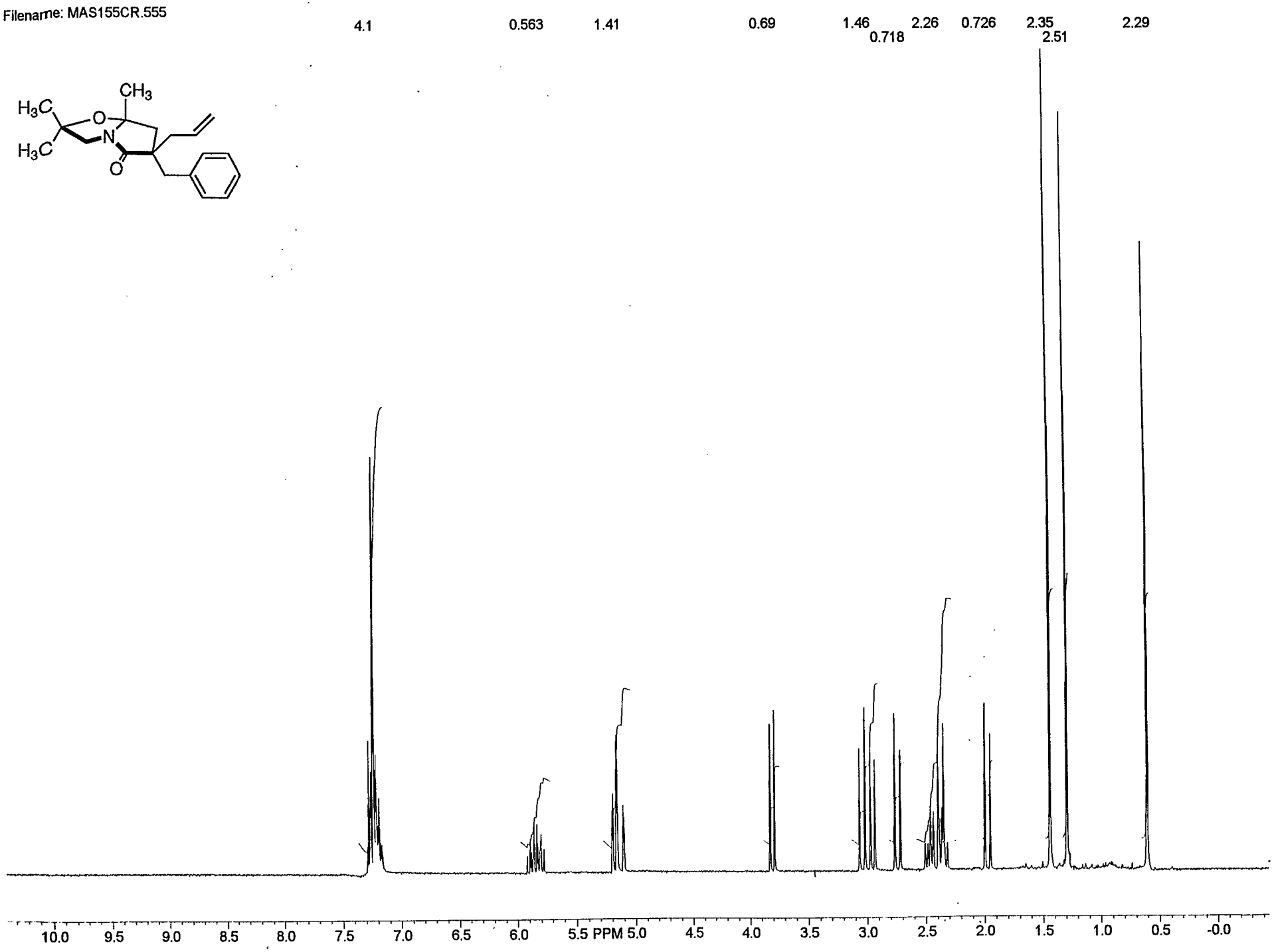

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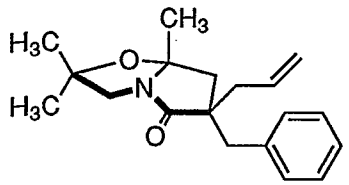

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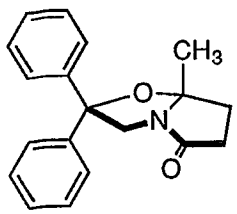

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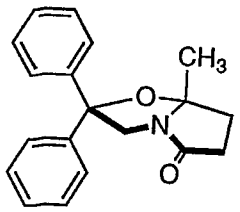

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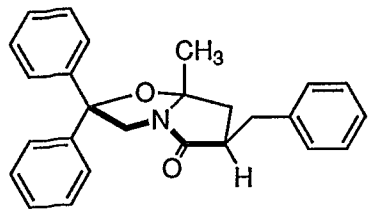

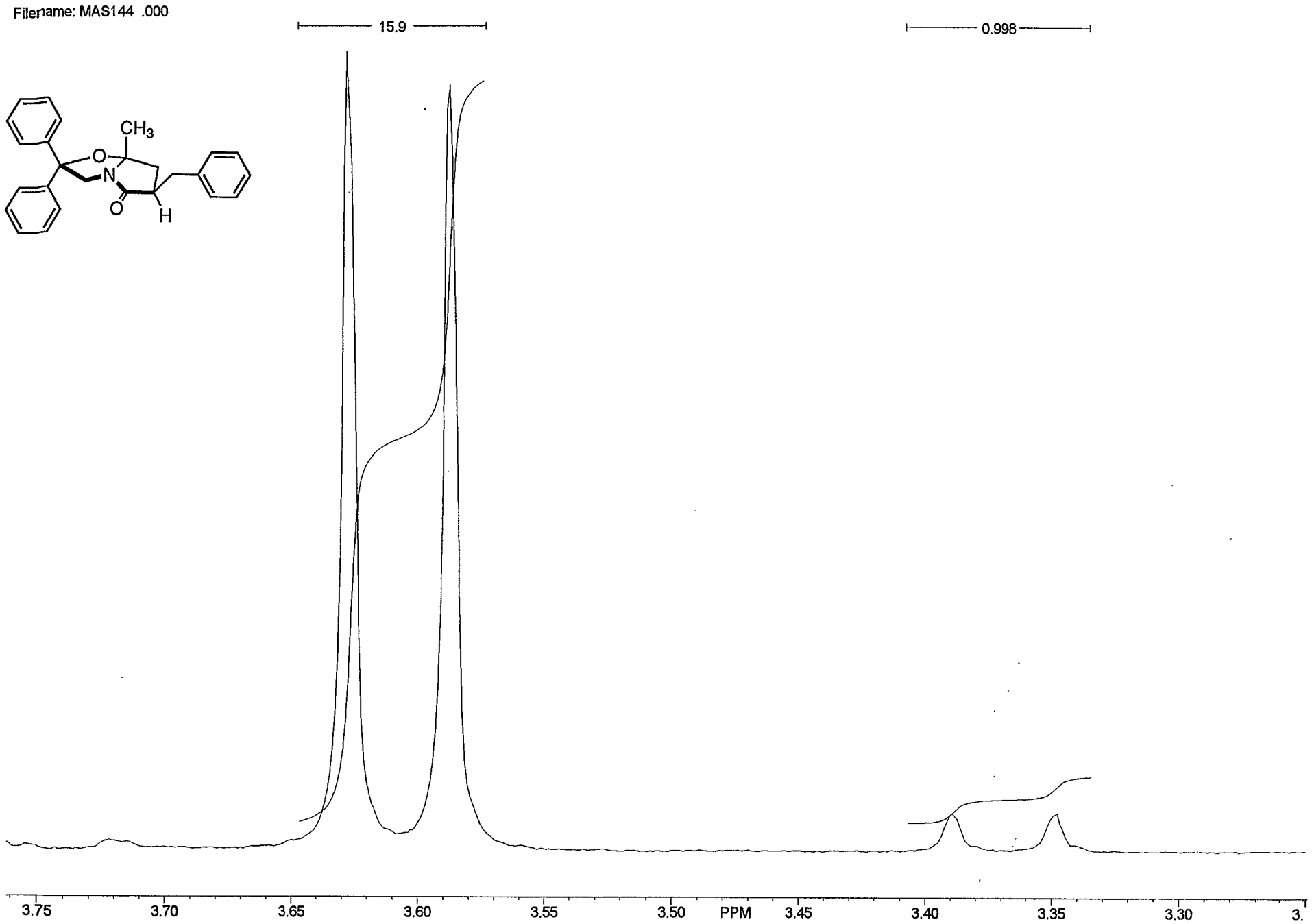

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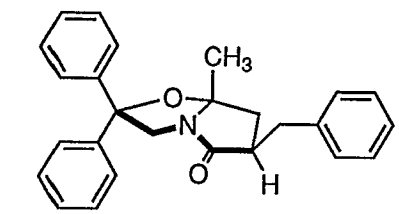
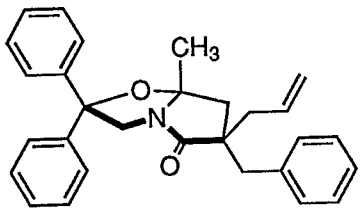


Filename: MAS152H .007



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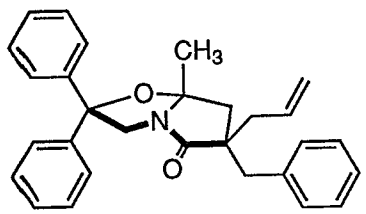
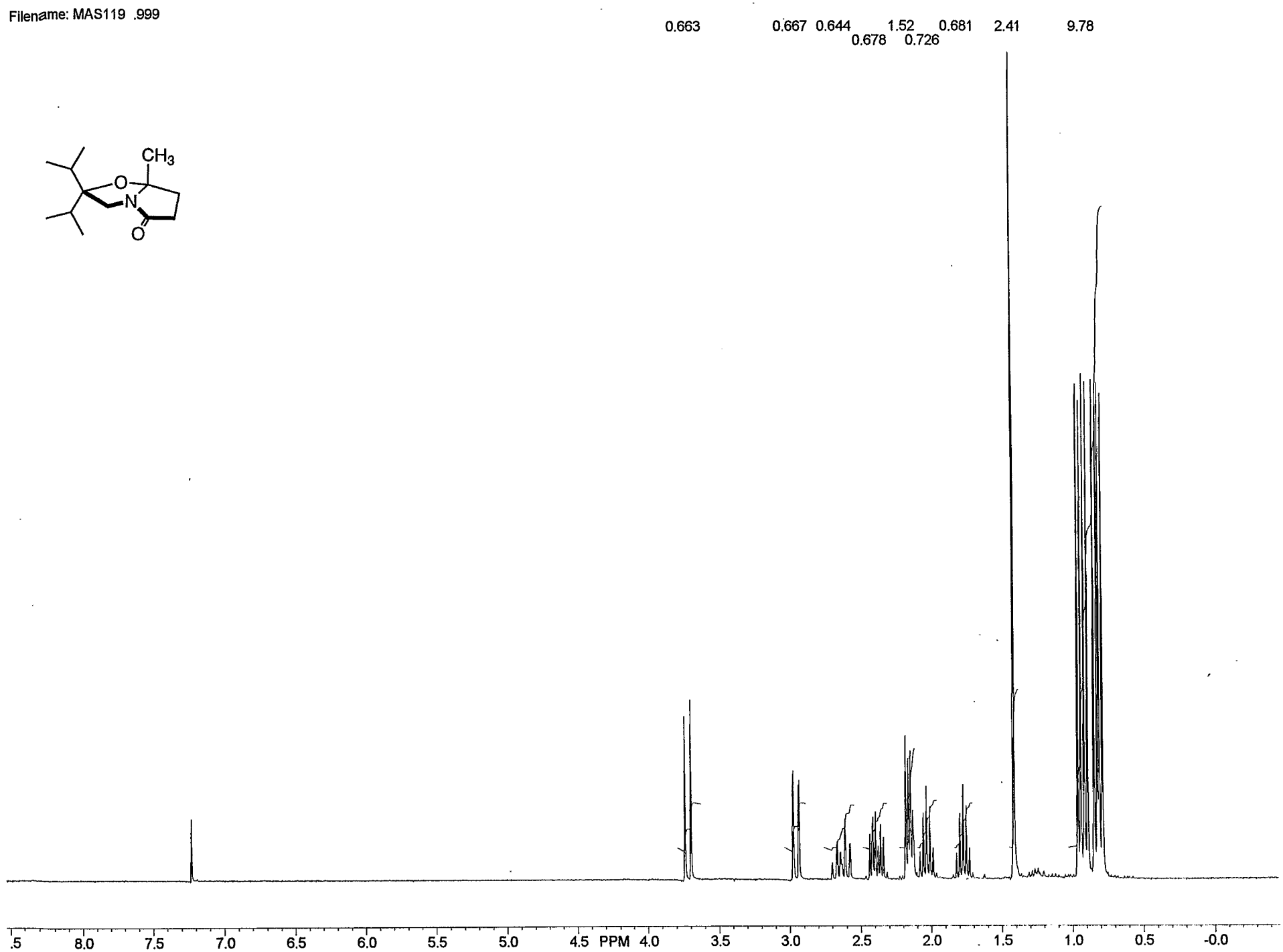
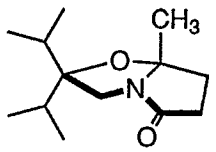
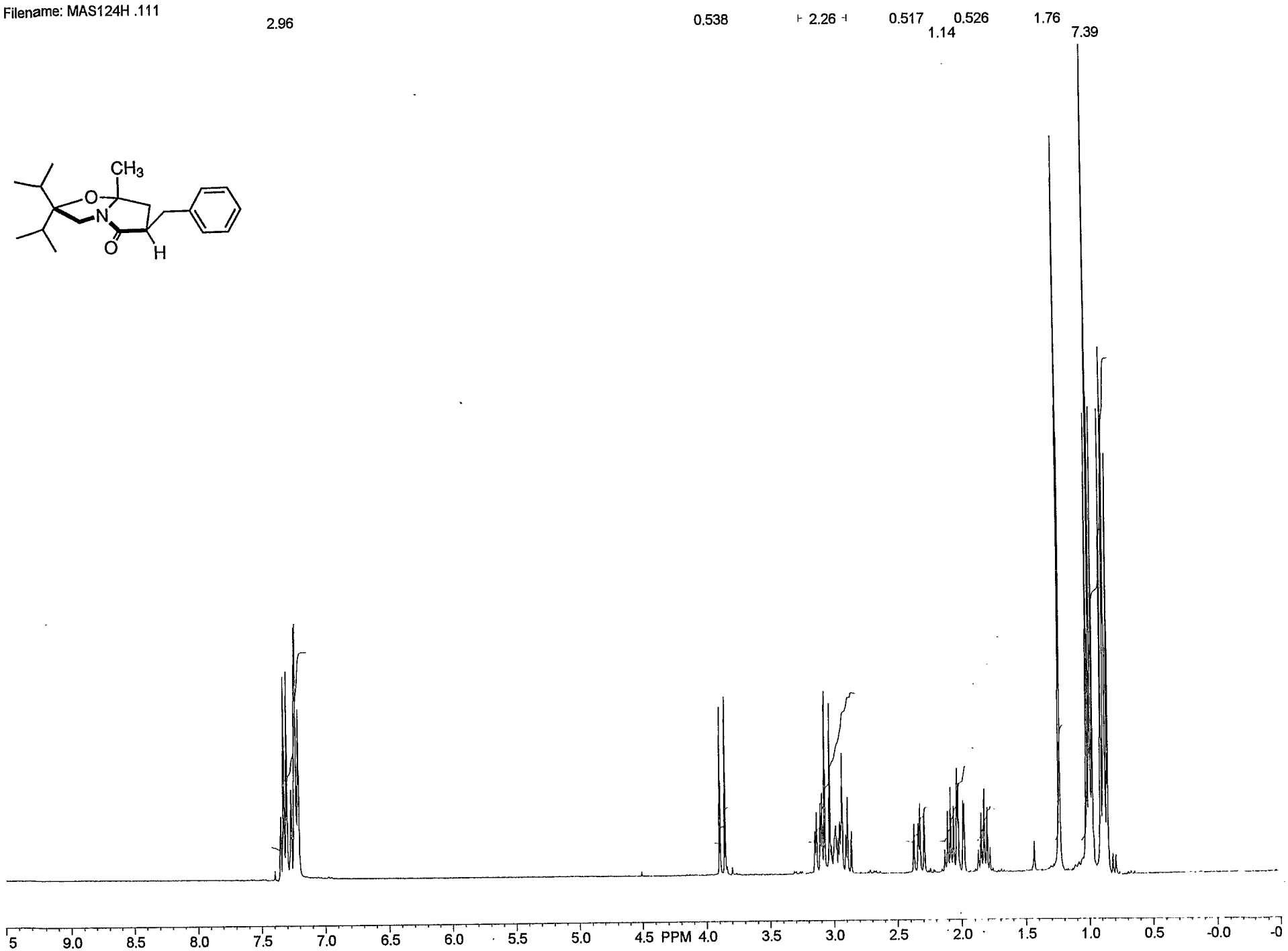
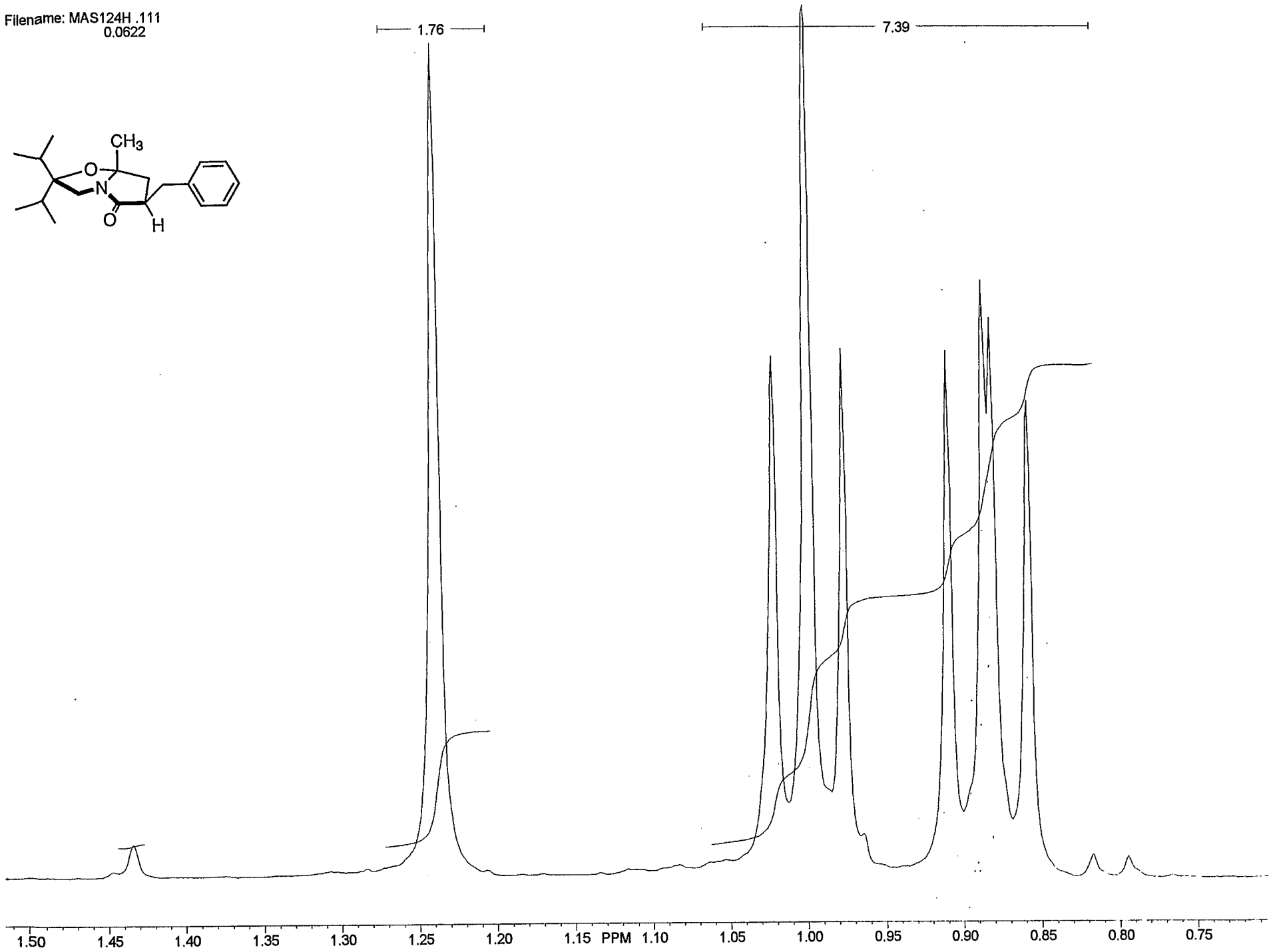




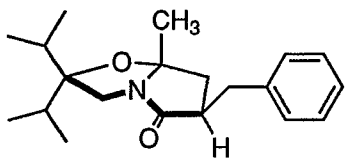
Filename: MAS119C .555

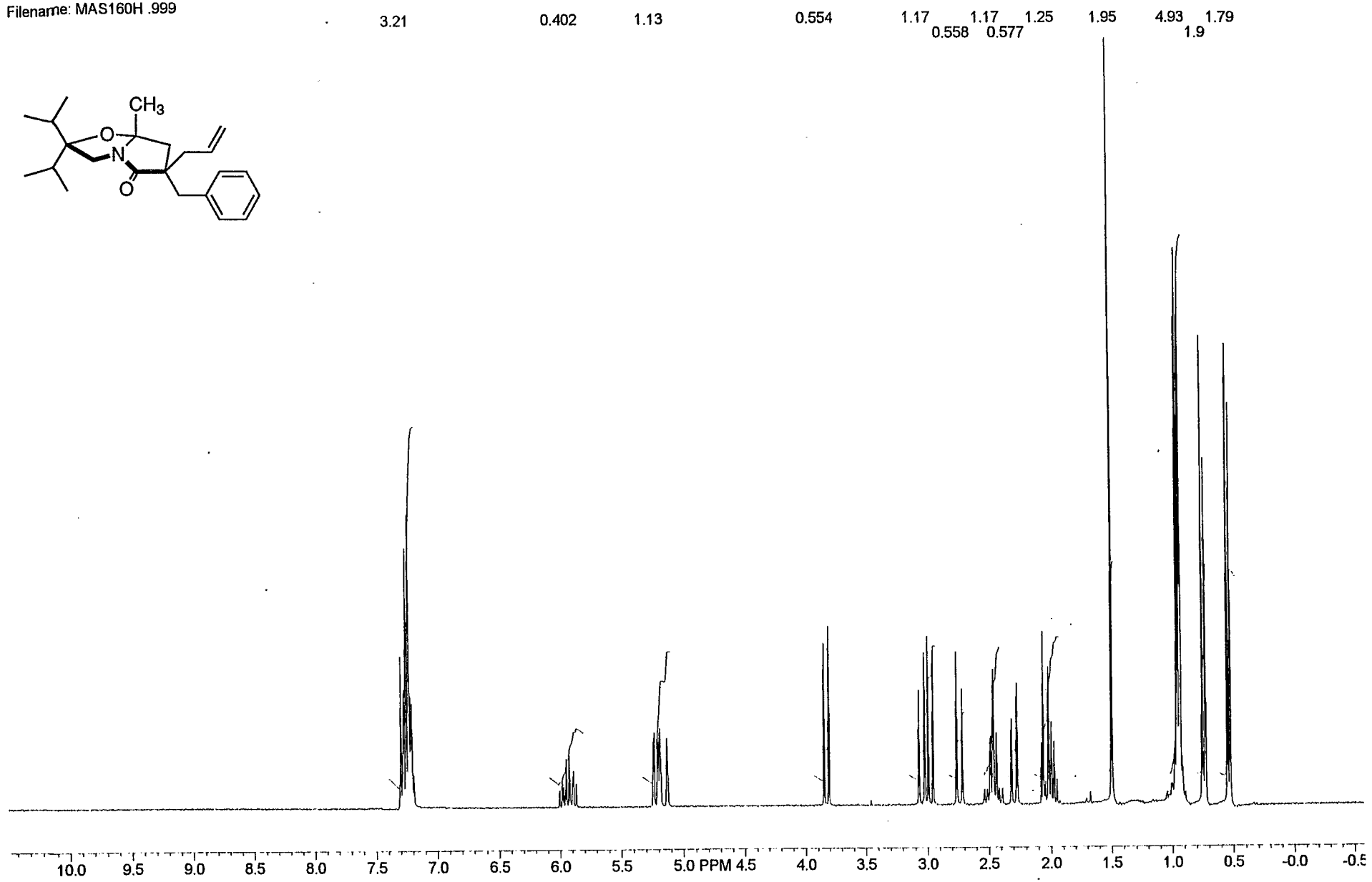




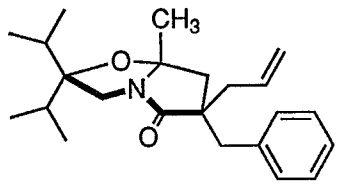


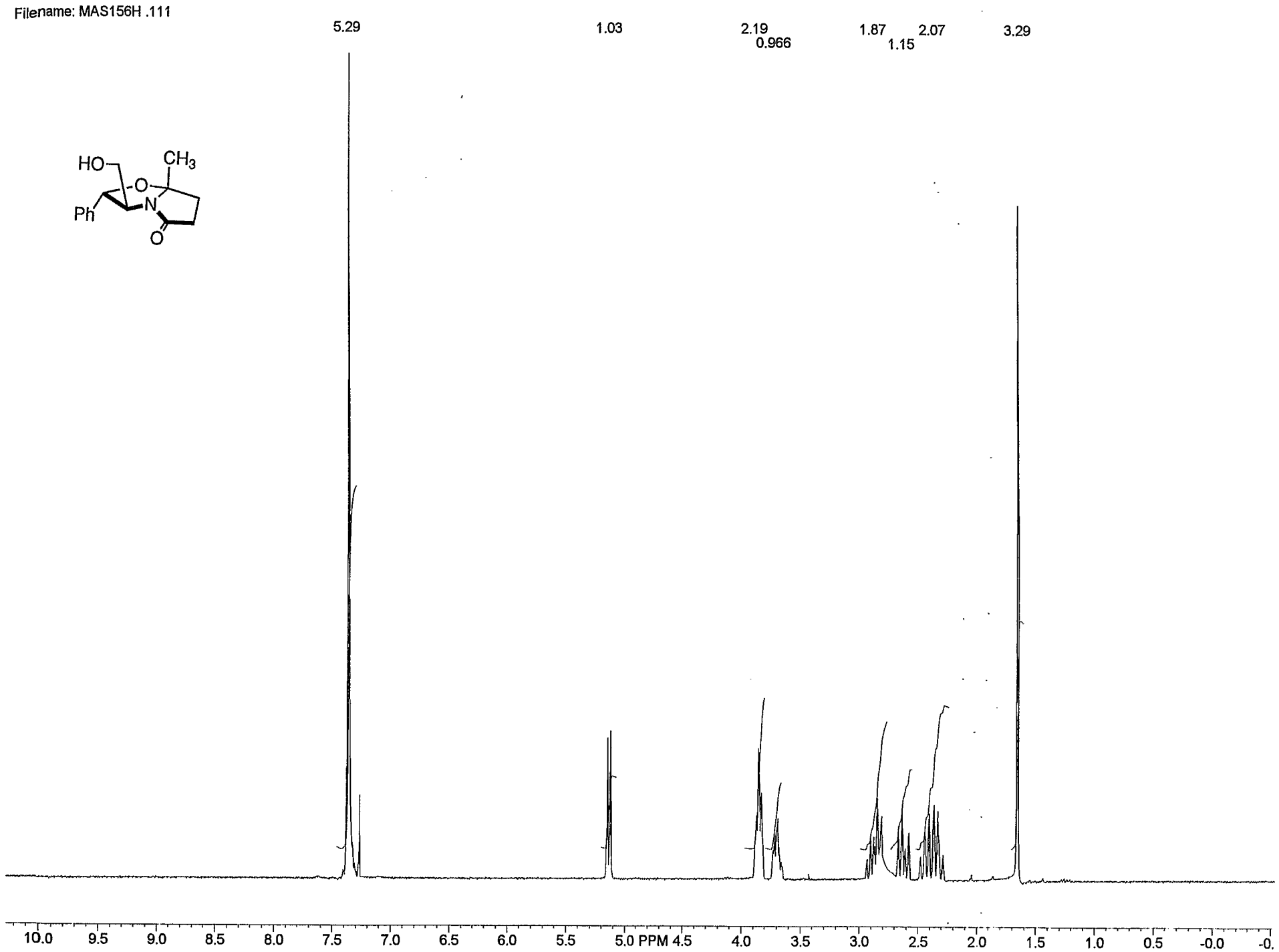
Filename: MAS124C .111



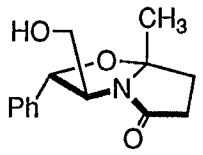


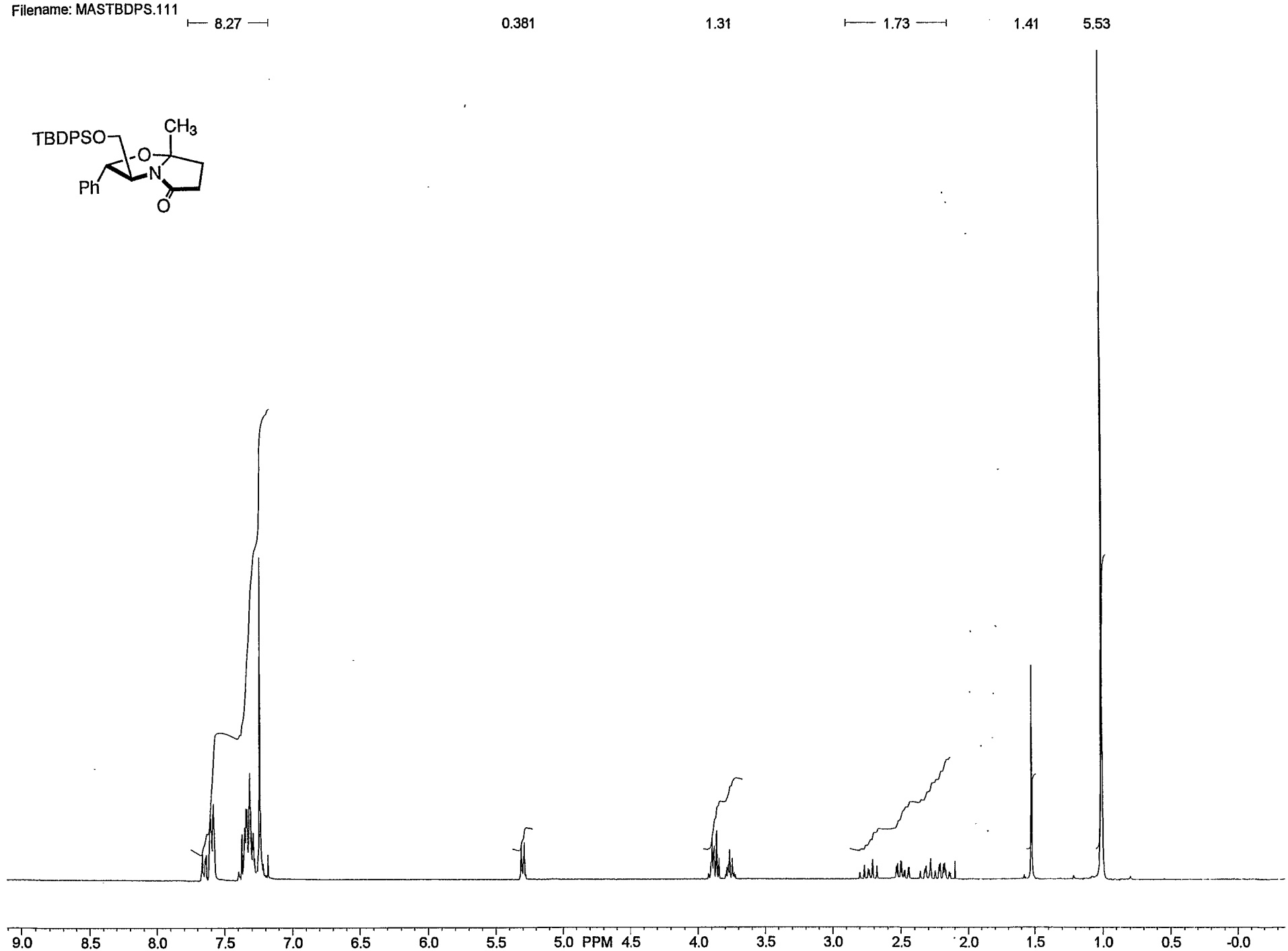
Filename: MAS160C .123





Filename: MAS156C .222





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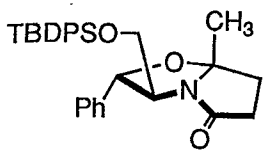
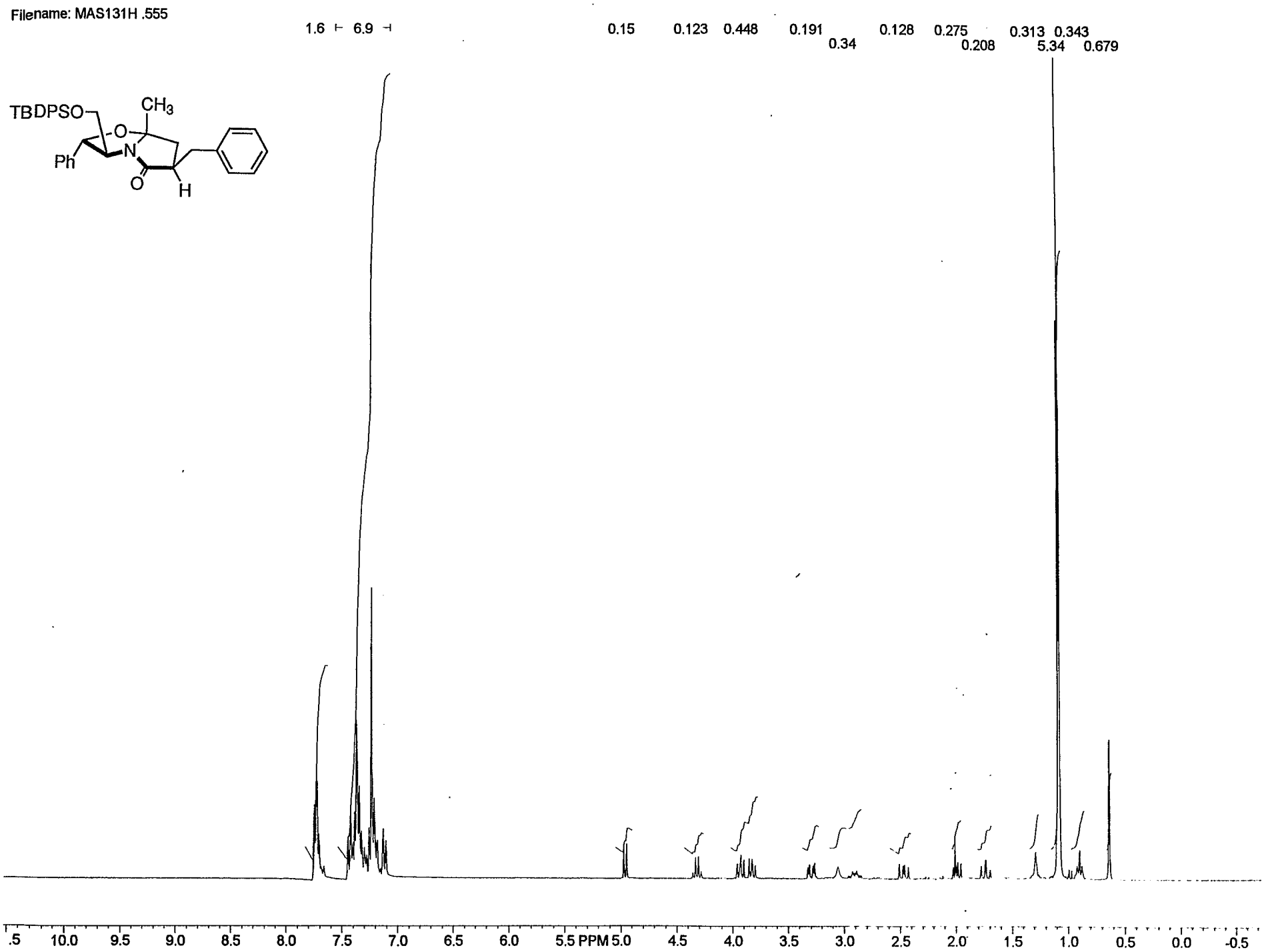
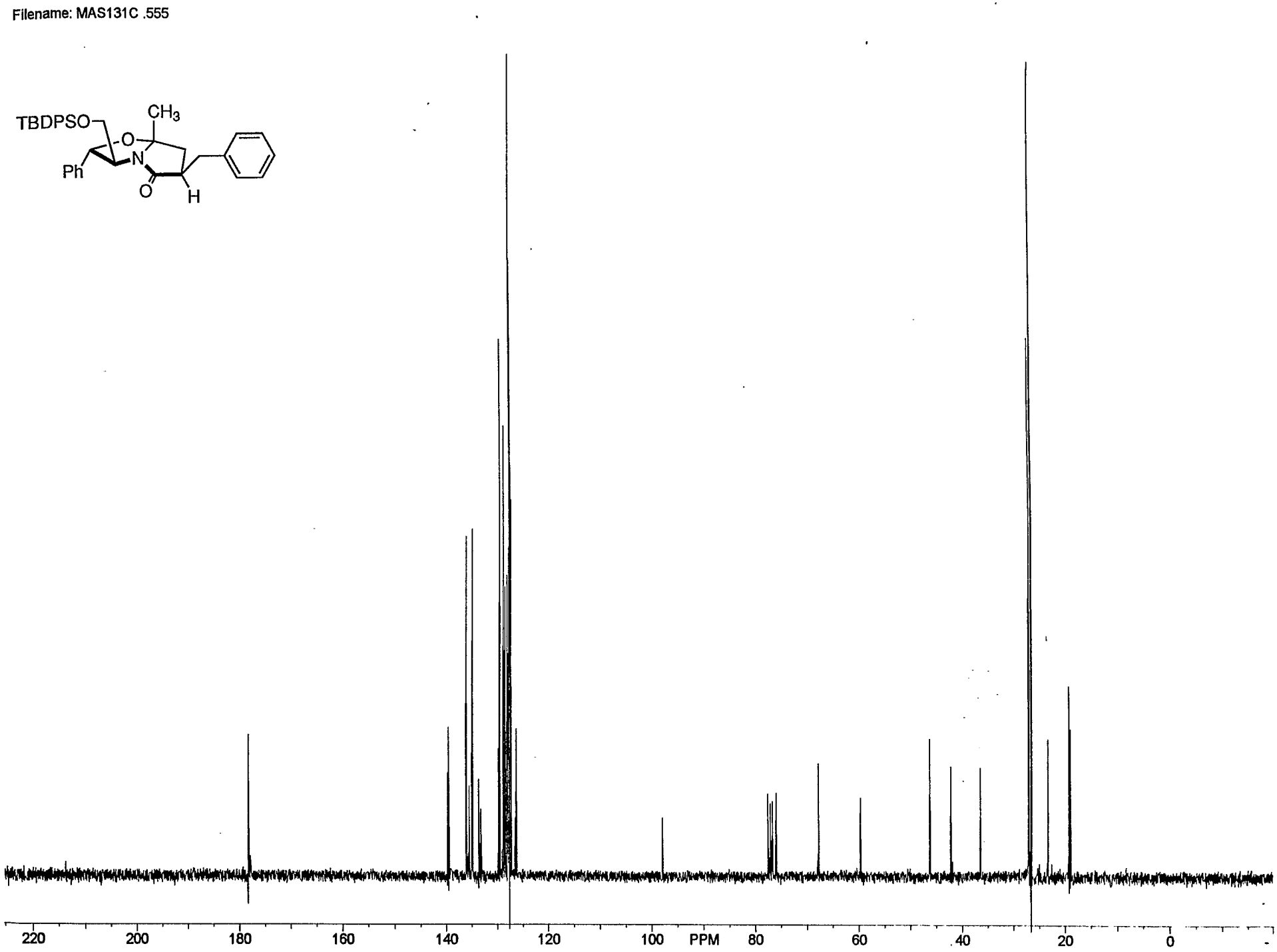
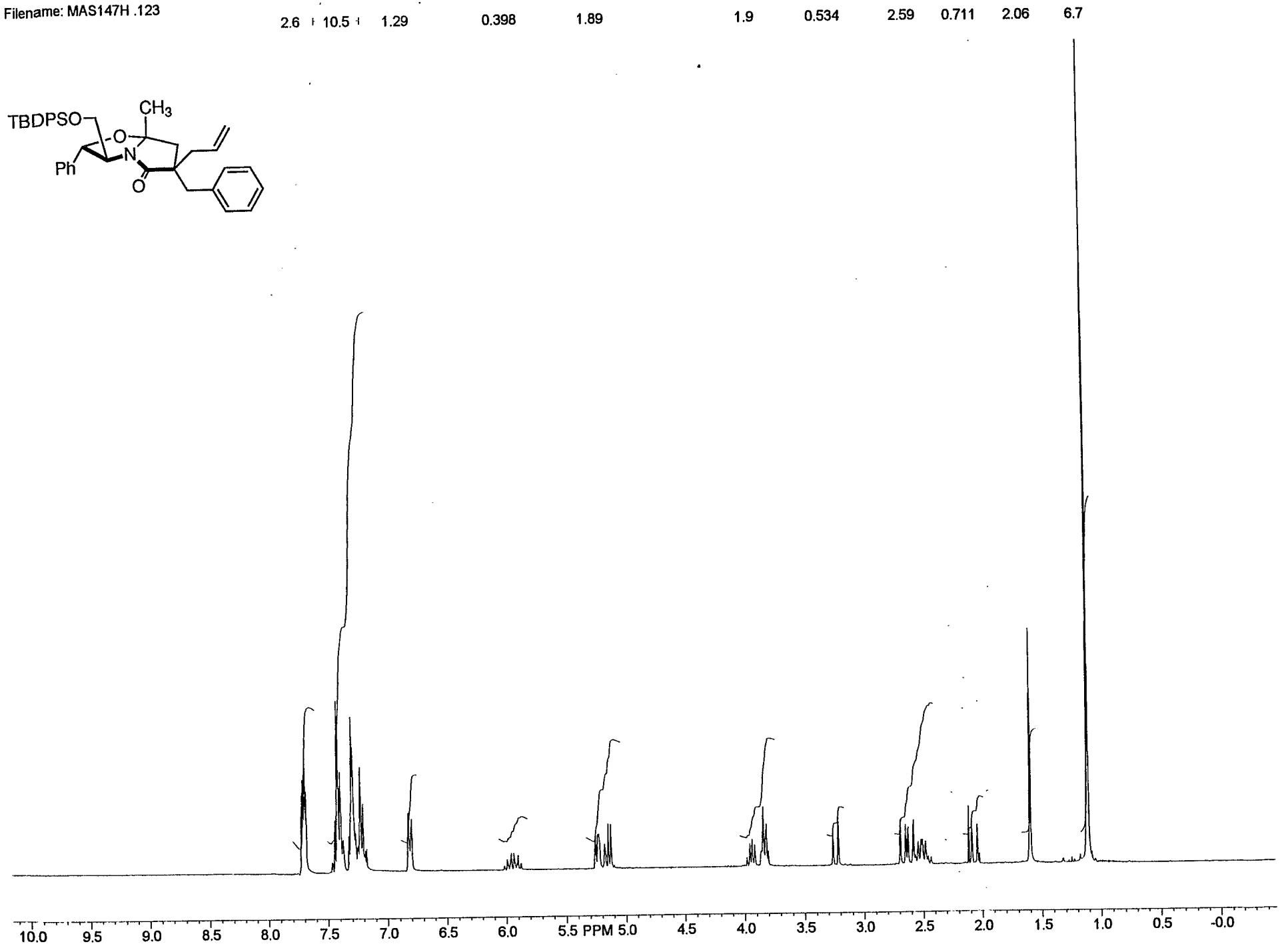
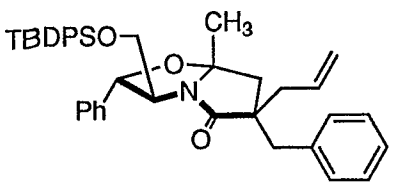


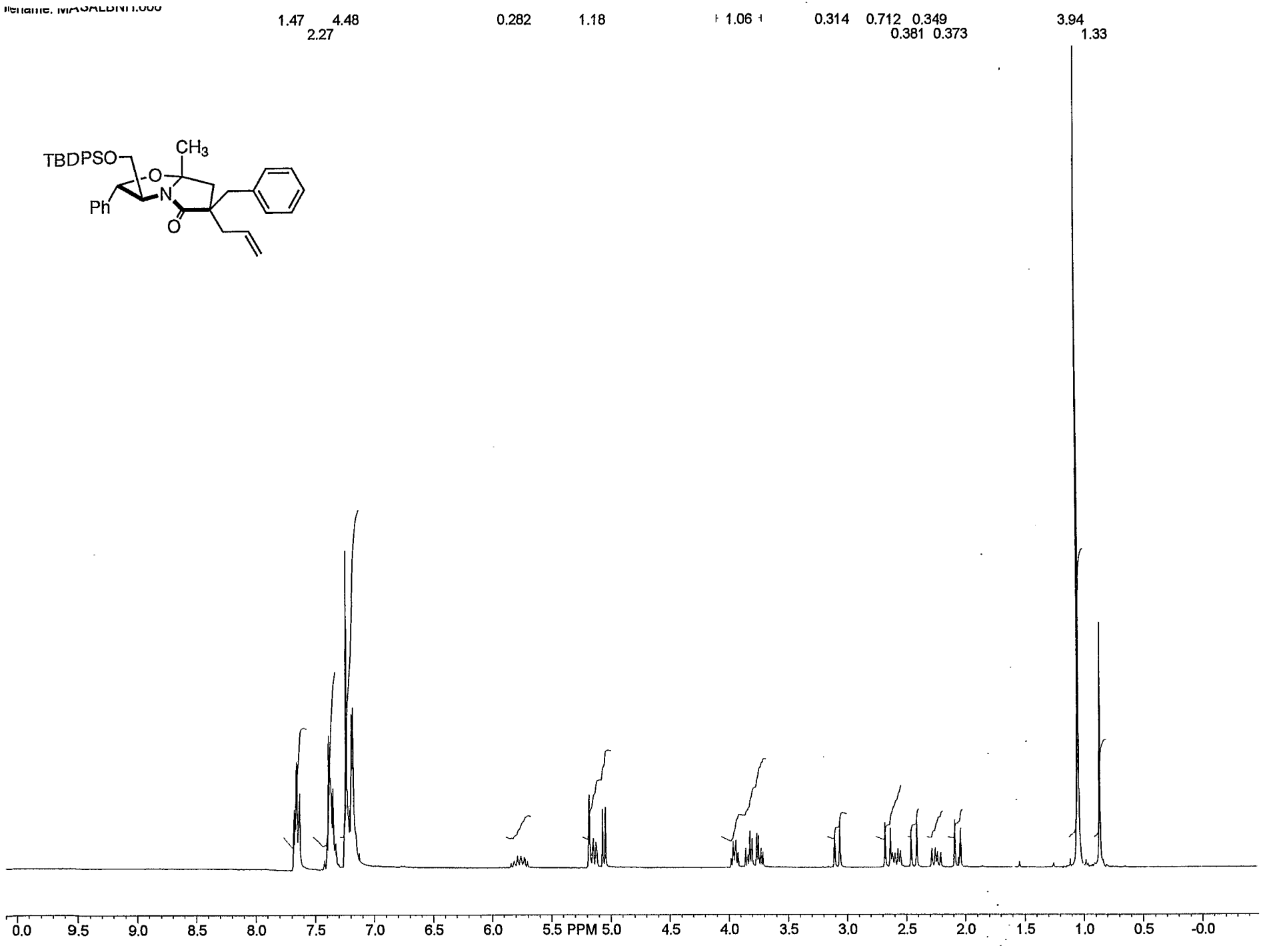




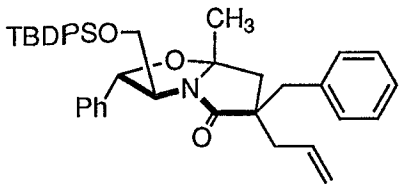


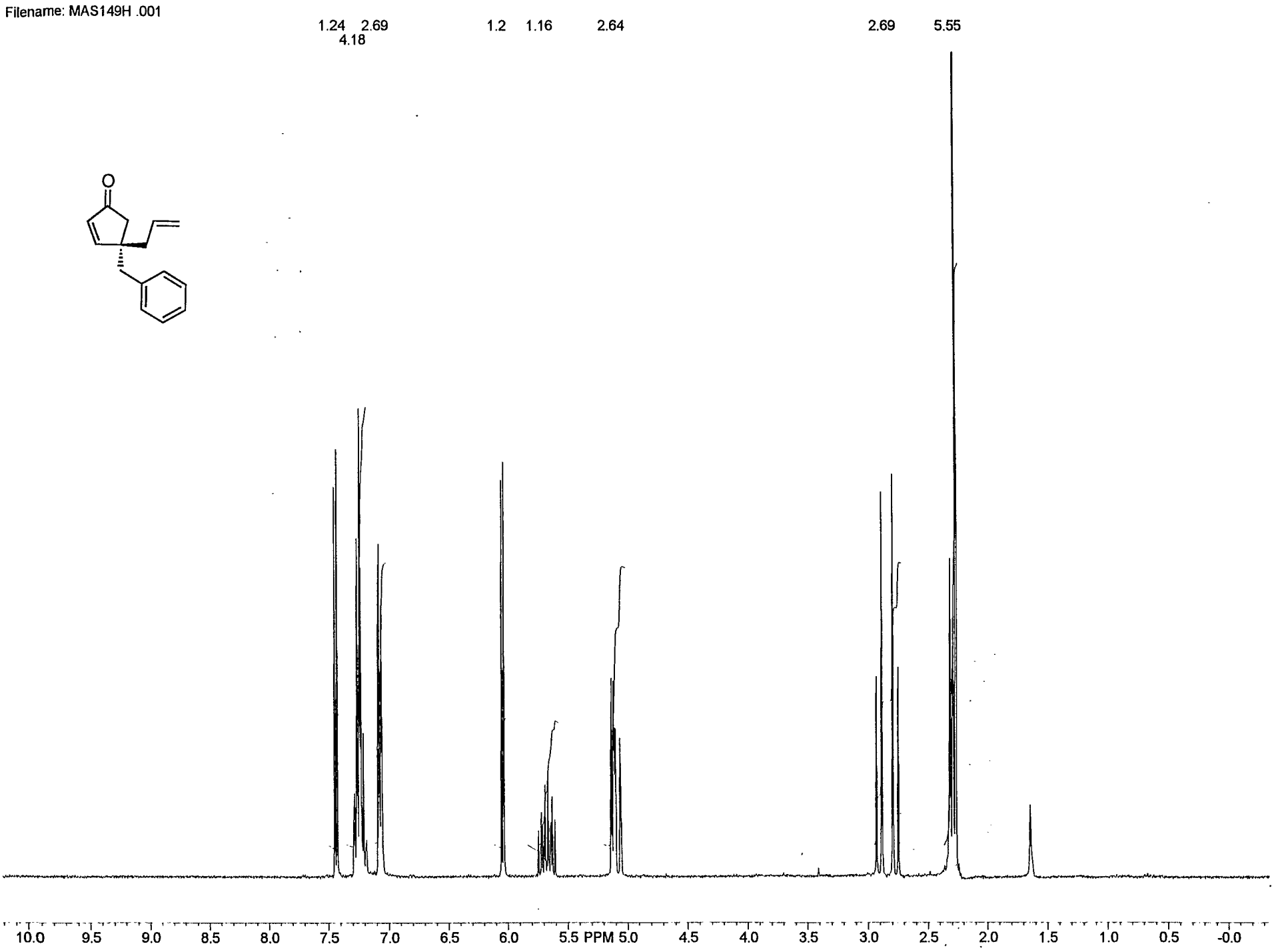
Filename: MAS147C .123





Filename: MASALBNC.000





Filename: MAS149C .222