Room Temperature Hydroamination of Alkenyl Ureas Catalyzed by a Gold(I) Carbene Complex

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Supporting Information

Experimental procedures, analytical and spectroscopic data, and copies of NMR spectra for heterocycles and selected compounds (54 pages).

Experimental

General Methods. Reactions were performed under a nitrogen atmosphere utilizing standard Shlenk and drybox techniques unless specified otherwise. NMR were obtained on a Varian spectrometer operating at 400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR in $CDCl_3$ at 25 °C unless stated otherwise. IR spectra were obtained on a Nicolet Avatar 360-FT IR spectrometer. Gas chromatography was performed on a HP 5890 gas chromatography equipped with a 25 m polydimethylsiloxane capillary column. Column chromatography was performed employing 230-450 mesh silica gel (Sorbent Technologies). All compounds were isolated as colorless oils unless noted otherwise. Elemental analyses were performed by Complete Analysis Laboratories (Parsippany, NJ). Thin layer chromatography (TLC) was performed on silica gel 60 F_{254}. Room temperature is 22-24 °C.

1,4-Dioxane (anhydrous Acros), methanol (anhydrous Aldrich), Au(Me_2S)Cl (Aldrich), and **4** (Strem) were used as received. Tetrahydrofuran (THF) and diethyl ether were distilled from sodium benzophenone ketyl, and $CDCl_3$ (Cambridge Isotope Labs) was distilled from CaH. 2,2-Diphenyl-4-pentenylamine (**S1**),[S1] *C*-[1-(2-methylallyl)-cyclohexyl]methylamine (**S2**),[S1] *C*-(1-but-3-enyl-cyclohexyl)methylamine (**S3**),[S1] 2-isopropyl-4-pentenylamine (**S4**)[S1] 2,2-dimethyl-4-pentenenitrile (**S5**),[S1] methyl-2-phenyl-4-pentenoate (**S6**),[S2] benzyl 2,2-diphenyl-4-pentenylcarbamate (**2a**),[S3] *N*-(2,2-diphenyl-4-pentenyl)acetamide (**2b**),[S4] *N*-(2,2-diphenyl-4-pentenyl)-*N*′-phenylurea (**2c**),[S4] and Au(**4**)Cl[S5] were synthesized employing published procedures.

Substrates

***N*-(2,2-Diphenyl-4-pentenyl)-*N′*-phenylurea (2c).** Phenylisocyanate (0.31 mL, 2.8 mmol) was added dropwise to a solution of **S1** (0.66 g, 2.8 mmol) in THF (10 mL) at 0 °C and the reaction mixture was stirred overnight. The resulting solution was diluted with ether (50 mL), washed with 1 M HCl (25 mL), sat. $NaHCO_3$ (25 mL), and brine (25 mL), dried ($MgSO_4$), and concentrated. The resulting white solid was chromatographed (ether–CH_2Cl_2 = 1:9) to give **2c** (0.79 g, 80%) as a white solid. mp 171-172.5 °C. TLC (ether–CH_2Cl_2 = 1:9): R_f = 0.64. ^{1}H NMR: δ 6.99-7.24 (m, 15 H), 6.56 (br s, 1 H), 5.40 (tdd, *J* = 7.2, 10.1, 17.1 Hz, 1 H), 4.89-4.96 (m, 2 H), 4.55 (t, *J* = 5.6 Hz, 1 H), 3.90 (d, *J* = 5.6 Hz, 2 H), 2.92 (d, *J* = 7.0 Hz, 2 H). ^{13}C{^{1}H} NMR: δ 155.9, 145.5, 138.4, 133.9, 129.3, 128.1, 126.5, 124.0, 121.5, 118.7, 50.3, 47.1, 42.0. IR (neat, cm^{-1}): 3324, 2360, 1642, 1550, 1232, 694. HRMS calcd (found) for $C_{24}H_{25}N_2O$ (MH^+): 357.1967 (357.1966).

N-(2,2-Diphenyl-4-pentenyl)-*N′*-ethylurea (**S7**), *N*-(4-bromophenyl)-*N′*-(2,2-diphenyl-4-pentenyl)urea (**S8**), *N*-(2,2-diphenyl-4-pentenyl)-*N′*-(4-methoxyphenyl)urea (**S9**), *N*-(4-acetylphenyl)-*N′*-(2,2-diphenyl-4-pentenyl)urea (**S10**), *N*-[1-(2-methylallyl)cyclohexylmethyl]-*N′*-phenylurea (**S11**), *N*-(1-but-3-enylcyclohexylmethyl)-*N′*-phenylurea (**S12**), *N*-(1-but-3-enylcyclohexylmethyl)-*N′*-ethylurea (**S13**), and *N*-(2-isopropyl-4-pentenyl)-*N′*-phenylurea (**S14**) were synthesized employing a procedure similar to that used to synthesize **2c**.

S7. White solid, 57%. mp 179.5-180 °C. TLC (ether–CH_2Cl_2 = 1:2): R_f = 0.49. ^{1}H NMR: δ 7.17-7.31 (m, 10 H), 5.45 (tdd, *J* = 7.2, 10.1, 17.1 Hz, 1 H), 4.95-5.02 (m, 2 H), 4.11 (br t, *J* = 5.6 Hz, 1 H), 3.88 (s, 3 H), 3.00-3.06 (m, 2 H), 2.88 (d, *J* = 7.0 Hz, 2 H), 1.02 (t, *J* = 7.2 Hz, 3 H). ^{13}C{^{1}H} NMR: δ 158.1, 145.7, 134.1, 128.4, 128.2, 126.5, 118.6, 50.5, 47.3, 41.9, 35.4, 15.5. IR (neat, cm^{-1}): 3347, 3290, 1615, 1574, 1494, 697. Anal. calcd (found) for $C_{20}H_{24}N_2O$: H, 7.84 (7.84); C, 77.89 (78.00). HRMS calcd (found) for $C_{20}H_{24}N_2O$ (M^+): 308.1889 (308.1886).

S8. White solid, 68%. mp 219-220 °C. TLC (ether-CH_2Cl_2 = 1:19): R_f = 0.53. ^{1}H NMR (d_6-DMSO): δ 8.69 (br s, 1 H), 7.19-7.36 (m, 14 H), 5.56 (br t, J = 5.8 Hz, 1 H), 5.45 (tdd, J = 7.0, 12.3, 17.1 Hz, 1 H), 4.90-4.99 (m, 2 H), 3.90 (d, J = 5.6 Hz, 2 H), 2.88 (d, J = 7.0 Hz, 2 H). ^{13}C{^{1}H} NMR (d_6-DMSO): δ 154.8, 145.7, 139.8, 134.3, 131.4, 128.1, 127.7, 126.0, 119.3, 118.1, 112.2, 49.7, 45.4, 40.9. IR (neat, cm^{-1}): 3337, 1647, 1549, 1489, 1233, 697. Anal. calcd (found) for $C_{24}H_{23}BrN_2O$: H, 5.32 (5.23); C, 66.21 (66.07). HRMS calcd for $C_{24}H_{23}{}^{79}BrN_2O$ (M^+): 434.0994 (434.0994).

S9. White solid, 48%. mp 177-177.5 °C. TLC (ether-CH_2Cl_2 = 1:9): R_f = 0.38. ^{1}H NMR: δ 7.09-7.26 (m, 10 H), 6.92-6.95 (m, 2 H), 6.73-6.77 (m, 2 H), 6.14 (br s, 1 H), 5.42 (tdd, J = 7.2, 10.1, 17.1 Hz, 1 H), 4.92-4.99 (m, 2 H), 4.29 (br t, J = 5.5 Hz, 1 H), 3.91 (d, J = 5.6 Hz, 2 H), 3.79 (s, 3 H), 2.82 (d, J = 7.0 Hz, 2 H). ^{13}C{^{1}H} NMR: δ 157.2, 156.6, 145.5, 133.9, 130.6, 128.4, 128.1, 126.5, 125.4, 118.7, 114.7, 55.6, 50.5, 47.1, 42.1. IR (neat, cm^{-1}): 3331, 1642, 1554, 1508, 1235, 696. Anal. calcd (found) for$C_{25}H_{26}N_2O_2$: H, 6.78 (6.75); C, 77.69 (77.74). HRMS calcd (found) for $C_{25}H_{26}N_2O_2$ (M^+): 386.1994 (386.1989).

S10. White, waxy solid, 88%. TLC (ether-CH_2Cl_2 = 1:9): R_f = 0.39. ^{1}H NMR: δ 7.76-7.79 (m, 2 H), 7.44 (br s, 1 H), 7.14-7.30 (m, 12 H), 5.42 (tdd, J = 7.0, 10.1, 17.1 Hz, 1 H), 4.93-5.00 (m, 2 H), 4.86 (br t, J = 5.6 Hz, 1 H), 3.97 (d, J = 5.8 Hz, 2 H), 2.87 (d, J = 7.0 Hz, 2 H), 2.47 (s, 3 H). ^{13}C{^{1}H} NMR: δ 197.8, 155.0, 145.4, 144.2, 133.8, 131.2, 130.1, 128.4, 128.1, 126.6, 118.8, 118.0, 50.2, 47.0, 42.0, 26.5. IR (neat, cm^{-1}): 3343, 1660, 1533, 1223, 1176, 699. Anal. calcd (found) for $C_{26}H_{26}N_2O_2$: H, 6.58 (6.54); C, 78.36 (78.56). HRMS calcd (found) for $C_{26}H_{26}N_2O_2$ (M^+): 398.1994, (398.2002).

S11. White solid, 85%. TLC (ether–CH_2Cl_2 = 1:19): R_f = 0.41. ^{1}H NMR: δ 7.86 (s, 1 H), 7.31 (d, J = 8.4 Hz, 2 H), 7.22 (t, J = 7.8 Hz, 2 H), 6.99 (t, J = 7.2 Hz, 1 H), 5.81 (br t, J = 5.6 Hz, 1 H), 4.78 (s, 1 H), 4.61 (s, 1 H), 3.20 (d, J = 6.0 Hz, 2 H), 1.99 (s, 2 H), 1.72 (s, 3 H), 1.31-1.44 (m, 10 H).

$^{13}C\{^{1}H\}$ NMR: δ 157.1, 143.1, 139.3, 129.1, 123.1, 120.4, 114.9, 46.4, 44.4, 37.6, 33.9, 26.2, 25.5, 21.8. IR (neat, cm^{-1}): 3361, 2928, 1642, 1559, 1236, 893. mp 99.5-100.5 °C. Anal. calcd (found) for $C_{18}H_{26}N_2O$: H, 9.15 (9.11); C, 75.48 (75.45). HRMS calcd (found) for $C_{18}H_{26}N_2O$ (M^+): 286.2045, (286.2051).

S12. White solid, 83%. TLC (ether–CH_2Cl_2 = 1:9): R_f = 0.65. ^{1}H NMR: δ 7.93 (br s, 1 H), 7.30 (d, *J* = 7.9 Hz, 2 H), 7.21 (d, *J* = 7.6 Hz, 2 H), 6.97 (t, *J* = 6.7 Hz, 1 H), 5.87 (br t, *J* = 5.6 Hz, 1 H), 5.74 (tdd, *J* = 6.5, 10.3, 16.9 Hz, 1 H), 4.86-4.98 (m, 2 H), 3.13 (d, *J* = 6.0 Hz, 2 H), 1.90-1.96 (m, 2 H), 1.20-1.44 (m, 12 H). $^{13}C\{^{1}H\}$ NMR: δ 157.1, 139.4, 139.4, 129.0, 122.9, 120.1, 114.2, 46.4, 36.4, 34.7, 33.5, 27.5, 26.3, 21.5. IR (neat, cm^{-1}): 3333, 2925, 1645, 1557, 1233, 694. Anal. calcd (found) for $C_{18}H_{26}N_2O$: H, 9.15 (9.29); C, 75.48 (75.32). HRMS calcd (found) for $C_{18}H_{27}N_2O$ (M^+): 287.2123 (287.2119).

S13. Colorless oil, 99%. TLC (ether–CH_2Cl_2 = 1:2): R_f = 0.51. ^{1}H NMR: δ 5.79 (tdd, *J* = 6.5, 10.3, 17.1 Hz, 1 H), 4.89-5.01 (m, 2 H), 4.83 (br t, *J* = 5.1 Hz, 1 H), 4.71 (br t, *J* = 5.5 Hz, 1 H), 3.18 (dq, *J* = 5.6, 7.2 Hz, 2 H), 3.07 (d, *J* = 6.0 Hz, 2 H), 1.93-1.99 (m, 2 H), 1.23-1.48 (m, 12 H), 1.11 (t, *J* = 7.2 Hz, 3 H). $^{13}C\{^{1}H\}$ NMR: δ 158.9, 139.6, 114.2, 46.5, 36.3, 35.4, 34.9, 33.7, 27.5, 26.4, 21.6, 15.7. IR (neat, cm^{-1}): 3353, 2924, 2857, 1629, 1568, 1253. Anal. calcd (found) for $C_{14}H_{26}N_2O$: H, 10.99 (11.10); C, 70.54 (70.52). HRMS calcd (found) for $C_{14}H_{26}N_2O$ (M^+): 238.2045 (238.2047).

S14. White solid, 38%. TLC (EtOAc–hexanes = 1:2): R_f = 0.29. ^{1}H NMR (300 MHz): δ 7.68 (br s, 1 H), 7.20-7.32 (m, 4 H), 6.96-7.02 (m, 1 H), 5.64-5.78 (m, 2 H), 4.91-5.01 (m, 2 H), 3.08-3.26 (m, 2 H), 2.04-2.13 (m, 1 H), 1.88-1.98 (m, 1 H), 1.63-1.76 (m, 1 H), 1.34-1.44 (m, 1 H), 0.85 (d, *J* = 6.9 Hz, 3 H), 0.84 (d, *J* = 6.9 Hz, 3 H). $^{13}C\{^{1}H\}$ NMR: δ 156.9, 139.4, 137.5, 129.0, 122.9, 120.0, 116.1, 44.3, 41.0, 33.5, 28.3, 19.6, 19.1. IR (neat, cm^{-1}): 3358, 2958, 1642, 1555, 1241, 694. Anal.

calcd (found) for $C_{15}H_{22}N_2O$: H, 9.00 (9.07); C, 73.13 (73.27). HRMS calcd (found) for $C_{15}H_{22}N_2O$ (M^+): 246.1732 (246.1731).

***N*-(2,2-Dimethyl-1-phenyl-4-pentenyl)-*N*′-phenylurea (S15).** A solution of phenyl magnesium bromide (1 M in THF, 15 mL, 15 mmol) and **S5** (1.08 g, 9.89 mmol) in ether (60 mL) was refluxed for 17 h. The resulting suspension was cooled to –15 °C, treated with methanol (17 mL), stirred for 5 min, cooled to –78 °C, and treated with $NaBH_4$ (920 mg, 24.3 mmol) added in one portion. The reaction mixture was warmed slowly to room temperature and stirred for an additional 1 h. The resulting suspension was treated with 1 M NaOH (50 mL) and extracted with ether (2 × 50 mL). The combined organic extracts were washed aqueous sodium hydroxide (1 M, 5 mL) and brine (45 mL), dried ($MgSO_4$), and concentrated to yield 2,2-dimethyl-1-phenyl-4-pentenylamine (**S16**, 760 mg, 41%, 93% pure) that was used in the subsequent step without further purification.

Phenylisocyanate (210 μL, 1.93 mmol) was added dropwise to a solution of **S16** (380 mg, 2.01 mmol) in THF (10 mL) at 0 °C and the reaction was stirred overnight. The resulting solution was diluted with ether (25 mL), washed with 1 M HCl (15 mL), sat. aqueous $NaHCO_3$ (15 mL), and brine (15 mL), dried ($MgSO_4$), and concentrated. The resulting residue was chromatographed (ether–CH_2Cl_2 = 1:30) to give **S15** (450 mg, 76%) as a white solid. TLC (ether–CH_2Cl_2 = 1:30): R_f = 0.45. ^{1}H NMR: δ 7.73 (br s, 1 H), 7.14-7.19 (m, 9 H), 6.95-7.01 (m, 1 H), 6.48 (br s, 1 H), 5.81 (tdd, J = 7.3, 10.1, 17.3 Hz, 1 H), 4.98-5.05 (m, 2 H), 4.72 (d, J = 8.7 Hz, 1 H), 1.92-2.05 (m, 2 H), 0.82 (s, 3 H), 0.78 (s, 3 H). ^{13}C{^{1}H} NMR: δ 156.3, 140.4, 139.1, 134.8, 129.1, 128.5, 127.9, 127.1, 123.1, 120.2, 118.1, 62.0, 44.2, 37.8, 24.1, 23.5. IR (neat, cm^{-1}): 3345, 1642, 1549, 1498, 1234, 696. Anal. calcd (found) for $C_{20}H_{24}N_2O$: H, 7.84 (7.86); C, 77.89 (77.78). HRMS calcd (found) for $C_{20}H_{24}N_2O$ (M^+): 308.1889 (308.1888).

***N*-(2,2-Dimethyl-1-phenyl-4-pentenyl)-*N′*-ethylurea (S17). S17** was synthesized in 66% yield as a colorless oil that solidified to a white solid over several days employing a procedure similar to that used to synthesize **S15**. TLC (ether–CH_2Cl_2 = 1:9): R_f = 0.22. ^{1}H NMR: δ 7.20-7.29 (m, 5 H), 5.78-5.91 (m, 2 H), 4.95-5.10 (m, 3 H), 4.54 (d, J = 8.2 Hz, 1 H), 3.03-3.16 (m, 2 H), 1.98-2.11 (m, 2 H), 0.96 (t, J = 7.2 Hz, 3 H), 0.87 (s, 3 H), 0.83 (s, 3 H). ^{13}C{^{1}H} NMR: δ 158.5, 140.8, 135.0, 128.5, 127.8, 127.0, 117.9, 62.2, 44.2, 37.9, 35.2, 24.2, 23.4, 15.5. IR (neat, cm^{-1}): 3348, 2969, 1628, 1559, 1252, 703. Anal. calcd (found) for $C_{16}H_{24}N_2O$: H, 9.29 (9.14); C, 73.81 (73.78). HRMS calcd (found) for $C_{16}H_{24}N_2O$ (M^+): 260.1889 (260.1889).

***N*-Benzyl-*N′*-4-pentenylurea** (**S18**). 4-Pentenitrile (4.38 g, 54.0 mmol) was added to a suspension of $LiAlH_4$ (8.15 g, 215 mmol) in ether (250 mL) at 0 °C. The reaction mixture was warmed to room temperature, stirred overnight, cooled to 0 °C, and quenched by successive addition of water (11.5 mL), 15% NaOH (11.5 mL), and water (11.5 mL). The resulting suspension was warmed to room temperature, filtered through Celite, and eluted with ether (200 mL). The resulting solution was carefully concentrated to yield 4-pentenylamine[S6] (**S19**, 38% w/w in ether, 3.31 g, 72%). **S18** was synthesized from **S19** employing a procedure similar to that used to synthesize **2c**.

For S19: ^{1}H NMR: δ 5.80 (tdd, J = 6.5, 10.3, 17.1 Hz, 1 H), 4.92-5.04 (m, 2 H), 2.70 (t, J = 7.1 Hz, 2 H), 2.06-2.11 (m, 2 H), 1.50-1.57 (m, 2 H), 1.41 (br. s, 2 H). ^{13}C{^{1}H} NMR: δ 138.5, 114.8, 41.8, 32.8, 31.2.

For S18: White solid, 70%. TLC (ether-CH_2Cl_2 = 1:2): R_f = 0.60. ^{1}H NMR: δ 7.18-7.27 (m, 5 H), 5.73 (tdd, J = 6.7, 10.3, 16.9 Hz, 1 H), 5.63 (br t, J = 6.0 Hz, 1 H), 5.33 (br t, J = 5.8 Hz, 1 H), 4.91-4.99 (m, 2 H), 4.22 (d, J = 5.8 Hz, 2 H), 3.02-3.07 (m, 2 H), 1.96-2.01 (m, 2 H), 1.46 (quintet, J = 7.3 Hz, 2 H). ^{13}C{^{1}H} NMR: δ 159.0, 139.7, 138.0, 128.6, 127.3, 127.1, 115.0, 44.2, 39.9, 31.1, 29.5.

IR (neat, cm^{-1}): 3329, 2927, 1620, 1584, 1262, 692. Anal. calcd (found) for $C_{13}H_{18}N_2O$: H, 8.31 (8.40); C, 71.53 (71.18). HRMS calcd (found) for $C_{13}H_{18}N_2O$ (M^+): 218.1419 (218.1420).

***N*-Ethyl-*N′*-(2-phenyl-4-pentenyl)urea (S21).** **S6** in THF (35 mL) was added to a solution of KOH (89%, 5.9 g, 94 mmol) in water (25 mL). MeOH (50 mL) was added and the reaction mixture was heated at 40 °C for 19 h. The resulting mixture was cooled to room temperature, acidified with concentrated HCl (10 mL), and extracted with EtOAc (3 × 75 mL). The combined organic extracts were washed with 1 M HCl (5 mL) and brine (45 mL), dried ($MgSO_4$), and concentrated to yield 2-phenyl-4-pentenoic acid[S2] (**S22**, 3.77 g, 92%) as a yellow oil.

Oxalyl chloride (1.10 mL, 12.6 mmol) was added over 10 min to a solution of **S22** (1.53 g, 8.68 mmol) and toluene (10 mL), stirred for 3 h, and concentrated to ~5 mL under reduced pressure. The resulting solution was added over 15 min to a solution of ammonia in toluene (10 mL) at –78 °C. The reaction mixture was warmed to room temperature, stirred overnight, and concentrated under vacuum to give a pale yellow oil that was partitioned between CH_2Cl_2 (50 mL) and 10% NaOH (50 mL). The layers were separated and the aqueous layer extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were washed with brine (30 mL), dried ($MgSO_4$) and concentrated. The resulting residue was chromatographed (EtOAc–CH_2Cl_2 = 1:4) to give 2-phenyl-4-pentenamide[S2] (**S23**, 1.05 g, 69%) as a white solid. mp 60-61 °C.

A solution of **S23** (653 mg, 3.73 mmol) in ether (10 mL) was added to a suspension of $LiAlH_4$ (580 mg, 15.3 mmol) in ether (40 mL) and the resulting suspension was refluxed for 16 h. The reaction mixture was cooled to 0 °C and quenched by successive addition of water (0.8 mL), 15% NaOH (0.8 mL), and water (0.8 mL). The resulting suspension was warmed to room temperature, filtered through Celite, and eluted with ether (150 mL). The solution was carefully concentrated to yield 2-phenyl-4-

pentenylamine[S2] (**S24**, 75% w/w in ether, 0.60 g, 100%). **S21** was synthesized from **S24** employing a procedure similar to that used to synthesize **S15**.

For S21: Colorless, viscous oil, 72%. TLC (ether–CH_2Cl_2 = 1:3): R_f = 0.34. ^{1}H NMR: δ 7.17-7.34 (m, 6 H), 5.68 (tdd, *J* = 7.2, 10.1, 17.1 Hz, 1 H), 4.94-5.03 (m, 2 H), 4.11 (br t, *J* = 5.6 Hz, 1 H), 3.65 (ddd, *J* = 5.5, 7.3, 13.0 Hz, 1 H), 3.16 (ddd, *J* = 4.4, 9.2, 13.5 Hz, 1 H), 3.09 (dt, *J* = 5.6, 7.2 Hz, 2 H), 2.82-2.90 (m, 1 H), 2.33-2.46 (m, 2 H), 1.05 (t, *J* = 7.2 Hz, 3 H). ^{13}C{^{1}H} NMR: δ 158.3, 142.7, 136.2, 128.7, 128.0, 126.8, 116.6, 46.1, 45.5, 38.3, 35.3, 15.5. IR (neat, cm^{-1}): 3332, 1630, 1566, 1256, 913, 698. Anal. calcd (found) for $C_{14}H_{20}N_2O$: H, 8.68 (8.76); C, 72.38 (72.21). HRMS calcd (found) for $C_{14}H_{20}N_2O$ (M^+): 232.1576 (232.1581).

For S22: ^{1}H NMR: δ 11.87 (br s, 1 H), 7.26-7.37 (m, 5 H), 5.74 (tdd, *J* = 6.8, 10.3, 17.1 Hz, 1 H), 5.02-5.12 (m, 2 H), 3.66 (t, *J* = 7.5 Hz, 1 H), 2.81-2.88 (m, 1 H), 2.51-2.58 (m, 1 H). ^{13}C{^{1}H} NMR: δ 179.9, 137.9, 135.0, 128.9, 128.2, 127.7, 117.4, 51.5, 37.2.

For S23: TLC (EtOAc–CH_2Cl_2 = 1:4): R_f = 0.32. ^{1}H NMR: δ 7.24-7.35 (m, 5 H), 6.02 (br s, 1 H), 5.71 (tdd, *J* = 7.0, 9.7, 16.7, 1 H), 5.53 (br s, 1 H), 4.96-5.08 (m, 2 H), 3.46 (t, *J* = 7.5 Hz, 1 H), 2.84-2.92 (m, 1 H), 2.48-2.55 (m, 1 H). ^{13}C{^{1}H} NMR: δ 175.7, 139.4, 135.8, 128.9, 128.1, 127.5, 116.9, 52.6, 37.2.

For S24: ^{1}H NMR: δ 7.17-7.34 (m, 5 H), 5.68 (tdd, *J* = 6.5, 10.1, 17.1 Hz, 1 H), 4.92-5.01 (m, 2 H), 2.96 (dd, *J* = 4.6, 12.1 Hz, 1 H), 2.84 (dd, *J* = 8.7, 12.1 Hz, 1 H), 2.64-2.71 (m, 1 H), 2.31-2.44 (m, 2 H), 1.47 (br s, 2 H). ^{13}C{^{1}H} NMR: δ 143.1, 136.7, 128.7, 128.1, 126.7, 116.3, 49.5, 47.5, 38.5.

***N*-Phenyl-*N′*-(2-phenyl-4-pentenyl)urea (S25).** **S25** was synthesized from **S24** employing a procedure similar to that used to synthesize **S15**. White solid, 82%. TLC (ether-CH_2Cl_2 = 1:19): R_f = 0.37. ^{1}H NMR: δ 7.37 (br s, 1 H), 7.00-7.28 (m, 10 H), 5.61 (tdd, *J* = 7.0, 10.1, 17.1 Hz, 1 H), 5.47 (br t, *J* = 5.3 Hz, 1 H), 4.90-4.97 (m, 2 H), 3.53 (td, *J* = 6.5, 13.3 Hz, 1 H), 3.20 (ddd, *J* = 5.0, 8.7, 13.5 Hz,

1 H), 2.76-2.83 (m, 1 H), 2.27-2.42 (m, 2 H). $^{13}C\{^1H\}$ NMR: δ 156.4, 142.4, 139.0, 136.0, 129.1, 128.7, 127.9, 126.8, 123.3, 120.5, 116.7, 45.9, 45.3, 38.1. IR (neat, cm^{-1}): 3322, 1643, 1547, 1496, 1235, 694. Anal. calcd (found) for $C_{18}H_{20}N_2O$: H, 7.19 (7.32); C, 77.11 (77.00). HRMS calcd (found) for $C_{18}H_{20}N_2O$ (M^+): 280.1576 (280.1574).

Heterocyclic Products

Phenyl 2-methyl-4,4-diphenyl-pyrrolidine-1-carboxlamide (3c).[S4] Dioxane (0.50 mL) was added to a mixture of **2c** (90 mg, 0.25 mmol), Au(**4**)Cl (7.5 mg, 0.012 mmol), and AgOTf (3.4 mg, 0.013 mmol) and the resulting suspension was stirred at room temperature for 18 h. The resulting mixture was concentrated and chromatographed (ether–CH_2Cl_2 = 1:30) to give **5** (86 mg, 96%) as white microcrystals. mp 184.5-186 °C. TLC (ether-CH_2Cl_2 = 1:30): R_f = 0.41. ^1H NMR: δ 7.44 (d, J = 7.7 Hz, 2 H), 7,13-7.30 (m, 12 H), 7.01 (tt, J = 1.2, 7.3 Hz, 1 H), 6.54 (br s, 1 H), 4.60 (d, J = 10.6 Hz, 1 H), 3.79-3.87 (m, 1 H), 3.75 (d, J = 10.8 Hz, 1 H), 2.84 (ddd, J = 1.4, 6.3, 12.3 Hz, 1 H), 2.35 (dd, J = 9.2, 12.3 Hz, 1 H), 1.34 (d, 3 H). $^{13}C\{^1H\}$ NMR: δ 154.2, 145.6, 145.2, 139.2, 128.9, 128.7, 128.5, 126.8, 126.6, 126.4, 122.9, 119.8, 56.2, 52.8, 52.1, 46.6, 20.8. IR (neat, cm^{-1}): 3267, 1645, 1538, 1443, 1388, 695. HRMS calcd (found) for $C_{24}H_{25}N_2O$ (MH^+): 357.1967 (357.1969).

The remaining nitrogen heterocycles were synthesized employing a procedure analogous to that used to synthesize **3c**.

Benzyl 2-methyl-4,4-diphenylpyrrolidinecarbamate (3a).[S3] Viscous colorless oil. TLC (EtOAc-hexanes = 1:5): R_f = 0.41. ^1H NMR (1:1 ratio of rotomers): δ 7.11-7.40 (m, 15 H), [5.31 (d, J = 12.4 Hz), 5.09 (d, J = 12.4 Hz), 1:1, 1 H], [5.18 (abq, J = 12.4 Hz), 1:1, 1 H], [4.74 (dd, J = 2.0, 11.6 Hz), 4.58 (dd, J = 1.6, 11.6 Hz), 1:1, 1 H], 3.65-3.81 (m, 2 H), 2.80-2.86 (m, 1 H), [2.31 (dd, J = 9.6, 12.4 Hz), 2.26 (dd, J = 9.6, 12.8 Hz), 1:1, 1 H], [1.36 (d, J = 6.0 Hz), 1.29 (d, J = 6.0 Hz), 1:1, 3 H].

$^{13}C\{^1H\}$ NMR: δ [155.7, 154.9, (1:1)], [146.0, 146.0, (1:1)], [145.5, 145.3, (1:1)], [137.4, 137.3, (1:1)], 128.8, 128.8, 128.8, 128.7, 128.3, 128.3, 128.1, 127.8, 127.1, 126.8, 126.8, 126.7, 126.7, 126.6, [67.1, 66.9, (1:1)], 56.2, [53.1, 53.1, (1:1)], [52.9, 52.5, (1:1)], [47.2, 46.3, (1:1)], [21.5, 20.4, (1:1)]. IR (neat, cm^{-1}): 3031, 2963, 1700, 1447, 1216, 1095. Anal. calcd (found) for $C_{25}H_{25}NO_2$: H, 6.78 (6.59); C, 80.83 (80.83); N, 3.77 (3.80).

1-(2-Methyl-4,4-diphenyl-pyrrolidin-1-yl)-ethanone (3b).[S4] White solid. TLC (ether–CH_2Cl_2 = 1:2): R_f = 0.57. ^1H NMR (1:1 mixture of rotomers): δ 7.13-7.33 (m, 10 H), [4.99 (dd, J = 2.4, 12.1 Hz), 4.29 (dd, J = 1.9, 10.8 Hz), 1 H], [4.04 (qdd, J = 6.5, 6.5, 8.9 Hz), 3.77 (qdd, J = 6.2, 6.2, 12.6 Hz), 1 H], [3.94 (d, J = 10.9 Hz), 3.58 (d, J = 12.1 Hz), 1 H], [3.00 (ddd, J = 2.6, 6.8, 12.6 Hz), 2.93 (ddd, J = 1.9, 7.0, 12.8), 1 H], [2.40 (dd, J = 8.7, 12.5 Hz), 2.23 (dd, J = 9.1, 12.8 Hz), 1 H], [2.11 (s), 2.02 (s), 3 H], [1.33 (d, J = 6.2 Hz), 1.32 (d, J = 6.2 Hz), 3 H]. $^{13}C\{^1H\}$ NMR (1:1 mixture of rotomers): δ 169.9, 168.9, 145.8, 145.7, 145.2, 145.0, 128.8, 128.7, 128.7, 128.7, 126.8, 126.7, 126.7, 126.5, 126.5, 126.4, 58.1, 54.6, 53.1, 52.8, 52.5, 52.3, 47.4, 45.7, 23.5, 22.1, 21.6, 20.2. IR (neat, cm^{-1}): 2969, 2876, 1637, 1412, 1347, 699. Anal. calcd (found) for $C_{19}H_{21}NO$: H, 7.58 (7.38); C, 81.68 (81.80).

Ethyl 2-methyl-4,4-diphenyl-pyrrolidine-1-carboxamide (S26). Colorless oil. TLC (ether–CH_2Cl_2 = 1:4): R_f = 0.35. ^1H NMR: δ 7.09-7.28 (m, 10 H), 4.48 (d, J = 10.9 Hz, 1 H), 4.13 (br t, J = 5.1 Hz, 1 H), 3.62 (d, J = 10.6 Hz, 1 H), 3.58-3.66 (m, 1 H), 3.21-3.36 (m, 1 H), 2.76 (ddd, J = 1.7, 6.3, 12.1 Hz, 1 H), 2.32 (dd, J = 9.1, 12.3 Hz, 1 H), 1.26 (d, J = 6.0 Hz, 3 H), 1.13 (t, J = 7.2 Hz, 3 H). $^{13}C\{^1H\}$ NMR: δ 157.0, 145.9, 145.6, 128.6, 128.6, 127.0, 126.6, 126.6, 126.4, 56.1, 52.9, 51.8, 47.1, 35.6, 21.0, 15.9. IR (neat, cm^{-1}): 3332, 2967, 1625, 1530, 1336, 698. Anal. calcd (found) for $C_{20}H_{24}N_2O$: H, 7.84 (7.79); C, 77.89 (78.04). HRMS calcd (found) for $C_{20}H_{24}N_2O$ (M^+): 308.1889, found 308.1888.

4-Bromophenyl 2-methyl-4,4-diphenylpyrrolidine-1-carboxamide (S27). White solid. TLC (ether–CH_2Cl_2 = 1:19): R_f = 0.69. ^{1}H NMR: δ 7.15-7.40 (m, 14 H), 6.20 (s, 1 H), 4.59 (d, J = 10.1 Hz, 1 H), 3.79-3.85 (d, J = 10.8 Hz, 1 H), 2.89 (dd, J = 5.1, 11.3 Hz, 1 H), 2.40 (dd, J = 9.2, 12.5 Hz, 1 H), 1.37 (d, J = 6.2 Hz, 3 H). ^{13}C{^{1}H} NMR: δ 153.8, 145.5, 145.1, 138.3, 131.9, 128.8, 128.7, 126.9, 126.8, 126.7, 126.5, 121.2, 115.5, 56.3, 52.9, 52.3, 46.9, 20.9. IR (neat, cm^{-1}): 2972, 1643, 1518, 1401, 1238, 698. Anal. calcd (found) for $C_{24}H_{23}BrN_2O$: H, 5.32 (5.20); C, 66.21 (66.02). HRMS calcd (found) for $C_{24}H_{23}{}^{79}BrN_2O$ (M^+): 434.0994 (434.0999).

4-Methoxyphenyl 2-methyl-4,4-diphenylpyrrolidine-1-carboxamide (S28). White solid. TLC (ether–CH_2Cl_2 = 1:9): R_f = 0.52. ^{1}H NMR: δ 7.14-7.33 (m, 12 H), 6.85 (d, J = 8.9 Hz, 2 H), 6.07 (s, 1 H), 4.61 (d, J = 10.1 Hz, 1 H), 3.77-3.83 (m, 1 H), 3.79 (s, 3 H), 3.76 (d, J = 10.6 Hz, 1 H), 2.86 (dd, J = 6.3, 12.1 Hz, 1 H), 2.40 (dd, J = 9.2, 12.1 Hz, 1 H), 1.37 (d, J = 6.2 Hz, 3 H). ^{13}C{^{1}H} NMR: δ 155.9, 154.6, 145.7, 145.3, 132.2, 128.8, 128.7, 127.0, 126.8, 126.6, 122.0, 114.3, 56.3, 55.7, 52.9, 52.2, 47.0, 20.9. IR (neat, cm^{-1}): 3301, 1640, 1511, 1372, 1232, 699. Anal. calcd (found) for $C_{25}H_{26}N_2O_2$: H, 6.78 (6.56); C, 77.69 (77.42). HRMS calcd (found) for $C_{25}H_{26}N_2O_2$ (M^+): 386.1994 (386.1996).

4-Acetylphenyl 2-methyl-4,4-diphenylpyrrolidine-1-carboxyamide (S29). White solid. TLC (ether–CH_2Cl_2 = 1:9): R_f = 0.35. ^{1}H NMR: δ 7.89 (d, J = 8.9 Hz, 2 H), 7.53 (d, J = 8.7 Hz, 2 H), 7.14-7.31 (m, 10 H), 6.71 (br s, 1 H), 4.61 (d, J = 9.9 Hz, 1 H), 3.82-3.90 (m, 1 H), 3.80 (d, J = 10.8 Hz, 1 H), 2.89 (dd, J = 6.5, 12.1 Hz, 1 H), 2.54 (s, 3 H), 2.39 (dd, J = 9.2, 12.3 Hz, 1 H), 1.37 (d, J = 6.2 Hz, 3 H). ^{13}C{^{1}H} NMR: δ 197.2, 153.4, 145.4, 145.0, 144.0, 131.6, 129.9, 128.8, 128.7, 126.8, 126.7, 126.4, 118.4, 56.3, 52.9, 52.4, 46.7, 26.5, 20.8. IR (neat, cm^{-1}): 1653, 1519, 1367, 1250, 1176, 699. HRMS calcd (found) for $C_{26}H_{26}N_2O_2$ (M^+): 398.1994 (398.1997).

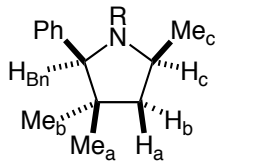
Phenyl 3-methyl-2-aza-spiro[4.5]decane-2-carboxamide (S30). White solid. TLC (ether-CH_2Cl_2 = 1:19): R_f = 0.50. ^{1}H NMR: δ 7.62 (t, J = 8.0 Hz, 2 H), 7.25-7.29 (m, 2 H), 6.98-7.02 (m, 1 H), 6.13 (br s, 1 H), 3.32 (s, 2 H), 1.83 (s, 2 H), 1.54 (s, 6 H), 1.38-1.59 (m, 10 H). ^{13}C{^{1}H} NMR: δ 153.8, 139.4, 128.9, 122.7, 119.8, 61.7, 58.4, 54.2, 40.0, 37.6, 28.9, 26.0, 23.5. IR (neat, cm^{-1}): 3297, 2924, 2854, 1637, 1367, 757. Anal. calcd (found) for $C_{17}H_{24}N_2O$: H, 8.88 (8.82); C, 74.96 (74.92). HRMS calcd (found) for $C_{17}H_{24}N_2O$ (M^+): 286.2045 (286.2043).

Ethyl 3,3,5-trimethyl-2-phenyl-pyrrolidine-1-carboxamide (S31). Chromatography of the crude reaction product gave three fractions, one of which consisted of a >20:1 mixture of *cis*-**S31**:*trans*-**S31**, a second that consisted of a 14:1 mixture of *cis*-**S31**:*trans*-**S31**, and a third that consisted of a 1:2.8 mixture of *cis*-**S31**:*trans*-**S31**. Spectroscopic analysis of these fractions allowed assignment of the ^{1}H and ^{13}C{^{1}H} NMR resonances corresponding to *cis*-**S31** and *trans*-**S31**, respectively. Combination of these fractions gave **S31** [99%, 3.9:1 (cis/trans)] as a white solid. TLC (ether–CH_2Cl_2 = 1:5): R_f = 0.44. ^{1}H NMR (*cis*-**S31**): δ 7.23-7.37 (m, 5 H), 4.19 (s, 1 H), 4.09-4.18 (m, 1 H), 3.80 (br t, J = 5.5 Hz, 1 H), 3.00-3.19 (m, 2 H), 1.76 (dd, J = 6.7, 12.5 Hz, 1 H), 1.53 (d, J = 6.2 Hz, 3 H), 1.51 (dd, J = 10.3, 12.8 Hz, 1 H), 1.18 (s, 3 H), 0.92 (t, J = 7.2 Hz, 3 H), 0.57 (s, 3 H). ^{13}C{^{1}H} NMR (*cis*-**S31**): δ 158.3, 141.2, 128.7, 127.8, 127.2, 74.0, 52.9, 45.9, 42.1, 35.2, 29.6, 25.3, 21.1, 15.5. ^{1}H NMR (*trans*-**S31**): δ 7.26-7.32 (m, 3 H), 7.08 (d, J = 7.5 Hz, 2 H), 4.29-4.37 (m, 1 H), 4.26 (s, 1 H), 3.78 (br t, J = 5.8 Hz, 1 H), 2.88-3.13 (m, 2 H), 2.10 (dd, J = 9.1, 13.0 Hz, 1 H), 1.50 (d, J = 6.3 Hz, 3 H), 1.46 (dd, J = 3.6, 13.0 Hz, 1 H), 1.31 (s, 3 H), 0.71 (t, J = 7.2 Hz, 3 H), 0.57 (s, 3 H). ^{13}C{^{1}H} NMR (*trans*-**S31**): δ 157.2, 140.8, 128.6, 127.7, 127.2, 72.8, 54.3, 45.2, 42.5, 35.2, 30.5, 25.9, 22.2, 15.3. IR (neat, cm^{-1}): 3397, 2963, 1626, 1519, 1324, 697. HRMS calcd (found) for $C_{16}H_{24}N_2O$ (M^+): 260.1889 (260.1894).

The stereochemistry of the major diastereomer of **S31** (*cis*-**S31**) was determined via ^{1}H-^{1}H NOESY analysis (Figures S1 and S3). A cis relationship between Me_a and H_{Ph} was established by the

much stronger cross peak between Me_b and H_{Bn} relative to the cross peak between Me_a and H_{Bn} and from the presence of a cross peak between Me_a and H_{Ph} and the absence of a detectable cross peak between Me_b and H_{Ph}. The cis relationship between H_b and Me_b was established by the greater magnitude of the Me_b/H_b cross peak relative to the Me_a/H_b cross peak. The overlapping resonances corresponding to H_a and Me_c in the ^1H NMR spectrum of *cis*-**S31** complicated, stereochemical analysis. Nevertheless, the cis relationship between H_a and Me_c was established from the NOESY spectrum. First, was the presence of a cross peak between H_a/Me_c and Me_a and the absence of a cross peak between H_a/Me_c and Me_b. Second was the presence of a cross peak between H_{Ph} and H_a/Me_c and the absence of cross peaks between either H_{Ph} and H_c or between H_{Ph} and H_b. Therefore H_a and Me_c must be cis to one another and, because H_b is trans to H_{Ph}, Me_c must be cis to H_{Ph}. Taken together, these data establish the cis relationship between Me_c and H_{Ph}.

Figure S1. Relevant cross-peaks and NOE enhancements observed in the ^1H-^1H NOESY spectrum of *cis*-**S31** (all values reported are absolute enhancements and not standardized).



cis-**S31** (R = CONHEt)

NOE enhancements

$H_{Ph} \rightarrow H_b = 3.4\%$
$H_{Ph} \rightarrow Me_c = 6.4\%$
$H_{Ph} \rightarrow Me_a = 4.3\%$

$Me_a \rightarrow H_{Bn} = 2.4\%$
$Me_a \rightarrow H_b = 1.8\%$
$Me_a \rightarrow H_a = 4.6\%$

$Me_b \rightarrow H_{Bn} = 5.6\%$
$Me_b \rightarrow H_b = 4.0\%$

Phenyl 3,3,5-trimethyl-2-phenyl-pyrrolidine-1-carboxamide (S32). Chromatography of the crude reaction product gave two fractions, one of which consisted of a >20:1 mixture of *cis*-**S32**:*trans*-

S32 and a second that consisted of 3.4:1 mixture of *cis*-**S32**:*trans*-**S32**. Spectroscopic analysis of these fractions allowed assignment of the ^{1}H and ^{13}C{^{1}H} NMR resonances corresponding to *cis*-**S32** and *trans*-**S32**. Combination of these fractions gave a 3.6:1 mixture of *cis*-**S32**:*trans*-**S32** (92%) as a white solid. TLC (ether–CH_2Cl_2 = 1:19): R_f = 0.54. ^{1}H NMR (*cis*-**S32**): δ 7.32-7.45 (m, 5 H), 7.15-7.19 (m, 2 H), 7.07-7.09 (m, 2 H), 6.92 (td, *J* = 1.2, 7.2 Hz, 1 H), 5.92 (s, 1 H), 4.37 (s, 1 H), 4.21-4.29 (m, 1 H), 1.85 (dd, *J* = 6.5, 12.6 Hz, 1 H), 1.61 (dd, *J* = 10.1, 12.6 Hz, 1 H), 1.58 (d, *J* = 6.0 Hz, 3 H), 1.25 (s, 3 H), 0.64 (s, 3 H). ^{13}C{^{1}H} NMR (*cis*-**S32**): δ 155.3, 140.4, 139.1, 129.1, 128.8, 128.3, 127.4, 122.6, 119.1, 74.3, 53.1, 45.8, 42.2, 29.6, 25.2, 20.6. ^{1}H NMR (*trans*-**S32**): δ 6.89-7.46 (m, 10 H), 5.94 (s, 1 H), 4.46 (s, 1 H), 4.40-4.44 (m, 1 H), 2.17 (dd, *J* = 9.1, 13.0 Hz, 1 H), 1.59 (d, *J* = 6.3 Hz, 3 H), 1.54 (dd, *J* = 3.6, 13.0 Hz, 1 H), 1.36 (s, 3 H), 0.63 (s, 3 H). ^{13}C{^{1}H} NMR (*trans*-**S32**): δ 154.2, 140.0, 139.0, 128.8, 128.7, 128.1, 127.4, 122.7, 119.5, 73.0, 54.5, 45.2, 42.6, 30.3, 25.8, 22.0. IR (neat, cm^{-1}): 3409, 2961, 1664, 1524, 1440, 1331. HRMS calcd (found) for $C_{20}H_{24}N_2O$ (M^+): 308.1889 (308.1892).

Phenyl 2-methyl-4-phenyl-pyrrolidine-1-carboxamide (S33). Chromatography of the crude reaction product gave two fractions, one of which consisted of a >20:1 mixture of *cis*-**S33**:*trans*-**S33** and a second that consisted of 3.7:1 mixture of *cis*-**S33**:*trans*-**S33**. Spectroscopic analysis of these fractions allowed assignment of the ^{1}H and ^{13}C{^{1}H} NMR resonances corresponding to *cis*-**S33** and *trans*-**S33**. Combination of these fractions gave **S33** [99%, 2.9:1 (cis/trans)] as a white solid. TLC (ether–CH_2Cl_2 = 1:19): R_f = 0.19. ^{1}H NMR (*cis*-**S33**): δ 7.22-7.40 (m, 9 H), 6.96-7.01 (m, 1 H), 6.23 (br s, 1 H), 4.06-4.14 (m, 1 H), 3.96 (dd, *J* = 8.0, 8.2 Hz, 1 H), 3.25-3.42 (m, 2 H), 2.52-2.58 (m, 1 H), 1.77 (dt, *J* = 9.4, 9.6 Hz, 1 H), 1.41 (d, *J* = 6.0 Hz, 3 H). ^{13}C{^{1}H} NMR (*cis*-**S33**): δ 154.2, 140.3, 139.3, 129.0, 128.8, 127.3, 127.1, 122.9, 119.6, 54.0, 53.5, 43.4, 42.1, 21.3. ^{1}H NMR (*trans*-**S33**): δ 7.22-7.40 (m, 9 H), 6.96-7.01 (m, 1 H), 6.22 (br s, 1 H), 4.27-4.33 (m, 1 H), 3.87 (dd, *J* = 8.4, 8.5 Hz, 1 H), 3.59-3.68 (m, 1 H), 3.34-3.40 (m, 1 H), 2.23 (dt, *J* = 8.0, 12.1 Hz, 1 H), 1.98 (dd, *J* = 6.5, 12.3 Hz, 1 H), 1.34 (d, *J* = 6.5

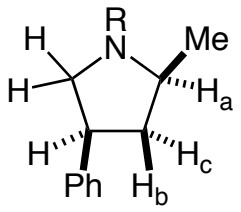
Hz, 3 H). $^{13}C\{^1H\}$ NMR (*trans*-**S33**): δ 153.7, 140.8, 139.2, 129.0, 128.9, 127.2, 127.2, 122.9, 119.6, 53.5, 53.0, 42.2, 40.0, 21.1. IR (neat, cm^{-1}): 3276, 1639, 1532, 1443, 1377, 756. HRMS calcd (found) for $C_{18}H_{20}N_2O$ (M^+): 280.1576 (280.1574).

Ethyl 2-methyl-4-phenyl-pyrrolidine-1-carboxamide (S34). Chromatography of the crude reaction product gave two fractions, one of which consisted of a >20:1 mixture of *cis*-**S34**:*trans*-**S34** and a second that consisted of 3.0:1 mixture of *cis*-**S34**:*trans*-**S34**. Spectroscopic analysis of these fractions allowed assignment of the ^1H and $^{13}C\{^1H\}$ NMR resonances corresponding to *cis*-**S34** and *trans*-**S34**. Combination of these fractions gave a 3.3:1 mixture of *cis*-**S34**:*trans*-**S34 S34** (84%) as a white solid. TLC (ether–CH_2Cl_2 = 1:19): R_f = 0.21. ^1H NMR (*cis*-**S34**): δ 7.22-7.34 (m, 5 H), 4.13 (br t, J = 5.3 Hz, 1 H), 3.86-4.03 (m, 2 H), 3.21-3.67 (m, 4 H), 2.50-2.56 (m, 1 H), 1.69-1.78 (m, 1 H), 1.37 (d, J = 6.2 Hz, 3 H), 1.15 (t, J = 7.3 Hz, 3 H). $^{13}C\{^1H\}$ NMR (*cis*-**S34**): δ 157.1, 140.8, 128.7, 127.2, 126.9, 53.5, 53.1, 43.2, 42.3, 35.5, 21.5, 15.8. ^1H NMR (*trans*-**S34**): δ 7.21-7.33 (m, 5 H), 4.18 (br t, J = 6.2 Hz, 1 H), 3.73 (dd, J = 8.4, 8.5 Hz, 1 H), 3.54-3.62 (m, 1 H), 3.20-3.36 (m, 4 H), 2.13-2.21 (m,1 H), 1.94 (dd, J = 6.2, 12.1 Hz, 1 H), 1.27 (d, J = 6.3 Hz, 3 H), 1.13 (t, J = 7.2 Hz, 3 H). $^{13}C\{^1H\}$ NMR (*trans*-**S34**): δ 156.6, 141.2, 128.7, 127.2, 127.0, 53.1, 52.7, 42.1, 40.1, 35.4, 21.2, 15.9. IR (neat, cm^{-1}): 3335, 2968, 1626, 1532, 1369, 761. HRMS calcd (found) for $C_{14}H_{20}N_2O$ (M^+): 232.1576 (232.1569).

The cis-stereochemistry of the major diastereomer of **S34** was established by combined ^1H-^1H NOESY and ^1H-^1H COSY analysis of the major diastereomer of **S34** (Figures S2, S4, & S5). 1H assignments were made on the basis of ^1H-^1H COSY analysis. The cis relationship between the menthyl group and phenyl group of the pyrrolidine ring was established from the presence of a cross peak between the aryl protons and the methyl group. Furthermore, the cis relationship between H_{Ph} and H_b was established by the presence of a cross peak between H_{Ph} and H_b and the absence of a cross peak

betweeh H_{Ph} and H_c. The cis relationship between H_b and Me was established by the presence of a cross peak between Me and H_b and the absence of a cross peak between Me and H_c.

Figure S2. Proton assignments for *cis*-**S34**.



cis-**S34** (R = CONHEt)

Phenyl 4-isopropyl-2-methyl-pyrrolidine-1-carboxamide (S35). Chromatography of the crude reaction product gave two fractions, one of which consisted of a 6.3:1 mixture of *cis*-**S35**:*trans*-**S35**, and a second that consisted of 4.1:1 mixture of *cis*-**S35**:*trans*-**S35**. Spectroscopic analysis of these fractions allowed assignment of the ^{1}H and ^{13}C{^{1}H} NMR resonances corresponding to *cis*-**S35** and partial assignment of the ^{1}H and ^{13}C{^{1}H} NMR resonances corresponding to *trans*-**S35**. Combination of these fractions gave a 5.5:1 mixture of *cis*-**S35**:*trans*-**S35**. **S35** (98%) as a white solid. TLC (ether–CH_2Cl_2 = 1:11): R_f = 0.62. ^{1}H NMR (*cis*-**S35**): δ 7.37-7.42 (m, 2 H), 7.25-7.29 (m, 2 H), 6.98-7.02 (m, 1 H), 6.11 (br s, 1 H), 3.92-4.01 (m, 1 H), 3.72 (t, J = 8.4 Hz, 1 H), 2.99-3.04 (m, 1 H), 2.32 (td, J = 6.7, 12.5 Hz, 1 H), 1.73-1.85 (m, 1 H), 1.44-1.53 (m, 1 H), 1.34 (d, J = 6.0 Hz, 3 H), 1.20-1.28 (m, 2 H), 0.92-0.96 (m, 6 H). ^{13}C{^{1}H} NMR (*cis*-**S35**): δ 154.3, 139.4, 128.9, 122.7, 119.5, 54.0, 51.6, 45.7, 40.0, 32.1, 21.6, 21.4, 21.2. ^{1}H NMR (*trans*-**S35**, partial): δ 6.14 (br s, 1 H), 4.14-4.21 (m, 1 H), 3.61 (dd, J = 8.0, 8.7 Hz, 1 H), 3.00-3.05 (m, 1 H), 2.07-2.19 (m, 1 H), 1.63-1.72 (m, 1 H), 1.34 (d, J = 6.0 Hz, 3 H). ^{13}C{^{1}H} NMR (*trans*-**S35**): δ 154.3, 139.4, 128.9, 122.7, 119.6, 53.5, 50.7, 44.4, 37.4, 32.5, 21.3, 21.2, 21.0. IR (neat, cm^{-1}): 3223, 2959, 1633, 1443, 1385, 756. Anal. calcd (found) for

$C_{15}H_{22}N_2O$: H, 9.00 (9.00); C, 73.13 (72.90). HRMS calcd (found) for $C_{15}H_{22}N_2O$ (M^+): 246.1732 (246.1731).

Benzyl 2-methyl-pyrrolidine-1-carboxamide (S36). TLC (ether–CH_2Cl_2 = 1:2): R_f = 0.46. White solid. ^{1}H NMR: δ 7.22-7.33 (m, 5 H), 4.53 (br t, 1 H), 4.36-4.48 (m, 2 H), 3.96-4.03 (m, 1 H), 3.21-3.34 (m, 2 H), 1.82-2.03 (m, 3 H), 1.54-1.61 (m, 1 H), 1.18 (d, J = 6.3 Hz, 3 H). ^{13}C{^{1}H} NMR: δ 156.6, 140.0, 128.6, 127.8, 127.2, 52.8, 45.9, 44.7, 32.9, 23.6, 20.7. IR (neat, cm^{-1}): 3334, 2962, 1626, 1533, 1389, 1350. HRMS calcd (found) for $C_{13}H_{18}N_2O$ (M^+): 218.1419 (218.1418).

Ethyl 3-methyl-2-aza-spiro[5.5]undecane-2-carboxamide (S37). TLC (ether–CH_2Cl_2 = 1:3): R_f = 0.50. Colorless oil. ^{1}H NMR: δ 4.41 (br t, J = 5.3 Hz, 1 H), 4.08-4.16 (m, 1 H), 3.64 (d, J = 13.5 Hz, 1 H), 3.13-3.29 (m, 2 H), 2.48 (d, J = 13.5 Hz, 1 H), 1.76-1.86 (m, 1 H), 1.17-1.43 (m, 13 H), 1.08 (t, J = 6.7 Hz, 3 H), 1.07 (d, J = 7.0 Hz, 3 H). ^{13}C{^{1}H} NMR: δ 157.8, 47.2, 46.2, 38.1, 35.7, 33.1, 31.4, 30.2, 26.7, 25.7, 21.8, 21.5, 15.7, 15.6. IR (neat, cm^{-1}): 3344, 2925, 2855, 1617, 1532, 1295. HRMS calcd (found) for $C_{14}H_{26}N_2O$ (M^+): 238.2045 (238.2043).

Figure S3. ^{1}H-^{1}H NOESY of *cis*-**S31**.

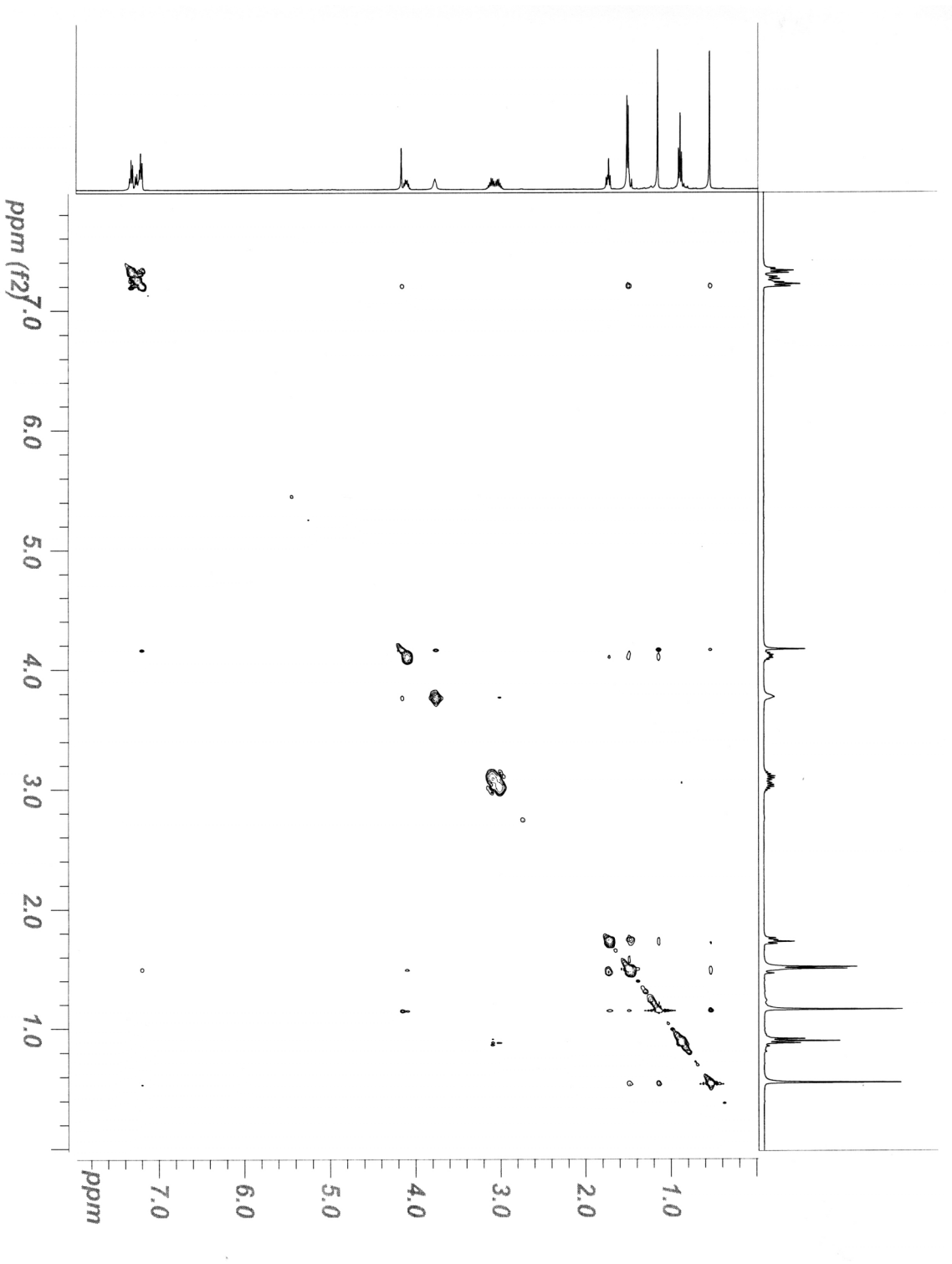


Figure S4. Partial ^{1}H-^{1}H COSY of *cis*-**S34**.

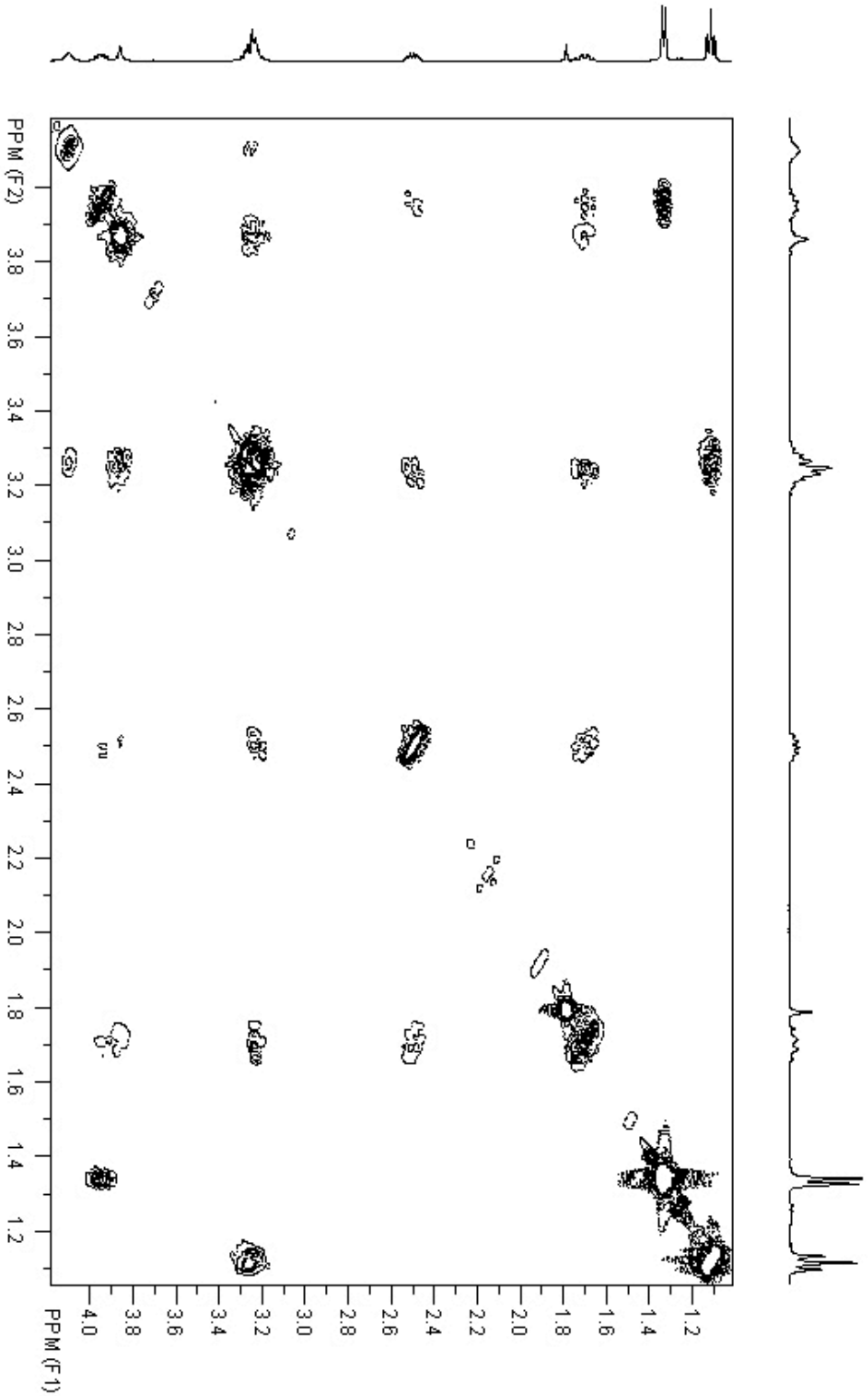


Figure S5. Partial ^{1}H-^{1}H NOESY of *cis*-**S34**.

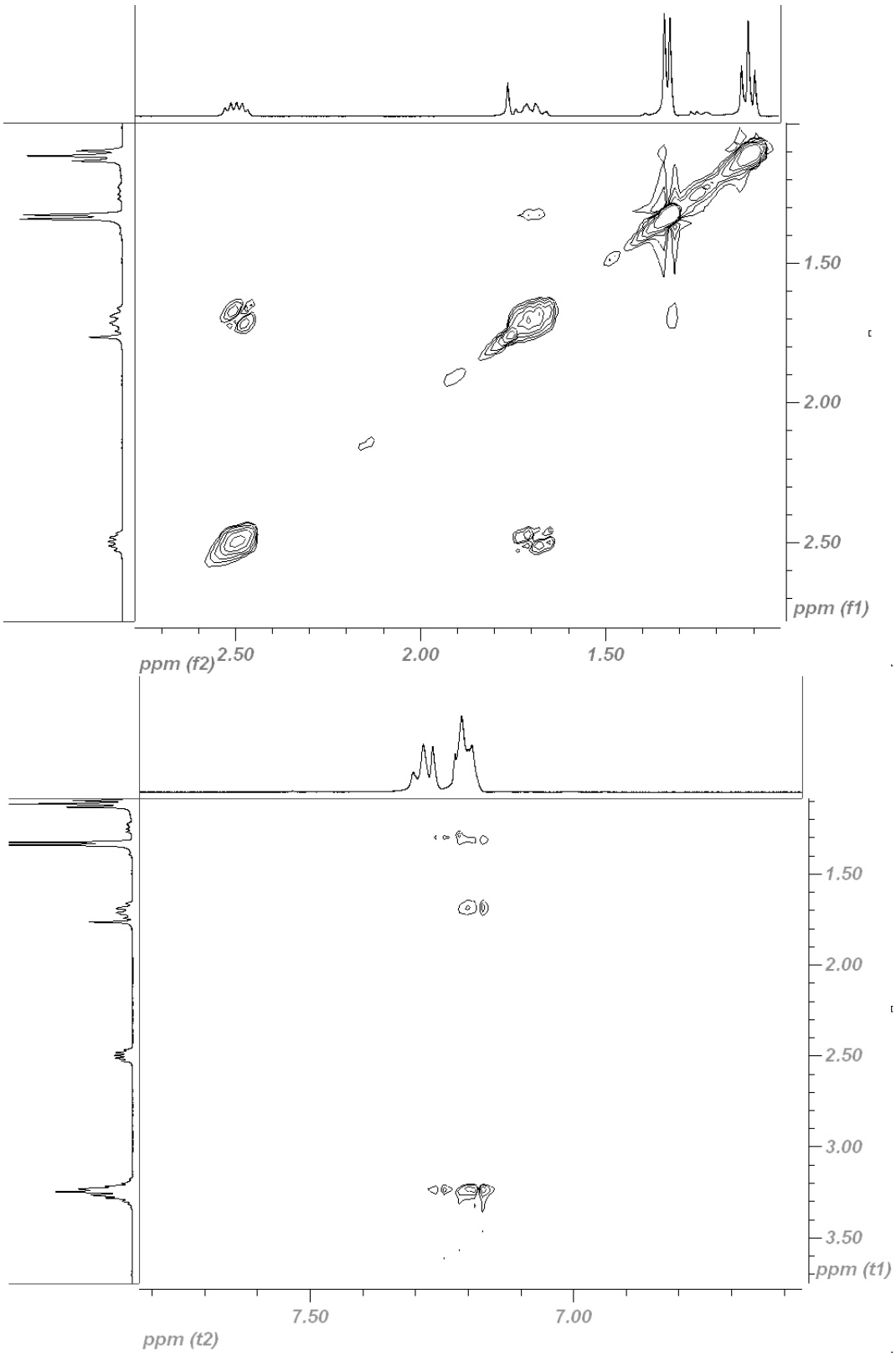


Figure S6. ^{1}H NMR spectrum of **2c**.

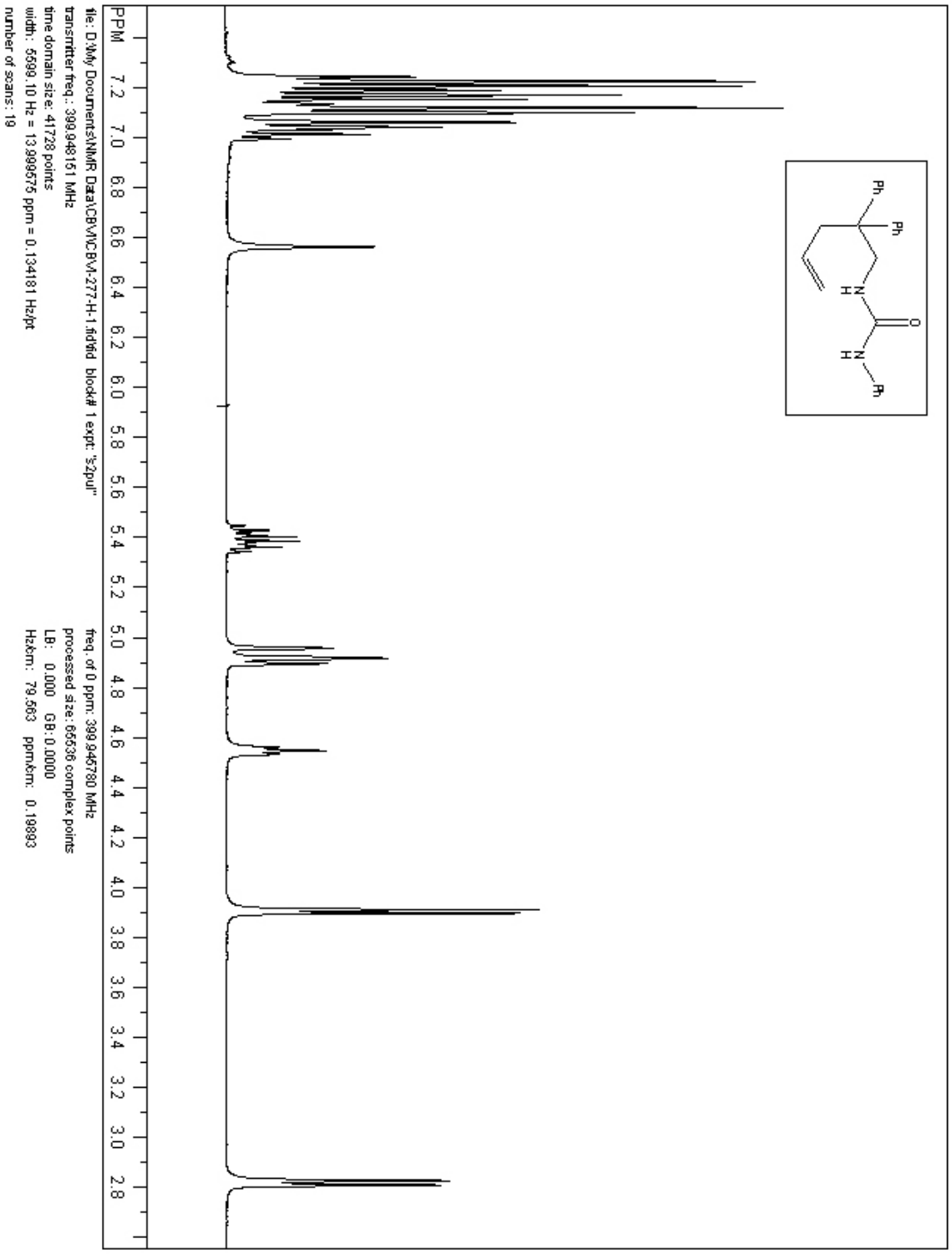


Figure S7. $^{13}C\{^{1}H\}$ NMR spectrum of **2c**.

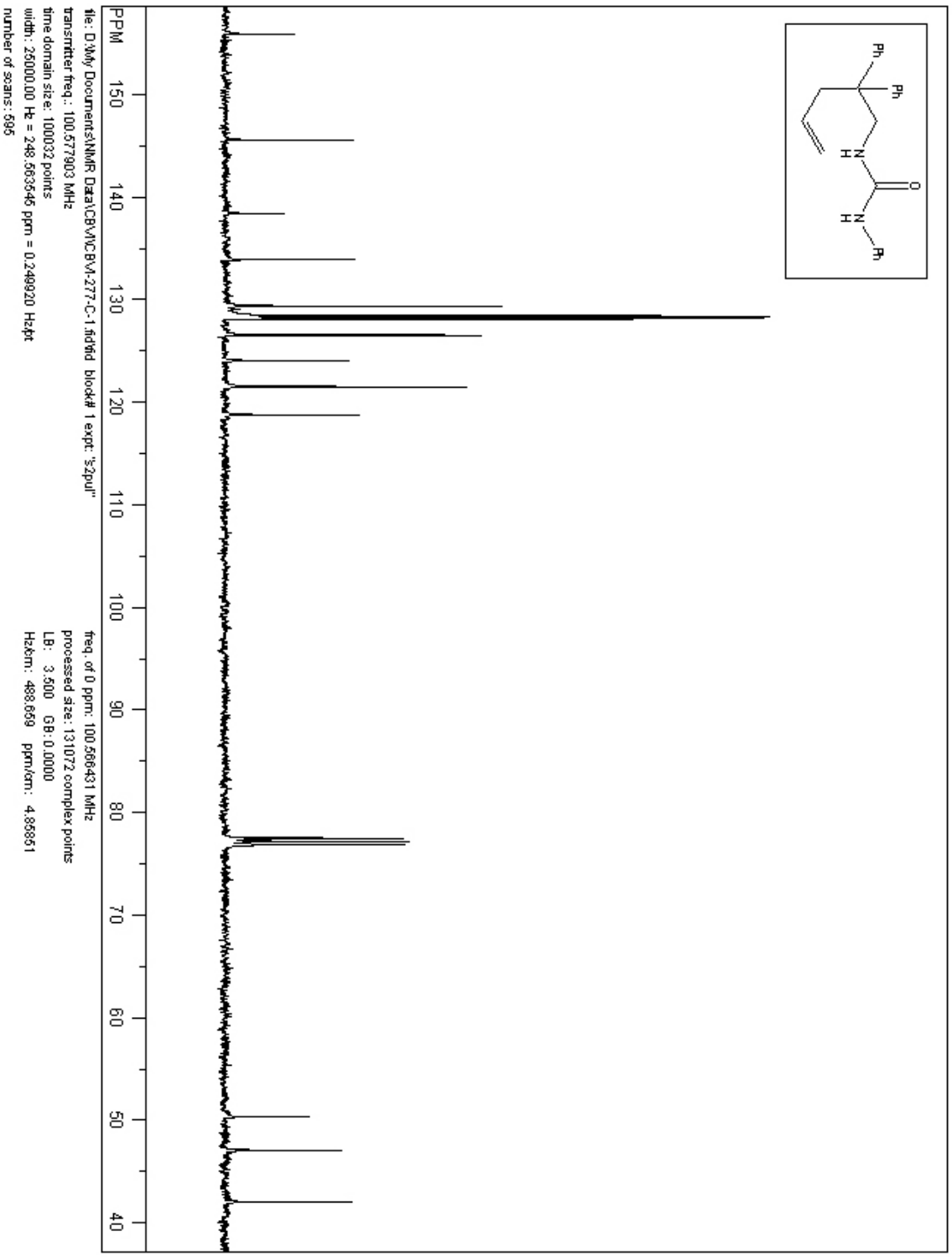


Figure S8. ^{1}H NMR spectrum of **3c**.

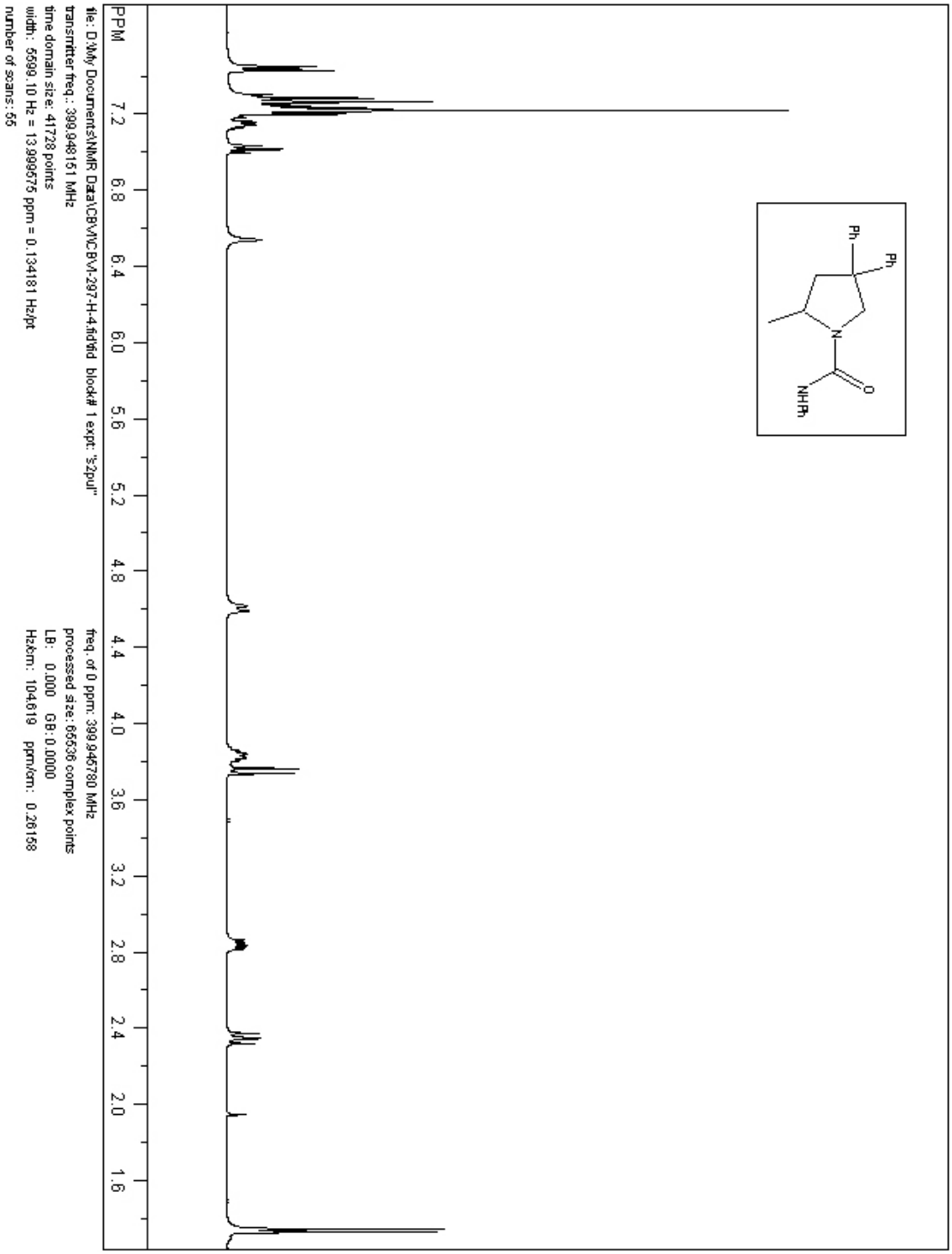


Figure S9. $^{13}C\{^{1}H\}$ NMR spectrum of **3c**.

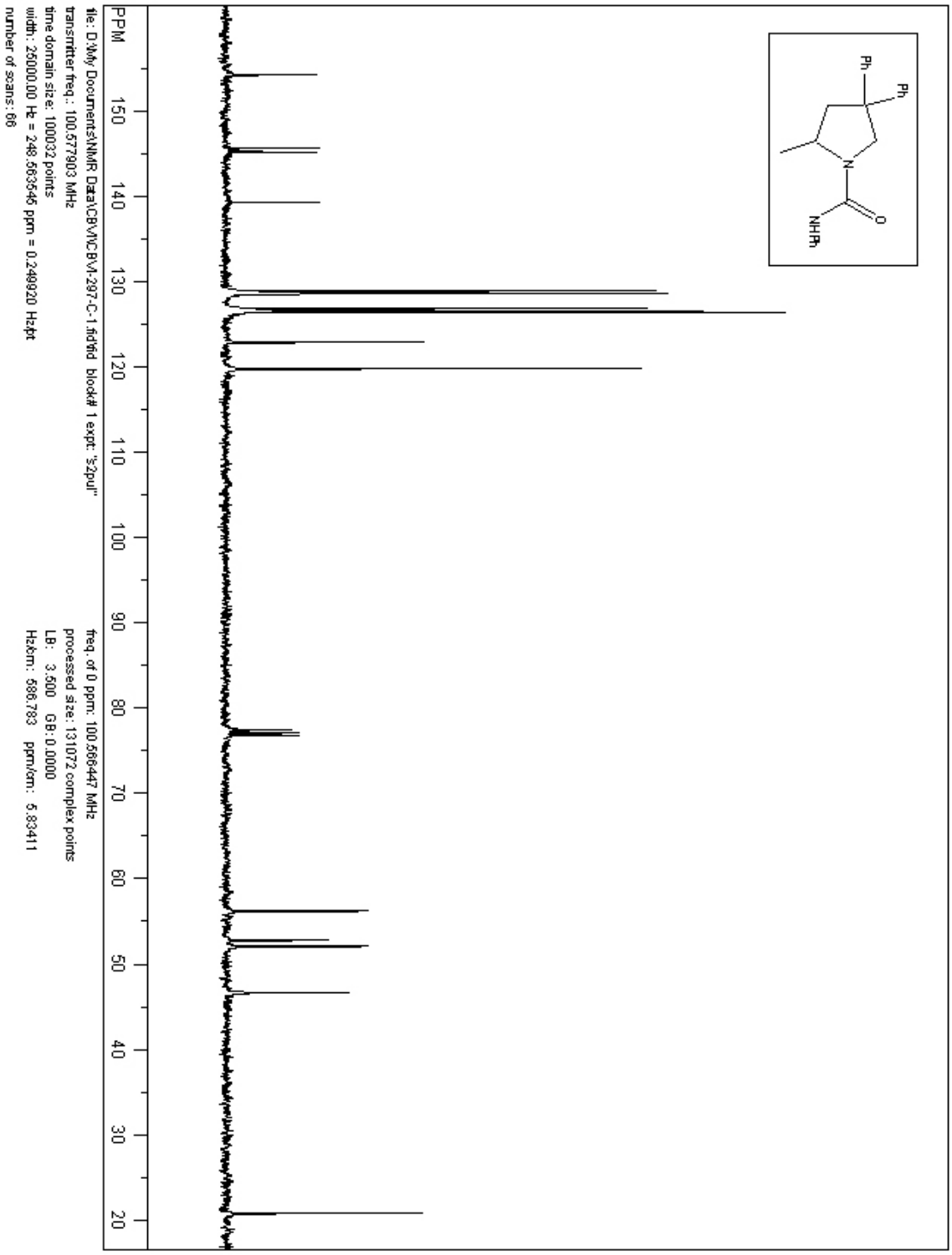


Figure S10. ^{1}H NMR spectrum of **3b**.

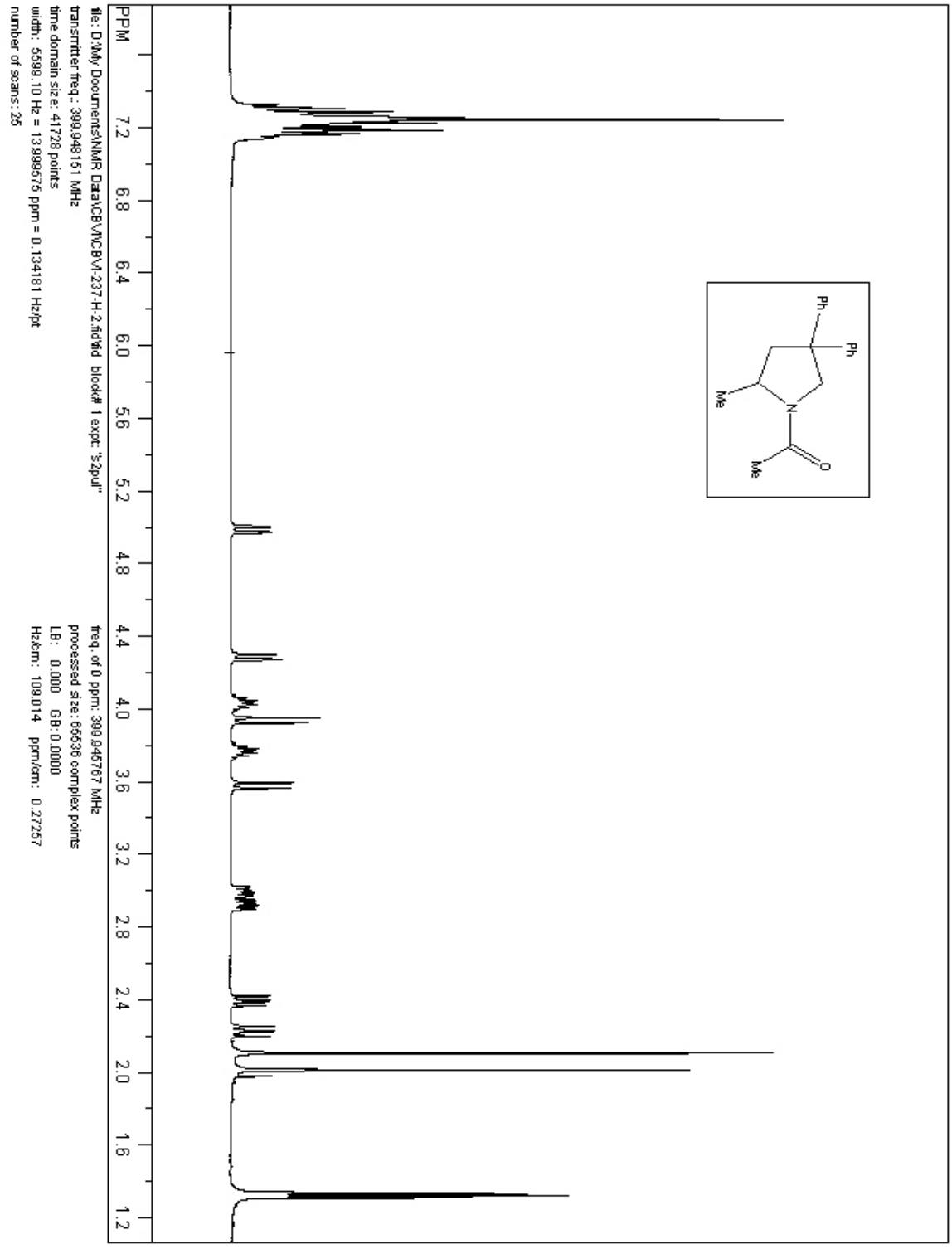


Figure S11. $^{13}C\{^{1}H\}$ NMR spectrum of **3b**.

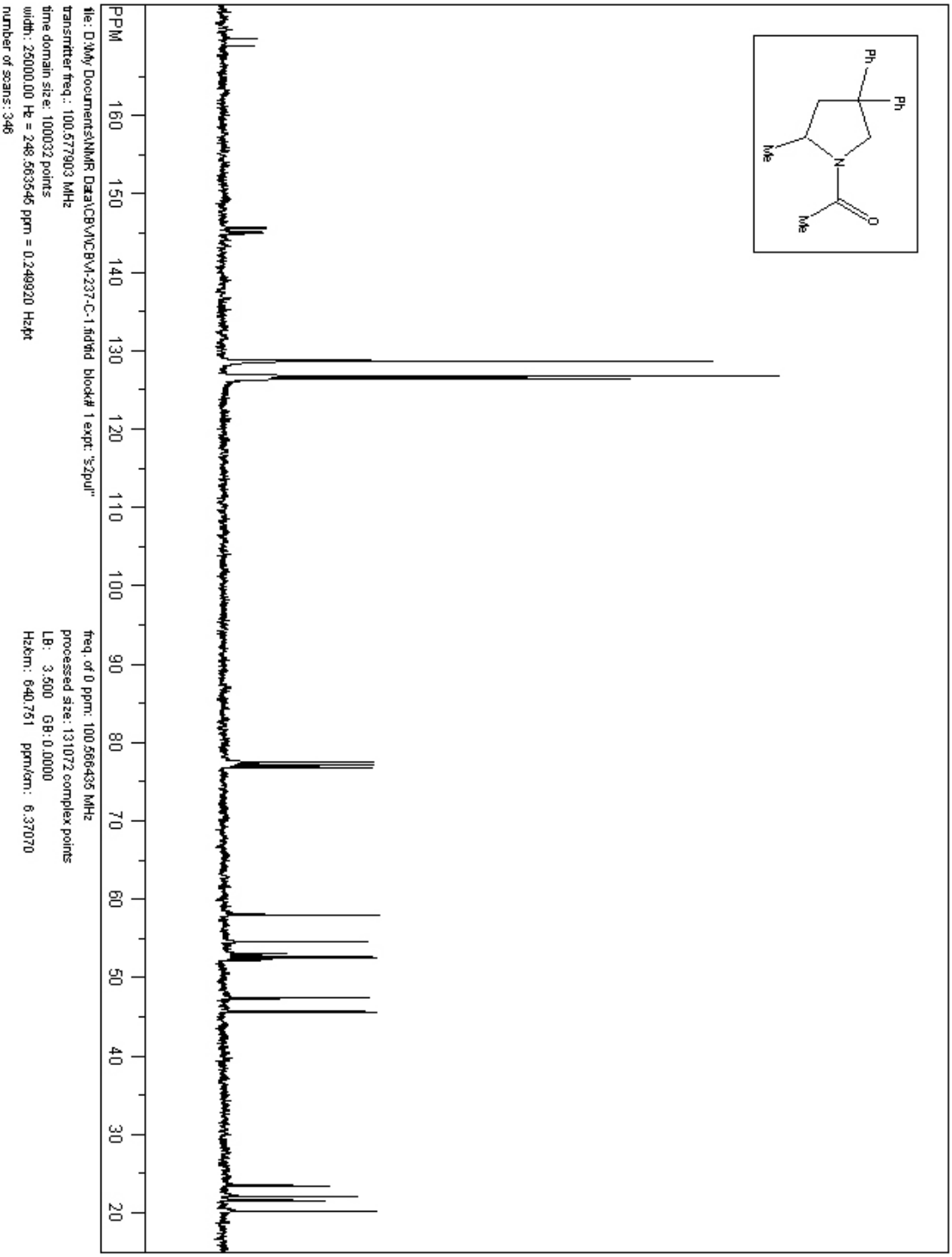


Figure S12. ^{1}H NMR spectrum of **3a**.

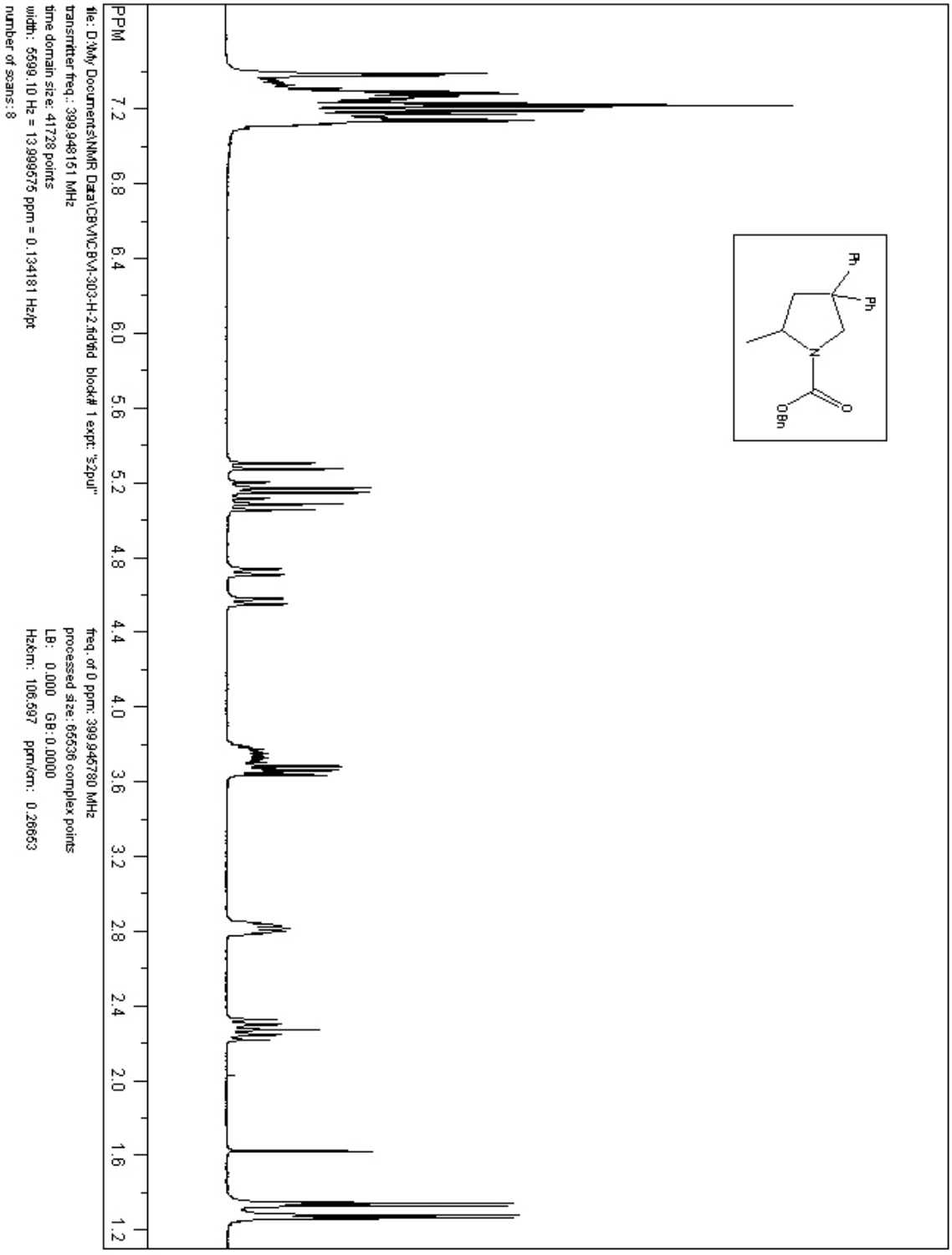


Figure S13. $^{13}C\{^{1}H\}$ NMR spectrum of **3a**.

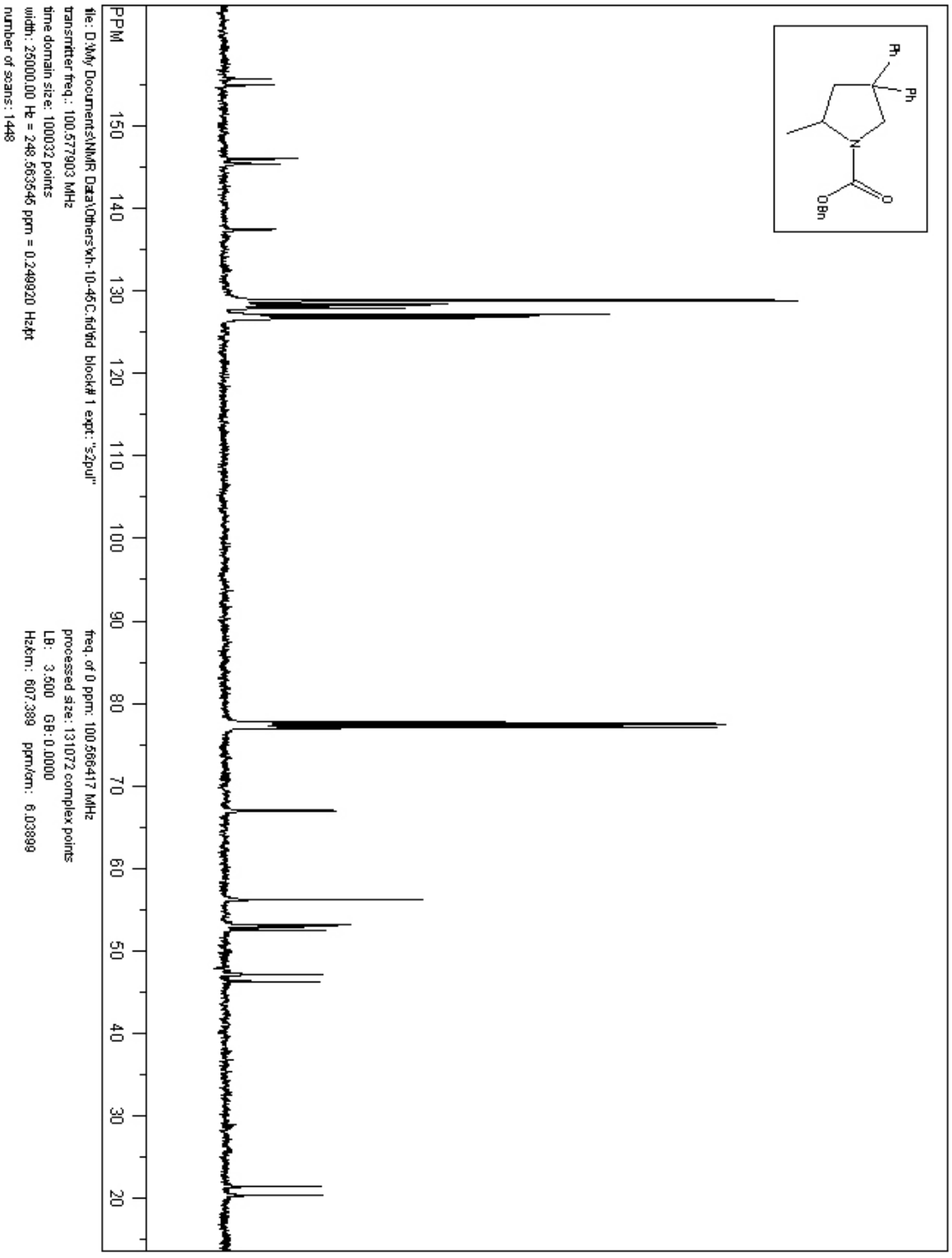


Figure S14. ^{1}H NMR spectrum of **S26**.

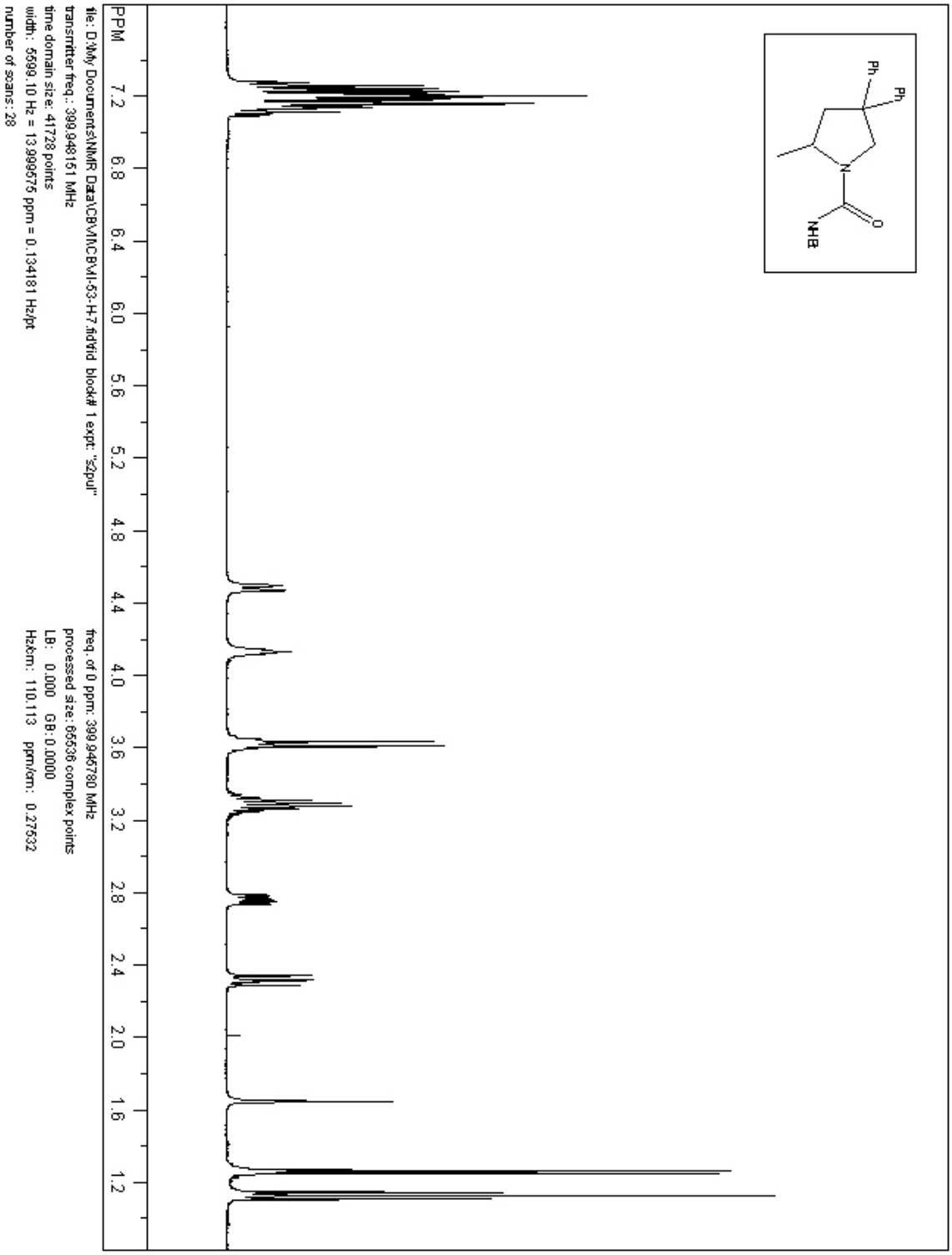


Figure S15. $^{13}C\{^{1}H\}$ NMR spectrum of **S26**.

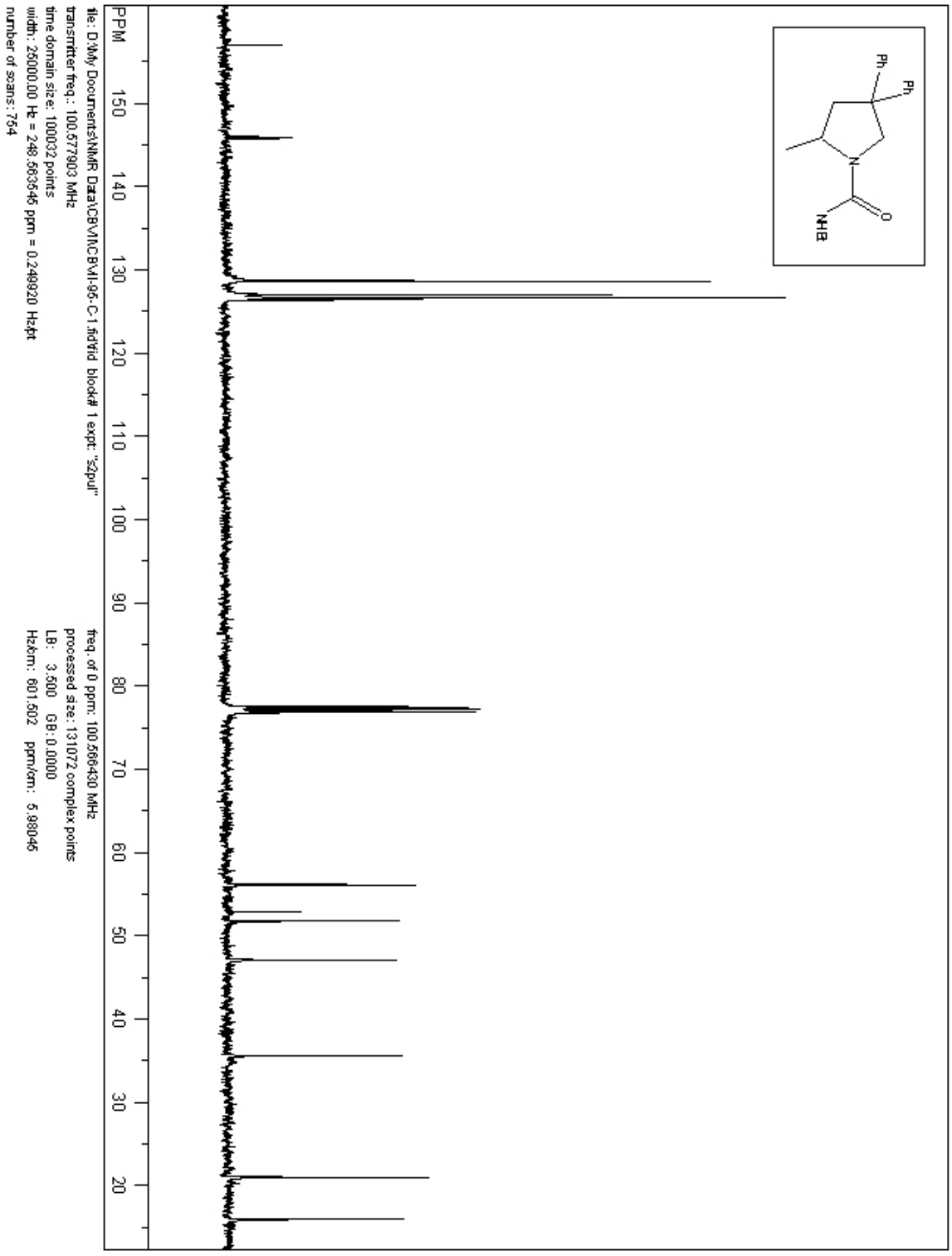


Figure S16. ^{1}H NMR spectrum of **S27**.

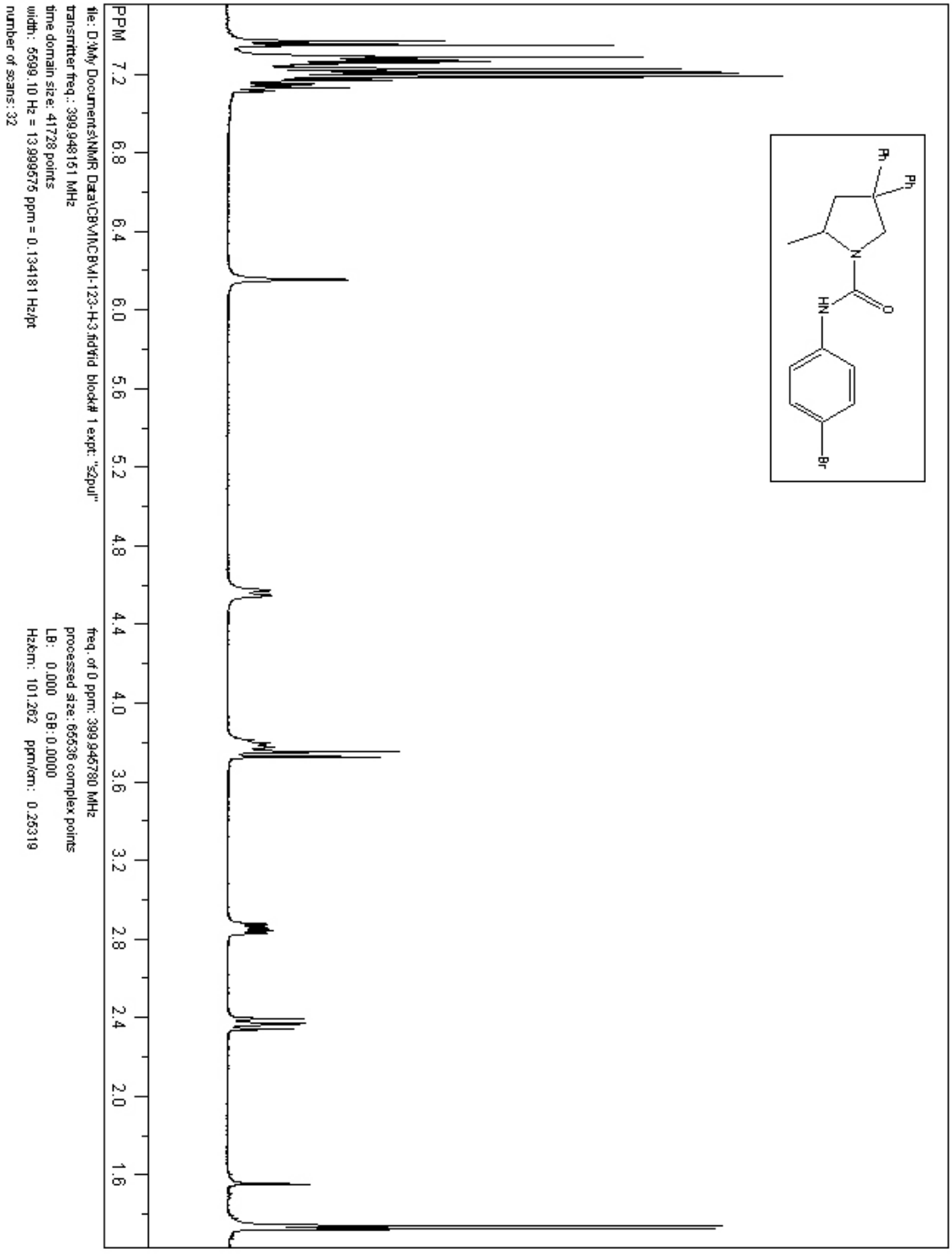


Figure S17. $^{13}C\{^{1}H\}$ NMR spectrum of **S27**.

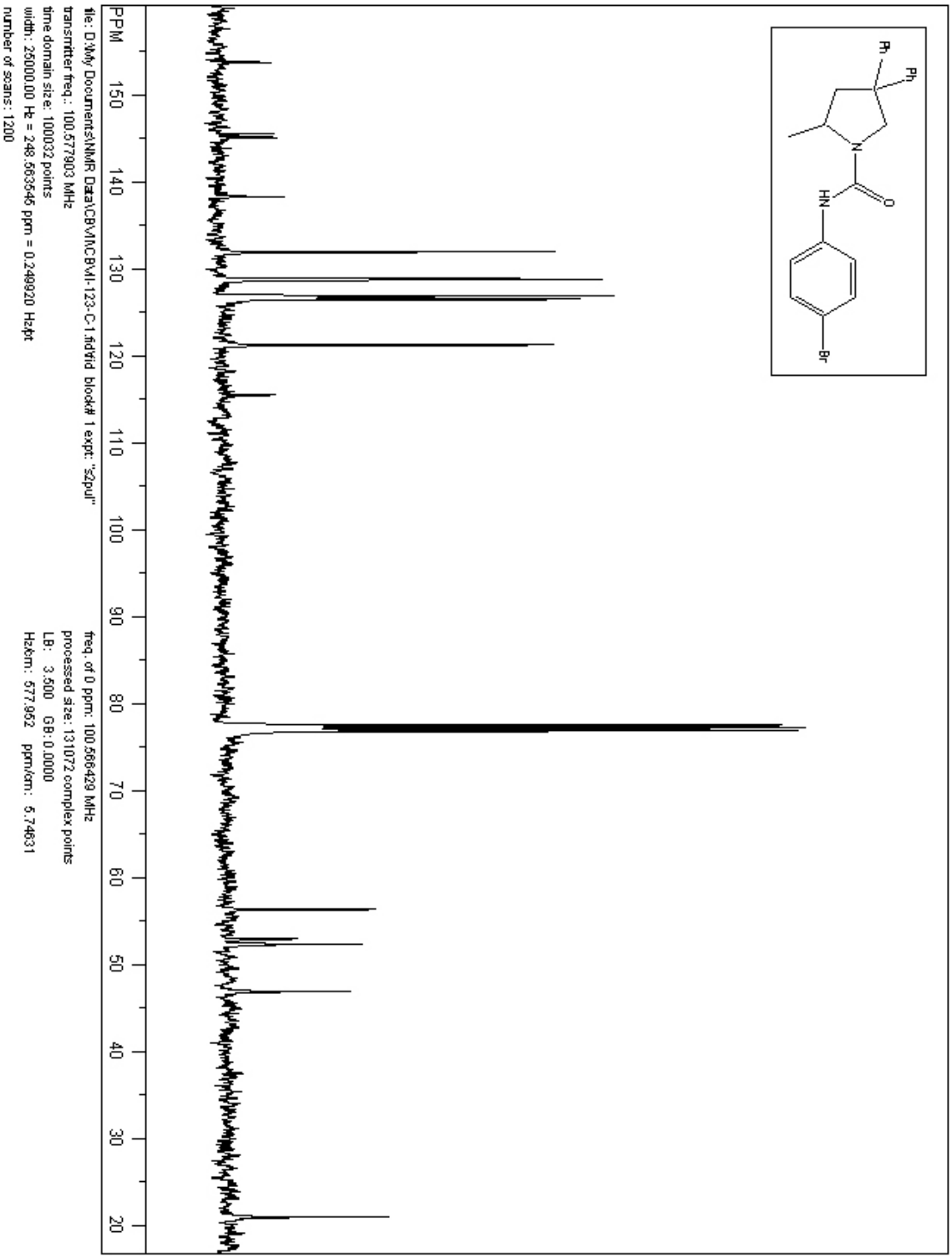


Figure S18. ^{1}H NMR spectrum of **S28**.

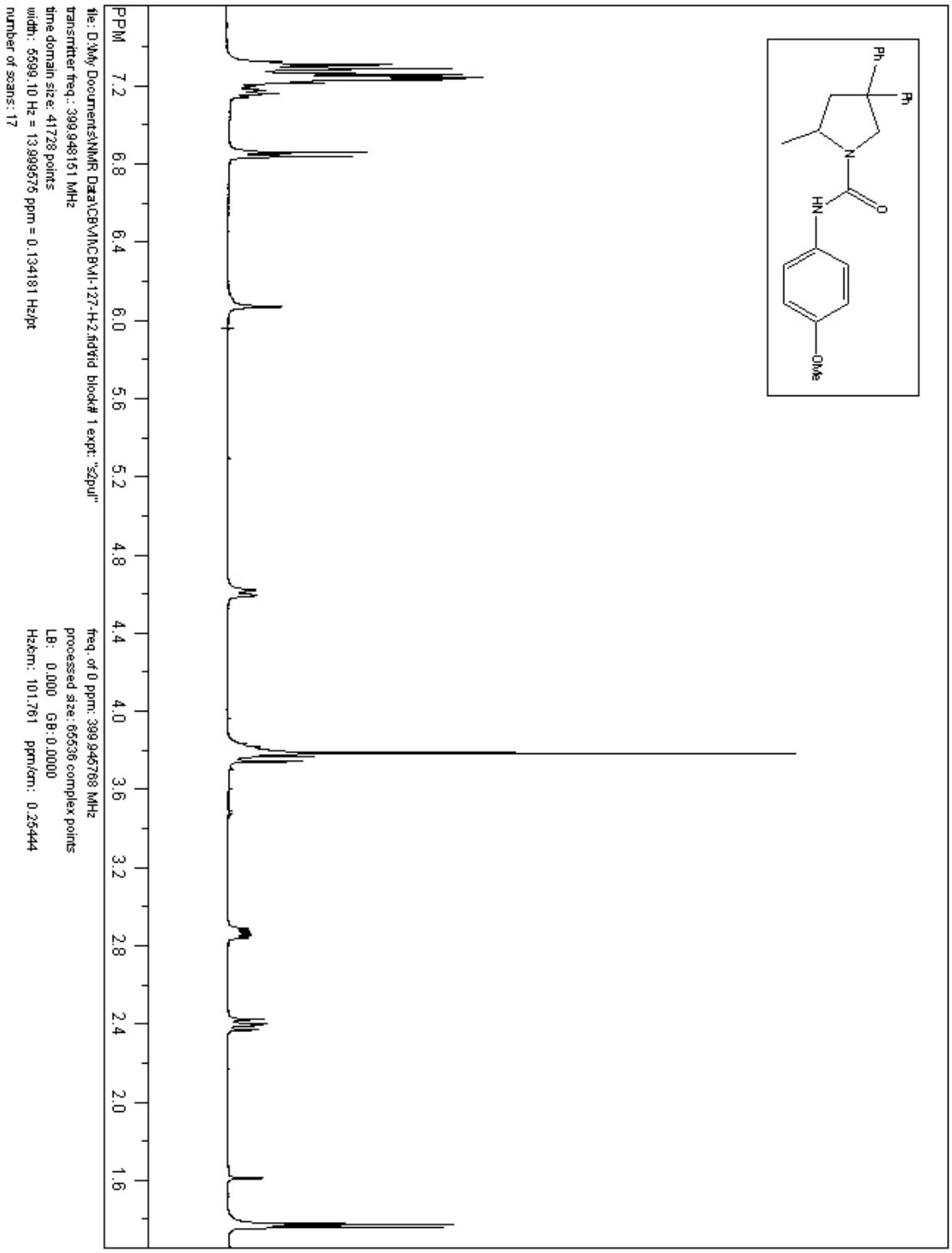


Figure S19. $^{13}C\{^{1}H\}$ NMR spectrum of **S28**.

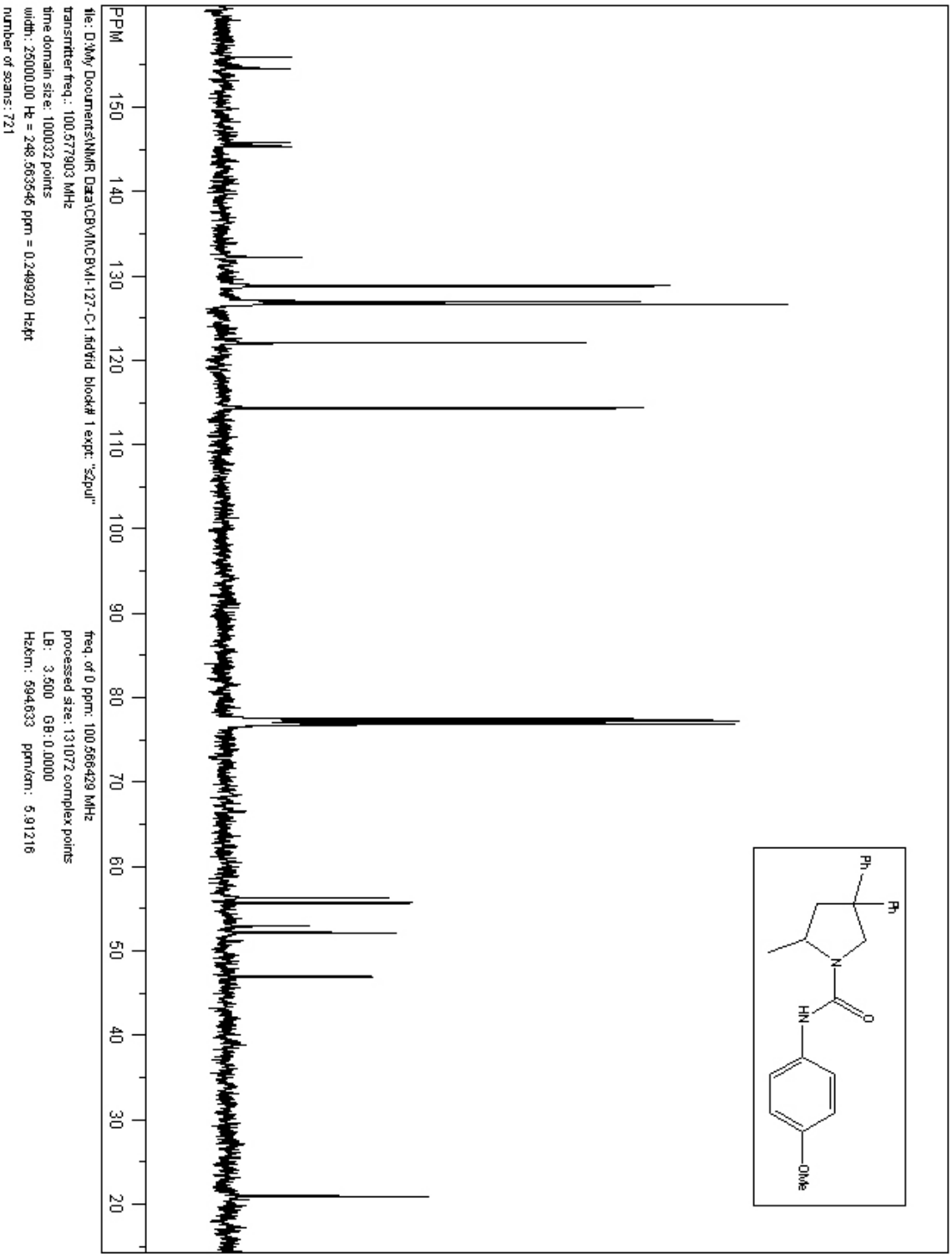


Figure S20. ^{1}H NMR spectrum of **S29**.

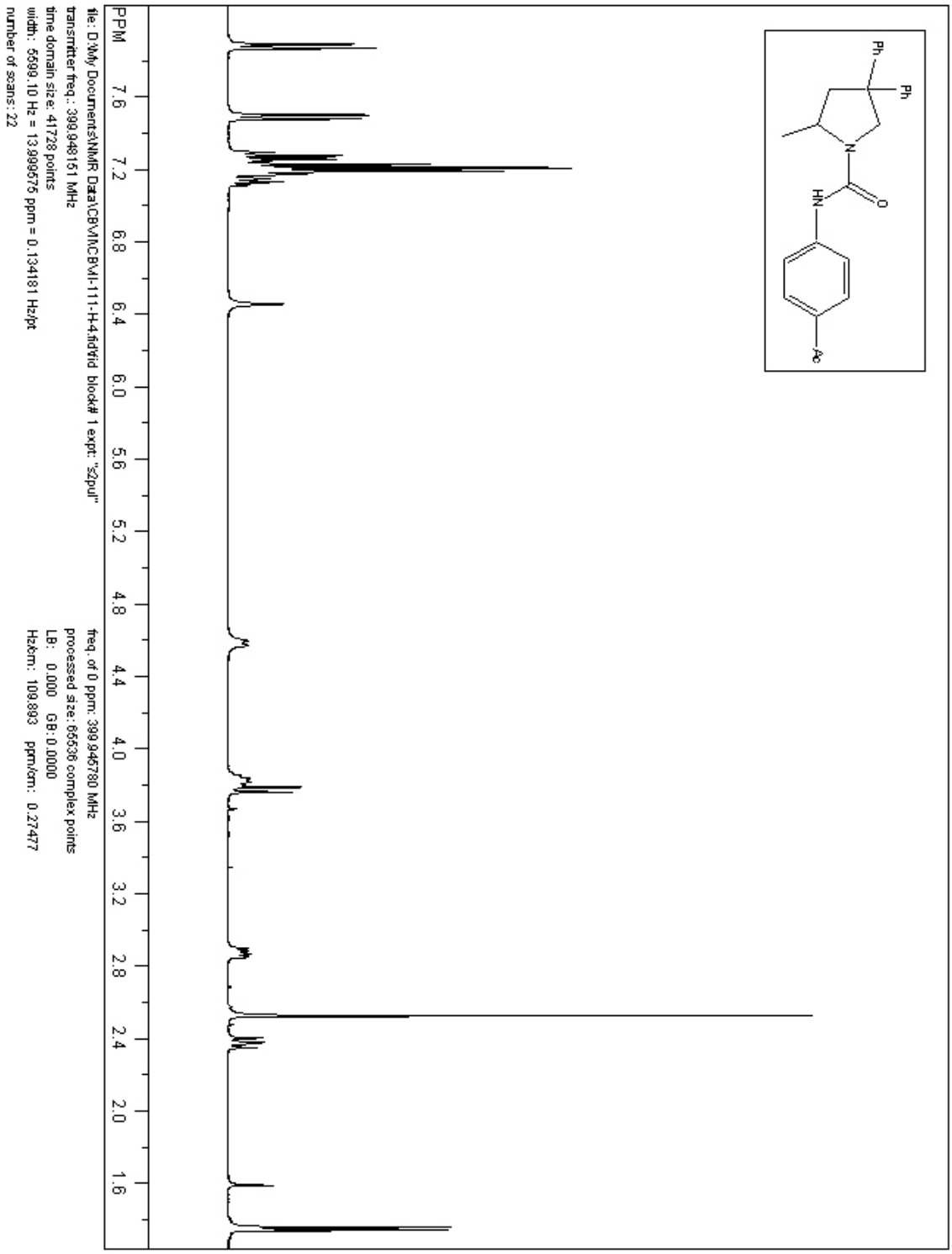


Figure S21. $^{13}C\{^{1}H\}$ NMR spectrum of **S29**.

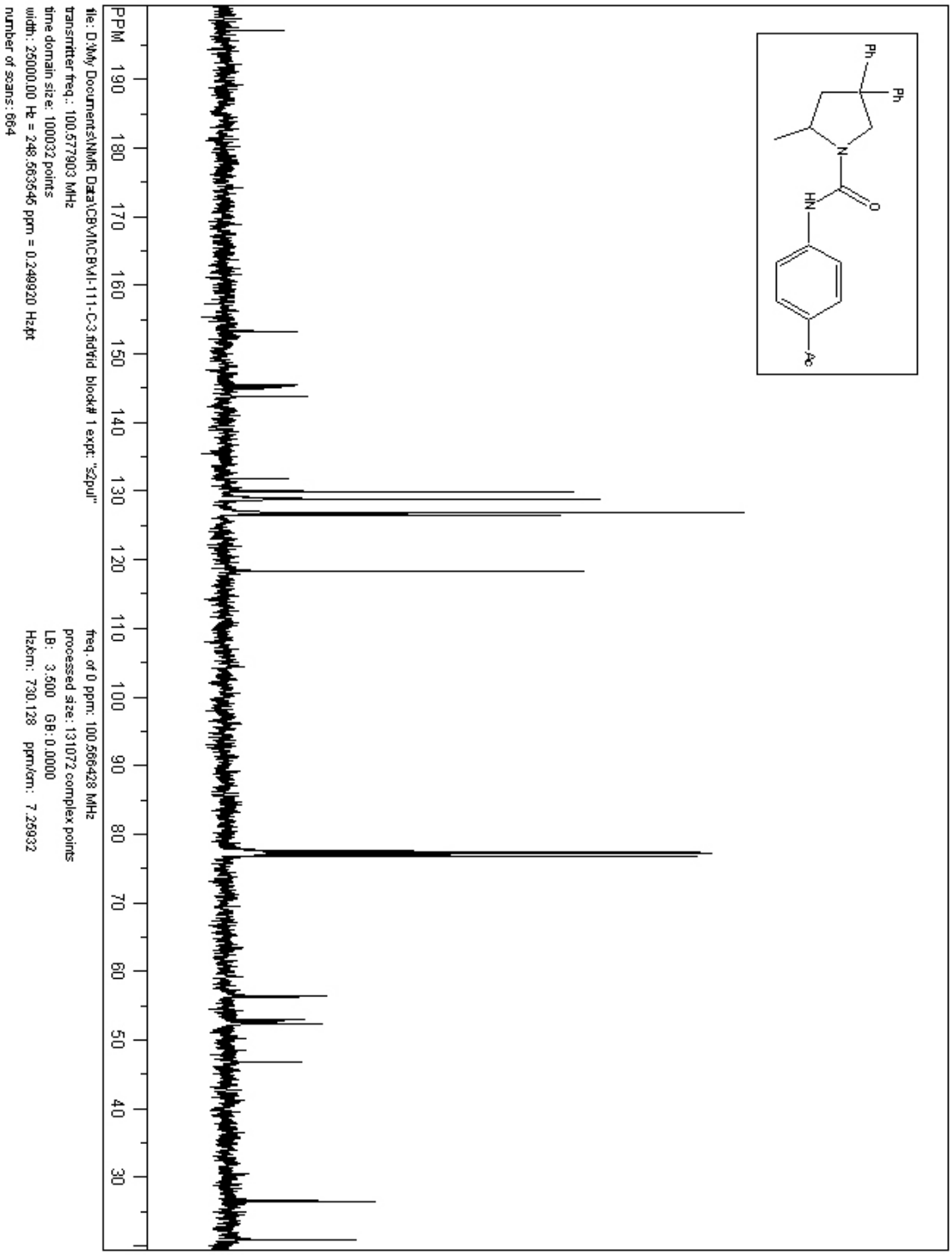


Figure S22. ^{1}H NMR spectrum of **S30**.

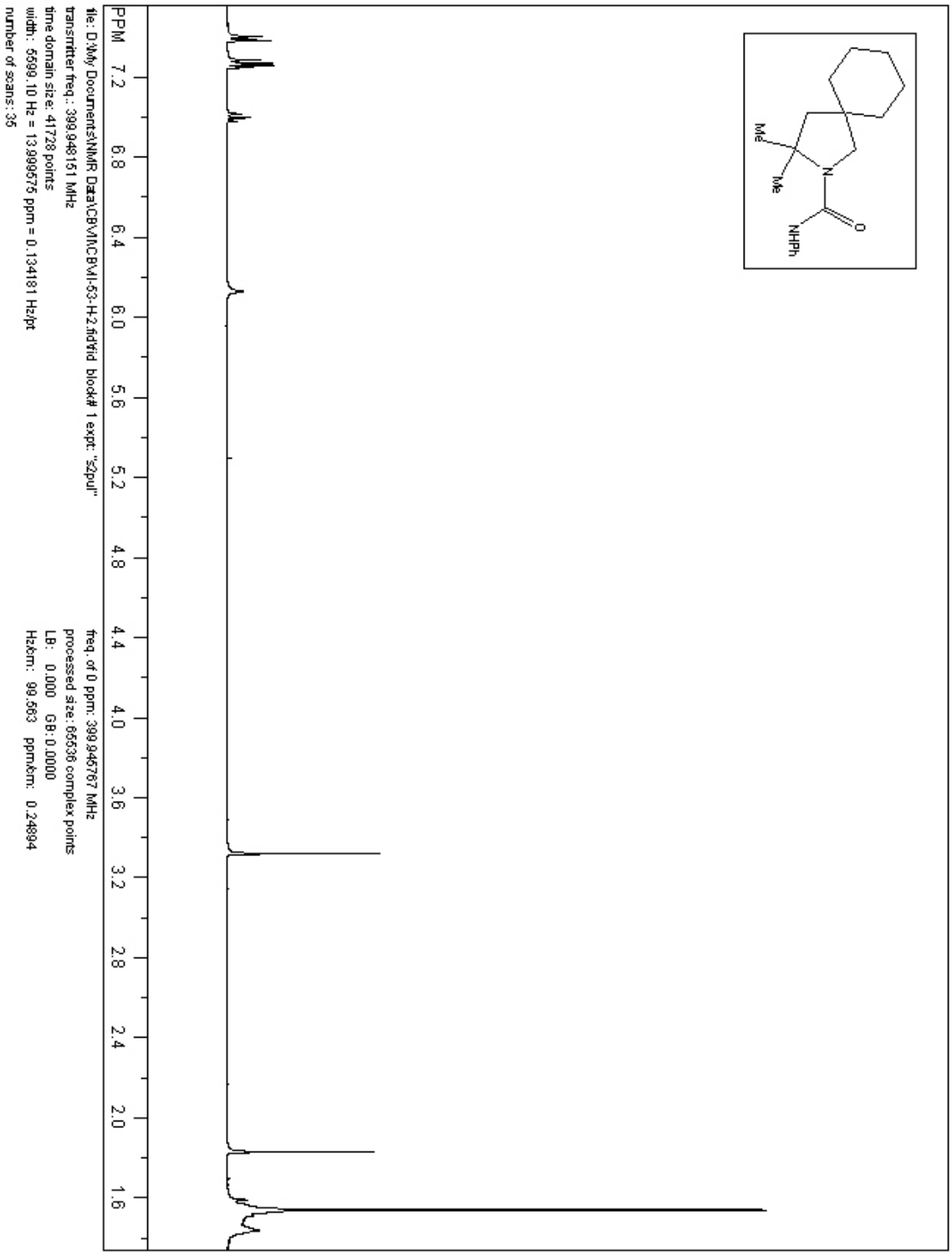


Figure S23. $^{13}C\{^{1}H\}$ NMR spectrum of **S30**.

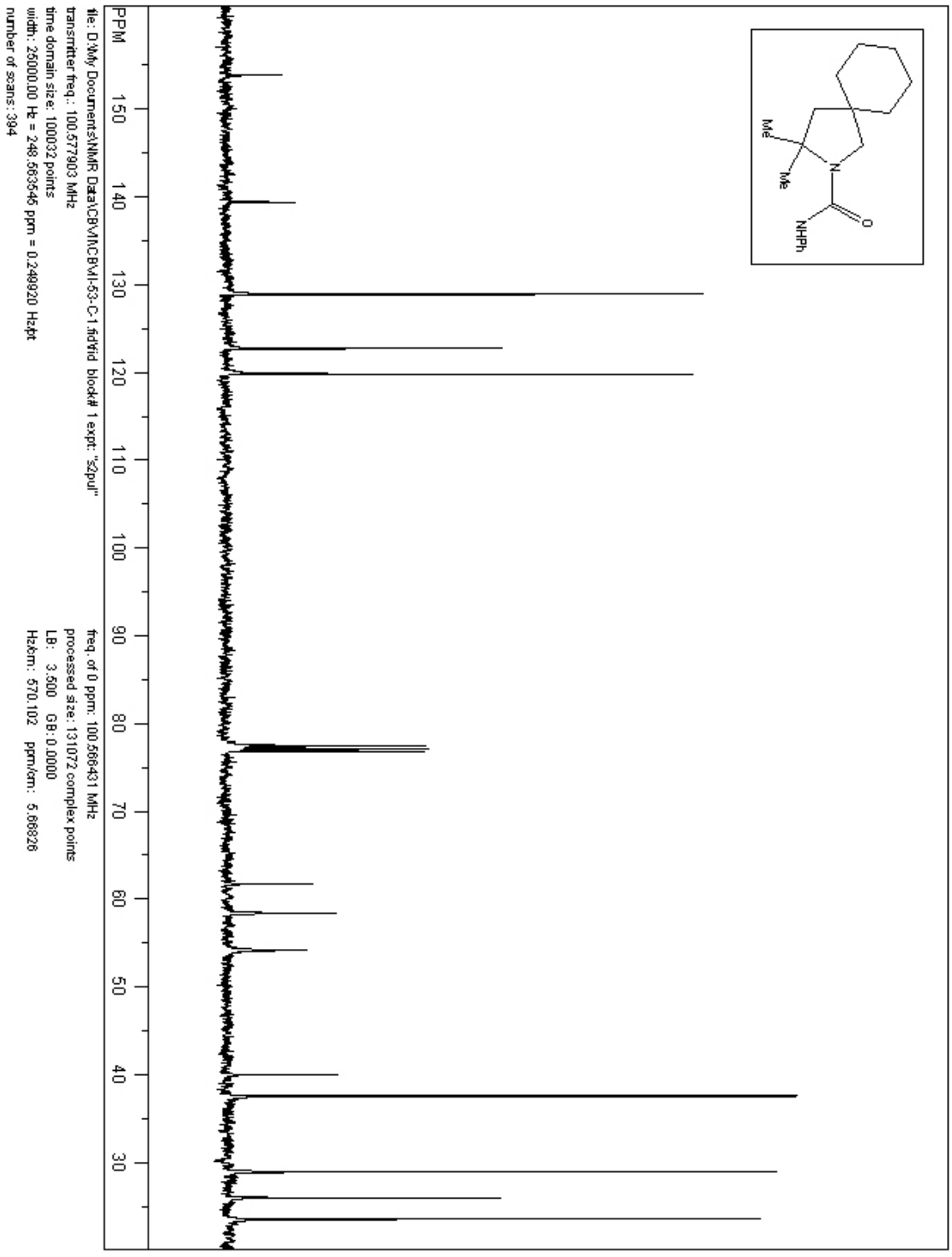


Figure S24. ^{1}H NMR spectrum (14:1-cis:trans) **S31**.

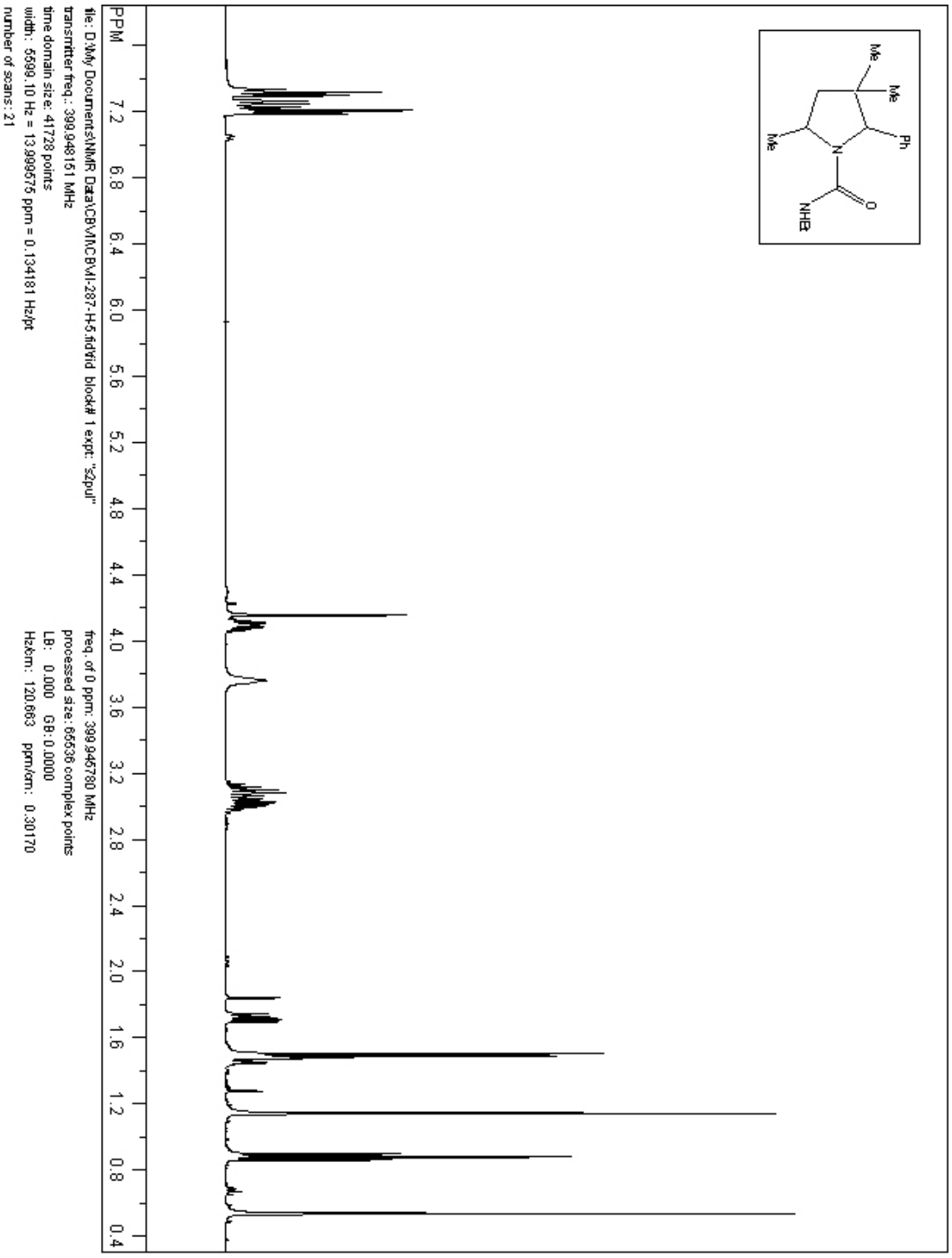


Figure S25. $^{13}C\{^{1}H\}$ NMR (>20:1-cis:trans) spectrum of **S31**.

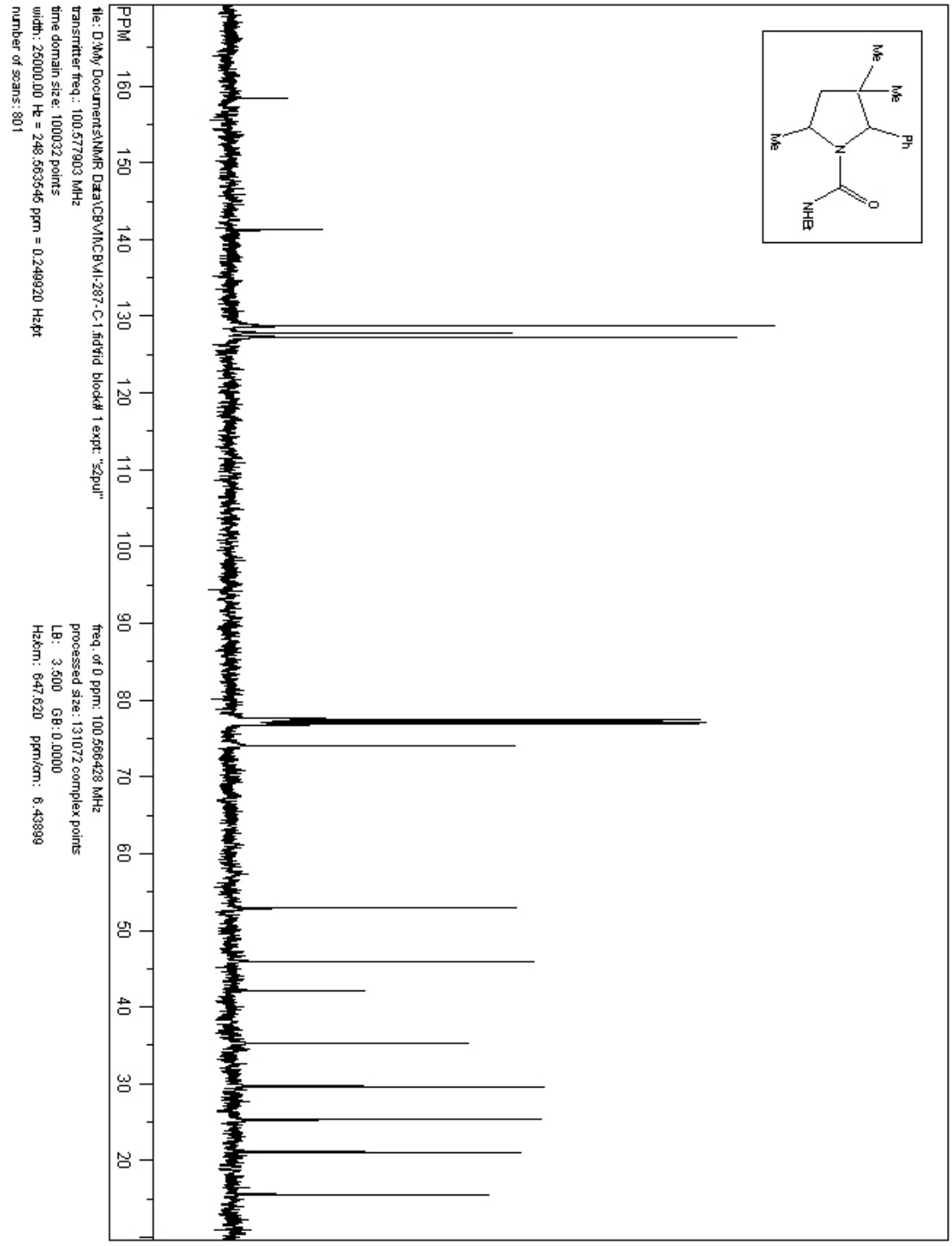


Figure S26. ^{1}H NMR spectrum of the cis-diastereomer of **S32**.

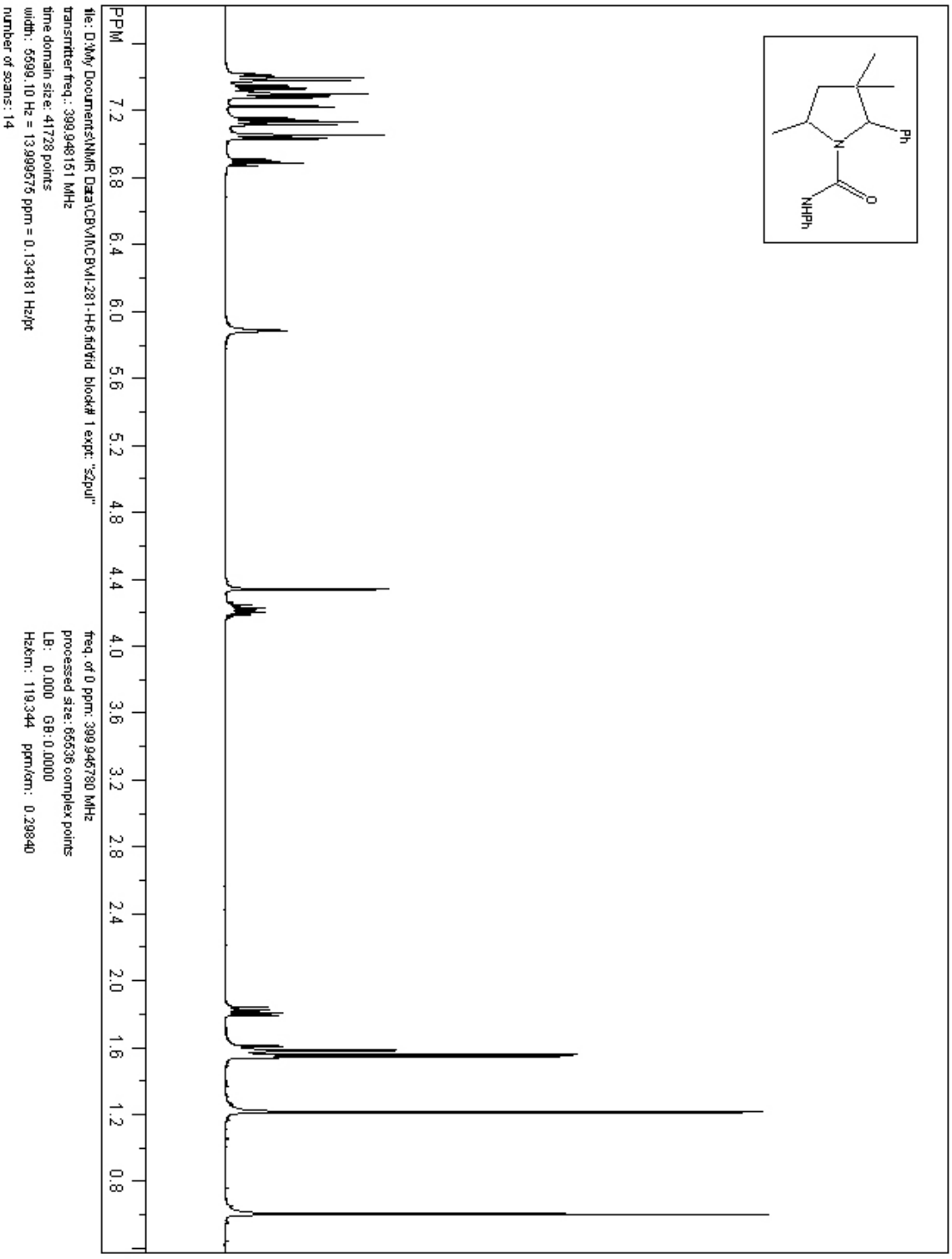


Figure S27. $^{13}C\{^{1}H\}$ NMR spectrum of cis-diastereomer of **S32**.

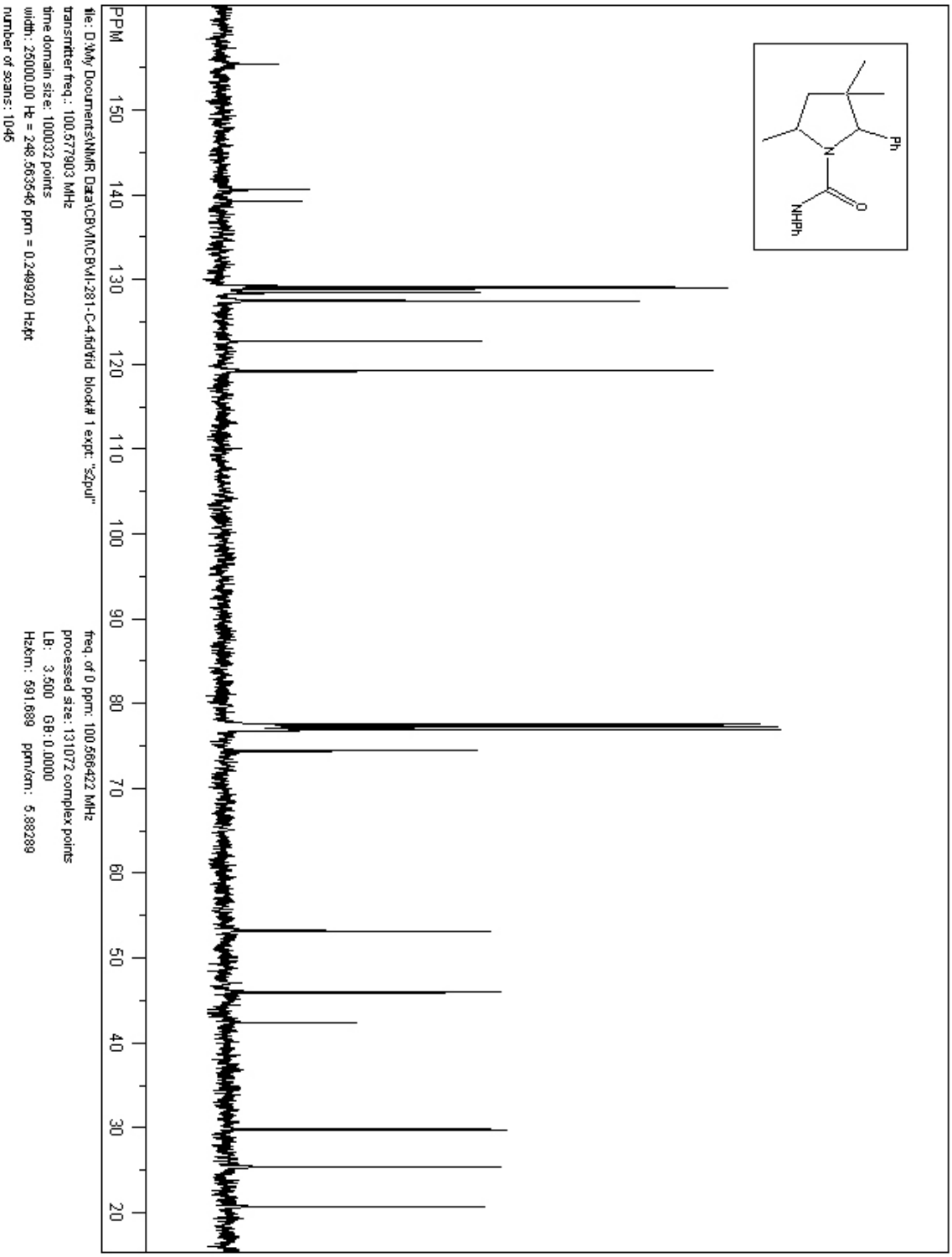


Figure S28. ^{1}H NMR (3.7:1-cis:trans) spectrum of **S33**.

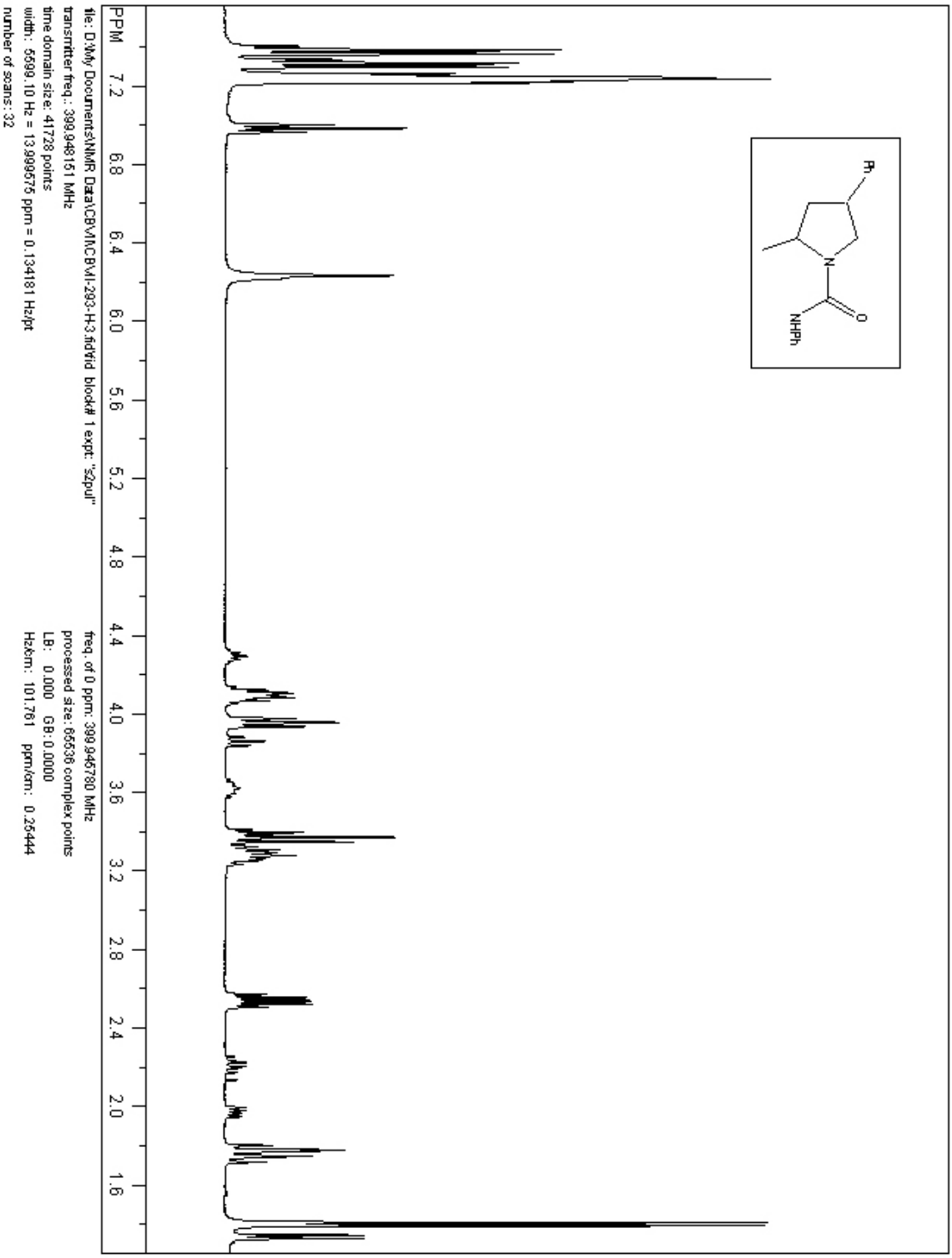


Figure S29. $^{13}C\{^{1}H\}$ NMR (3.7:1-cis:trans) spectrum of **S33**.

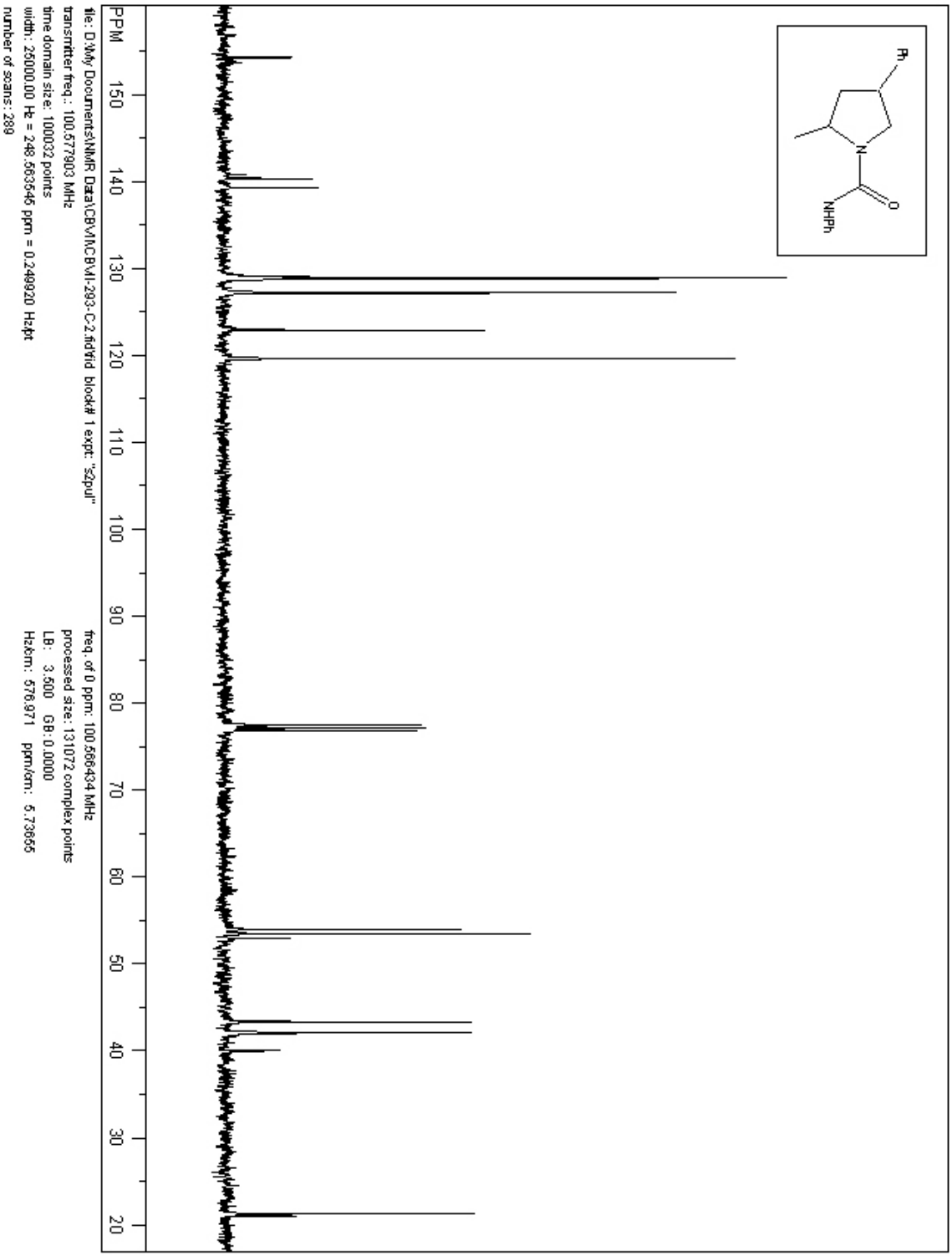


Figure S30. ^{1}H NMR (3.0:1-cis:trans) spectrum of **S34**.

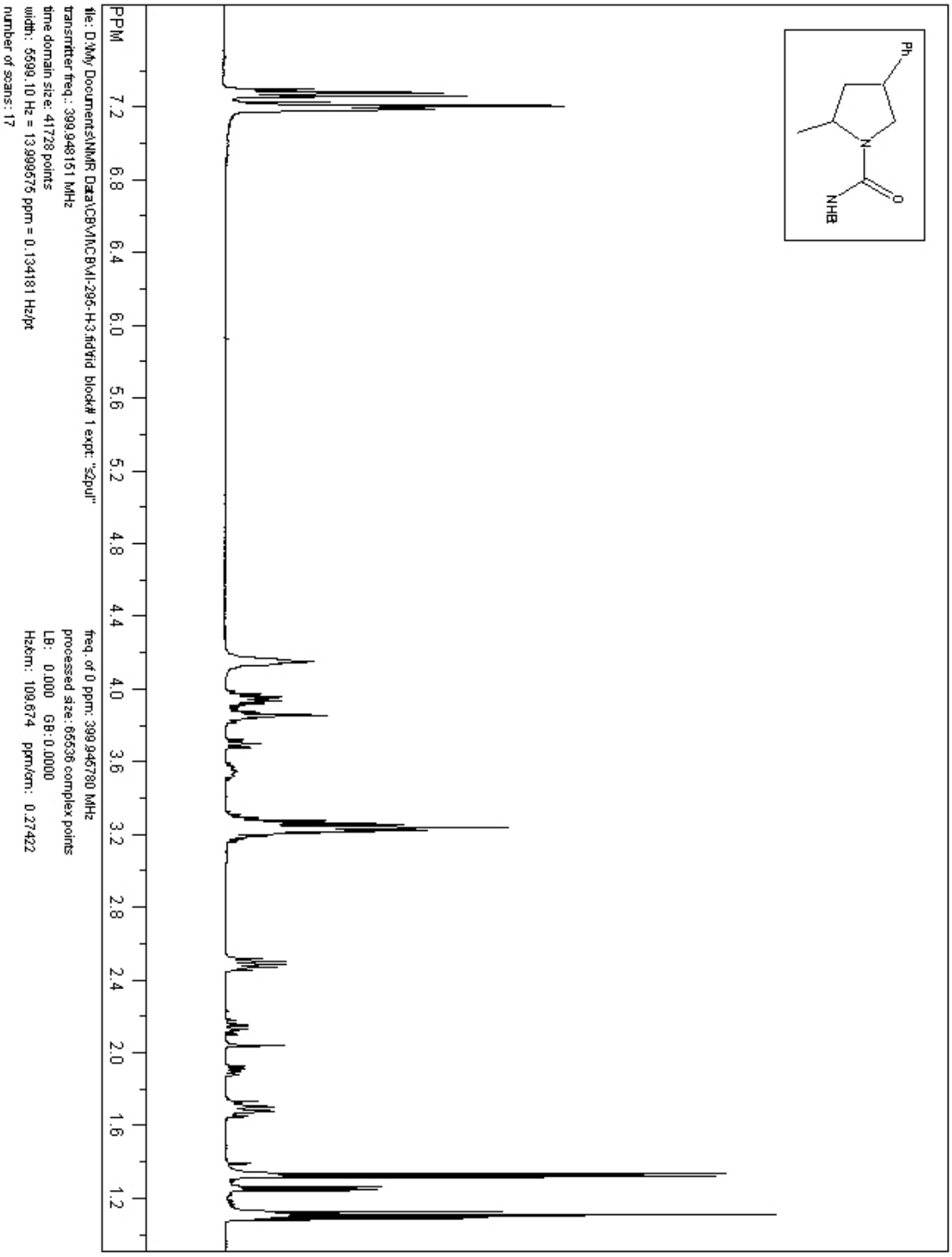


Figure S31. $^{13}C\{^{1}H\}$ NMR (3.0:1-cis:trans) spectrum of **S34**.

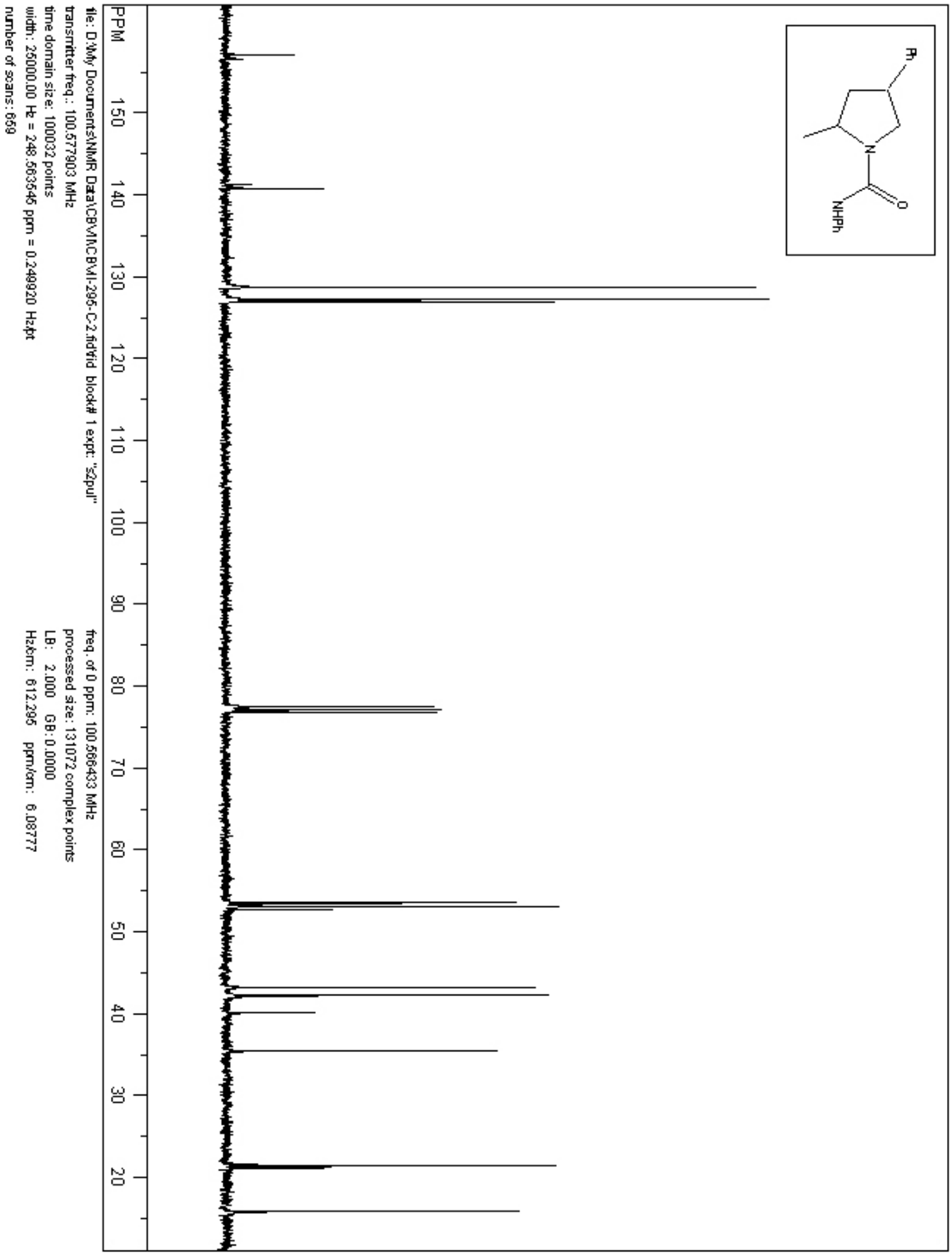


Figure S32. ^{1}H NMR (4.1:1-cis:trans) spectrum of **S35**.

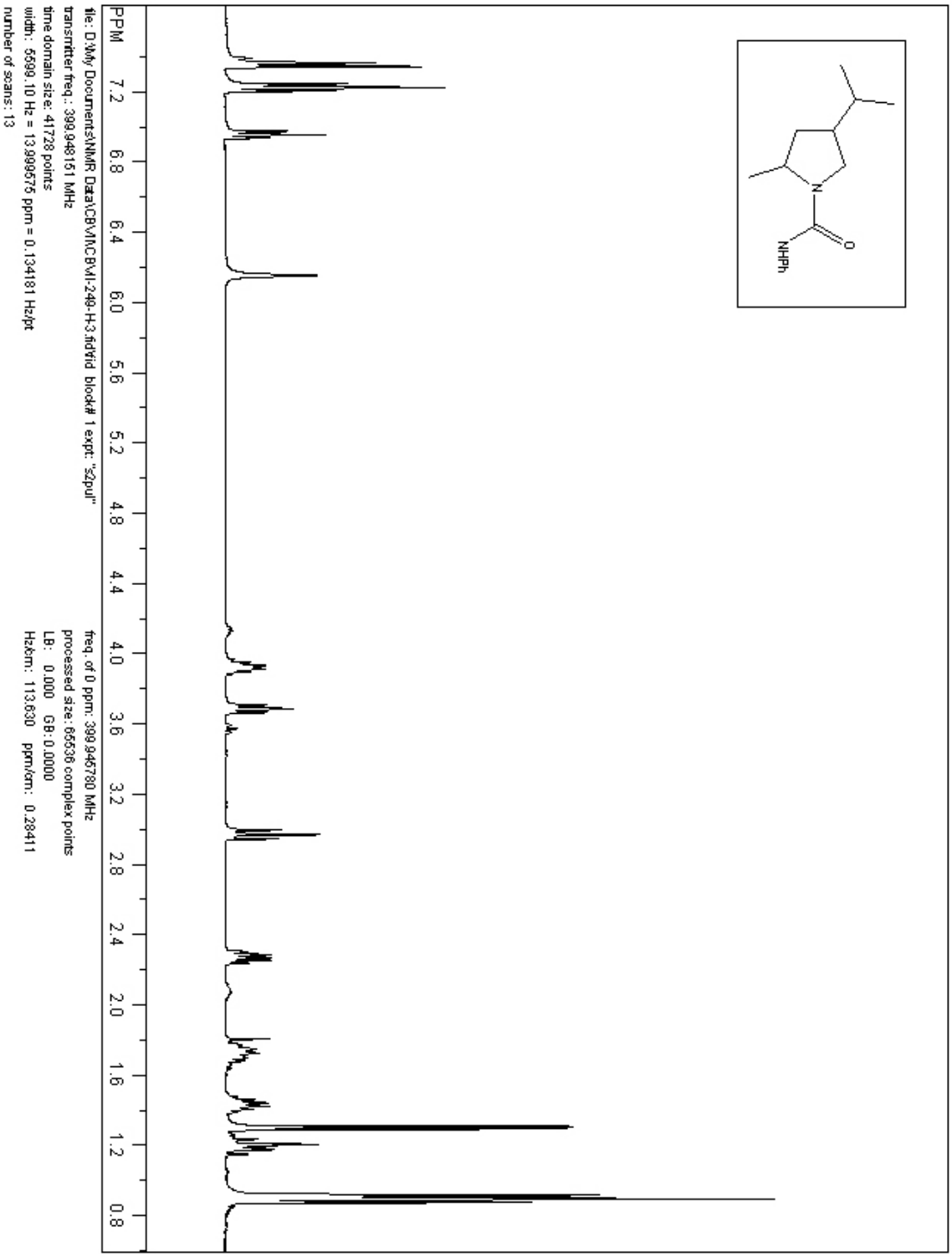


Figure S33. $^{13}C\{^{1}H\}$ (4.1:1-cis:trans) NMR spectrum of **S35**.

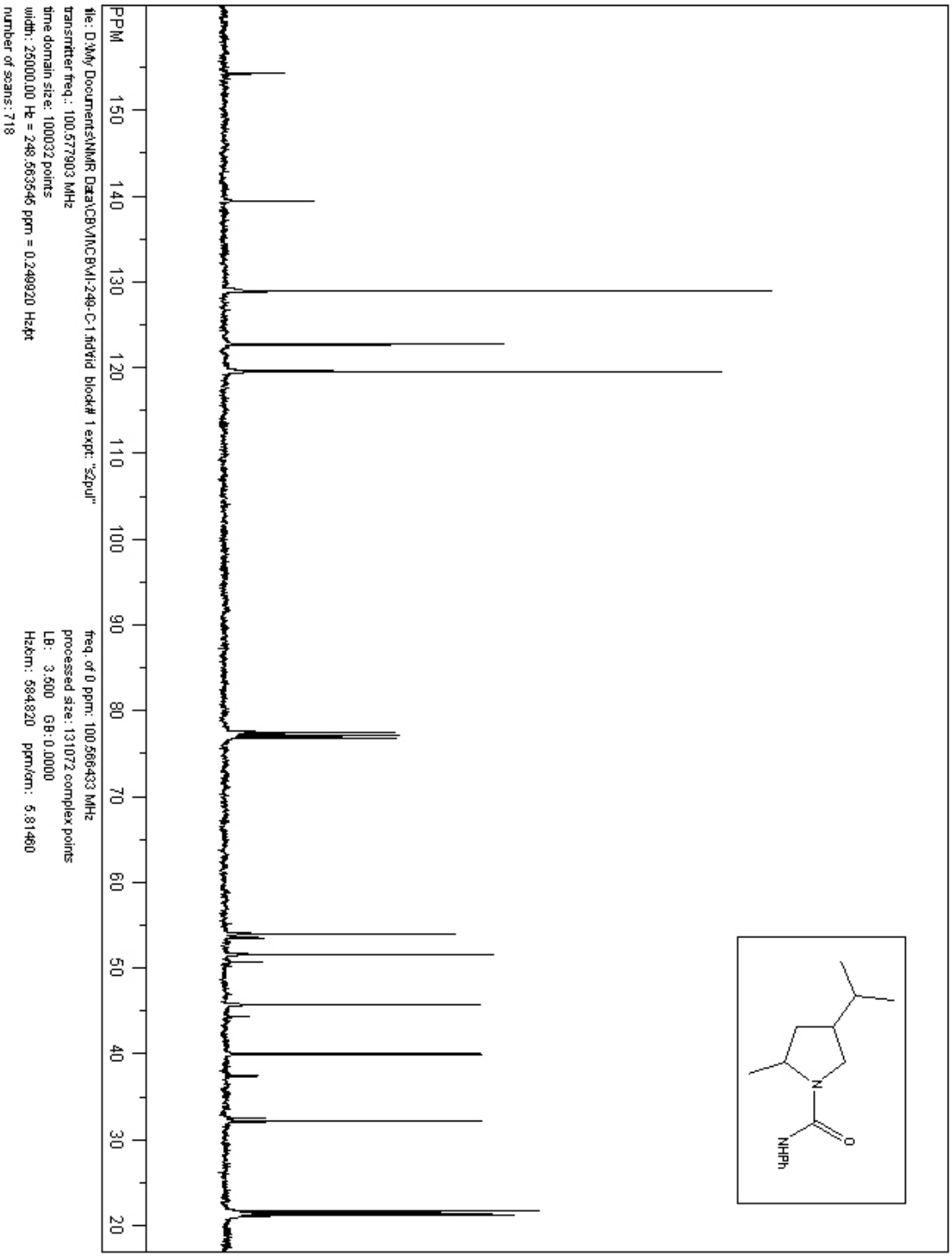


Figure S34. ^{1}H NMR spectrum of **S36**.

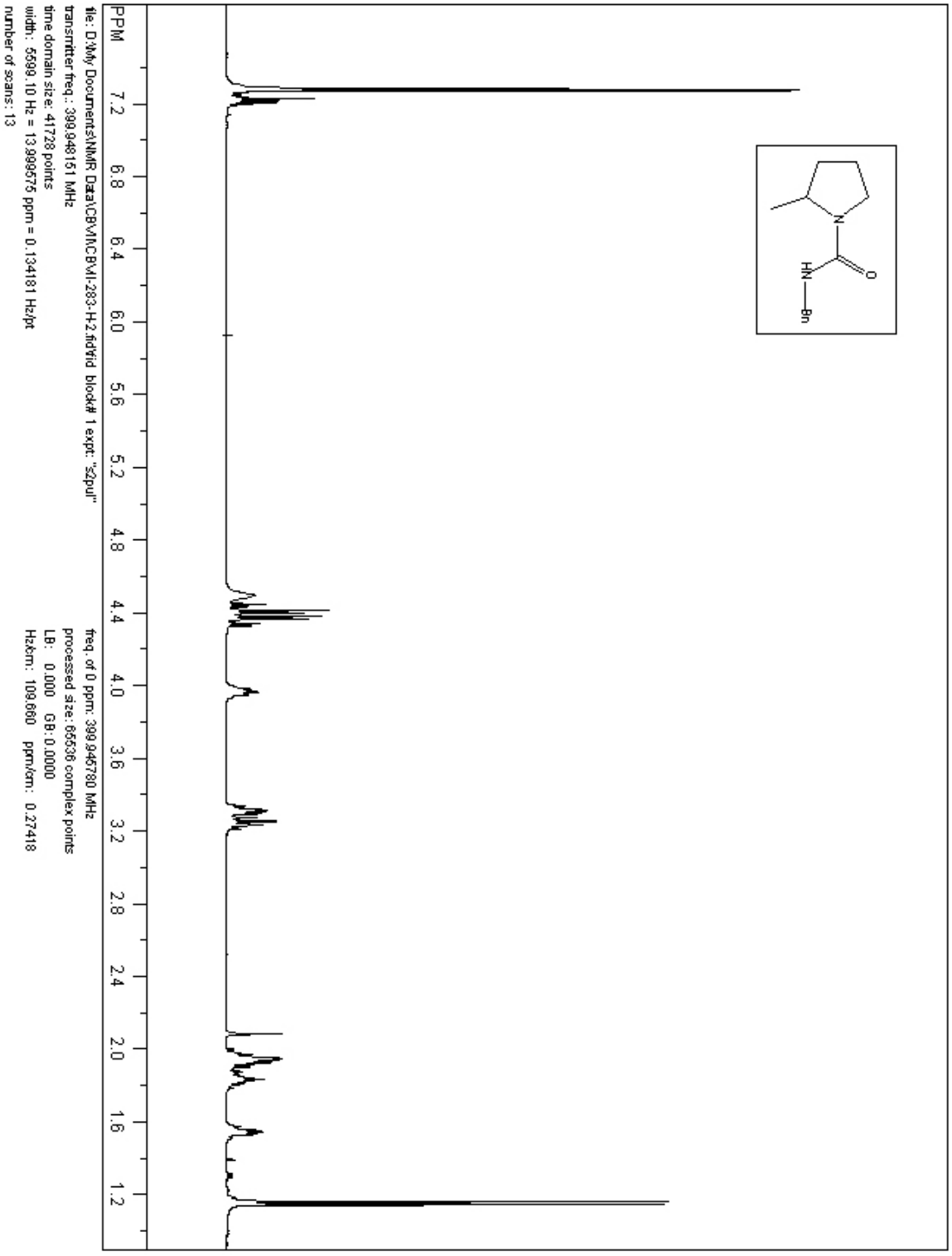


Figure S35. $^{13}C\{^{1}H\}$ NMR spectrum of **S36**.

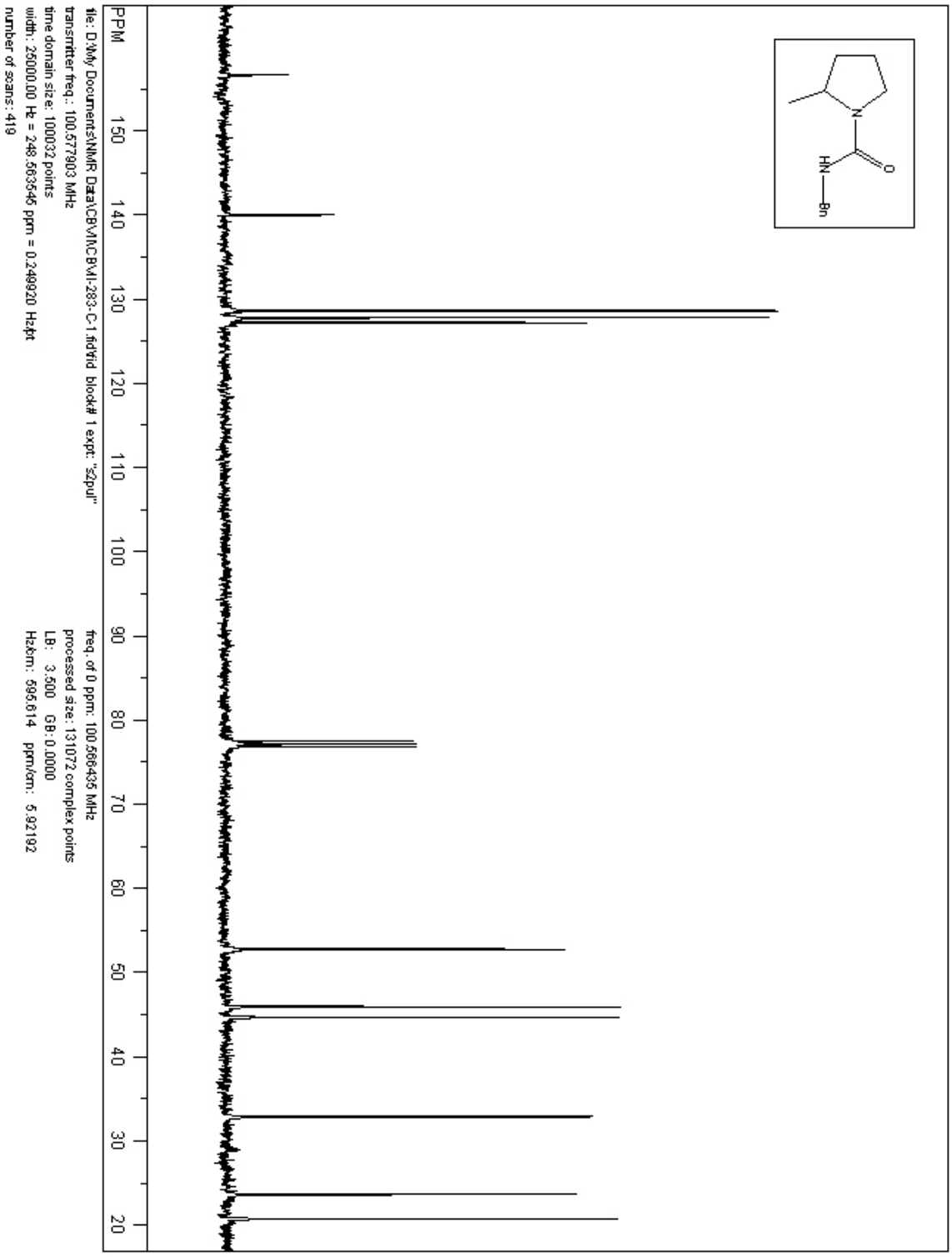


Figure S36. ^{1}H NMR spectrum of **S37**.

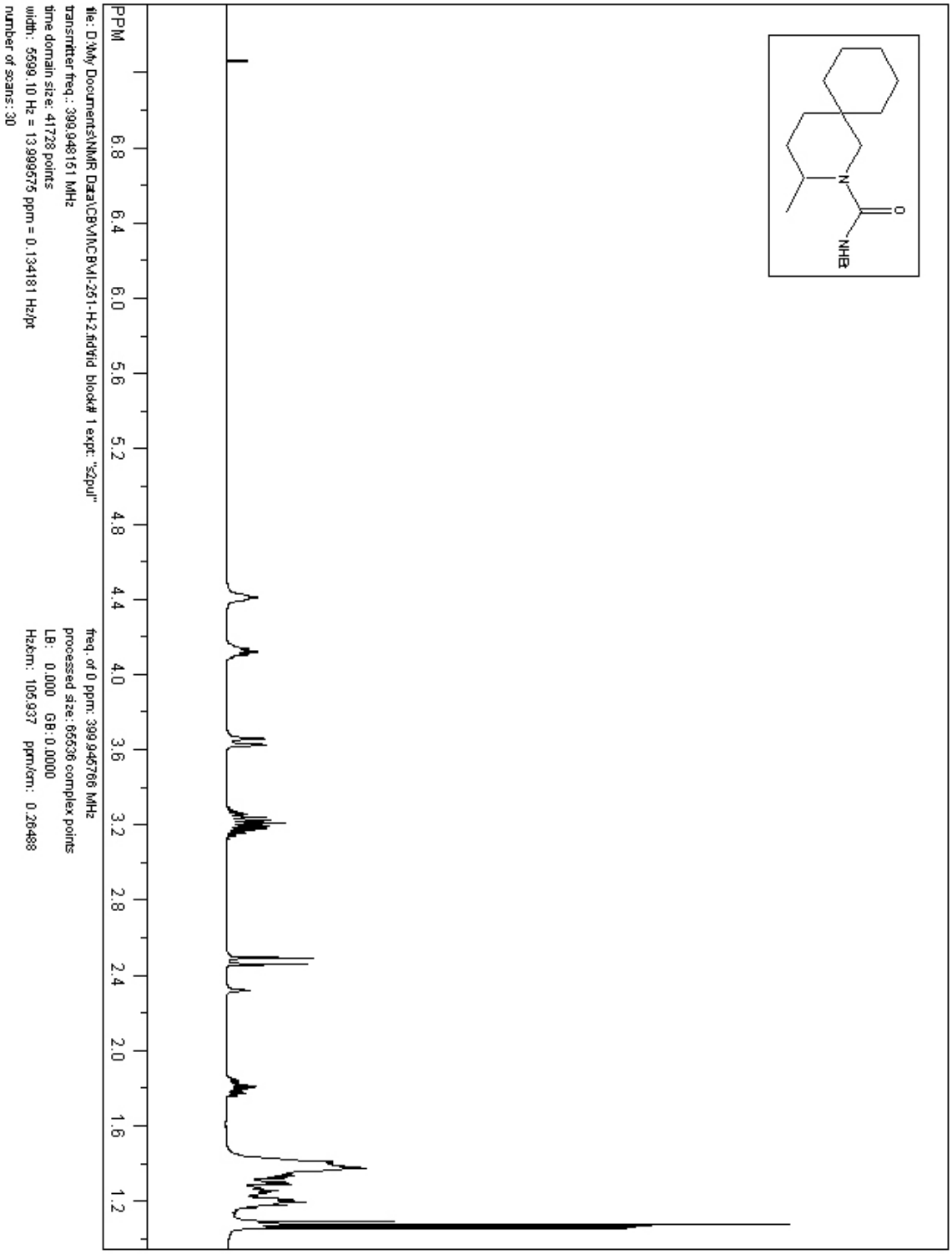
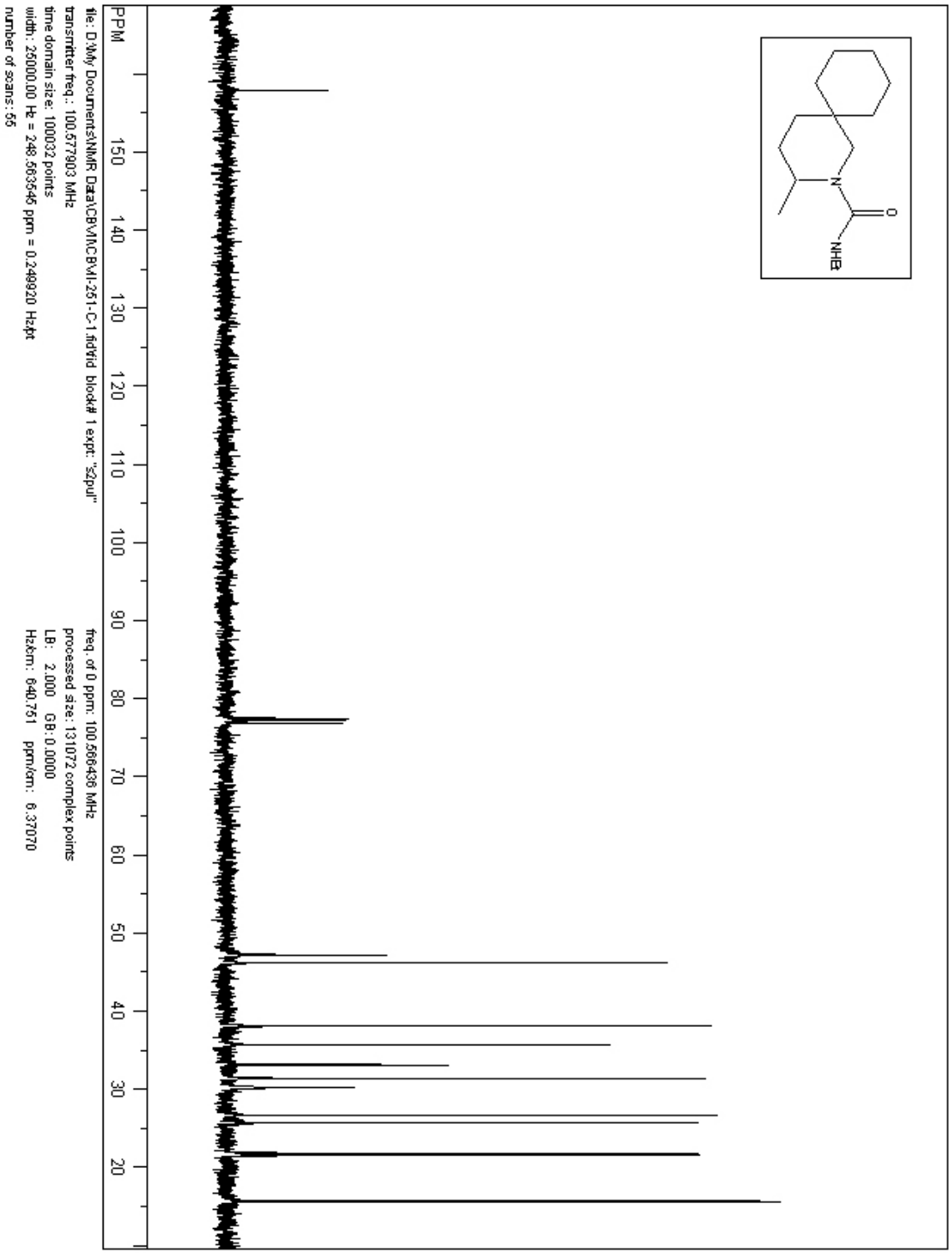


Figure S37. $^{13}C\{^{1}H\}$ NMR spectrum of **S37**.



References.

S1) Bender, C. F.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **2005**, *127*, 1070.

S2) Pour, M.; Špulák, M.; Balšánek, V.; Kuneš, J.; Kubanová, P.; Buchta, V. *Biorg. & Med. Chem.* **2003**, *11*, 2843.

S3) Han, X.; Widenhoefer, R. A. *Angew. Chem. Int. Ed.* **2006**, *45*, 1747.

S4) Bender, C. F.; Widenhoefer, R. A. *Chem. Commun*. **2006**, DOI: 10.1039/b608638a.

S5) de Frémont, P.; Scott, N. M.; Stevens, E. D.; Nolan, S. P. *Organometallics* **2005**, *24*, 2411.

S6) El Samii, Z. K. M.; Al Ashmawy, M. I.; Mellor, J. M. *J. Chem. Soc., Perkin Trans. 1* **1988**, 2517.