Synthesis of 7-Epineoptilocaulin, Mirabilin B, and Isoptilocaulin. A Unified Biosynthetic Proposal for the Ptilocaulin and Batzelladine Alkaloids. Synthesis and Structure Revision of Netamines E and G

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Supporting Information

Experimental Section

General Experimental Methods

Reactions were conducted in flame or oven-dried glassware under a nitrogen atmosphere and were stirred magnetically. The phrase "concentrated" refers to removal of solvents by means of a rotary-evaporator attached to a diaphragm pump (15-60 Torr) followed by removal of residual solvents at < 1 Torr with an vacuum pump. Flash chromatography was performed on silica gel 60 (230-400 mesh). Analytical thin layer chromatography (TLC) was performed using silica gel 60 F-254 pre-coated glass plates (0.25 mm). TLC Plates were analyzed by short wave UV illumination, or by dipping in vanillin stain (27 g of vanillin in 380 mL of EtOH, 50 mL of water and 20 mL of concentrated sulfuric acid) and heating on a hot plate. THF and ether were dried and purified by distillation from sodium/benzophenone. Pyridine, Et_3N, benzene, toluene, MeOH, and CH_2Cl_2 were distilled from CaH_2. ^1H and ^{13}C NMR spectra were obtained on a 400 MHz spectrometer in $CDCl_3$ with tetramethylsilane as internal standard unless the use of a 500 or 800 MHz spectrometer is specifically indicated. Chemical shifts are reported in δ (ppm downfield from tetramethylsilane). Coupling constants are reported in Hz with multiplicities denoted as s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), m (multiplet) and br (broad). IR spectra were acquired on an FT-IR spectrometer and are reported in wave numbers (cm^{-1}). High resolution mass spectra were obtained using the following ionization techniques: chemical ionization (CI), electron impact (EI), electrospray ionization analyzed by quadrupole time of flight (QTof) . Optical rotation values were measured on a polarimeter using a cell with a path length of 1 dm.

***tert*-Butyl 3-Oxooctanoate (35)** was prepared by the literature procedure.[20] A solution of *n*-hexanoyl chloride (4.15 mL, 29.7 mmol) in CH_2Cl_2 (10 mL) was added dropwise to a solution of Meldrum's acid (3.97 g, 27.5 mmol) in pyridine (5 mL) at 10 °C. The red solution was stirred for 4.5 h at 25 °C, and then 2 M aqueous HCl (30 mL) was added. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 25 mL). The combined organic layers were washed with water (10 mL), dried over Na_2SO_4, and concentrated to yield 6.51 g of crude 5-hexanoyl-2,2-dimethyl-1,3-dioxan-4,6-dione as a red oil. A solution of this red oil in *t*-BuOH (20 mL) was refluxed overnight,

cooled to 25 °C, diluted with EtOAc (80 mL), washed with saturated Na_2CO_3 (10 mL) and brine (10 mL), dried over Na_2SO_4, and concentrated to yield 4.99 g of crude **35**. Flash chromatography on silica gel (30:1 hexanes/EtOAc) gave 3.85 g (66%) of **35** as a yellow oil: ^{1}H NMR 3.34 (s, 2), 2.52 (t, 2, J = 7.3), 1.65-1.55 (m, 2), 1.47 (s, 9), 1.35-1.24 (m, 4), 0.89 (t, 3, J = 6.8).

(±)-2-Butyl-5-(3*Z*-hexenyl)-cyclohex-2-en-1-one (36). To a stirred solution of *β*-keto ester **35** (3.82 g, 17.8 mmol) and 2*E*,6*Z*-nonadienal (**34**) (3.0 mL, 17.8 mmol) in *t*-BuOH (15 mL) was added a catalytic amount of *t*-BuOK (100 mg, 0.89 mmol, 0.05 equiv) at 0 °C under N_2. The reaction mixture was stirred at 0 °C for 30 min and an additional 0.2 equiv of *t*-BuOK (400 mg, 3.56 mmol) was added. The mixture was heated at reflux for 17 h, cooled to 25 °C, quenched with 1 M aqueous HCl (10 mL), and diluted with ether (80 mL). The separated organic layer was washed with brine (20 mL), dried over Na_2SO_4, and concentrated to yield 6.0 g of crude *tert*-butyl 3-butyl-6-(3*Z*-hexenyl)-2-oxocyclohex-3-ene-1-carboxylate as a yellow oil.

To a solution of this ester in toluene (35 mL) was added *p*-TsOH (685 mg, 3.6 mmol). The reaction mixture was heated at 80 °C for 16 h, cooled to 25 °C, and diluted with EtOAc (50 mL). The solution was washed with saturated $NaHCO_3$ (15 mL), 1 M aqueous HCl (10 mL), and brine (10 mL), dried over $MgSO_4$, and concentrated to yield 4.7 g of crude **36** as a yellow oil. Flash chromatography on silica gel (70:1 hexanes/EtOAc) gave 3.20 g (77%) of **36** as a yellow oil: ^{1}H NMR 6.67 (br d, 1, J = 5.6), 5.38 (dtt, 1, J = 11, 6.7, 0.7), 5.29 (dtt, 1, J = 11, 6.7, 0.7), 2.54 (br d, 1, J = 13), 2.43 (br dd, 1, J = 14.6, 6.1), 2.17 (br t, 2, J = 7.2), 2.13-1.96 (m, 7), 1.46-1.24 (m, 6), 0.95 (t, 3, J = 7.4), 0.89 (t, 3, J = 7.0); ^{13}C NMR 199.7, 144.0, 139.7, 132.2, 128.2, 44.8, 35.7, 35.0, 32.5, 30.7, 29.0, 24.0, 22.4, 20.5, 14.3, 13.9; IR (neat) 1681, 1674; HRMS (EI) calcd for $C_{16}H_{26}O$ (M^+) 234.1984, found 234.1984.

(*R*)-2-Butyl-5-(3*Z*-hexenyl)-cyclohex-2-en-1-one (*R*-36). *β*-Keto ester **35** (284 mg, 1.3 mmol) was added to a mixture of catalyst **43**[33] (79 mg, 0.13 mmol) and 2*E*,6*Z*-nonadienal (**34**) (0.22 mL, 1.3 mmol) at 25 °C. The reaction mixture was stirred for 16 h and treated with toluene (5 mL) and *p*-TsOH (45.4 mg, 0.26 mmol). The reaction mixture was heated at 80°C for 23 h, cooled to 25 °C, diluted with ether (60 mL), and washed with saturated $NaHCO_3$ (15 mL), 1 M aqueous HCl (10 mL), and brine (10 mL), dried over $MgSO_4$, and concentrated to yield 258 mg of crude (*R*)-**36** as a yellow oil.

Flash chromatography on silica gel (70:1 hexanes/EtOAc) gave 168 mg (55%) of (*R*)-**36** as a yellow oil: $[\alpha]_D^{25}$ – 21.2 (*c* 1.16, $CHCl_3$).

(±)-2-Butyl-5-(3*Z*-hexenyl)-3-methylcyclohex-2-en-1-one (37). A flask containing $CeCl_3 \bullet 7 H_2O$ (3.5g, 9.4 mmol) and a magnetic stirring bar was evacuated and heated slowly to 140 °C over 2 h. The magnetically-stirred white solid was heated overnight at 140 °C, cooled, purged with nitrogen, treated with 35 mL of dry THF, and agitated at 25 °C for 3 h. MeLi (1.6 M solution in ether), (5.9 mL, 9.4 mmol) was added dropwise to the suspension of cerium chloride at –78 °C and the solution was stirred for 1.5 h at –78 °C. Ketone **36** (468 mg, 1.96 mmol) was added over 5 min and the reaction was stirred for 30 min, treated with 10% aqueous acetic acid (10 mL), warmed to 25 °C, and diluted with ether. The two layers were separated and the organic layer was washed with brine (15 mL), saturated $NaHCO_3$ (10 mL), and brine (10 mL), dried over $MgSO_4$, and concentrated to yield 490 mg of crude 2-butyl-5-(3*Z*-hexenyl)-1-methylcyclohex-2-en-1-ol as a yellow oil. To a solution of this alcohol in CH_2Cl_2 (20 mL) was added PCC (847 mg, 3.93 mmol) and NaOAc (80 mg, 0.97 mmol). The resulting dark red-black mixture was stirred for 4 h at 25 °C and poured onto a flash chromatography silica gel column. Elution with 1:1 hexanes/CH_2Cl_2 gave 386 mg (79%) of **37** as a yellow oil: ^{1}H NMR 5.38 (br dt, 1, *J* = 10.4, 7.2), 5.29 (br dt, 1, *J* = 10.4, 7.2), 2.51 (br d, 1, *J* = 12), 2.38-2.19 (m, 3), 2.15-1.96 (m, 7), 1.93 (s, 3), 1.44-1.17 (m, 6), 0.96 (t, 3, *J* = 7.2), 0.89 (t, 3, *J* = 6.8); ^{13}C NMR 199.0, 154.1, 135.6, 132.1, 128.3, 44.1, 39.4, 35.8, 33.9, 31.3, 24.9, 24.0, 22.8, 21.2, 20.5, 14.3, 14.0; IR (neat) 1665; HRMS (EI) calcd for $C_{17}H_{28}O$ (M^+) 248.2137, found 248.2140.

An identical reaction with (*R*)-**36** afforded (*S*)-**37**: $[\alpha]_D^{25}$ + 53.6 (*c* 1.16, $CHCl_3$).

(±)-(2β,3α,5α)-2-Butyl-5-(3*Z*-hexenyl)-3-methylcyclohexanone (38). A solution of cyclohexenone **37** (295 mg, 1.19 mmol) and *tert*-BuOH (1.0 mL, 10.5 mmol) in 5 mL of THF was added dropwise and with vigorous stirring to a solution of Li (168 mg, 24 mmol) in 50 mL of liquid NH_3 at –33 °C. The resulting solution was stirred for 30 min, solid NH_4Cl was added until the blue solution turned colorless, and the NH_3 was evaporated. The residual material was partitioned between ether (50 mL) and brine (15 mL). The two layers were separated and the aqueous layer was extracted with ether (2 × 40 mL). The combined organic layers were washed with 1 M HCl (10 mL) and brine

(10 mL), dried over $MgSO_4$ and concentrated to yield 292 mg of crude **38** as a yellow oil. Flash chromatography on silica gel (70:1 hexanes/EtOAc) gave 217 mg (73%) of **38** as a 10:1 mixture of **38** and minor isomers: ^{1}H NMR 5.37 (br dt, 1, *J* = 10.4, 6.8), 5.27 (br dt, 1, *J* = 10.4, 6.8), 2.40 (br d, 1, *J* = 12.2), 2.08-1.83 (m, 7), 1.80-1.22 (m, 10), 1.16 (ddd, 1, *J* =12, 12, 12), 1.06 (d, 3, *J* = 6.1), 0.95 (t, 3, *J* = 7.5), 0.95 (t, 3, *J* = 6.8); ^{13}C NMR (**38**) 212.3, 132.1, 128.4, 56.7, 48.5, 41.6, 38.0, 37.6, 37.1, 29.6, 25.3, 24.2, 23.2, 20.8, 20.5, 14.3, 14.0; (partial data for minor isomer(s)) 57.2, 54.2, 48.6, 45.3, 39.3, 37.9, 35.7, 34.9, 34.9, 34.5, 34.4, 34.0, 29.8, 26.0, 25.5, 24.4, 24.3, 22.9, 22.7, 20.4, 14.0; IR (neat) 1711; HRMS (EI) calcd for $C_{17}H_{30}O$ (M^+) 250.2297, found 250.2299.

An identical reaction with (*S*)-**37** afforded (5*S*)-**38**: $[\alpha]_D^{25}$ – 15.2 (*c* 0.91, $CHCl_3$).

(±)-(1α,3α,4β)-4-Butyl-3-methyl-5-oxocyclohexanepropanal (39). Cyclohexanone **38** (200 mg, 0.80 mmol) was dissolved in CH_2Cl_2 (15 mL). The reaction mixture was cooled to –78 °C and O_3 was passed through until the color of the solution turned light blue. Then PPh_3 (315 mg, 1.2 mmol) was added to the solution and the mixture was warmed up to 25 °C. After stirring for 4 h, the mixture was concentrated and the residue was purified by flash chromatography on MeOH-deactivated silica gel (8:1 hexanes/EtOAc) to give 168 mg (93%) of a 10:1 mixture of **39** and minor isomers as a colorless oil: ^{1}H NMR 9.78 (s, 1), 2.48 (t, 2, *J* = 7.3), 2.39 (br d, 1, *J* = 12.4), 2.00 (t, 1, *J* = 12.4), 1.95-1.82 (m, 2), 1.80-1.40 (m, 6), 1.37-1.24 (m, 4), 1.18 (ddd, 1, *J* = 12.4, 12.4, 12.4), 1.06 (d, 3, *J* = 6.7), 0.88 (t, 3, *J* = 6.4); (partial data for minor isomers) 0.99 (d, 3, *J* = 6.7), 0.78 (d, 3, *J* = 6.7); ^{13}C NMR 211.5, 201.8, 56.6, 48.1, 41.3, 41.1, 37.8, 37.3, 29.5, 28.8, 25.2, 23.1, 20.7, 14.0; IR (neat) 2861, 1724, 1709; The aldehyde decomposed prior to HRMS analysis.

An identical reaction with (5*S*)-**38** afforded (1*S*)-**39**: $[\alpha]_D^{25}$ – 10.1 (*c* 0.76, $CHCl_3$).

(±)-(5β,6α,7aβ)- and (7a*S*)-(5α,6α,7aβ)-5-Butyl-1,2,5,6,7,7a-hexahydro-6-methyl-4*H*-inden-4-one (25). To a solution of cyclohexanepropanal **39** (55 mg, 0.25 mmol) in 3.0 mL of DME was added 0.1 mL of 6 M aqueous HCl. The mixture was irradiated at 55 °C for 10 min using a microwave reactor and cooled to 25 °C. The mixture was quenched with 5% $NaHCO_3$ solution (2 mL) and diluted with ether (60 mL). The layers were separated and the organic layer was washed with brine (10 mL), dried over $MgSO_4$, and concentrated to yield 61 mg of crude **25** as a yellow oil. Flash chromatography on

silica gel (60:1 hexanes/EtOAc) gave 39 mg (76%) of **25** as a 4:1 mixture of trans and cis isomers that was used for the next reaction. Preparative TLC of the mixture gave *trans*-**25** as a colorless oil: ^{1}H NMR 6.58 (br ddd, 1 *J* = 2.5, 2.5, 2.5), 2.94-2.78 (m, 1), 2.44-2.32 (m, 2), 2.27 (dddd, 1 *J* = 12.8, 6.8, 6.8, 1.8), 2.06-1.97 (m, 1), 1.98-1.74 (m, 4), 1.65-1.41 (m, 2), 1.40-1.16 (m, 3), 1.14 (ddd, 1 *J* = 11.6, 11.6, 12.0), 1.05 (d, 3, *J* = 6), 0.89 (t, 3, *J* = 7.2); ^{13}C NMR 200.8, 144.8, 137.8, 56.2, 44.4, 41.0, 34.0, 33.1, 31.7, 28.2, 26.2, 23.3, 20.9, 14.0; IR (neat) 1682, 1616; HRMS (EI) calcd for $C_{14}H_{22}O$ (M^+) 206.1672, found 206.1671.

An identical reaction with (1*S*)-**39** afforded optical pure (7a*S*)-**25** as a 4:1 mixture of trans and cis isomers.

(5*R*)-(1β, 5β)-2-Butyl-5-(3*Z*-hexenyl)cyclohex-2-en-1-ol (44). To a cooled (-10 °C) solution of cyclohexenone (5*R*)-**36** (47.5 mg, 0.20 mmol) and $CeCl_3$•7 H_2O (113.6 mg, 0.30 mmol) in MeOH (6 mL) was added $NaBH_4$ (15.4 mg, 0.41 mmol). The resulting suspension was stirred at 0 °C for 1.5 h. The reaction mixture was quenched with saturated NH_4Cl (2 mL) and diluted with ether (20 mL). The organic layer was separated and the aqueous layer was extracted with ether (2 × 20 mL). The combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, and concentrated to yield 49 mg of crude **44**. Flash chromatography on silica gel (30:1 hexanes/EtOAc) gave 48 mg (100%) of **44** as a yellow oil: ^{1}H NMR 5.46 (br, 1), 5.40-5.27 (m, 2), 4.28-4.18 (m, 1), 2.28-1.94 (m, 8), 1.73-1.41 (m, 3), 1.41-1.24 (m, 5), 1.18 (ddd, 1, *J* = 10.4, 10.4, 11.6), 0.96 (t, 3, *J* = 7.2), 0.91 (t, 3, *J* = 7.2); ^{13}C NMR 140.4. 131.8, 128.9, 123.1, 69.3, 40.1, 36.5, 32.9, 32.3, 32.2, 30.1, 24.3, 22.6, 20.5, 14.4, 14.0; HRMS (EI) calcd for $C_{16}H_{28}O$ (M^+) 236.2140, found 236.2138.

(*S*)-Mosher ester of 44 (45). Oxalyl chloride (90 μL, 1.0 mmol) was added to a solution of (*S*)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (47 mg, 0.2 mmol) and DMF (15 μL, 0.2 mmol) in 1.5 mL of hexane and the mixture was stirred for 1 h at 25 °C, filtered, and concentrated. The resulting acid chloride was dissolved in 1.5 mL of CH_2Cl_2 and an aliquot of 0.3 mL of this solution was stirred with **44** (3.1 mg, 0.013 mmol) and pyridine (16 μL) for overnight at 45 °C. The mixture was quenched with a saturated NH_4Cl solution (1 mL) and extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated to yield 10.6 mg of crude **45**. Flash chromatography on

silica gel (50:1 hexanes/EtOAc) gave 5.5 mg (91%) of (*S*)-Mosher ester **45** as a colorless oil: ^{1}H NMR 7.59-7.53 (m, 2), 7.42-7.37 (m, 3), 5.65 (br t, 1, *J* = 7.2), 5.56 (br d, 1, *J* = 4.8), 5.38 (br dt, 1, *J* = 10.8, 6.8), 5.29 (br dt, 1, *J* = 10.8, 6.8), 3.59 (s, 3), 2.28 (br dd, 1, *J* = 12, 6), 2.18-1.93 (m, 7), 1.83-1.60 (m, 3), 1.43-1.03 (m, 6), 0.96 (t, 3, *J* = 7.2), 0.81 (t, 3, *J* = 7.2).

(*R*)-Mosher ester of 44 (46). The analogous reaction of (*R*)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (47 mg, 0.2 mmol) and **44** (3.2 mg, 0.014 mmol) gave 5.9 mg (94%) of (*R*)-Mosher ester **46** as a colorless oil: ^{1}H NMR 7.60-7.49 (m, 2), 7.46-7.33 (m, 3), 5.63 (br t, 1, *J* = 7.2), 5.60 (br d, 1, *J* = 4.8), 5.37 (br dt, 1, *J* = 10.8, 7.2), 5.28 (br dt, 1, *J* = 10.8, 7.2), 3.53 (s, 3), 2.22 (br dd, 1, *J* = 12.4, 6), 2.16-1.94 (m, 7), 1.94-1.82 (m, 1), 1.76-1.61 (m, 2), 1.41-1.13 (m, 6), 0.96 (t, 3, *J* = 7.2), 0.87 (t, 3, *J* = 7.2).

(±)-4-Butyl-3-methyl-5-oxocyclohex-3-enepropanal (59). Cyclohexenone **37** (140 mg, 0.57 mmol) and pyridine (0.15 mL) were added to CH_2Cl_2 (15 mL). The mixture was cooled to –78 °C and O_3 was passed through for 100 s. The reaction was checked by TLC every 20 s until the starting material spot almost disappeared. The desired product is destroyed by O_3 if the reaction is run for a longer time. The mixture was concentrated and the residue was purified by flash chromatography on MeOH-deactivated silica gel (10:1 hexanes/EtOAc) to give 84 mg (66%) of **59** as a colorless oil: ^{1}H NMR 9.80 (s, 1), 2.54-2.46 (m, 3), 2.35 (br dd, 1, *J* = 18.4, 3.8), 2.26 (t, 2, *J* = 7.2), 2.17-1.98 (m, 3), 1.94 (s, 3), 1.78-1.58 (m, 2), 1.37-1.16 (m, 4), 0.89 (t, 3, *J* = 7.2); ^{13}C NMR 201.7, 198.2, 153.7, 135.8, 43.7, 40.9, 39.2, 33.8, 31.3, 27.6, 24.9, 22.8, 21.2, 14.0; IR (neat) 1724, 1661, 1630; HRMS (EI) calcd for $C_{14}H_{22}O_2$ (M^+) 222.1620, found 222.1620.

(±)-5-Butyl-1,2,7,7a-tetrahydro-6-methyl-4*H*-inden-4-one (60). To a solution of cyclohexenepropanal **59** (13 mg, 0.058 mmol) in 1.5 mL of DME was added 0.05 mL of 6 M aqueous HCl. The mixture was irradiated at 55 °C for 5 min using a microwave reactor and cooled to 25 °C. The mixture was quenched with 5% $NaHCO_3$ solution (1 mL) and diluted with ether (60 mL). The layers were separated and the organic layer was washed with brine (10 mL), dried over $MgSO_4$, and concentrated to yield 20 mg of crude **60** as a yellow oil. Flash chromatography on silica gel (10:1 hexanes/EtOAc) gave 8.3 mg (70%) of **60** as a colorless oil: ^{1}H NMR 6.65 (br d, 1 *J* = 2.6), 3.14-3.00

(m, 1), 2.54 (dd, 1, *J* = 12.4, 6), 2.54-2.46 (m, 1), 2.46-2.36 (m, 2), 2.31 (br dt, 2, *J* = 12.4, 8), 2.18 (dd, 1, *J* = 17.2, 11.2), 1.97 (s, 3), 1.65-1.49 (m, 1), 1.41-1.20 (m, 4), 0.90 (t, 3, *J* = 6.8); ^{13}C NMR 186.1, 153.9, 142.4, 137.4, 136.3, 42.1, 40.7, 32.3, 32.1, 31.3, 25.1, 22.9, 21.7, 14.0; IR (neat) 1647, 1624; HRMS (EI) calcd for $C_{14}H_{20}O$ (M^+) 204.1514, found 204.1514.

(5*S*)-2-Butyl-5-(3*Z*-hexenyl)-3-propylcyclohex-2-en-1-one (61). A flask containing $CeCl_3$•7 H_2O (3.0g, 8.1 mmol) and a magnetic stirring bar was evacuated and heated slowly to 140 °C over 2 h. The magnetically-stirred white solid was heated overnight at 140 °C, cooled, purged with nitrogen, treated with 35 mL of dry THF, and agitated at 25 °C for 3 h. Propylmagnesium chloride (2 M solution in ether), (4.1 mL, 8.1 mmol) was added dropwise to the suspension of cerium chloride at 0 °C and the solution was stirred for 1.5 h at 0 °C. Ketone (5*R*)-**36** (382 mg, 1.6 mmol) was added over 5 min and the reaction was stirred for 30 min, treated with 10% aqueous acetic acid (10 mL), warmed to 25 °C, and diluted with ether. The two layers were separated and the organic layer was washed with brine (15 mL), saturated $NaHCO_3$ (10 mL), and brine (10 mL), dried over $MgSO_4$, and concentrated to yield 490 mg of crude 2-butyl-5-(3*Z*-hexenyl)-1-propylcyclohex-2-en-1-ol as a yellow oil. To a solution of this alcohol in CH_2Cl_2 (15 mL) was added PCC (690 mg, 3.2 mmol) and NaOAc (66 mg, 0.8 mmol). The resulting dark red-black mixture was stirred for 4 h at 25 °C and poured onto a flash chromatography silica gel column. Elution with 1:1 hexanes/CH_2Cl_2 gave 345 mg (78%) of **61** as a yellow oil: $[\alpha]_D^{25}$ + 39.5 (*c* 0.99, $CHCl_3$); ^{1}H NMR 5.38 (br dt, 1, *J* = 11.2, 7.2), 5.29 (br dt, 1, *J* = 11.2, 7.2), 2.51 (br d, 1, *J* = 14), 2.35 (br d, 1, *J* = 12), 2.29-2.19 (m, 4), 2.13-1.92 (m, 7), 1.50 (tq, 2, *J* = 7.2 7.2), 1.39 (dt, 2, *J* = 6, 7.6), 1.35-1.21 (m, 4), 0.97 (t, 3, *J* = 7.2), 0.96 (t, 3, *J* = 7.2), 0.89 (t, 3, *J* = 7.2); ^{13}C NMR 199.4, 157.8, 135.5, 132.1, 128.3, 44.3, 37.1, 36.9, 35.8, 34.1, 31.9, 24.8, 24.0, 23.0, 21.2, 20.5, 14.3, 14.3, 14.0; IR (neat) 1667; HRMS (EI) calcd for $C_{19}H_{32}O$ (M^+) 276.2453, found 276.2454.

(5*S*)-(2β,3α,5α)-2-Butyl-5-(3*Z*-hexenyl)-3-propylcyclohexanone (62). To a cold (–33 °C) solution of Li (125 mg, 18 mmol) in 50 mL of liquid NH_3 was added a solution of cyclohexenone **61** (242 mg, 0.88 mmol) and *t*-BuOH (1.0 mL, 10.5 mmol) in 4 mL of THF dropwise and with vigorous stirring. The resulting solution was allowed to stir for 30 min, solid NH_4Cl was added until the blue solution turned colorless, and the NH_3 was evaporated. The residual material was partitioned between

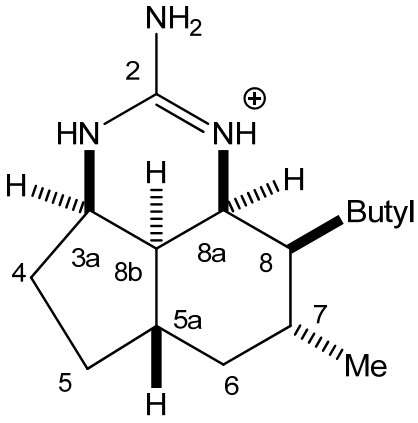
ether (50 mL) and brine (15 mL). The two layers were separated and the aqueous layer was extracted with ether (2 × 40 mL). The combined organic layers were washed with 1 M HCl (10 mL) and brine (10 mL), dried over $MgSO_4$ and concentrated to yield 244 mg of crude **62** as a yellow oil. Flash chromatography on silica gel (70:1 hexanes/EtOAc) gave 191 mg (78%) of **62** as a 7:1 mixture of isomers: $[\alpha]_D^{25}$ – 24.3 (*c* 0.94, $CHCl_3$); ^{1}H NMR (*trans*-**62**) 5.37 (br dt, 1, *J* = 10.8, 6.8), 5.27 (br dt, 1, *J* = 10.8, 6.8), 2.41 (ddd, 1, *J* = 12.8, 3.8, 1.9), 2.10-1.90 (m, 7), 1.76-1.18 (m, 14), 1.09 (ddd, 1, *J* = 11.6, 11.6, 12.8), 0.96 (t, 3, *J* = 7.6), 0.91 (t, 3, *J* = 7.6), 0.89 (t, 3, *J* = 7.6); ^{13}C NMR (*trans*-**62**) 212.6, 132.1, 128.4, 54.8, 48.5, 41.7, 37.9, 37.8, 37.2, 36.2, 29.6, 25.2, 24.2, 23.2, 20.5, 19.2, 14.4, 14.3, 14.0; (partial data for minor isomer(s)) 55.6, 54.7, 48.3, 45.1, 39.4, 39.4, 36.9, 36.6, 35.8, 34.6, 34.3, 33.8, 31.6, 30.9, 29.7, 29.4, 29.1, 25.7, 24.4, 24.3, 22.9, 22.6, 20.3, 20.2, 13.9; IR (neat) 1712; HRMS (EI) calcd for $C_{19}H_{34}O$ (M^+) 278.2610, found 278.2612.

(1*S*)-(1α,3α,4β)-4-Butyl-5-oxo-3-propylcyclohexanepropanal (63). Cyclohexanone **62** (103 mg, 0.37 mmol) was dissolved in CH_2Cl_2 (8 mL). The reaction mixture was cooled to –78 °C and O_3 was passed through until the color of the solution turned light blue. Then PPh_3 (485 mg, 1.8 mmol) was added to the solution and the mixture was warmed up to 25 °C. After stirring for 4 h, the mixture was concentrated and the residue was purified by flash chromatography on MeOH-deactivated silica gel (6:1 hexanes/EtOAc) to give 85.3 mg (91%) of **63** as a 7:1 mixture of isomers: $[\alpha]_D^{25}$ – 22.6 (*c* 1.12, $CHCl_3$); ^{1}H NMR 9.78 (s, 1), 2.48 (t, 2, *J* = 7.2), 2.40 (br dt, 1, *J* = 13.2, 3.1), 2.05-1.91 (m, 3), 1.77-1.37 (m, 6), 1.36-1.17 (m, 8), 1.12 (ddd, 1, *J* = 12, 12, 12), 0.92 (t, 3, *J* = 7.2), 0.89 (t, 3, *J* = 7.2); ^{13}C NMR (*trans*-**63**) 211.9, 201.8, 54.6, 48.1, 41.5, 41.1, 37.8, 37.7, 36.1, 29.5, 28.9, 25.1, 23.1, 19.2, 14.3, 14.0; (partial data for minor isomer(s)) 55.4, 54.6, 48.0, 47.9, 44.7, 41.3, 41.2, 39.2, 37.5, 35.7, 34.5, 34.2, 33.8, 31.7, 31.5, 30.8, 29.7, 29.0, 28.6, 28.3, 25.6, 22.8, 22.6, 20.3, 20.2, 13.9; IR (neat) 1709; HRMS (EI) calcd for $C_{16}H_{28}O_2$ (M^+) 252.20893, found 252.20887.

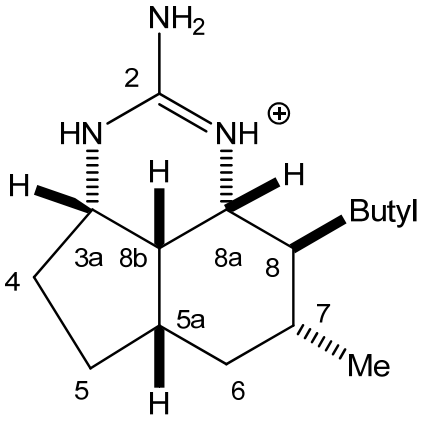
(7a*S*)-(5β,6α,7aβ)-5-Butyl-1,2,5,6,7,7a-hexahydro-6-propyl-4*H*-inden-4-one and (7a*S*)-(5α,6α,7aβ)-5-Butyl-1,2,5,6,7,7a-hexahydro-6-propyl-4*H*-inden-4-one (64). To a solution of cyclohexanepropanal **63** (83 mg, 0.33 mmol) in 3.5 mL of DME was added 0.12 mL of 6 M aqueous HCl. The mixture was irradiated at 55 °C for 10 min using a microwave reactor and cooled to 25 °C.

The mixture was quenched with 5% $NaHCO_3$ solution (2 mL) and diluted with ether (60 mL). The layers were separated and the organic layer was washed with brine (10 mL), dried over $MgSO_4$, and concentrated to yield 91 mg of crude **64** as a yellow oil. Flash chromatography on silica gel (60:1 hexanes/EtOAc) gave 60 mg (78%) of an 8:4:2:1 mixture of the trans and cis isomers of **64** and the two isomers with a β-propyl group as determined by the absorptions for the alkene hydrogen at δ 6.61, 6.47, 6.53 and 6.44, respectively, that was used for the synthesis of netamine E (**65**): ^{1}H NMR (*trans*-**64**) 6.61 (br d, 1 *J* = 2.6), 2.94-2.78 (m, 1), 2.50-2.34 (m, 2), 2.34-2.24 (m, 1), 2.15 (dt, 1, *J* = 12.8, 4), 2.03-1.74 (m, 3), 1.65-1.39 (m, 4), 1.39-1.10 (m, 6), 1.03 (ddd, 1, *J* = 12.4, 12.4, 12.4), 0.92 (t, 3, *J* = 7.2), 0.89 (t, 3, *J* = 7.2); ^{13}C NMR (*trans*-**64**) 201.2, 144.9, 138.1, 54.2, 44.1, 38.5, 37.1, 36.6, 33.2, 31.8, 28.4, 27.1, 23.2, 19.4, 14.4, 14.1; (*cis*-**64**) 203.5, 144.5, 136.9, 52.8, 45.7, 39.5, 34.8, 33.6, 33.3, 32.2, 29.5, 25.0, 22.8, 20.4, 14.2, 14.0; (trans diastereomer with a β-propyl group) 204.0, 144.1, 137.9, 54.3, 40.9, 39.0, 36.0, 34.8, 33.7, 31.9, 30.9, 29.6, 22.6, 20.4, 14.1, 14.0; (cis diastereomer with a β-propyl group) 204.3, 145.7, 135.9, 55.0, 41.3, 38.2, 34.1, 32.0, 30.3, 29.9, 29.3, 25.3, 22.8, 20.2, 14.1, 14.0; IR (neat) 1683, 1620; HRMS (EI) calcd for $C_{16}H_{26}O$ (M^+) 234.1984, found 234.1985.

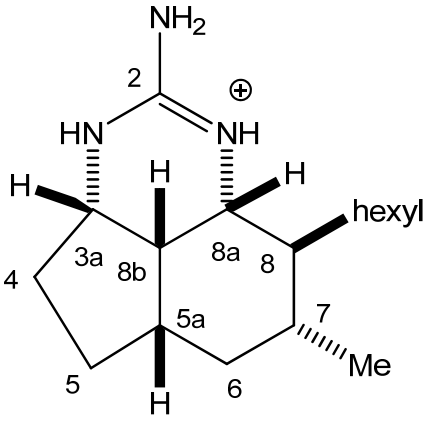
Table S1. ^{1}H and ^{13}C NMR Spectra of Saturated Tricyclic Guanidines 27, 41, and 68 in $CDCl_3$.



27[a]



41[a]

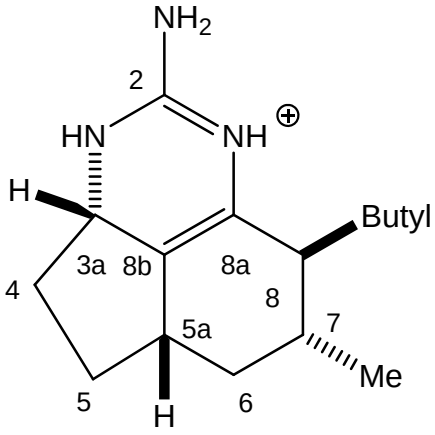


revised structure of netamine C (**68**)[b]

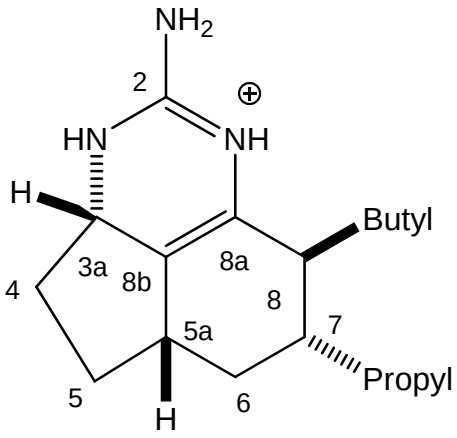
Atom #	C	H	C	H	C	H
1N		7.63		7.64		7.67
2	154.2		154.8		154.9	
2N		7.32		7.05		6.93
3N		8.20		7.61		7.53
3a	51.6	3.79 (5.6, 5.6)	53.8	3.89 (6, 4.2)	53.7	3.86 (6.2, 3.9)
4β	31.7	1.72	33.4	1.66	33.4	1.63
4α		2.10		1.93 (13.2, 5.8)		1.84 (13.0, 5.5)
5β	29.1	1.92	30.5	1.97 (12.9, 7.1, 7.1)	30.4	1.94
5α		1.20		1.37		1.30
5a	36.3	1.75	35.8	2.10	35.8	2.08
6β	39.6	1.91	35.2	1.63	35.1	1.63 (12.7, 4.8, 4.8)
6α		0.86 (12, 12, 12)		1.13 (13, 13, 13)		1.06 (12.7, 12, 12)
7	32.4	1.48	34.6	1.25	34.5	1.21
8	46.2	1.16	44.7	1.46	45.0	1.36
8a	47.0	3.77 (2.7, 2.7)	50.0	3.54 (4.9, 1.1)	49.8	3.51 (5, 1.5)
8b	46.1	1.49	34.8	2.34 (11.4, 5.7, 5.7)	34.8	2.32 (11.2, 5.9, 5.9)
1’	27.4	1.70, 1.52	34.5	1.35, 1.30	34.7	1.28
2’	29.0	1.50, 1.20	29.8	1.35, 1.25	27.5	1.31
3’	22.7	1.41, 1.35	22.9	1.36, 1.30	29.4	1.28
4	14.2	0.94	14.0	0.92	31.7	1.28
5’					22.6	1.27
6’					14.0	0.89
1”	20.1	0.96	23.4	1.09	23.1	1.02

a) This work. Coupling constants (all doublets) are given in parentheses. b) Data from reference 8. Chemical shifts are for netamine C. Coupling constants (all doublets) given in parentheses are for netamine A because coupling constants for netamine C were not provided.

Table S2. ^{1}H and ^{13}C NMR Spectra of 7-Epineoptilocaulin (5) and Netamine E (65) in CD_3OD.



7-epineoptilocaulin (**5**)[a]



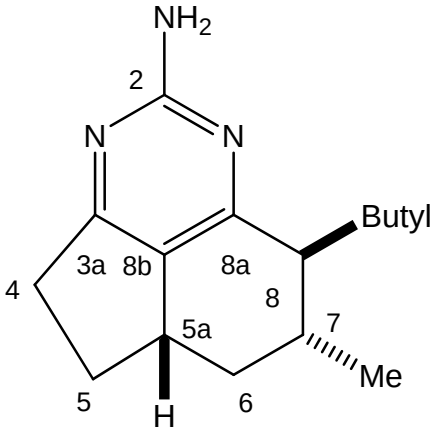
revised structure of netamine E (**65**)[b]

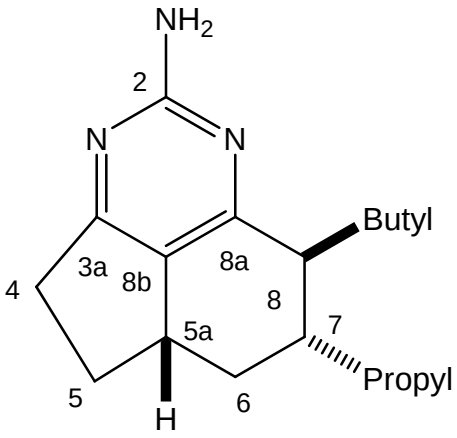
Atom #	C	H	C	H
2	154.8		155.0	
2N				
3a	53.7	4.25 (7.0, 6.4)	54.3	4.29 (6.8, 6.8)
4	33.8	1.68	34.4	1.70
4		2.17		2.22
5	30.4	1.28	30.8	1.30
5		1.97		2.05
5a	37.7	2.44	38.0	2.45
6β	40.1	1.94	36.9	2.15
6α		0.88 (12, 12, 12)		0.72 (12, 12, 12)
7	33.6	1.68	38.7	1.60
8	44.0	1.88	42.5	1.98
8a	128.8		129.2	
8b	119.1		119.8	
1'	28.4	1.68	29.1	1.70
2'	27.3	1.25, 1.14	27.8	1.25
3'	24.2	1.33	24.7	1.38
4'	14.4	0.92	14.9	0.95
1"	20.4	1.04	37.7	1.55, 1.25
2"			21.7	1.50, 1.35
3"			15.2	0.95

a) This work and references 5 and 13. Coupling constants (all doublets) are given in parentheses. b) Data this work and from reference 8.

Differences in the C-6 to C-8 region are due to the different side chains at C-7.

Table S3. ^{1}H and ^{13}C NMR Spectra of Mirablin B (9) and Netamine G (66) in $CDCl_3$.



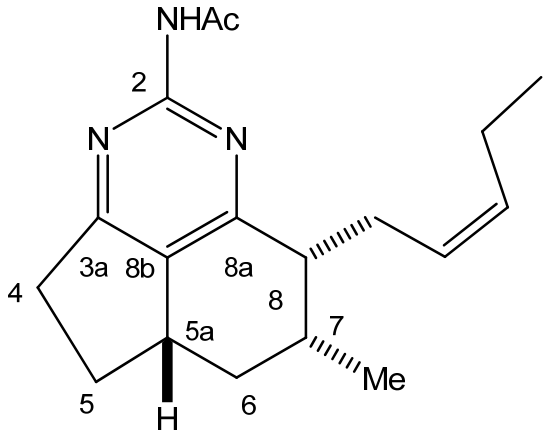


	Mirablin B (**9**)[a]		revised structure of netamine G (**66**)[b]	
Atom #	C	H	C	H
2	163.1		162.8	
2N		4.90		5.19
3a	174.5		174.8	
4β	34.1	2.90	34.0	2.95
4α		2.58 (16.4, 8.8)		2.60 (16.4, 8.4)
5β	33.0	2.35 (12.4, 7.2, 7.2)	32.9	2.38 (12.0, 7.2, 7.2)
5α		1.51		1.55
5a	37.7	2.90	37.3	2.90
6β	39.8	2.03	35.9	2.22 (12.4, 3.8, 3.8)
6α		0.91 (12, 12, 12)		0.78 (12, 12, 12)
7	33.6	1.88	38.5	1.75
8	47.0	2.20 (10.2, 4.4, 4.4)	44.0	2.30 (8.8, 4.4, 4.4)
8a	166.0		166.1	
8b	125.9		126.4	
1'	30.4	2.08, 1.78	30.5	2.04, 1.76
2'	27.7	1.32, 1.05	27.5	1.31, 1.12
3'	23.2	1.28	23.1	1.31
4'	14.0	0.87	14.1	0.89
1"	21.0	1.09 (6.8)	36.8	1.58, 1.27
2"			20.1	1.50, 1.31
3"			14.3	0.96

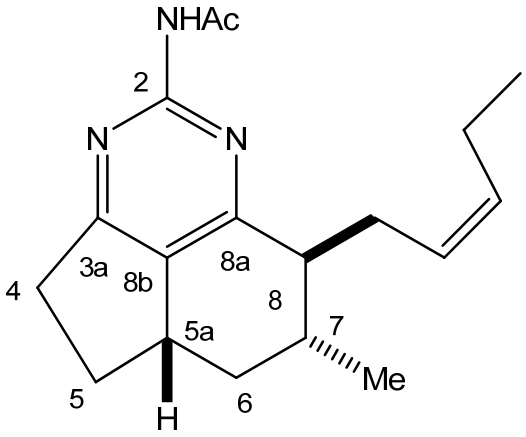
a) This work and references 5 and 13. Coupling constants (all doublets) are given in parentheses. b) Data this work and from reference 8.

Differences in the C-6 to C-8 region are due to the different side chains at C-7.

Table S4. Comparison of the ^{1}H and ^{13}C NMR Spectral Data of *N*-Acetylmirabilin A (*N*-Ac-8) and *N*-Acetylmirabilin C (*N*-Ac-10) in $CDCl_3$.



N-Acetylmirabilin A[a] (*N*-Ac-**8**)

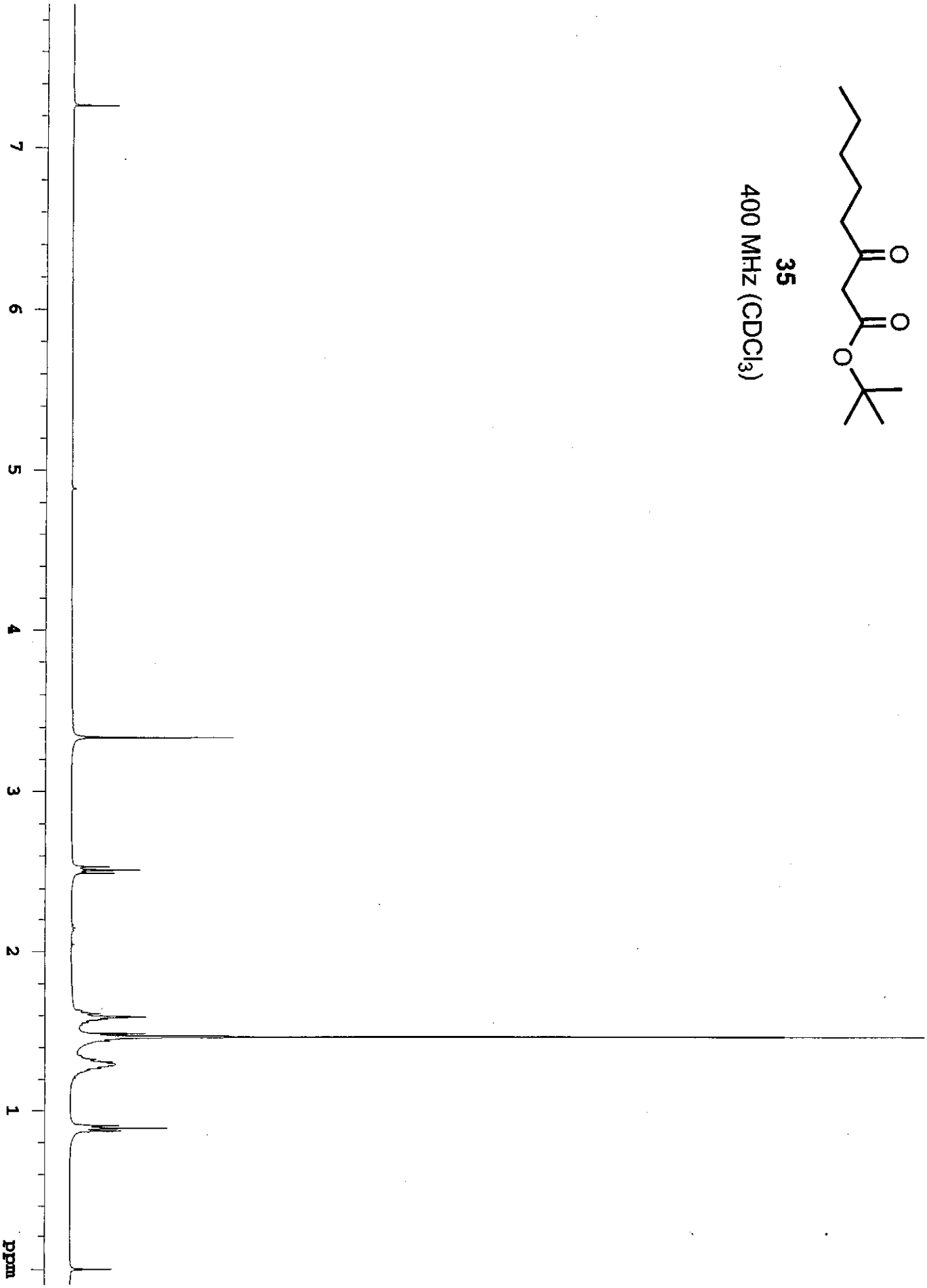


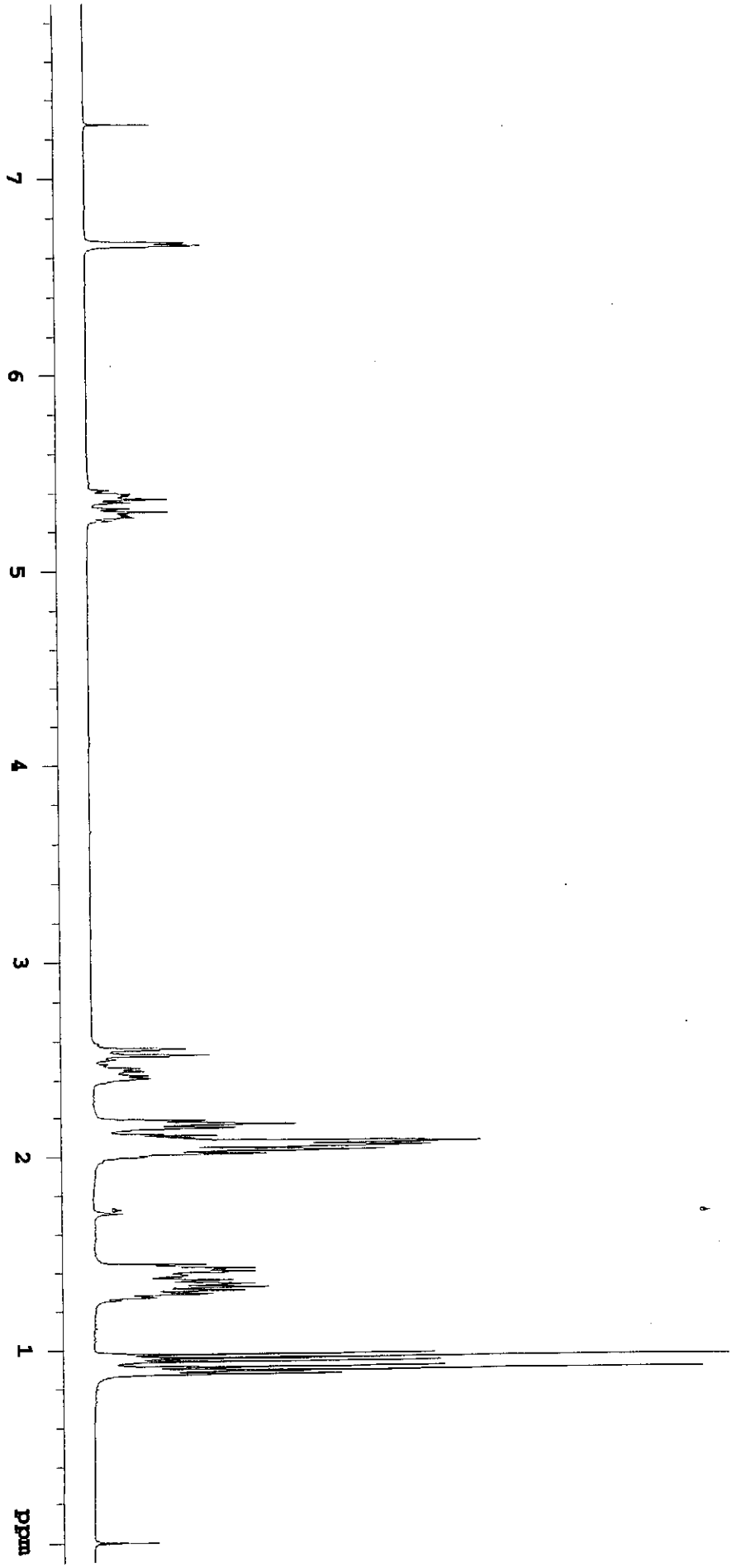
N-Acetylmirabilin C[a] (*N*-Ac-**10**)

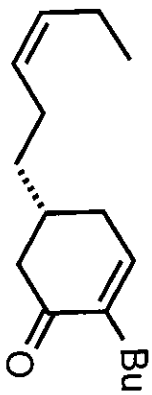
Atom #[b]		C	H	C	H
2	2	156.6		156.8	
3a	4	175.0		175.1	
4	5	34.0	2.75 (17.0, 8.2)	33.7	2.71 (17.0, 8.4)
			2.99 (17.0, 11.7, 7.1)		3.02 (17.0, 11.9, 7.4)
5	6	33.6	1.59 (11.9, 11.7, 11.7, 8.2)	33.1	1.58 (12.3, 11.9, 10.3, 8.4)
			2.40 (11.9, 7.1, 6.8)		2.40 (12.2, 7.4, 7.3)
5a	7	39.0	2.97 (11.7, 11.7, 6.8, 5.6)	37.8	2.98 (12.0, 10.3, 7.3, 4.4)
6	8	33.9	1.23 (12.7, 11.7, 11.7)	39.0	0.99 (12.2, 12.2, 12.0)
			1.84 (12.7, 5.6, 2.6)		2.05 (12.2, 4.4, 3.1)
7	9	34.4	2.20 (11.7, 5.4, 2.6, 7.1 (q))	33.6	1.90 (12.2, 9.5, 3.1, 6.6 (q))
8	10	43.1	2.88 (5.7, 5.5, 5.4)	47.0	2.36 (9.5, 4.7, 4.4, 1.5)
8a	11	165.6		165.3	
8b	12	130.4		131.2	
1’	1’	27.9	2.31 (15.1, 6.7, 5.5)	27.6	2.67 (14.9, 4.4, 4.4)
			2.45 (15.1, 6.7, 5.7)		2.86 (14.9, 4.9, 4.7)
2’	2’	128.0	5.10 (11.0, 6.7, 6.7)	125.7	5.17 (10.7, 4.9, 4.7, 2.0)
3’	3’	130.2	5.25 (11.0, 6.8, 6.8)	132.0	5.39 (10.7, 7.3, 7.3)
4’	4’	29.3	1.91	29.5	2.03
5’	5’	22.6	1.29	22.8	1.33
6’	6’	13.8	0.85	13.8	0.89
1”	C9Me	18.9	1.11 (7.1)	20.6	1.12 (6.6)

a) Data from reference 4. Coupling constants (all doublets) are given in parentheses. *N*-Acetyl protons and carbons are not shown b) Ptilocaulin numbering in left column. Numbering in the right column is from reference 4.

Note the significant differences for H-6 as a function of C-8 geometry.


35
400 MHz ($CDCl_3$)
7
6
5
4
3
2
1
ppm

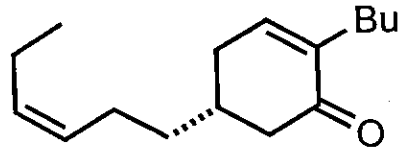




36

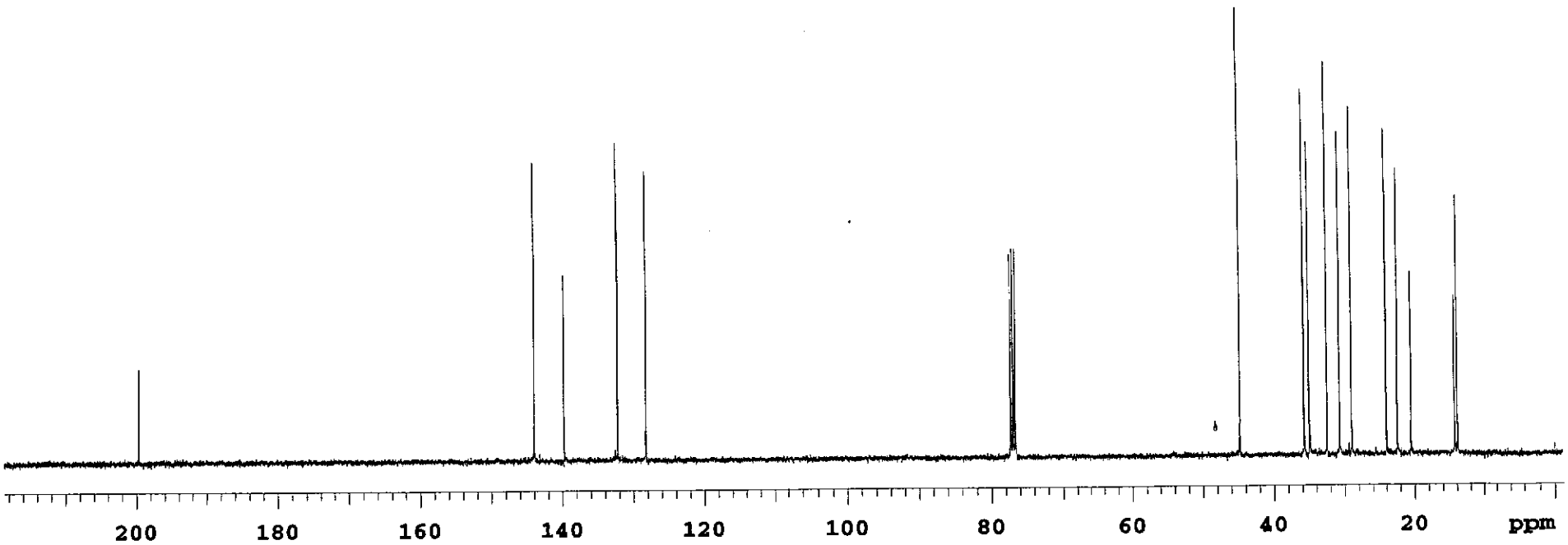
400 MHz ($CDCl_3$)

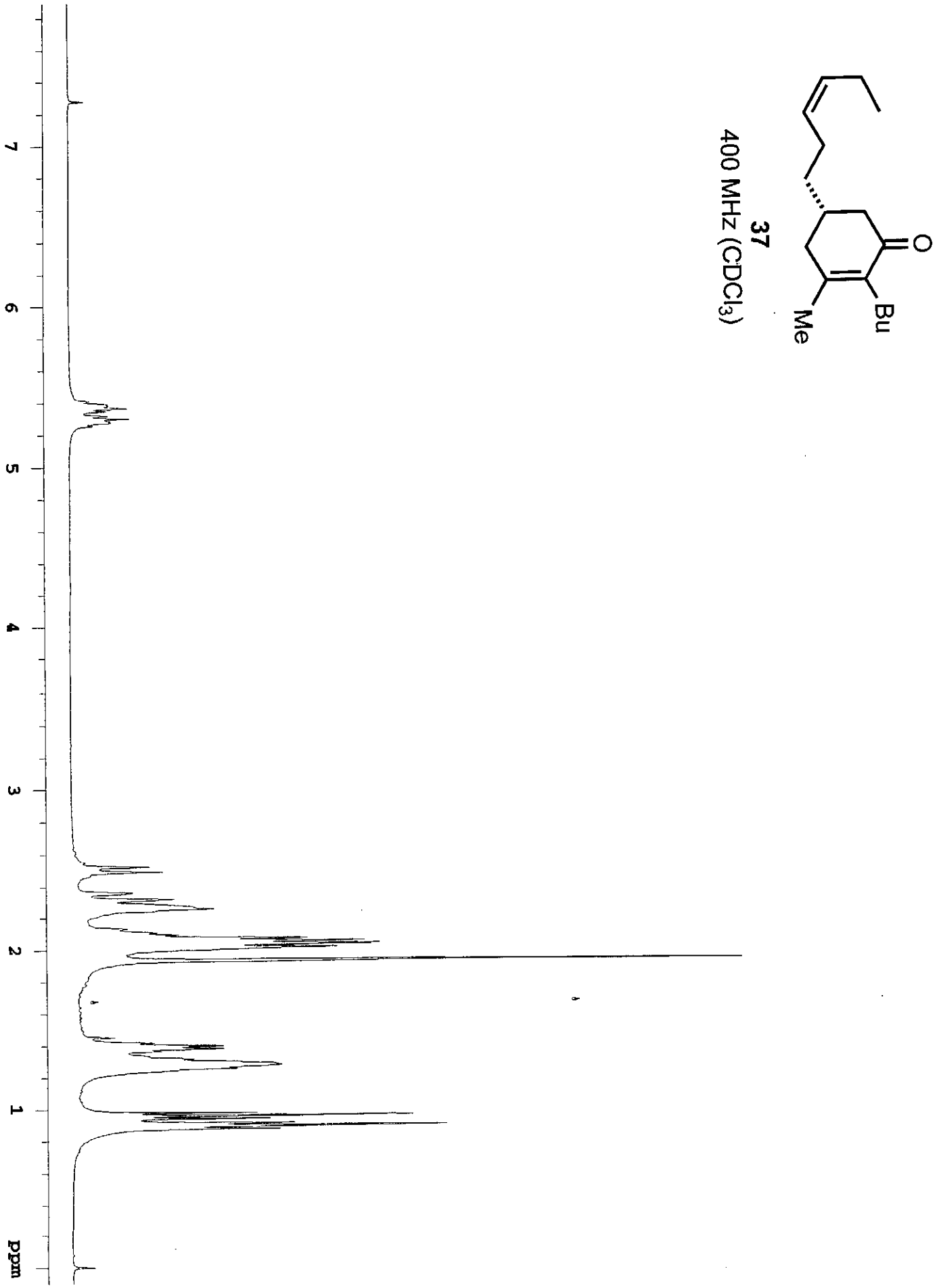
INDEX	FREQUENCY	PPM	HEIGHT
1	20070.326	199.653	15.2
2	14471.705	143.960	48.0
3	14047.497	139.740	30.1
4	13289.112	132.195	51.2
5	12888.557	128.211	46.5
6	7772.129	77.314	32.8
7	7740.084	76.996	33.8
8	7708.040	76.677	33.8
9	4503.597	44.800	72.1
10	3592.619	35.738	58.9
11	3518.612	35.002	50.4
12	3263.782	32.467	63.3
13	3085.249	30.691	52.0
14	2912.819	28.976	56.0
15	2415.367	24.027	52.3
16	2255.908	22.441	46.0
17	2060.590	20.498	29.6
18	1434.960	14.274	25.7
19	1397.575	13.903	41.7



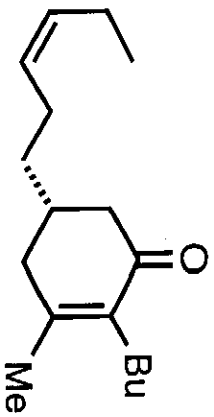
36

400 MHz ($CDCl_3$)



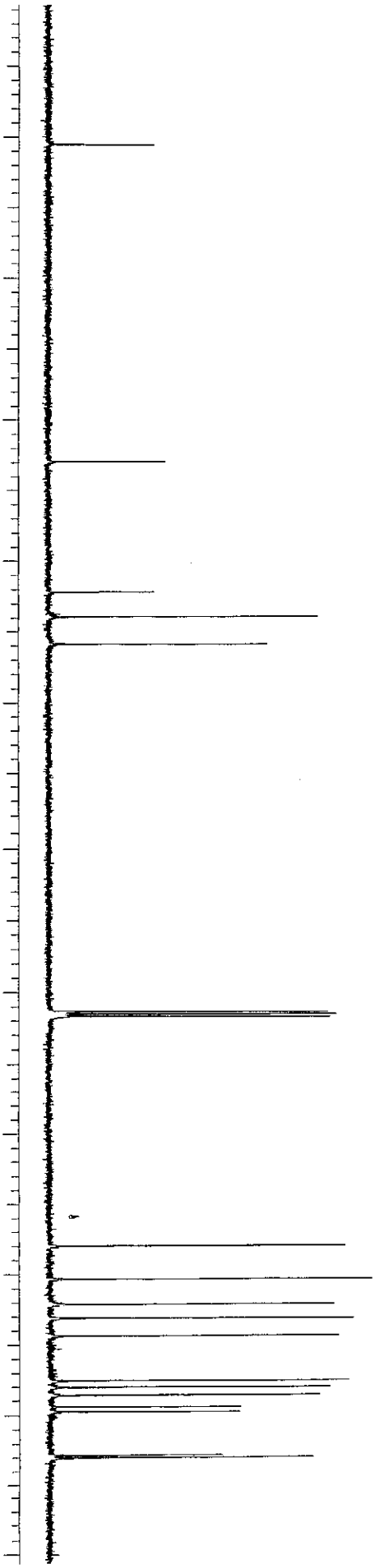

7
6
5
4
3
2
1
ppm
37
400 MHz ($CDCl_3$)
O
Bu
Me

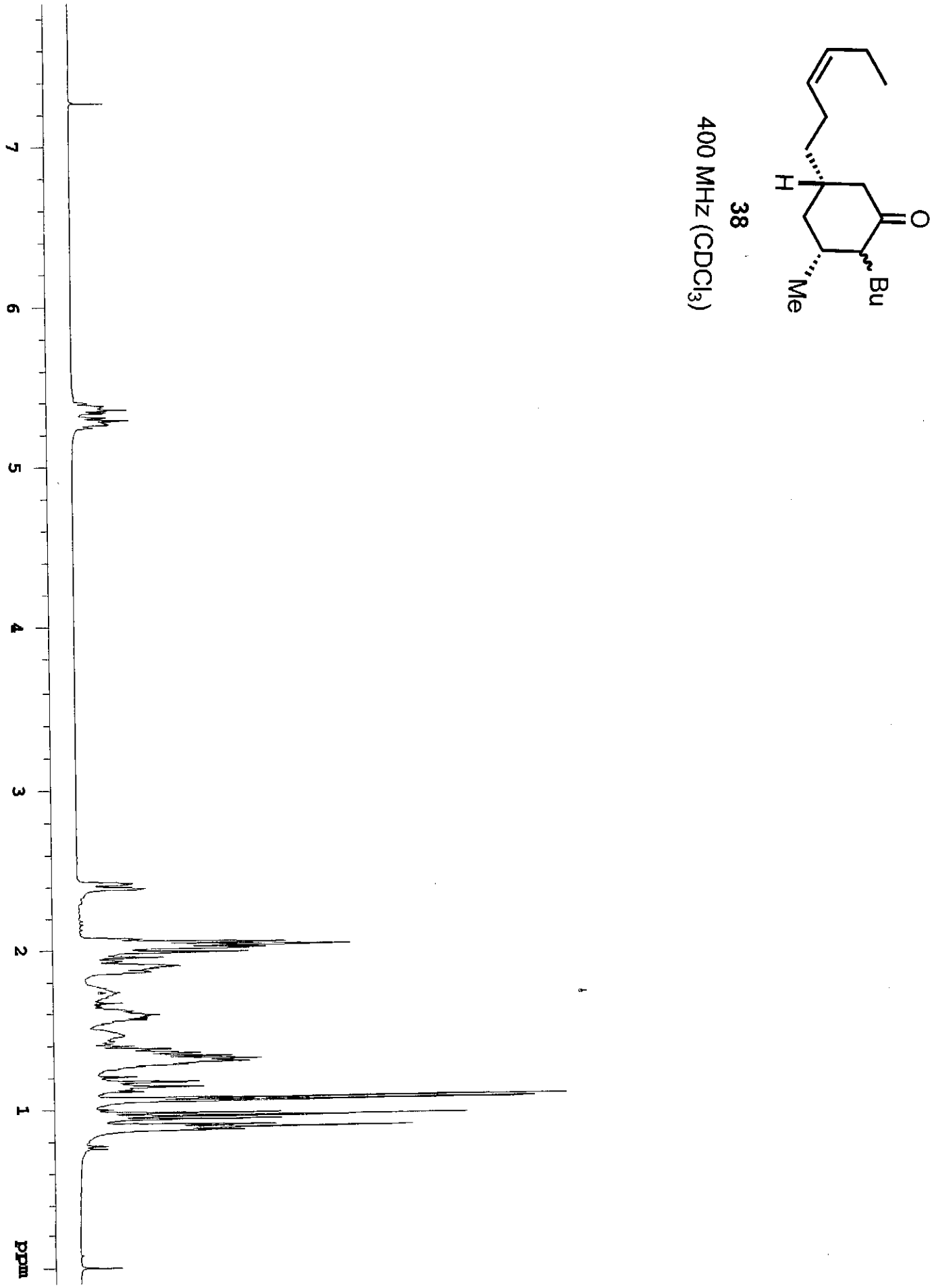
INDEX	FREQUENCY	PPM	HEIGHT
1	19998.738	198.957	17.1
2	15487.341	154.075	19.0
3	13634.104	135.638	17.2
4	13283.142	132.147	43.4
5	12894.030	128.276	35.3
6	7771.499	77.314	44.8
7	7739.454	76.996	46.2
8	7707.410	76.677	45.2
9	4432.010	44.092	47.6
10	3956.685	39.363	51.9
11	3594.277	35.758	45.7
12	3403.537	33.860	48.9
13	3144.892	31.287	46.4
14	2500.952	24.881	48.1
15	2410.922	23.985	45.0
16	2294.952	22.831	43.5
17	2127.863	21.169	30.9
18	2060.722	20.501	30.6
19	1435.856	14.285	27.9
20	1404.574	13.973	42.3

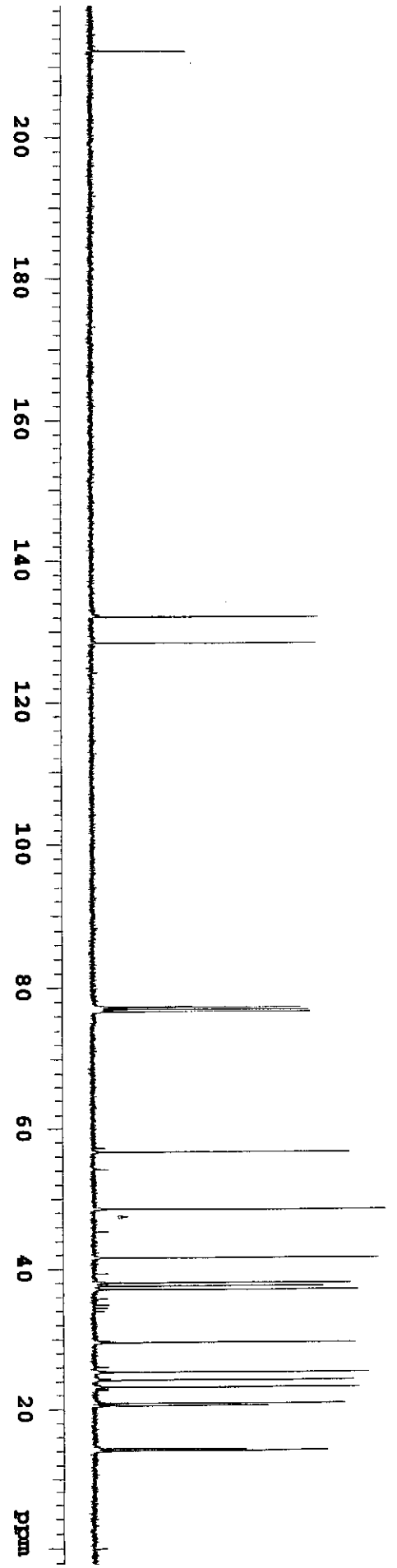


37

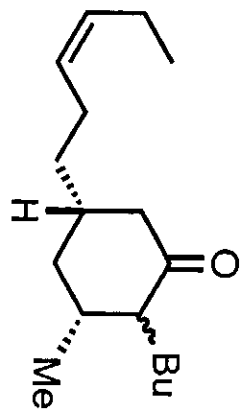
400 MHz ($CDCl_3$)




38
400 MHz ($CDCl_3$)
H
O
Bu
Me
7
6
5
4
3
2
1
ppm

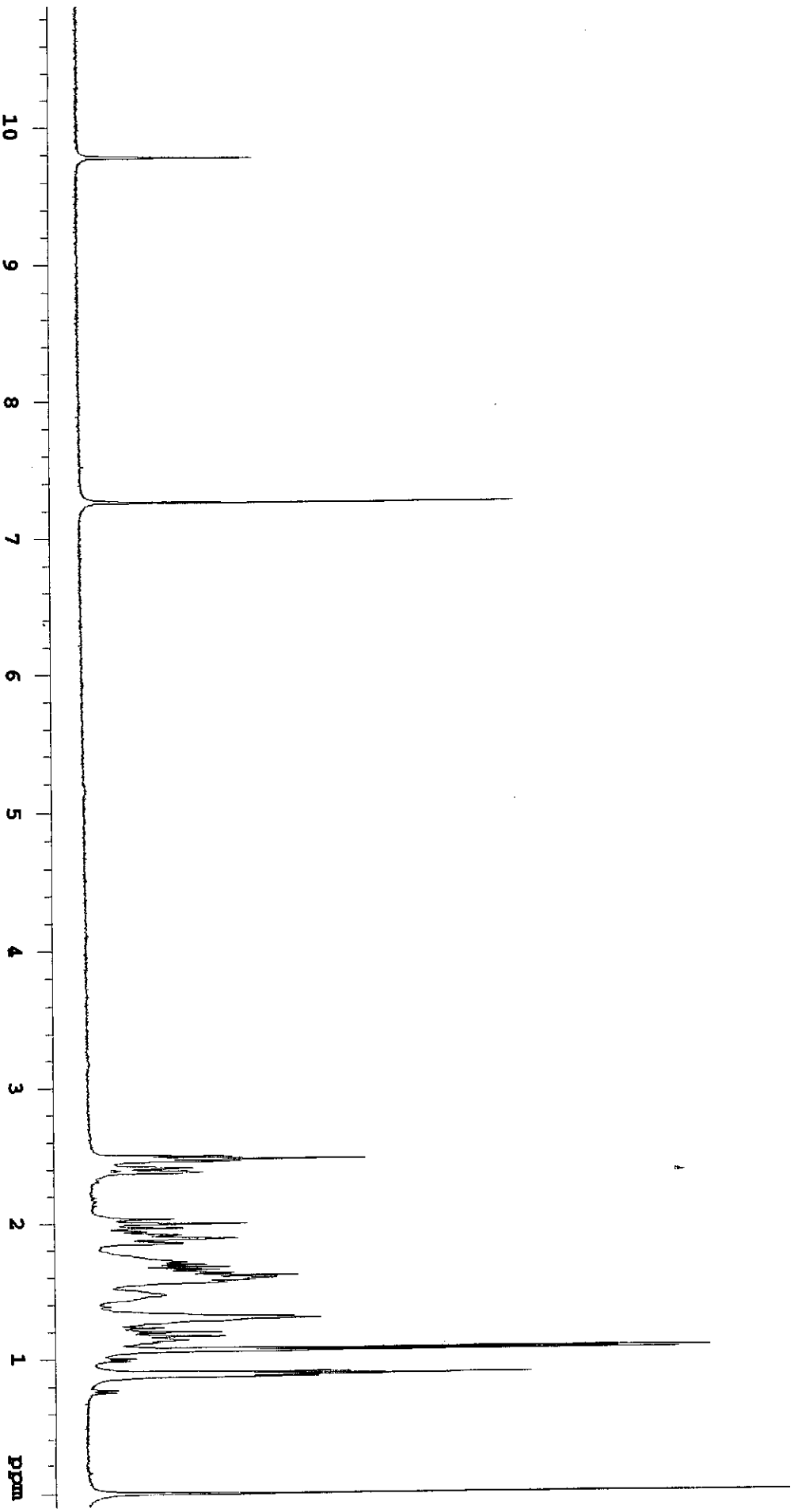


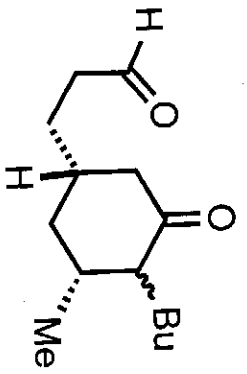
INDEX	FREQUENCY	PPM	HEIGHT
1	21335.121	212.252	15.4
2	13273.657	132.052	36.6
3	12905.146	128.386	36.2
4	7771.933	77.319	33.5
5	7739.889	77.000	34.8
6	7707.844	76.681	35.0
7	5698.200	56.688	41.3
8	4871.912	48.468	47.0
9	4178.378	41.568	45.8
10	3822.838	38.031	41.4
11	3777.060	37.576	37.0
12	3726.705	37.075	42.6
13	2970.609	29.553	42.1
14	2543.349	25.302	44.2
15	2428.142	24.156	41.8
16	2327.431	23.154	42.6
17	2091.676	20.809	40.3
18	2060.394	20.498	28.1
19	1437.053	14.296	24.6
20	1408.061	14.008	37.6



38

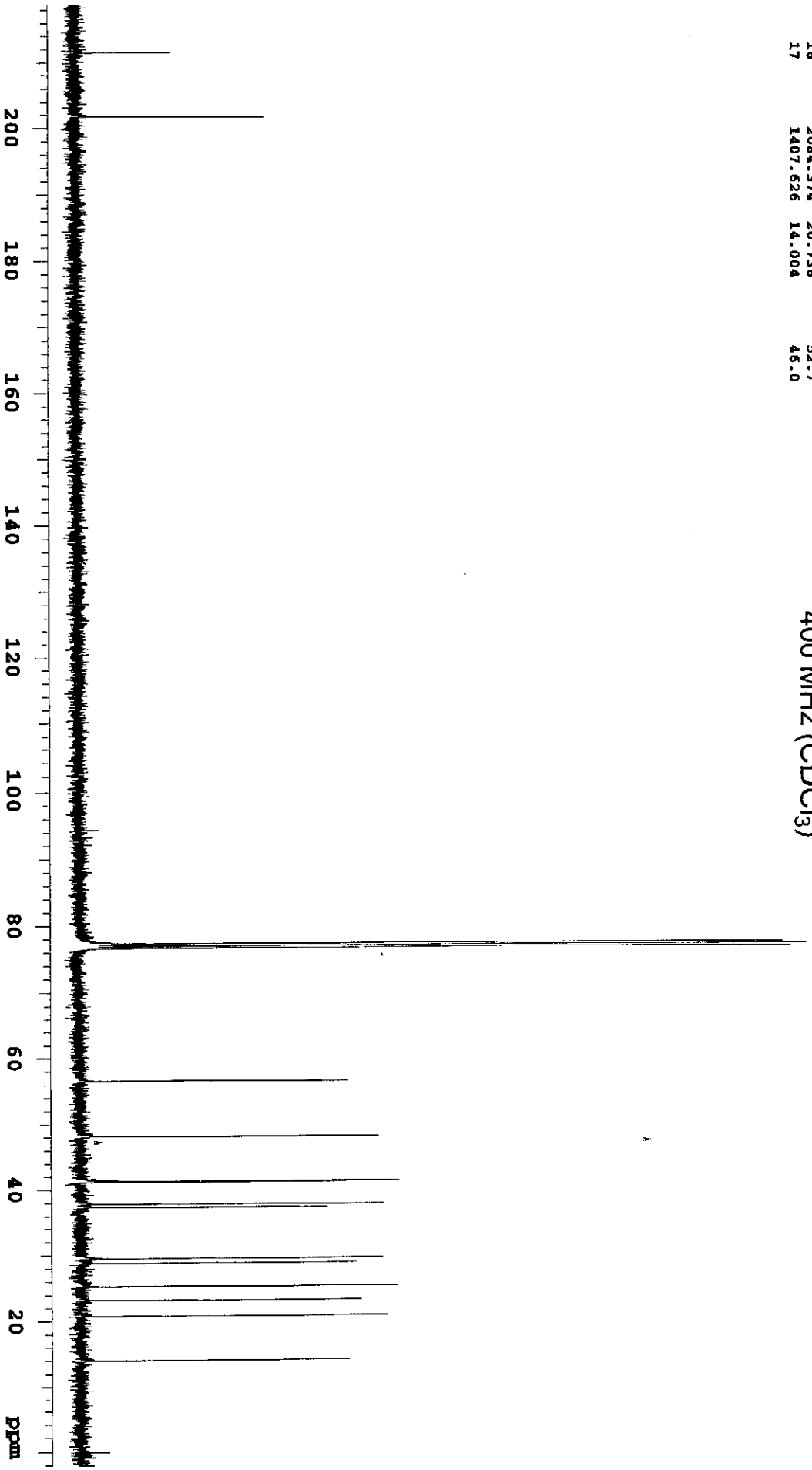
400 MHz ($CDCl_3$)



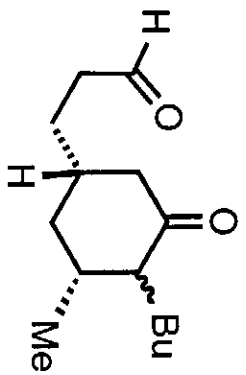


39

400 MHz ($CDCl_3$)

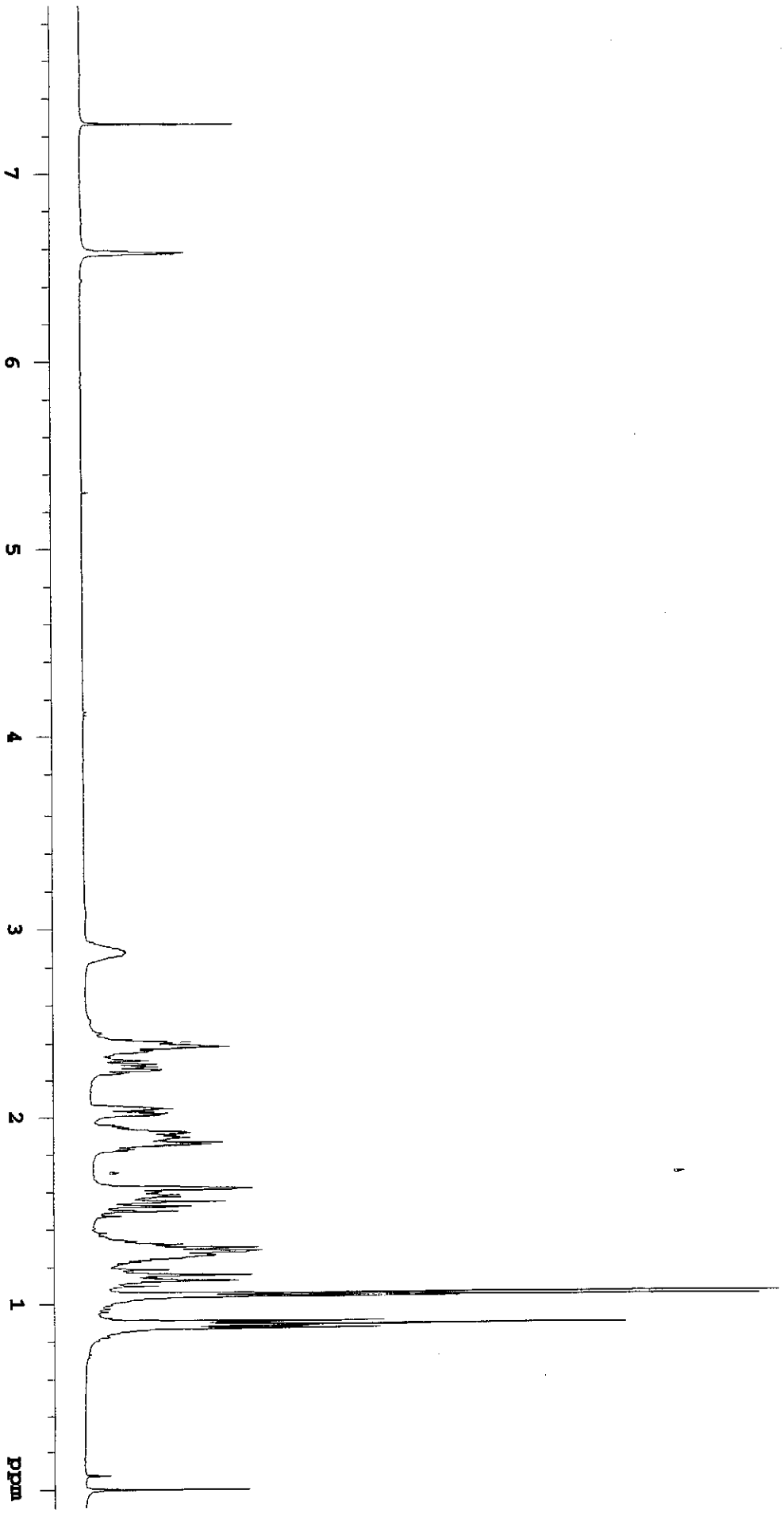


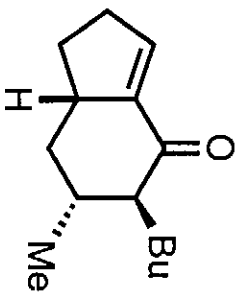
INDEX	FREQUENCY	PPM	HEIGHT
1	21258.391	211.488	16.2
2	20284.088	201.796	32.4
3	7771.498	77.314	120.9
4	7739.454	76.996	124.9
5	7707.409	76.677	122.3
6	5685.558	56.563	46.1
7	4834.854	48.099	51.3
8	4153.529	41.321	55.0
9	4134.455	41.131	45.7
10	3801.803	37.822	52.1
11	3749.922	37.306	42.6
12	2964.070	29.488	51.9
13	2893.115	28.782	47.4
14	2536.811	25.237	54.4
15	2325.470	23.135	48.3
16	2084.374	20.736	52.7
17	1407.626	14.004	46.0



39

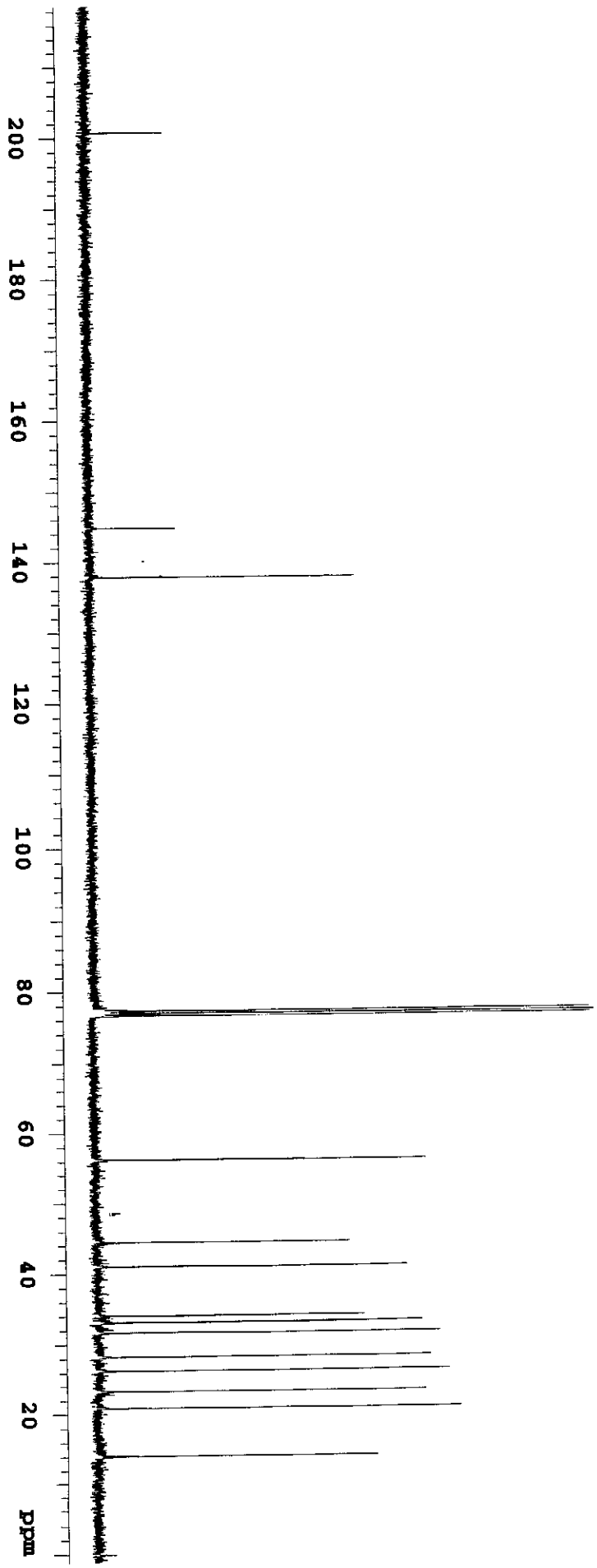
400 MHz ($CDCl_3$)



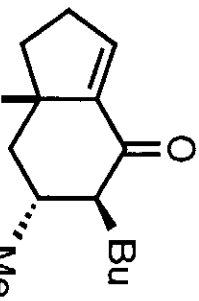


trans-**25**

400 MHz ($CDCl_3$)

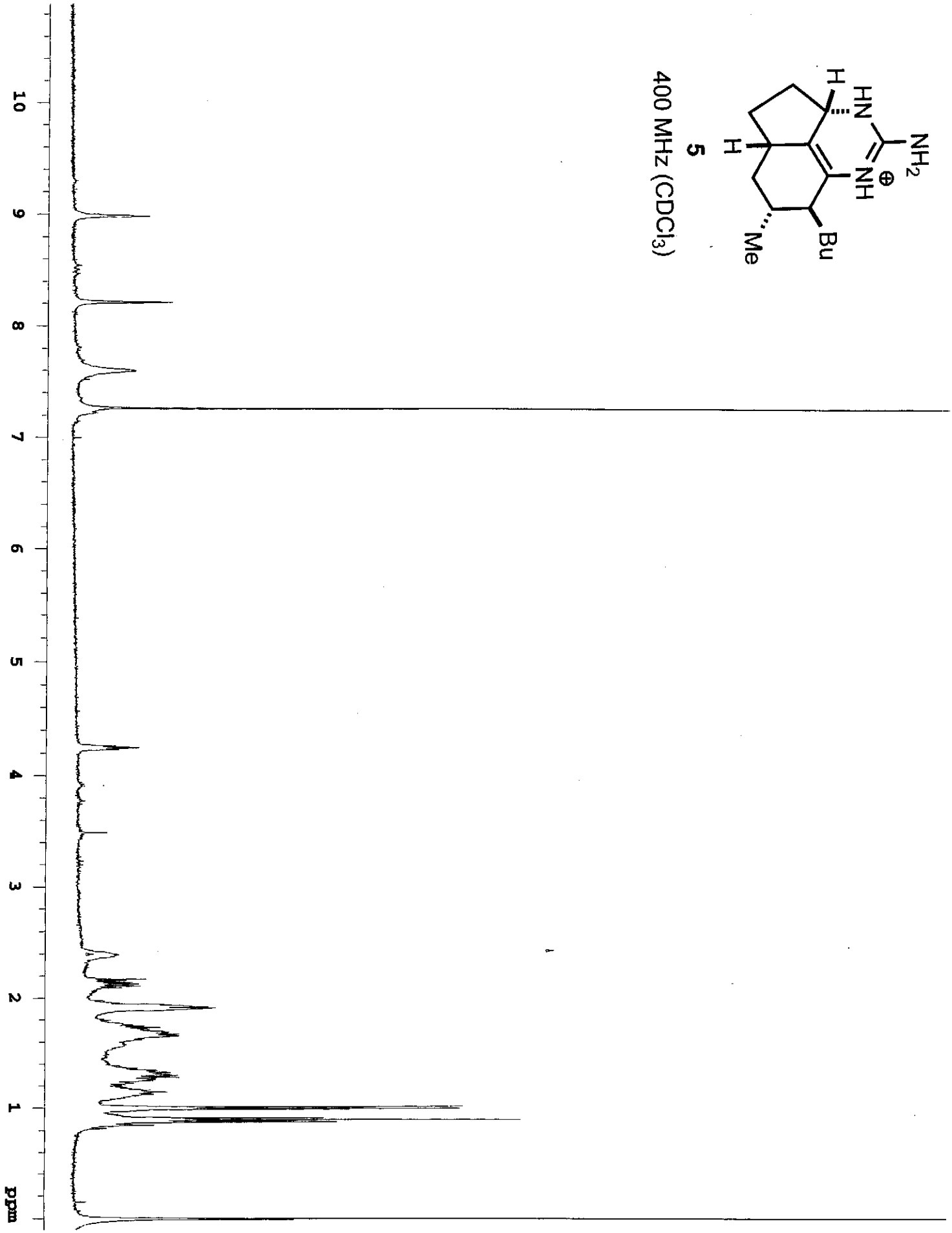


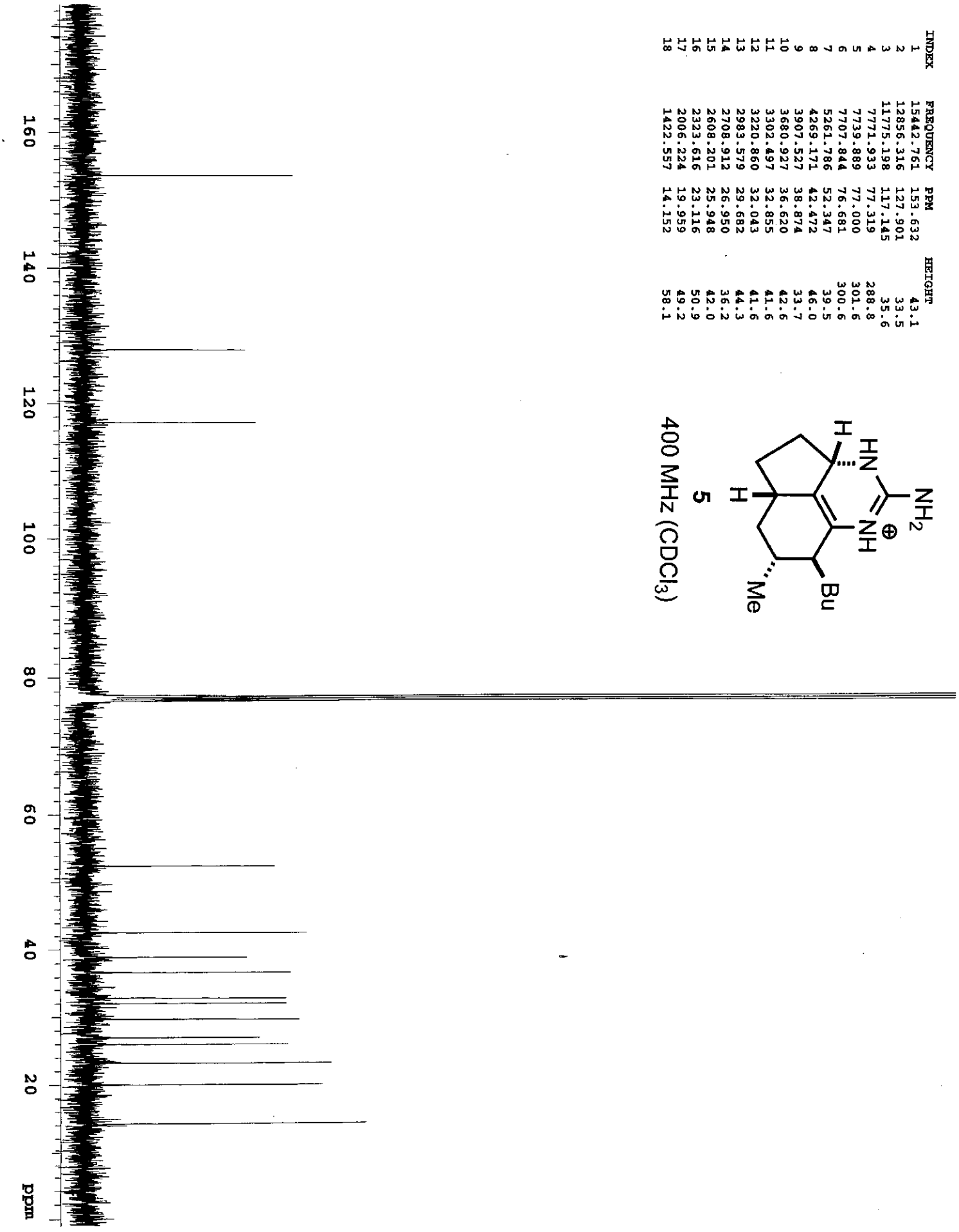
INDEX	FREQUENCY	PPM	HEIGHT
1	20181.088	200.771	12.5
2	14553.474	144.785	14.0
3	13853.074	137.817	42.8
4	7771.498	77.314	79.6
5	7739.454	76.996	80.5
6	7707.409	76.677	79.8
7	5647.410	56.183	53.3
8	4465.581	44.426	40.9
9	4124.536	41.033	50.2
10	3421.848	34.042	43.2
11	3331.055	33.139	52.4
12	3186.855	31.704	55.2
13	2836.655	28.220	53.7
14	2637.522	26.239	56.8
15	2338.441	23.264	52.9
16	2098.870	20.881	58.6
17	1407.626	14.004	45.0



trans-**25**

400 MHz ($CDCl_3$)

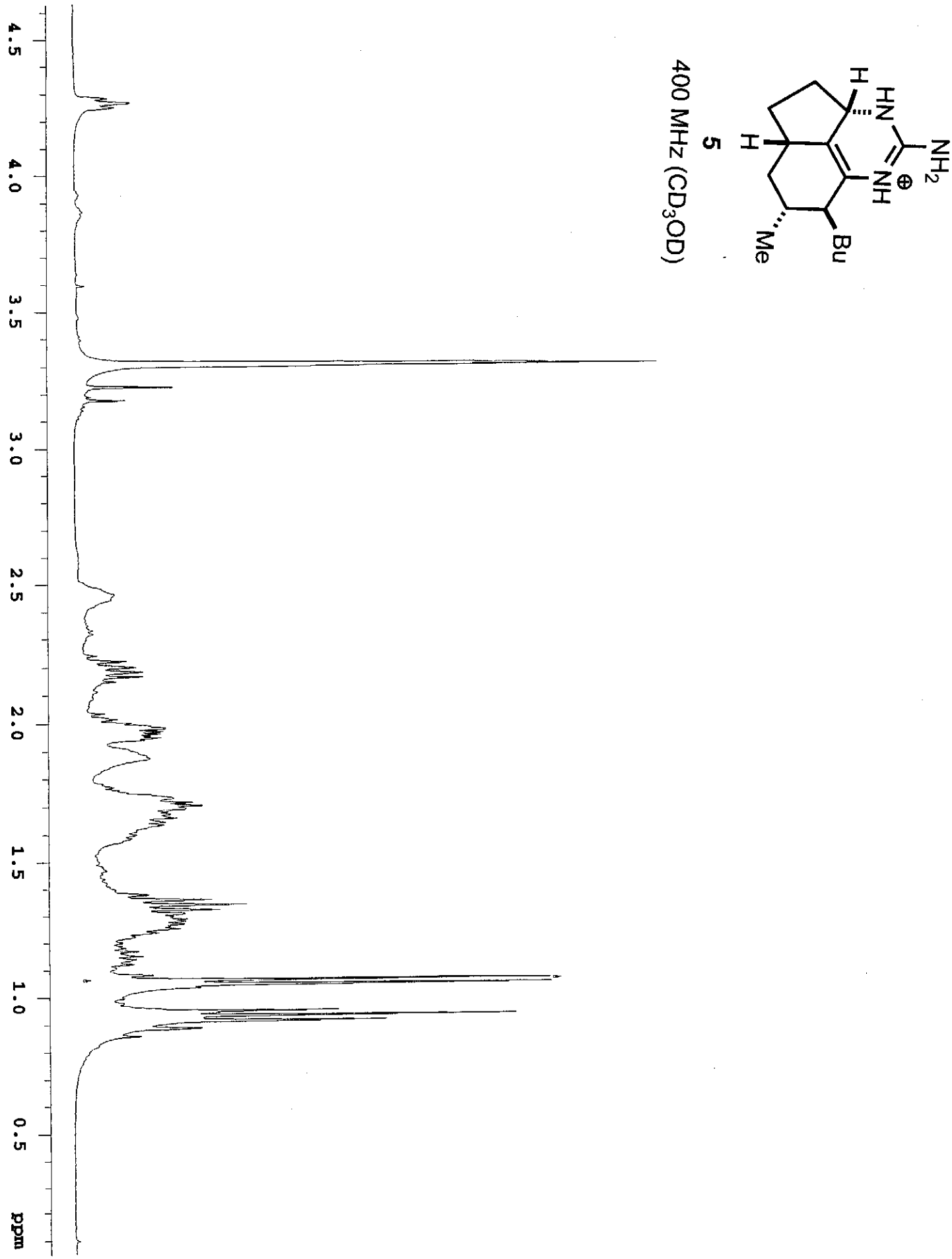

400 MHz (CDCl3)
HN
NH2
NH
H
H
Me
Bu
10
9
8
7
6
5
4
3
2
1
ppm

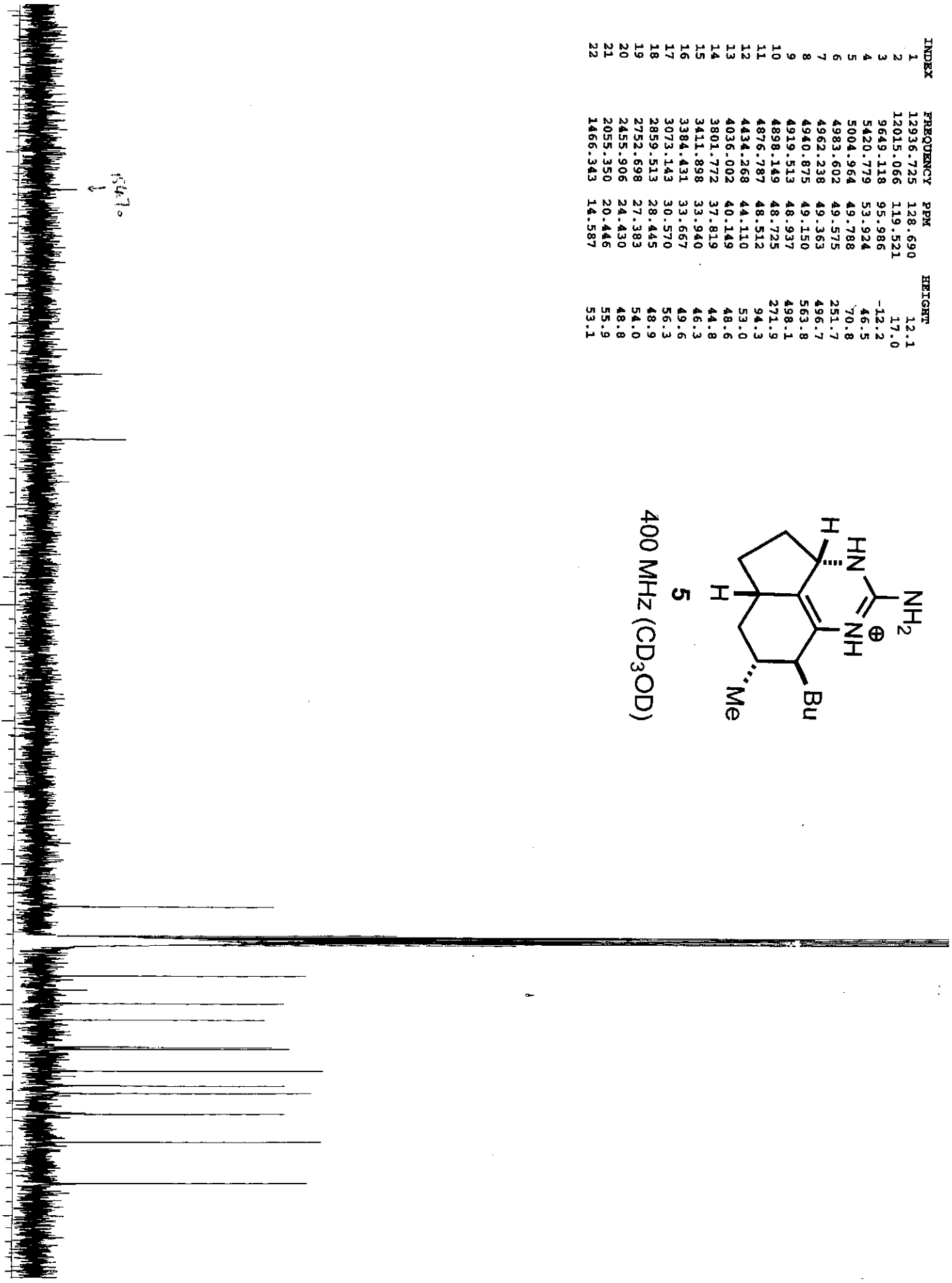


INDEX	FREQUENCY	PPM	HEIGHT
1	15442.761	153.632	43.1
2	12856.316	127.901	33.5
3	11775.198	117.145	35.6
4	7771.933	77.319	288.8
5	7739.889	77.000	301.6
6	7707.844	76.681	300.6
7	5261.786	52.347	39.5
8	4269.171	42.472	46.0
9	3907.527	38.874	33.7
10	3680.927	36.620	42.6
11	3302.497	32.855	41.6
12	3220.860	32.043	41.6
13	2983.579	29.682	44.3
14	2708.912	26.950	36.2
15	2608.201	25.948	42.0
16	2323.616	23.116	50.9
17	2006.224	19.959	49.2
18	1422.557	14.152	58.1

5

400 MHz ($CDCl_3$)

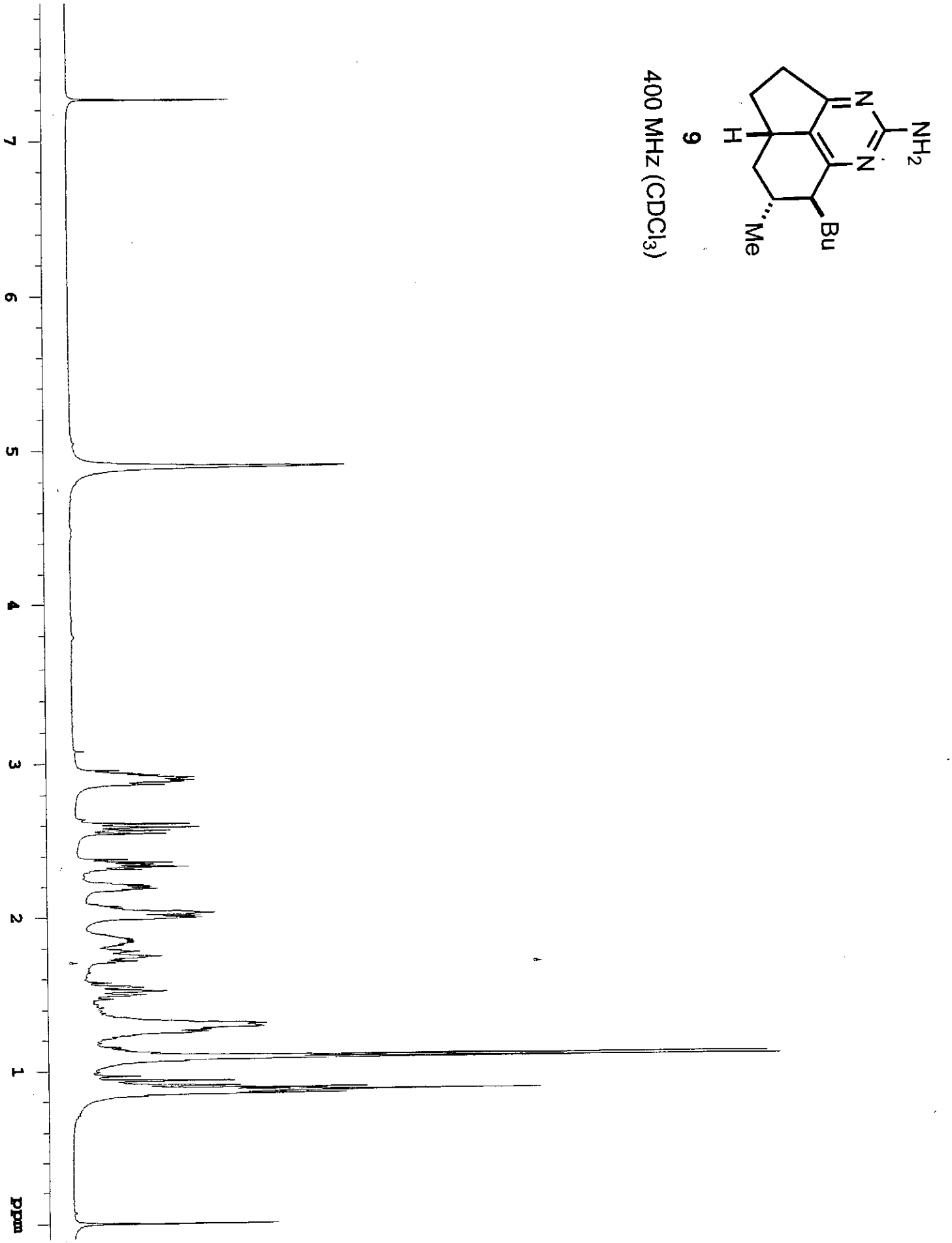

4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
400 MHz (CD_3OD)
5
H
HN
NH_2
NH
H
Me
Bu



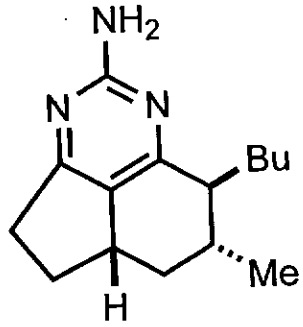
INDEX	FREQUENCY	PPM	HEIGHT
1	12936.725	128.690	12.1
2	12015.066	119.521	17.0
3	9649.118	95.986	-12.2
4	5420.779	53.924	46.5
5	5004.964	49.788	70.8
6	4983.602	49.575	251.7
7	4962.238	49.363	496.7
8	4940.875	49.150	563.8
9	4919.513	48.937	498.1
10	4898.149	48.725	271.9
11	4876.787	48.512	94.3
12	4434.268	44.110	53.0
13	4036.002	40.149	48.6
14	3801.772	37.819	44.8
15	3411.898	33.940	46.3
16	3384.431	33.667	49.6
17	3073.143	30.570	56.3
18	2859.513	28.445	48.9
19	2752.698	27.383	54.0
20	2455.906	24.430	48.8
21	2055.350	20.446	55.9
22	1466.343	14.587	53.1

5

400 MHz (CD_3OD)

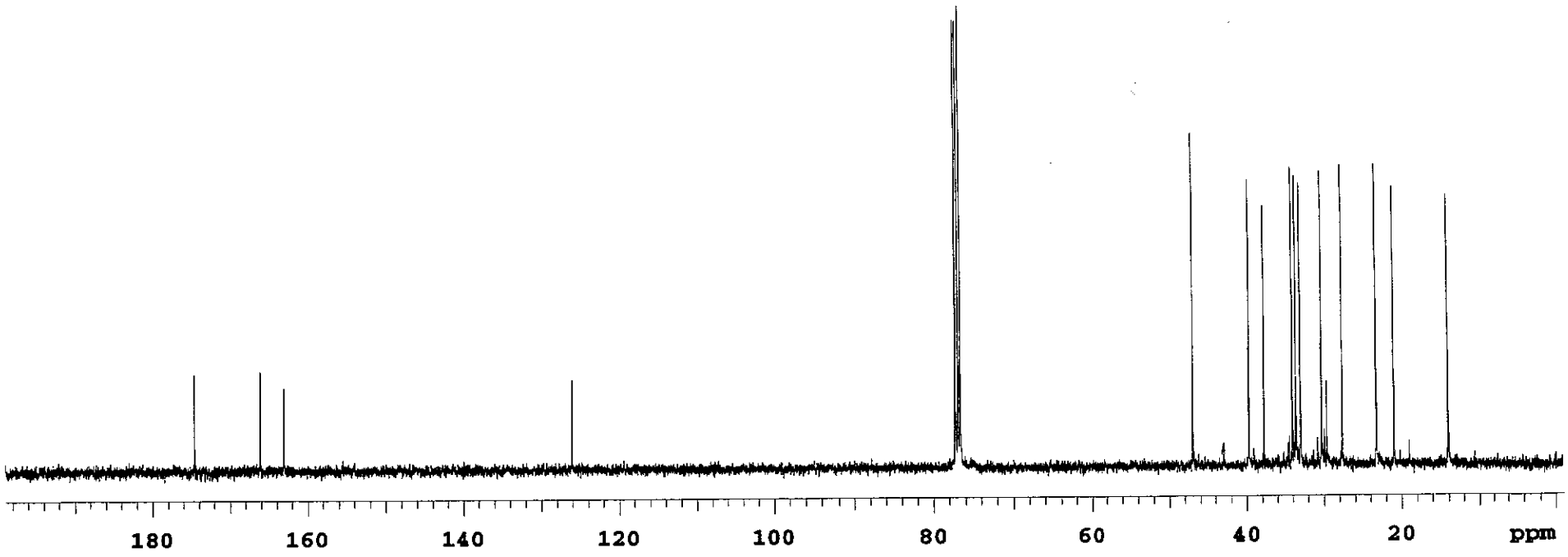

400 MHz ($CDCl_3$)
9
NH_2
N
N
H
Me
Bu
7
6
5
4
3
2
1
ppm

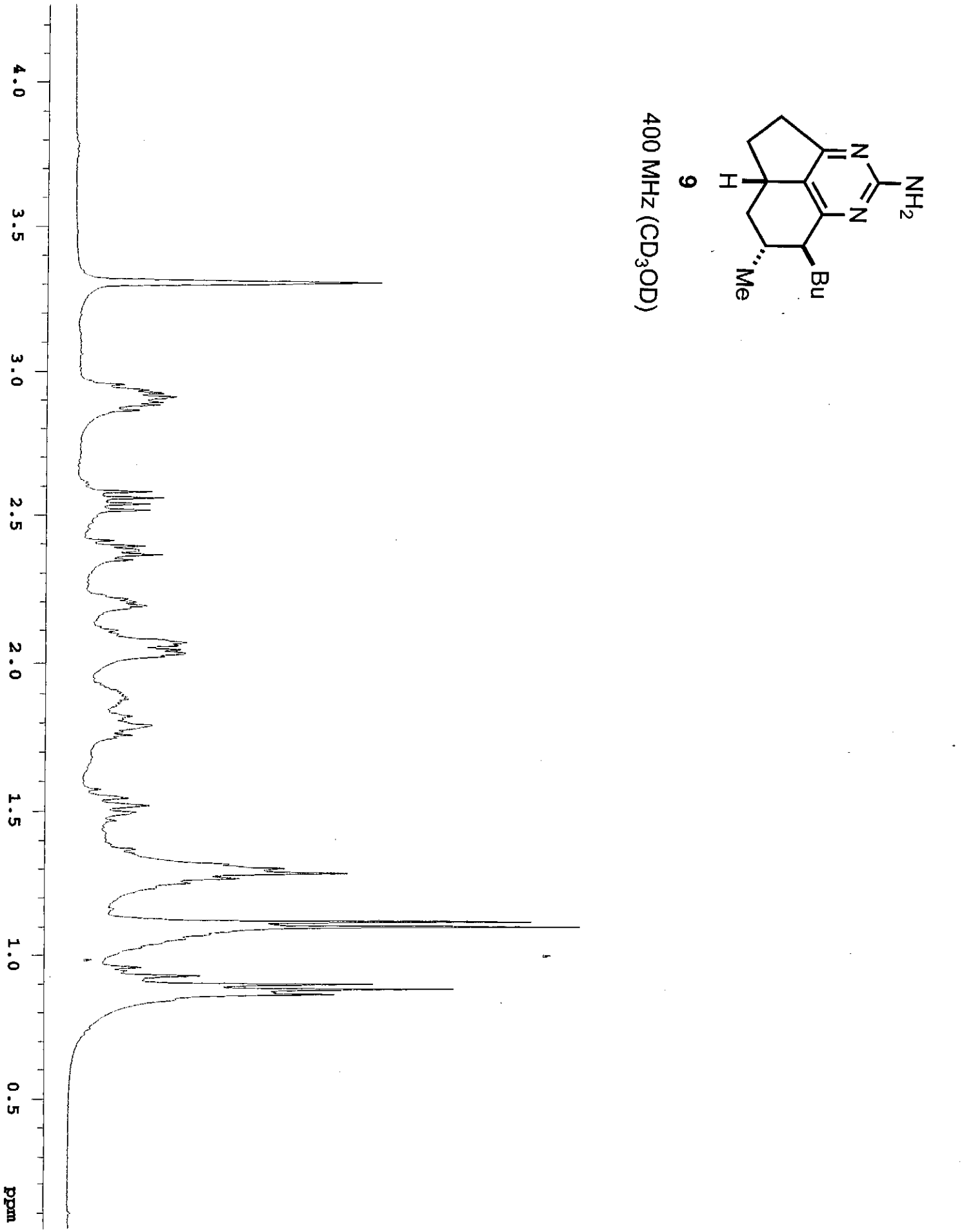
INDEX	FREQUENCY	PPM	HEIGHT
1	17549.629	174.592	15.7
2	16698.162	166.121	16.1
3	16392.977	163.085	13.5
4	12670.482	126.052	14.7
5	7771.498	77.314	72.0
6	7739.454	76.996	71.9
7	7708.172	76.684	74.3
8	4722.699	46.984	53.7
9	3994.833	39.742	46.0
10	3792.647	37.731	41.9
11	3423.374	34.057	48.1
12	3379.885	33.625	46.6
13	3322.663	33.055	45.5
14	3047.233	30.315	47.4
15	2981.618	29.663	13.7
16	2779.433	27.651	48.3
17	2339.204	23.271	48.5
18	2108.789	20.979	44.8
19	1412.967	14.057	43.5



9

400 MHz ($CDCl_3$)

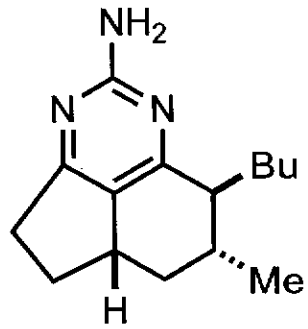




400 MHz (CD_3OD)

9

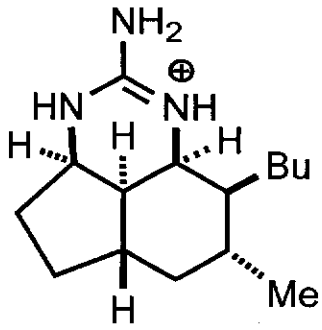
INDEX	FREQUENCY	PPM	HEIGHT
1	17719.336	176.280	12.3
2	16848.795	167.619	14.4
3	12753.975	126.882	10.5
4	5004.562	49.788	54.0
5	4983.199	49.575	161.4
6	4961.836	49.363	302.1
7	4940.473	49.150	343.0
8	4919.110	48.937	299.9
9	4896.984	48.717	150.4
10	4875.621	48.505	54.0
11	4860.362	48.353	50.8
12	4118.762	40.975	45.2
13	3930.310	39.100	41.6
14	3551.118	35.328	44.6
15	3461.851	34.440	44.9
16	3447.355	34.296	43.6
17	3135.303	31.191	46.1
18	2885.051	28.702	41.1
19	2463.896	24.512	41.7
20	2150.318	21.392	44.1
21	1462.126	14.546	40.4



9

400 MHz (CD_3OD)

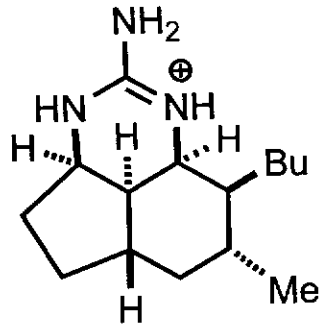
NAME	min
EXPNO	1
PROCNO	1
Date_	20080528
Time	10.23
INSTRUM	spect
PROBHD	5 mm CPTCI 1H-
PULPROG	zg
TD	65536
SOLVENT	CDCl3
NS	8
DS	2
SWH	8802.817 Hz
FIDRES	0.134320 Hz
AQ	3.7224948 sec
RG	11.3
DW	56.800 usec
DE	6.50 usec
TE	-27.3 K
D1	0.50000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	8.10 usec
PL1	2.50 dB
PL1W	8.47522545 W
SFO1	800.1340006 MHz
SI	32768
SF	800.1300000 MHz
WDW	no
SSB	0
LB	0.00 Hz
GB	0
PC	1.00



27

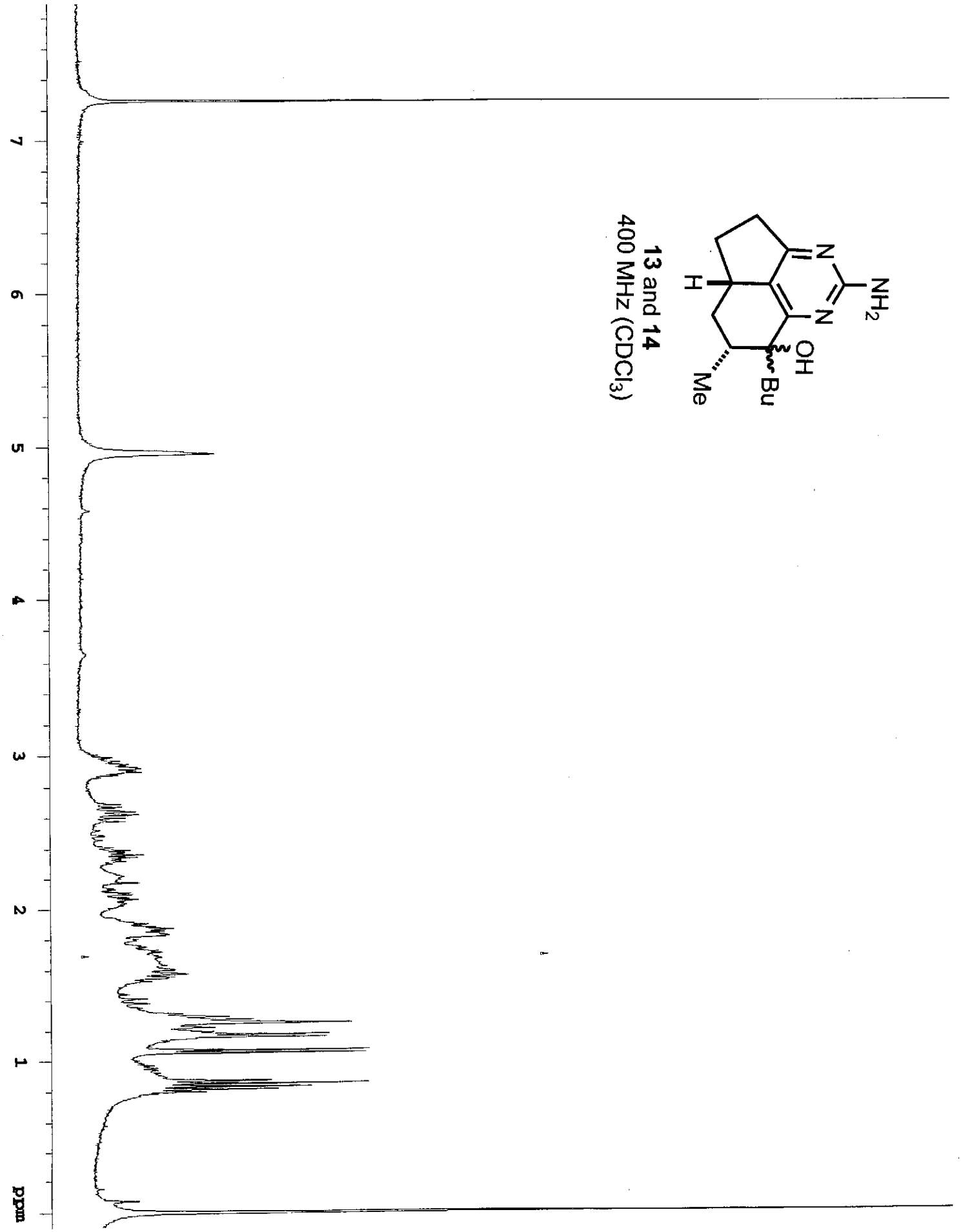
800 MHz ($CDCl_3$)

INDEX	FREQUENCY	PPM	HEIGHT
1	15503.230	154.221	30.3
2	7771.366	77.307	479.3
3	7740.084	76.996	499.6
4	7708.040	76.677	501.7
5	5187.974	51.608	44.2
6	4723.330	46.986	49.4
7	4645.507	46.212	52.5
8	4630.248	46.060	49.6
9	3981.730	39.609	42.8
10	3652.893	36.338	45.2
11	3260.730	32.437	47.1
12	3182.145	31.655	37.3
13	2925.790	29.105	49.2
14	2916.634	29.014	54.8
15	2757.175	27.427	40.6
16	2284.138	22.722	55.0
17	2024.730	20.141	57.4
18	1424.279	14.168	61.4

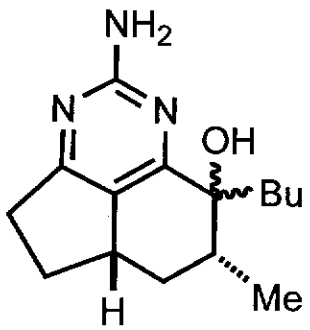


27

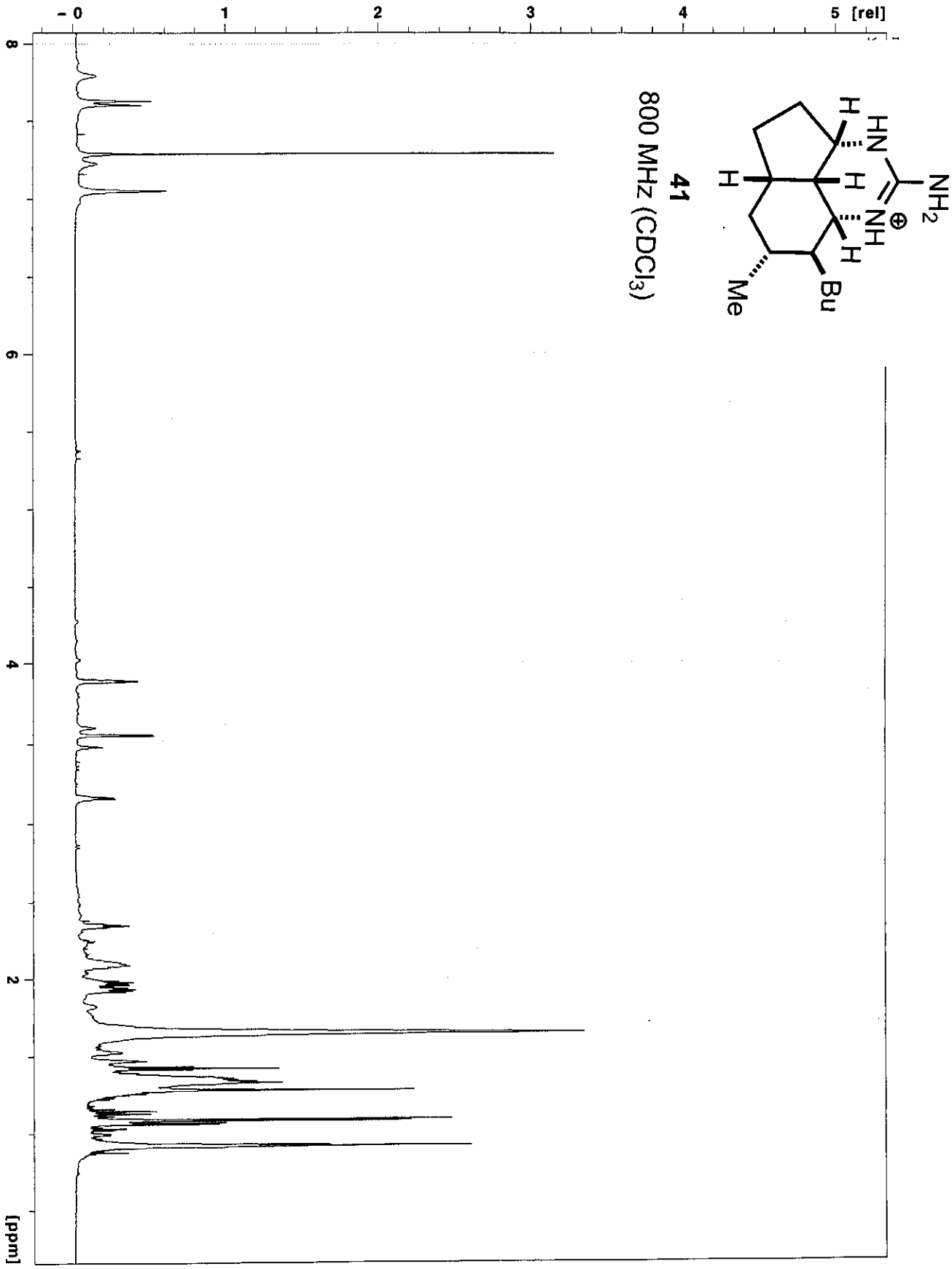
400 MHz ($CDCl_3$)

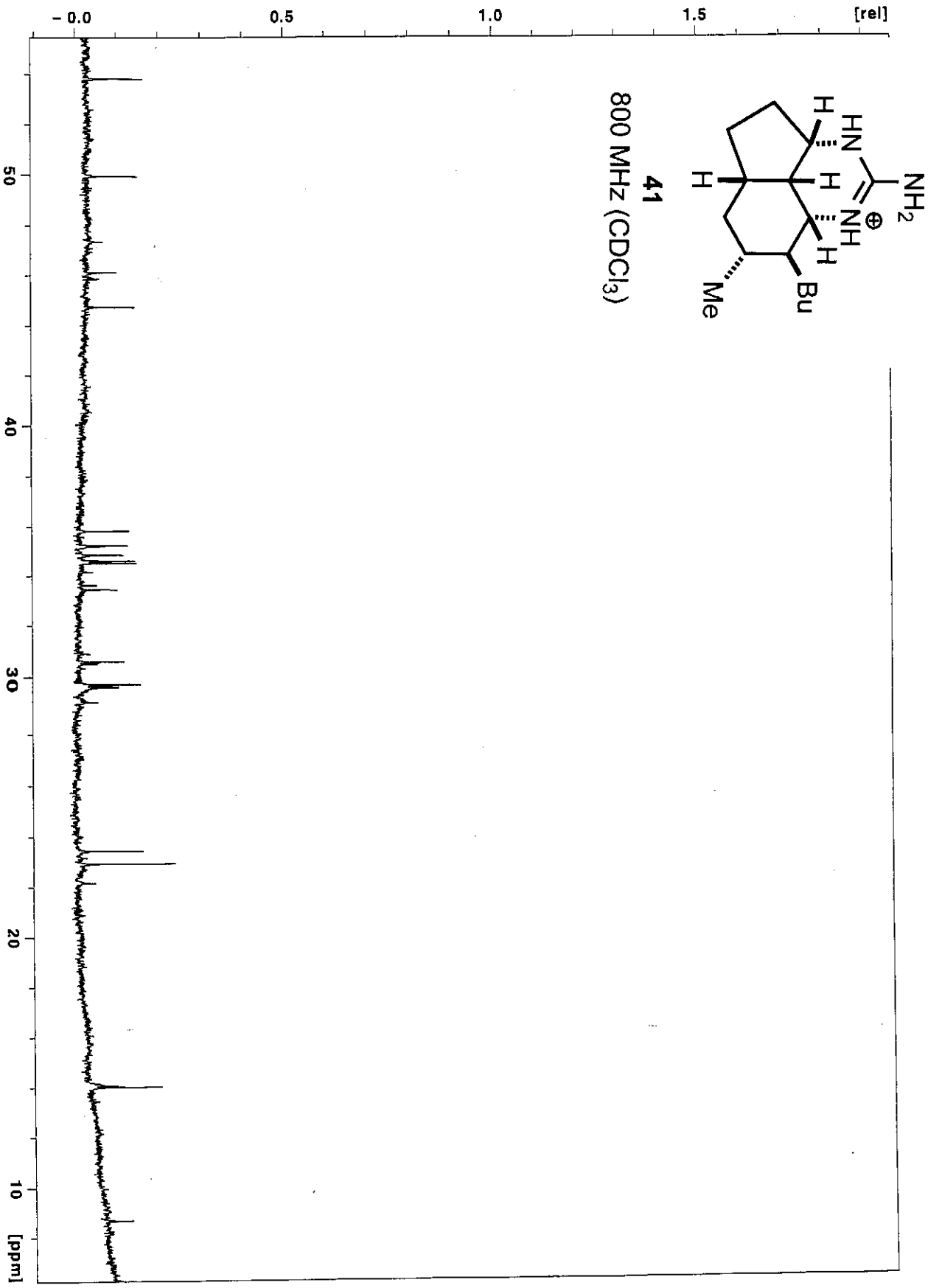

7
6
5
4
3
2
1
ppm
13 and 14
400 MHz (CDCl3)
NH2
N
N
H
OH
Bu
Me

INDEX	FREQUENCY	PPM	HEIGHT
1	9709.046	77.255	791.2
2	9677.001	77.000	829.3
3	9644.957	76.745	835.9
4	5283.099	42.038	25.9
5	4818.455	38.340	24.0
6	4753.603	37.824	47.3
7	4694.091	37.351	33.8
8	4673.492	37.187	53.7
9	4621.610	36.774	42.2
10	4422.477	35.190	49.4
11	4285.144	34.097	31.7
12	4253.099	33.842	55.1
13	4205.032	33.459	41.4
14	4182.144	33.277	46.9
15	3400.107	27.055	49.5
16	3386.373	26.945	31.6
17	2953.010	23.497	30.9
18	2906.470	23.127	38.0
19	1966.500	15.647	32.4
20	1890.966	15.046	45.9
21	1755.922	13.972	43.8
22	1740.663	13.850	24.5
23	-1.944	-0.015	33.4

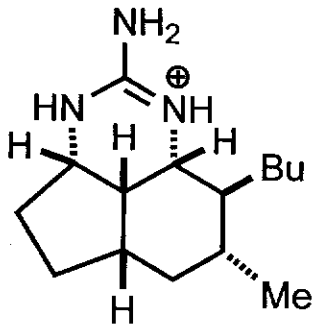


13 and **14**
500 MHz ($CDCl_3$)


– 0
1
2
3
4
5 [rel]
8
6
4
2
[ppm]
41
800 MHz ($CDCl_3$)
H
HN
H
NH
H
NH_2
H
Me
Bu

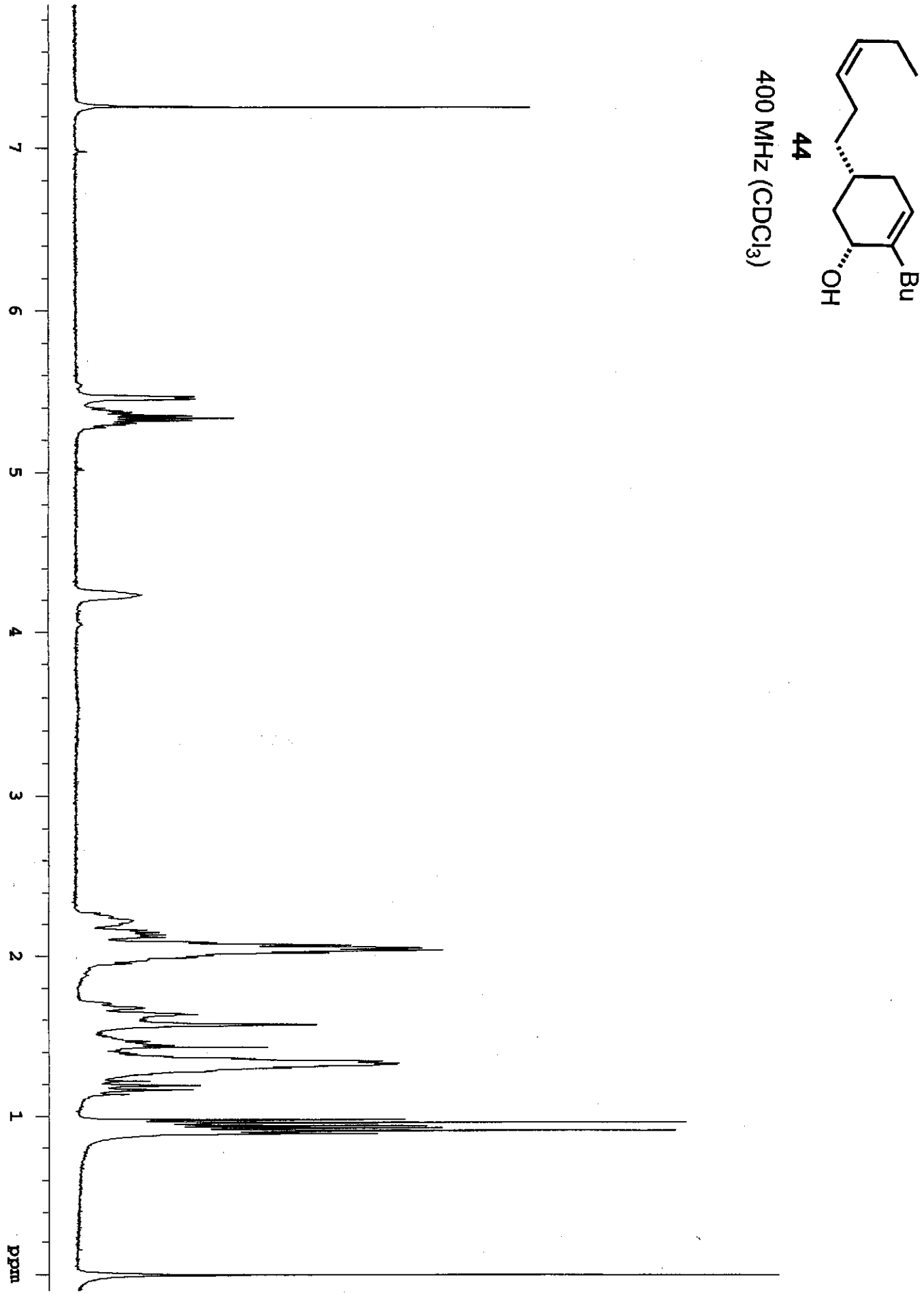

– 0.0
0.5
1.0
1.5
[rel]
50
40
30
20
10
[ppm]
41
800 MHz ($CDCl_3$)
H
HN
H
NH
H
NH_2
H
Me
Bu

INDEX	FREQUENCY	PPM	HEIGHT
1	15554.021	154.726	20.9
2	7772.563	77.319	594.7
3	7740.519	77.000	625.0
4	7708.475	76.681	620.4
5	5405.853	53.776	40.1
6	5016.742	49.905	39.4
7	4486.483	44.630	40.5
8	3593.054	35.742	37.9
9	3537.357	35.188	36.6
10	3522.098	35.037	24.2
11	3495.395	34.771	47.1
12	3475.557	34.574	46.0
13	3467.928	34.498	50.1
14	3383.239	33.655	20.6
15	3354.246	33.367	34.0
16	3065.083	30.490	45.0
17	2991.076	29.754	65.8
18	2984.209	29.686	103.3
19	2943.772	29.284	24.5
20	2352.476	23.402	47.2
21	2302.121	22.901	70.3
22	2229.639	22.180	23.0
23	1408.691	14.013	53.5



41

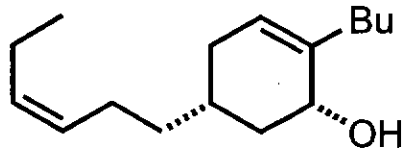
400 MHz ($CDCl_3$)



400 MHz ($CDCl_3$)

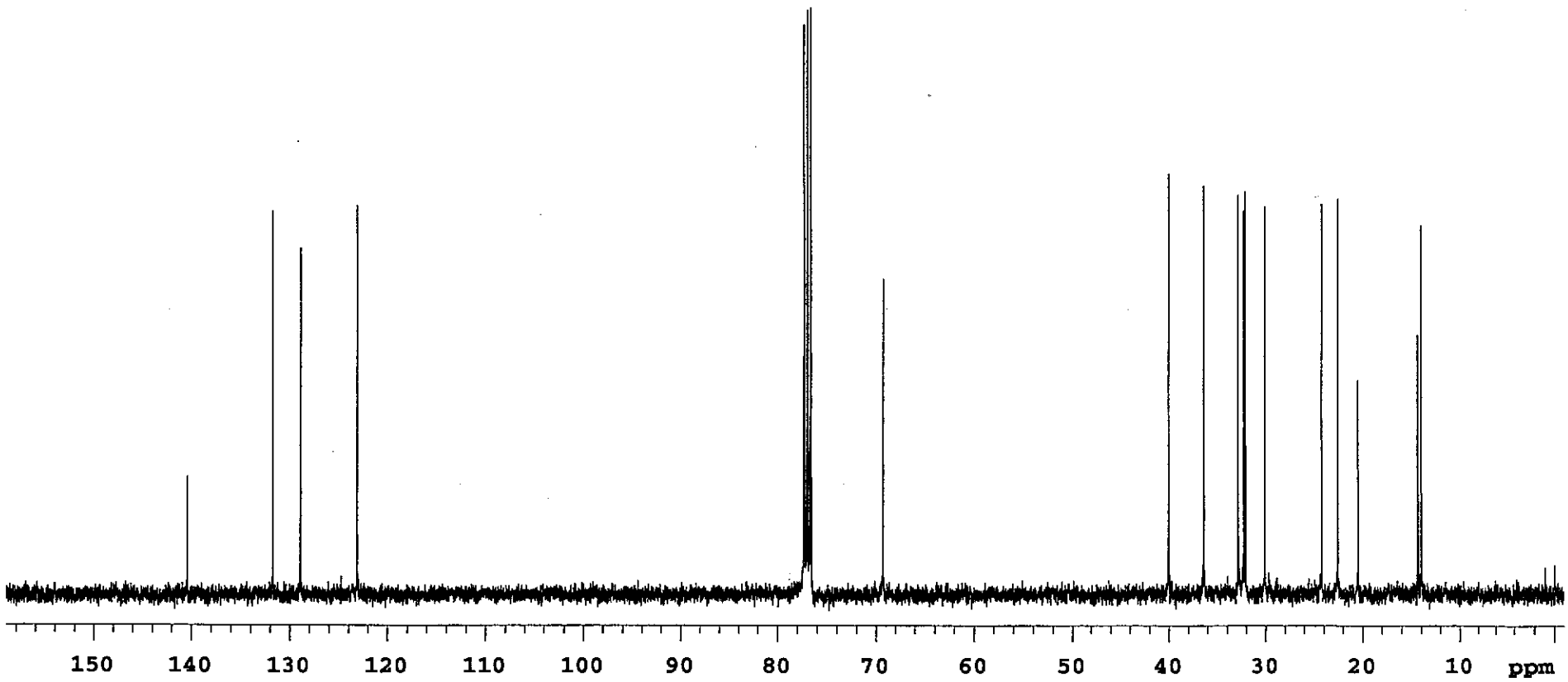
44

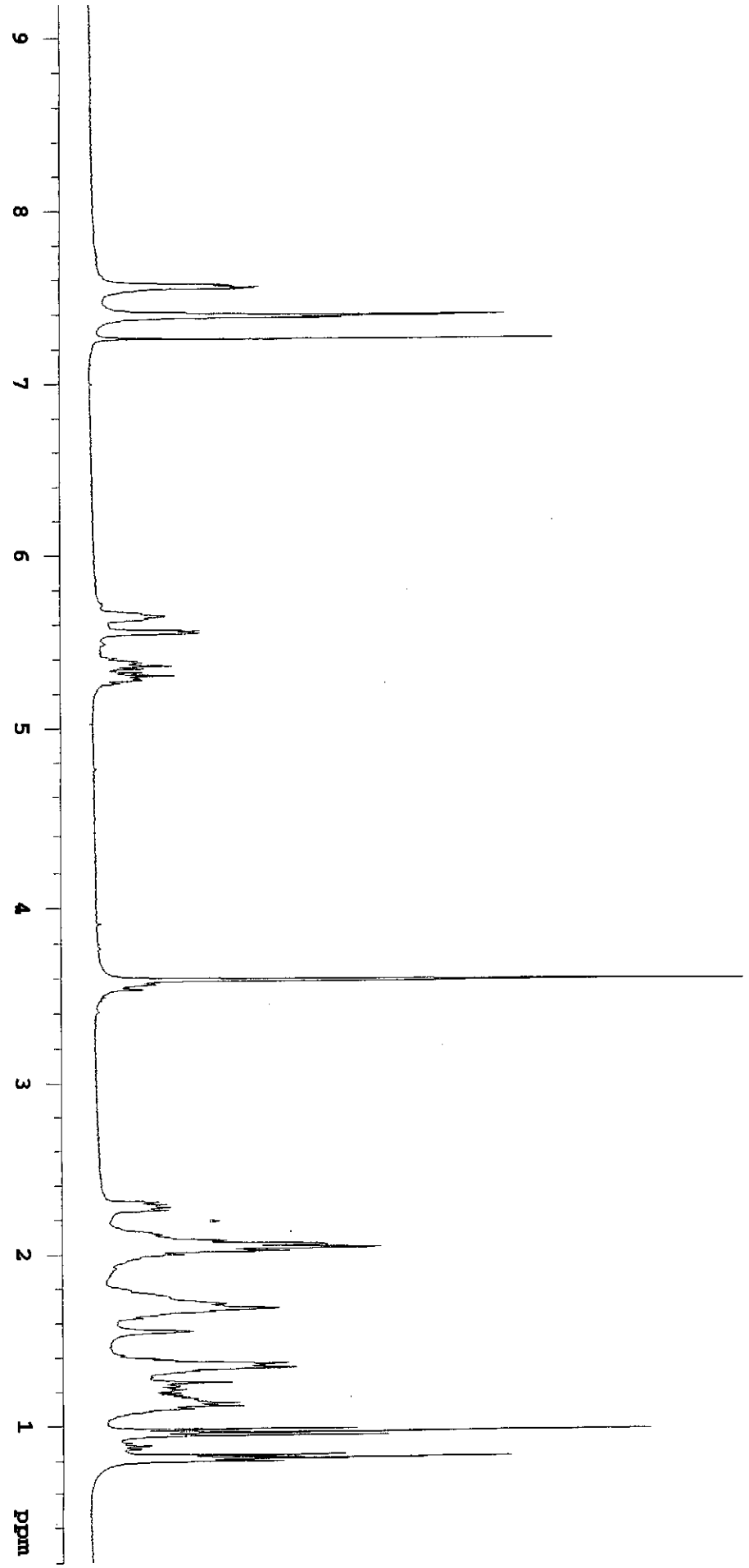
INDEX	FREQUENCY	PPM	HEIGHT
1	14117.930	140.440	19.3
2	13244.364	131.750	61.7
3	12959.788	128.919	55.7
4	12374.613	123.098	62.6
5	7771.800	77.311	91.9
6	7740.519	77.000	94.2
7	7708.476	76.681	94.6
8	6966.899	69.304	50.9
9	4028.056	40.070	67.9
10	3666.423	36.472	66.0
11	3304.789	32.875	64.5
12	3249.858	32.328	62.0
13	3232.310	32.154	65.2
14	3028.605	30.128	62.6
15	2440.379	24.276	63.1
16	2268.717	22.568	63.9
17	2061.198	20.504	34.8
18	1443.980	14.364	42.0
19	1409.648	14.023	59.5



44

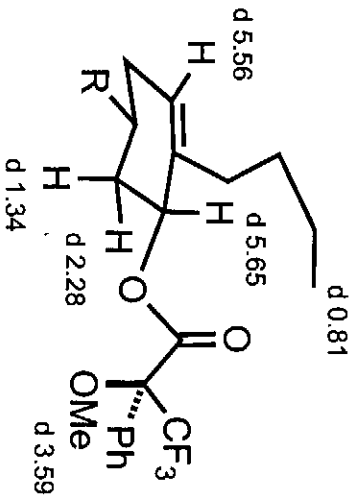
400 MHz ($CDCl_3$)

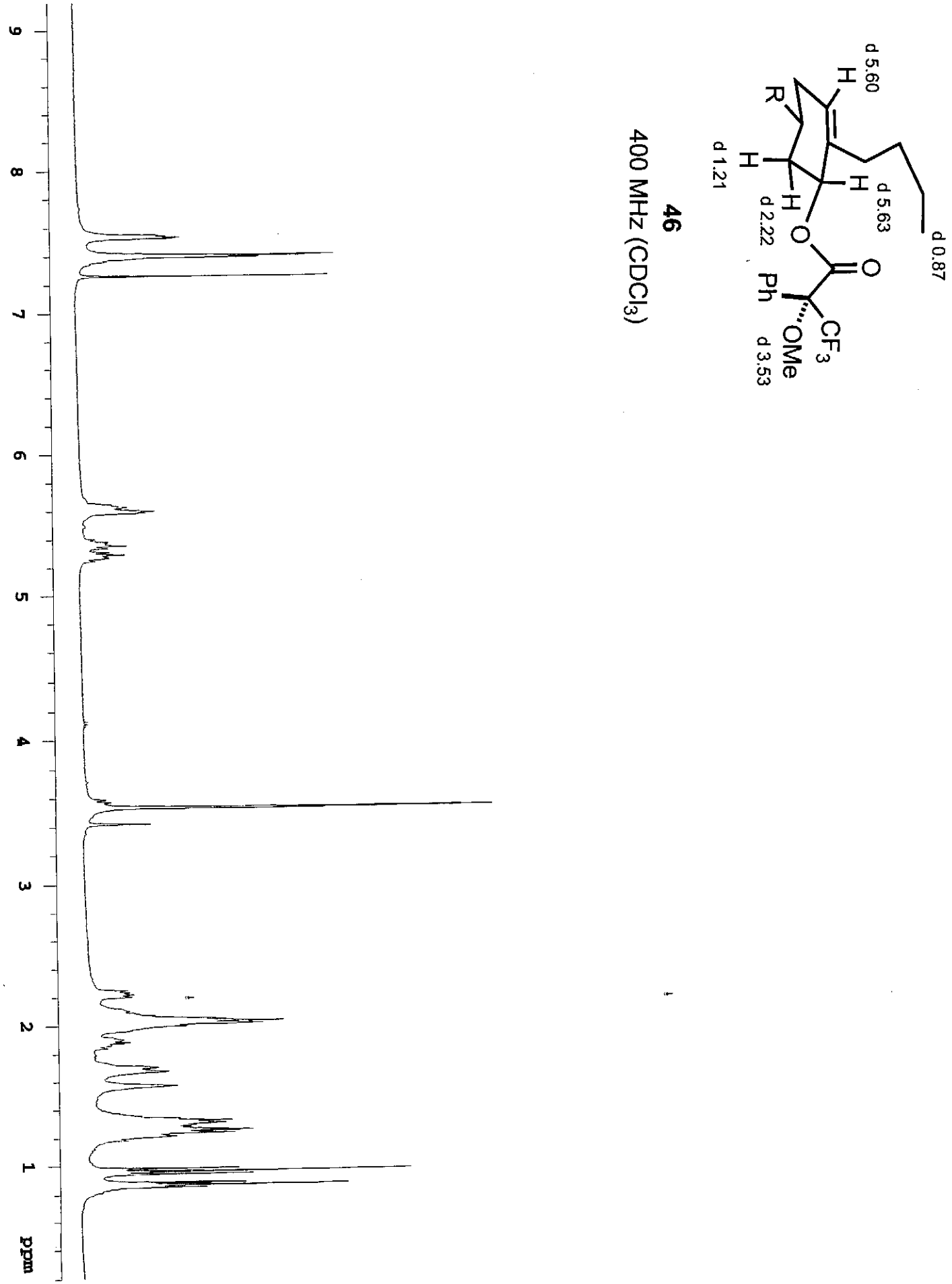


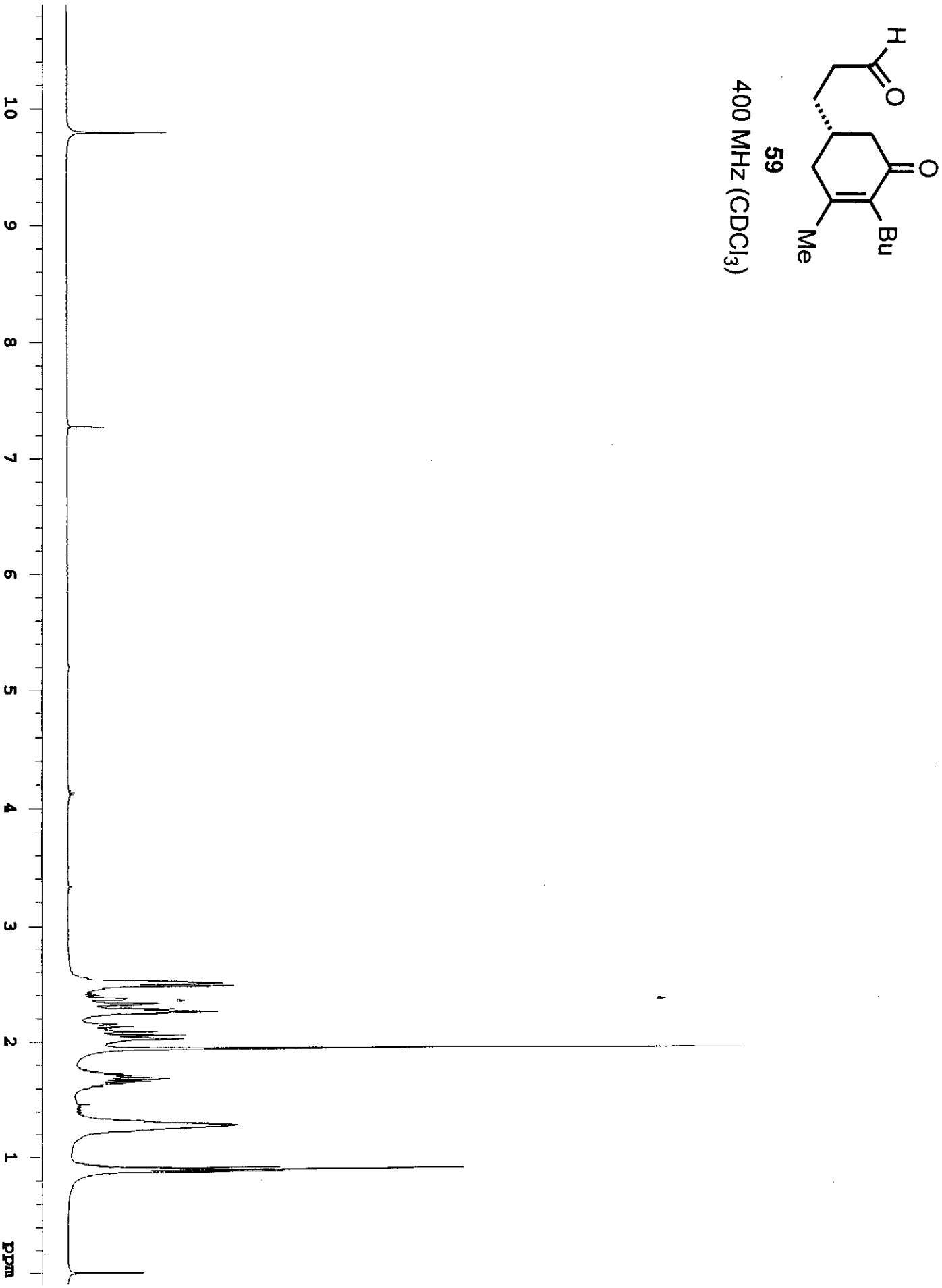


45

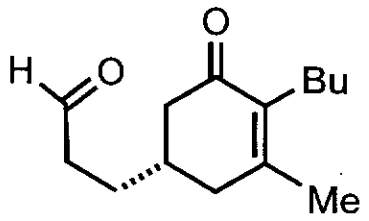
400 MHz ($CDCl_3$)




9
8
7
6
5
4
3
2
1
ppm
46
400 MHz ($CDCl_3$)
d 5.60
d 5.63
d 0.87
d 1.21
d 2.22
d 3.53
R
H
O
Ph
OMe
CF_3

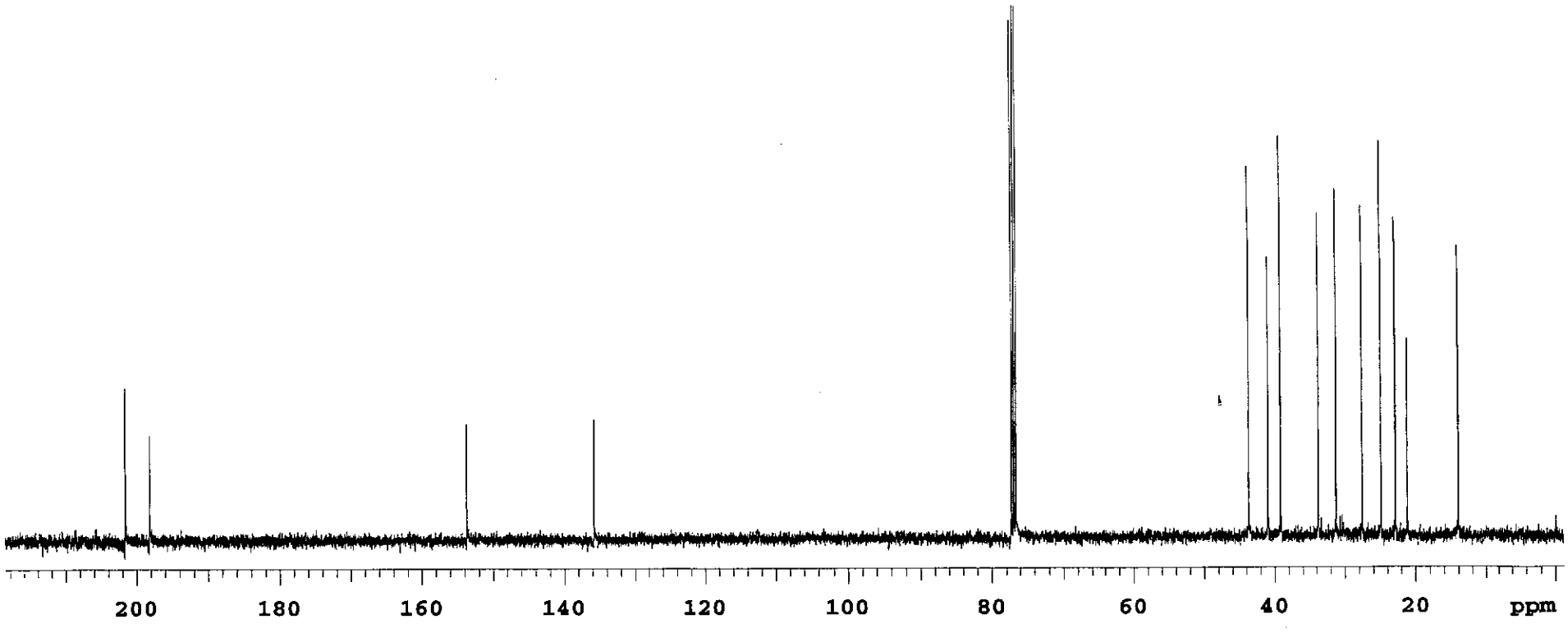

H
O
O
Bu
Me
59
400 MHz ($CDCl_3$)
10
9
8
7
6
5
4
3
2
1
ppm

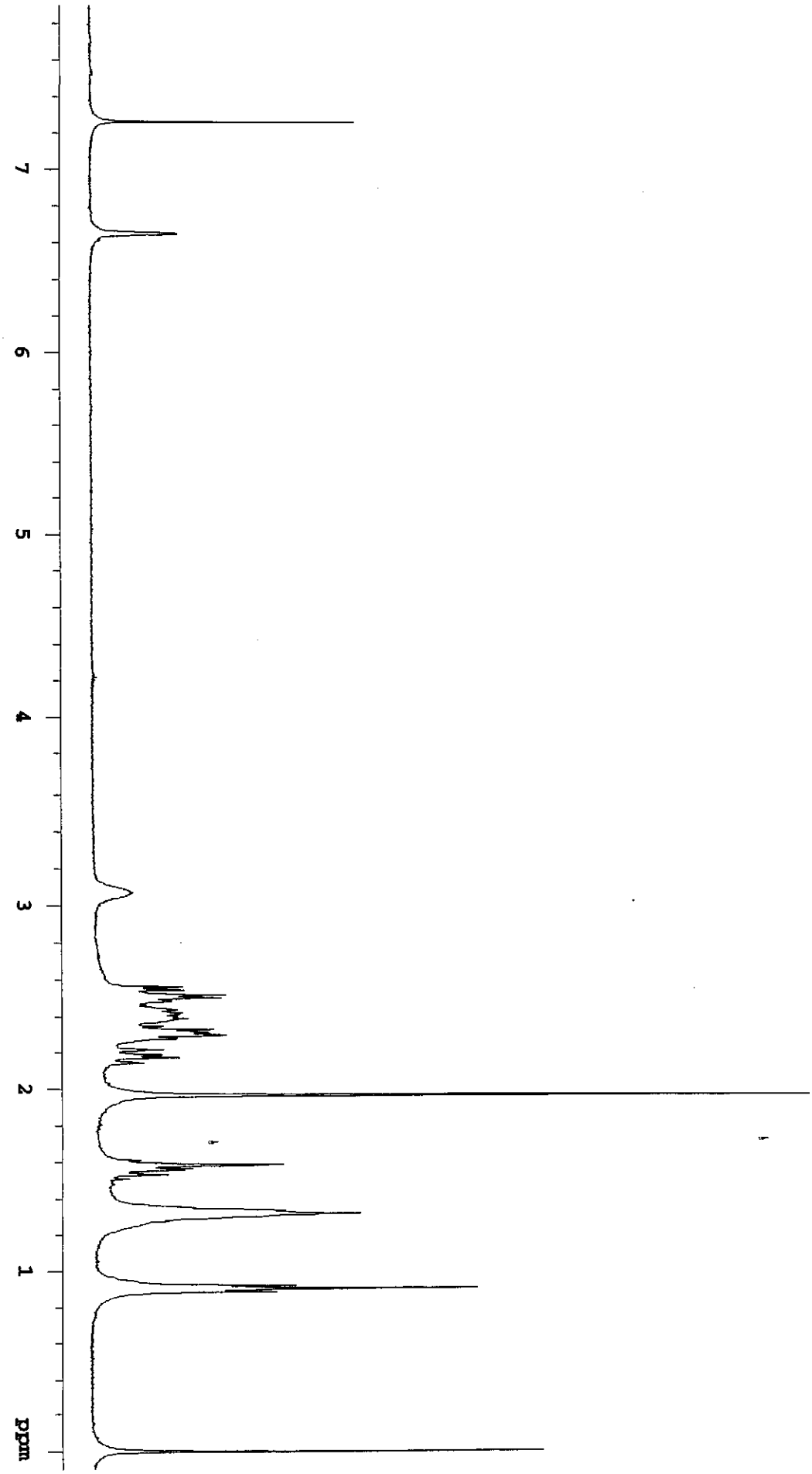
INDEX	FREQUENCY	PPM	HEIGHT
1	20273.709	201.676	24.5
2	19928.850	198.245	16.9
3	15451.783	153.709	18.7
4	13654.243	135.828	19.4
5	7772.563	77.319	83.5
6	7740.519	77.000	86.0
7	7708.475	76.681	85.7
8	4394.165	43.712	59.8
9	4115.683	40.941	45.2
10	3937.150	39.165	64.7
11	3394.683	33.769	52.3
12	3142.143	31.257	56.2
13	2770.580	27.561	53.4
14	2502.780	24.897	63.9
15	2296.017	22.840	51.6
16	2128.165	21.170	32.1
17	1404.114	13.968	47.0

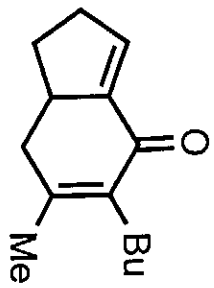


59

400 MHz ($CDCl_3$)

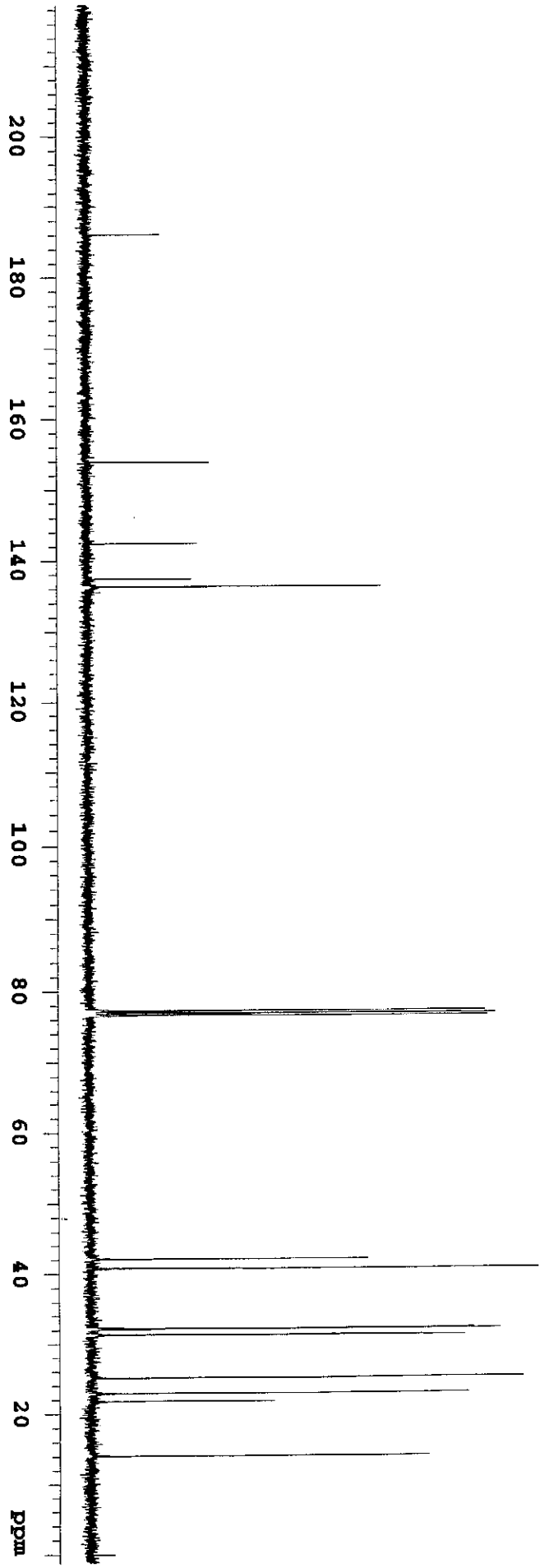




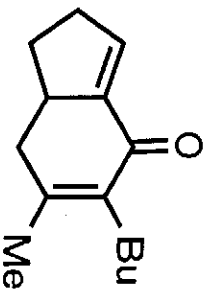


60

400 MHz ($CDCl_3$)

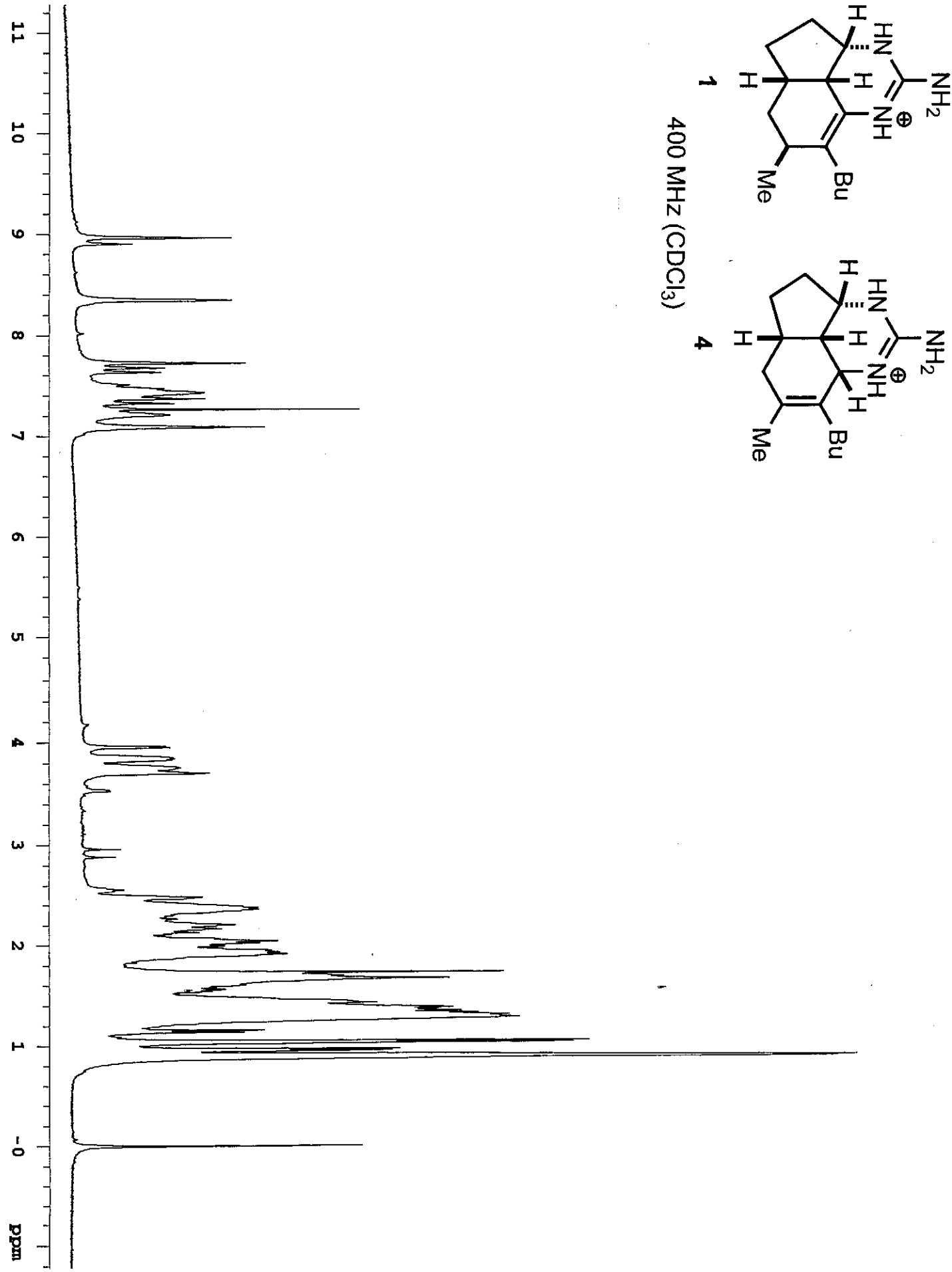


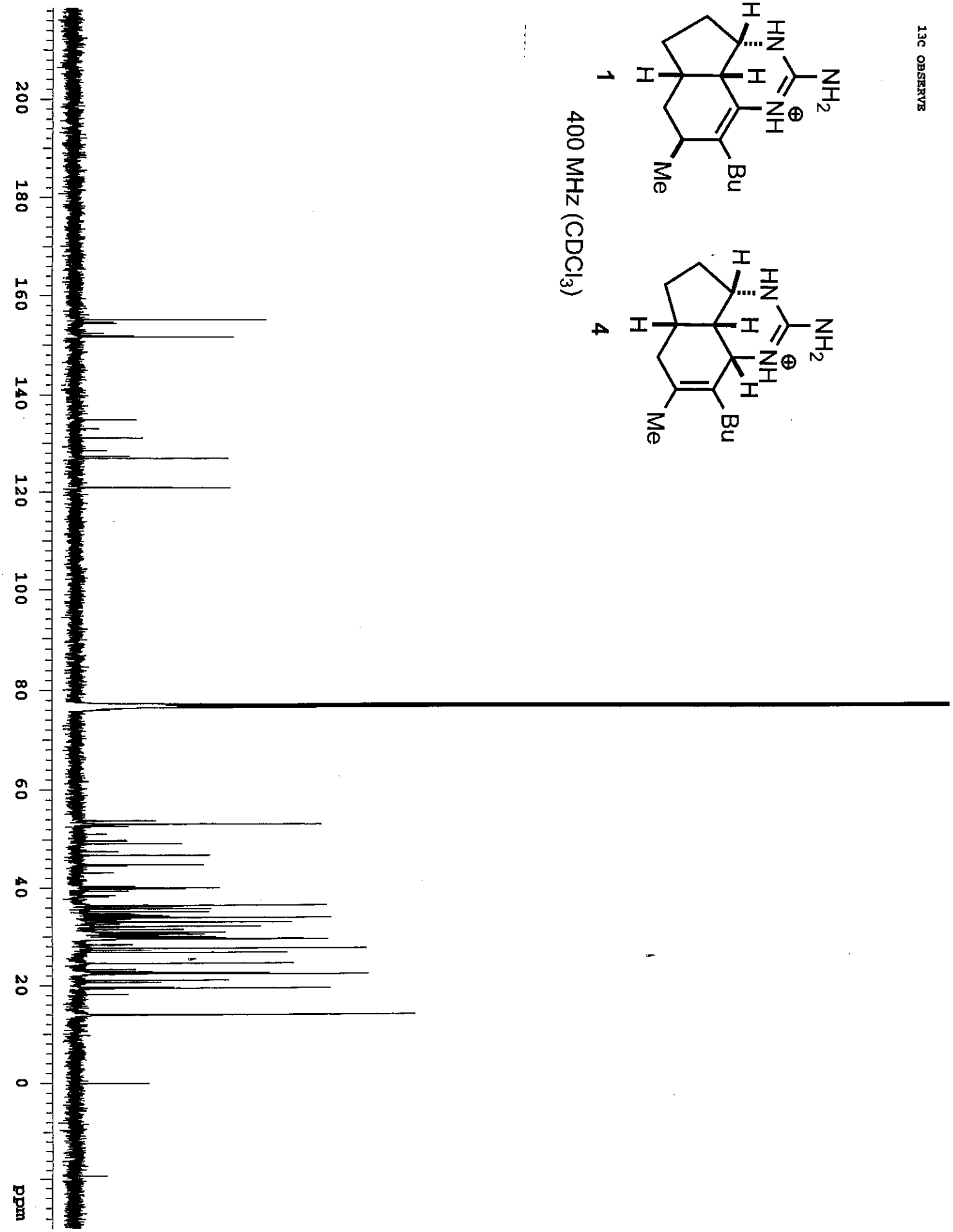
INDEX	FREQUENCY	PPM	HEIGHT
1	18707.346	186.094	11.9
2	15471.621	153.906	19.9
3	14311.917	142.370	17.9
4	13812.177	137.399	16.9
5	13703.836	136.321	47.3
6	7772.563	77.319	63.9
7	7740.519	77.000	65.6
8	7708.475	76.681	64.4
9	4232.417	42.103	45.0
10	4094.320	40.729	72.4
11	3235.987	32.190	61.9
12	3228.358	32.115	66.1
13	3142.906	31.265	60.6
14	2521.091	25.079	69.8
15	2299.069	22.870	61.1
16	2186.150	21.747	29.9
17	1406.403	13.990	54.4

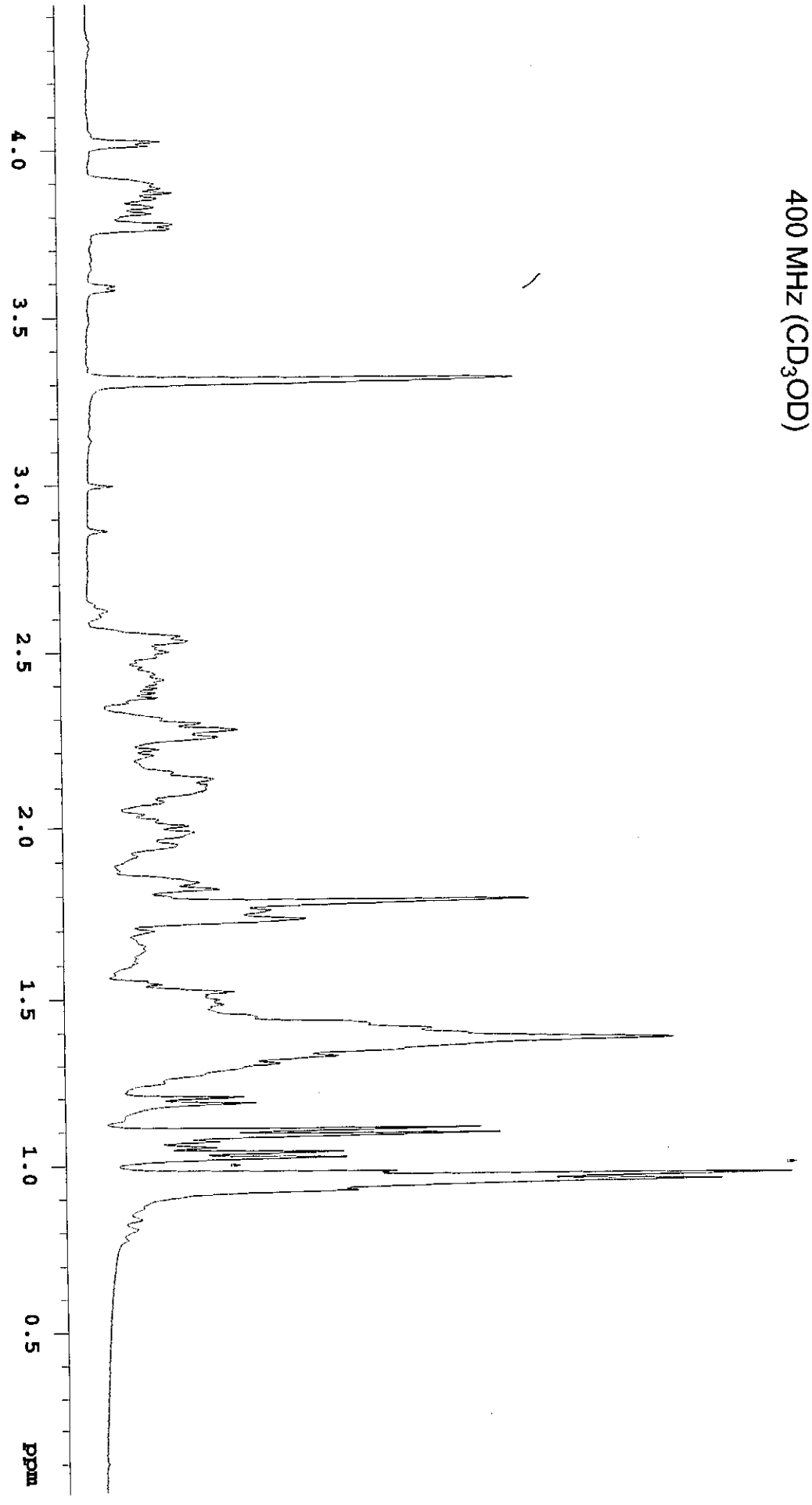


60

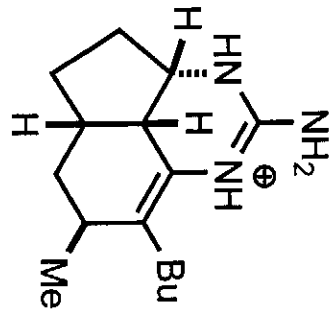
400 MHz ($CDCl_3$)


11
10
9
8
7
6
5
4
3
2
1
-0
ppm
400 MHz ($CDCl_3$)
1
4
H
HN
NH
NH_2
Me
Bu

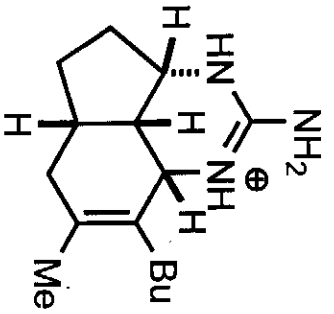

13C OBSERVE
400 MHz (CDCl3)
1
4
NH2
NH
HN
H
Me
Bu
200
180
160
140
120
100
80
60
40
20
0
ppm



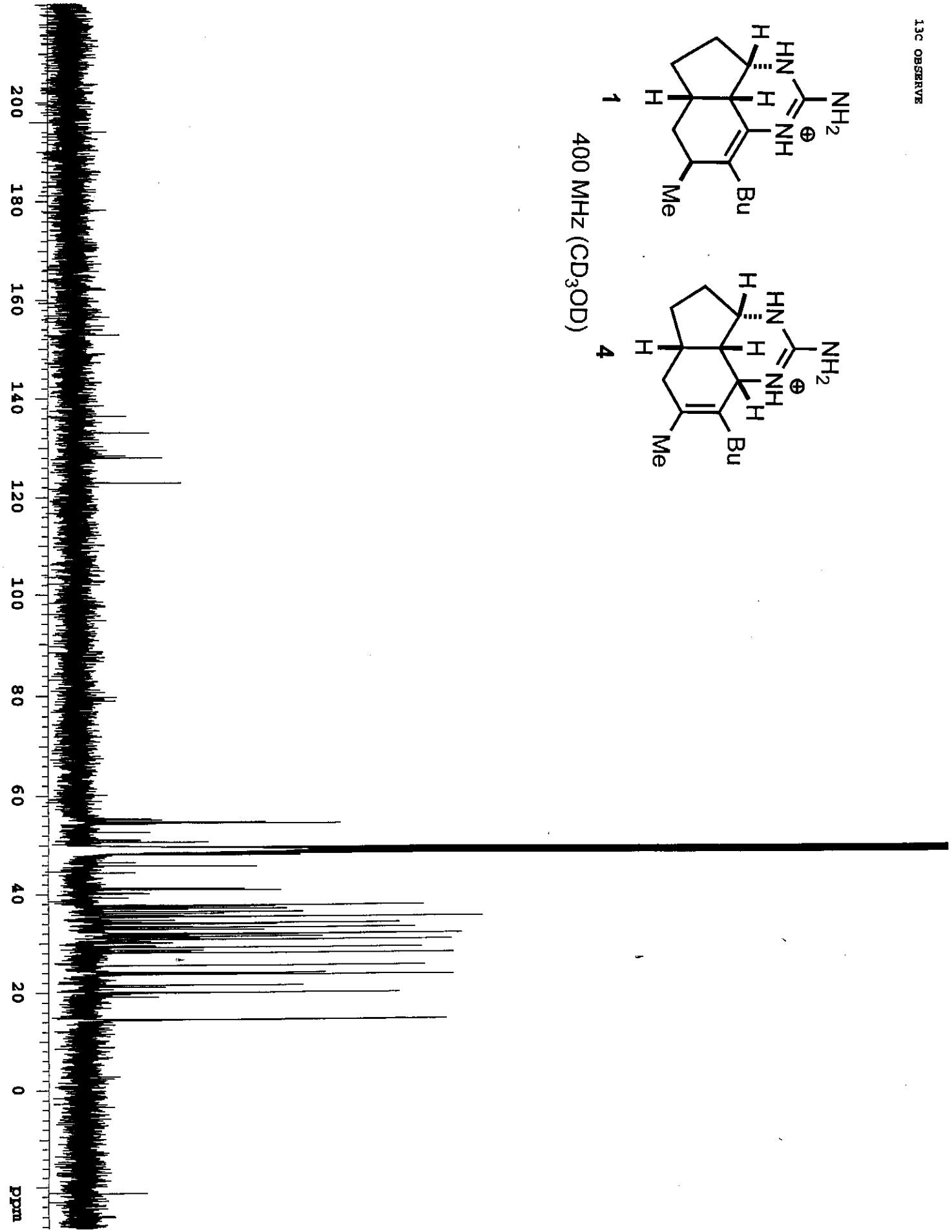
400 MHz (CD_3OD)

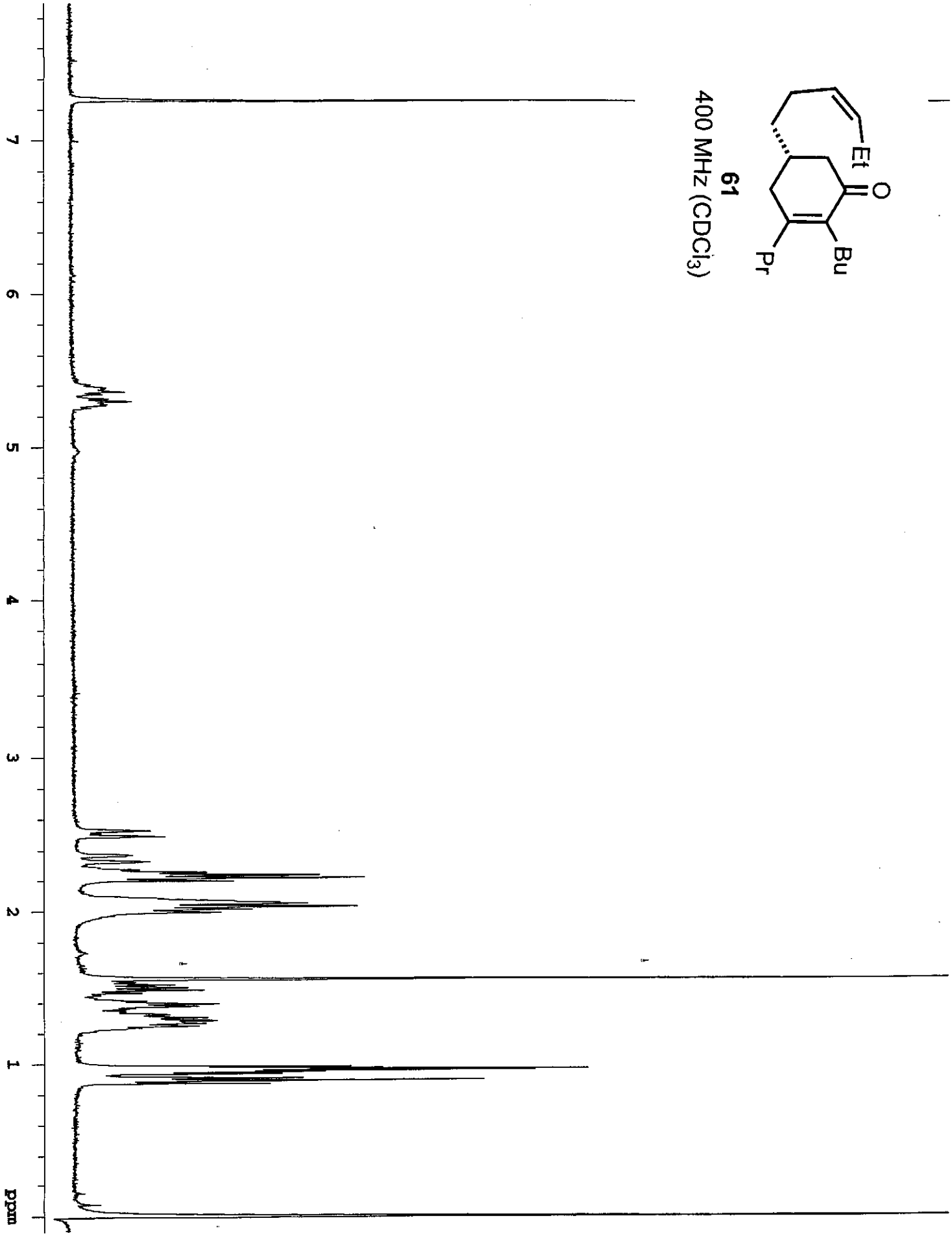


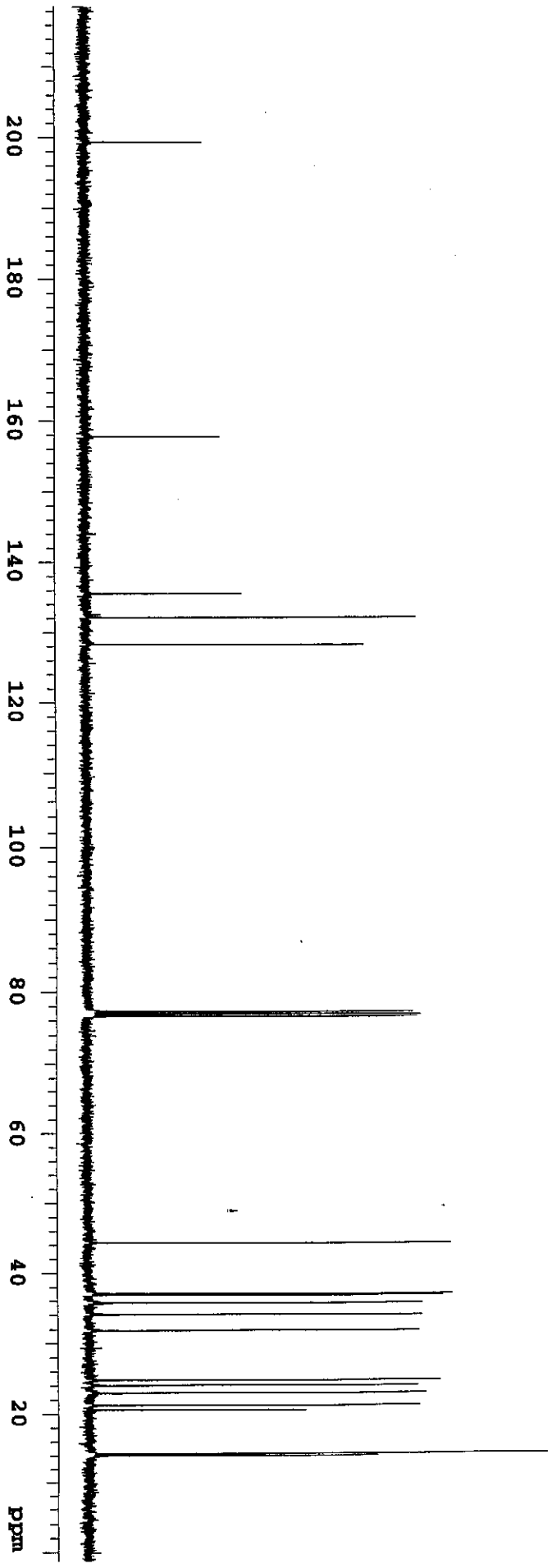
1



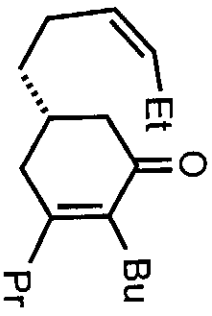
4


13C OBSERVE
400 MHz (CD_3OD)
1
4
Me
Bu
NH
NH_2
H
HN
200
180
160
140
120
100
80
60
40
20
0
ppm


61
400 MHz ($CDCl_3$)
Et
O
Bu
Pr
7
6
5
4
3
2
1
ppm

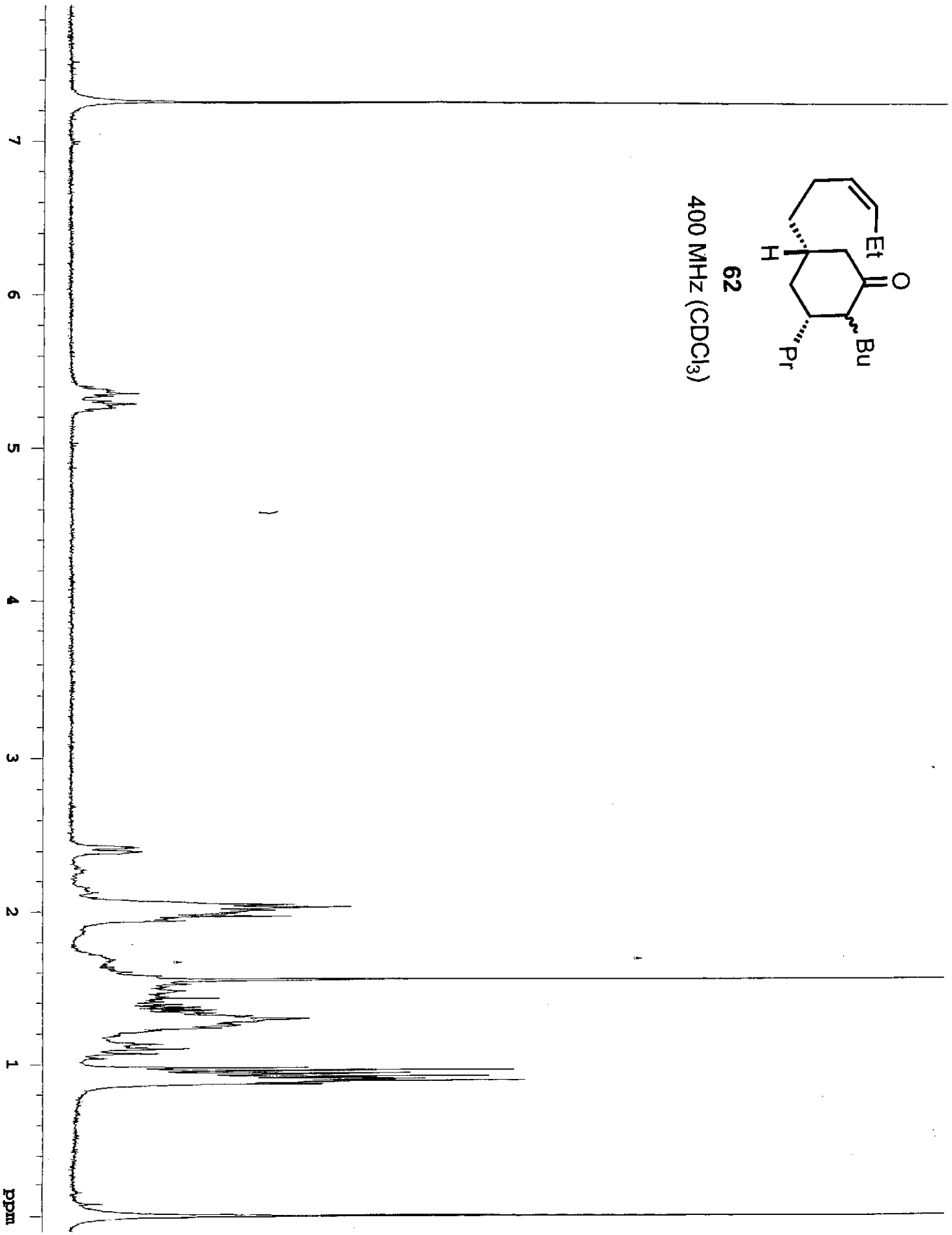


INDEX	FREQUENCY	PPM	HEIGHT
1	20045.970	199.410	18.9
2	15862.010	157.790	21.8
3	13633.545	135.522	25.4
4	13283.274	132.137	53.3
5	12897.227	128.297	45.1
6	7772.563	77.319	52.8
7	7740.519	77.000	54.0
8	7708.476	76.681	53.5
9	4453.013	44.297	58.7
10	3726.695	37.072	58.9
11	3706.095	36.867	57.5
12	3594.706	35.759	54.1
13	3428.386	34.104	54.1
14	3204.844	31.881	53.6
15	2493.022	24.800	57.0
16	2415.202	24.026	53.3
17	2307.627	22.955	54.7
18	2130.625	21.195	53.6
19	2062.724	20.519	35.3
20	1437.114	14.296	74.1
21	1405.833	13.985	46.8

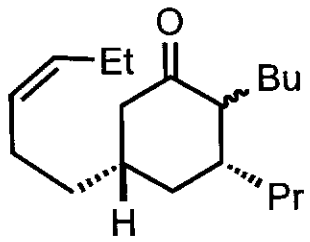


61

400 MHz ($CDCl_3$)

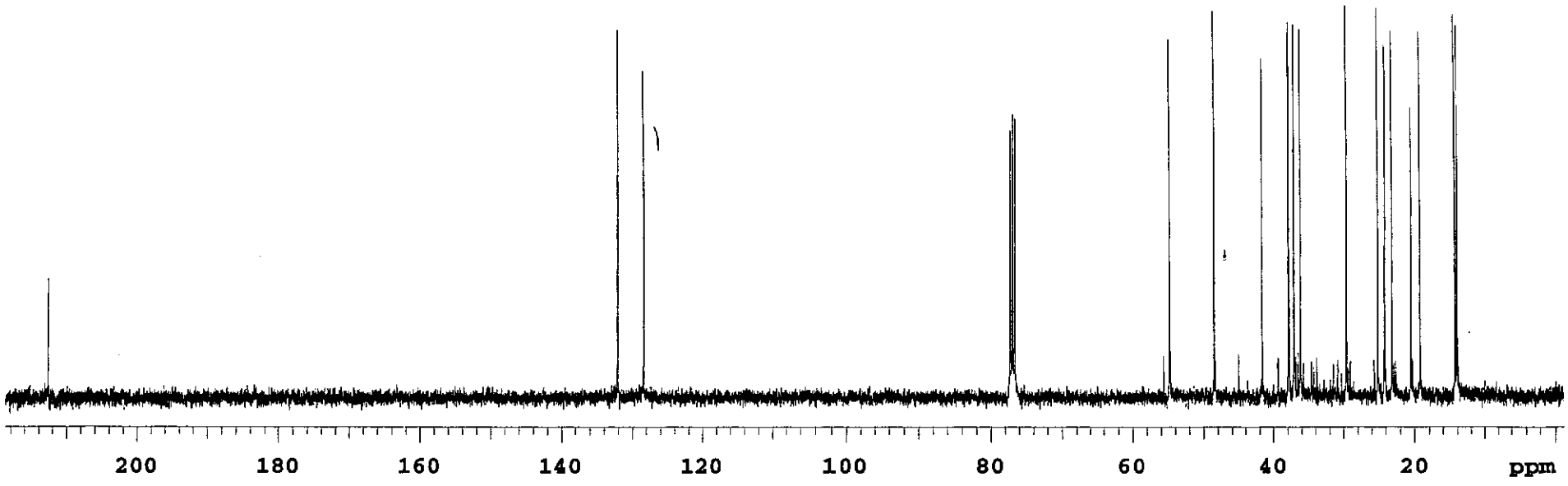

Et
O
H
Bu
Pr
62
400 MHz ($CDCl_3$)
7
6
5
4
3
2
1
ppm

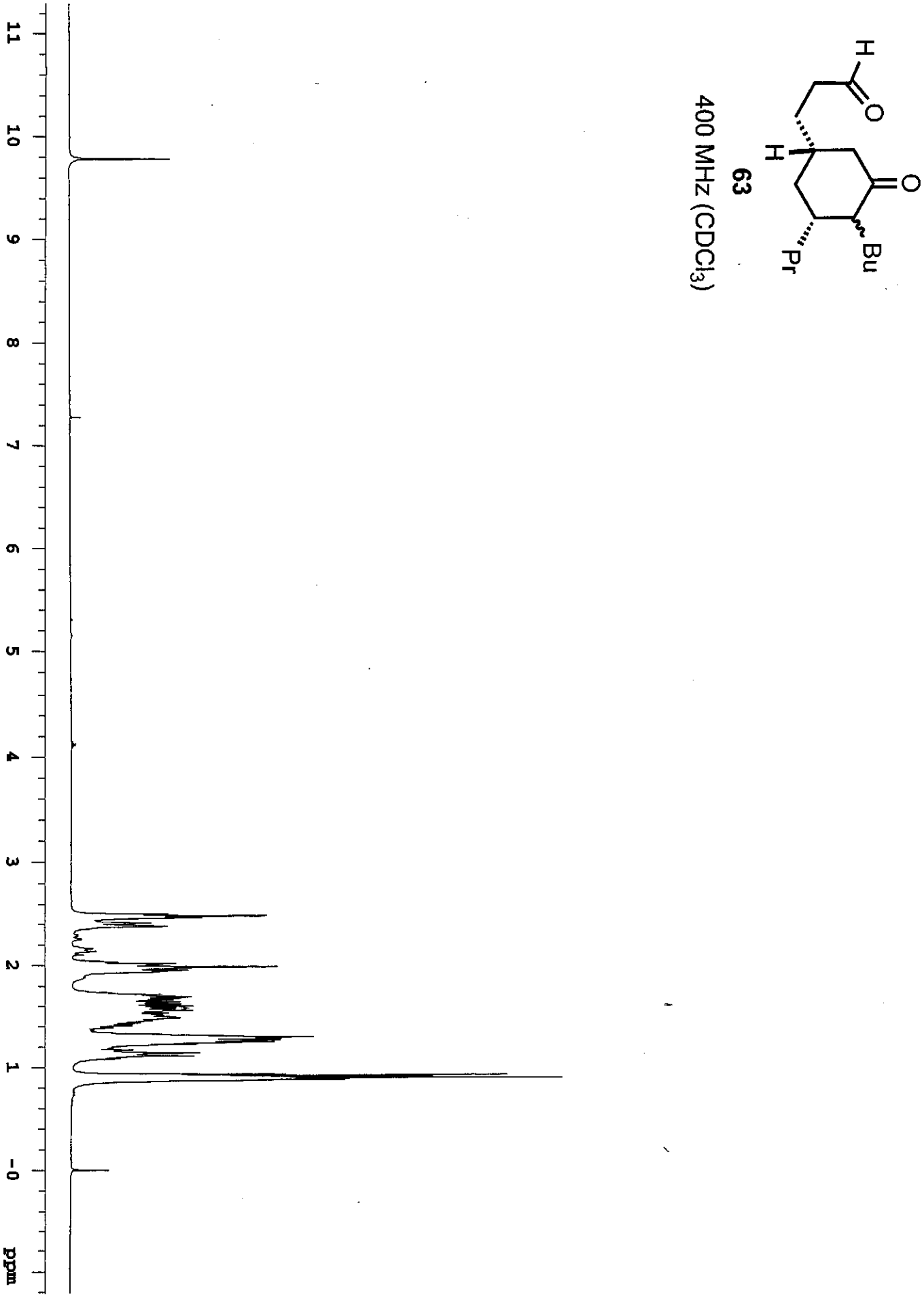
INDEX	FREQUENCY	PPM	HEIGHT
1	21375.754	212.639	19.2
2	13274.616	132.051	59.2
3	12907.631	128.401	52.6
4	7772.129	77.314	43.0
5	7740.084	76.996	45.6
6	7708.040	76.677	44.9
7	5506.129	54.773	57.6
8	4876.685	48.512	62.2
9	4196.123	41.742	54.6
10	3813.115	37.932	58.7
11	3804.723	37.848	60.4
12	3735.293	37.157	60.0
13	3641.448	36.224	59.4
14	2974.619	29.590	63.1
15	2529.049	25.158	62.7
16	2429.101	24.164	56.7
17	2328.390	23.162	58.9
18	2061.353	20.506	46.5
19	1931.649	19.215	58.9
20	1442.590	14.350	61.6
21	1439.538	14.320	49.1
22	1409.783	14.024	59.9



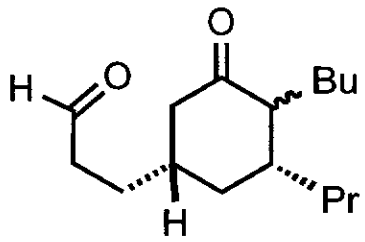
62

400 MHz ($CDCl_3$)



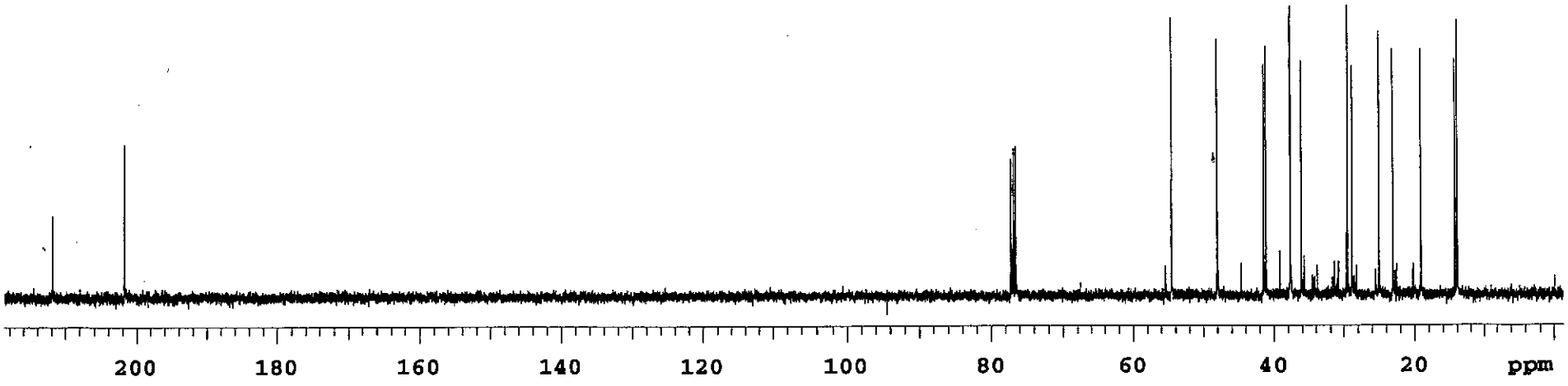

11
10
9
8
7
6
5
4
3
2
1
-0
ppm
400 MHz ($CDCl_3$)
63
H
O
H
O
Pr
Bu

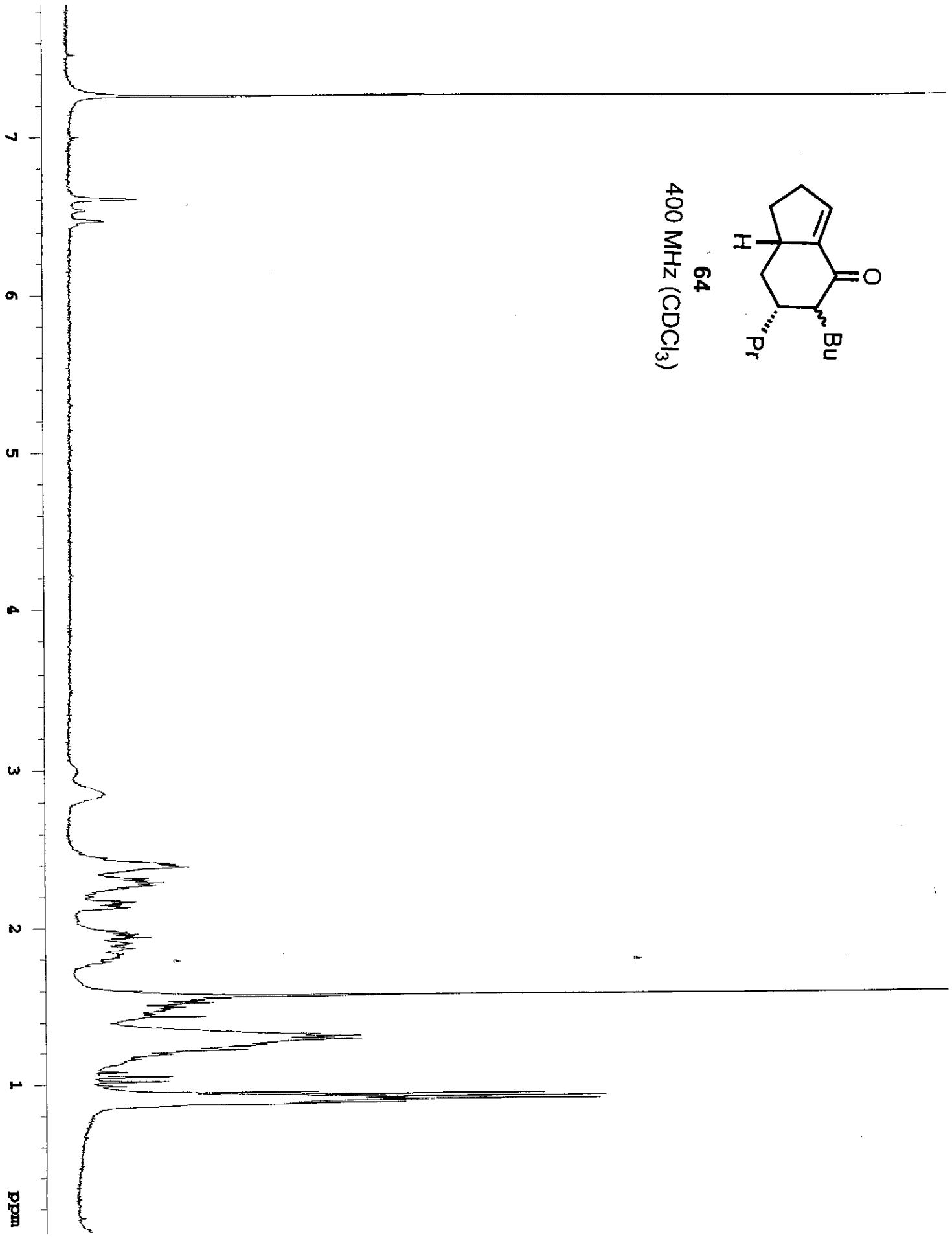
INDEX	FREQUENCY	PPM	HEIGHT
1	21301.005	211.895	13.1
2	20287.059	201.809	24.7
3	7771.800	77.311	22.2
4	7740.519	77.000	23.9
5	7708.476	76.681	24.3
6	5493.663	54.649	44.9
7	4835.246	48.099	41.5
8	4170.726	41.489	37.4
9	4134.104	41.125	40.4
10	3798.411	37.785	45.1
11	3789.256	37.694	46.8
12	3629.801	36.108	37.9
13	2967.570	29.520	46.8
14	2904.246	28.890	37.1
15	2522.776	25.096	42.6
16	2325.938	23.138	39.9
17	1925.395	19.153	39.8
18	1440.928	14.334	38.2
19	1408.122	14.008	44.4



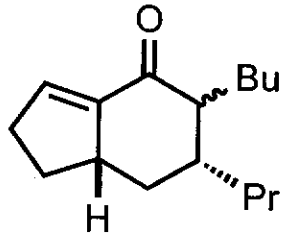
63

400 MHz ($CDCl_3$)



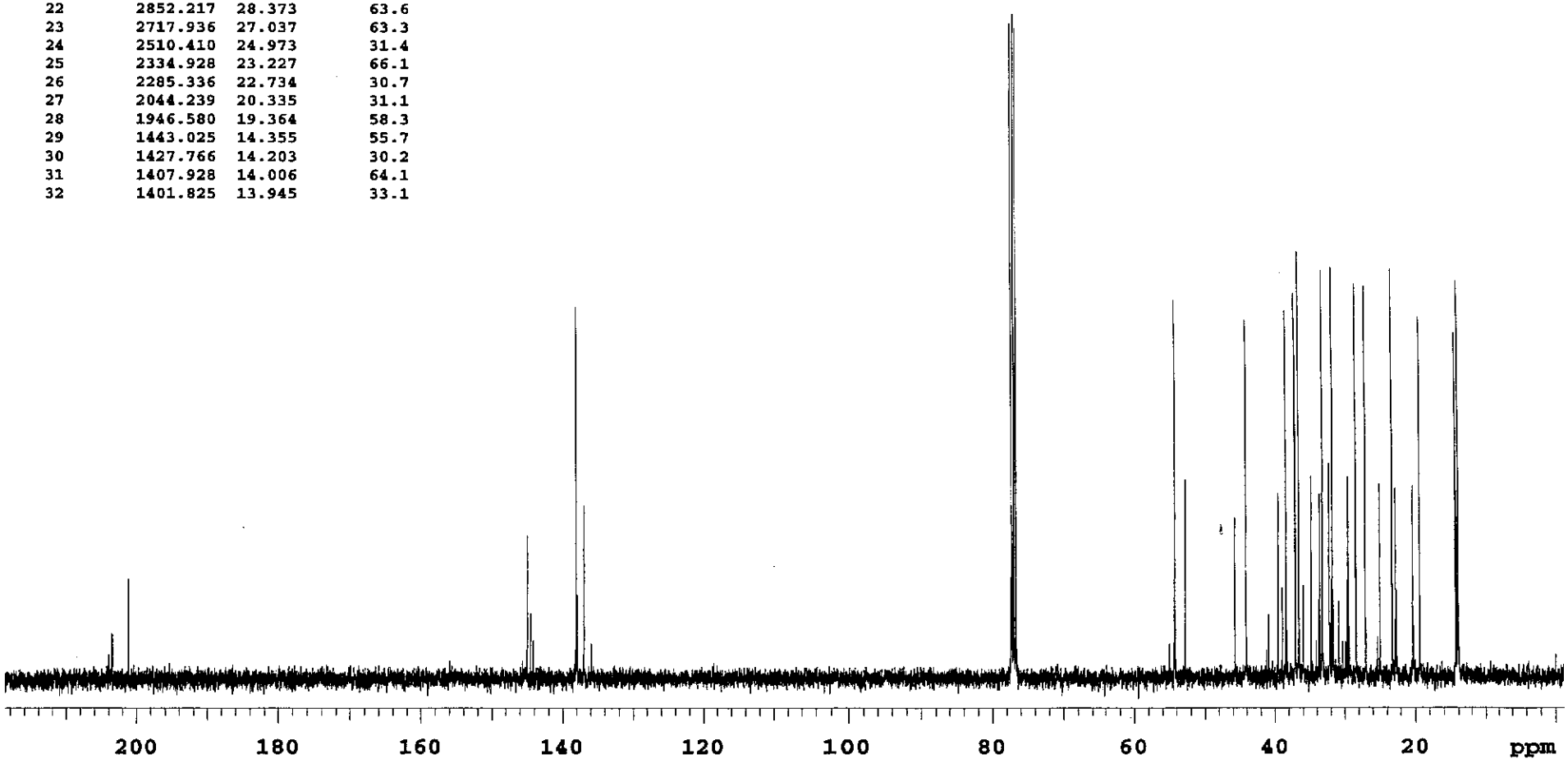

7
6
5
4
3
2
1
ppm
H
O
Bu
Pr
64
400 MHz ($CDCl_3$)

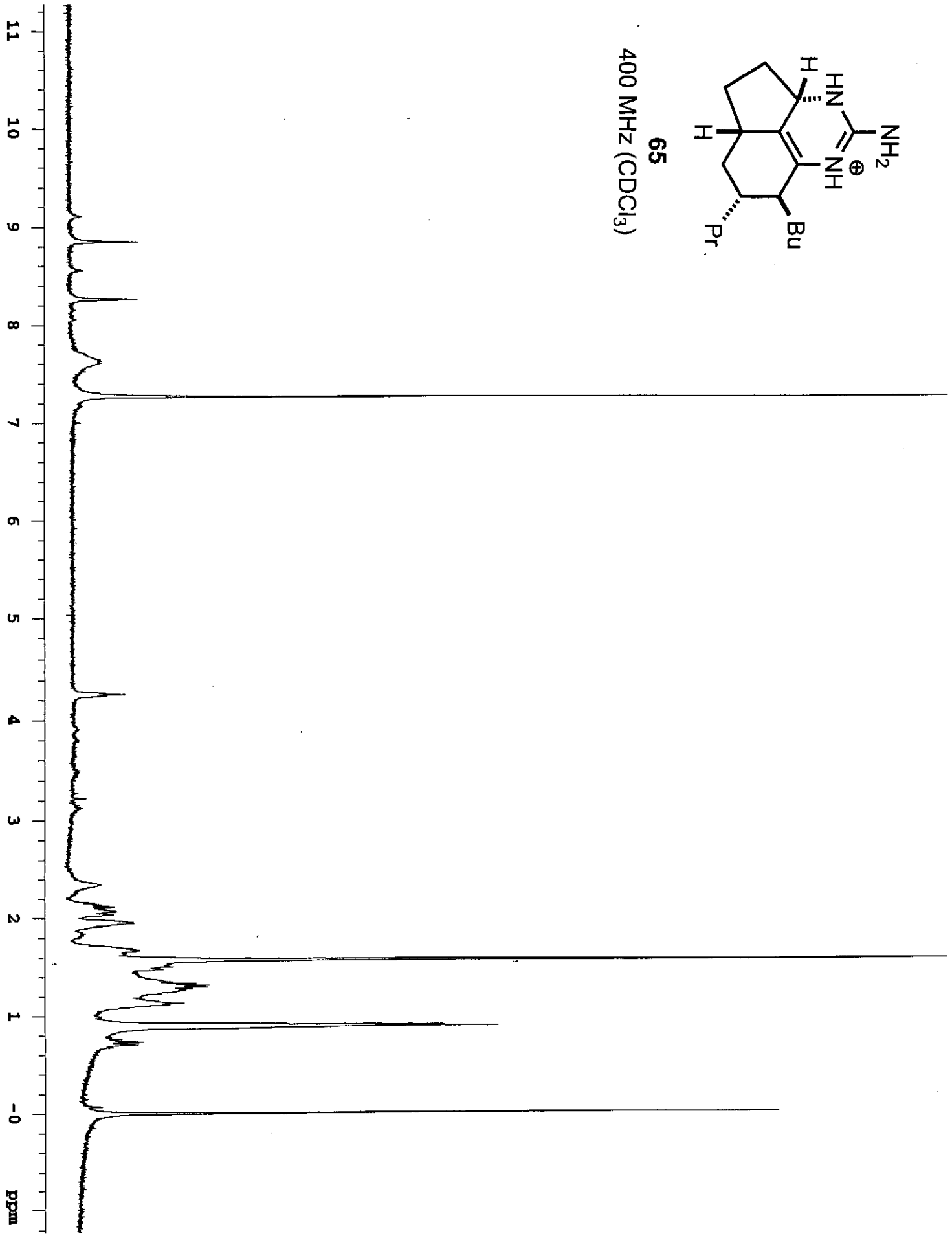
INDEX	FREQUENCY	PPM	HEIGHT
1	14568.272	144.920	23.2
2	13880.080	138.074	60.0
3	13767.162	136.951	28.0
4	7772.563	77.319	105.9
5	7740.519	77.000	107.4
6	7709.238	76.689	105.1
7	5447.816	54.193	61.2
8	5301.327	52.736	32.1
9	4593.298	45.693	26.0
10	4436.127	44.129	58.0
11	3968.431	39.477	29.9
12	3862.380	38.422	59.4
13	3728.861	37.093	62.2
14	3677.743	36.585	68.9
15	3496.920	34.786	32.6
16	3373.321	33.557	29.8
17	3342.039	33.245	30.0
18	3337.461	33.200	65.9
19	3234.461	32.175	34.6
20	3189.447	31.728	66.4
21	2963.610	29.481	32.5
22	2852.217	28.373	63.6
23	2717.936	27.037	63.3
24	2510.410	24.973	31.4
25	2334.928	23.227	66.1
26	2285.336	22.734	30.7
27	2044.239	20.335	31.1
28	1946.580	19.364	58.3
29	1443.025	14.355	55.7
30	1427.766	14.203	30.2
31	1407.928	14.006	64.1
32	1401.825	13.945	33.1

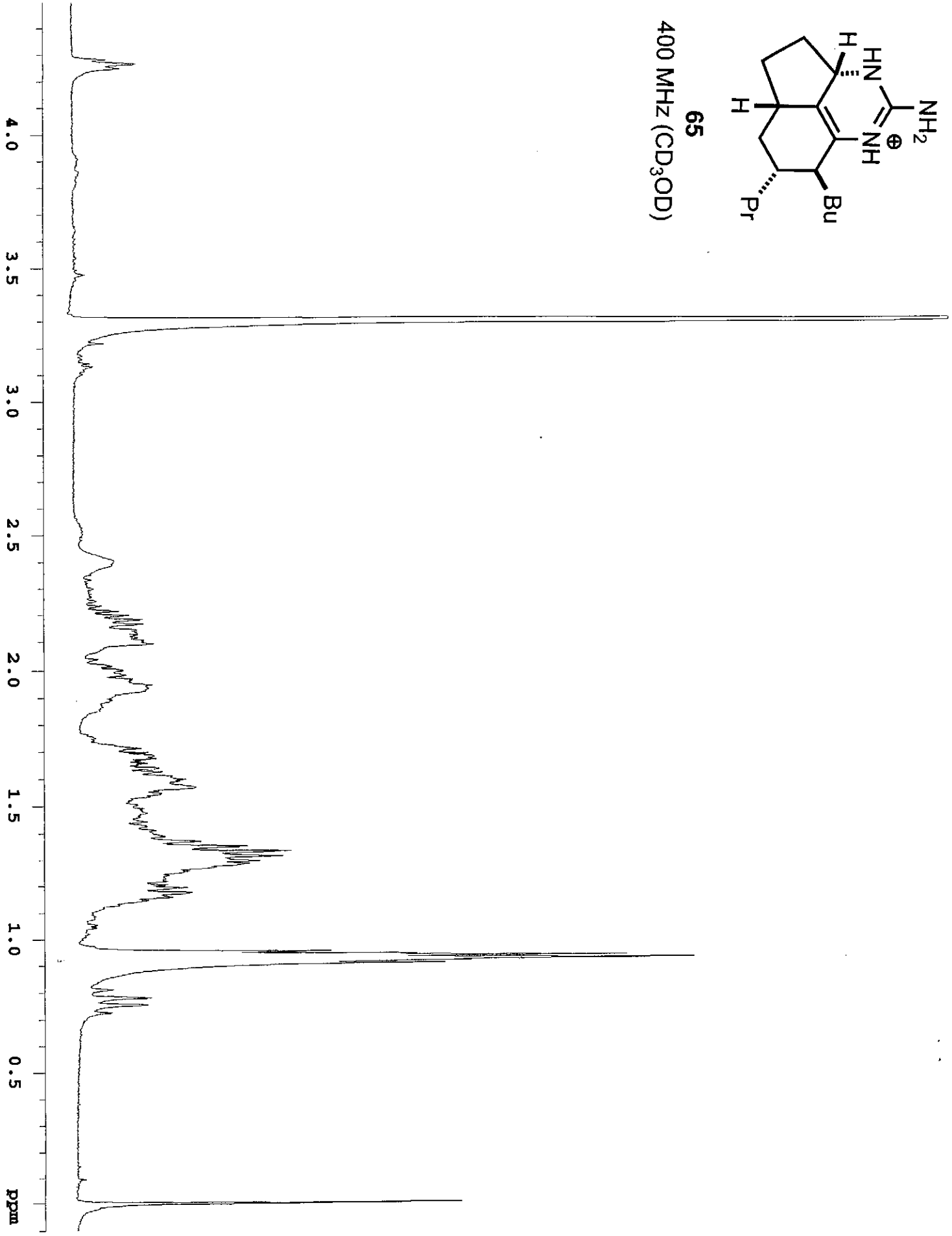


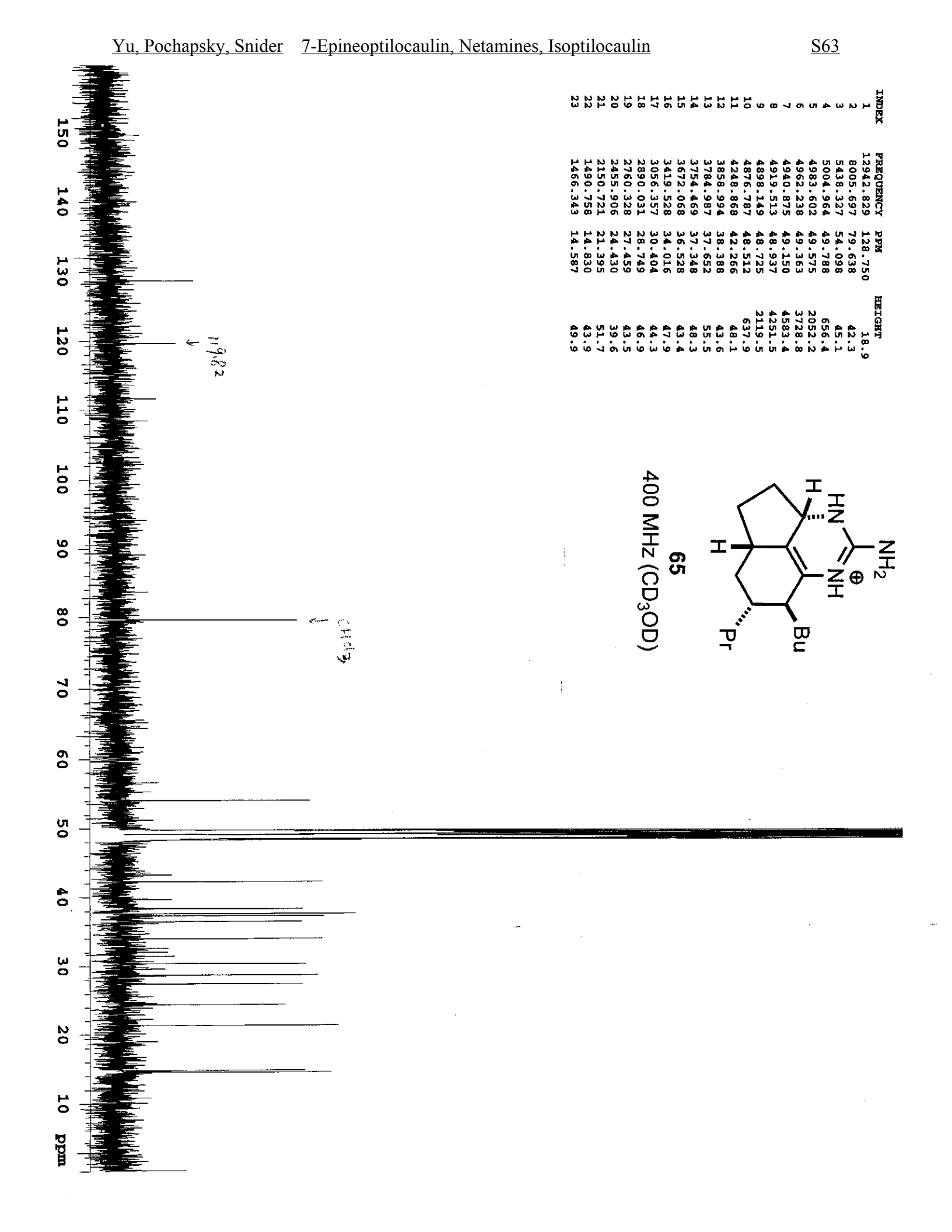
64

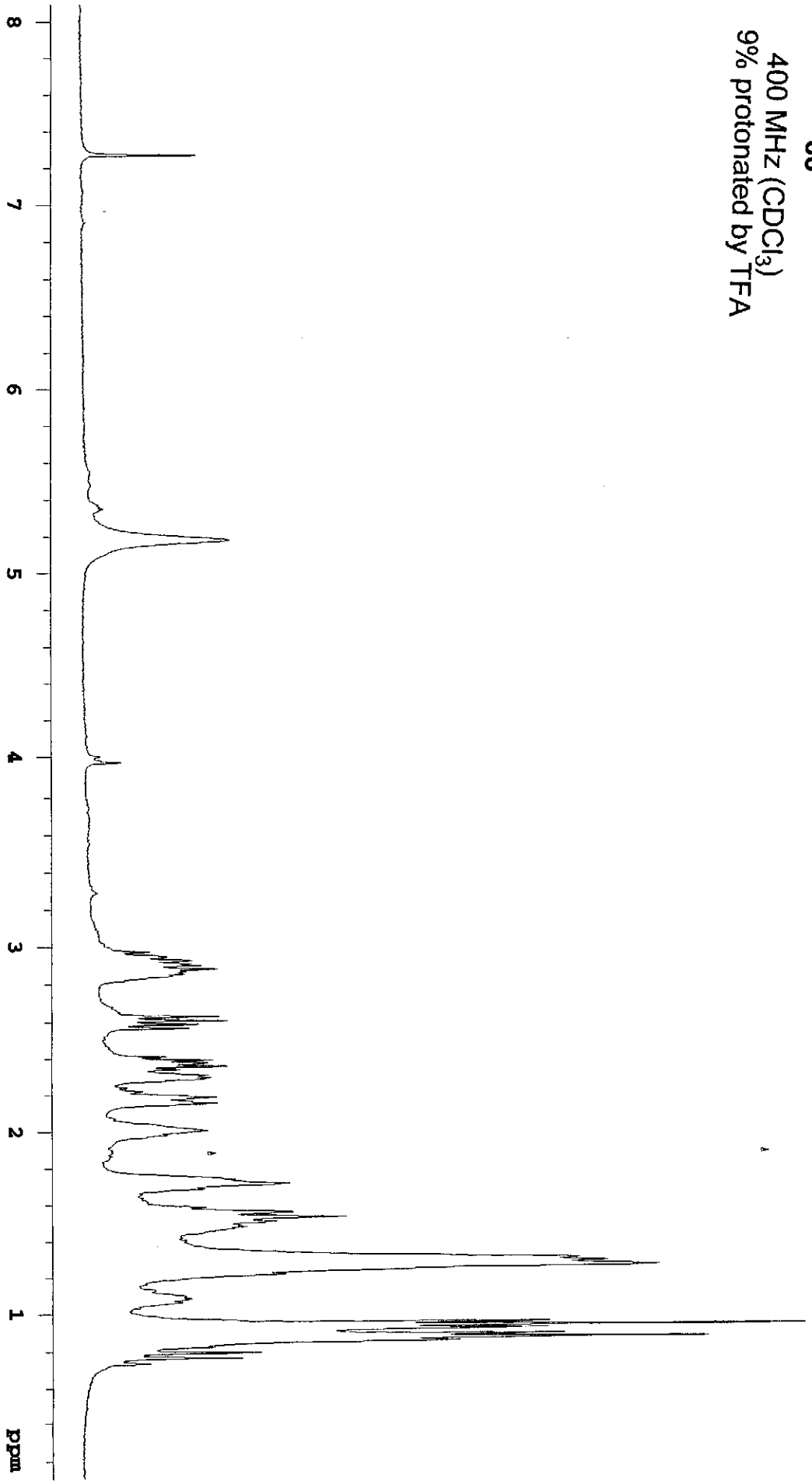
400 MHz ($CDCl_3$)




65
400 MHz (CDCl3)
H
HN
NH2
H
NH
Pr
Bu
11
10
9
8
7
6
5
4
3
2
1
-0
ppm

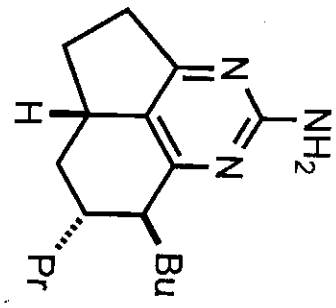

65
400 MHz (CD_3OD)
H
HN
NH_2
H
NH
Pr
Bu
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


INDEX FREQUENCY PPM HEIGHT
1 12942.829 128.750 18.9
2 8005.697 79.638 42.3
3 5438.327 54.098 45.1
4 5004.964 49.788 656.4
5 4983.602 49.575 2052.2
6 4962.238 49.363 3728.8
7 4940.875 49.150 4583.4
8 4919.513 48.937 4251.5
9 4898.149 48.725 2119.5
10 4876.787 48.512 637.9
11 4248.868 42.266 48.1
12 3858.994 38.388 43.6
13 3784.987 37.652 55.5
14 3754.469 37.348 48.3
15 3672.068 36.528 43.4
16 3419.528 34.016 47.9
17 3056.357 30.404 44.3
18 2890.031 28.749 46.9
19 2760.328 27.459 43.5
20 2455.906 24.430 39.6
21 2150.721 21.395 51.7
22 1490.758 14.830 43.9
23 1466.343 14.587 49.9
NH2
HN
NH
H
H
Pr
Bu
65
400 MHz (CD3OD)
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

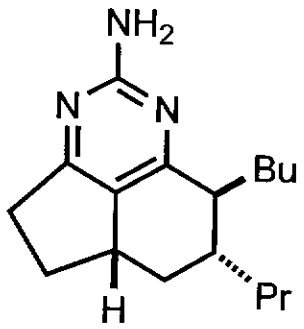


400 MHz ($CDCl_3$)
9% protonated by TFA

66

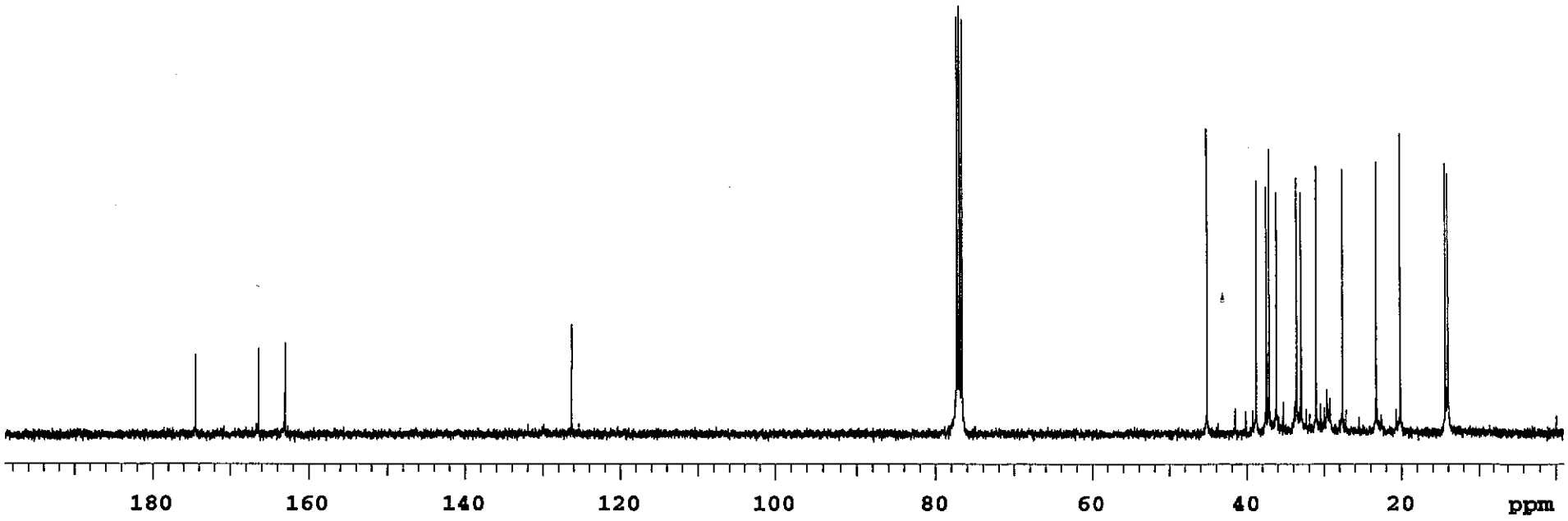


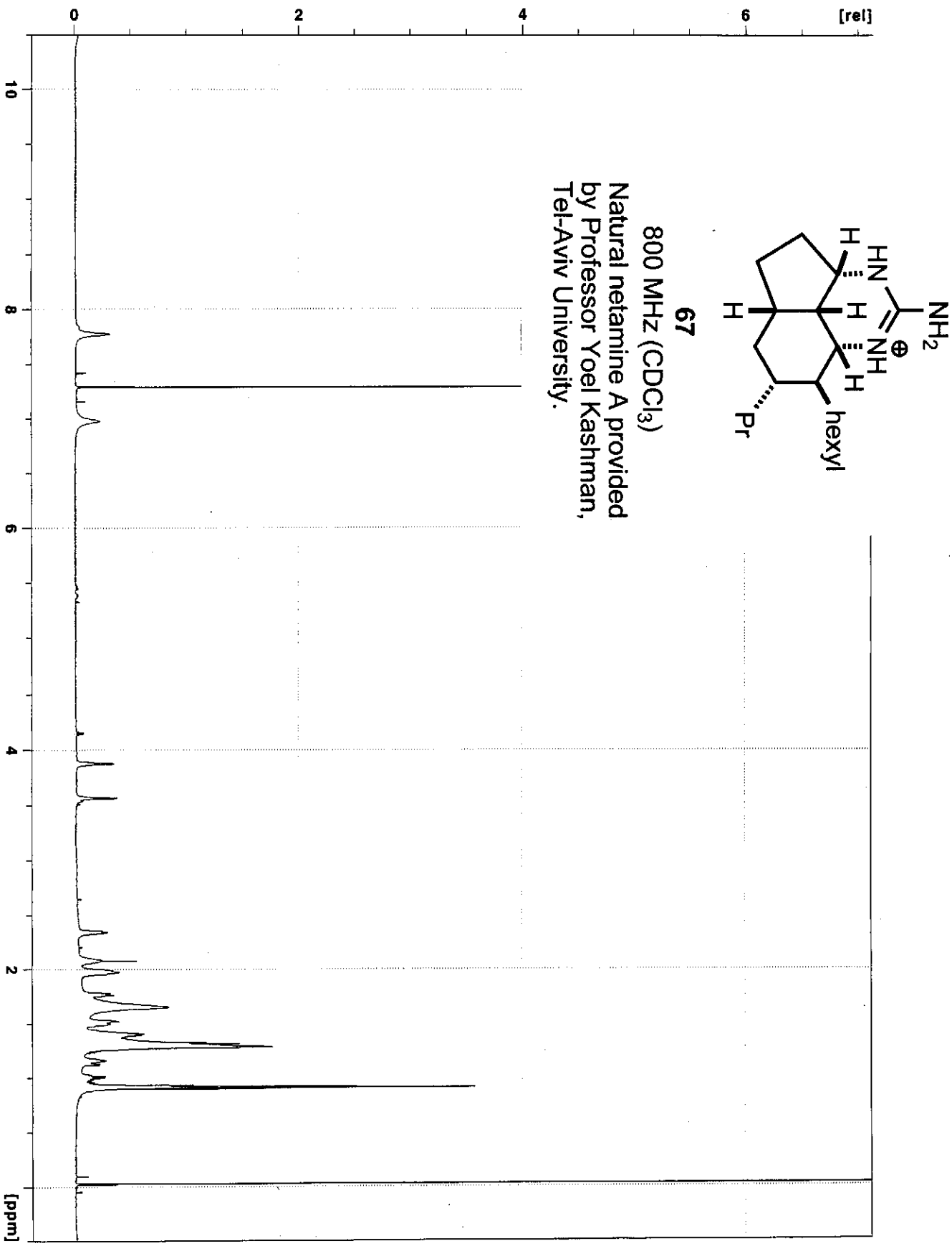
INDEX	FREQUENCY	PPM	HEIGHT
1	17540.776	174.490	12.8
2	16727.457	166.399	13.9
3	16391.754	163.059	14.8
4	12699.777	126.333	17.9
5	7772.564	77.319	67.4
6	7740.519	77.000	69.3
7	7708.475	76.681	67.0
8	4541.417	45.176	49.3
9	3902.054	38.816	41.0
10	3769.298	37.496	40.0
11	3732.676	37.131	46.0
12	3640.358	36.213	39.1
13	3377.898	33.602	41.4
14	3319.150	33.018	39.1
15	3123.069	31.067	43.3
16	2779.736	27.652	42.8
17	2336.454	23.242	44.0
18	2027.454	20.168	48.5
19	1447.603	14.400	43.6
20	1411.743	14.044	42.0

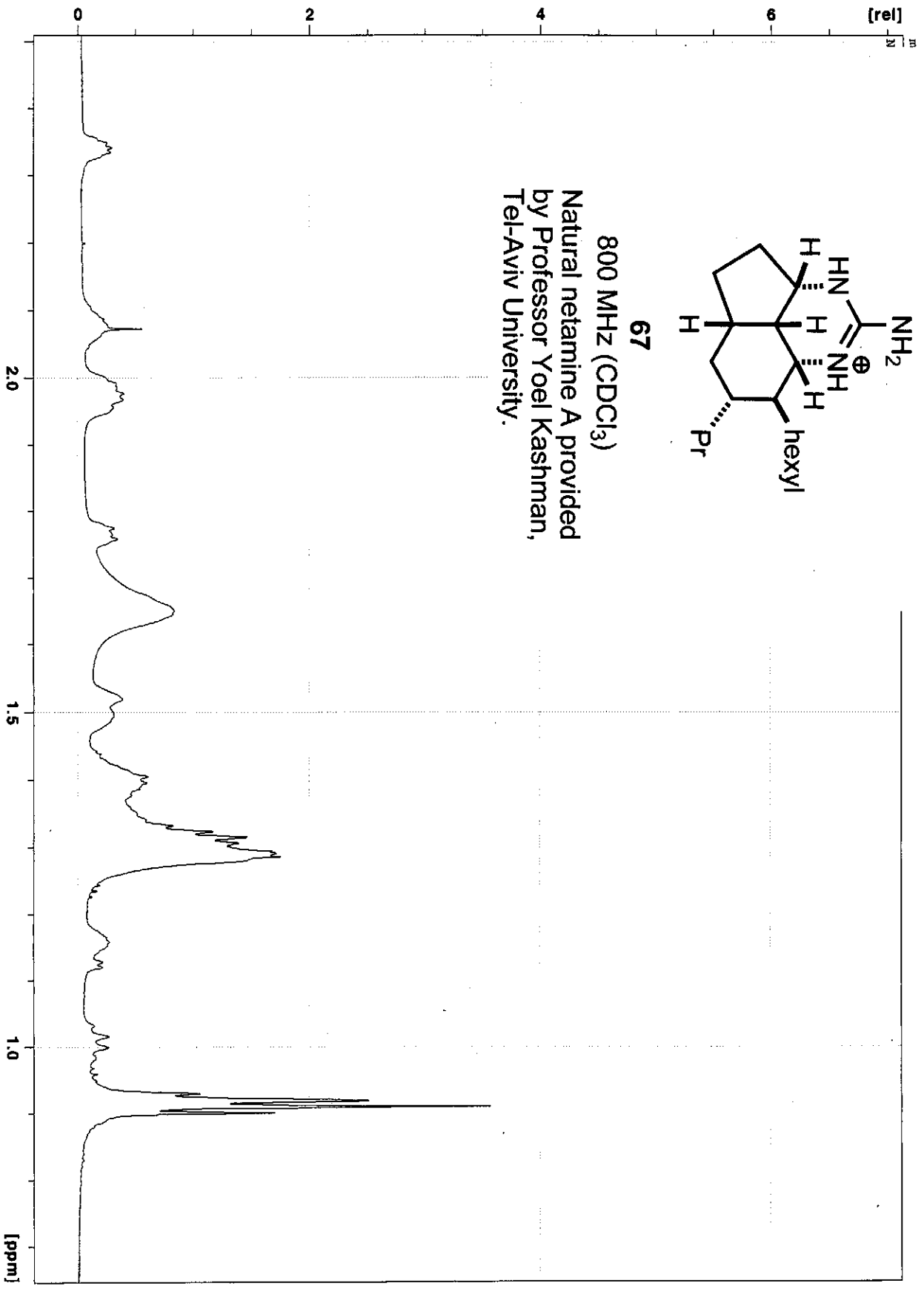


66

400 MHz ($CDCl_3$)
9% protonated by TFA



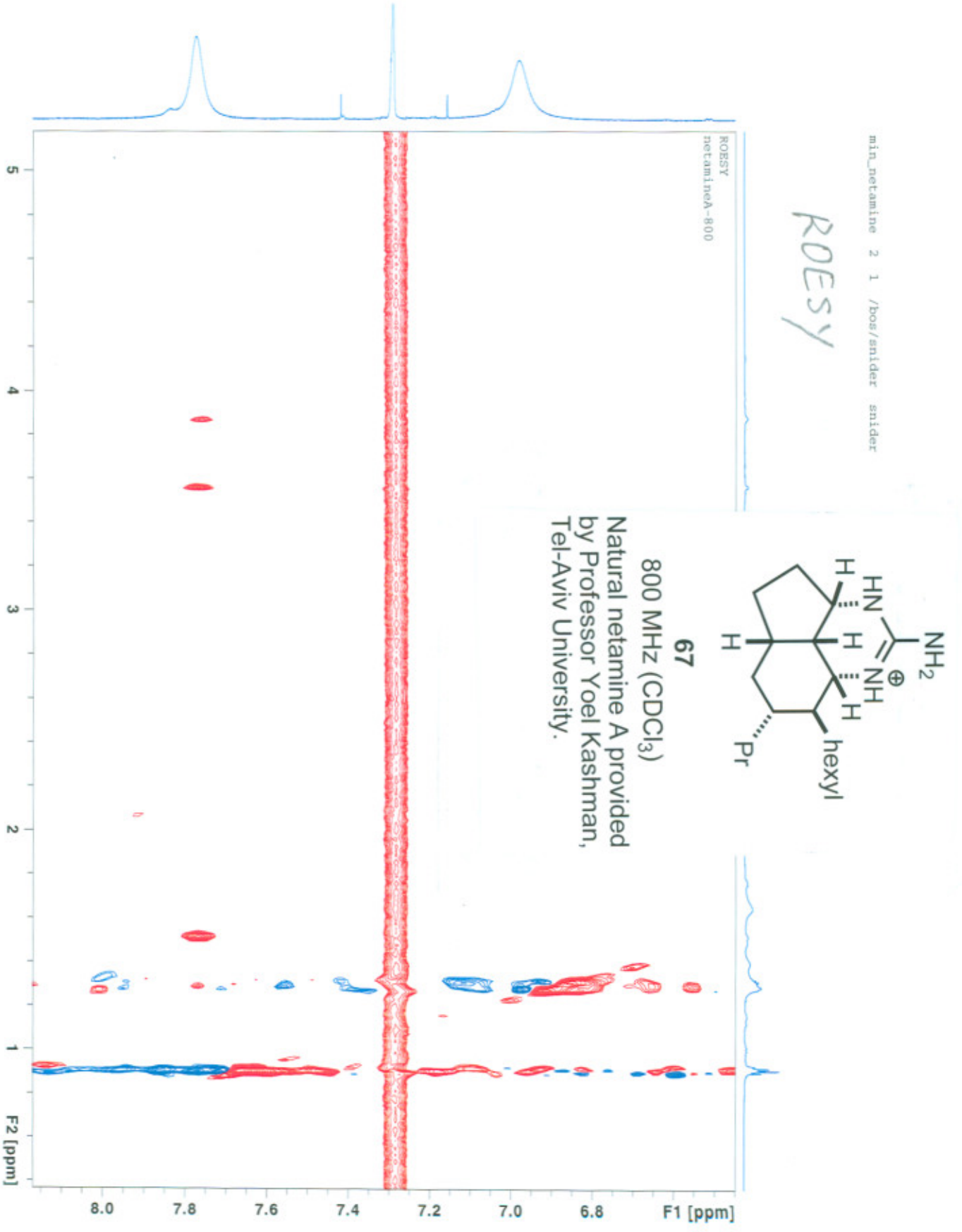

0
2
4
6
[rel]
10
8
6
4
2
[ppm]
67
800 MHz (CDCl3)
Natural netamine A provided
by Professor Yoel Kashman,
Tel-Aviv University.
HN
NH2
NH
H
Pr
hexyl



67

800 MHz ($CDCl_3$)

Natural netamine A provided by Professor Yoel Kashman, Tel-Aviv University.


ROESY
netamineA-800
min_netamine 2 1 /bos/snider snider
ROESY
67
800 MHz (CDCl3)
Natural netamine A provided
by Professor Yoel Kashman,
Tel-Aviv University.
NH2
HN
NH
H
Pr
hexyl
F2 [ppm]
F1 [ppm]
8.0
7.8
7.6
7.4
7.2
7.0
6.8
1
2
3
4
5