Stereoselective Synthesis of Complex Polycyclic Aziridines: Use of the Brønsted Acid-Catalyzed aza-Darzens Reaction to Prepare an Orthogonally Protected Mitomycin C Intermediate with Maximal Convergency

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Experimental Section

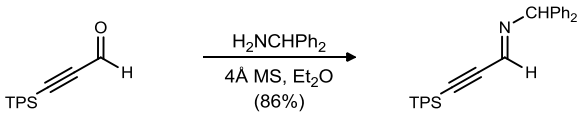
Flame-dried (under vacuum) glassware was used for all reactions. All reagents and solvents were commercial grade and purified prior to use when necessary. Diethyl ether (Et_2O), tetrahydrofuran (THF), dichloromethane (CH_2Cl_2), and benzene (C_6H_6) were dried by passage through a column of activated alumina as described by Grubbs.[1] Benzene was additionally passed through a column containing activated Q-5 reactant. Flash column chromatography was performed using Sorbent Technologies 40-63 mm, pore size 60 Å silica gel with solvent systems indicated. Analytical thin layer column chromatography was performed using Sorbent Technologies 250 mm glass-backed UV254 silica gel plates that were visualized by fluorescence upon 250 nm radiation and/or the by use of ceric ammonium molybdate, ninhydrin, *p*-anisaldehyde and potassium permanganate. Solvent removal was effected by rotary evaporation under vacuum (~ 25-40 mm Hg). IR spectra were recorded on a Nicolet Avatar 360 spectrophotometer and are reported in wavenumbers (cm^{-1}). Liquids and oils were analyzed as neat films on a NaCl plate (transmission), whereas solids were applied to a diamond plate (ATR).

Nuclear magnetic resonance spectra (NMR) were acquired on a Varian INOVA-400 (400 MHz), VXR-400 (400 MHz), INOVA-500 (500 MHz), BRUKER DRX-500 (500 MHz), BRUKER DRX-600 (600 MHz), Bruker AV-400 (400 MHz) or Bruker AV II-600 (600 MHz) spectrometers. All chemical shifts were measured relative to residual solvent peaks as an internal standard set to δ 7.26 and δ 77.1 ($CDCl_3$), unless otherwise specified.

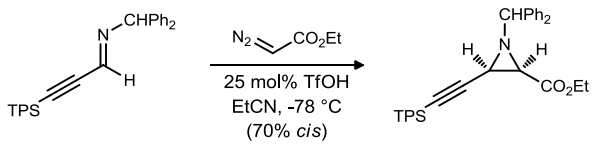
[1] A. B. Pangborn, M. A. Giardello, R. H. Grubbs, R. K. Rosen, F. J. Timmers, *Organometallics* 1996, **15**, 1518.

Mass spectra were recorded on a Kratos MS-80 spectrometer by use of the ionization techniques specified (CI, EI or ESI). Ratios of diastereomers and isomeric products were measured directly from integration of ^{1}H NMR absorptions of protons common to the components.

3-(Triphenylsilyl)prop-2-yn-1-ol and 3-(triphenylsilyl)propiolaldehyde were prepared according to literature procedures,[2] and matched previously reported spectral data.[3]



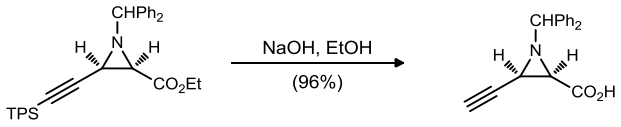
(*E*)-1,1-Diphenyl-N-(3-(triphenylsilyl)prop-2-ynylidene)methanamine (4). The alkynyl aldehyde (0.51 g, 1.6 mmol) and 4 Å molecular sieves were stirred in diethyl ether (20 mL). Diphenylmethyl amine (280 μL, 1.63 mmol) was then added and the mixture was stirred until ^{1}H NMR spectroscopy of an aliquot revealed complete aldehyde consumption. The mixture was filtered, dichloromethane was added to the filter cake to dissolve the white solid and the mixture was refiltered. The solvent was removed and the product (488 mg) was precipitated by the addition of a few drops of diethyl ether and hexanes, as a white solid as the *E*-isomer. The mother liquor was purified by flash chromatography (Al_2O_3, 10% ethyl acetate in hexanes) to afford the remainder of the aldimine (total yield: 678 mg, 86%). R_f = 0.50 (20% EtOAc/hexanes); IR (film) 3068, 3025, 2852, 1607, 1430, 1114 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.67 (d, *J* = 6.6 Hz, 6H), 7.46-7.25 (m, 19H), 5.54 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 145.3, 142.5, 135.8, 132.4, 130.3, 128.7, 128.3, 128.2, 127.9, 127.8, 127.5, 105.3, 94.3, 78.9; HRMS (EI): Exact mass calcd for $C_{34}H_{28}NSi$ $[M+H]^+$ 478.1986, found 478.1973.



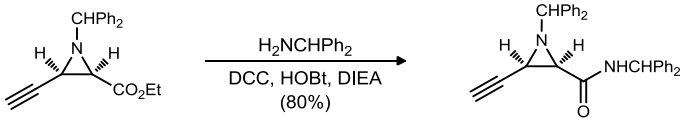
Ethyl-1-benzhydryl-3-((triphenylsilyl)ethynyl)aziridine-2-carboxylate (5). To a propionitrile solution (5 mL) of the aldimine (0.50 g, 1.1 mmol) at -78 °C was added triflic acid (23.5 μL, 293 μmol). After 5 min, ethyl diazoacetate (132 μL, 1.26 mmol) was added dropwise to the cold solution. The mixture was stirred at -78 °C for 6 h, and then quenched by the addition of a satd aq $NaHCO_3$ solution (5 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were dried (Na_2SO_4), filtered, and concentrated to give the crude product (4.4:1 of *cis*:*trans*, ^{1}H NMR). The addition of a few drops of dichloromethane and hexanes precipitated the *cis*-aziridine as a white solid (302 mg). The mother liquor was purified by flash chromatography (SiO_2, 0-20% ethyl acetate in hexanes) to afford an additional 112 mg of the *cis*-isomer and 108 mg pure *trans*-isomer. *cis*: 414 mg (70%); R_f = 0.38 (20% EtOAc/hexanes); IR (film) 3068, 2982, 2177, 1752, 1430, 1188, 1113 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65-7.63 (m, 6H), 7.54 (d, *J* = 7.3 Hz, 2H), 7.47-7.23 (m, 17H), 4.20-4.01 (m, 2H), 3.99 (s, 1H), 2.64 (d, *J* = 6.4 Hz, 2H), 1.11 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) ppm 167.3, 153.1, 141.8, 135.7, 133.3, 130.0, 128.7, 128.6, 128.0, 127.60,

[2] J. R. Hwu, P. S. Furth, *J. Am. Chem. Soc.* 1989, **111**, 8834.
[3] 3-(triphenylsilyl)prop-2-yn-1-ol: S. Morikawa, S. Yamazaki, M. Tsukada, S. Izuhara, T. Morimoto, K. Kakiuchi, *J. Org. Chem.* 2007, **72**, 6459; 3-(triphenylsilyl)propiolaldehyde: E. V. Arshavskaya, L. D. Lezhava, A. M. Sladkov, *B. Acad. Sci. USSR CH+* 1979, 200.

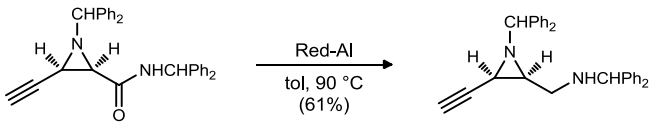
127.59, 127.5, 105.1, 83.2, 77.1, 61.4, 45.0, 34.7, 14.3; HRMS (EI): Exact mass calcd for $C_{38}H_{34}NO_2Si$ $[M+H]^+$ 564.2353, found 564.2358. *trans*: 108 mg (18%); R_f = 0.43 (20% EtOAc/hexanes); IR (film) 3068, 2980, 2172, 1742, 1429, 1187, 1114 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.55-7.53 (m, 6H), 7.45-7.43 (m, 2H), 7.40-7.15 (m, 17H), 4.54 (s, 1H), 4.21-4.10 (m, 2H), 3.29 (d, *J* = 2.8 Hz, 1H), 2.58 (d, *J* = 2.6 Hz, 1H), 1.24 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) ppm 168.8, 142.8, 141.4, 135.7, 132.9, 130.2, 128.7, 128.4, 128.2, 127.6, 127.4, 127.1, 104.3, 86.0, 71.4, 61.5, 45.7, 34.8, 14.2; HRMS (EI): Exact mass calcd for $C_{38}H_{34}NO_2Si$ $[M+H]^+$ 564.2353, found 564.2342.



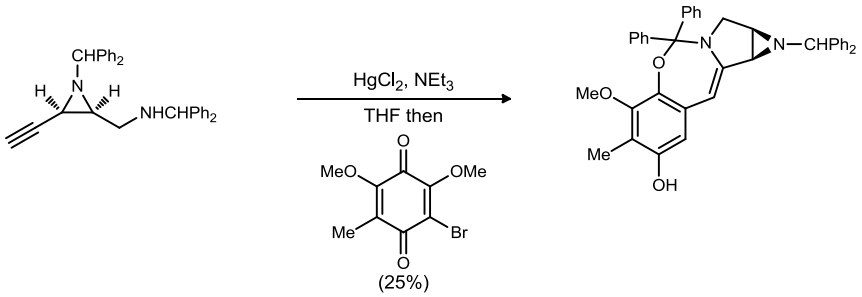
1-Benzhydryl-3-ethynylaziridine-2-carboxylic acid (S1). The ethyl ester (14.3 g, 25.4 mmol) in 95% aqueous ethanol (300 mL) was treated with sodium hydroxide (2.0 g, 51 mmol) and the suspension was stirred overnight. Ethanol was evaporated, water was added and the aqueous layer was washed with diethyl ether. The aqueous layer was acidified to pH < 2 with aq 1N hydrochloric acid, and the resulting solid was dissolved in dichloromethane. The organic layer was separated, dried (Na_2SO_4), filtered and the solvent was removed to afford the alkynyl carboxylic acid as a white solid (6.7 g, 96% yield). mp 136.5-138 °C; R_f = 0.09 (40% EtOAc/hexanes); IR (film) 3288, 3090, 3061, 3029, 1718, 1700, 1498, 1454, 1247, 1063 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.4 Hz, 2H), 7.40-7.28 (m, 8H), 3.97 (s, 1H), 2.75 (d, *J* = 6.6 Hz, 1H), 2.71 (dd, *J* = 6.6, 1.5 Hz, 1H), 2.29 (d, *J* = 1.5 Hz, 1H) (O*H* not observed); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 168.9, 141.0, 140.9, 129.2, 129.0, 128.4, 128.0, 127.6, 127.3, 77.7, 76.4, 72.5, 44.4, 34.5; HRMS (EI) Exact mass calcd for $C_{18}H_{14}NO_2$ $[M-H]^+$ 276.1025, found 276.1034.



1-Benzhydryl-3-ethynylaziridine-2-carboxylic acid benzhydryl amide (6). The carboxylic acid (1.3 g, 3.7 mmol), 1,3-dicyclohexylcarbodiimide (DCC) (1.35 g, 6.56 mmol), and 1-hydroxybenzotriazole (HOBt) (890 mg, 6.56 mmol) were dissolved in dichloromethane (94 mL). Then diisopropylethylamine (0.82 mL, 4.69 mmol) and diphenyl methyl amine (1.13 mL, 6.56 mmol) were added to the solution, and the mixture was stirred at room temperature for 3 days. A 1 M HCl solution was added and the layers were separated. The organic layer was washed with 1 M HCl, brine, and 1 M sodium bicarbonate, and then dried (Na_2SO_4), filtered, and concentrated to afford a solid. The crude material was purified by flash column chromatography (SiO_2, 10-40% ethyl acetate in hexanes) to give an off-white solid (1.68 g, 80%). mp 50-52 °C; R_f = 0.34 (40% EtOAc/hexanes); IR (film) 3390, 3294, 3086, 3061, 2924, 1683, 1515, 1493, 1454 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 7.4 Hz, 2H), 7.37-7.21 (m, 16H), 7.02-7.00 (m, 2H), 6.20 (d, *J* = 8.9 Hz, 1H), 3.82 (s, 1H), 2.62 (d, *J* = 6.6 Hz, 1H), 2.54 (dd, *J* = 6.6, 1.7 Hz, 1H), 1.92 (d, *J* = 1.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 165.8, 141.5, 141.4, 141.2, 141.1, 128.8, 128.6, 128.51, 128.48, 128.4, 128.04, 127.97, 127.6, 127.5, 127.4, 127.3, 127.2, 127.0, 78.6, 76.5, 71.6, 56.1, 45.4, 34.8; HRMS (EI) Exact mass calcd for $C_{31}H_{26}N_2O$ $[M]^+$ 442.2045, found 442.2039.

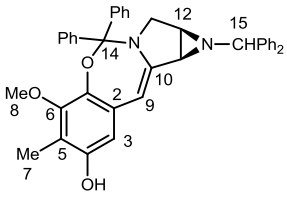


Benzhydryl-(1-benzhydryl-3-ethynylaziridin-2-ylmethyl) amine (7). The amide (15.1 mg, 33.8 μmol) was dissolved in toluene (1.1 mL), then Red-Al (65 % w/v) (105 μL, 33.8 μmol) was added dropwise (note: reaction bubbled vigorously). The reaction was heated to 90 °C for 4 h, then cooled to rt and quenched by the addition of $Na_2SO_4 \cdot 10H_2O$. The mixture was stirred at rt for 30 min, filtered, and the solvent was removed. The product was purified by flash column chromatography (SiO_2, 25-40% ethyl acetate in hexanes) to give a white solid (8.9 mg, 61%). mp 109-111 °C; R_f = 0.51 (40% EtOAc/hexanes); IR (film) 3286, 3060, 3026, 2850, 1493, 1453, 1029 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 7.2 Hz, 2H), 7.36-7.30 (m, 4H), 7.26-7.16 (m, 14H), 4.67 (s, 1H), 3.66 (s, 1H), 2.80 (dd, *J* = 12.3, 5.0 Hz, 1H), 2.68 (dd, *J* = 12.3, 7.1 Hz, 1H), 2.19 (dd, *J* = 6.2, 1.8 Hz, 1H), 2.16 -2.12 (m, 1H), 2.07 (d, *J* = 1.8 Hz, 1H) (N*H* not observed); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 144.1, 143.9, 142.9, 142.4, 128.7, 128.5, 128.4, 127.9, 127.7, 127.4, 127.3, 127.2, 127.0, 80.8, 78.0, 70.2, 67.1, 48.0, 45.0, 32.7; HRMS (EI) Exact mass calcd for $C_{31}H_{29}N_2$ $[M+H]^+$ 429.2331, found 429.2313.



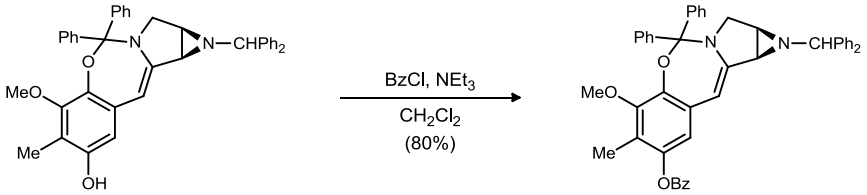
***N,O*-Ketal (11).** The alkynyl amine (15 mg, 35 μmol) and mercuric chloride (7 mg, 27 μmol) were dissolved in THF (175 μmol), and treated with triethylamine (25 μL, 18 μmol). The reaction mixture was stirred for 4 h at rt, then the quinone (9 mg, 35 μmol) was added and the solution was stirred for an additional 4 h. The solvent was removed and the residue was purified by flash chromatography (neutral alumina, 20-40-80% ethyl acetate in hexanes) afforded the title compound as a green-yellow solid (6 mg, 30%). R_f = 0.30 (30% EtOAc/hexanes); IR (film) 3061, 3028, 2921, 1636, 1577 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.4 Hz, 2H), 7.46 (d, *J* = 7.2 Hz, 2H), 7.39-7.22 (m, 16 H), 5.90 (s, 1H), 5.19 (s, 1H), 3.91 (s, 3H), 3.76 (s, 1H), 3.17 (dd, *J* = 10.6, 3.4 Hz, 1H), 3.10 (d, *J* = 10.6 Hz, 1H), 2.93 (d, *J* = 5.3 Hz, 1H), 2.61 (dd, *J* = 4.8, 3.6 Hz, 1H), 2.07 (s, 3H) (O*H* not observed); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 150.9, 149.2, 144.2, 144.0, 143.6, 143.5, 141.7, 139.9, 129.3, 128.6, 128.30, 128.27, 128.2, 127.9, 127.7 (2C), 127.5, 127.3 (2C), 113.5, 108.7, 97.9, 96.8, 74.8, 61.1, 55.7, 50.6, 41.5, 9.1; HRMS (EI): Exact mass calcd for $C_{39}H_{35}N_2O_3$ $[M+H]^+$ 579.2642, found 579.2632.

Structural Assignment of *N,O*-ketal 11

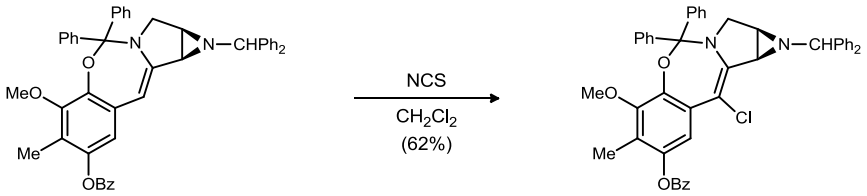


All the 1D and 2D NMR experiments were carried out on a Varian I400 (400 MHz) instrument in $CDCl_3$. The ^1H NMR experiment confirmed the hydroquinone ring proton H_3 (5.90 ppm). The corresponding ^{13}C chemical shift appeared at 108.7 ppm. The enamine olefin proton H_9 appeared at 5.19 ppm, with the corresponding ^{13}C chemical shift at 97.9 ppm. The two protons (H_3, H_9) showed $^3J_{HC}$ correlations with each other in a CIGAR experiment. Critically, the *N,O*-ketal carbon (C_{14}) was observed

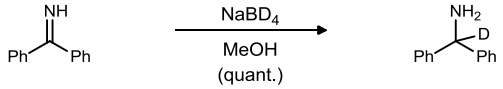
at 96.8 ppm. The aziridine diphenylmethyl methine proton (H_{15}) was assigned at 3.76 ppm, based on the $^3J_{HC}$ correlations with the aziridine ring carbons C_{11} and C_{12}. The absence of peaks in 175-185 ppm region in the ^{13}C experiment indicated that the quinone ring of the starting material was present in its reduced form. HMQC, CIGAR and COSY experiments allowed assignment of all the other proton and carbon peaks. The presence of only one methoxy group indicated that the Michael reaction occurred with the regiochemistry depicted (i.e. substitution of the methoxy group in preference to the bromide). The loss of bromide was confirmed by mass spectroscopic analysis. The IR experiment revealed the presence of a broad band at ~3300 cm^{-1} confirming the presence of the phenol hydroxyl group.



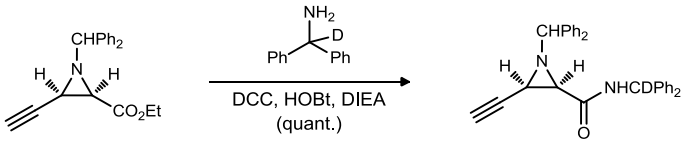
Benzoyl *N,O*-ketal (S2). To a solution of the *N,O*-ketal (25 mg, 38 μmol) in dichloromethane (1 mL) was added triethylamine (16 μL, 114 μmol) and benzoyl chloride (8.8 μL, 66 μmol) at 0 °C and stirred for 5 min. The reaction mixture was warmed to room temperature and stirred for an additional 30 min. It was then diluted with dichloromethane (5 mL), washed with water and brine, dried (Na_2SO_4), filtered, and then concentrated. The residue was purified via column chromatography (SiO_2, 0-20% ethyl acetate in hexanes) to afford the benzoate as a white solid (23 mg, 80% yield). R_f = 0.33 (20% EtOAc/hexanes); IR (film) 3059, 2922, 1732, 1653, 1609, 1444 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 7.6 Hz, 2H), 7.59 (dd, *J* = 15.8, 7.7 Hz, 4H), 7.46 (dd, *J* = 18.7, 7.6 Hz, 4H), 7.38-7.20 (m, 15H), 6.39 (s, 1H), 5.29 (s, 1H), 3.94 (s, 3H), 3.76 (s, 1H), 3.19 (dd, *J* = 10.5, 3.2 Hz, 1H), 3.09 (d, *J* = 10.8 Hz, 1H), 2.95 (d, *J* = 4.9 Hz, 1H), 2.63 (t, *J* = 3.8 Hz, 1H), 2.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 165.0, 150.8, 145.5, 144.7, 144.5, 143.8, 143.6, 143.2, 139.6, 133.5, 130.2, 129.8 129.2, 128.9, 128.7, 128.3, 128.2, 127.9, 127.6, 127.4 127.1, 119.3, 115.6, 97.9, 97.0, 74.8, 61.2, 55.7, 50.4, 41.5, 9.9; HRMS (EI): Exact mass calcd for $C_{46}H_{38}N_2O_4$ $[M]^+$ 682.2832, found 682.2790.



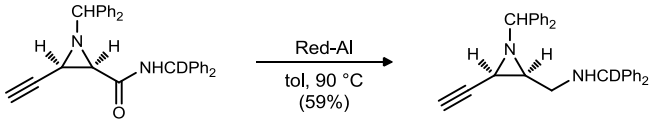
Chloro *N,O*-ketal (12). To a solution of the *N,O*-ketal (20 mg, 29 μmol) in dichloromethane (1 mL) was added *N*-chlorosuccinimide (3.5 mg, 29 μmol) and the mixture was stirred for 30 min. The mixture was filtered through a plug of Celite, the solid was washed with dichloromethane, and the filtrate was concentrated. The crude solid was purified via column chromatography (SiO_2, 0-20% ethyl acetate in hexanes) to afford the chloride as a white crystalline solid (13 mg, 62% yield). R_f = 0.45 (20% EtOAc/hexanes); IR (film) 3060, 2958, 2923, 2851, 1734, 1595, 1449, 1409, 1095 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 8.14 (d, *J* = 7.1 Hz, 2H), 7.60 (dd, *J* = 7.4, 7.4 Hz, 2H), 7.55 (d, *J* = 7.4 Hz, 2H), 7.47 (dd, *J* = 7.9, 7.7 Hz, 3H), 7.44 (d, *J* = 7.3 Hz, 2H), 7.35-7.28 (m, 9H), 7.25-7.22 (m, 5H), 7.02 (s, 1H), 3.92 (s, 3H), 3.86 (s, 1H), 3.63 (d, *J* = 5.0 Hz, 1H), 3.22 (dd, *J* = 10.7, 3.5 Hz, 1H), 3.18 (d, *J* = 10.7 Hz, 1H), 2.60 (dd, *J* = 4.9, 3.7 Hz, 1H), 2.03 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 164.9, 150.7, 144.7, 144.6, 143.3, 143.3, 142.7, 138.8, 133.5, 130.2, 129.7, 128.9, 128.6 (2C) 128.5, 128.5 (2C), 128.1, 127.9, 127.7, 127.5, 127.4, 127.3, 127.1, 121.0, 115.0, 102.4, 97.4, 74.7, 61.2, 56.5, 50.8, 40.6, 9.8; HRMS (EI): Exact mass calcd for $C_{46}H_{38}ClN_2O_4$ $[M+H]^+$ 717.2515, found 717.2305.



Deuterodiphenyl methylamine (S3). To a methanolic solution (3 mL) of the imine (100 mg, 556 μmol) was added sodium borodeuteride (70 mg, 1.7 mmol), and the mixture was stirred overnight, quenched with water, and then extracted with dichloromethane. The organic layer was dried (Na_2SO_4), filtered, and concentrated to afford the deuteroamine as a colorless oil (100 mg, quant). R_f = 0.35 (30% EtOAc/hexanes); IR (film) 3368, 3297, 3020, 1491, 1446 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41-7.39 (m, 4H), 7.36-7.32 (m, 4H), 7.28-7.23 (m, 2H), 1.83 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 145.6, 128.6, 127.04, 126.97, 59.4 (t, *J* = 20.7 Hz); HRMS (EI): Exact mass calcd for $C_{13}H_{12}DN$ $[M]^+$ 184.1111, found 184.1101.

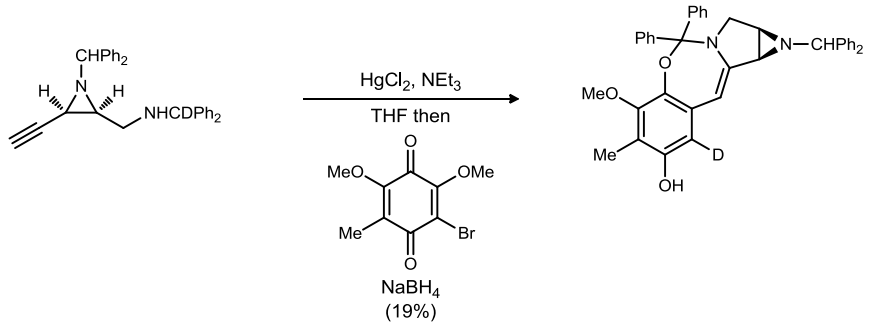


***N*,1-Dibenzhydryl-3-ethynylaziridine-2-deuterocarboxamide (S4).** The carboxylic acid (500 mg, 1.80 mmol), 1,3-dicyclohexylcarbodiimide (DCC) (870 mg, 3.25 mmol), and 1-hydroxybenzotriazole (HOBt) (440 mg, 3.25 mmol) were dissolved in dichloromethane (0.04 M). Diisopropylethylamine (410 μL, 2.35 mmol) and deuteroamine (600 μL, 3.25 mmol) were added to the solution, and the mixture was stirred at room temperature for 24 h. A 1 M HCl solution was added and the layers were separated. The organic layer was washed with 1 M HCl, brine, and 1 M sodium bicarbonate, and then dried (Na_2SO_4), filtered, and concentrated. The crude oil was purified by flash column chromatography (Al_2O_3, 0-40% ethyl acetate in hexanes) to give the amide as an oil (790 mg, quant). R_f = 0.46 (50% EtOAc/hexanes); IR (film) 3387, 3297, 3059, 1696, 1507, 1496, 1448 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.3 Hz, 2H), 7.36-7.23 (m, 16H), 7.04-7.02 (m, 2H), 3.84 (s, 1H), 2.64 (d, *J* = 6.6 Hz, 1H), 2.57 (dd, *J* = 6.6, 1.9 Hz, 1H), 1.93 (d, *J* = 1.9 Hz, 1H) (N*H* not observed); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 165.8, 141.5, 141.4, 141.2, 128.8, 128.6, 128.52, 128.47, 128.40, 128.0, 127.9, 127.6, 127.5, 127.4, 127.3, 127.2, 127.0, 126.94, 126.90, 78.6, 76.4, 71.6, 55.9 (t, *J* = 20.7 Hz), 45.4, 34.8; HRMS (CI) Exact mass calcd for $C_{31}H_{26}DN_2O$ $[M+H]^+$ 444.2181, found 444.2180.



***N*-((1-Benzhydryl-3-ethynylaziridin-2-yl)methyl)-1,1-deuterodiphenylmethanamine (13).** The amide (800 mg, 1.81 mmol) was dissolved in toluene (0.03 M), and then treated with Red-Al (65 % w/v) (1.63 mL, 5.42 mmol) dropwise (note: reaction bubbled vigorously). The reaction was heated to 90 °C for 3 h, then cooled to rt and quenched by the addition of $Na_2SO_4 \cdot 10H_2O$. The mixture was stirred at rt for 30 min, filtered through Celite, and concentrated. The product was purified by flash column chromatography (SiO_2, 0-20% ethyl acetate in hexanes) to give the amine as an oil (462 mg, 59%). R_f = 0.37 (20% EtOAc/hexanes); IR (film) 3288, 3055, 1488, 1448 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 7.3 Hz, 2H), 7.36-7.30 (m, 4H), 7.26-7.17 (m, 14H), 3.66 (s, 1H), 2.80 (dd, *J* = 12.3, 5.0 Hz, 1H), 2.68 (dd, *J* = 12.3, 7.1 Hz, 1H), 2.19 (dd, *J* = 6.2, 1.6 Hz,

1H), 2.16-2.13 (m, 1H), 2.07 (d, *J* = 1.6 Hz, 1H) (N*H* not observed); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 144.1, 143.9, 142.9, 142.4, 128.7, 128.5, 128.4, 127.9, 127.7, 127.4, 127.3, 127.2, 127.0, 80.8, 78.0, 70.2, 66.7 (t, *J* = 20.8 Hz), 48.0, 45.0, 32.7; HRMS (EI) Exact mass calcd for $C_{31}H_{28}DN_2$ $[M+H]^+$ 430.2404, found 430.2395.



Deutero *N,O*-ketal 14. The deutero amine (150 mg, 349 μmol) and mercuric chloride (48 mg, 175 μmol) were dissolved in THF (3 mL), and treated with triethyl amine (292 μL, 2.10 mmol). The reaction mixture was stirred for 90 min at rt, after which quinone (91 mg, 349 μmol) and sodium borohydride (27 mg, 698 μmol) were added, and the mixture was stirred overnight. The mixture was filtered through Celite and the solvent was evaporated. Purification by flash chromatography (neutral alumina, 0-40% ethyl acetate in hexanes) afforded the ketal as a colorless oil (39 mg, 19%). R_f = 0.18 (20% EtOAc/hexanes); IR (film) 3361, 2921, 1649, 1446, 1092 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.5 Hz, 2H), 7.45 (d, *J* = 7.4 Hz, 2H), 7.39-7.22 (m, 16H), 5.22 (s, 1H), 3.91 (s, 3H), 3.76 (s, 1H), 3.19-3.16 (m, 1H), 3.11-3.08 (m, 1H), 2.94 (d, *J* = 4.6 Hz, 1H), 2.62 (t, *J* = 3.8 Hz, 1H), 2.07 (s, 3H) (O*H* not observed); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 150.9, 149.1, 144.1, 143.9, 143.5, 143.4, 141.6, 139.7, 129.2, 128.6, 128.4, 128.2, 128.1, 127.8, 127.6, 127.4, 127.2, 113.4, 108.5 (t, *J* = 20.7 Hz), 97.8, 96.7, 74.8, 61.1, 55.7, 50.5, 41.5, 9.0; HRMS (EI): Exact mass calcd for $C_{39}H_{34}DN_2O_3$ $[M+H]^+$ 580.2705, found 580.2681.

Stereoselective Synthesis of Complex Polycyclic Aziridines: Use of the Brønsted Acid-Catalyzed aza-Darzens Reaction to Prepare an Orthogonally Protected Mitomycin C Intermediate with Maximal Convergency

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S-II-X

Figure 1. ^{1}H NMR ($CDCl_3$) of **4**.

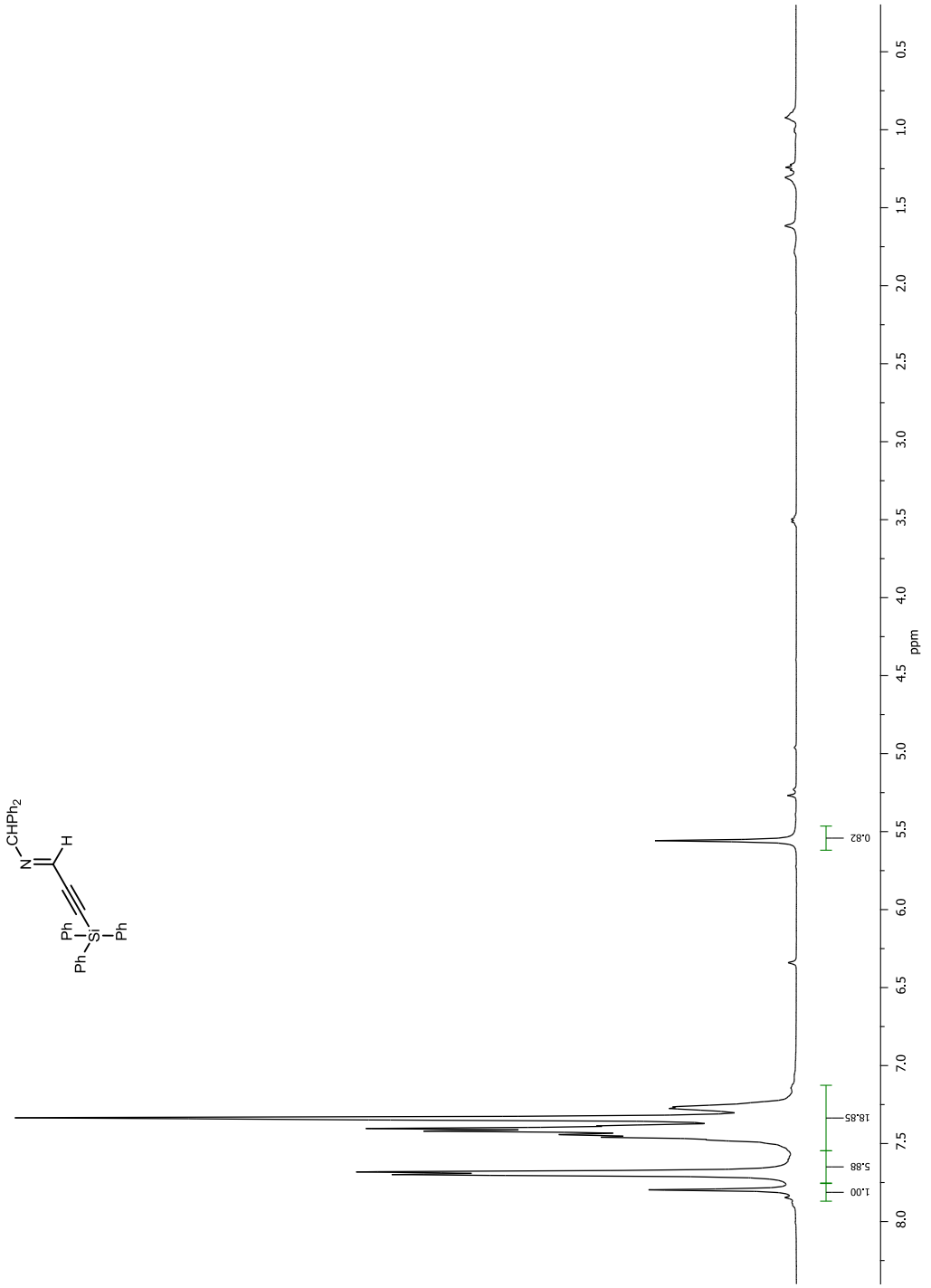


Figure 2. ^{13}C NMR ($CDCl_3$) of **4**.

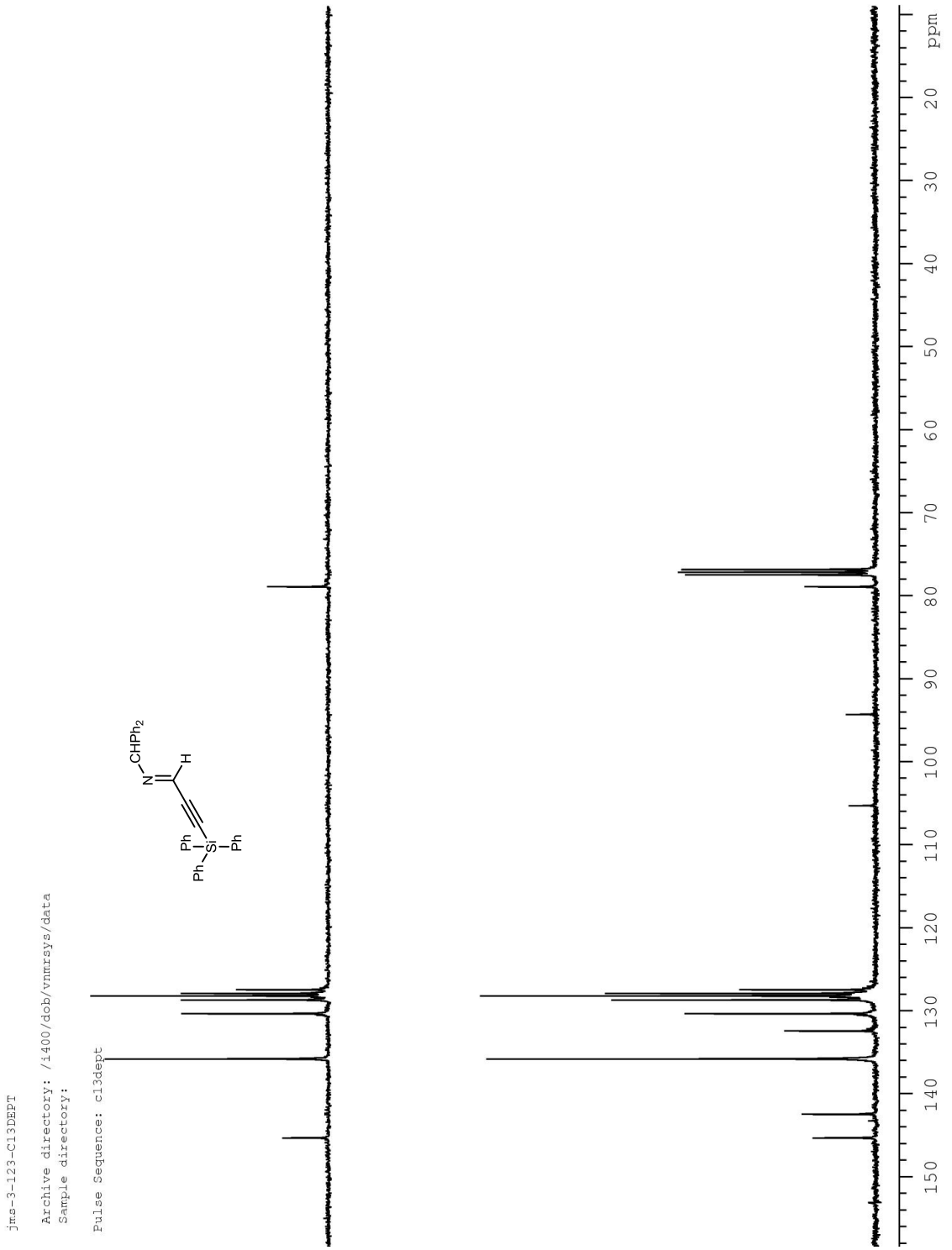


Figure 3. ^{1}H NMR ($CDCl_3$) of **5**.

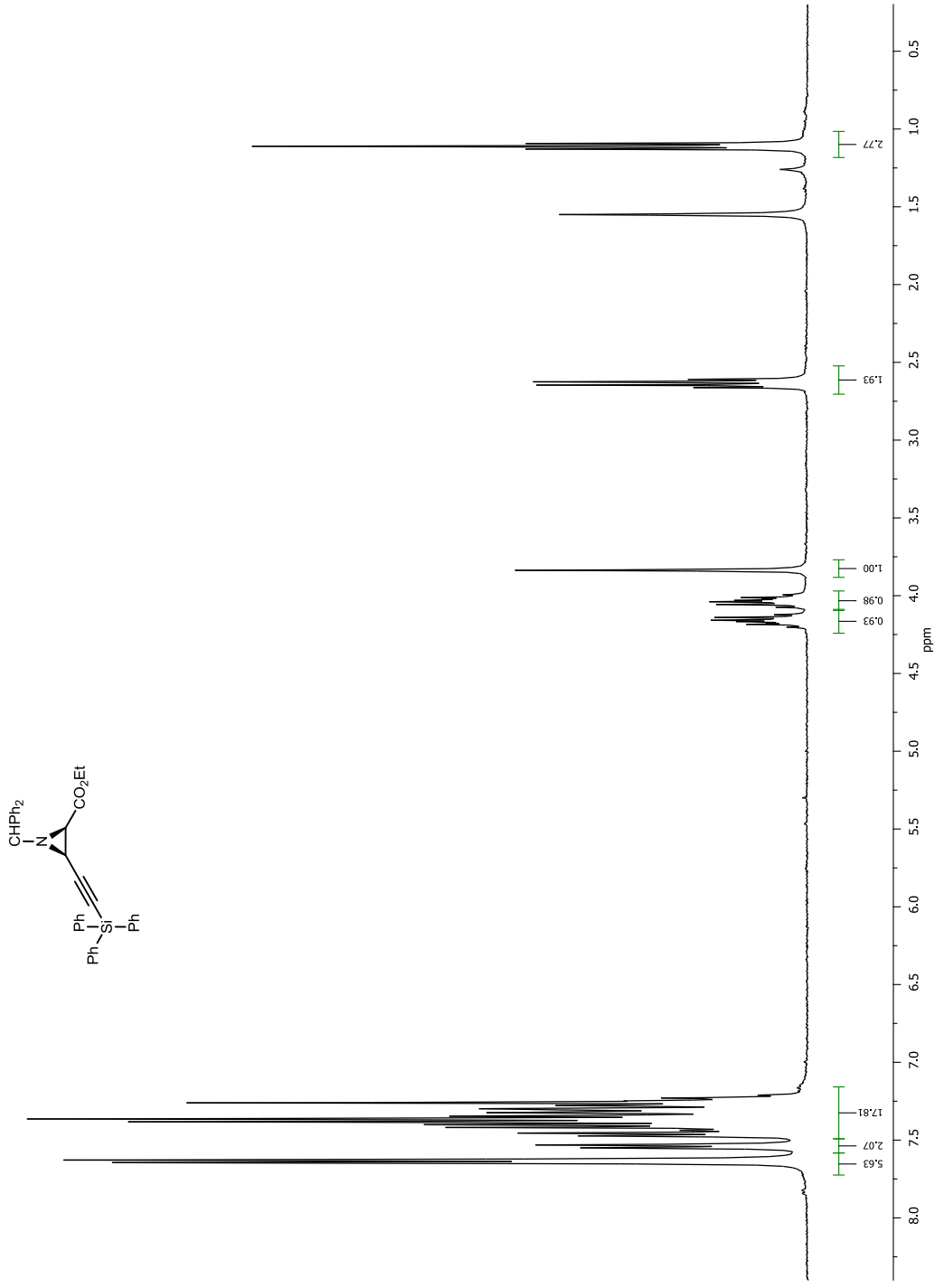


Figure 4. ^{13}C NMR ($CDCl_3$) of **5**.

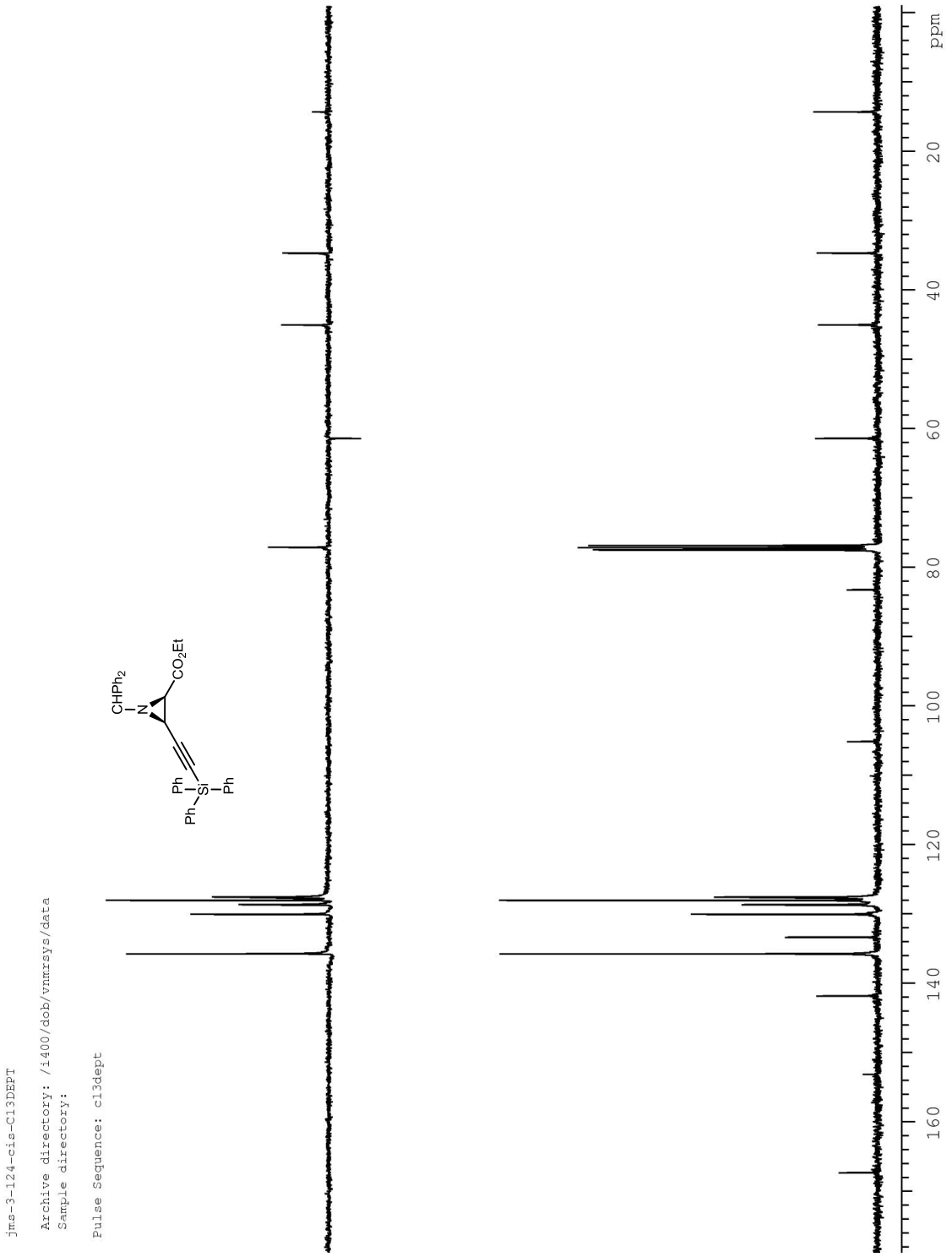


Figure 5. ^{1}H NMR ($CDCl_3$) of S1**.**

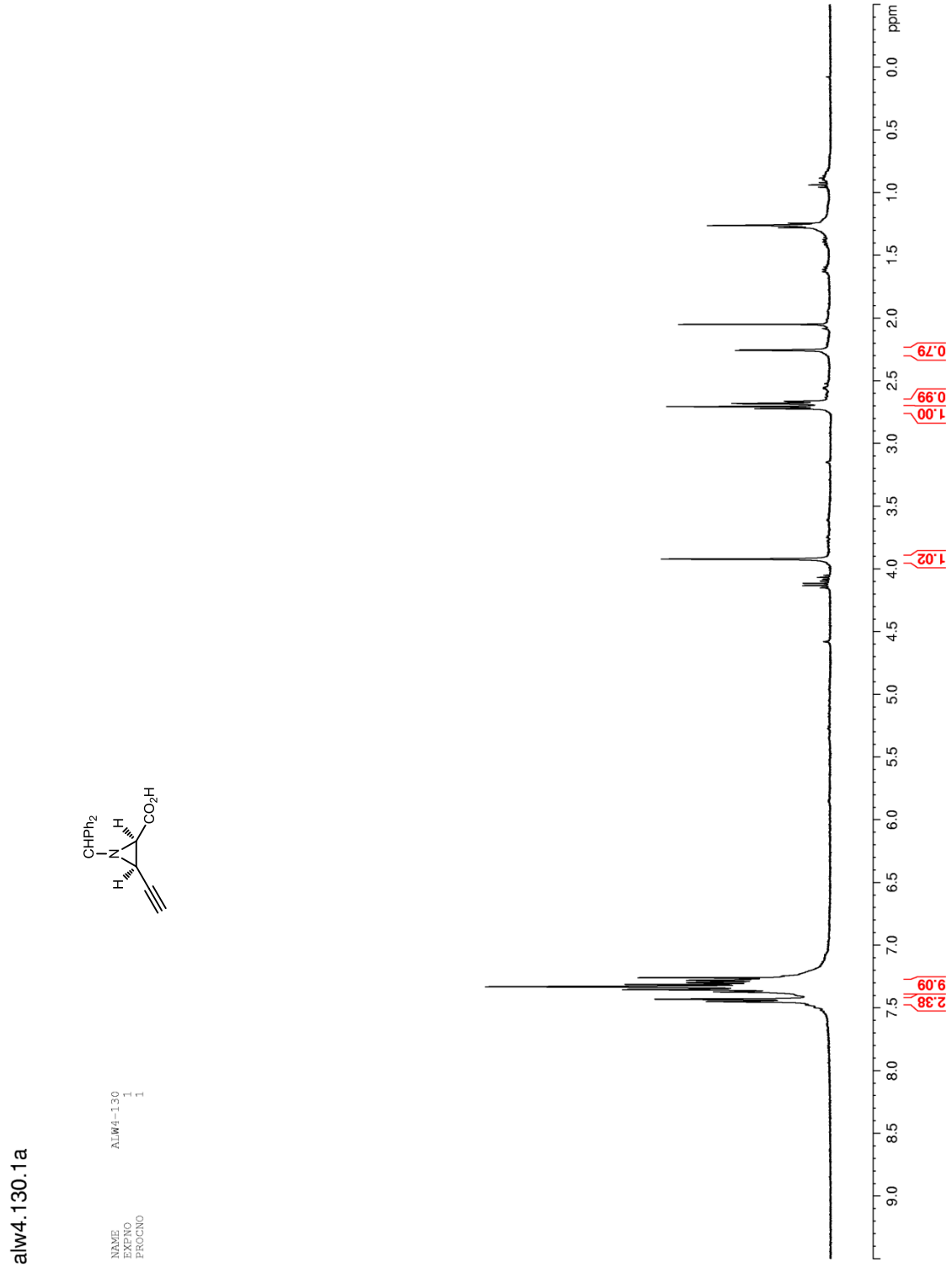


Figure 6. ^{13}C NMR ($CDCl_3$) of **S1**.

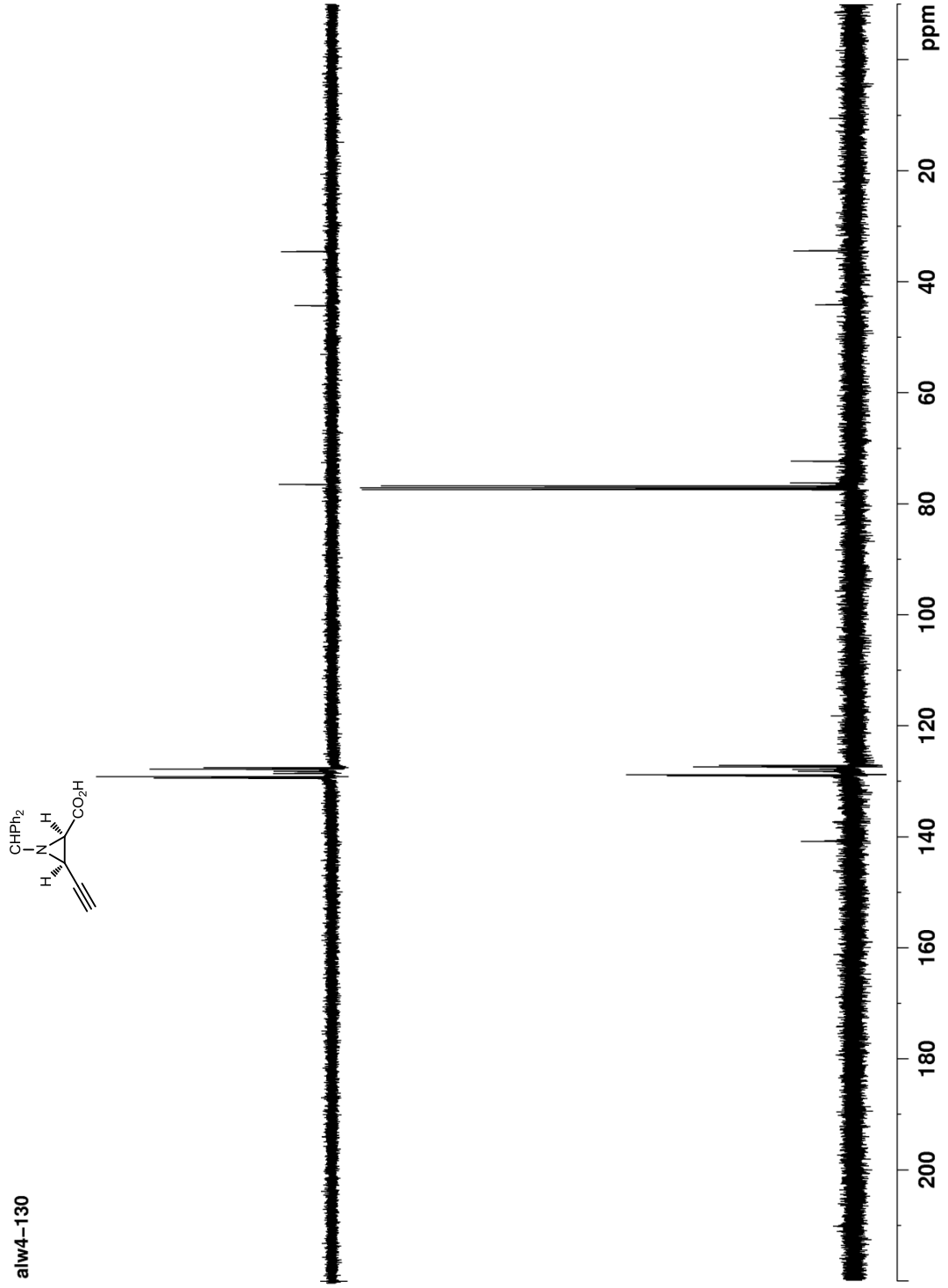


Figure 7. ^{1}H NMR ($CDCl_3$) of **6**.

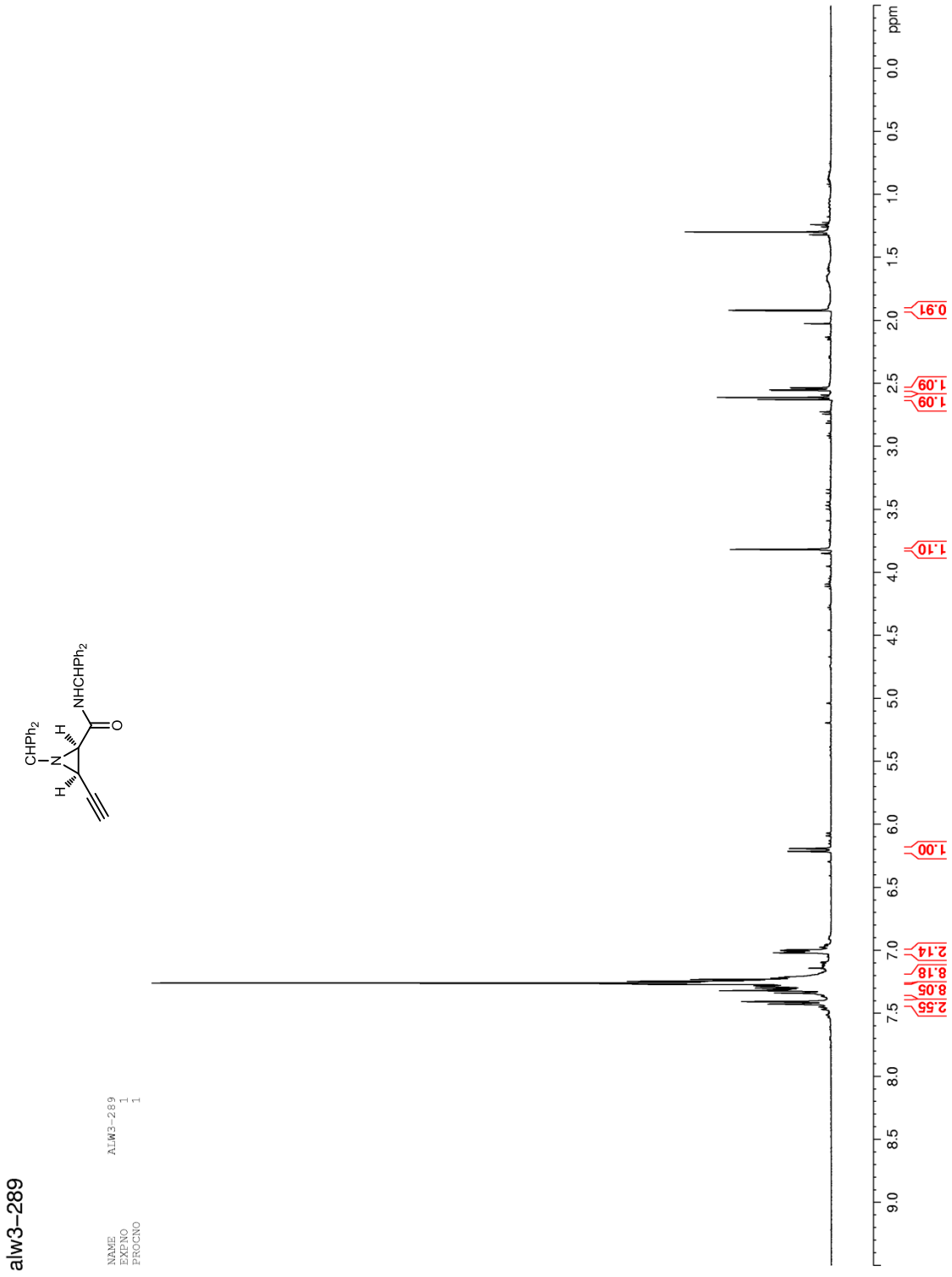


Figure 8. ^{13}C NMR ($CDCl_3$) of **6**.

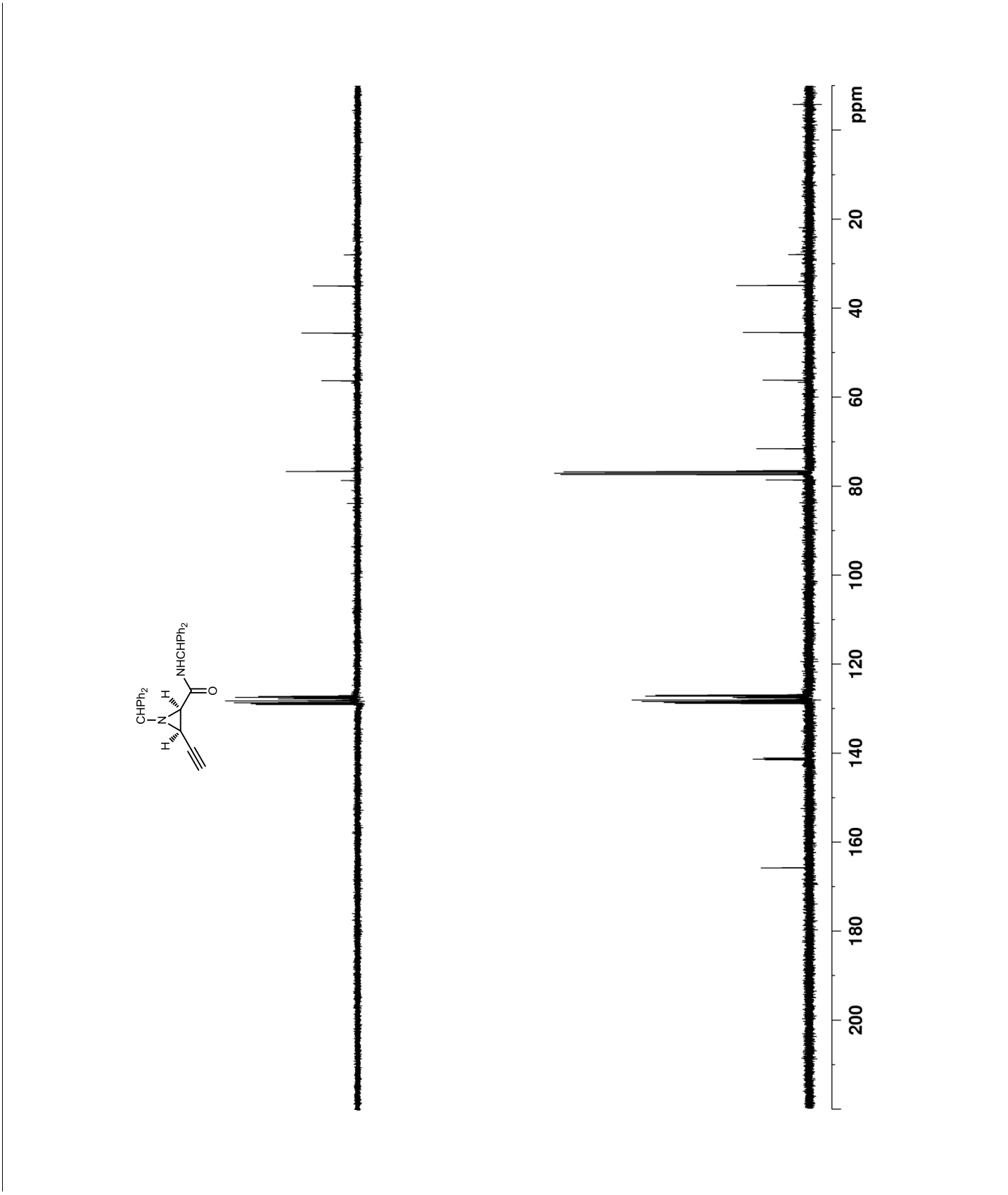


Figure 9. ^{1}H NMR ($CDCl_3$) of **7**.

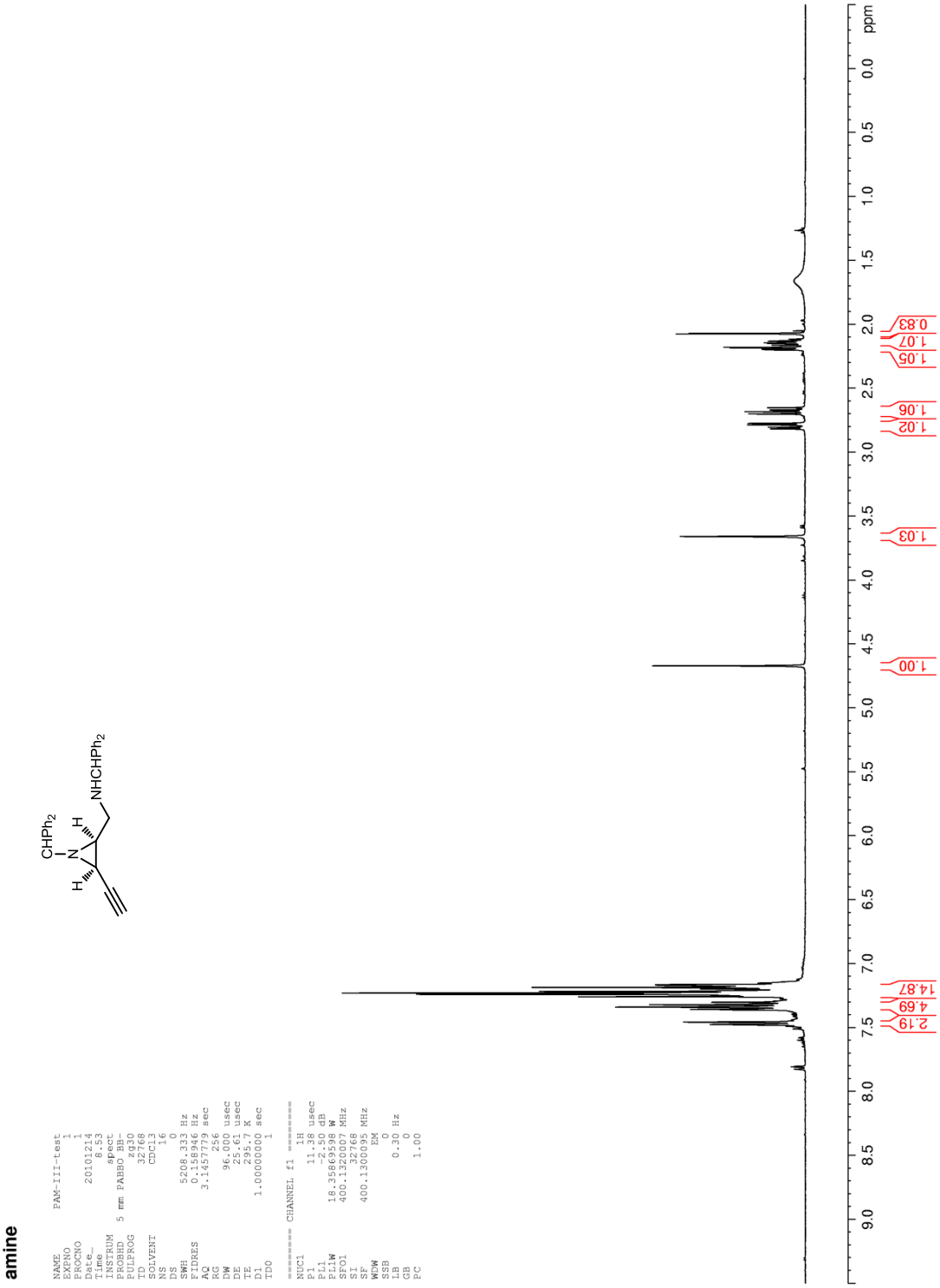


Figure 10. ^{13}C NMR ($CDCl_3$) of **7**.

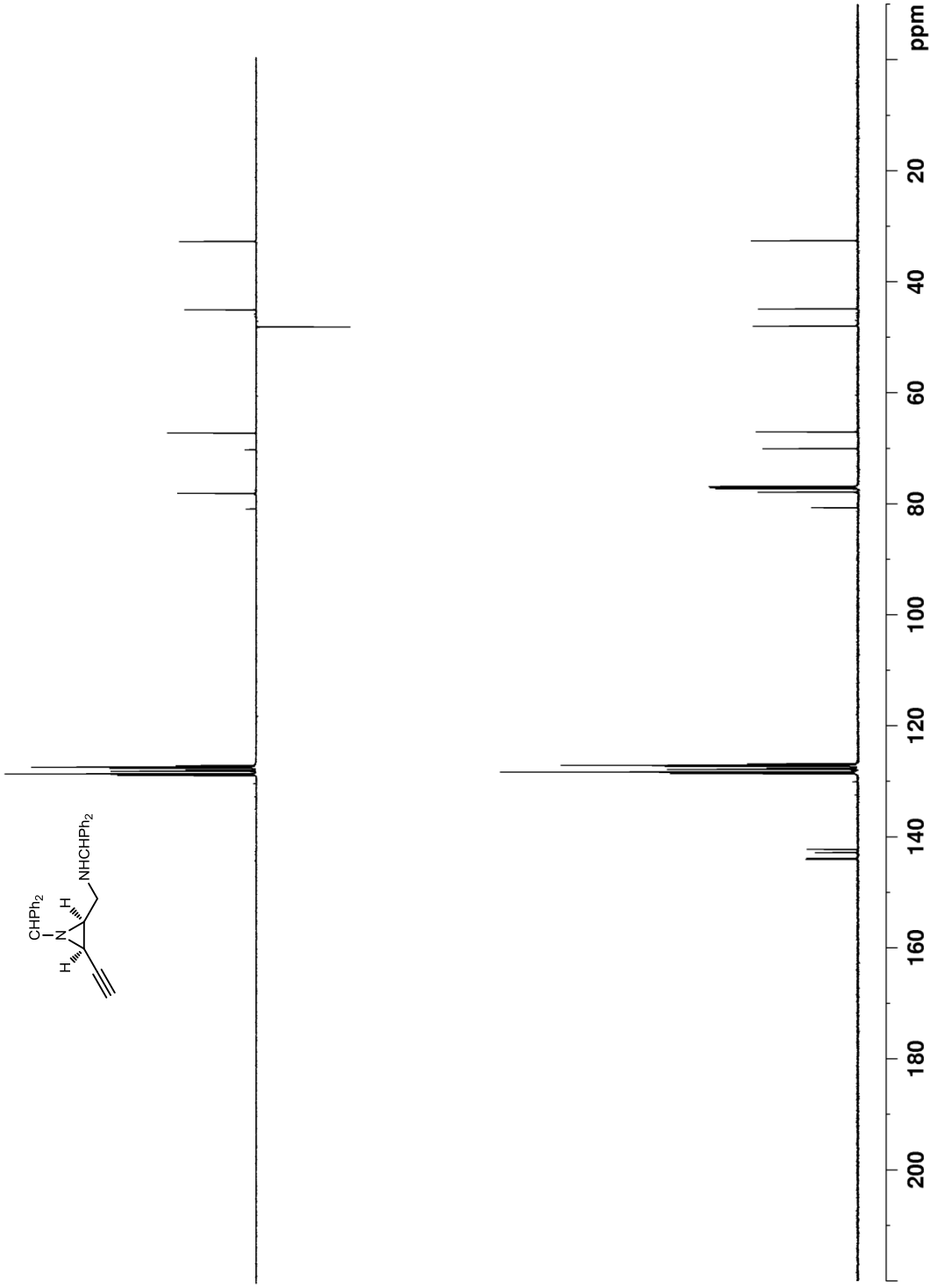


Figure 11. ^{1}H NMR ($CDCl_3$) of **11**.

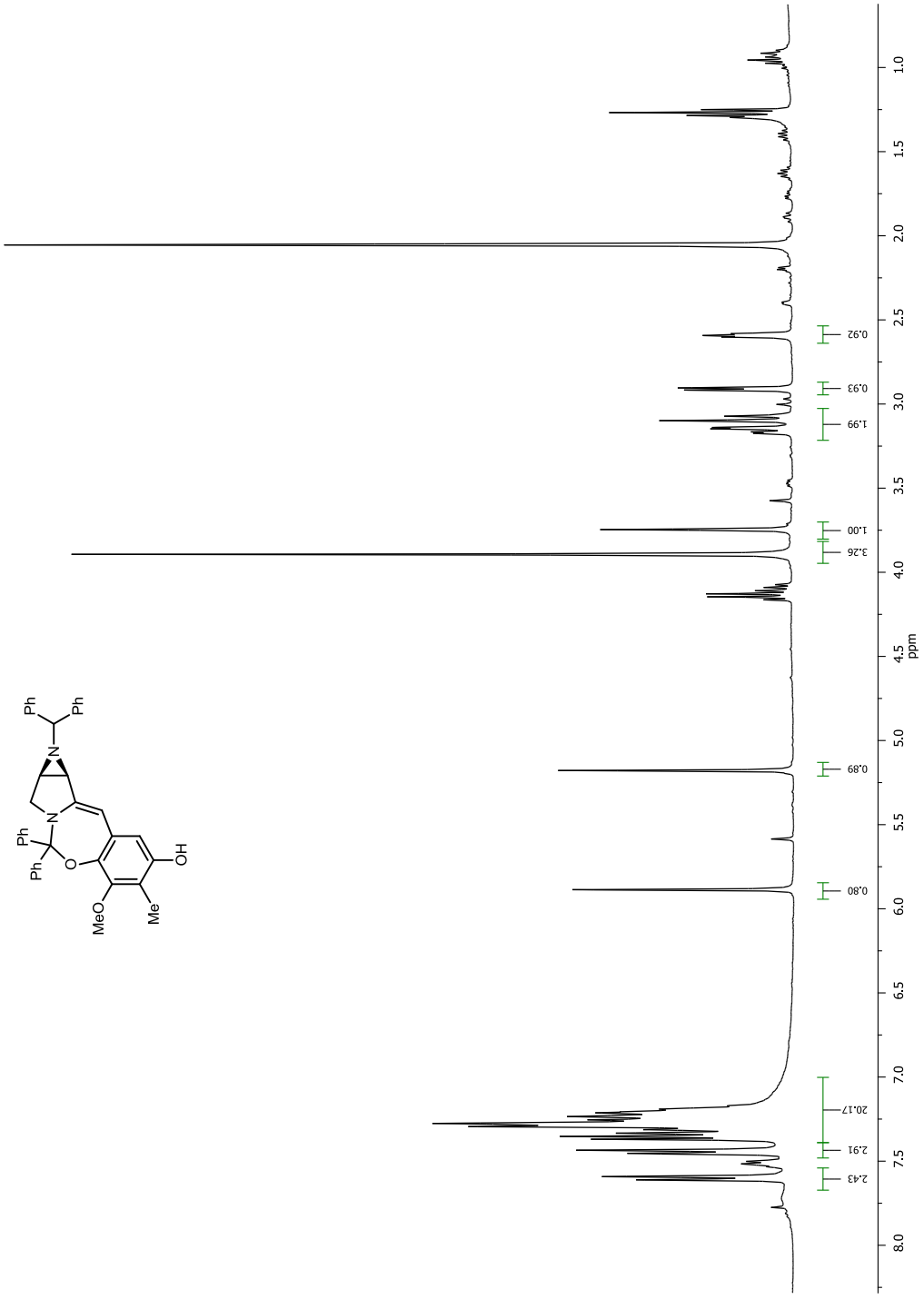


Figure 12. ^{13}C NMR ($CDCl_3$) of **11**.

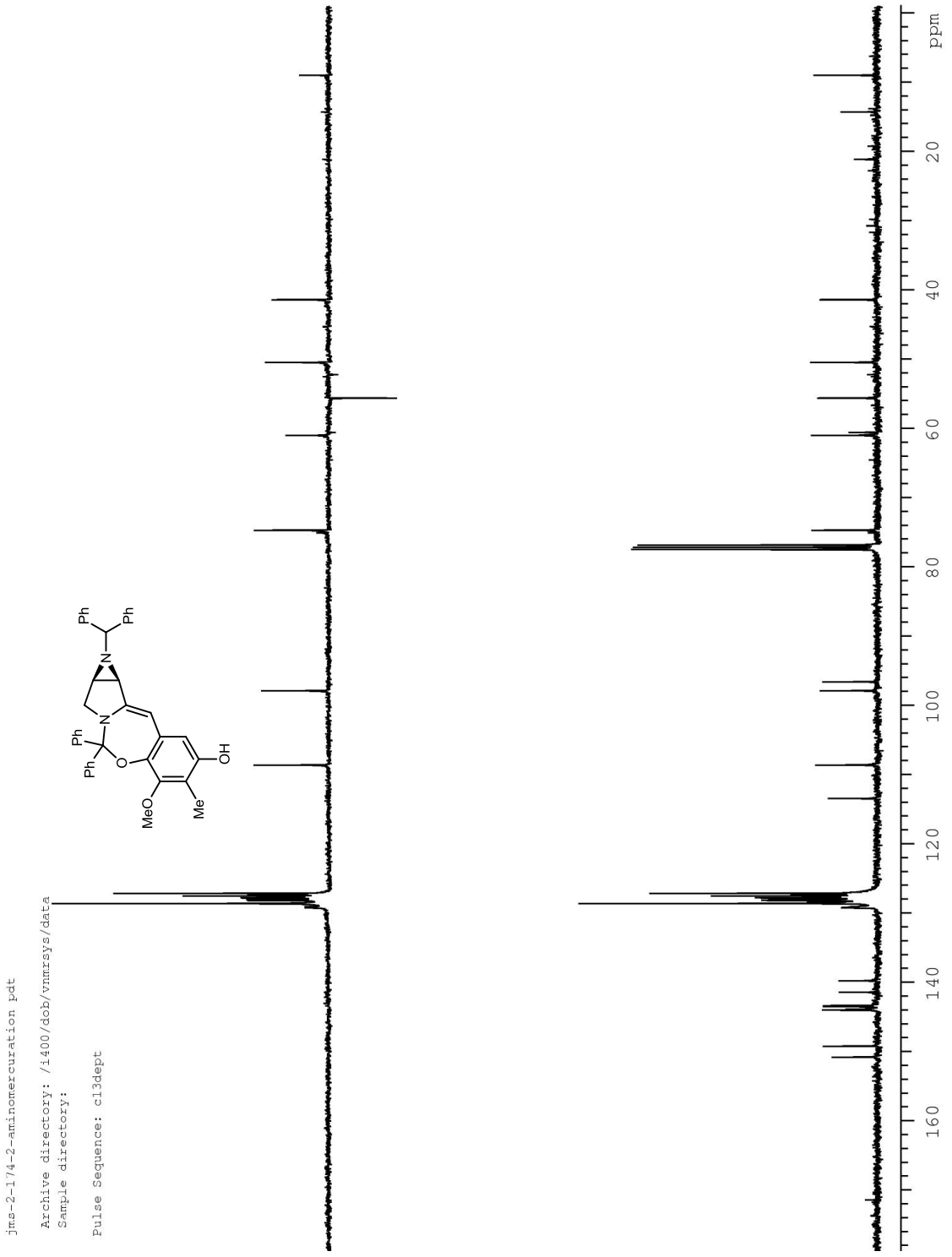


Figure 13. ^{1}H NMR ($CDCl_3$) of **S2**.

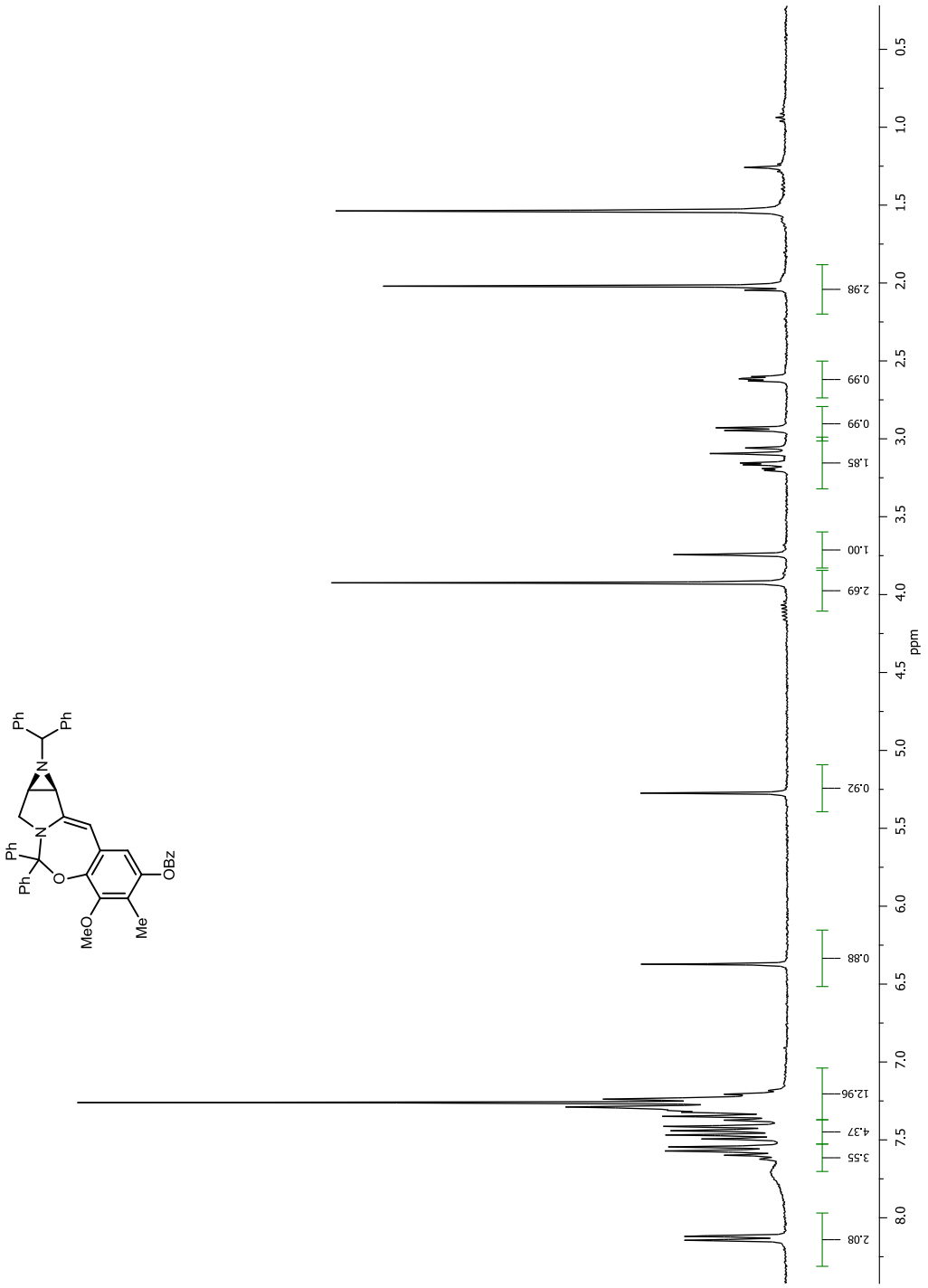


Figure 14. ^{13}C NMR ($CDCl_3$) of **S2**.

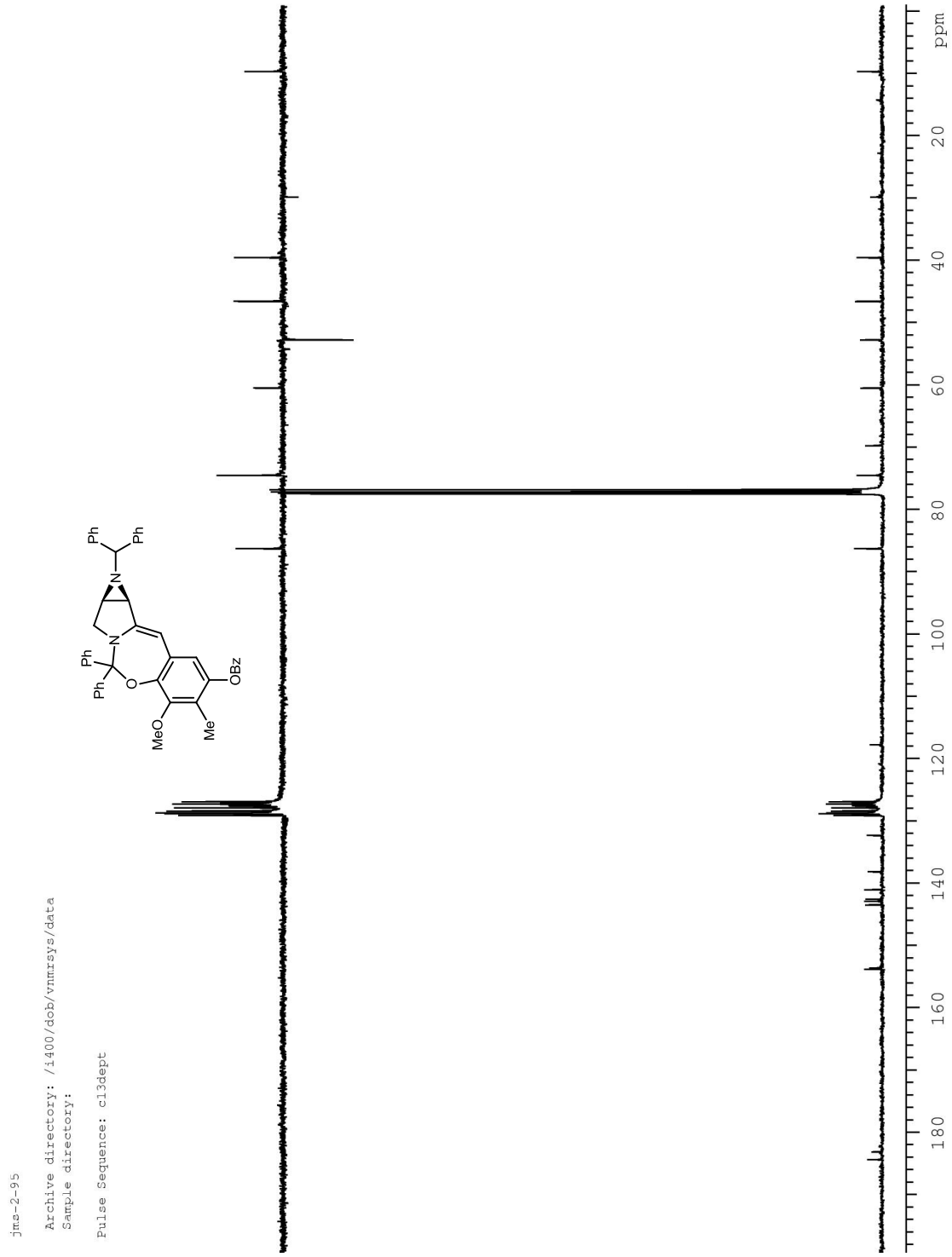


Figure 15. ^{1}H NMR ($CDCl_3$) of **12**.

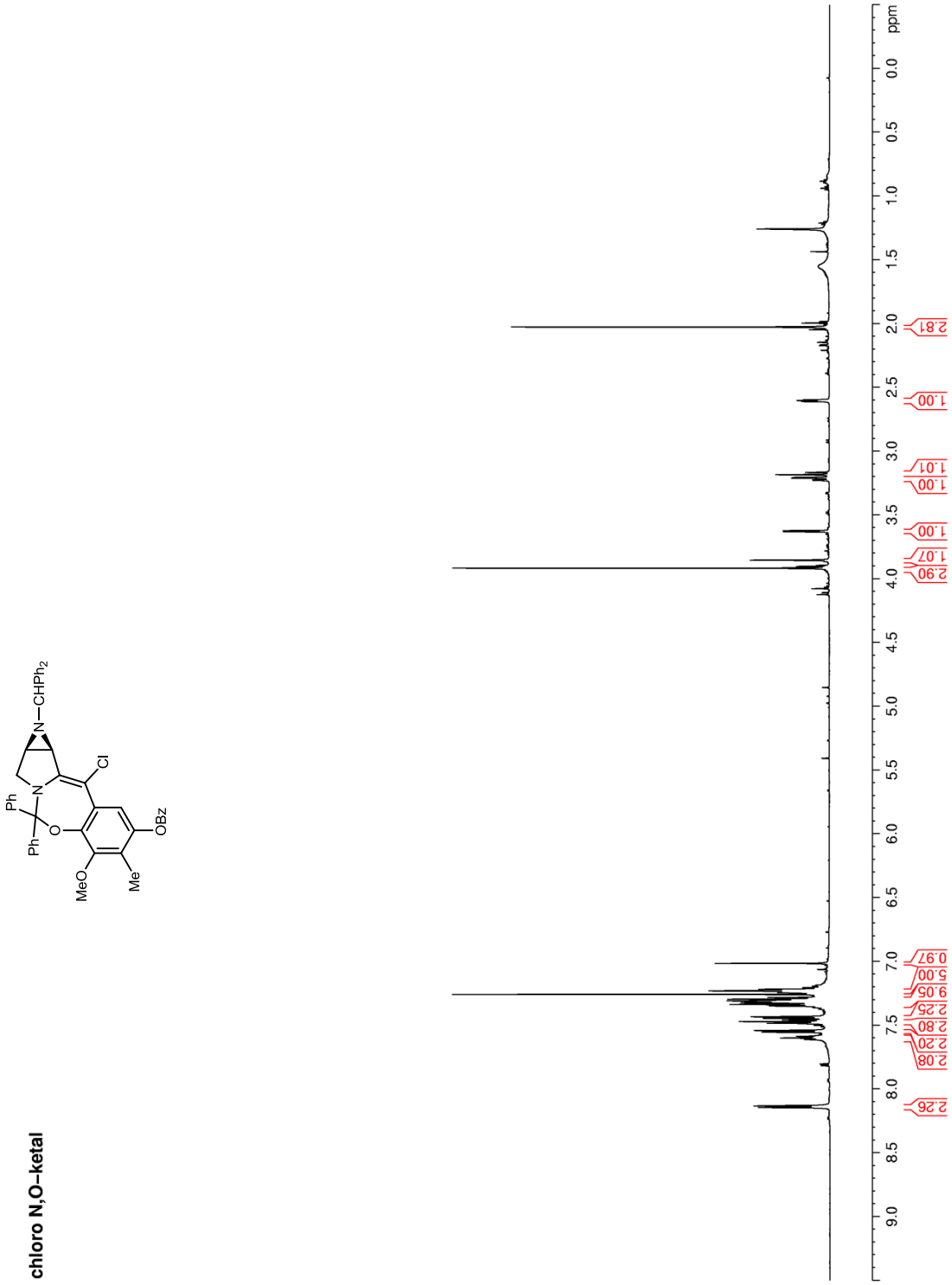


Figure 16. ^{13}C NMR ($CDCl_3$) of **12**.

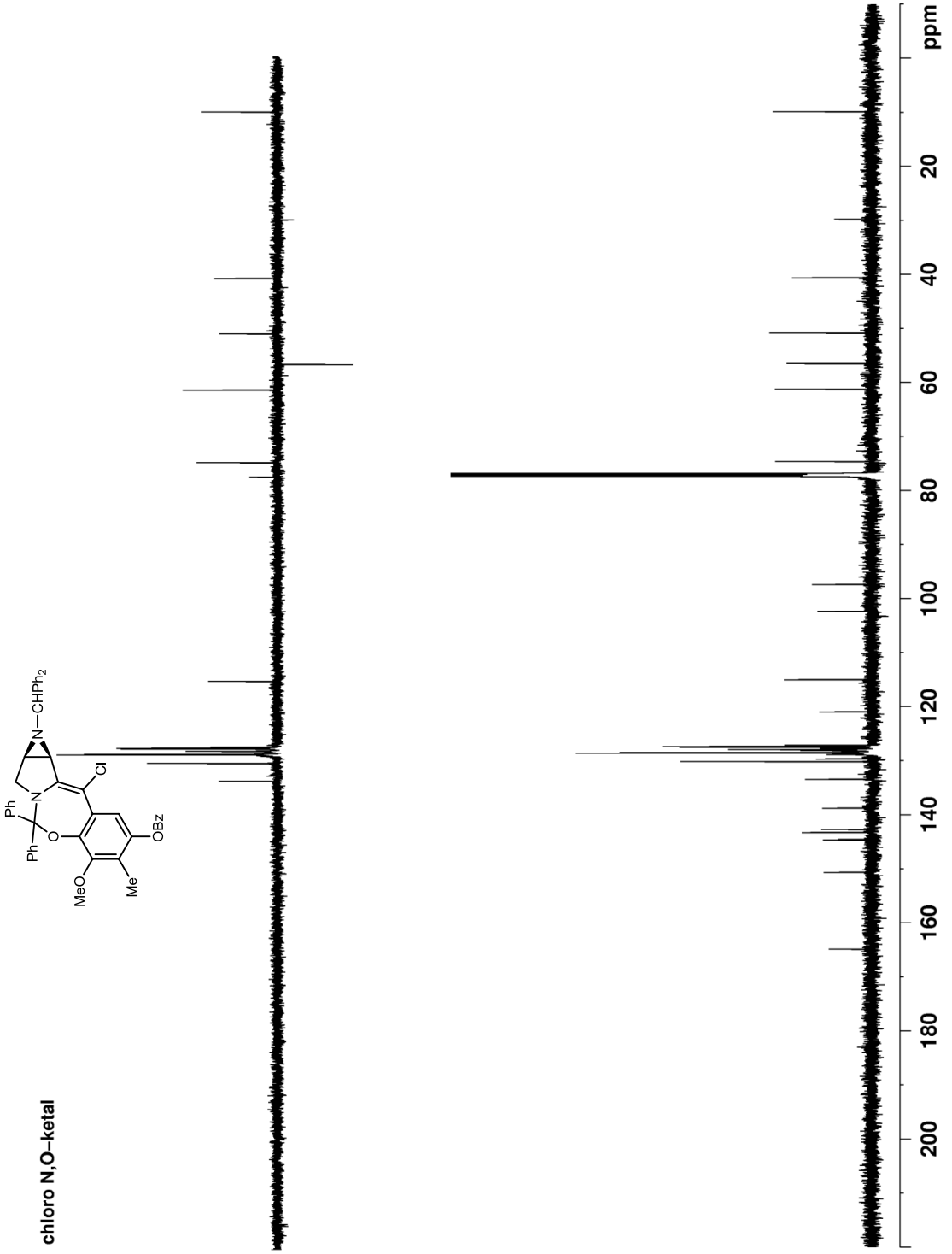


Figure 17. ^{1}H NMR ($CDCl_3$) of **S4**.

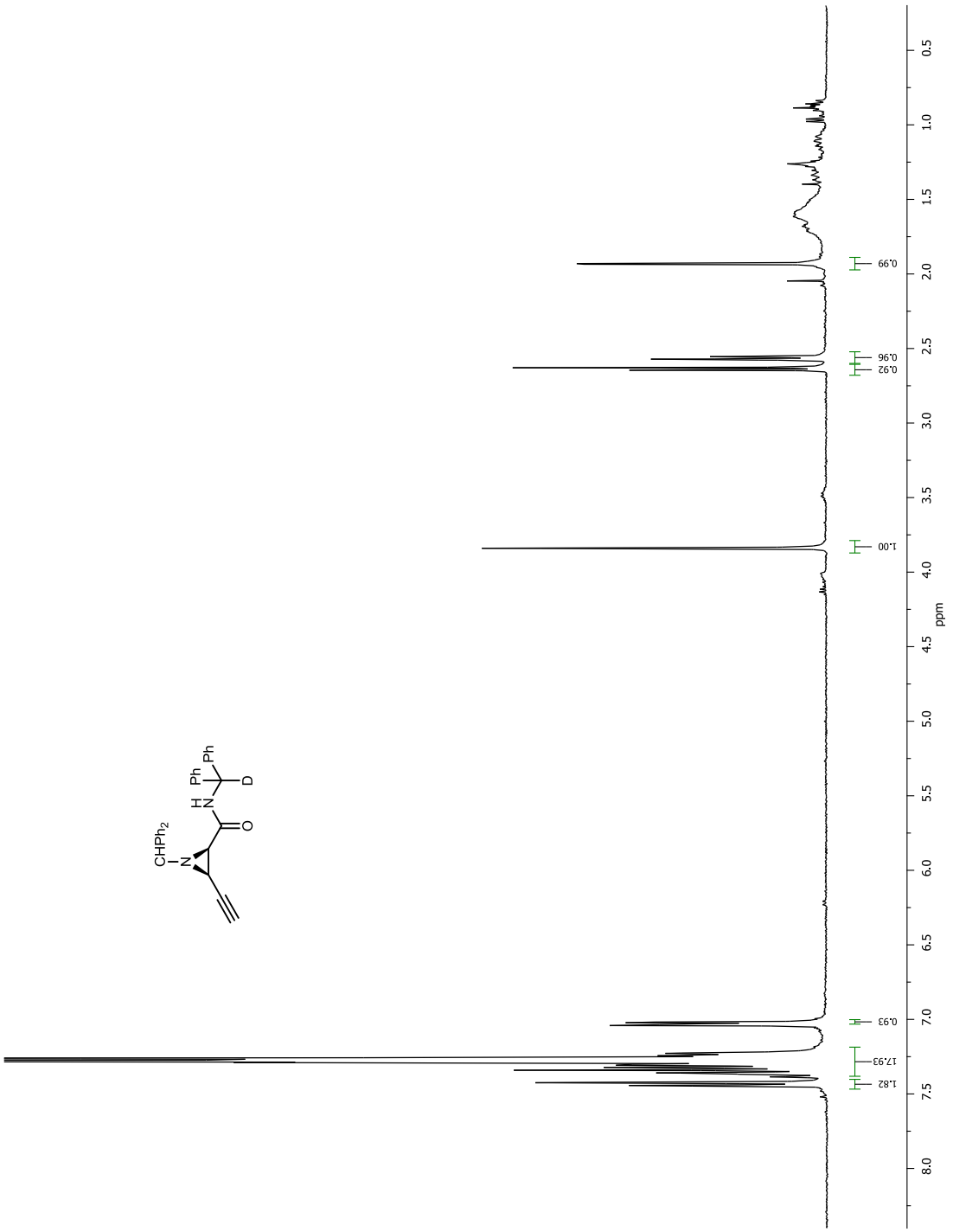


Figure 18. ^{13}C NMR ($CDCl_3$) of **S4**.

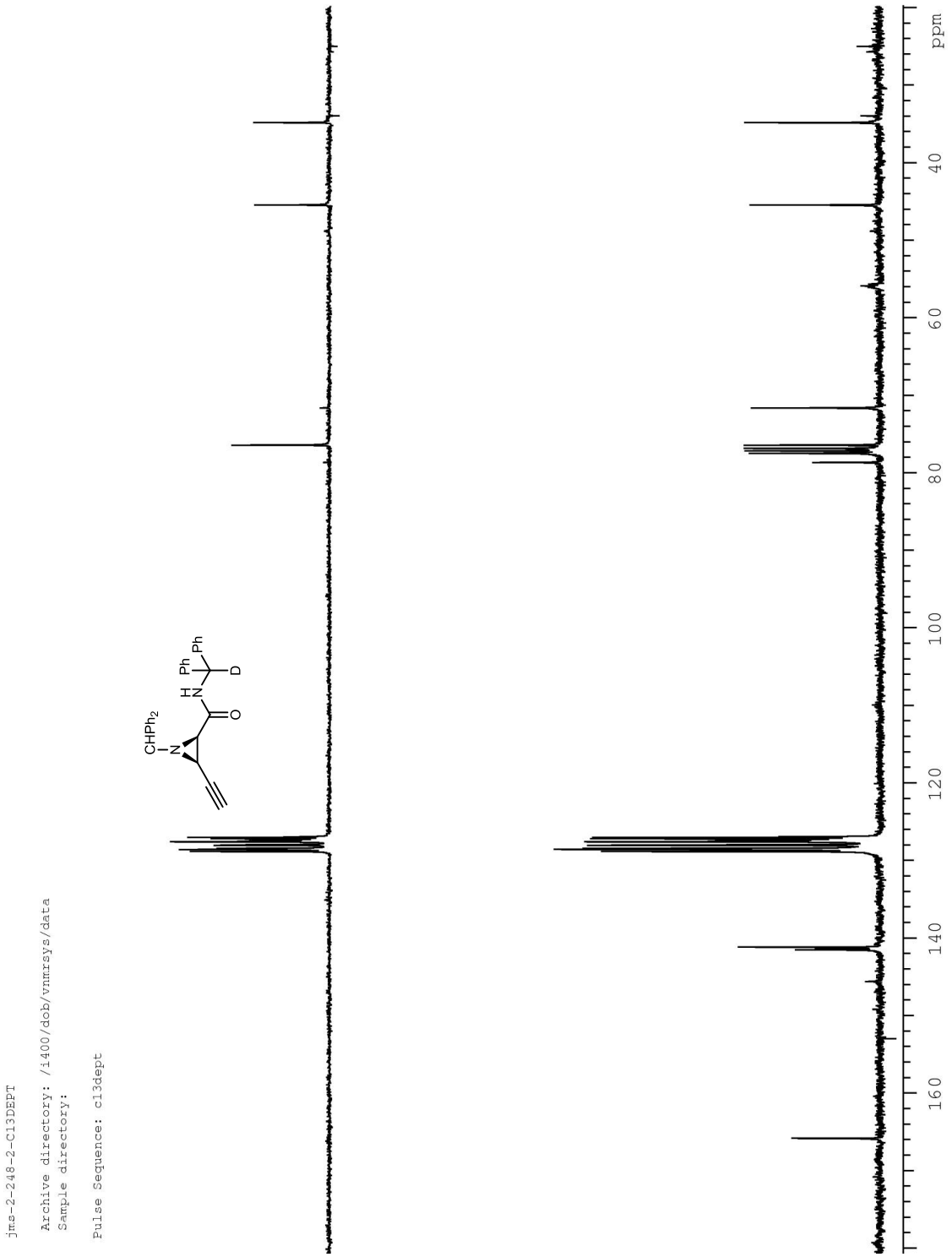


Figure 19. ^{1}H NMR ($CDCl_3$) of **13**.

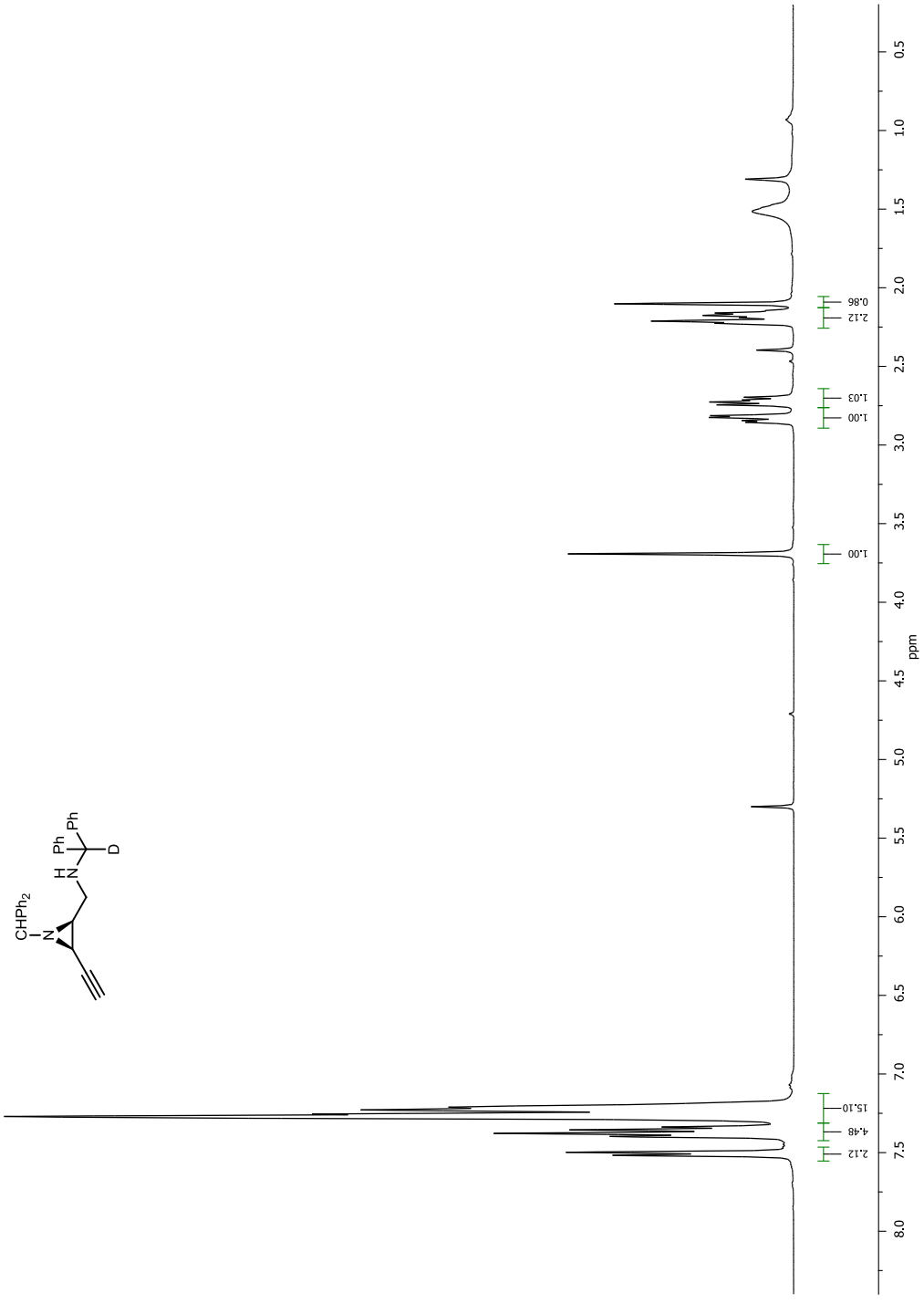


Figure 20. ^{13}C NMR ($CDCl_3$) of **13**.

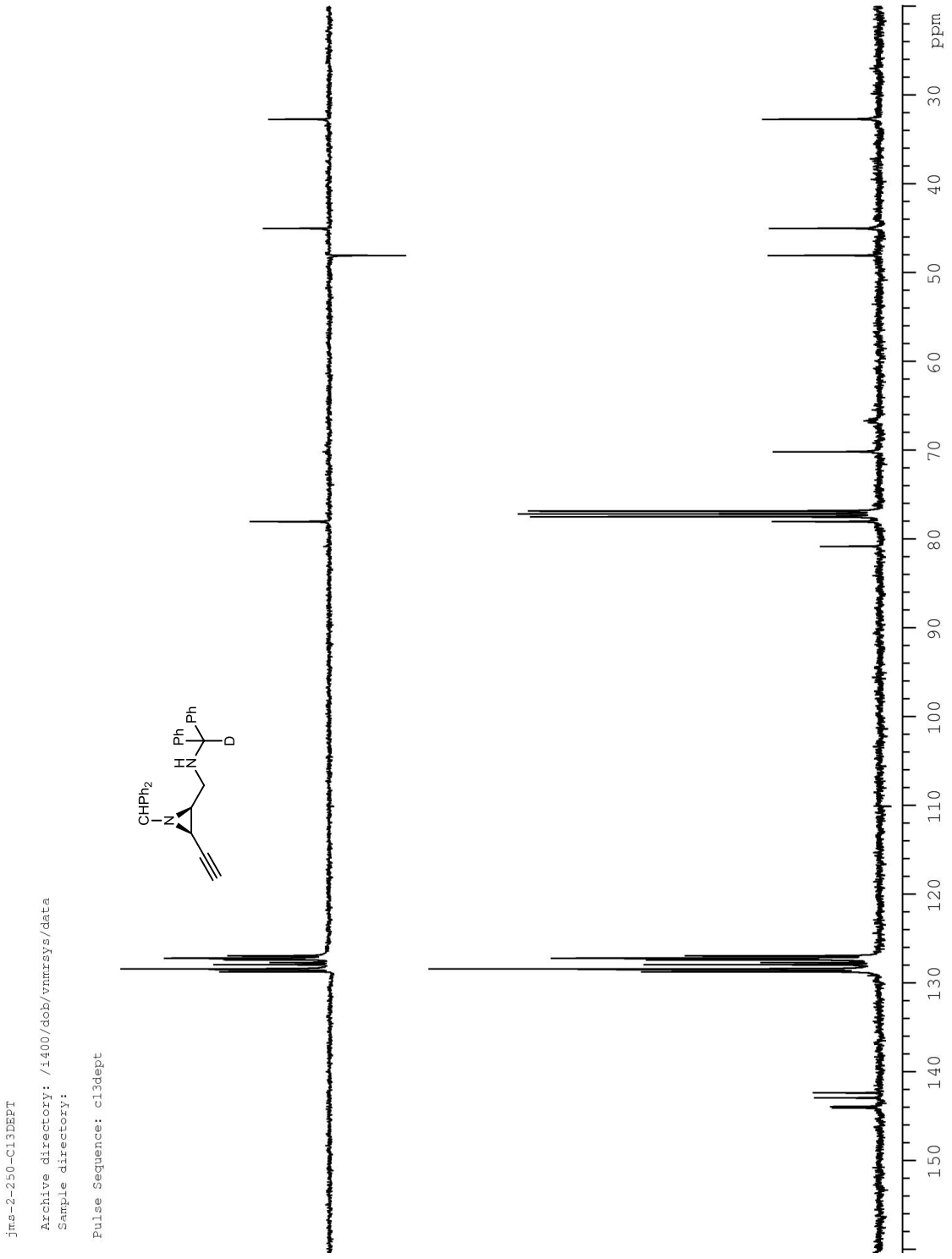


Figure 21. ^{1}H NMR ($CDCl_3$) of **14**.

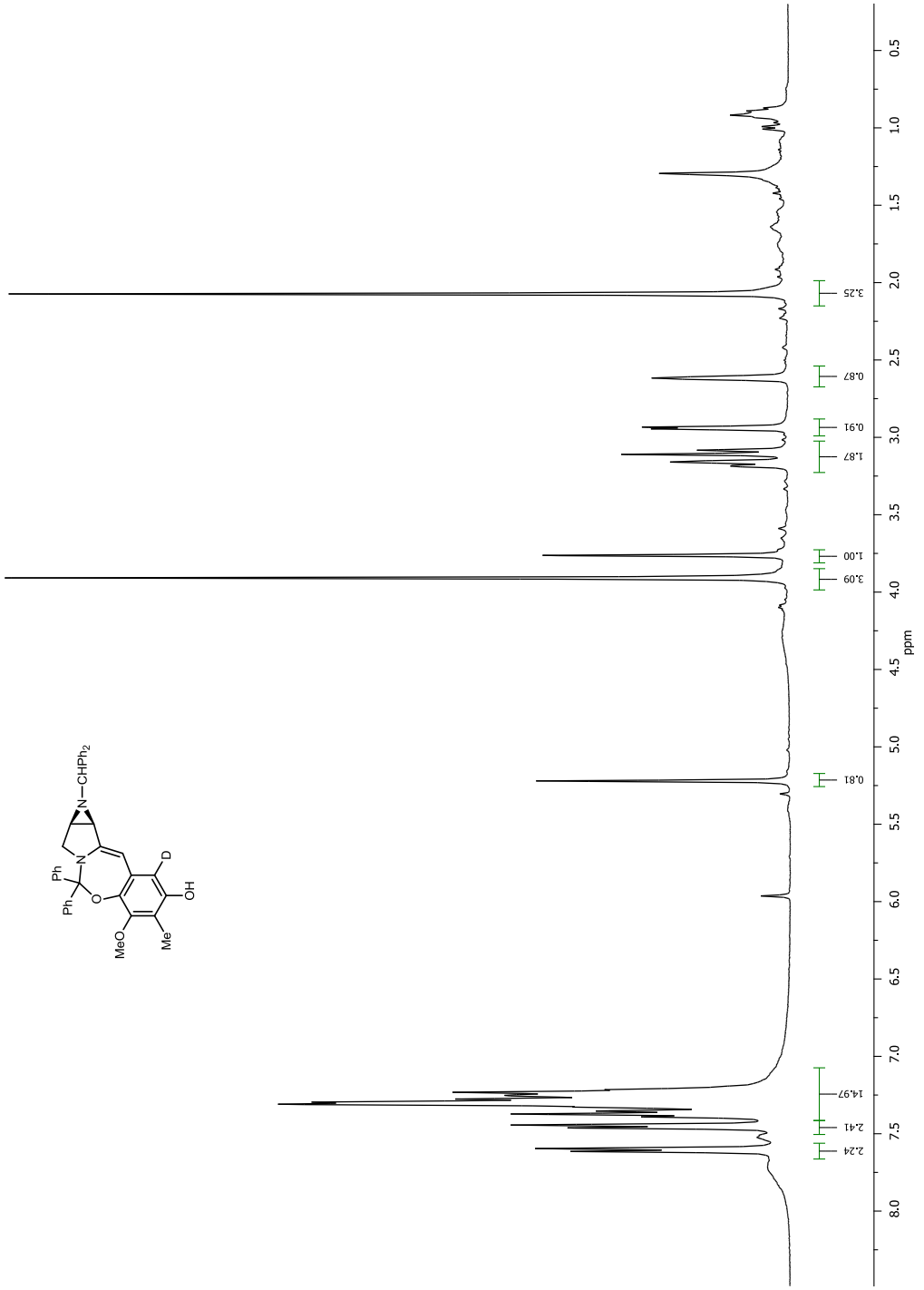
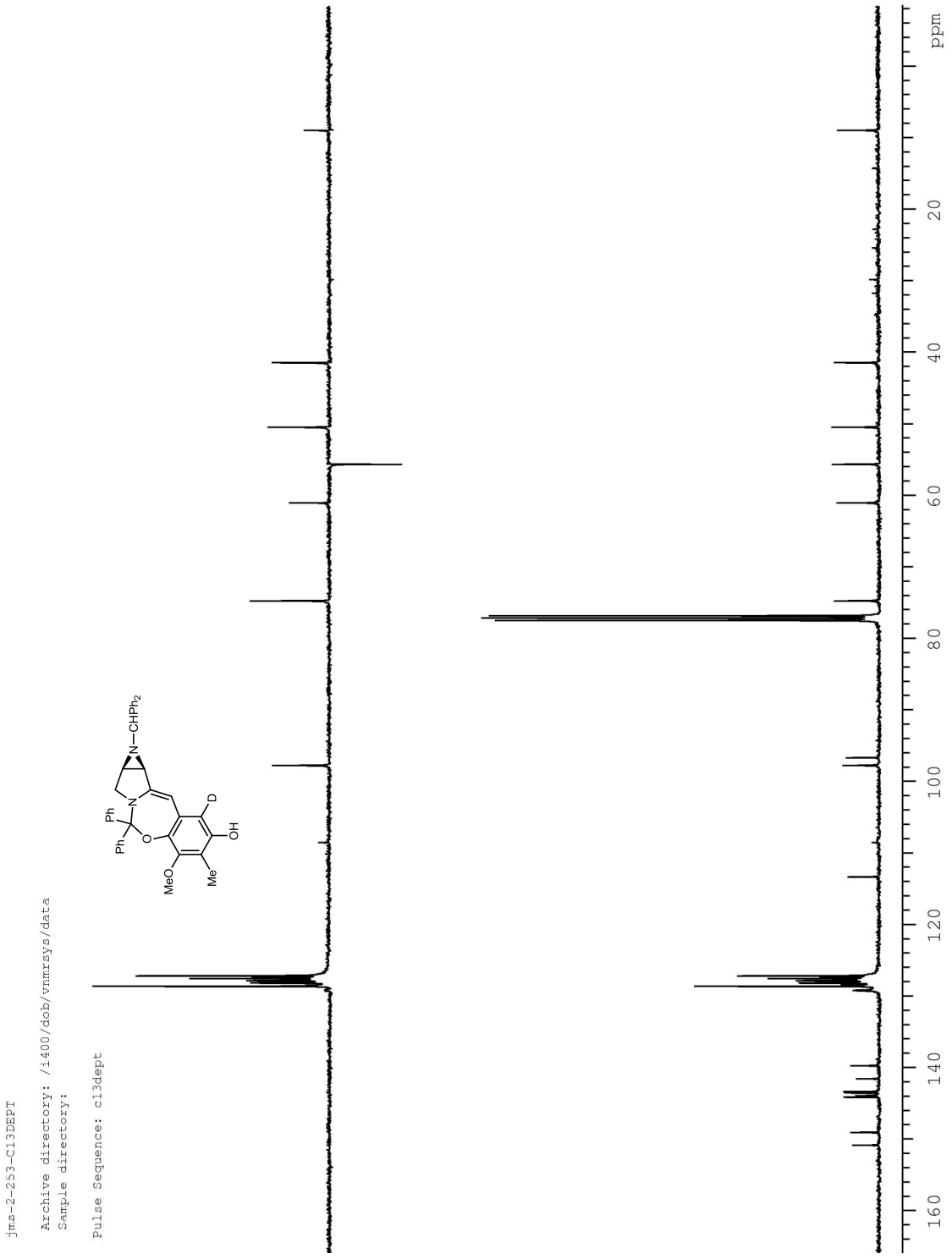
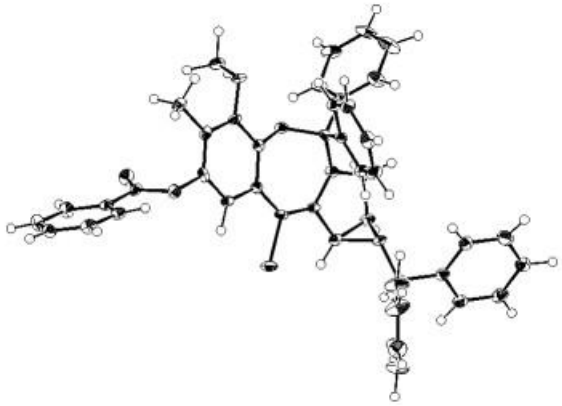


Figure 22. ^{13}C NMR ($CDCl_3$) of **14**.



X-ray Crystal Analysis of 12.

Figure 23. Crystal Structure of **12**



Note: Data were collected on a Bruker SMART 6000 sealed-tube system comprising a three-circle platform goniostat, an HOG crystal monochromator, a four kilopixel by four kilopixel single-chip CCD-based detector, a K761 high voltage generator, and a PC interface running Bruker's SMART software.

Table 1. Fractional Coordinates and Isotropic Thermal Parameters for **12**

Atom	x	y	z	Uiso
Cl(1)	9827(1)	844(1)	4639(1)	24(1)
O(10)	10237(2)	3213(1)	3856(1)	18(1)
O(42)	9727(2)	4255(1)	4894(1)	20(1)
O(45)	8510(2)	2517(1)	6852(1)	19(1)
O(47)	6845(2)	2783(1)	6246(2)	26(1)
N(5)	12270(3)	994(2)	3056(2)	17(1)
N(8)	11193(2)	2301(2)	3187(2)	17(1)
C(2)	10182(3)	1708(2)	4298(2)	16(1)
C(3)	10753(3)	1723(2)	3600(2)	15(1)
C(4)	11034(3)	1075(2)	3110(2)	18(1)
C(6)	11623(3)	1315(2)	2370(2)	18(1)
C(7)	11681(3)	2118(2)	2388(2)	18(1)
C(9)	11318(3)	2999(2)	3562(2)	17(1)
C(11)	9924(3)	3004(2)	4626(2)	15(1)
C(12)	9586(3)	3553(2)	5145(2)	18(1)
C(13)	9117(3)	3423(2)	5900(2)	18(1)
C(14)	9007(3)	2701(2)	6098(2)	17(1)
C(15)	9361(3)	2150(2)	5614(2)	16(1)
C(16)	9840(3)	2283(2)	4848(2)	16(1)
C(17)	12624(3)	246(2)	2915(2)	18(1)
C(18)	12925(3)	-94(2)	3750(2)	20(1)
C(19)	12851(4)	-824(2)	3839(3)	34(1)
C(20)	13182(4)	-1153(2)	4587(3)	39(1)
C(21)	13598(4)	-759(2)	5232(3)	33(1)
C(22)	13686(5)	-27(2)	5155(3)	40(1)
C(23)	13346(4)	303(2)	4409(3)	40(1)
C(24)	13609(3)	238(2)	2360(2)	20(1)
C(25)	13741(3)	-318(2)	1799(2)	22(1)
C(26)	14634(4)	-320(2)	1284(3)	27(1)
C(27)	15423(4)	204(2)	1317(3)	29(1)
C(28)	15307(4)	754(2)	1896(3)	30(1)
C(29)	14427(3)	767(2)	2408(3)	23(1)
C(30)	12162(3)	3005(2)	4300(2)	17(1)
C(31)	12763(3)	2400(2)	4521(2)	22(1)
C(32)	13490(3)	2421(2)	5206(2)	27(1)

C(33)	13647(3)	3053(2)	5644(2)	26(1)
C(34)	13063(3)	3658(2)	5413(2)	23(1)
C(35)	12309(3)	3636(2)	4753(2)	21(1)
C(36)	11547(3)	3560(2)	2906(2)	17(1)
C(37)	12586(4)	3848(2)	2810(2)	28(1)
C(38)	12750(4)	4375(2)	2201(3)	41(1)
C(39)	11866(4)	4597(2)	1705(3)	36(1)
C(40)	10833(4)	4299(2)	1792(2)	27(1)
C(41)	10681(4)	3778(2)	2385(2)	22(1)
C(43)	8838(4)	4492(2)	4347(3)	25(1)
C(44)	8727(4)	4017(2)	6441(3)	23(1)
C(46)	7393(3)	2603(2)	6857(2)	19(1)
C(48)	6932(3)	2446(2)	7671(2)	18(1)
C(49)	7619(3)	2349(2)	8377(2)	21(1)
C(50)	7119(4)	2231(2)	9127(3)	24(1)
C(51)	5991(3)	2211(2)	9179(3)	21(1)
C(52)	5314(4)	2306(2)	8479(3)	27(1)
C(53)	5792(3)	2420(2)	7728(2)	24(1)
H(54)	1057(3)	66(2)	321(2)	50
H(55)	1156(3)	108(2)	190(2)	25(12)
H(56)	1248(3)	229(2)	232(2)	16(10)
H(57)	1121(2)	228(2)	193(2)	9(9)
H(58)	918(3)	166(2)	582(2)	22(10)
H(59)	1201(3)	-6(2)	267(2)	50
H(60)	1247(4)	-112(2)	340(3)	70(16)
H(61)	1303(3)	-166(2)	463(2)	49(13)
H(62)	1397(3)	-98(2)	581(3)	64(15)
H(63)	1408(4)	28(2)	556(3)	66(16)
H(64)	1349(4)	82(3)	432(3)	77(17)
H(65)	1310(3)	-63(2)	176(2)	42(13)
H(66)	1475(3)	-68(2)	97(2)	31(12)
H(67)	1608(3)	17(2)	92(3)	50
H(68)	1593(3)	105(2)	191(2)	31(12)
H(69)	1429(3)	109(2)	279(2)	55(15)
H(70)	1265(2)	194(2)	425(2)	3(8)
H(71)	1394(3)	202(2)	537(2)	29(11)
H(72)	1421(2)	307(2)	613(2)	11(9)
H(73)	1320(3)	414(2)	570(2)	26(10)
H(74)	1187(3)	404(2)	464(2)	36(12)
H(75)	1328(3)	375(2)	315(2)	27(11)
H(76)	1359(3)	450(2)	214(2)	45(13)
H(77)	1199(3)	494(2)	125(3)	53(14)
H(78)	1028(2)	445(2)	144(2)	1(9)
H(79)	992(2)	361(2)	245(2)	5(9)
H(80)	886(3)	426(2)	385(2)	27(12)
H(81)	895(3)	506(2)	427(2)	48(13)
H(82)	811(3)	445(2)	465(2)	16(10)
H(83)	923(3)	445(2)	638(2)	47(13)
H(84)	796(3)	414(2)	634(2)	44(13)
H(85)	887(3)	388(2)	701(3)	47(14)
H(86)	842(3)	241(2)	837(2)	50
H(87)	760(3)	217(2)	958(2)	32(12)
H(88)	566(3)	215(2)	968(2)	30(12)
H(89)	454(3)	224(2)	853(2)	43(14)
H(90)	532(3)	248(2)	723(2)	15(9)

Notes:

1) Fractional coordinates are X 10**4 for non-hydrogen atoms and X 10**3 for hydrogen atoms. Uiso values are all X 10**3.

2) Isotropic values for those atoms refined anisotropically are calculated as one third of the trace of the orthogonalized Uij tensor.

3) Parameters without standard deviations were not varied.

Table 2. Anisotropic Thermal Parameters for **12**

Atom	U11	U22	U33	U23	U13	U12
Cl(1)	39(1)	12(1)	23(1)	2(1)	7(1)	-1(1)
O(10)	23(2)	14(1)	16(2)	-2(1)	2(1)	-1(1)
O(42)	27(2)	10(1)	23(2)	-1(1)	-1(1)	2(1)
O(45)	22(2)	22(2)	15(2)	2(1)	3(1)	1(1)
O(47)	25(2)	32(2)	20(2)	3(1)	-2(1)	5(1)
N(5)	23(2)	10(2)	17(2)	-2(1)	-1(2)	4(1)
N(8)	25(2)	15(2)	12(2)	1(1)	1(2)	-1(2)
C(2)	17(2)	10(2)	20(2)	4(2)	-4(2)	-2(2)
C(3)	21(2)	11(2)	14(2)	-1(2)	-5(2)	-1(2)
C(4)	21(2)	15(2)	19(2)	-1(2)	-2(2)	1(2)
C(6)	25(2)	15(2)	14(2)	-2(2)	-4(2)	2(2)
C(7)	23(3)	15(2)	17(2)	3(2)	1(2)	-1(2)
C(9)	19(2)	14(2)	17(2)	1(2)	4(2)	-3(2)
C(11)	14(2)	18(2)	13(2)	0(2)	-2(2)	-1(2)
C(12)	17(2)	12(2)	25(2)	1(2)	-6(2)	3(2)
C(13)	18(2)	22(2)	14(2)	-6(2)	1(2)	2(2)
C(14)	13(2)	25(2)	11(2)	0(2)	-1(2)	-3(2)
C(15)	19(2)	13(2)	16(2)	4(2)	-2(2)	2(2)
C(16)	14(2)	17(2)	16(2)	2(2)	-2(2)	1(2)
C(17)	21(2)	12(2)	20(2)	-1(2)	-1(2)	2(2)
C(18)	21(2)	20(2)	18(2)	1(2)	6(2)	-1(2)
C(19)	52(3)	24(2)	26(3)	0(2)	-4(2)	-10(3)
C(20)	59(4)	20(2)	38(3)	10(2)	-4(3)	-10(3)
C(21)	41(3)	36(3)	23(3)	7(2)	1(2)	6(2)
C(22)	67(4)	28(3)	24(3)	-6(2)	-11(3)	11(3)
C(23)	71(4)	24(3)	25(3)	3(2)	-7(3)	3(3)
C(24)	25(2)	16(2)	17(2)	2(2)	1(2)	3(2)
C(25)	22(3)	17(2)	27(3)	0(2)	-4(2)	1(2)
C(26)	37(3)	22(2)	22(3)	-4(2)	3(2)	5(2)
C(27)	31(3)	24(2)	33(3)	3(2)	9(2)	2(2)
C(28)	27(3)	26(3)	38(3)	5(2)	-3(2)	-2(2)
C(29)	24(2)	20(2)	24(3)	-2(2)	0(2)	1(2)
C(30)	20(2)	12(2)	17(2)	-2(2)	3(2)	-3(2)
C(31)	23(2)	16(2)	27(3)	0(2)	1(2)	0(2)
C(32)	29(3)	23(2)	30(3)	7(2)	-6(2)	4(2)
C(33)	18(2)	37(3)	21(2)	1(2)	-9(2)	-2(2)
C(34)	29(3)	22(2)	19(2)	-6(2)	5(2)	1(2)
C(35)	25(3)	18(2)	20(2)	-1(2)	2(2)	0(2)
C(36)	23(2)	14(2)	15(2)	-3(2)	-1(2)	0(2)
C(37)	30(3)	31(2)	23(3)	8(2)	-6(2)	-7(2)
C(38)	48(3)	41(3)	33(3)	14(2)	-5(3)	-21(3)
C(39)	54(3)	25(3)	30(3)	13(2)	1(3)	-15(2)
C(40)	45(3)	20(2)	15(2)	5(2)	-9(2)	2(2)
C(41)	29(3)	21(2)	16(2)	-6(2)	1(2)	-7(2)
C(43)	28(3)	15(2)	32(3)	0(2)	-2(2)	2(2)
C(44)	24(3)	21(2)	23(3)	-7(2)	-1(2)	5(2)
C(46)	16(2)	13(2)	27(3)	-10(2)	-1(2)	1(2)
C(48)	24(2)	12(2)	17(2)	-4(2)	1(2)	0(2)
C(49)	27(2)	16(2)	18(2)	-2(2)	-2(2)	3(2)
C(50)	30(3)	23(2)	17(2)	0(2)	-2(2)	2(2)
C(51)	29(3)	20(2)	16(2)	-2(2)	8(2)	-3(2)
C(52)	22(2)	31(3)	29(3)	0(2)	1(2)	-4(2)
C(53)	25(2)	29(2)	17(3)	5(2)	-3(2)	2(2)

Form of the anisotropic thermal parameter:
exp{ -2 pi**2 [h**2 (a*)**2 U11 + ... + 2 h k (a*) (b*) U12] }
All values are X 10**3

Table 3. Bond Distances (Å) for **12**

A	B	Distance
Cl(1)	C(2)	1.767(3)
O(10)	C(11)	1.372(4)
O(10)	C(9)	1.464(4)
O(42)	C(12)	1.388(4)
O(42)	C(43)	1.437(5)
O(45)	C(46)	1.362(4)
O(45)	C(14)	1.422(4)
O(47)	C(46)	1.217(4)
N(5)	C(6)	1.462(4)
N(5)	C(17)	1.485(4)
N(5)	C(4)	1.509(5)
N(8)	C(3)	1.390(4)
N(8)	C(9)	1.446(4)
N(8)	C(7)	1.480(5)
C(2)	C(3)	1.345(5)
C(2)	C(16)	1.466(5)
C(3)	C(4)	1.494(5)
C(4)	C(6)	1.485(5)
C(4)	H(54)	0.97(4)
C(6)	C(7)	1.506(5)
C(6)	H(55)	0.88(3)
C(7)	H(56)	1.03(3)
C(7)	H(57)	0.96(3)
C(9)	C(36)	1.526(5)
C(9)	C(30)	1.541(5)
C(11)	C(12)	1.398(5)
C(11)	C(16)	1.402(5)
C(12)	C(13)	1.386(5)
C(13)	C(14)	1.398(5)
C(13)	C(44)	1.501(5)
C(14)	C(15)	1.372(5)
C(15)	C(16)	1.409(5)
C(15)	H(58)	1.00(3)
C(17)	C(24)	1.519(5)
C(17)	C(18)	1.525(5)
C(17)	H(59)	1.01(4)
C(18)	C(19)	1.377(5)
C(18)	C(23)	1.381(6)
C(19)	C(20)	1.402(6)
C(19)	H(60)	1.01(4)
C(20)	C(21)	1.359(6)
C(20)	H(61)	0.97(4)
C(21)	C(22)	1.380(6)
C(21)	H(62)	1.09(4)
C(22)	C(23)	1.404(6)
C(22)	H(63)	0.98(4)
C(23)	H(64)	0.99(5)
C(24)	C(25)	1.393(5)
C(24)	C(29)	1.400(5)
C(25)	C(26)	1.390(6)
C(25)	H(65)	0.98(4)
C(26)	C(27)	1.368(6)
C(26)	H(66)	0.86(4)
C(27)	C(28)	1.402(6)
C(27)	H(67)	1.04(4)
C(28)	C(29)	1.374(5)
C(28)	H(68)	0.94(4)
C(29)	H(69)	0.88(4)
C(30)	C(31)	1.386(5)
C(30)	C(35)	1.398(5)
C(31)	C(32)	1.389(5)
C(31)	H(70)	0.97(3)
C(32)	C(33)	1.388(5)

C(32)	H(71)	0.96(4)
C(33)	C(34)	1.379(5)
C(33)	H(72)	1.02(3)
C(34)	C(35)	1.379(5)
C(34)	H(73)	1.03(4)
C(35)	H(74)	0.93(4)
C(36)	C(37)	1.382(5)
C(36)	C(41)	1.382(5)
C(37)	C(38)	1.413(5)
C(37)	H(75)	1.00(3)
C(38)	C(39)	1.378(6)
C(38)	H(76)	1.05(4)
C(39)	C(40)	1.380(6)
C(39)	H(77)	0.99(4)
C(40)	C(41)	1.385(5)
C(40)	H(78)	0.91(3)
C(41)	H(79)	0.98(3)
C(43)	H(80)	0.92(3)
C(43)	H(81)	1.08(4)
C(43)	H(82)	1.03(3)
C(44)	H(83)	1.02(4)
C(44)	H(84)	0.96(4)
C(44)	H(85)	0.96(4)
C(46)	C(48)	1.479(5)
C(48)	C(53)	1.387(5)
C(48)	C(49)	1.399(5)
C(49)	C(50)	1.392(5)
C(49)	H(86)	0.97(4)
C(50)	C(51)	1.371(5)
C(50)	H(87)	0.93(3)
C(51)	C(52)	1.385(5)
C(51)	H(88)	0.93(4)
C(52)	C(53)	1.380(5)
C(52)	H(89)	0.95(4)
C(53)	H(90)	0.98(3)

Table 4. Bond Angles (°) for **12**

A	B	C	Angle
C(11)	O(10)	C(9)	119.8(3)
C(12)	O(42)	C(43)	112.1(3)
C(46)	O(45)	C(14)	115.3(3)
C(6)	N(5)	C(17)	114.8(3)
C(6)	N(5)	C(4)	59.9(2)
C(17)	N(5)	C(4)	113.3(3)
C(3)	N(8)	C(9)	122.5(3)
C(3)	N(8)	C(7)	114.4(3)
C(9)	N(8)	C(7)	122.5(3)
C(3)	C(2)	C(16)	131.2(3)
C(3)	C(2)	Cl(1)	114.8(3)
C(16)	C(2)	Cl(1)	113.9(3)
C(2)	C(3)	N(8)	129.6(3)
C(2)	C(3)	C(4)	124.2(3)
N(8)	C(3)	C(4)	106.2(3)
C(6)	C(4)	C(3)	107.9(3)
C(6)	C(4)	N(5)	58.5(2)
C(3)	C(4)	N(5)	110.9(3)
C(6)	C(4)	H(54)	132(2)
C(3)	C(4)	H(54)	114(2)
N(5)	C(4)	H(54)	121(2)
N(5)	C(6)	C(4)	61.6(2)

N(5)	C(6)	C(7)	111.9(3)
C(4)	C(6)	C(7)	108.1(3)
N(5)	C(6)	H(55)	118(2)
C(4)	C(6)	H(55)	121(2)
C(7)	C(6)	H(55)	121(2)
N(8)	C(7)	C(6)	103.2(3)
N(8)	C(7)	H(56)	115.6(18)
C(6)	C(7)	H(56)	110.3(18)
N(8)	C(7)	H(57)	110.9(19)
C(6)	C(7)	H(57)	105.6(19)
H(56)	C(7)	H(57)	111(3)
N(8)	C(9)	O(10)	107.6(3)
N(8)	C(9)	C(36)	110.4(3)
O(10)	C(9)	C(36)	103.0(3)
N(8)	C(9)	C(30)	112.8(3)
O(10)	C(9)	C(30)	108.8(3)
C(36)	C(9)	C(30)	113.7(3)
O(10)	C(11)	C(12)	115.7(3)
O(10)	C(11)	C(16)	122.1(3)
C(12)	C(11)	C(16)	121.9(3)
C(13)	C(12)	O(42)	118.8(3)
C(13)	C(12)	C(11)	122.7(3)
O(42)	C(12)	C(11)	118.5(3)
C(12)	C(13)	C(14)	114.6(3)
C(12)	C(13)	C(44)	122.1(4)
C(14)	C(13)	C(44)	123.2(3)
C(15)	C(14)	C(13)	124.2(3)
C(15)	C(14)	O(45)	117.3(3)
C(13)	C(14)	O(45)	118.5(3)
C(14)	C(15)	C(16)	121.1(3)
C(14)	C(15)	H(58)	115.0(18)
C(16)	C(15)	H(58)	123.6(19)
C(11)	C(16)	C(15)	115.5(3)
C(11)	C(16)	C(2)	121.8(3)
C(15)	C(16)	C(2)	122.6(3)
N(5)	C(17)	C(24)	109.7(3)
N(5)	C(17)	C(18)	108.6(3)
C(24)	C(17)	C(18)	110.6(3)
N(5)	C(17)	H(59)	112(2)
C(24)	C(17)	H(59)	111(2)
C(18)	C(17)	H(59)	105(2)
C(19)	C(18)	C(23)	118.5(4)
C(19)	C(18)	C(17)	119.6(4)
C(23)	C(18)	C(17)	121.8(4)
C(18)	C(19)	C(20)	120.6(4)
C(18)	C(19)	H(60)	120(3)
C(20)	C(19)	H(60)	119(3)
C(21)	C(20)	C(19)	120.6(4)
C(21)	C(20)	H(61)	123(2)
C(19)	C(20)	H(61)	116(2)
C(20)	C(21)	C(22)	119.8(4)
C(20)	C(21)	H(62)	125(2)
C(22)	C(21)	H(62)	115(2)
C(21)	C(22)	C(23)	119.6(4)
C(21)	C(22)	H(63)	123(3)
C(23)	C(22)	H(63)	116(3)
C(18)	C(23)	C(22)	120.9(4)
C(18)	C(23)	H(64)	118(3)
C(22)	C(23)	H(64)	120(3)
C(25)	C(24)	C(29)	117.8(4)
C(25)	C(24)	C(17)	120.2(4)
C(29)	C(24)	C(17)	122.0(3)
C(26)	C(25)	C(24)	120.2(4)
C(26)	C(25)	H(65)	126(2)
C(24)	C(25)	H(65)	113(2)
C(27)	C(26)	C(25)	122.1(4)
C(27)	C(26)	H(66)	117(3)

C(25)	C(26)	H(66)	120(3)
C(26)	C(27)	C(28)	117.8(4)
C(26)	C(27)	H(67)	119(2)
C(28)	C(27)	H(67)	123(2)
C(29)	C(28)	C(27)	120.9(4)
C(29)	C(28)	H(68)	128(2)
C(27)	C(28)	H(68)	111(2)
C(28)	C(29)	C(24)	121.1(4)
C(28)	C(29)	H(69)	127(3)
C(24)	C(29)	H(69)	112(3)
C(31)	C(30)	C(35)	120.0(4)
C(31)	C(30)	C(9)	121.4(3)
C(35)	C(30)	C(9)	118.6(3)
C(30)	C(31)	C(32)	119.5(4)
C(30)	C(31)	H(70)	122.6(18)
C(32)	C(31)	H(70)	117.6(18)
C(33)	C(32)	C(31)	120.2(4)
C(33)	C(32)	H(71)	118(2)
C(31)	C(32)	H(71)	122(2)
C(34)	C(33)	C(32)	120.2(4)
C(34)	C(33)	H(72)	120.0(18)
C(32)	C(33)	H(72)	119.8(18)
C(33)	C(34)	C(35)	120.2(4)
C(33)	C(34)	H(73)	122(2)
C(35)	C(34)	H(73)	118.0(19)
C(34)	C(35)	C(30)	119.9(4)
C(34)	C(35)	H(74)	118(2)
C(30)	C(35)	H(74)	122(2)
C(37)	C(36)	C(41)	119.3(4)
C(37)	C(36)	C(9)	122.4(4)
C(41)	C(36)	C(9)	118.3(3)
C(36)	C(37)	C(38)	120.2(4)
C(36)	C(37)	H(75)	128(2)
C(38)	C(37)	H(75)	111(2)
C(39)	C(38)	C(37)	119.4(5)
C(39)	C(38)	H(76)	127(2)
C(37)	C(38)	H(76)	113(2)
C(38)	C(39)	C(40)	120.3(4)
C(38)	C(39)	H(77)	119(3)
C(40)	C(39)	H(77)	120(3)
C(39)	C(40)	C(41)	119.9(4)
C(39)	C(40)	H(78)	117.6(19)
C(41)	C(40)	H(78)	122(2)
C(36)	C(41)	C(40)	120.9(4)
C(36)	C(41)	H(79)	122.3(18)
C(40)	C(41)	H(79)	116.6(18)
O(42)	C(43)	H(80)	110(2)
O(42)	C(43)	H(81)	106(2)
H(80)	C(43)	H(81)	111(3)
O(42)	C(43)	H(82)	108.3(19)
H(80)	C(43)	H(82)	116(3)
H(81)	C(43)	H(82)	104(3)
C(13)	C(44)	H(83)	109(2)
C(13)	C(44)	H(84)	114(2)
H(83)	C(44)	H(84)	111(3)
C(13)	C(44)	H(85)	108(2)
H(83)	C(44)	H(85)	103(3)
H(84)	C(44)	H(85)	111(3)
O(47)	C(46)	O(45)	122.6(4)
O(47)	C(46)	C(48)	124.4(4)
O(45)	C(46)	C(48)	112.9(3)
C(53)	C(48)	C(49)	120.3(4)
C(53)	C(48)	C(46)	118.4(3)
C(49)	C(48)	C(46)	121.3(4)
C(50)	C(49)	C(48)	117.8(4)
C(50)	C(49)	H(86)	120(2)
C(48)	C(49)	H(86)	122(2)

C(51)	C(50)	C(49)	121.6(4)
C(51)	C(50)	H(87)	123(2)
C(49)	C(50)	H(87)	116(2)
C(50)	C(51)	C(52)	120.4(4)
C(50)	C(51)	H(88)	121(2)
C(52)	C(51)	H(88)	118(2)
C(53)	C(52)	C(51)	119.0(4)
C(53)	C(52)	H(89)	123(2)
C(51)	C(52)	H(89)	118(2)
C(52)	C(53)	C(48)	120.9(4)
C(52)	C(53)	H(90)	119.7(19)
C(48)	C(53)	H(90)	119.4(19)

Table 5. Torsional Angles (°) for **12**

A	B	C	D	Torsion Angle
C(16)	C(2)	C(3)	N(8)	-0.3(7)
Cl(1)	C(2)	C(3)	N(8)	-177.2(3)
C(16)	C(2)	C(3)	C(4)	179.9(4)
Cl(1)	C(2)	C(3)	C(4)	3.0(5)
C(9)	N(8)	C(3)	C(2)	14.8(6)
C(7)	N(8)	C(3)	C(2)	-174.3(4)
C(9)	N(8)	C(3)	C(4)	-165.4(3)
C(7)	N(8)	C(3)	C(4)	5.5(4)
C(2)	C(3)	C(4)	C(6)	177.6(3)
N(8)	C(3)	C(4)	C(6)	-2.2(4)
C(2)	C(3)	C(4)	N(5)	-120.1(4)
N(8)	C(3)	C(4)	N(5)	60.0(4)
C(17)	N(5)	C(4)	C(6)	-106.2(3)
C(6)	N(5)	C(4)	C(3)	-98.7(3)
C(17)	N(5)	C(4)	C(3)	155.1(3)
C(17)	N(5)	C(6)	C(4)	103.6(3)
C(17)	N(5)	C(6)	C(7)	-157.0(3)
C(4)	N(5)	C(6)	C(7)	99.4(4)
C(3)	C(4)	C(6)	N(5)	104.0(3)
C(3)	C(4)	C(6)	C(7)	-1.6(4)
N(5)	C(4)	C(6)	C(7)	-105.6(3)
C(3)	N(8)	C(7)	C(6)	-6.3(4)
C(9)	N(8)	C(7)	C(6)	164.6(3)
N(5)	C(6)	C(7)	N(8)	-61.5(4)
C(4)	C(6)	C(7)	N(8)	4.5(4)
C(3)	N(8)	C(9)	O(10)	-54.4(4)
C(7)	N(8)	C(9)	O(10)	135.5(3)
C(3)	N(8)	C(9)	C(36)	-166.0(3)
C(7)	N(8)	C(9)	C(36)	23.8(5)
C(3)	N(8)	C(9)	C(30)	65.6(4)
C(7)	N(8)	C(9)	C(30)	-104.5(4)
C(11)	O(10)	C(9)	N(8)	86.3(4)
C(11)	O(10)	C(9)	C(36)	-157.1(3)
C(11)	O(10)	C(9)	C(30)	-36.2(4)
C(9)	O(10)	C(11)	C(12)	126.6(3)
C(9)	O(10)	C(11)	C(16)	-59.7(5)
C(43)	O(42)	C(12)	C(13)	-96.5(4)
C(43)	O(42)	C(12)	C(11)	83.5(4)
O(10)	C(11)	C(12)	C(13)	171.8(3)
C(16)	C(11)	C(12)	C(13)	-1.9(6)
O(10)	C(11)	C(12)	O(42)	-8.3(5)
C(16)	C(11)	C(12)	O(42)	178.0(3)
O(42)	C(12)	C(13)	C(14)	179.9(3)
C(11)	C(12)	C(13)	C(14)	-0.2(6)
O(42)	C(12)	C(13)	C(44)	1.8(6)
C(11)	C(12)	C(13)	C(44)	-178.2(4)
C(12)	C(13)	C(14)	C(15)	2.2(6)
C(44)	C(13)	C(14)	C(15)	-179.7(4)
C(12)	C(13)	C(14)	O(45)	-178.6(3)

C(44)	C(13)	C(14)	O(45)	-0.5(6)
C(46)	O(45)	C(14)	C(15)	-106.4(4)
C(46)	O(45)	C(14)	C(13)	74.3(4)
C(13)	C(14)	C(15)	C(16)	-2.2(6)
O(45)	C(14)	C(15)	C(16)	178.6(3)
O(10)	C(11)	C(16)	C(15)	-171.3(3)
C(12)	C(11)	C(16)	C(15)	2.0(6)
O(10)	C(11)	C(16)	C(2)	5.9(6)
C(12)	C(11)	C(16)	C(2)	179.2(4)
C(14)	C(15)	C(16)	C(11)	0.0(6)
C(14)	C(15)	C(16)	C(2)	-177.2(4)
C(3)	C(2)	C(16)	C(11)	11.3(6)
Cl(1)	C(2)	C(16)	C(11)	-171.7(3)
C(3)	C(2)	C(16)	C(15)	-171.7(4)
Cl(1)	C(2)	C(16)	C(15)	5.3(5)
C(6)	N(5)	C(17)	C(24)	78.2(4)
C(4)	N(5)	C(17)	C(24)	144.5(3)
C(6)	N(5)	C(17)	C(18)	-160.8(3)
C(4)	N(5)	C(17)	C(18)	-94.5(4)
N(5)	C(17)	C(18)	C(19)	154.2(4)
C(24)	C(17)	C(18)	C(19)	-85.4(5)
N(5)	C(17)	C(18)	C(23)	-30.5(6)
C(24)	C(17)	C(18)	C(23)	90.0(5)
C(23)	C(18)	C(19)	C(20)	0.8(7)
C(17)	C(18)	C(19)	C(20)	176.4(4)
C(18)	C(19)	C(20)	C(21)	-1.0(8)
C(19)	C(20)	C(21)	C(22)	0.6(8)
C(20)	C(21)	C(22)	C(23)	0.0(8)
C(19)	C(18)	C(23)	C(22)	-0.3(8)
C(17)	C(18)	C(23)	C(22)	-175.7(4)
C(21)	C(22)	C(23)	C(18)	-0.1(8)
N(5)	C(17)	C(24)	C(25)	-146.1(3)
C(18)	C(17)	C(24)	C(25)	94.1(4)
N(5)	C(17)	C(24)	C(29)	35.9(5)
C(18)	C(17)	C(24)	C(29)	-83.9(4)
C(29)	C(24)	C(25)	C(26)	-2.9(6)
C(17)	C(24)	C(25)	C(26)	179.1(4)
C(24)	C(25)	C(26)	C(27)	1.7(6)
C(25)	C(26)	C(27)	C(28)	0.0(6)
C(26)	C(27)	C(28)	C(29)	-0.3(6)
C(27)	C(28)	C(29)	C(24)	-1.0(6)
C(25)	C(24)	C(29)	C(28)	2.6(6)
C(17)	C(24)	C(29)	C(28)	-179.4(4)
N(8)	C(9)	C(30)	C(31)	3.6(5)
O(10)	C(9)	C(30)	C(31)	122.9(4)
C(36)	C(9)	C(30)	C(31)	-123.0(4)
N(8)	C(9)	C(30)	C(35)	-176.0(3)
O(10)	C(9)	C(30)	C(35)	-56.7(4)
C(36)	C(9)	C(30)	C(35)	57.4(5)
C(35)	C(30)	C(31)	C(32)	1.6(6)
C(9)	C(30)	C(31)	C(32)	-178.0(4)
C(30)	C(31)	C(32)	C(33)	-2.7(6)
C(31)	C(32)	C(33)	C(34)	1.6(6)
C(32)	C(33)	C(34)	C(35)	0.8(6)
C(33)	C(34)	C(35)	C(30)	-1.9(6)
C(31)	C(30)	C(35)	C(34)	0.8(6)
C(9)	C(30)	C(35)	C(34)	-179.6(4)
N(8)	C(9)	C(36)	C(37)	-104.6(4)
O(10)	C(9)	C(36)	C(37)	140.7(4)
C(30)	C(9)	C(36)	C(37)	23.3(5)
N(8)	C(9)	C(36)	C(41)	74.5(4)
O(10)	C(9)	C(36)	C(41)	-40.1(4)
C(30)	C(9)	C(36)	C(41)	-157.6(3)
C(41)	C(36)	C(37)	C(38)	1.9(6)
C(9)	C(36)	C(37)	C(38)	-179.0(4)
C(36)	C(37)	C(38)	C(39)	-0.1(7)
C(37)	C(38)	C(39)	C(40)	-1.0(7)

C(38)	C(39)	C(40)	C(41)	0.3(7)
C(37)	C(36)	C(41)	C(40)	-2.6(6)
C(9)	C(36)	C(41)	C(40)	178.2(3)
C(39)	C(40)	C(41)	C(36)	1.5(6)
C(14)	O(45)	C(46)	O(47)	4.2(5)
C(14)	O(45)	C(46)	C(48)	-176.5(3)
O(47)	C(46)	C(48)	C(53)	7.8(6)
O(45)	C(46)	C(48)	C(53)	-171.5(3)
O(47)	C(46)	C(48)	C(49)	-170.0(4)
O(45)	C(46)	C(48)	C(49)	10.7(5)
C(53)	C(48)	C(49)	C(50)	-0.3(6)
C(46)	C(48)	C(49)	C(50)	177.5(3)
C(48)	C(49)	C(50)	C(51)	-0.1(6)
C(49)	C(50)	C(51)	C(52)	0.3(6)
C(50)	C(51)	C(52)	C(53)	0.1(6)
C(51)	C(52)	C(53)	C(48)	-0.5(6)
C(49)	C(48)	C(53)	C(52)	0.6(6)
C(46)	C(48)	C(53)	C(52)	-177.2(4)

Table 6. Summary of X-Ray Crystallographic Data for **12**

Empirical Formula	C46H37ClN2O4
Color of Crystal:	colorless
Crystal Dimensions were:	0.40 x 0.05 x 0.03 mm.
Space Group:	P2(1)/c
Cell Dimensions (at 121(2) K; 868 reflections)	
a =	12.104(3)
b =	18.720(4)
c =	16.171(4)
alpha =	90
beta =	92.131(6)
gamma =	90
Z (Molecules/cell):	4
Volume:	3661.6(15)
Calculated Density:	1.301
Wavelength:	0.71073
Molecular Weight:	717.23
F(000):	1504
Linear Absorption Coefficient:	0.153