

Supporting Information

An Efficient Synthesis of D-*erythro*- and D-*threo*-Sphingosine from D-Glucose:

Olefin Cross Metathesis Approach

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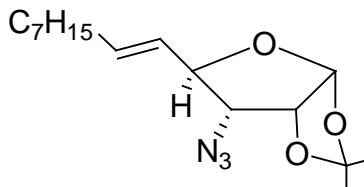
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General Experimental Methods. Melting points were recorded with Thomas Hoover melting point apparatus and are uncorrected. IR spectra were recorded with FTIR as a thin film or in nujol mull or using KBr pellets and are expressed in cm^{-1} . ^1H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded using CDCl_3 as a solvent. Chemical shifts were reported in δ unit (ppm) with reference to TMS as an internal standard and J values are given in Hz. Decoupling and DEPT experiments confirmed the assignments of the signals. Elemental analyses were carried out with C, H-analyzer. Optical rotations were measured using polarimeter at 25 °C. Thin layer chromatography was performed on pre-coated plates (0.25 mm, silica gel 60 F₂₅₄). Column chromatography was carried out with silica gel (100-200 mesh). The reactions were carried out in oven-dried glassware under dry N_2 . Methanol, pyridine, THF, dichloromethane were purified and dried before use. n-Hexane was used is the distillation fraction between 40-60 °C. Grubbs catalyst **A** and **B** were purchased from Aldrich. After decomposition of the reaction with water, the work-up involves- washing of combined organic layer with water, brine, drying over anhydrous sodium sulfate and evaporation of solvent at reduced pressure.

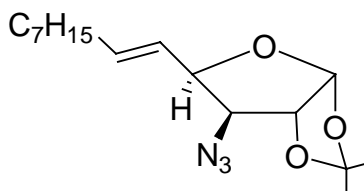
Cross coupled product 3a:



To a stirred solution of compound **2a** (0.10 g, 0.47 mmol) and 1-nonene (0.16 mL, 0.95 mmol) in dry DCM (15 mL) at 30 °C for 10 min was added the Grubbs catalyst **B** (0.04 g, 0.047 mmol). The mixture was stirred for 15 h and after completion of reaction (TLC monitoring), the solvent was evaporated and the crude product was purified by column chromatography to give cross-coupled product **3a**.

Yield: 83% (0.12 g, thick liquid). $[\alpha]_D = +55.0$ (c 0.5, CHCl_3); IR (KBr) 2930, 2110, 1590 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 0.95 (t, $J = 6.7$ Hz, 3H, CH_3), 1.27-1.62 (m, 10H, CH_2), 1.32 (s, 3H, CH_3), 1.53 (s, 3H, CH_3), 2.05-2.10 (m, 2H, H-7), 3.12 (dd, $J = 9.2, 4.3$ Hz, 1H, H-3), 4.39 (dd, $J = 9.2, 7.3$ Hz, 1H, H-4), 4.59 (dd, $J = 4.3, 3.5$ Hz, 1H, H-2), 5.34 (dd, $J = 15.4, 7.3$ Hz, 1H, H-5), 5.70 (d, $J = 3.5$ Hz, 1H, H-1), 5.89 (dt, $J = 15.4, 6.8$ Hz, 1H, H-6); ^{13}C NMR (75 MHz, CDCl_3): δ 14.2, 22.8, 26.1, 26.5, 28.6, 29.0 (s), 29.6, 31.7, 32.8, 68.2, 80.7, 83.4, 104.1, 111.2, 122.2, 137.8. Anal. Calcd. for $\text{C}_{16}\text{H}_{27}\text{N}_3\text{O}_3$: C, 62.11; H, 8.80. Found: C, 62.13; H, 8.73.

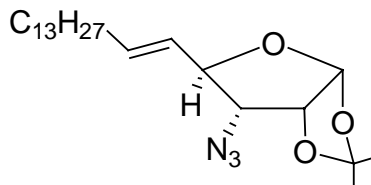
Cross coupled product 3b:



The same experimental procedure was followed, as was used for obtaining compound **3a** from **2a**, for the conversion of **2b** to give **3b**.

Yield: 86% (thick liquid). $[\alpha]_D = -44.4$ (c 0.2, CHCl_3); IR (neat) 2939, 2113, 1595 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 0.91 (t, $J = 6.7$ Hz, 3H, CH_3), 1.28-1.62 (m, 10H, CH_2), 1.30 (s, 3H, CH_3), 1.56 (s, 3H, CH_3), 2.09-2.16 (m, 2H, H-7), 3.84 (d, $J = 3.0$ Hz, 1H, H-3), 4.66 (d, $J = 3.8$ Hz, 1H, H-2), 4.72 (dd, $J = 7.4, 3.2$ Hz, 1H, H-4), 5.58 (dd, $J = 15.3, 7.4$ Hz, 1H, H-5), 5.93 (d, $J = 3.8$ Hz, 1H, H-1), 5.97 (dt, $J = 15.3, 7.3$ Hz, 1H, H-6); ^{13}C NMR (75 MHz, CDCl_3): δ 14.2, 22.7, 26.2, 26.6, 28.8, 29.2 (s), 29.8, 31.9, 32.5, 68.1, 80.7, 83.6, 104.2, 111.8, 122.3, 137.7. Anal. Calcd. for $\text{C}_{16}\text{H}_{27}\text{N}_3\text{O}_3$: C, 62.11; H, 8.80. Found: C, 62.17; H, 8.76.

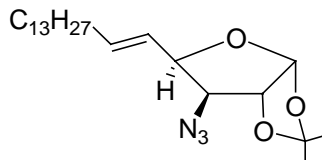
Cross coupled product 4a:



The same experimental procedure was followed, as was used for obtaining compound **3a** from **2a**, for the conversion of **2a** to give **4a**.

Yield: 85% (white solid, m.p. 48-50 °C). $[\alpha]_D = + 51.3$ (*c* 0.4, CHCl₃); IR (KBr) 2927, 2109, 1598 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 0.80 (t, *J* = 6.6 Hz, 3H, CH₃), 1.18-1.50 (m, 22H, CH₂), 1.28 (s, 3H, CH₃), 1.52 (s, 3H, CH₃), 1.98-2.08 (m, 2H, H-7), 3.11 (dd, *J* = 9.3, 4.4 Hz, 1H, H-3), 4.38 (dd, *J* = 9.3, 7.7 Hz, 1H, H-4), 4.61 (dd, *J* = 4.4, 3.8 Hz, 1H, H-2), 5.34 (dd, *J* = 15.1, 7.7 Hz, 1H, H-5), 5.71 (d, *J* = 3.8 Hz, 1H, H-1), 5.88 (dt, *J* = 15.1, 6.8 Hz, 1H, H-6); ¹³C NMR (75 MHz, CDCl₃): δ 14.2, 22.8, 26.3, 26.4, 28.7, 29.2, 29.4, 29.5, 29.6, 29.7 (s), 32.0, 32.5, 64.8, 78.7, 79.7, 103.6, 112.8, 124.9, 138.5. Anal. Calcd. for C₂₂H₃₉N₃O₃: C, 67.14; H, 9.99. Found: C, 67.17; H, 9.95.

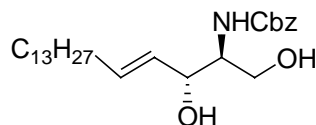
Cross coupled product 4b:



The same experimental procedure was followed, as was used for obtaining compound **3a** from **2a**, for the conversion of **2b** to give **4b**.

Yield: 87% (thick liquid). $[\alpha]_D = -40.0$ (c 0.2, CHCl_3); IR (neat) 2935, 2110, 1605 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 0.85 (t, $J = 6.8$ Hz, 3H, CH_3), 1.20-1.35 (m, 22H, CH_2), 1.45 (s, 3H, CH_3), 1.58 (s, 3H, CH_3), 1.97-2.14 (m, 2H, H-7), 3.84 (d, $J = 3.2$ Hz, 1H, H-3), 4.65 (d, $J = 3.9$ Hz, 1H, H-2), 4.71 (dd, $J = 7.4, 3.2$ Hz, 1H, H-4), 5.58 (dd, $J = 7.4, 15.3$ Hz, 1H, H-5), 5.92 (d, $J = 3.9$ Hz, 1H, H-1), 5.97 (dt, $J = 15.3, 6.6$ Hz, 1H, H-6); ^{13}C NMR (75 MHz, CDCl_3): δ 14.1, 22.7, 26.1, 26.5, 28.7, 29.1, 29.3, 29.4, 29.5, 29.6 (s), 31.9, 32.4, 68.1, 80.7, 83.7, 104.3, 111.8, 122.4, 137.8. Anal. Calcd. for $\text{C}_{22}\text{H}_{39}\text{N}_3\text{O}_3$ (393.56): C, 67.14; H, 9.99. Found: C, 67.19; H, 9.96.

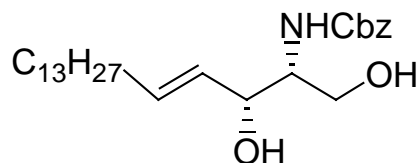
Cbz-D-erythro-Sphingosine 1c:



A solution of **4a** (0.10 g, 0.254 mmol) in TFA- H_2O (3 mL, 4:1) was stirred at 25 °C for 2.5 h. Trifluoroacetic acid was co-evaporated with benzene to furnish hemiacetal as a thick liquid. To an ice-cooled solution of hemiacetal (0.10 g, 0.28 mmol) in acetone-water (10 mL, 5:1) was added sodium metaperiodate (0.07 g, 0.34 mmol). After stirring the reaction for 2.5 h, workup and column purification (n-hexane/ethyl acetate = 4/1) afforded an aldehyde. To an ice-cooled suspension of LAH (0.04 g, 0.85 mmol) in THF (5 mL), the solution above aldehyde (0.10 g, 0.28 mmol) in THF (10 mL) was added slowly. The reaction mixture was stirred for 2 h at 25 °C and usual workup afforded *D-erythro*-sphingosine as a waxy solid. To an ice-cooled solution of *D-erythro*-sphingosine (0.09 g, 0.30 mmol) in methanol-water (10 mL, 9:1) was added benzylchloroformate (0.05 mL, 0.36 mmol) and sodium bicarbonate (0.07 g, 0.84 mmol). Reaction mixture was stirred for 6 h at 25 °C. Usual workup and purification by column chromatography afforded *Cbz-D-erythro-sphingosine 1c*.

Yield: 77% (0.07 g, white solid, m.p. 77-78 °C). $[\alpha]_D = + 2.8$ (*c* 0.5, CHCl₃); IR (neat) 3400-3200 (broad), 1695, 1612, 986 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 0.88 (t, *J* = 6.3 Hz, 3H, CH₃), 1.24-1.32 (m, 22H, CH₂), 1.96-2.08 (m, 2H, H-6), 2.45 (br, 2H, OH), 3.65-3.71 (m, 1H, H-2), 3.77-3.79 (m, 2H, H-1), 4.32-4.36 (m, 1H, H-3), 5.10 (s, 2H, COOCH₂Ph), 5.48 (dd, *J* = 15.1, 6.3 Hz, 1H, H-4), 5.68 (br, 1H, NH), 5.73 (dt, *J* = 15.4, 6.6 Hz, 1H, H-5), 7.25-7.33 (m, 5H, aromatic); ¹³C NMR (75 MHz, CDCl₃) δ 14.2, 22.8, 29.1, 29.2, 29.4, 29.6, 29.7 (s), 29.8 (s), 31.9, 32.2, 55.7, 64.4, 67.1, 73.5, 128.3, 128.1, 128.4 (s), 128.5, 134.8, 136.1, 156.5. Anal. Calcd for C₂₆H₄₃NO₄: C, 72.02; H, 10.00. Found: C, 72.07; H, 9.94.

Cbz-D-threo-Sphingosine 1d:



The same experimental procedure was followed, as was used for obtaining compound **1c** from **4a**, for the conversion of **4b** to give **1d**.

Yield: 75% (0.47 g, white solid, m.p. 47-50 °C). $[\alpha]_D = + 5.7$ (*c* 0.4, CHCl₃); IR (neat) 3400-3200 (broad), 1691, 1606, 1076 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 0.88 (t, *J* = 6.3 Hz, 3H, CH₃), 1.26-1.33 (m, 22H, CH₂), 1.98-2.08 (m, 2H, H-6), 2.43 (br, 2H, OH), 3.65-3.69 (m, 1H, H-2), 3.76-3.79 (m, 2H, H-1), 4.33-4.35 (m, 1H, H-3), 5.09 (s, 2H, COOCH₂Ph), 5.48 (dd, *J* = 15.4, 6.6 Hz, 1H, H-4), 5.69 (br, 1H, NH), 5.73 (dt, *J* = 15.4, 6.6 Hz, 1H, H-5), 7.24-7.34 (m, 5H, aromatic); ¹³C NMR (75 MHz, CDCl₃) δ 14.2, 22.8, 29.1, 29.2, 29.4, 29.6, 29.7 (s), 29.8 (s), 31.9, 32.3, 55.8, 64.0, 66.9, 73.1, 128.0, 128.4 (s), 128.5, 134.1, 136.2, 156.8. Anal. Calcd for C₂₆H₄₃NO₄: C, 72.02; H, 10.00. Found: C, 72.11; H, 9.98.

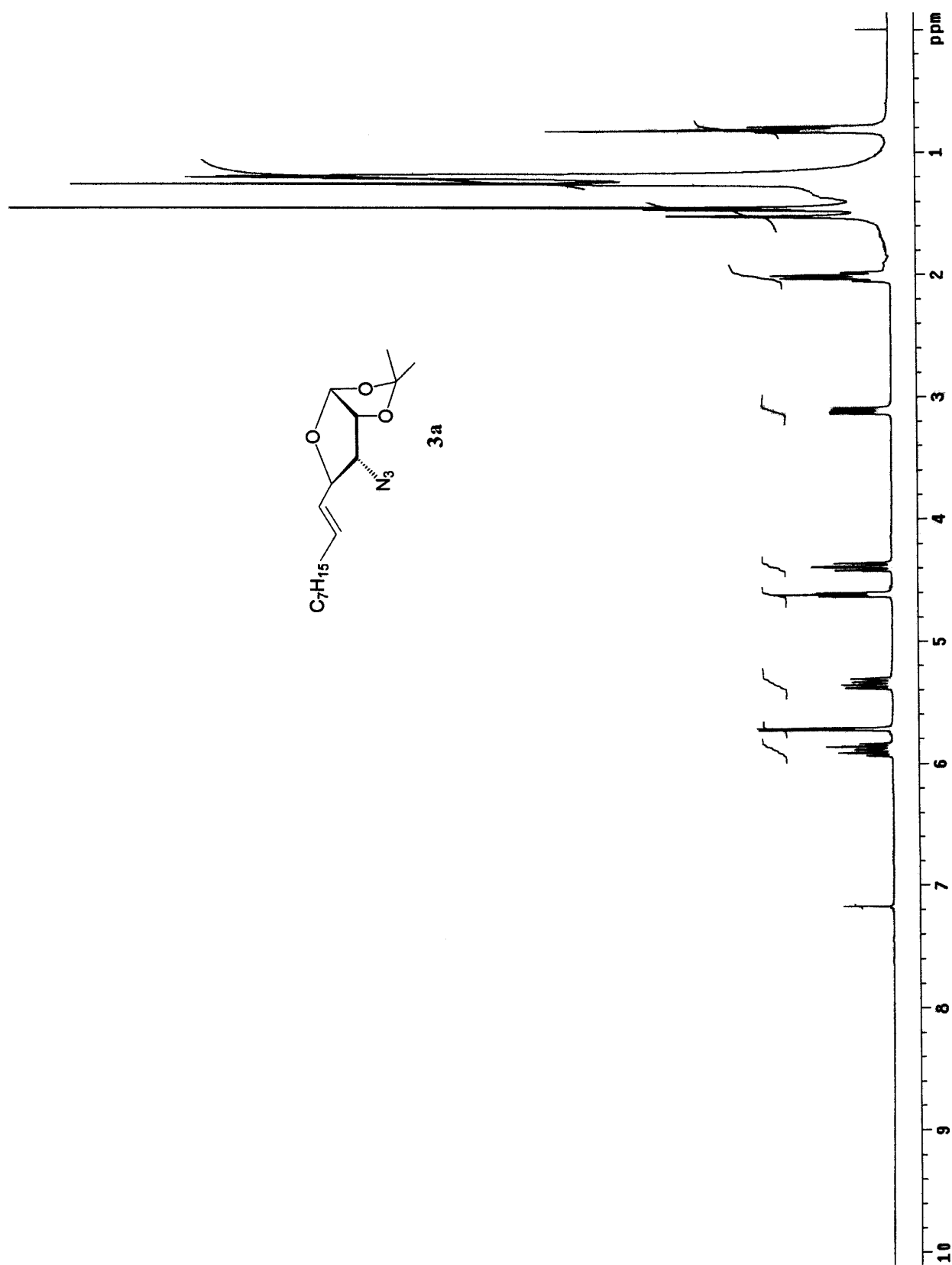


Figure 1: ^1H NMR (300 MHz, CDCl_3) spectrum of compound **3a**

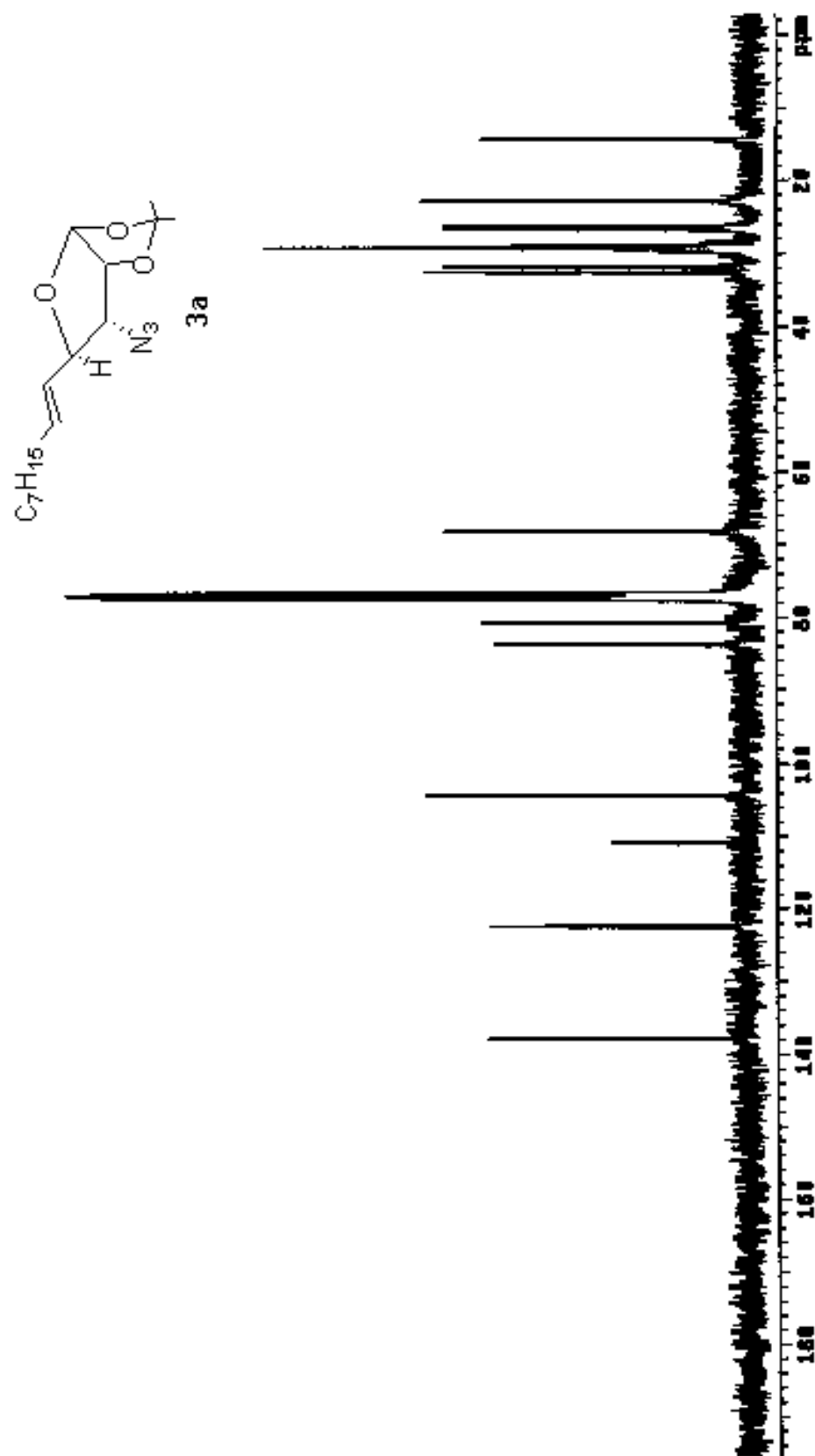


Figure 2: ¹³C NMR (75 MHz, CDCl₃) spectrum of the compound 3a

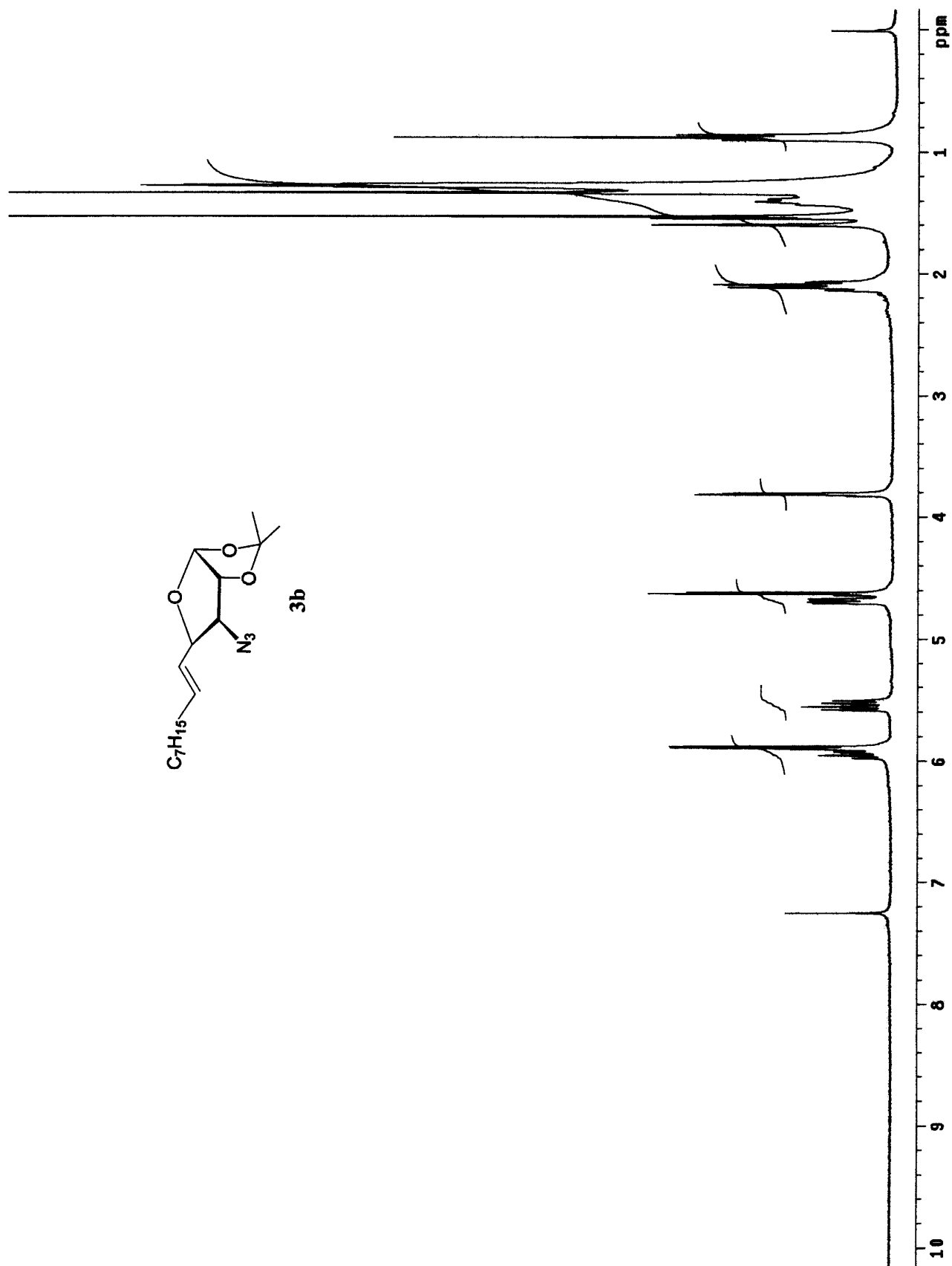
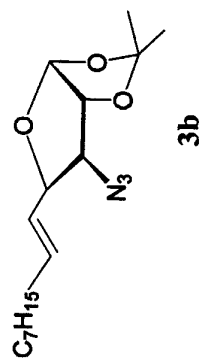


Figure 3: 1H NMR (300 MHz, $CDCl_3$) spectrum of compound **3b**

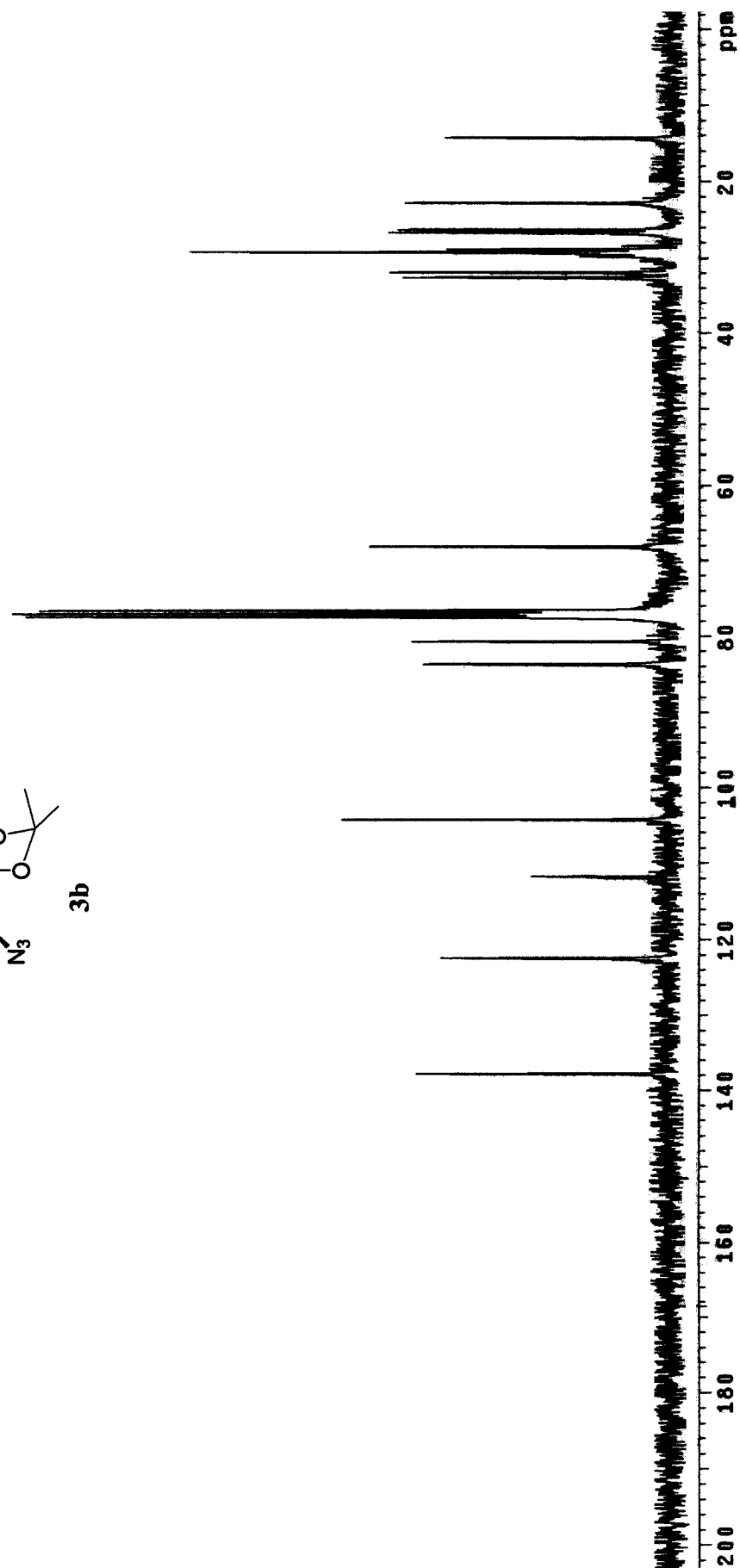
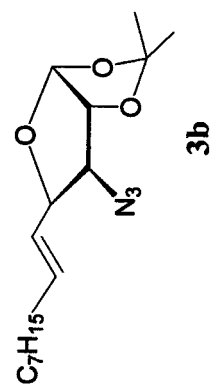


Figure 4: ^{13}C NMR (75 MHz, CDCl_3) spectrum of compound **3b**

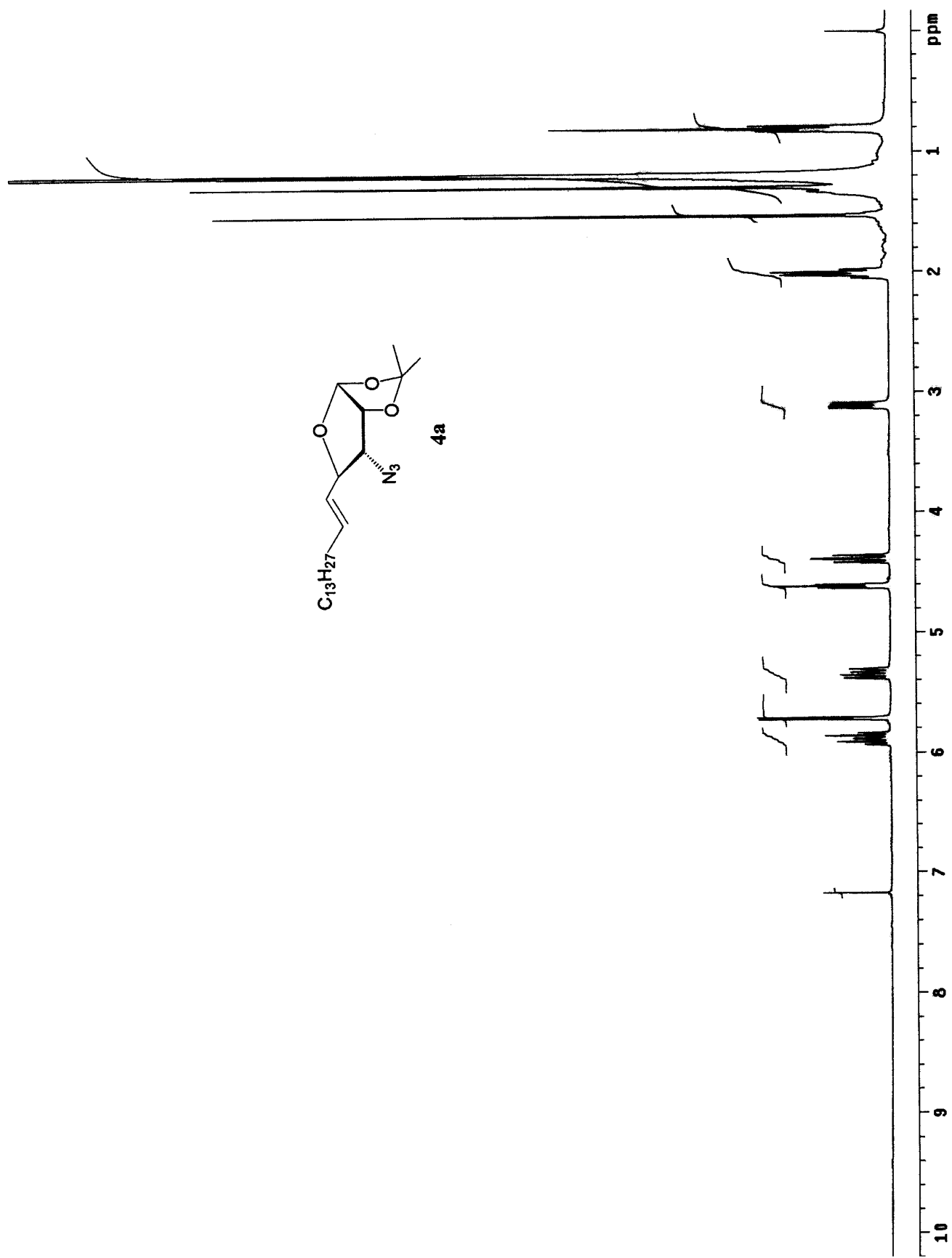


Figure 5 : ^1H NMR (300 MHz, CDCl_3) spectrum of compound **4a**

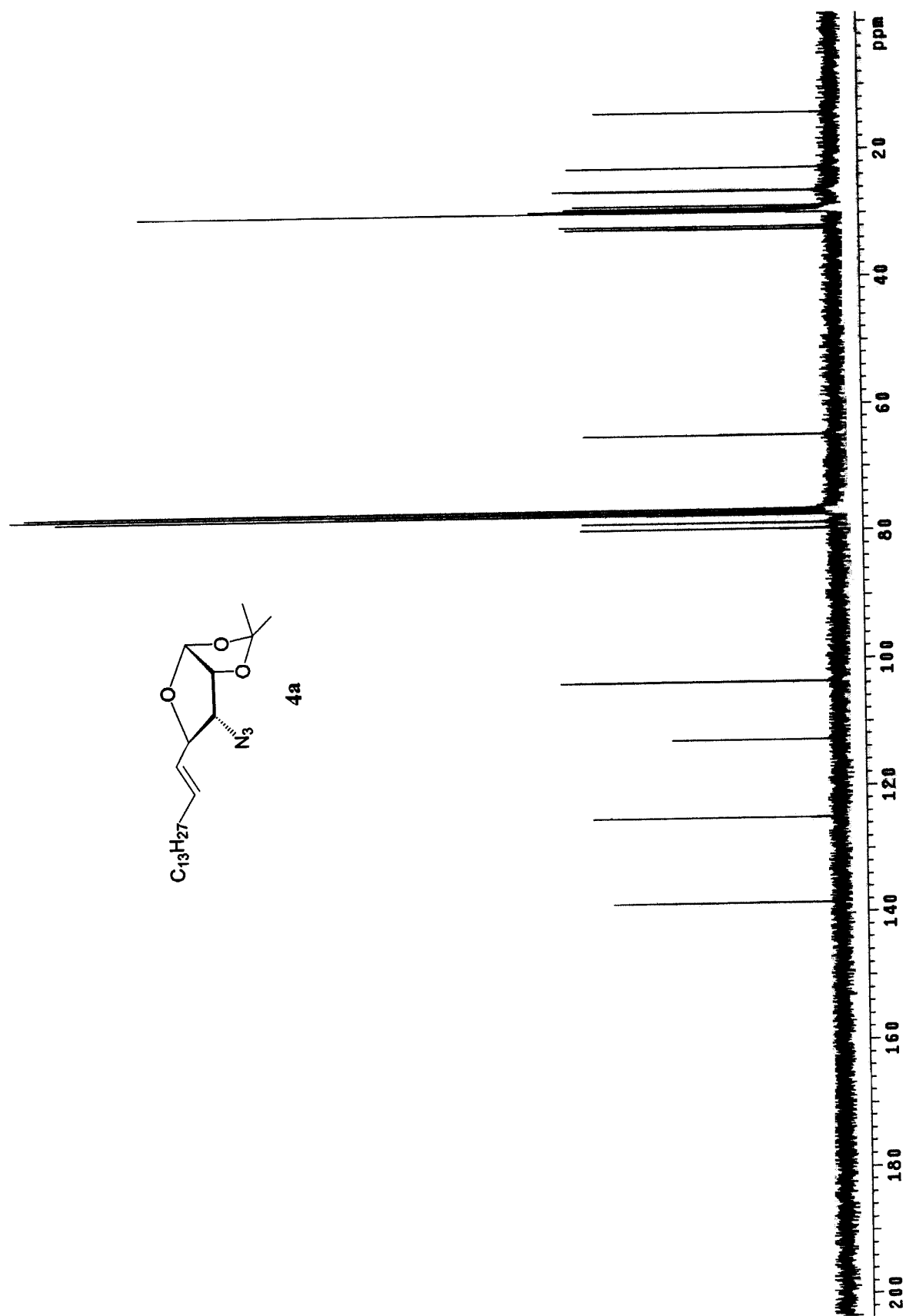


Figure 6: ^{13}C NMR (75 MHz, CDCl_3) spectrum of compound **4a**

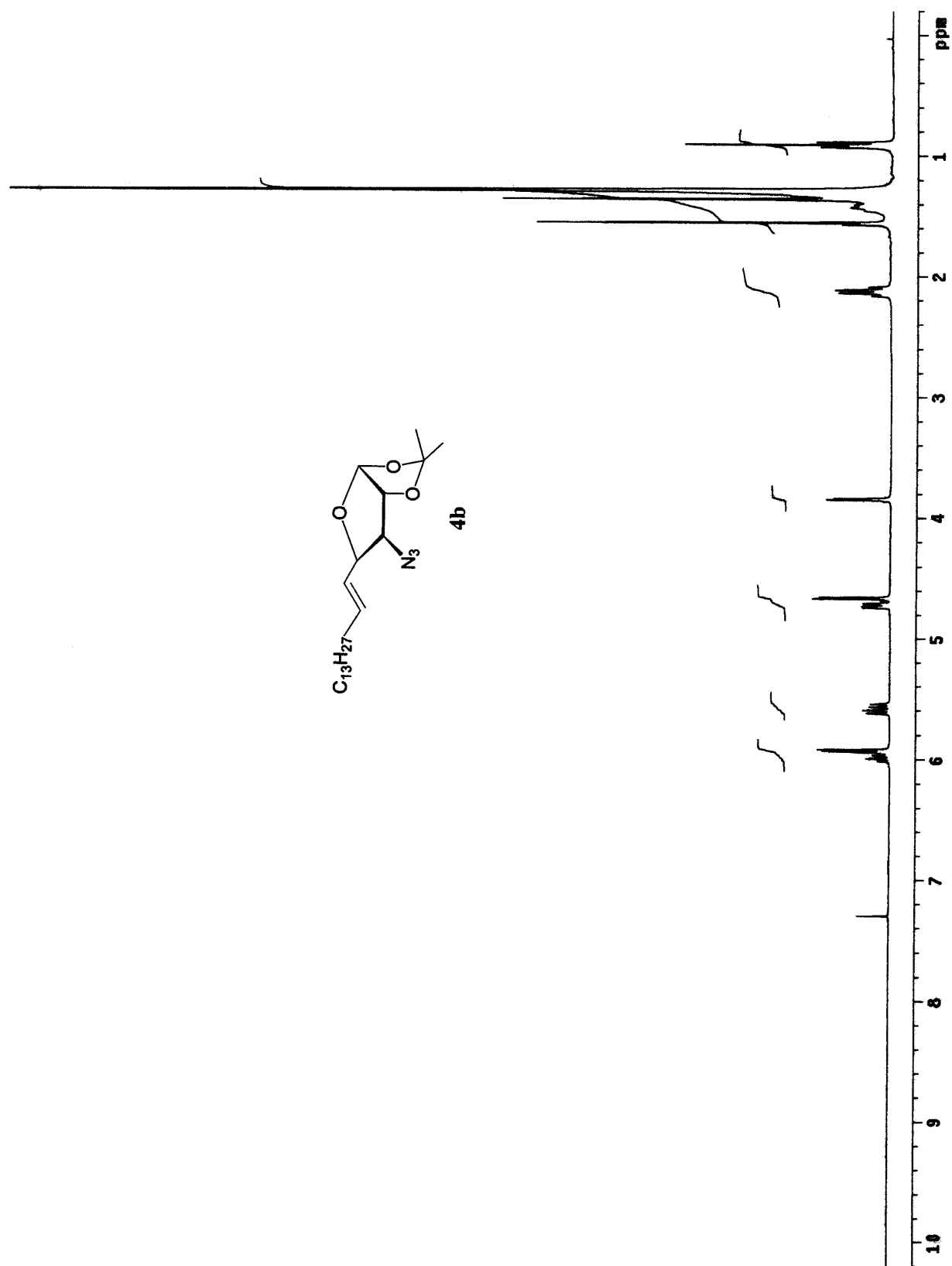


Figure 7: ^1H NMR (300 MHz, CDCl_3) spectrum of compound **4b**

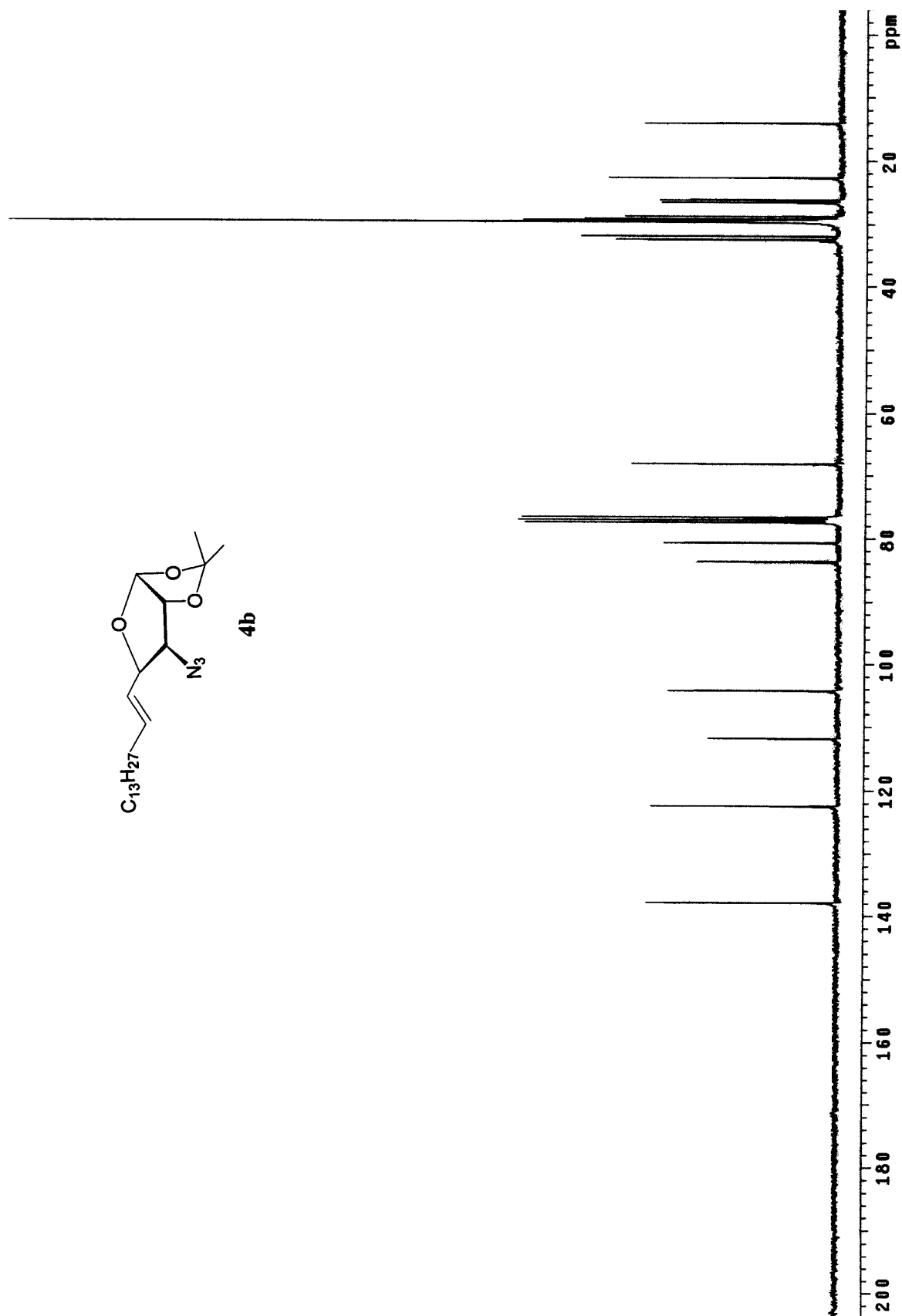


Figure 8: ^{13}C NMR (75 MHz, CDCl_3) spectrum of compound **4b**

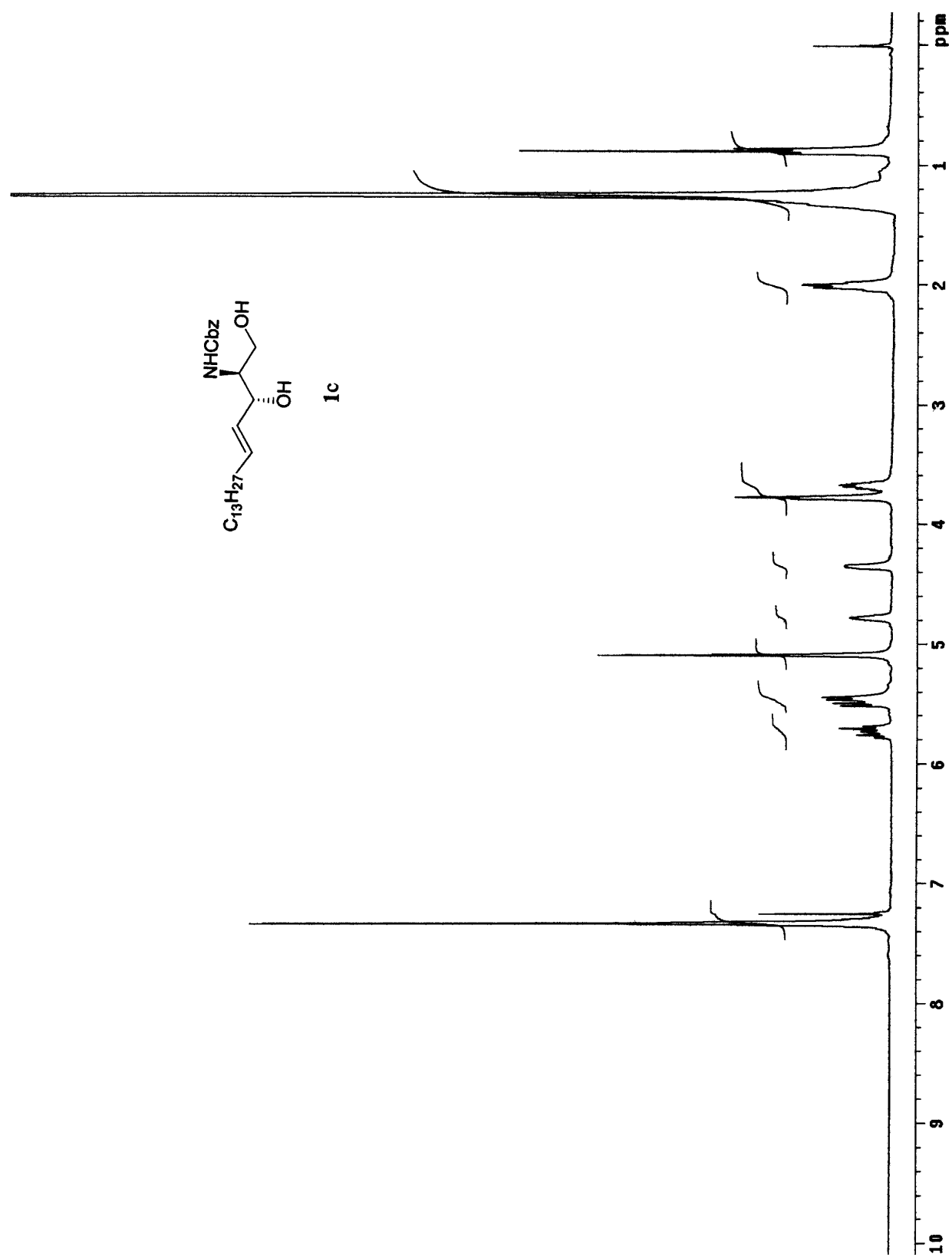


Figure 9: ¹H NMR (300 MHz, CDCl₃) spectrum of compound **1c**

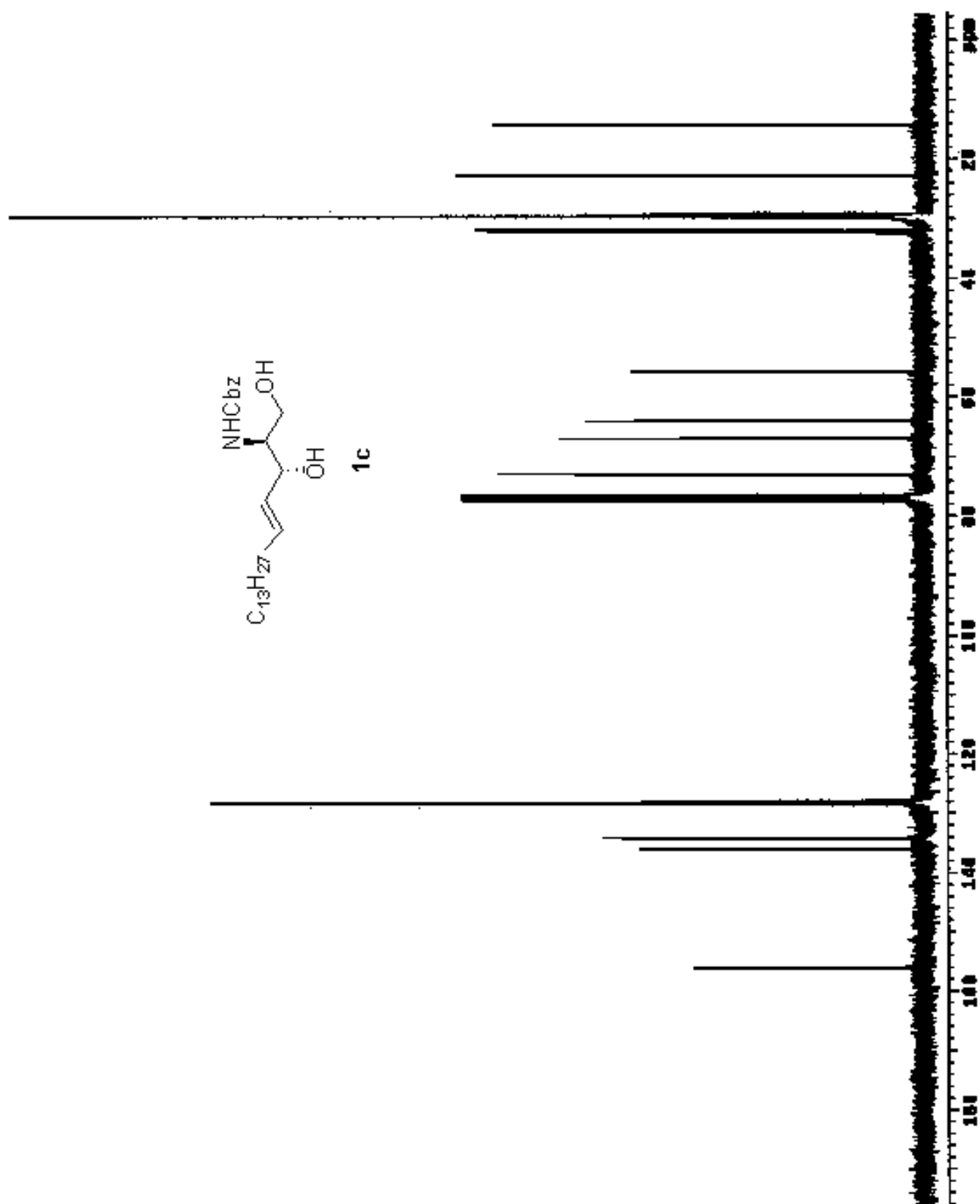


Figure 10: ¹³C NMR (75 MHz, CDCl₃) spectrum of the compound **1c**

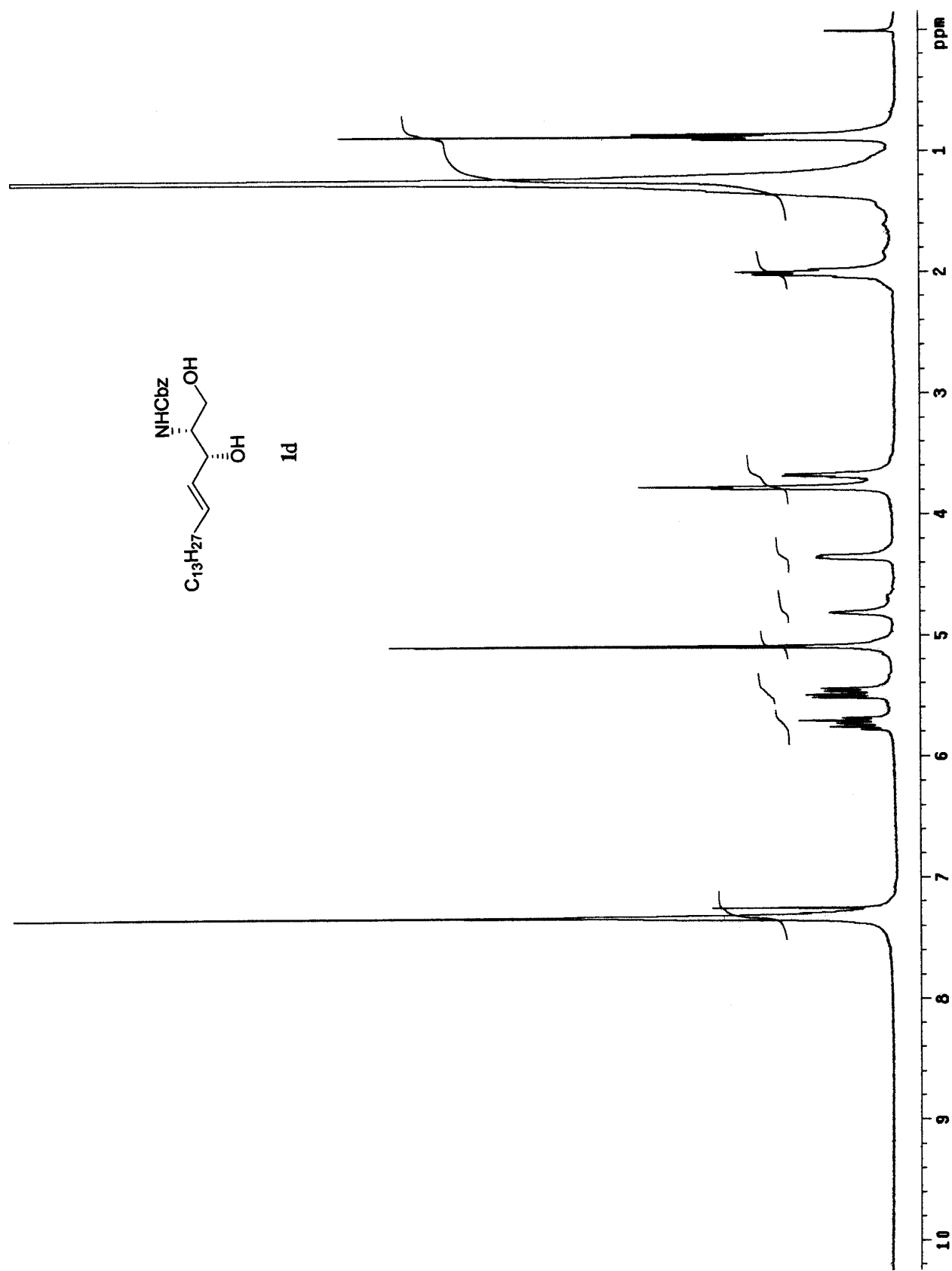


Figure 11: ¹H NMR (300 MHz, CDCl₃) spectrum of compound **1d**

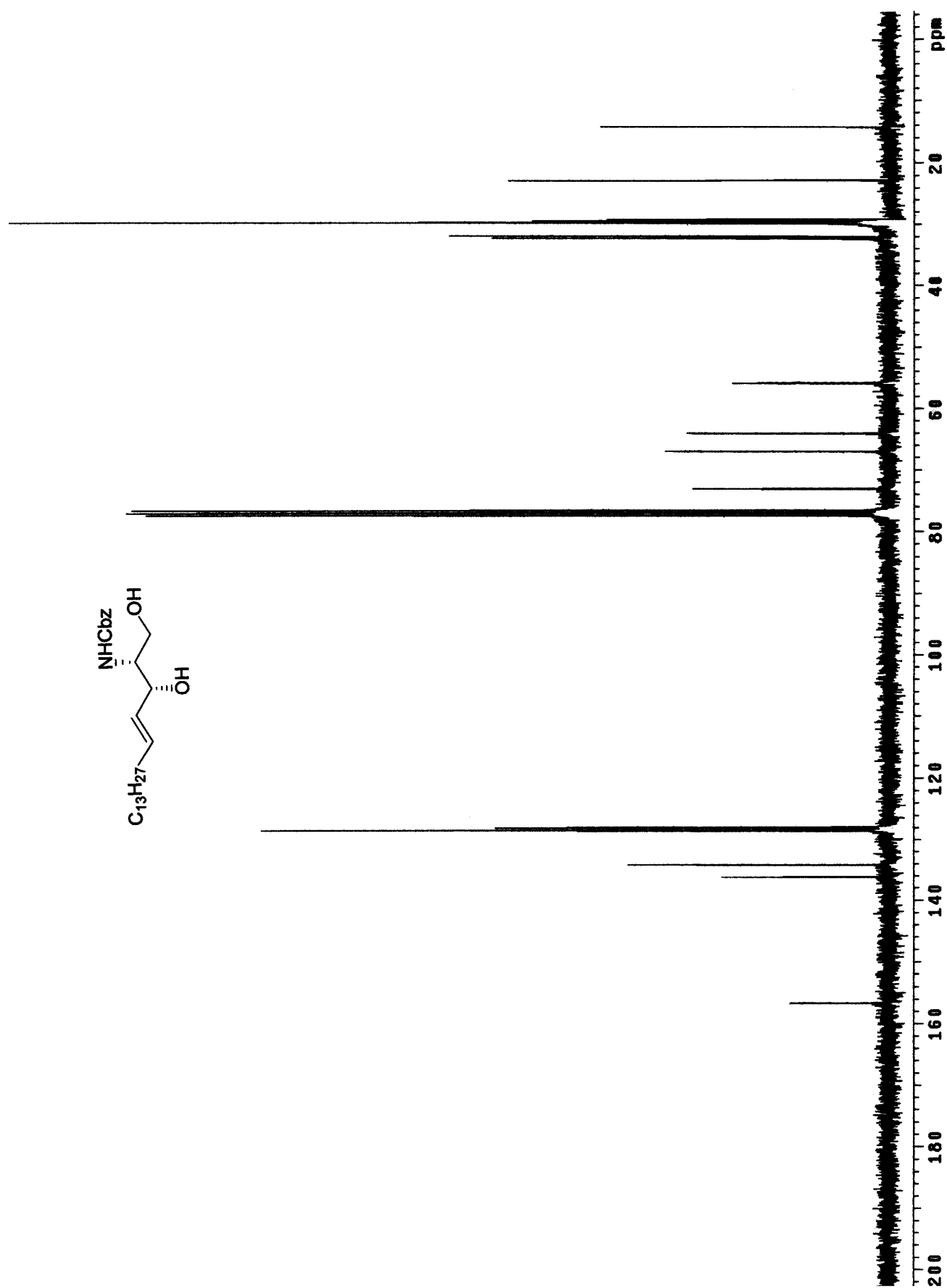
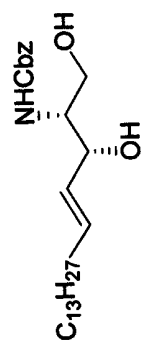


Figure 12: ^{13}C NMR (75 MHz, CDCl_3) spectrum of compound 1d