Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

How to Make Five Contiguous Stereocenters in One Reaction: Asymmetric Organocatalytic Synthesis of Pentasubstituted Cyclohexanes

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Contents

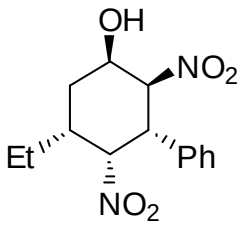
General Methods. NMR spectra were acquired on a Varian AS 400 spectrometer, running at 400 and 100 MHz for ^{1}H and ^{13}C, respectively. Chemical shifts (δ) are reported in ppm relative to residual solvent signals ($CHCl_3$, 7.26 ppm for ^{1}H NMR, $CDCl_3$, 77.0 ppm for ^{13}C NMR). The following abbreviations are used to indicate the multiplicity in ^{1}H NMR spectra: s, singlet; d, doublet; t, triplet; m, multiplet; bs, broad signal. ^{13}C NMR spectra were acquired on a broad band decoupled mode. Mass spectra were recorded on a Micromass LCT spectrometer using electrospray (ES^+) ionization techniques. Analytical thin layer chromatography (TLC) was performed using pre-coated aluminium-backed plates (Merck Kieselgel 60 F254) and visualized by ultraviolet irradiation or $KMnO_4$ dip. Melting points are uncorrected. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. The enantiomeric excess (*ee*) of the products was determined by chiral stationary phase HPLC (Daicel Chiralpak AS/AD columns).

Materials. Analytical grade solvents and commercially available reagents were used without further purification. For flash chromatography (FC) silica gel (Silica gel 60, 230-400 mesh, Fluka). Catalysts **3** were prepared according to literature procedure.[1]

[1] M. Marigo, T. C. Wabnitz, D. Fielenbach, K. A. Jørgensen, *Angew. Chem. Int. Ed.* **2005**, *44*, 794.

Experimental Procedures and Characterizations

General Procedure. An ordinary vial equipped with a magnetic stirring bar was charged with catalyst **3a** (0.04 mmol, 20 mol%), DABCO (0.02 mmol, 10 mol%) and CH_2Cl_2 (0.25 mL). Then, **2** (0.2 mmol) and the α,β-unsatured aldehyde **1** (0.2 mmol) were added. The stirring was maintained at room temperature until completion of the reaction and the crude reaction mixture was directly charged on silica gel and subjected to FC. Racemic samples were prepared using pyrrolidine (0.04 mmol, 20 mol%) instead of catalyst **3a**.



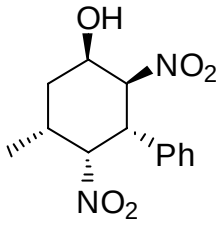
(1*R*,2*S*,3*R*,4*R*,5*R*)-5-Ethyl-2,4-dinitro-3-phenylcyclohexanol (4a). Following the general procedure **4a** was isolated by FC (*n*-hexane/AcOEt gradient from 9.5:0.5 to 8:2) in 45% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53-7.08 (m, 5H), 5.93 (dd, *J* = 12.4, 2.5 Hz, 1H), 5.02 (t, *J* = 4.4 Hz, 1H), 4.79 (bs, 1H), 4.17 (dd, *J* = 12.4 Hz, 1H), 2.58 (bs, 1H), 2.53-2.42 (m, 1H), 2.20 (td, *J* = 13.5, 2.0 Hz, 1H), 2.06 (td, *J* = 14.5, 4.2 Hz, 1H), 1.45-1.20 (m, 2H), 1.01 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.3, 129.3, 128.6, 127.0, 92.1, 85.9, 67.5, 41.7, 34.7, 32.1, 24.6, 11.3. HRMS: Calculated for $[C_{14}H_{18}N_2O_5Na]^+$: 317.1113; found: 317.1122. M.p. (*n*-hexane/AcOEt): 153-155 °C. The *ee* was determined by HPLC using a Chiralpak AS column [*n*-hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major} = 20.8 min, τ_{minor} = 24.4 min (90% *ee*). $[\alpha]_D^{rt}$: -49.8 (c = 0.75, $CHCl_3$).

The absolute configuration of the cyclohexane **4a** was determined by single-crystal X-ray analysis after transformation to the corresponding *p*-chlorobenzoate derivative. The same stereochemistry was assumed for assigning the absolute configuration of the rest of the compounds.

Both minor diastereoisomer was also isolated after FC. First stereoisomer after purification by FC **(1*R*,2*S*,3*R*,4*R*,5*R*)-5-Ethyl-2,4-**

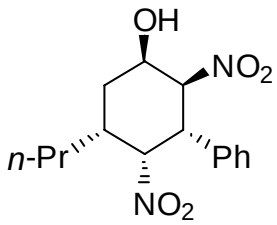
dinitro-3-phenylcyclohexanol (4a')[2] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.14 (m, 5H), 5.97 (dd, ***J*** = 12.3, 3.0 Hz, 1H), 4.92 (d, ***J*** = 4.5 Hz, 1H), 4.81 (t, ***J*** = 7.2 Hz, 1H), 4.18 (dd, ***J*** = 12.2, 4.5 Hz, 1H), 2.49 (bs, 1H), 2.34 (ddd, ***J*** = 14.9, 6.0, 2.8 Hz, 1H), 2.22-2.10 (m, 2H), 2.03-1.80 (m, 2H), 1.08 (t, ***J*** = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.8, 128.9, 126.6, 127.1, 92.8, 85.9, 68.2, 39.1, 37.9, 29.9, 27.5, 12.6.

Third stereoisomer after purification by FC **(1*R*,2*S*,3*S*,4*R*,5*R*)-5-Ethyl-2,4-dinitro-3-phenylcyclohexanol (4a'')** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.10 (m, 5H), 5.75 (dd, ***J*** = 12.2, 9.5 Hz, 1H), 4.95 (t, ***J*** = 3.8 Hz, 1H), 4.37-4.18 (m, 1H), 3.67 (dd, ***J*** = 12.2, 4.2 Hz, 1H), 2.30-1.98 (m, 4H), 1.52-1.29 (m, 2H), 1.03 (t, ***J*** = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.7, 129.4, 129.1, 127.4, 91.0, 89.9, 72.0, 47.8, 39.9, 33.2, 24.8, 11.4.

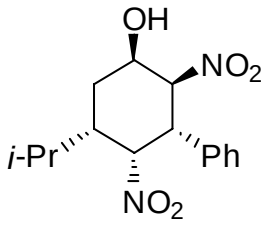


(1*R*,2*S*,3*R*,4*R*,5*R*)-5-Methyl-2,4-dinitro-3-phenylcyclohexanol (4b). Following the general procedure **4b** was isolated by FC (***n***-hexane/AcOEt gradient from 9.5:0.5 to 8:2) in 43% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.12 (m, 5H), 5.91 (dd, ***J*** = 12.4, 2.65 Hz, 1H), 4.92 (t, ***J*** = 4.6 Hz, 1H), 4.79-4.73 (m, 1H), 4.19 (dd, ***J*** = 12.4, 4.6 Hz, 1H), 2.82-2.69 (m, 1H), 2.65 (bs, 1H), 2.17 (td, ***J*** = 14.7, 2.2 Hz, 1H), 1.98 (td, ***J*** = 14.7, 3.7 Hz, 1H), 1.03 (d, ***J*** = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.3, 129.3, 128.6, 127.0, 93.9, 85.6, 67.6, 41.6, 33.7, 27.8, 16.8. HRMS: Calculated for $[C_{13}H_{16}N_2O_5Na]^+$: 303.0957; found: 303.0959. M.p. (***n***-hexane/AcOEt): 163-165 °C. The ***ee*** was determined by HPLC using a Chiralpak AS column [***n***-hexane/***i***-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major} = 30.6 min, τ_{minor} = 37.6 min (75% ***ee***). $[\alpha]_D^{rt}$: -51.1 (c = 0.4, $CHCl_3$).

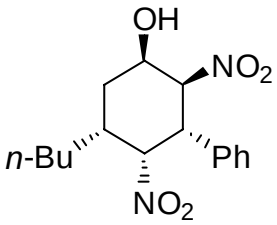
[2] Relative configuration determined by NOESY experiments. Absolute configuration assumed.



(1*R*,2*S*,3*R*,4*R*,5*R*)-2,4-Dinitro-3-phenyl-5-propyl-cyclohexanol (4c). Following the general procedure **4c** was isolated by FC (*n*-hexane/AcOEt gradient from 9.5:0.5 to 8:2) in 44% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.16 (m, 5H), 5.93 (dd, ***J*** = 12.5, 2.5 Hz, 1H), 4.98 (t, ***J*** = 4.5 Hz, 1H), 4.77 (bs, 1H), 4.17 (dd, ***J*** = 12.4, 4.5 Hz, 1H), 2.66-2.51 (m, 1H), 2.45 (bs, 1H), 2.21-2.11 (td, ***J*** = 13.9, 2.3 Hz, 1H), 2.05 (td, ***J*** = 14.4, 4.0 Hz, 1H), 1.49-1.14 (m, 4H), 0.92 (***t***, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.3, 129.3, 128.6, 127.0, 92.5, 85.9, 67.6, 41.762, 33.6, 32.6, 32.2, 19.8, 13.8. HRMS: Calculated for $[C_{15}H_{20}N_2O_5Na]^+$: 331.1270; found: 331.1267. M.p. (*n*-hexane/AcOEt): 130-132 °C. The ***ee*** was determined by HPLC using a Chiralpak AD column [*n*-hexane/***i***-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 15.3 min, τ_{minor} = 18.4 min (86% ***ee***). $[\alpha]_D^{rt}$: -52.3 (c = 0.5, $CHCl_3$).

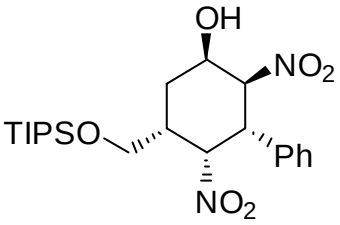


(1*R*,2*S*,3*R*,4*R*,5*S*)-5-*iso*-Propyl-2,4-dinitro-3-phenylcyclohexanol (4d). Following the general procedure **4d** was isolated by FC (*n*-hexane/AcOEt gradient from 9.5:0.5 to 8:2) in 38% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.28 (m, 3H), 7.23-7.15 (m, 2H), 5.90 (dd, ***J*** = 12.5 Hz, 1H), 5.13 (t, ***J*** = 4.0 Hz, 1H), 4.80 (bs, 1H), 4.15 (dd, ***J*** = 12.5 Hz, 1H), 2.41 (bs, 1H), 2.23-2.16 (m, 2H), 1.84-1.61 (m, 1H), 1.49-1.34 (m, 1H), 1.05 (d, ***J*** = 6.6 Hz, 3H), 0.98 (d, ***J*** = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.3, 129.3, 128.7, 127.0, 91.2, 85.8, 67.5, 42.0, 39.9, 30.2, 29.1, 20.7, 20.5. M.p. (*n*-hexane/AcOEt): 159-161 °C. The ***ee*** was determined by HPLC using a Chiralpak AS column [*n*-hexane/***i***-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major} = 19.8 min, τ_{minor} = 28.5 min (90% ***ee***). $[\alpha]_D^{rt}$: -50.0 (c = 0.4, $CHCl_3$).

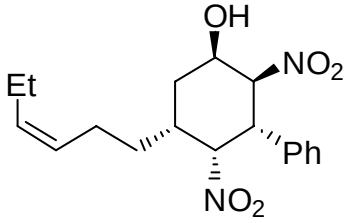


(1*R*,2*S*,3*R*,4*R*,5*R*)-5-Butyl-2,4-dinitro-3-phenylcyclohexanol (4e). Following the general procedure **4e** was isolated by FC (*n*-hexane/AcOEt gradient from 9.5:0.5 to 8:2) in 43% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.10 (m, 5H), 5.93 (dd, ***J*** = 12.2, 2.3 Hz, 1H), 4.99 (t, ***J*** = 4.4 Hz, 1H), 4.81-4.76 (m, 1H), 4.16 (dd, ***J*** = 12.4, 4.4 Hz, 1H), 2.63-

2.49 (m, 1H), 2.47-2.42 (m, 1H), 2.16 (t, ***J*** = 13.3 Hz, 1H), 2.05 (td, ***J*** = 7.9, 4.3 Hz, 1H), 1.46-1.16 (m, 6H), 0.89 (t, ***J*** = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.3, 129.3, 128.6, 127.0, 92.5, 85.9, 67.6, 41.7, 32.9, 32.2, 31.2, 28.8, 22.4, 13.8. HRMS: Calculated for $[C_{16}H_{22}N_2O_5Na]^+$: 345.1426; found: 345.1421. M.p. (***n***-hexane/AcOEt): 138-140 °C. The ***ee*** was determined by HPLC using a Chiralpak AD column [***n***-hexane/***i***-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 12.5 min, τ_{minor} = 18.8 min (87% ***ee***). $[\alpha]_D^{rt}$: -52.4 (c = 0.5, $CHCl_3$).

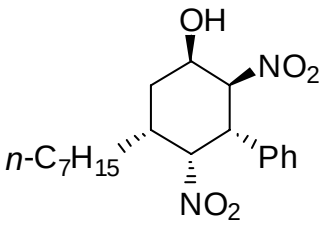


(1*R*,2*S*,3*R*,4*S*,5*R*)-5-(Tri(*iso*-propyl)syliloxymethyl)-2,4-dinitro-3-phenylcyclohexanol (4f). Following the general procedure **4f** was isolated by FC (***n***-hexane/AcOEt gradient from 9.5:0.5 to 8:2) in 56% yield. ^{1}H NMR (400 MHz, $CDCl_3$) (*denotes minor diastereoisomer d.r.: 80:20; $^+$denotes not well resolved signals) δ 7.48-7.05 (m, 5H), 7.48-7.05* (m, 5H), 5.91 (dd, ***J*** = 12.4, 2.5 Hz, 1H), 5.89* (dd, ***J*** = 12.4 Hz, 1H), 5.19*$^+$ (t, ***J*** = 4.9 Hz, 1H), 5.17 (t, ***J*** = 4.5 Hz, 1H), 4.86-4.80 (m, 1H), 4.77-4.70* (m, 1H), 4.23*$^+$ (dd, ***J*** = 4.8 Hz, 1H), 4.18 (dd, ***J*** = 12.3, 4.6 Hz, 1H), 4.09* (dd, ***J*** = 10.6, 6.9 Hz, 1H), 3.96* (dd, ***J*** = 10.7, 4.2 Hz, 1H), 3.72 (dd, ***J*** = 10.3, 5.2 Hz, 1H), 3.58 (dd, ***J*** = 10.3, 8.2 Hz, 1H), 2.86-2.74 (m, 1H), 2.67-2.59* (m, 1H), 2.59-2.46 (m, 1H), 2.52-2.46*$^+$ (m, 1H), 2.30 (dt, ***J*** = 14.1, 2.4 Hz, 1H), 2.06*$^+$ (dt, ***J*** = 15.5, 3.0 Hz, 1H), 2.00 (td, J = 14.3, 3.7 Hz, 1H), 1.19-0.98 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$) (*denotes minor diastereoisomer d.r.: 80:20) δ 134.7*, 134.2, 129.3, 129.2*, 128.7, 128.5*, 127.0, 126.9*, 90.6*, 89.8, 86.1, 85.5*, 67.4, 67.0*, 66.2*, 63.6, 41.7, 39.3*, 38.8*, 36.3, 30.6*, 29.1, 17.9, 17.9*, 11.7*, 11.7. HRMS: Calculated for $[C_{22}H_{36}N_2O_6SiNa]^+$: 475.2240; found: 475.2249. The ***ee*** was determined by HPLC using a Chiralpak AD column [***n***-hexane/***i***-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major} = 8.7 min, τ_{minor} = 7.9 min (94% ***ee***).

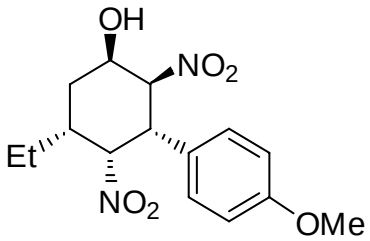


(1*R*,2*S*,3*R*,4*R*,5*R*)-5-(*cis*-Hex-3-enyl)-2,4-dinitro-3-phenylcyclohexanol (4g). Following the general procedure **4g** was isolated by FC (***n***-hexane/AcOEt

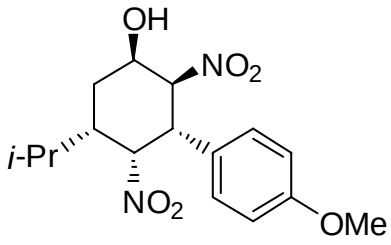
gradient from 9.5:0.5 to 8:2) in 52% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.12 (m, 5H), 5.92 (dd, ***J*** = 12.3, 2.3 Hz, 1H), 5.48-5.39 (m, 1H), 5.30-5.21 (m, 1H), 4.98 (t, ***J*** = 4.4 Hz, 1H), 4.78 (bs, 1H), 4.16 (dd, ***J*** = 12.4, 4.4 Hz, 1H), 2.66-2.53 (m, 2H), 2.21-1.98 (m, 6H), 1.42-1.25 (m, 2H), 0.96 (t, ***J*** = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.3, 133.2, 129.3, 128.6, 127.0, 126.9, 92.3, 85.9, 67.5, 41.7, 32.3, 32.2, 31.3, 23.9, 20.5, 14.3. HRMS: Calculated for $[C_{18}H_{24}N_2O_5Na]^+$: 371.1583; found: 371.1583. M.p. (***n***-hexane/AcOEt): 106-108 °C. The ***ee*** was determined by HPLC using a Chiralpak AD column [***n***-hexane/***i***-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 12.2 min, τ_{minor} = 13.6 min (86% ***ee***). $[\alpha]_D^{rt}$: -12.3 (c = 1.3, $CHCl_3$).



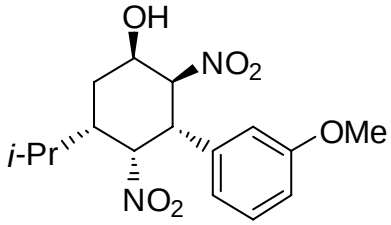
(1*R*,2*S*,3*R*,4*R*,5*R*)-5-Heptyl-2,4-dinitro-3-phenylcyclohexanol (4h). Following the general procedure **4h** was isolated by FC (*n*-hexane/AcOEt gradient from 9.5:0.5 to 8:2) in 50% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.10 (m, 5H), 5.92 (ddd, ***J*** = 12.2, 2.3, 1.0 Hz, 1H), 4.99 (t, ***J*** = 4.2 Hz, 1H), 4.81-4.74 (m, 1H), 4.16 (dd, ***J*** = 12.4, 4.4 Hz, 1H), 2.62-2.48 (m, 2H), 2.15 (t, ***J*** = 13.4 Hz, 1H), 2.04 (td, ***J*** = 14.4, 3.9 Hz, 1H), 1.52-1.12 (m, 12H), 0.87 (t, ***J*** = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.4, 129.3, 128.6, 127.0, 92.4, 85.9, 67.6, 41.7, 32.9, 32.3, 31.6, 31.5, 29.3, 29.0, 26.6, 22.5, 14.0. HRMS: Calculated for $[C_{19}H_{28}NO_5Na]^+$: 387.1896; found: 387.1896. M.p. (*n*-hexane/AcOEt): 104-106 °C. The ***ee*** was determined by HPLC using a Chiralpak AD column [*n*-hexane/***i***-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 9.9 min, τ_{minor} = 14.9 min (87% ***ee***). $[\alpha]_D^{rt}$: -22,3 (c = 1.0, $CHCl_3$).



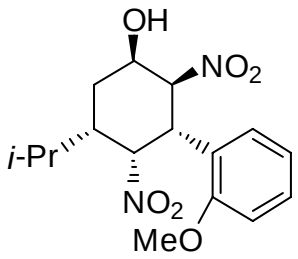
(1*R*,2*S*,3*R*,4*R*,5*R*)-5-Ethyl-3-(*p*-methoxyphenyl)-2,4-dinitrocyclohexanol (4i). Following the general procedure **4i** was isolated by FC (*n*-hexane/AcOEt gradient from 9.5:0.5 to 8:2) in 48% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (d, ***J*** = 8.7 Hz, 2H), 6.84 (d, ***J*** = 8.8 Hz, 2H), 5.88 (dd, ***J*** = 12.5, 2.5 Hz, 1H), 4.99 (t, ***J*** = 4.5 Hz, 1H), 4.79-4.71 (m, 1H), 4.10 (dd, ***J*** = 12.5, 4.5 Hz, 1H), 3.76 (s, 3H), 2.54 (dd, ***J*** = 2.8, 1.4 Hz, 1H), 2.51-2.39 (m, 1H), 2.18-2.09 (m, 1H), 2.05 (td, ***J*** = 14.5, 4.1 Hz, 1H), 1.42-1.23 (m, 2H), 1.01 (t, ***J*** = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 128.2, 126.0, 114.7, 92.2, 86.2, 67.5, 55.2, 41.1, 34.6, 32.0, 24.6, 11.3. HRMS: Calculated for $[C_{15}H_{20}N_2O_6Na]^+$: 347.1219; found: 347.1234. M.p. (*n*-hexane/AcOEt): 154-156 °C. The ***ee*** was determined by HPLC using a Chiralpak AD column [*n*-hexane/***i***-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major} = 31.9 min, τ_{minor} = 47.8 min (92% ***ee***). $[\alpha]_D^{rt}$: +44.7 (c = 0.3, $CHCl_3$).



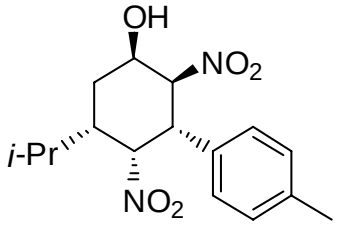
(1*R*,2*S*,3*R*,4*R*,5*S*)-5-*iso*-Propyl-3-(4-methoxyphenyl)-2,4-dinitrocyclohexanol (4j). Following the general procedure **4j** was isolated by FC (*n*-hexane/AcOEt gradient from 9.5:0.5 to 8:2) in 53% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 710 (td, ***J*** = 8.8, 2.0 Hz, 2H), 6.84 (td, ***J*** = 8.8, 2.0 Hz, 2H), 5.83 (dd, ***J*** = 12.5, 2.6 Hz, 1H), 5.10 (t, ***J*** = 4.0 Hz, 1H), 4.79-4.75 (m, 1H), 4.09 (dd, ***J*** = 12.5, 4.5 Hz, 1H), 3.76 (s, 3H), 2.59 (d, ***J*** = 2.9 Hz, 1H), 2.21-2.14 (m, 3H), 1.41 (m, 1H), 1.04 (d, ***J*** = 6.6 Hz, 3H), 0.97 (d, ***J*** = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 128.1, 126.1, 114.7, 91.3, 86.1, 67.5, 55.1, 41.3, 39.8, 30.1, 29.1, 20.7, 20.5. HRMS: Calculated for $[C_{16}H_{22}N_2O_6Na]^+$: 361.1376; found: 361.1373. M.p. (*n*-hexane/AcOEt): 195-198 °C. The ***ee*** was determined by HPLC using a Chiralpak AD column [*n*-hexane/***i***-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 18.8 min, τ_{minor} = 13.4 min (89% ***ee***). $[\alpha]_D^{rt}$: -51.2 (c = 0.3, $CHCl_3$).



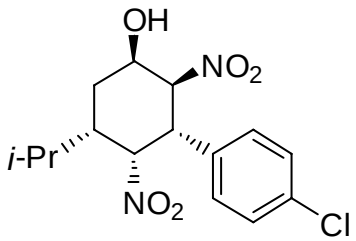
(1*R*,2*S*,3*R*,4*R*,5*S*)-5-*iso*-Propyl-3-(3-methoxyphenyl)-2,4-dinitrocyclohexanol (4k). Following the general procedure **4k** was isolated by FC (*n*-hexane/AcOEt gradient from 9.5:0.5 to 8:2) in 65% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (t, ***J*** = 8.0 Hz, 1H), 6.82 (ddd, ***J*** = 8.3, 2.4, 0.6 Hz, 1H), 6.75 (d, ***J*** = 7.9 Hz, 1H), 6.72 (t, ***J*** = 2.0 Hz, 1H), 5.86 (dd, ***J*** = 12.4, 2.6 Hz, 1H), 5.13 (t, ***J*** = 3.9 Hz, 1H), 4.82-4.76 (m, 1H), 4.12 (dd, ***J*** = 12.5, 4.4 Hz, 1H), 3.77 (s, 3H), 2.60 (d, ***J*** = 3.1 Hz, 1H), 2.22-2.14 (m, 3H), 1.46-1.35 (m, 1H), 1.04 (d, ***J*** = 6.6 Hz, 3H), 0.97 (d, ***J*** = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 135.9, 130.4, 118.9, 113.6, 113.3, 91.1, 85.8, 67.5, 55.1, 41.9, 39.9, 30.2, 29.1, 20.7, 20.5. HRMS: Calculated for $[C_{16}H_{22}N_2O_6Na]^+$: 361.1376; found: 361.1381. M.p. (*n*-hexane/AcOEt): 150-152 °C. The ***ee*** was determined by HPLC using a Chiralpak AD column [hexane/***i***-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 15.7 min, τ_{minor} = 11.8 min (90% ***ee***). $[\alpha]_D^{rt}$: -0.2 (c = 2, $CHCl_3$).



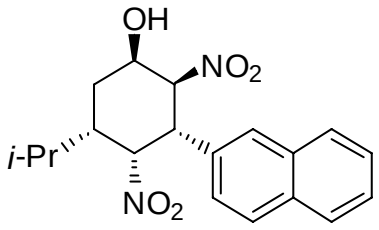
(1*R*,2*S*,3*R*,4*R*,5*S*)-5-*iso*-Propyl-3-(2-methoxyphenyl)-2,4-dinitrocyclohexanol (4l). Following the general procedure **4l** was isolated by FC (*n*-hexane/AcOEt gradient from 9.5:0.5 to 8:2) in 48% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.23 (m, 1H), 6.98 (d, ***J*** = 7.5 Hz, 1H), 6.91 (d, ***J*** = 8.3 Hz, 1H), 6.87 (td, ***J*** = 7.6, 0.9 Hz, 1H), 5.89 (d, ***J*** = 12.4 Hz, 1H), 5.24 (t, ***J*** = 3.6 Hz, 1H), 4.83-4.78 (m, 1H), 4.67 (d, ***J*** = 11.0 Hz, 1H), 3.90 (s, 3H), 2.43 (d, ***J*** = 2.9 Hz, 1H), 2.24-2.13 (m, 3H), 1.50-1.35 (m, 1H), 1.05 (d, ***J*** = 6.6 Hz, 3H), 0.97 (d, ***J*** = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 129.5, 125.3, 122.3, 121.1, 110.9, 94.4, 88.7, 85.5, 67.8, 55.6, 39.5, 34.5, 30.2, 29.1, 20.8, 20.5. HRMS: Calculated for $[C_{16}H_{22}N_2O_6Na]^+$: 361.1376; found: 361.1366. M.p. (*n*-hexane/AcOEt): 201-203 °C. The ***ee*** was determined by HPLC using a Chiralpak AD column [*n*-hexane/***i***-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 10.8 min, τ_{minor} = 9.6 min (90% ***ee***). $[\alpha]_D^{rt}$: -26.0 (c = 0.3, $CHCl_3$).



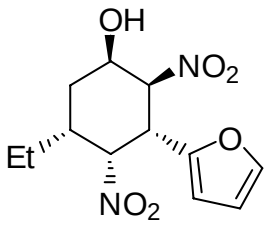
(1*R*,2*S*,3*R*,4*R*,5*S*)-5-*iso*-Propyl-3-(4-methylphenyl)-2,4-dinitrocyclohexanol (4m). Following the general procedure **4m** was isolated by FC (*n*-hexane/AcOEt gradient from 9.5:0.5 to 8:2) in 40% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 (d, ***J*** = 8.0 Hz, 2H), 7.06 (d, ***J*** = 8.2 Hz, 2H), 5.86 (dd, ***J*** = 12.5, 2.6 Hz, 1H), 5.11 (t, ***J*** = 4.0 Hz, 1H), 4.82-4.76 (m, 1H), 4.11 (dd, ***J*** = 12.5, 4.5 Hz, 1H), 2.56 (bs, 1H), 2.30 (s, 3H), 2.22-2.16 (m, 3H), 1.48-1.35 (m, 1H), 1.04 (d, ***J*** = 6.6 Hz, 3H), 0.97 (d, ***J*** = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 131.2, 130.0, 126.8, 91.3, 85.9, 67.5, 41.7, 39.8, 30.2, 29.1, 21.0, 20.7, 20.5. HRMS: Calculated for $[C_{16}H_{22}N_2O_5Na]^+$: 345.1426; found: 345.1422. M.p. (*n*-hexane/AcOEt): 220-223 °C. The ***ee*** was determined by HPLC using a Chiralpak AD column [*n*-hexane/***i***-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 12.3 min, τ_{minor} = 9.1 min (84% ***ee***). $[\alpha]_D^{rt}$: -9.3 (c = 1.0, $CHCl_3$).



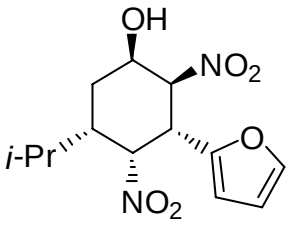
(1*R*,2*S*,3*R*,4*R*,5*S*)-3-(4-Chlorophenyl)-5-*iso*-propyl-2,4-dinitrocyclohexanol (4n). Following the general procedure **4n** was isolated by FC (*n*-hexane/AcOEt gradient from 9.5:0.5 to 8:2) in 47% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (td, ***J*** = 8.6, 2.0 Hz, 2H), 7.13 (td, ***J*** = 8.4, 1.9 Hz, 2H), 5.82 (dd, ***J*** = 12.4, 2.7 Hz, 1H), 5.09 (t, ***J*** = 4.1 Hz, 1H), 4.83-4.77 (m, 1H), 4.14 (dd, ***J*** = 12.4, 4.5 Hz, 1H), 2.61 (d, ***J*** = 3.2 Hz, 1H), 2.25-2.13 (m, 3H), 1.52-1.31 (m, 1H), 1.04 (d, ***J*** = 6.6 Hz, 3H), 0.97 (d, ***J*** = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.7, 133.0, 129.6, 128.4, 91.0, 85.7, 67.5, 41.4, 39.8, 30.2, 29.1, 20.7, 20.5. M.p. (*n*-hexane/AcOEt): 206-208 °C. The ***ee*** was determined by HPLC using a Chiralpak AD column [*n*-hexane/***i***-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 22.2 min, τ_{minor} = 12.2 min (88% ***ee***). $[\alpha]_D^{rt}$: -38.8 (c = 1.0, $CHCl_3$).



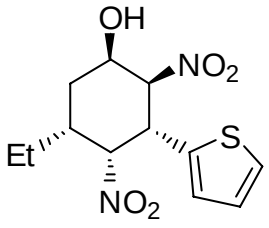
(1*R*,2*S*,3*R*,4*R*,5*S*)-5-*iso*-Propyl-3-(naphthalene-2-yl)-2,4-dinitrocyclohexanol (4o). Following the general procedure **4o** was isolated by FC (*n*-hexane/AcOEt gradient from 9.5:0.5 to 8:2) in 61% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86-7.74 (m, 3H), 7.65-7.61 (m, 1H), 7.52-7.44 (m, 2H), 7.32 (dd, ***J*** = 8.5, 1.8 Hz, 1H), 6.03 (dd, ***J*** = 12.5 2.6 Hz, 1H), 5.24 (t, ***J*** = 3.9 Hz, 1H), 4.88-4.82 (m, 1H), 4.33 (dd, ***J*** = 12.4, 4.4 Hz, 1H), 2.61 (d, ***J*** = 2.6 Hz, 1H), 2.30-2.17 (m, 3H), 1.50-1.38 (m, 1H), 1.06 (d, ***J*** = 6.6 Hz, 3H), 0.99 (d, ***J*** = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.2, 133.0, 131.8, 129.3, 128.0, 127.6, 126.5, 126.5, 125.9, 124.8, 91.1, 85.9, 67.6, 42.1, 39.9, 30.2, 29.1, 20.8, 20.5. HRMS: Calculated for $[C_{19}H_{22}N_2O_5Na]^+$: 381.1426; found: 381.1446. M.p. (*n*-hexane/AcOEt): 207-209 °C. The ***ee*** was determined by HPLC using a Chiralpak AD column [*n*-hexane/***i***-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 20.3 min, τ_{minor} = 12.4 min (88% ***ee***). $[\alpha]_D^{rt}$: -56.5 (c = 0.2, $CHCl_3$).



(1*R*,2*S*,3*R*,4*R*,5*R*)-5-Ethyl-3-(furan-2-yl)-2,4-dinitrocyclohexanol (4p). Following the general procedure **4p** was isolated by FC (*n*-hexane/AcOEt gradient from 9.5:0.5 to 8:2) in 60% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (dd, ***J*** = 1.8, 0.7 Hz, 1H), 6.28 (dd, ***J*** = 3.3, 1.8 Hz, 1H), 6.17 (td, ***J*** = 3.4, 0.7 Hz, 1H), 5.73 (dd, ***J*** = 12.3, 2.6 Hz, 1H), 5.18 (t, ***J*** = 4.4 Hz, 1H), 4.77-4.72 (m, 1H), 4.31 (dd, ***J*** = 12.2, 4.6 Hz, 1H), 2.46 (dd, ***J*** = 3.0, 1.9 Hz, 1H), 2.45-2.35 (m, 1H), 2.14-1.98 (m, 2H), 1.43-1.19 (m, 2H), 1.03 (t, ***J*** = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.3, 142.9, 110.6, 107.7, 89.5, 85.5, 67.2, 36.3, 34.0, 31.9, 24.6, 11.3. HRMS: Calculated for $[C_{12}H_{16}N_2O_6Na]^+$: 307.0906; found: 307.0898. The ***ee*** was determined by HPLC using a Chiralpak AS column [*n*-hexane/***i***-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major} = 22.0 min, τ_{minor} = 24.7 min (86% ***ee***). $[\alpha]_D^{rt}$: -40.0 (c = 1.0, $CHCl_3$).

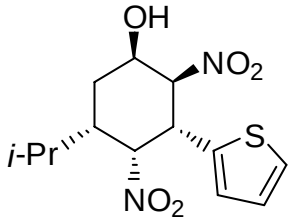


(1*R*,2*S*,3*R*,4*R*,5*S*)-3-(Furan-2-yl)-5-*iso*-propyl-2,4-dinitrocyclohexanol (4q). Following the general procedure **4q** was isolated by FC (*n*-hexane/AcOEt gradient from 9.5:0.5 to 8:2) in 43% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, ***J*** = 1.4 Hz, 1H), 6.28 (dd, ***J*** = 3.2, 1.9 Hz, 1H), 6.17 (d, ***J*** = 3.3 Hz, 1H), 5.69 (dd, ***J*** = 12.3, 2.6 Hz, 1H), 5.32-5.27 (m, 1H), 4.79-4.74 (m, 1H), 4.30 (dd, ***J*** = 12.3, 4.5 Hz, 1H), 2.51 (bs, 1H), 2.21-2.07 (m, 3H), 1.48-1.37 (m, 1H), 1.07 (d, ***J*** = 6.5 Hz, 3H), 0.97 (d, ***J*** = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.3, 142.9, 110.6, 107.7, 88.7, 85.3, 67.2, 39.1, 36.6, 30.3, 29.0, 20.7, 20.5. HRMS: Calculated for $[C_{13}H_{18}N_2O_6Na]^+$: 321.1063; found: 321.1063. M.p. (*n*-hexane/AcOEt): 108-109 °C. The ***ee*** was determined by HPLC using a Chiralpak AD column [*n*-hexane/***i***-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 16.0 min, τ_{minor} = 11.1 min (88% ***ee***). $[\alpha]_D^{rt}$: -60.8 (c = 0.8, $CHCl_3$).



(1*R*,2*S*,3*R*,4*R*,5*R*)-5-Ethyl-2,4-dinitro-3-(thiophen-2-yl)-cyclohexanol (4r). Following the general procedure **4r** was isolated by FC (*n*-hexane/AcOEt gradient from

9.5:0.5 to 8:2) in 42% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (ddd, ***J*** = 5.1, 1.1, 0.5 Hz, 1H), 6.94 (dd, ***J*** = 5.0, 3.7 Hz, 1H), 6.92-6.89 (m, 1H), 5.85 (dd, ***J*** = 12.2, 2.6 Hz, 1H), 5.10 (t, ***J*** = 4.5 Hz, 1H), 4.80-4.73 (m, 1H), 4.44 (dd, ***J*** = 12.2, 4.5 Hz, 1H), 2.58 (d, ***J*** = 2.2 Hz, 1H), 2.53-2.43 (m, 1H), 2.18-2.00 (m, 2H), 1.50-1.22 (m, 2H), 1.04 (t, ***J*** = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.3, 127.4, 125.6, 125.6, 92.1, 87.4, 67.4, 37.4, 34.4, 31.9, 24.7, 11.3. HRMS: Calculated for $[C_{12}H_{16}N_2O_5SNa]^+$: 323.0678; found: 323.0661. The ***ee*** was determined by HPLC using a Chiralpak AD column [***n***-hexane/***i***-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 19.9 min, τ_{minor} = 25.6 min (80% ***ee***). $[\alpha]_D^{rt}$: -29.8 (c = 1.5, $CHCl_3$).



(1*R*,2*S*,3*R*,4*R*,5*S*)-5-*iso*-Propyl-2,4-dinitro-3-(thiophen-2-yl)cyclohexanol (4s). Following the general procedure **4s** was isolated by FC (***n***-hexane/AcOEt gradient from 9.5:0.5 to 8:2) in 43% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (td, ***J*** = 5.1, 1.3 Hz, 1H), 6.92 (ddd, ***J*** = 5.1, 3.6, 1.5 Hz, 1H), 6.90-6.85 (m, 1H), 5.80 (dd, ***J*** = 12.2, 2.6 Hz, 1H), 5.16 (t, ***J*** = 3.8 Hz, 1H), 4.76 (bs, 1H), 4.41 (dd, ***J*** = 12.2, 4.5 Hz, 1H), 2.46 (bs, 1H), 2.25-2.08 (m, 3H), 1.49-1.36 (m, 1H), 1.07 (d, ***J*** = 6.6 Hz, 3H), 0.98 (d, J = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.3, 127.4, 125.6, 125.5, 91.3, 87.2, 67.3, 39.6, 37.6, 29.9, 29.1, 20.7, 20.5,. HRMS: Calculated for $[C_{13}H_{18}N_2O_5SNa]^+$: 337.0834; found: 307.0825. M.p. (***n***-hexane/AcOEt): 155-158 °C. The ***ee*** was determined by HPLC using a Chiralpak AD column [***n***-hexane/***i***-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 14.7 min, τ_{minor} = 11.3 min (90% ***ee***). $[\alpha]_D^{rt}$: -84.4 (c = 0.3, $CHCl_3$).

NMR spectra of compounds 4a-s

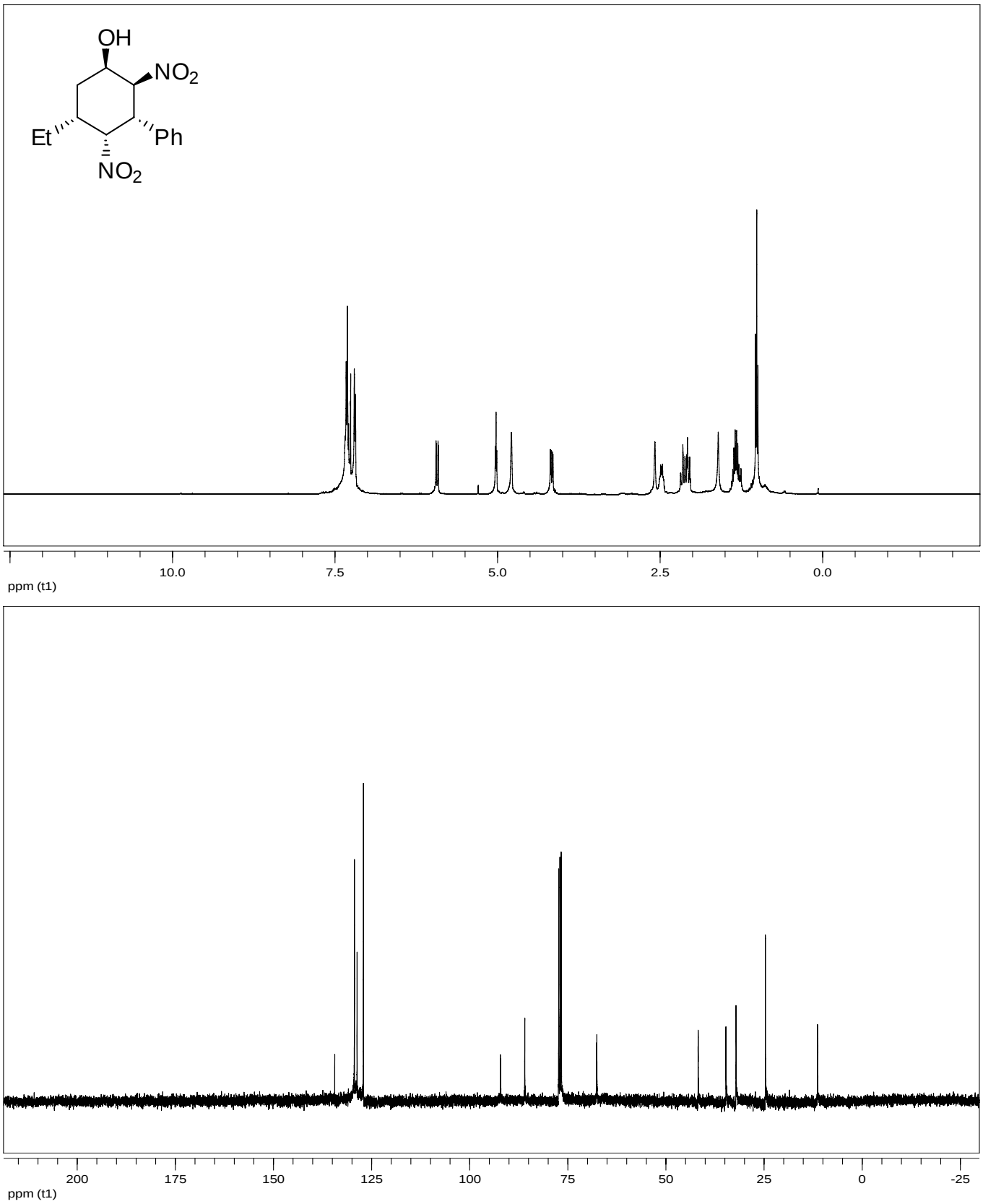


Figure 1a. NMR spectra of compound **4a**.

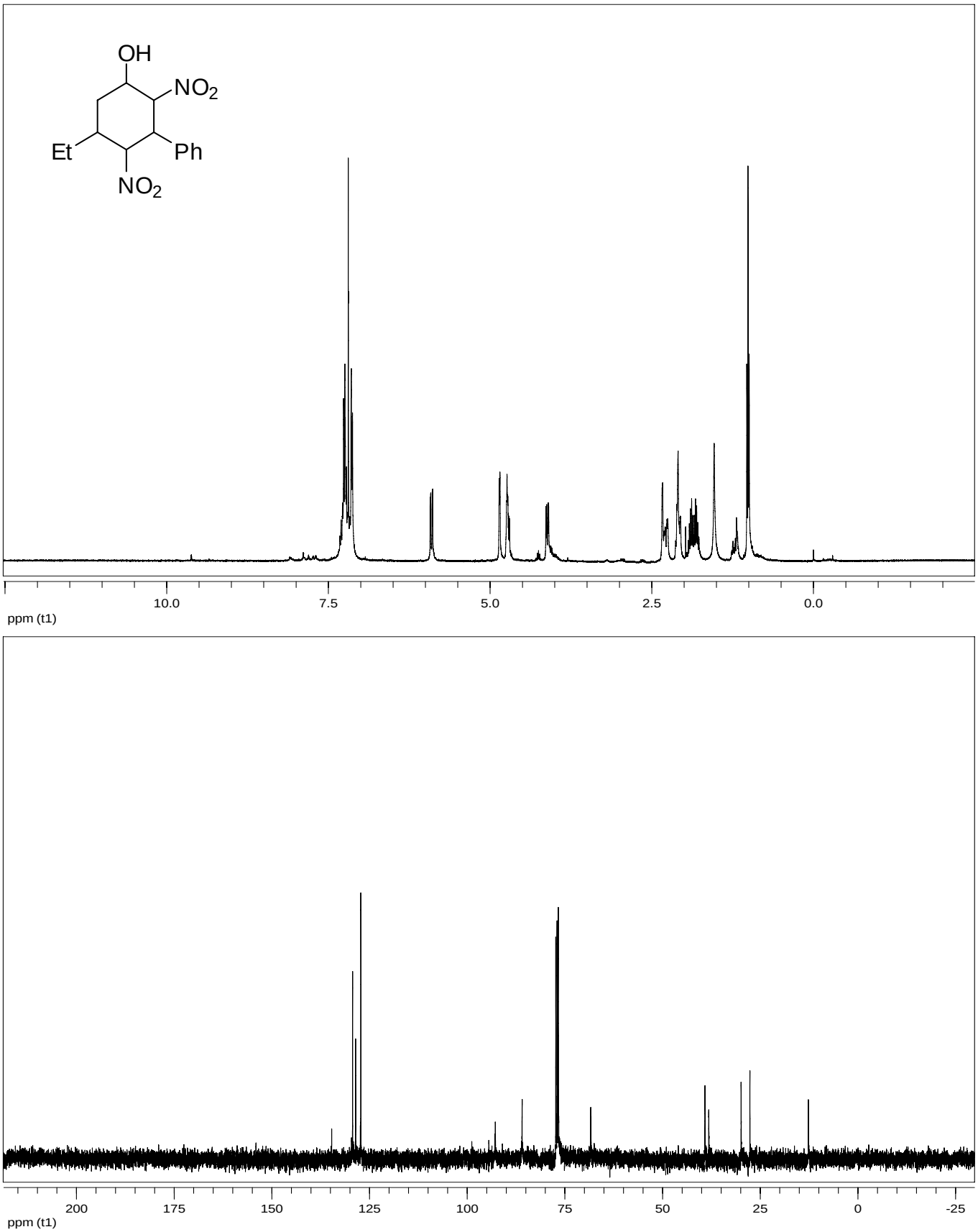


Figure 1b. NMR spectra of compound **4a′**.

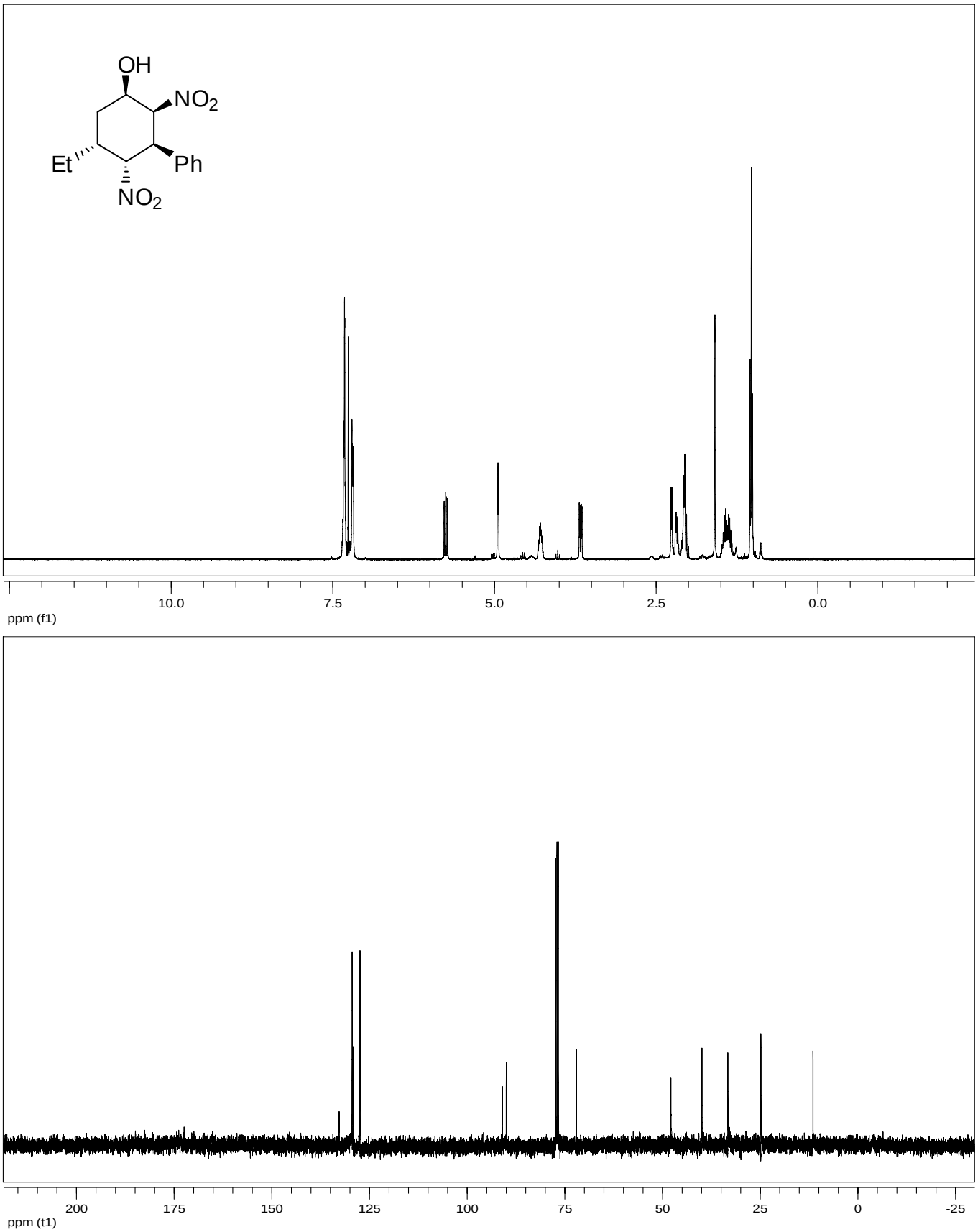


Figure 1c. NMR spectra of compound **4a''**.

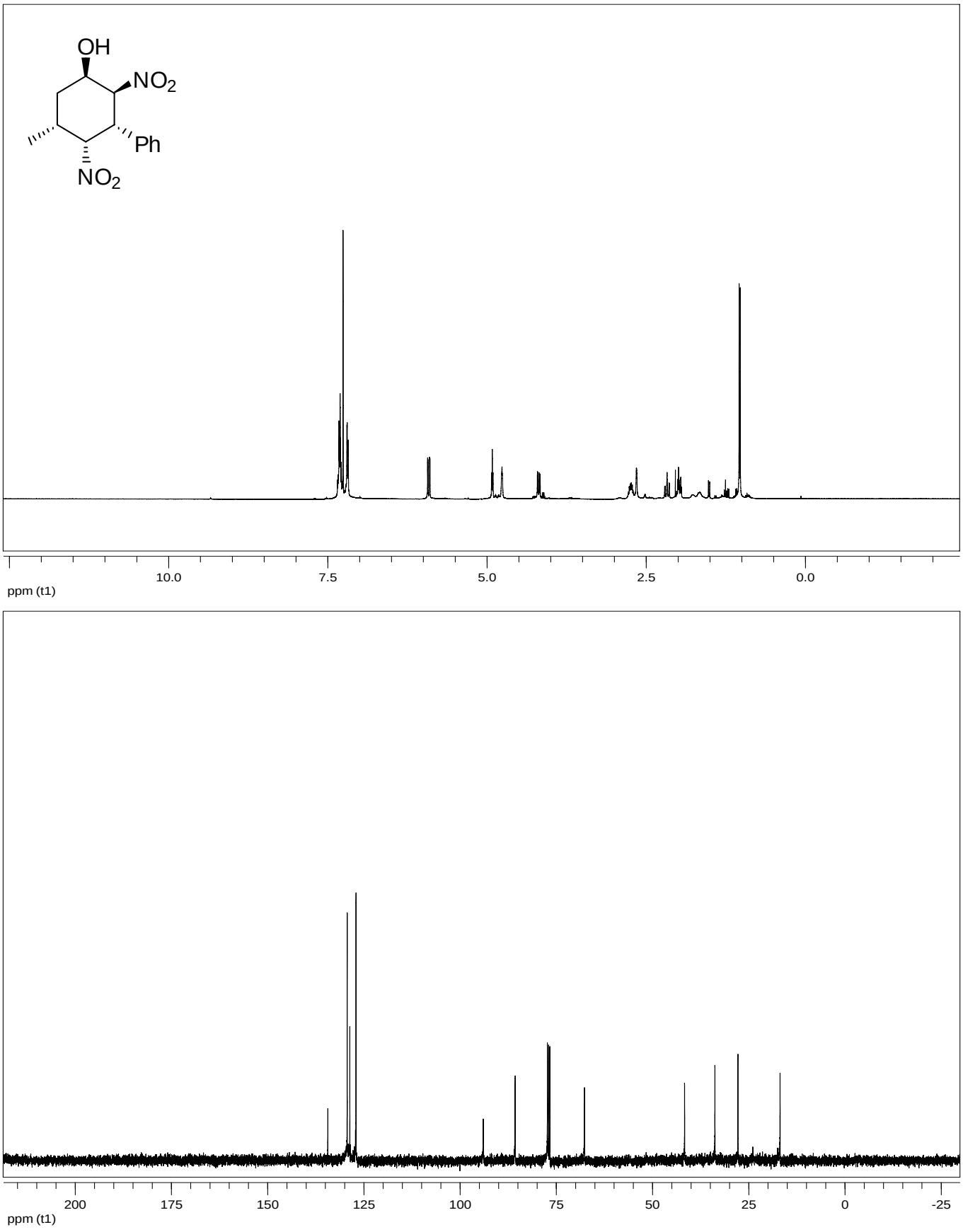


Figure 2. NMR spectra of compound **4b**.

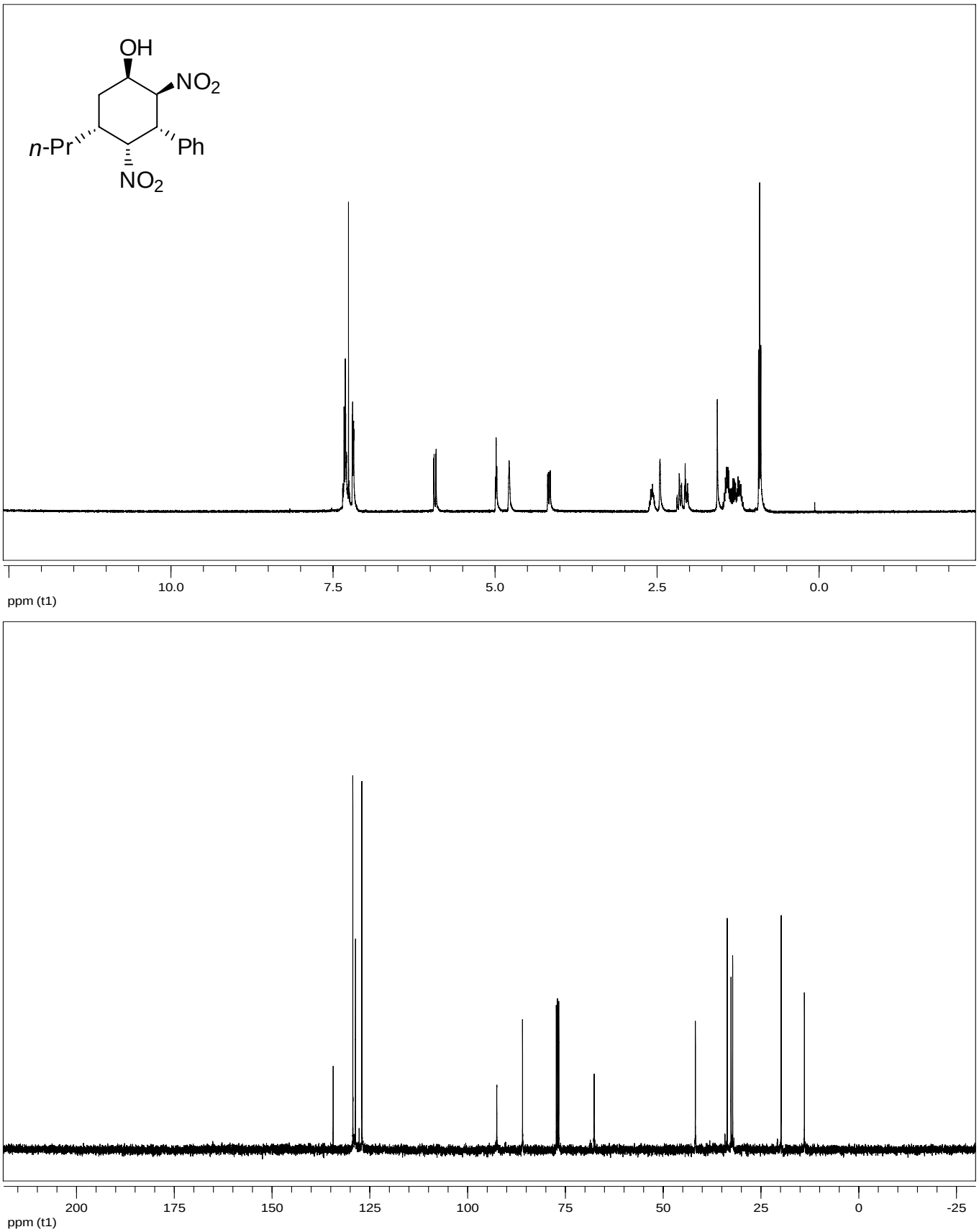


Figure 3. NMR spectra of compound **4c**.

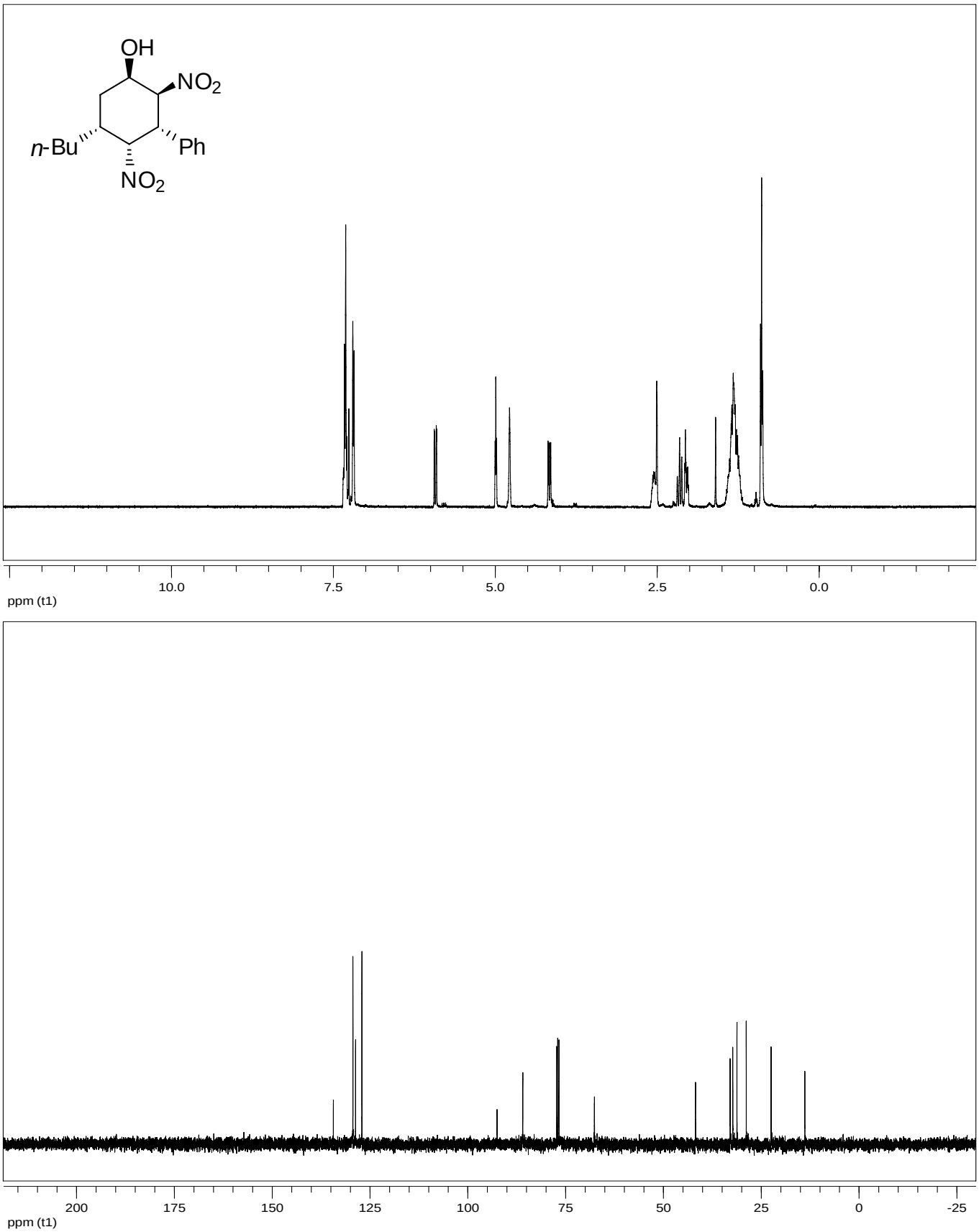


Figure 4. NMR spectra of compound **4e**.

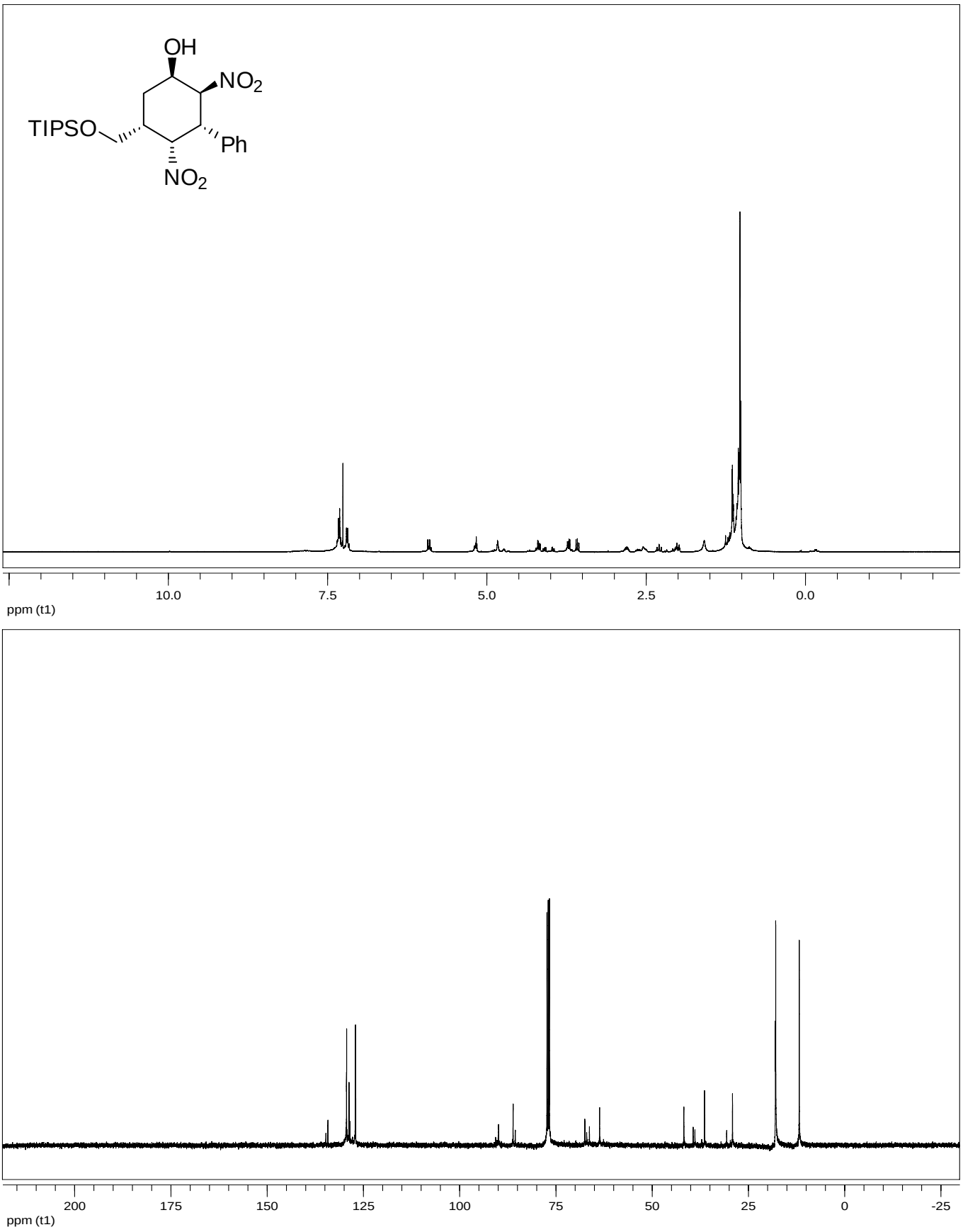


Figure 5. NMR spectra of compound **4f**.

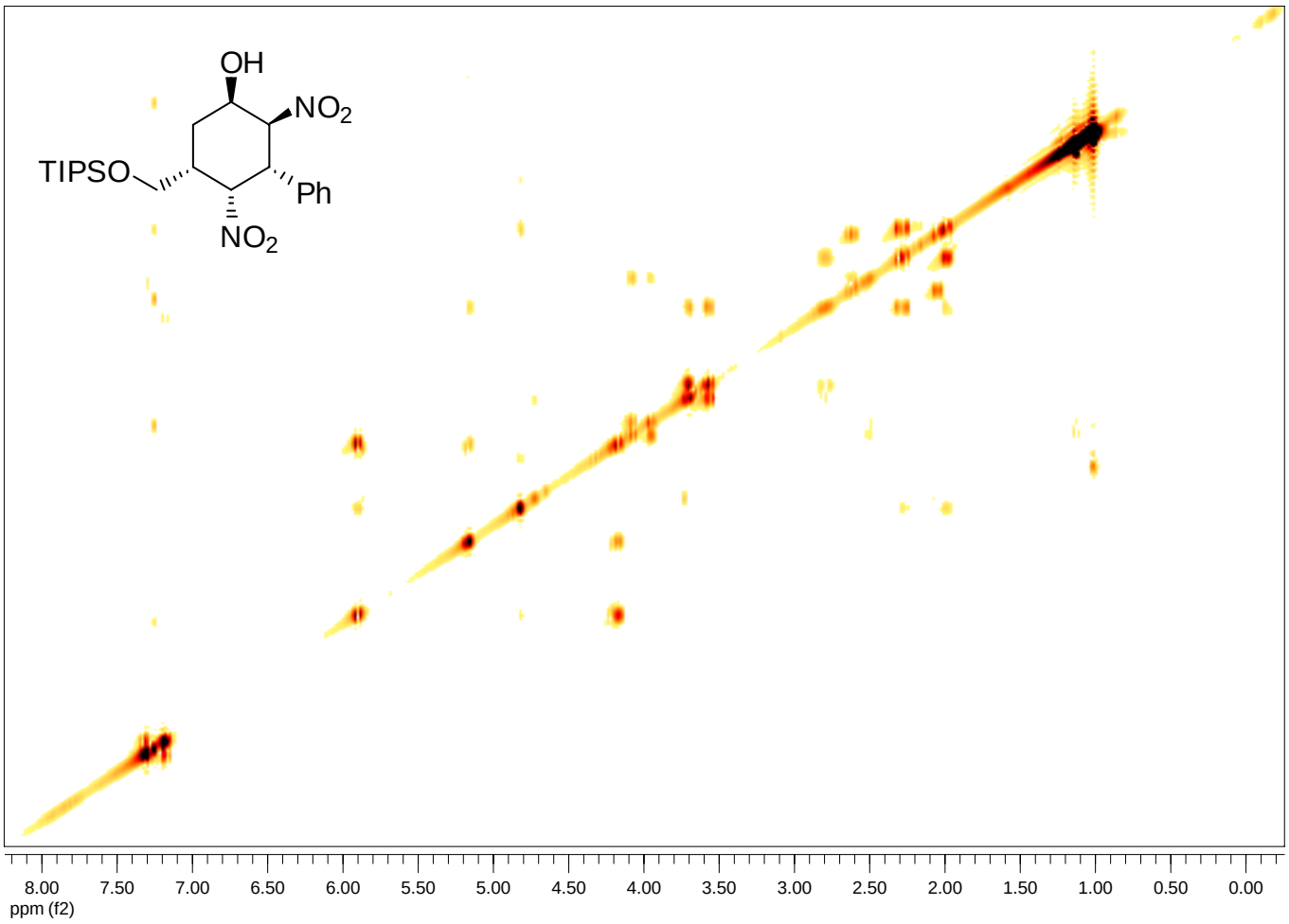


Figure 6. COSY spectra of compound **4f**.

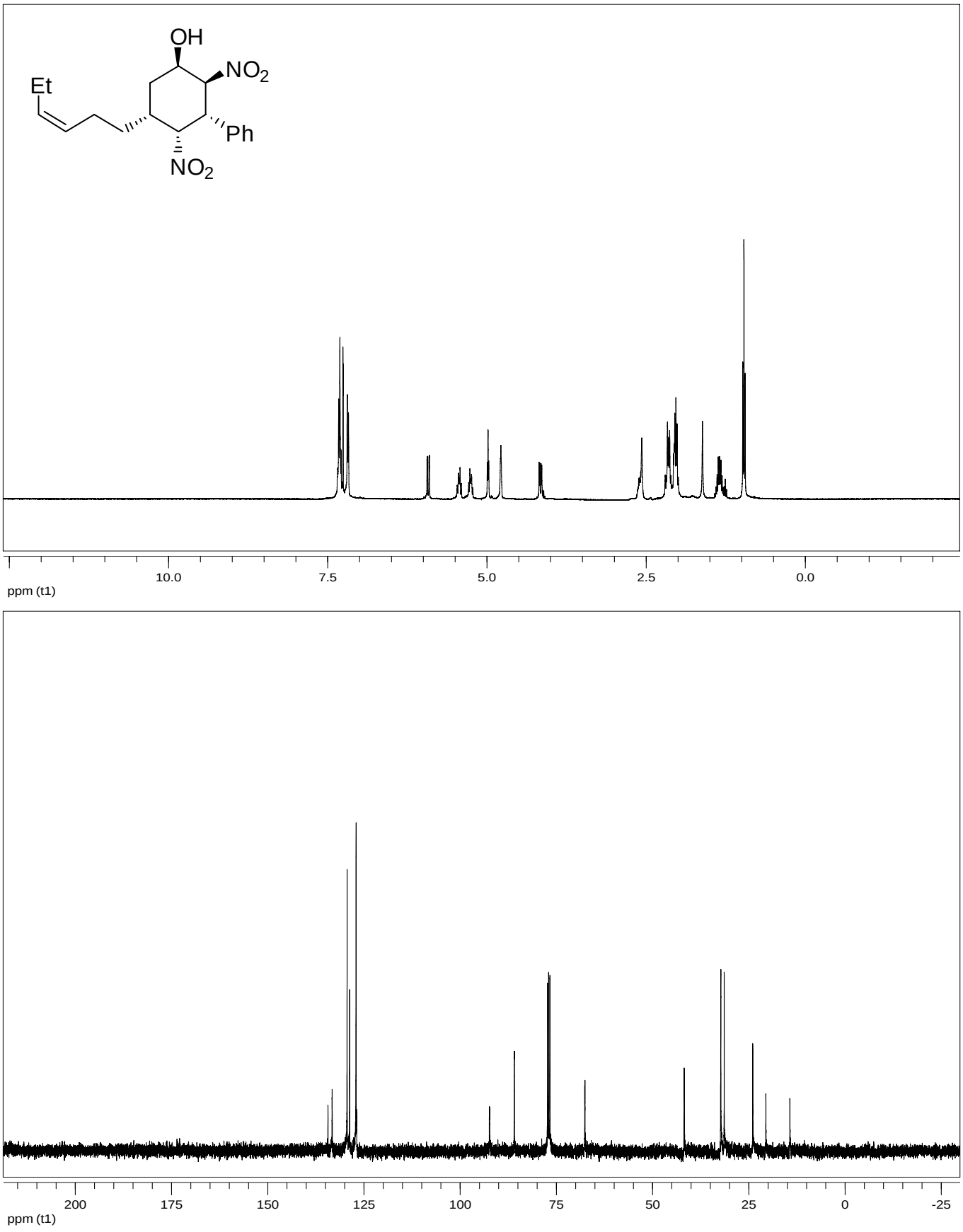


Figure 7. NMR spectra of compound **4g**.

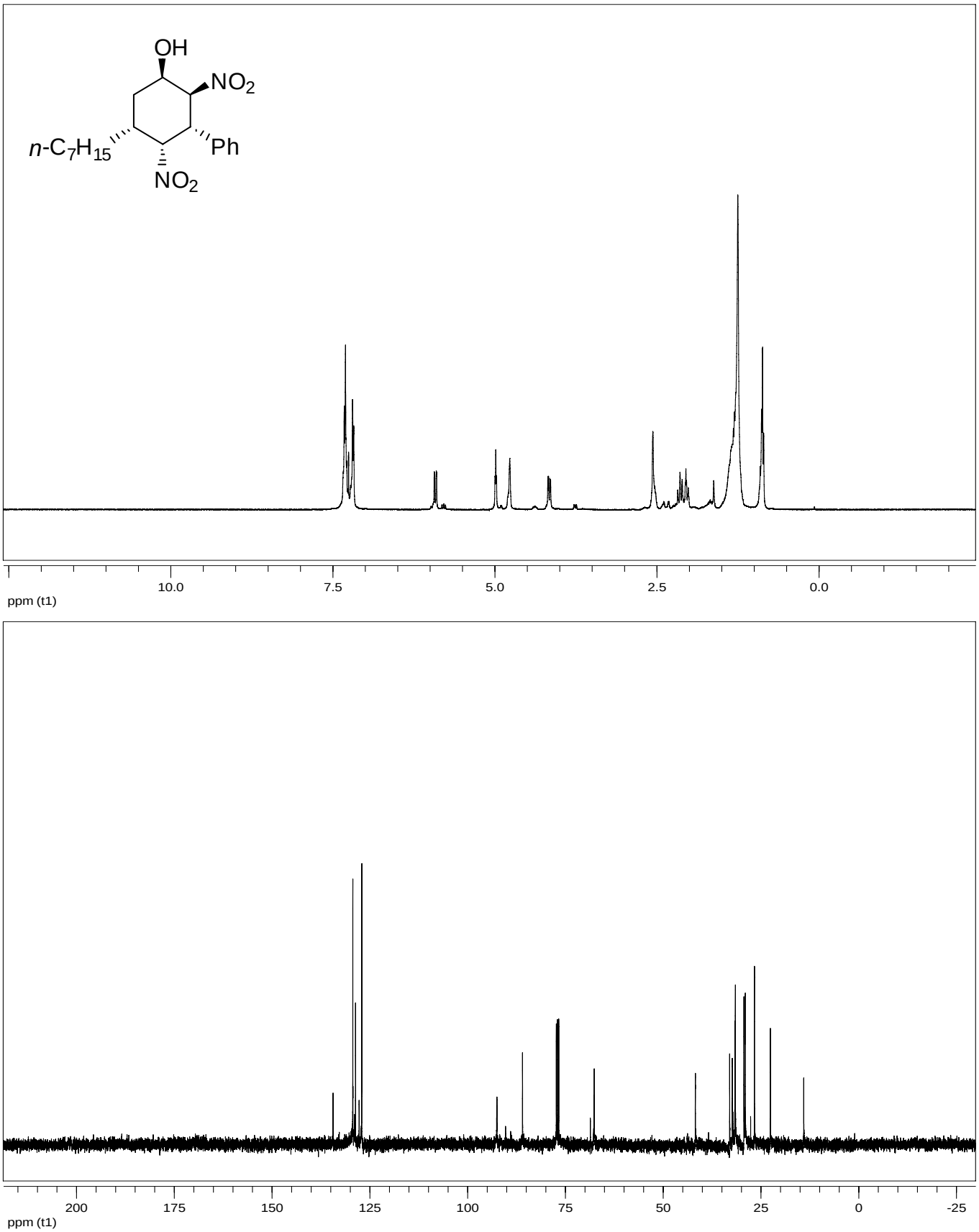


Figure 8. NMR spectra of compound **4h**.

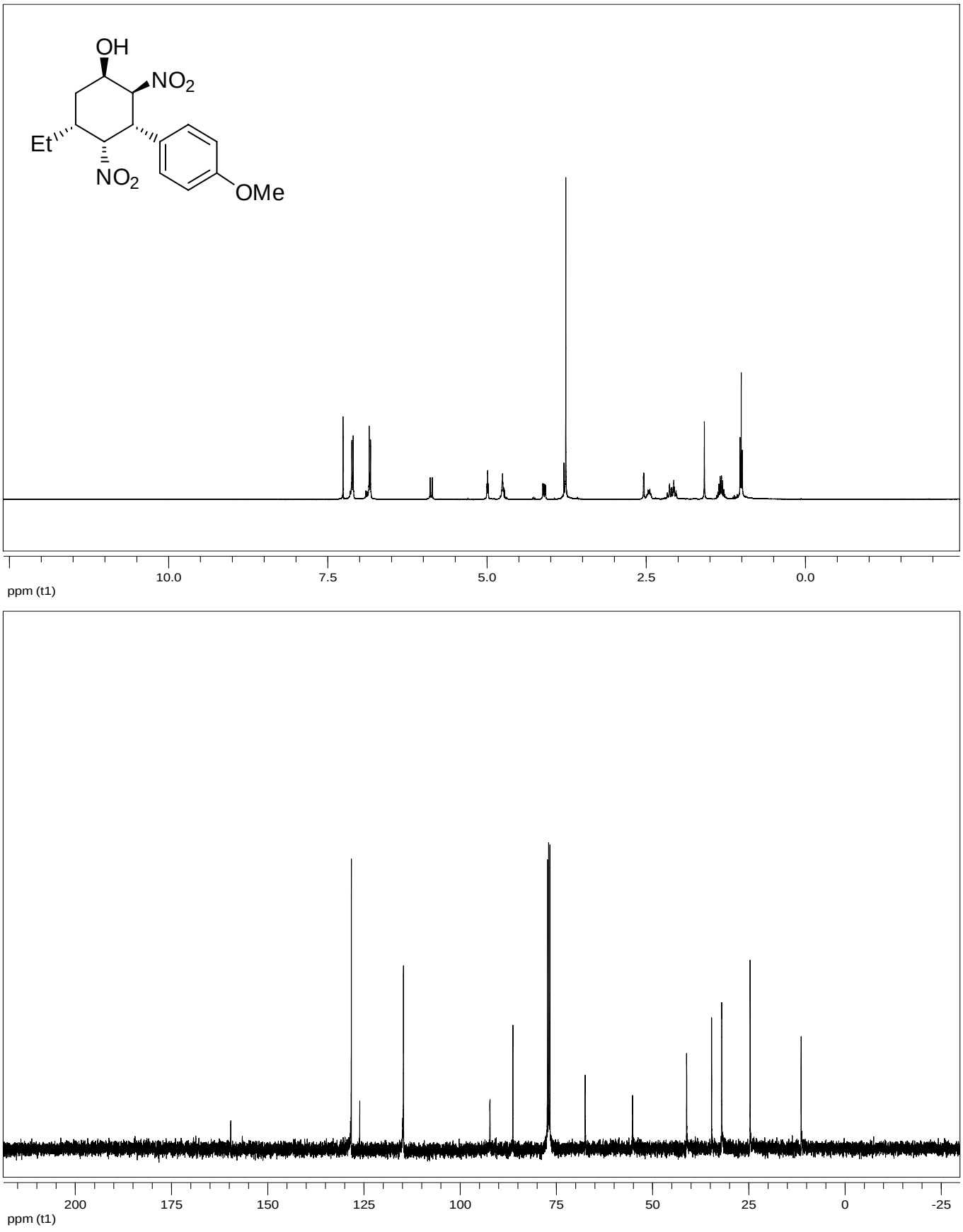
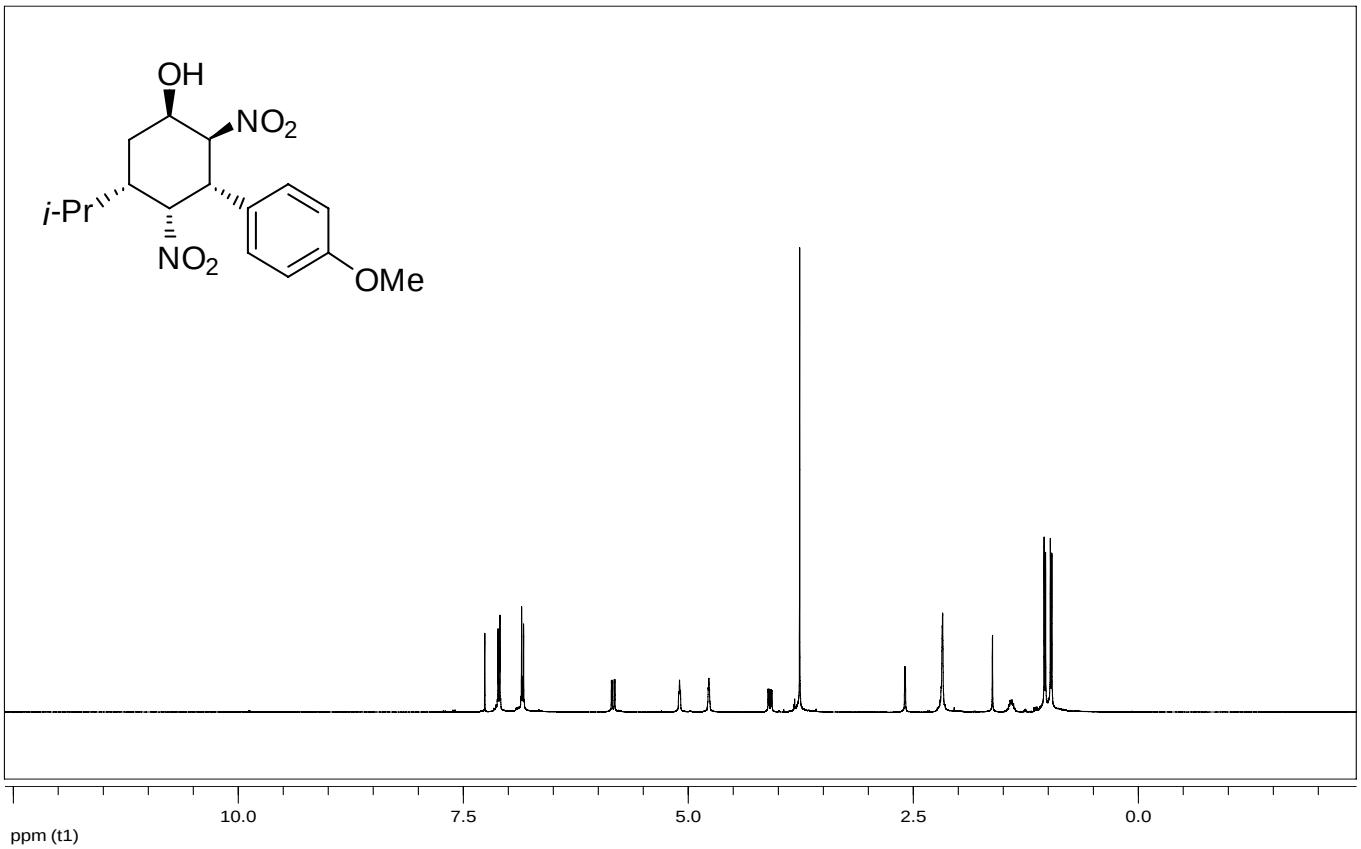


Figure 9. NMR spectra of compound **4i**.



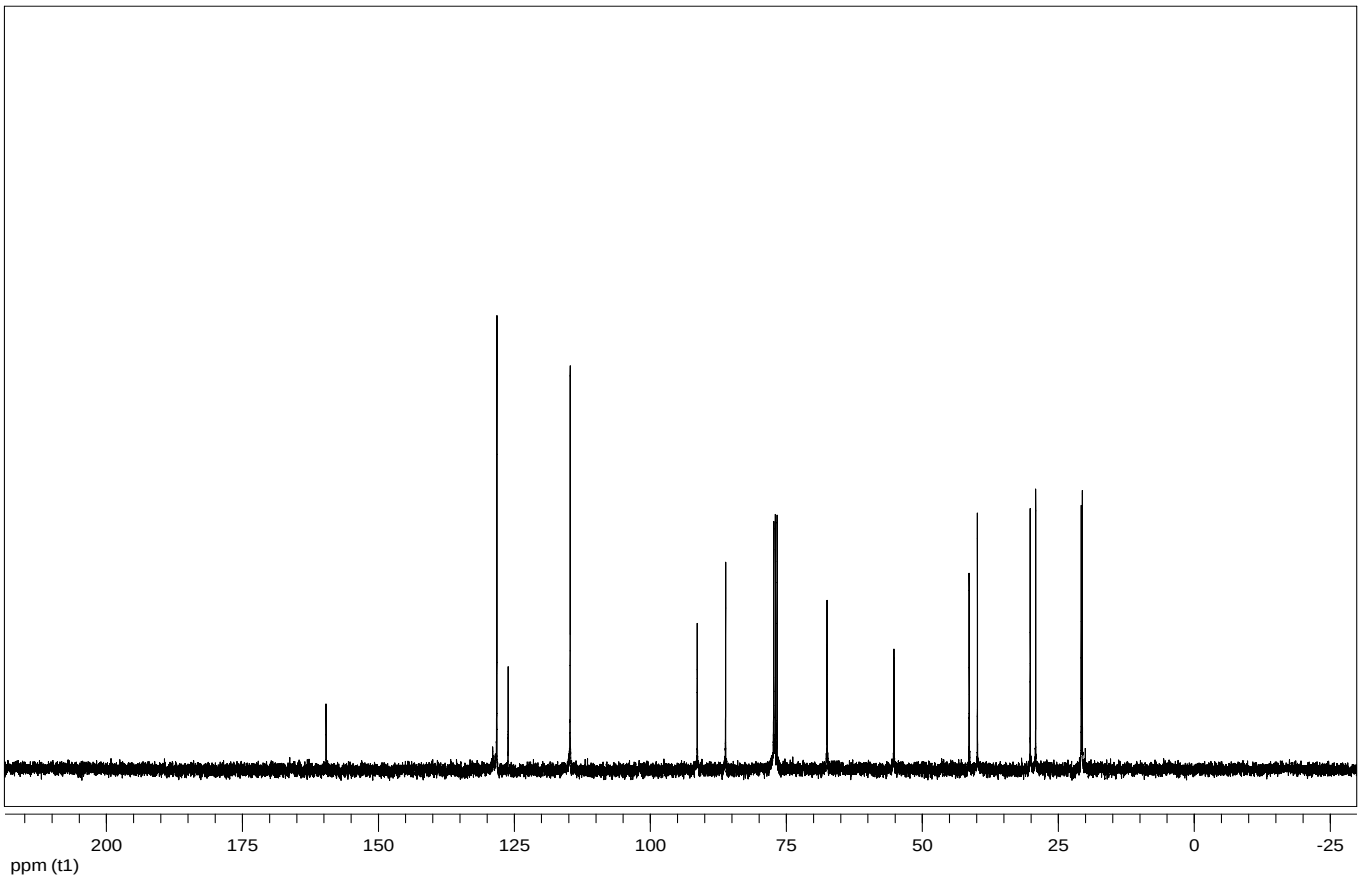
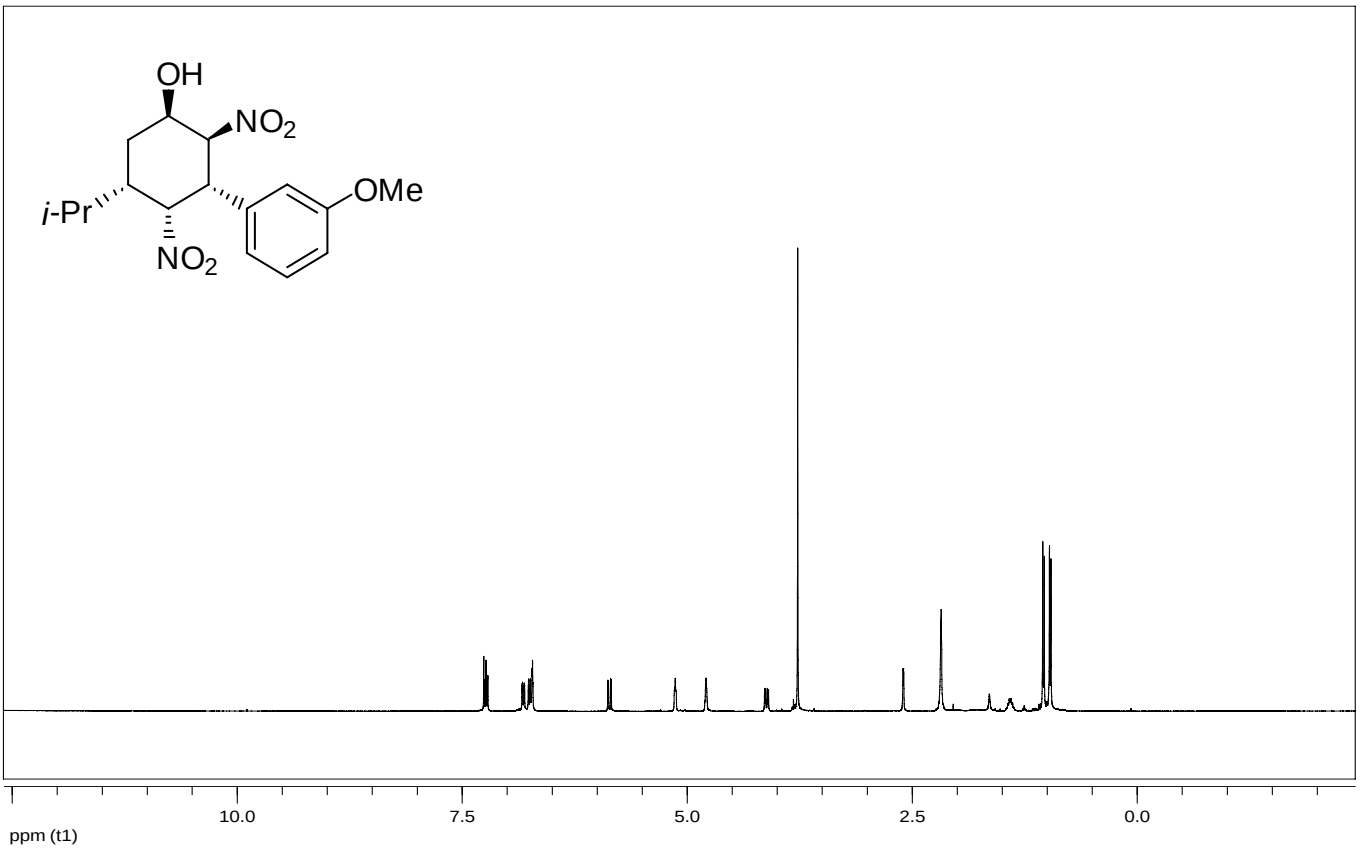


Figure 10. NMR spectra of compound **4j**.



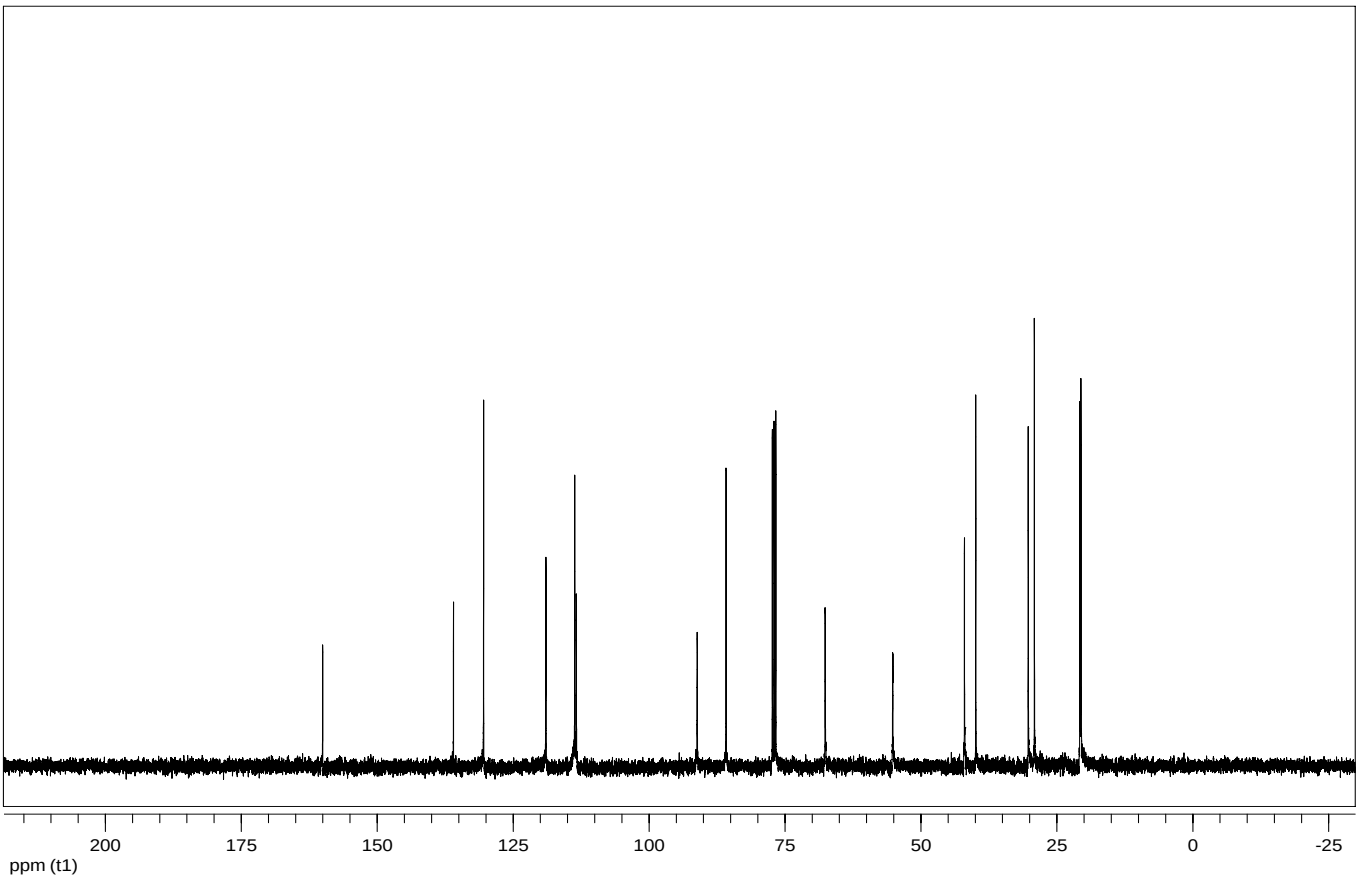
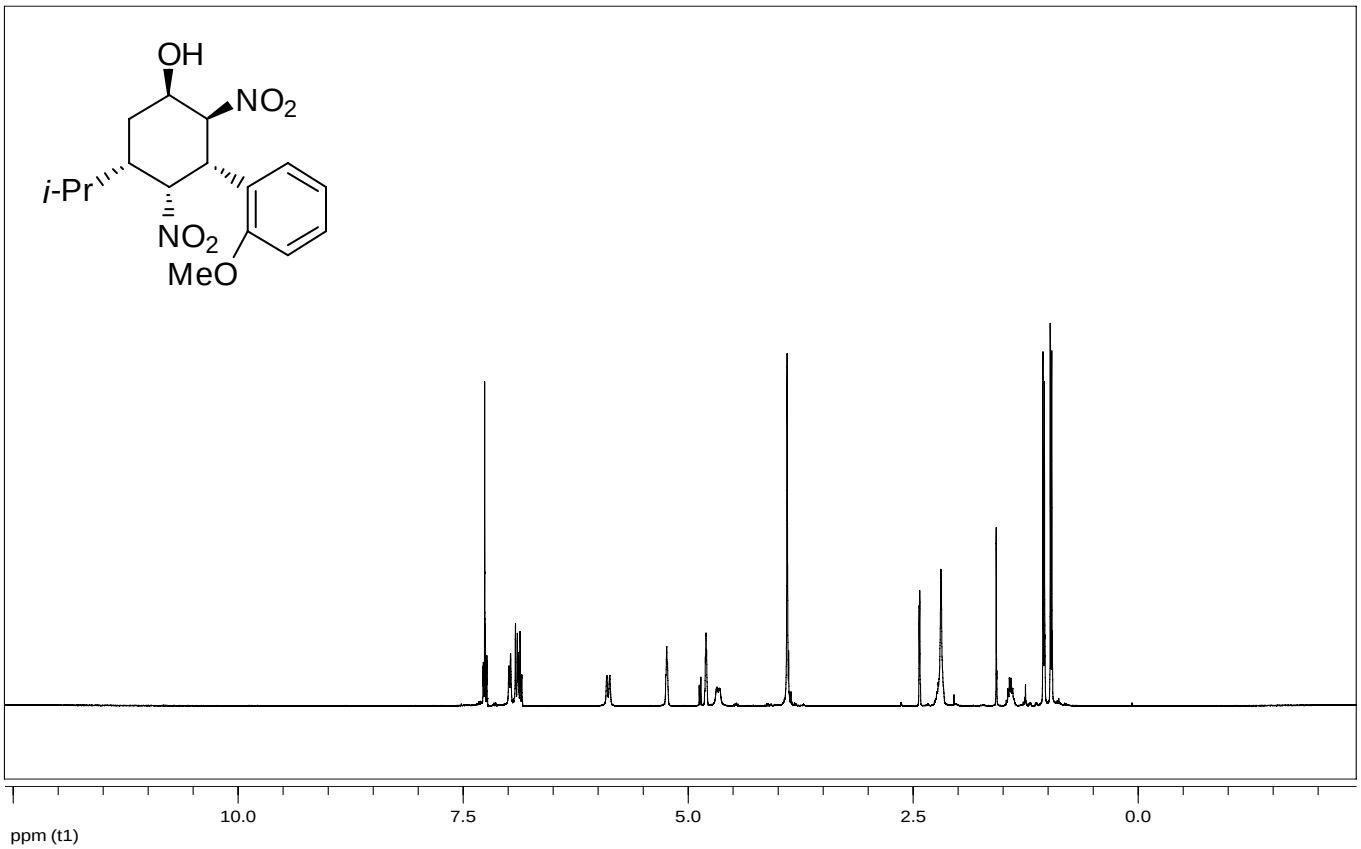


Figure 11. NMR spectra of compound **4k**.



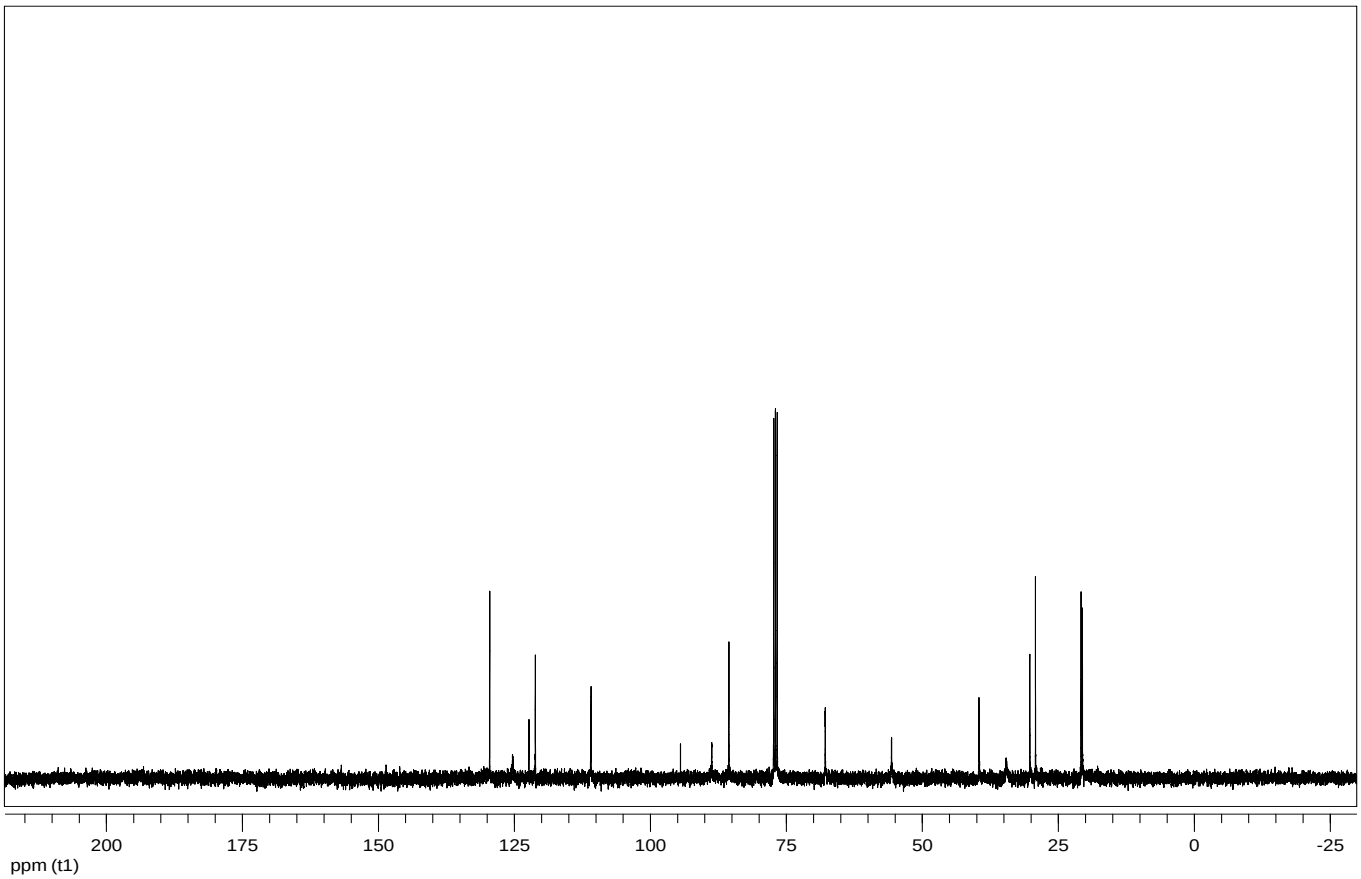


Figure 12. NMR spectra of compound **4l**.

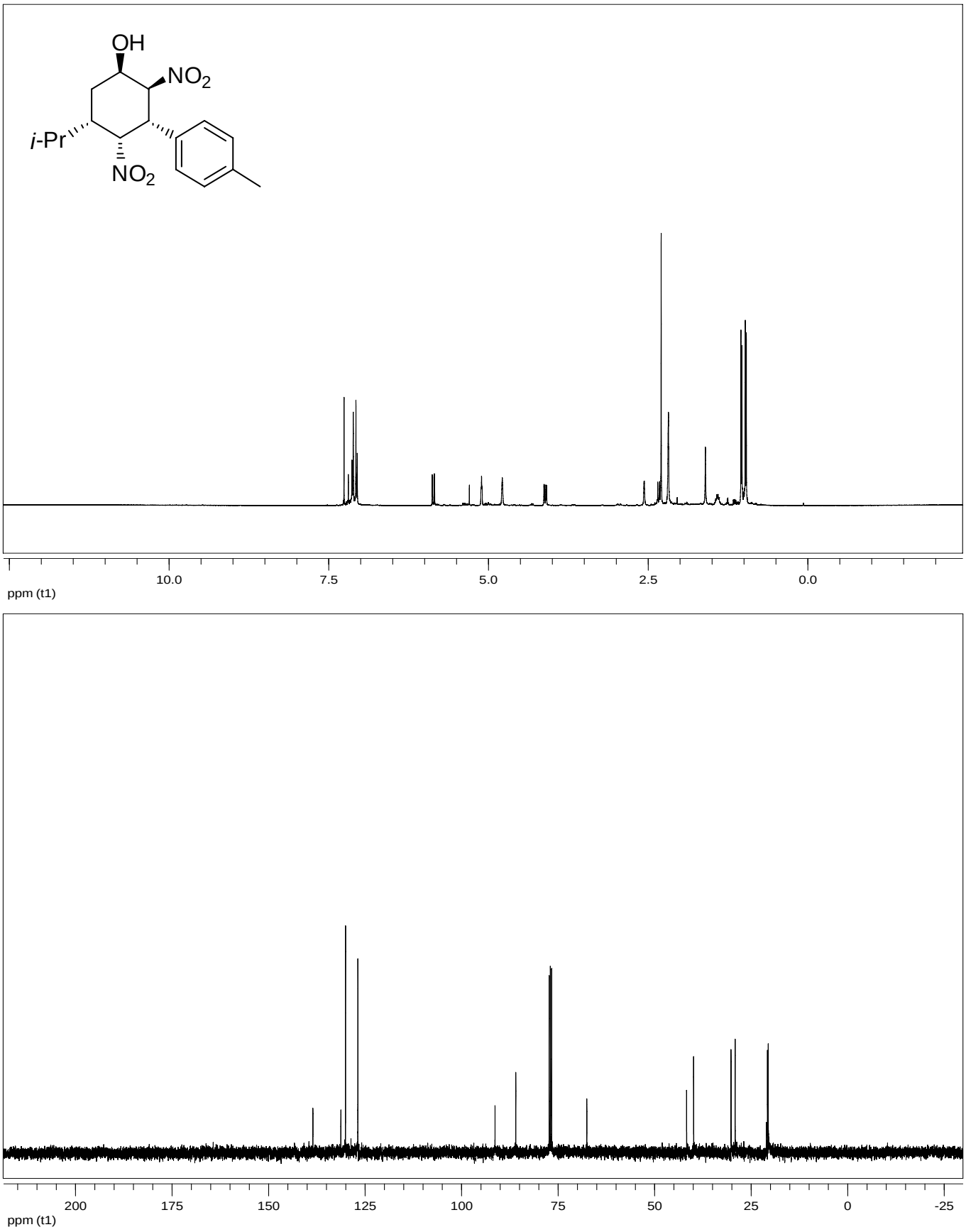
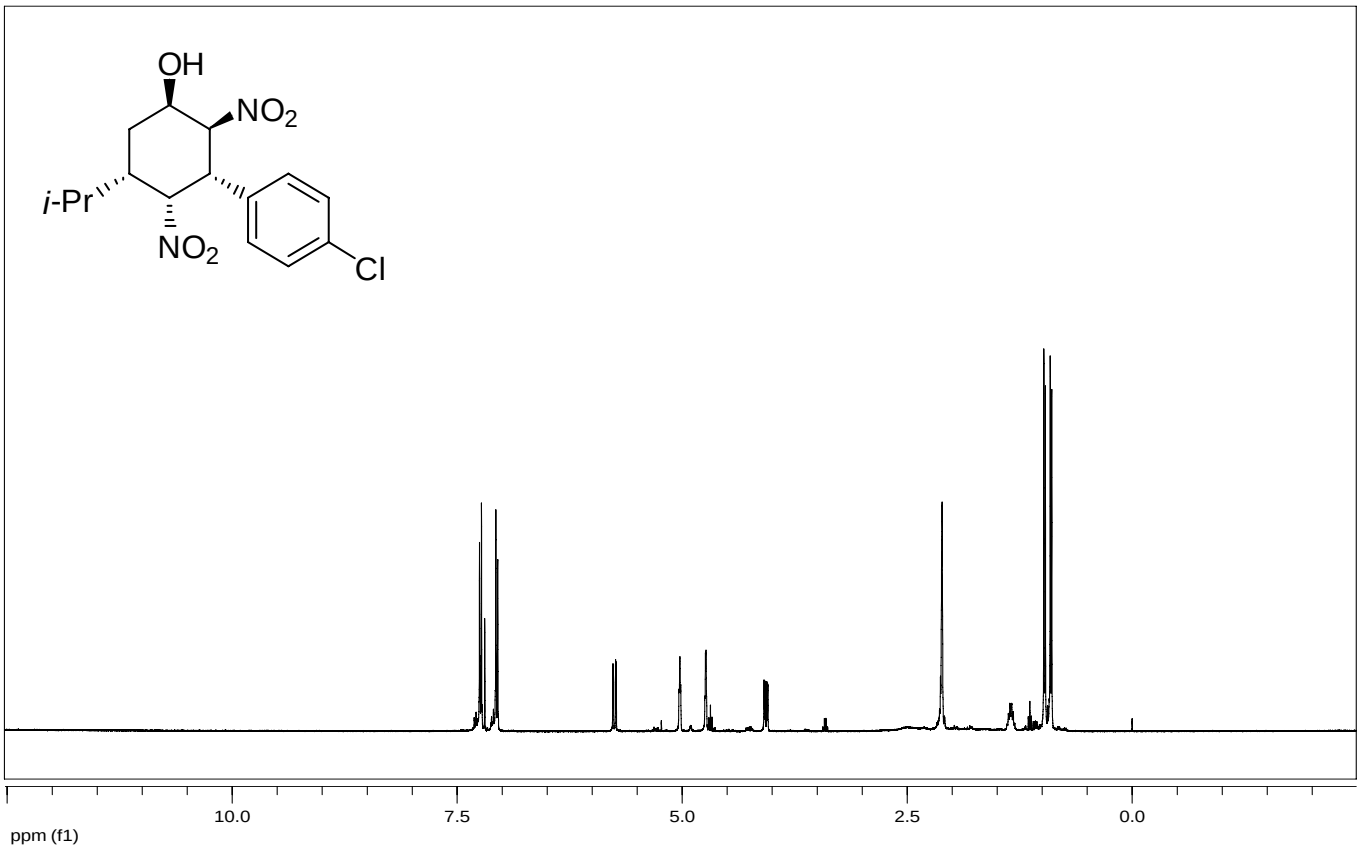


Figure 13. NMR spectra of compound **4m.**



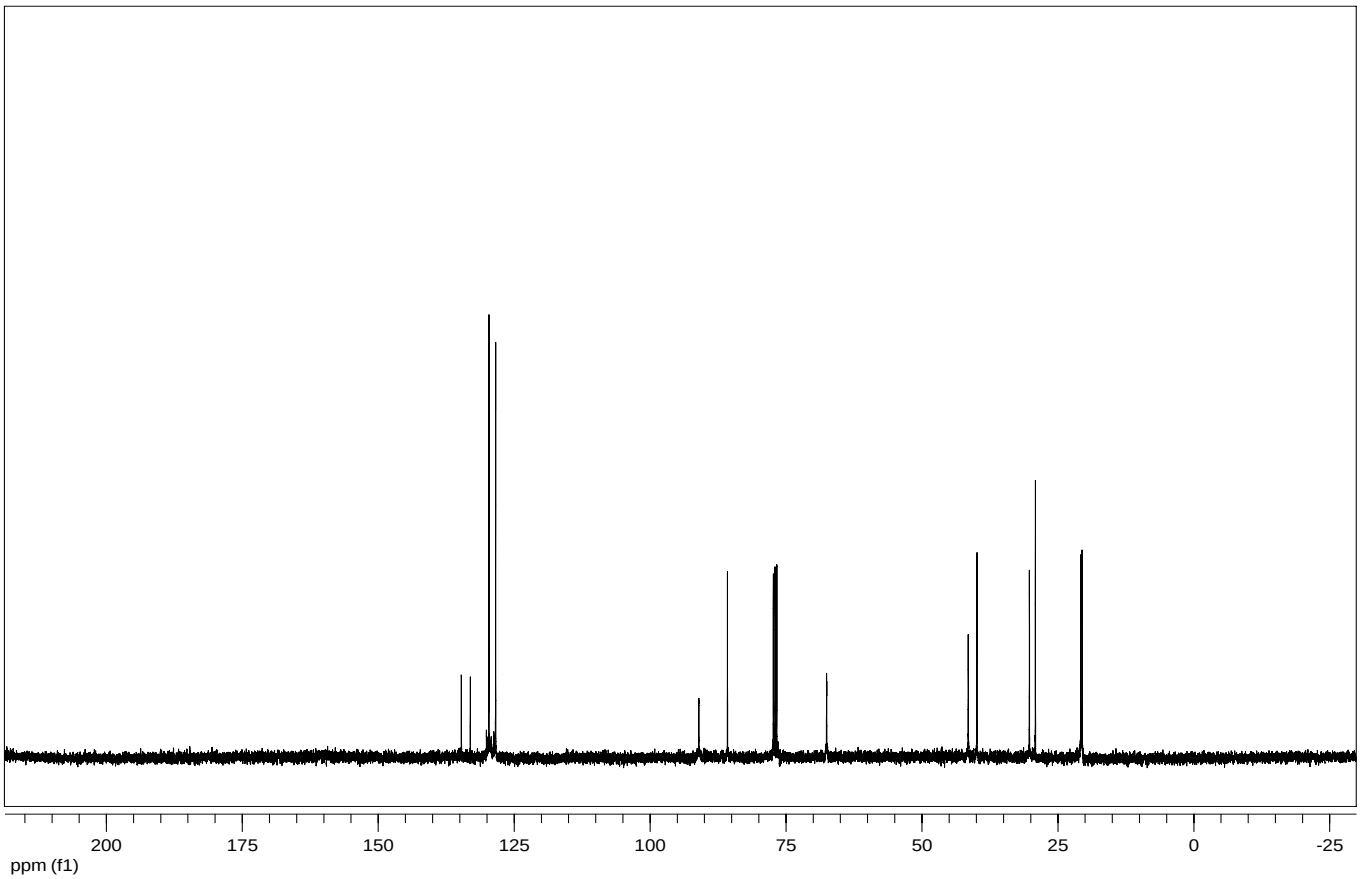


Figure 14. NMR spectra of compound **4n**.

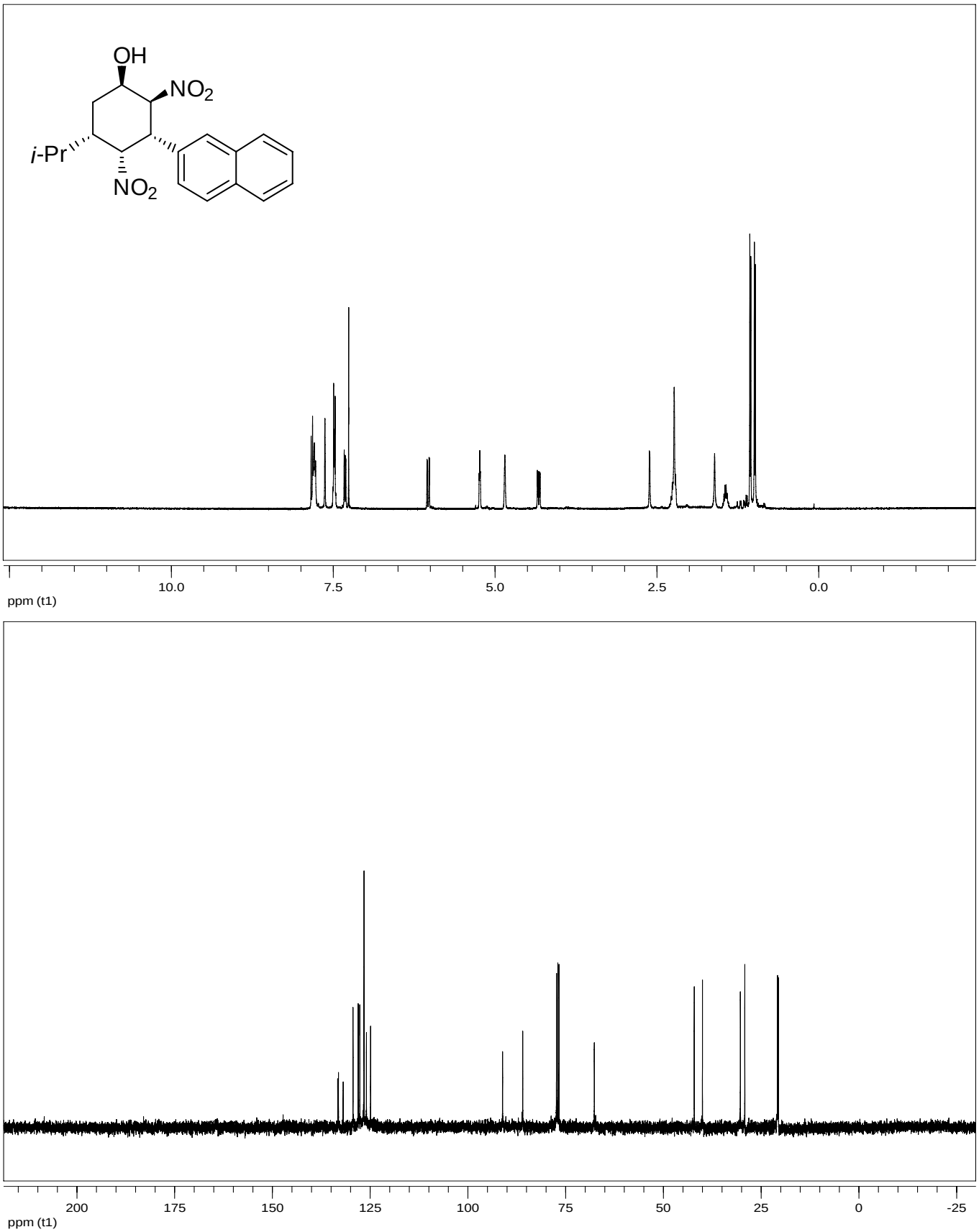


Figure 15. NMR spectra of compound **4o**.

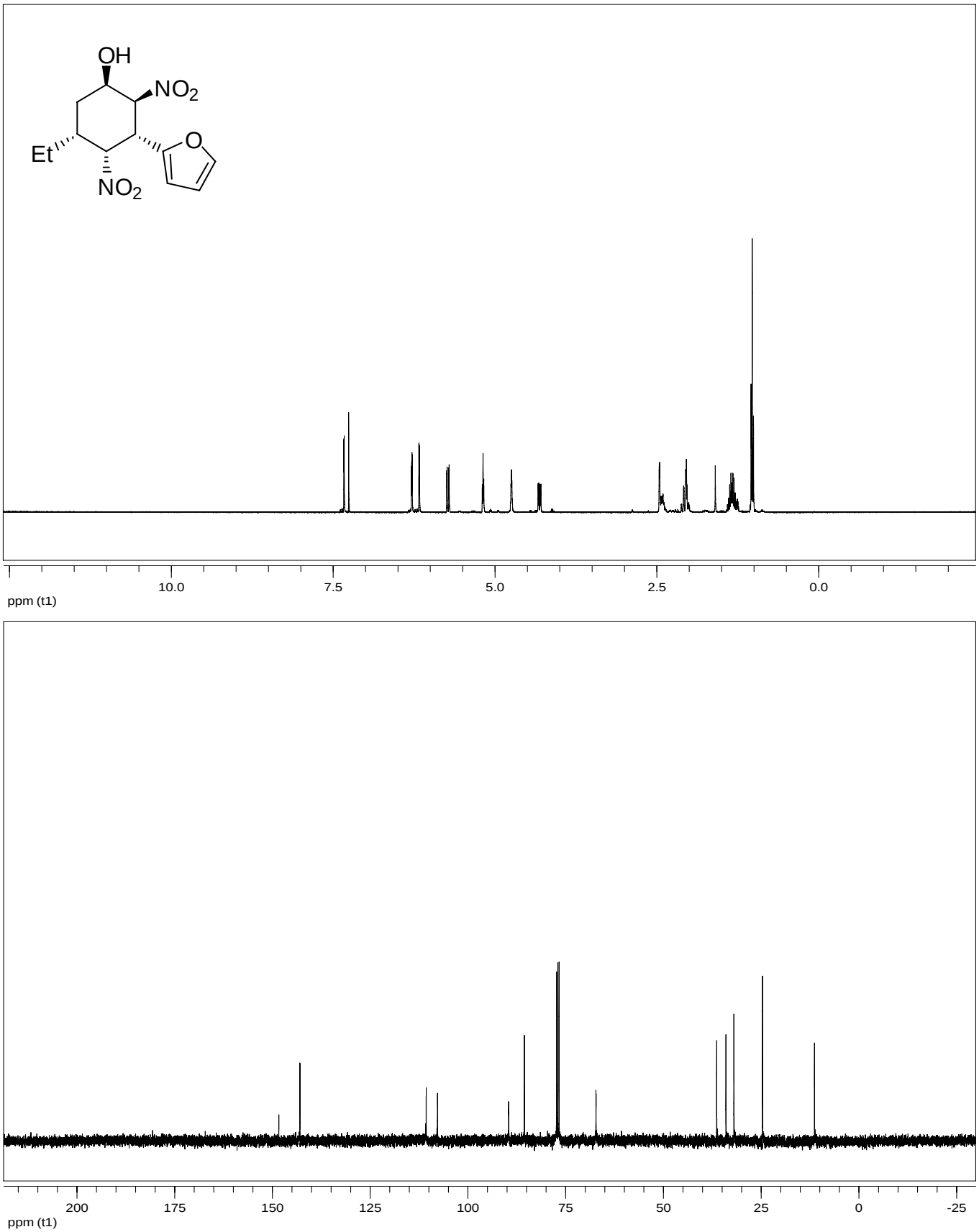


Figure 16. NMR spectra of compound **4p**.

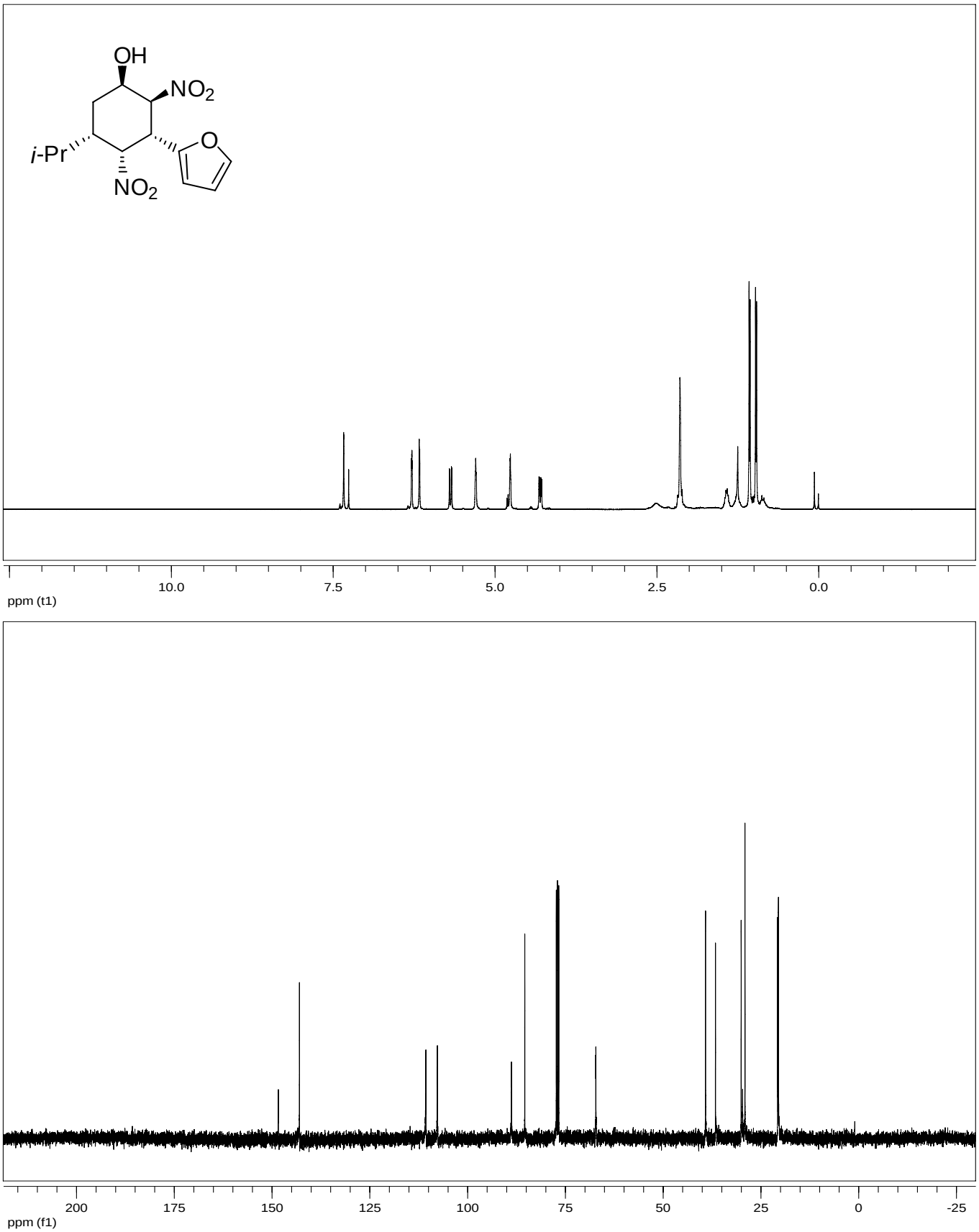


Figure 17. NMR spectra of compound **4q**.

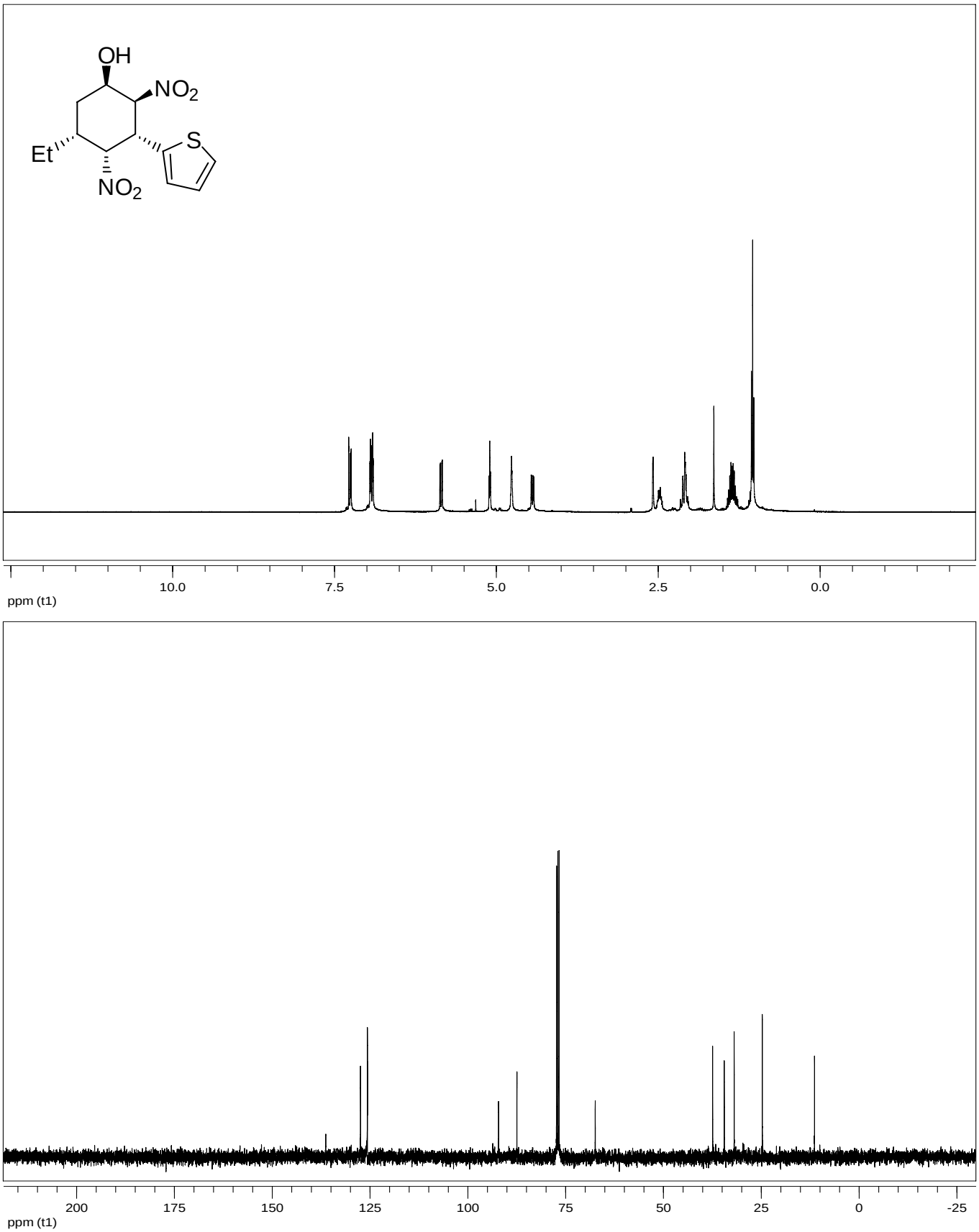


Figure 18. NMR spectra of compound **4r**.

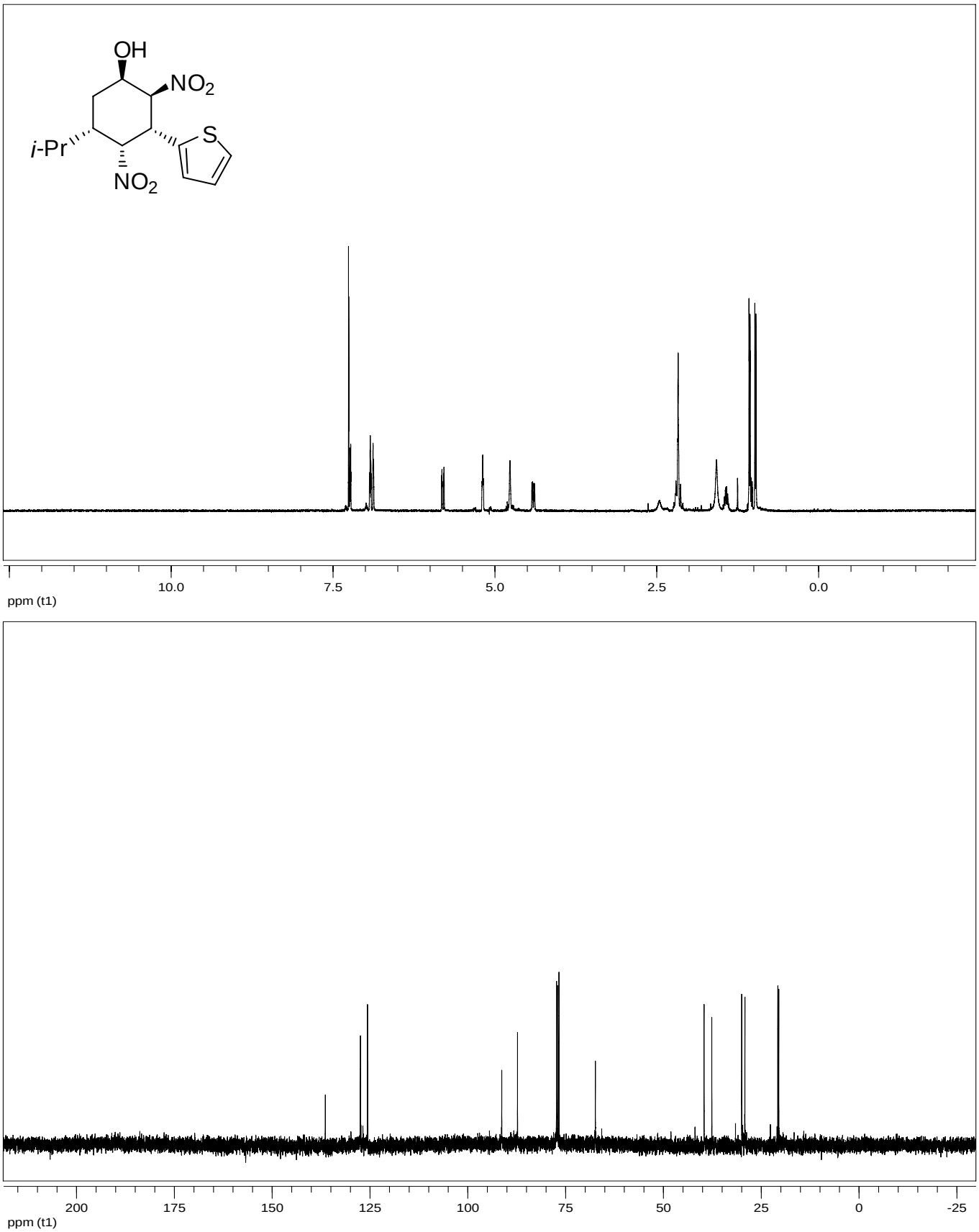


Figure 19. NMR spectra of compound **4s.**