Supplementary Material (ESI) for Chemical Communications

A Modular and Organocatalytic Asymmetric Approach to γ-Butyrolactone Autoregulators from *Streptomycetes*

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Contents

1. General Methods.

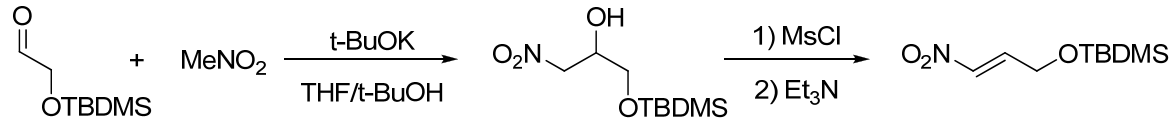
NMR spectra were acquired on a Varian AS 400 spectrometer, running at 400 and 100 MHz for ^{1}H and ^{13}C, respectively. Chemical shifts (δ) are reported in ppm relative to residual solvent signals ($CHCl_3$, 7.26 ppm for ^{1}H NMR, $CDCl_3$, 77.0 ppm for ^{13}C NMR). The following abbreviations are used to indicate the multiplicity in ^{1}H NMR spectra: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; bs, broad signal. ^{13}C NMR spectra were acquired on a broad band decoupled mode. In order to characterize ^{1}H and ^{13}C NMR spectra of diastereomeric (or keto-enol) mixtures, the following notations are used. *denotes the minor diastereomer (or the enol form); $^{+}$denotes overlap of signals from both diastereomers (both the keto and the enol form), the number of protons (or carbons) given in the parentheses represent the sum of protons (or carbons) from both diastereomers (keto-enol forms). 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 AD and Daicel Chiralcel OD columns) or by GC using a chiral Chrompack CP Chiralsil-Dex Cβ column. Unless otherwise noted, 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) and Iatrobeads (Iatron Laboratories Inc. 6RS-8060) were used.

2. Preparation of the catalysts

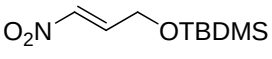
Catalysts **3a-d** were prepared according to the literature procedure.[1]

[1] B. Vakulya, S. Varga, A. A. Csámpai, T. Soós, *Org. Lett.* **2005**, *7*, 1967.

3. Preparation of the electrophile



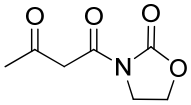
(*E*)-*tert*-butyldimethyl(3-nitroallyloxy)silane (2)



The silyloxyacetaldehyde[2] (2 mmol) and $MeNO_2$ (183 mg, 3 mmol) were dissolved in 1:1 THF(dry)/*t*-BuOH (1 mL). *t*-BuOK (22.4 mg, 0.2 mmol) was then added at 0 °C. The mixture was allowed to slowly warm up to rt and stirred over night under N_2 atmosphere. The reaction was then diluted with H_2O (10 mL) and drops of brine, extracted with EtOAc (3 x 15 mL), dried over $MgSO_4$ and concentrated *in vacuo*. To the afforded crude Henry addition product in anhyd. CH_2Cl_2 (10 mL) was added $MeSO_2Cl$ (356 mg, 3.1 mmol) at 0 °C in one portion. Et_3N (628 mg, 6.2 mmol) was then slowly added over 5 min. The reaction was stirred at 0 °C for 3 min and quenched with 1 M $KHSO_4$. The aq. phase was extracted twice with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by FC (5:95 to 1:4 EtOAc/hexane) provided the nitroalkene **2** as a yellowish liquid in 64% yield over 2 steps. ^{1}H NMR (400 MHz, $CDCl_3$) 7.32 (dt, *J* = 12.98, 3.03 Hz, 1H), 7.17 (dt, *J* = 12.97, 2.39 Hz, 1H), 4.44 (dd, *J* = 3.02, 2.42 Hz, 2H), 0.94-0.91 (m, 9H), 0.10-0.09 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.8, 139.3, 59.7, 25.7 (3C), 18.2, -5.6 (2C). HRMS: Calculated for $[C_9H_{19}NNaO_3Si]^+$: 240.1026; found: 240.1030.

4. Preparation of the nucleophiles

Nucleophiles **1a**-**b** are commercially available and were used as received. Nucleophile **1c** was synthesized according to the literature procedure.[3]

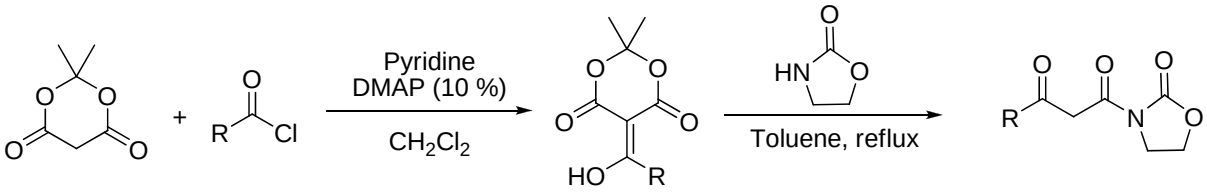


1-(2-Oxooxazolidin-3-yl)butane-1,3-dione (1d). The procedure reported by M. P. Doyle et al.[4] was applied. *n*-BuLi (6.25 mL of the 1.6 M solution in hexane, 10.0 mmol) was added drop-

[2] Prepared according the procedure presented by Shibasaki et al.: M. Sodeoka, H. Yamada, M. Shibasaki, *J. Am. Chem. Soc.* **1990**, *112*, 4906.
[3] T. Inokuchi, H. Kawafuchi, *J. Org. Chem.* **2006**, *71*, 947.
[4] M. P. Doyle, R. L. Dorow, J. W. Terpstra, R. A. Rodenhouse, *J. Org. Chem.* **1985**, *50*, 1663.

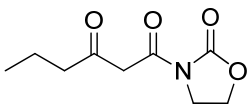
wise to a stirring solution of 2-oxazolidinone (1.67 g, 9.5 mmol) in dry THF (20 mL) at -78 °C (Note: The oxazolidinone was not fully soluble). The mixture was then allowed to warm up to -40 °C. After recooling to -78 °C, the lithiated oxazolidinone was treated with a solution of diketene (0.87 mL, 11.0 mmol) in THF (5 mL). After the addition was complete, the mixture was maintained at -78 °C for additionally 30 min before slowly warming up to rt. The reaction is quenched with NH_4Cl (sat.), extracted with CH_2Cl_2, dried and concentrated ***in vacuo***. Subsequent FC (silica gel, 2:1 pentane/EtOAc) afforded **2d** in 74% yield as an off-white solid. ^1H NMR (400 MHz, $CDCl_3$). Keto/enol ratio: 7:1; δ ppm 6.33* (s, 1H), 4.33$^+$ (t, ***J*** = 8.12 Hz, 4H), 3.93$^+$ (t, ***J*** = 8.22 Hz, 4H), 3,90 (s, 2H), 2.15 (s, 3H), 1.93* (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.0, 166.2$^+$ (2C), 153.5$^+$ (2C), 89.1*, 62.1, 61.8*, 50.6, 41.8, 41.7*, 29.8, 21.7*. HRMS: Calculated for $[C_7H_9NNaO_4]^+$: 194.0424; found: 194.0430. M.p. (pentane/EtOAc): 54 °C.

General procedure: The protocol reported by C. Marchi et al. was used for preparation of nucleophiles **1e-j**.[5]

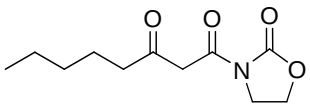


Meldrum's acid (2.00 g, 13.8 mmol), dimethylaminopyridine (0.34, 2.7 mmol) and anhyd. pyridine (2.23 mL, 27.6 mmol) were dissolved in anhyd. CH_2Cl_2 (50 mL) with stirring under N_2 atmosphere. The solution was cooled to 0 °C and the corresponding alkanoyl chloride (20.7 mmol) was added. The mixture was stirred for 2 h at 0 °C and slowly allowed to warm up to rt. After stirring for additionally 15 h, the solvent was evaporated and oxazolidin-2-one (1.8 g, 20.7 mmol) and anhyd. toluene (50 mL) were added. The mixture was refluxed for 5 h and concentrated ***in vacuo***. FC on silica-gel afforded the pure products. Solid products **1d-i** were further recrystallized from pentane/EtOAc.

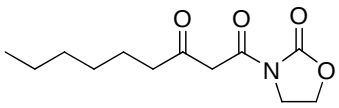
[5] C. Marchi, E. Trepat, M. Moreno-Manãs, A. Vallribera, E. Molins, ***Tetrahedron*** **2002**, ***58***, 5699.



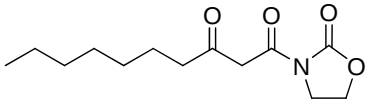
1-(2-Oxooxazolidin-3-yl)hexane-1,3-dione (1e). Following the general procedure **1e** was isolated by FC (petane/EtOAc 2:1) in 92% yield. ^{1}H NMR (400 MHz, $CDCl_3$). Keto/enol ratio: >20:1; δ ppm 6.49* (s, 1H), 4.44^{+} (t, ***J*** = 8.12 Hz, 4H), 4.07^{+} (t, ***J*** = 8.14 Hz, 4H), 4.03 (s, 2H), 2.53 (t, ***J*** = 7.33 Hz, 2H), 2.27* (t, ***J*** = 7.35 Hz, 2H) 1.63^{+} (tq, ***J*** = 7.39, 7.39 Hz, 4H), 0.93^{+} (t, ***J*** = 7.42 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.2, 166.6^{+} (2C), 153.6^{+} (2C), 88.8*, 62.1, 61.8*, 50.1, 44.5, 42.0, 41.8*, 37.5*, 19.7*, 16.6, 13.4*, 13.4. HRMS: Calculated for $[C_9H_{13}NNaO_4]^{+}$: 222.0737; found: 222.0740. M.p. (pentane/EtOAc): 58 °C.



1-(2-Oxooxazolidin-3-yl)octane-1,3-dione (1f). Following the general procedure **1f** was isolated by FC (pentane/EtOAc 2:1) in 98% yield. ^{1}H NMR (400 MHz, $CDCl_3$). Keto/enol ratio: 11:1; δ ppm 6.45* (s, 1H), 4.41^{+} (t, ***J*** = 8.08 Hz, 4H), 4.04^{+} (t, ***J*** = 8.11 Hz, 4H), 4.00 (s, 2H), 2.52 (t, ***J*** = 7.43 Hz, 2H), 2.25* (t, ***J*** = 7.62 Hz, 2H), 1.65-1.51^{+} (m, 4H), 1.36-1.19^{+} (m, 8H), 0.86^{+} (t, ***J*** = 6.79 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.4, 166.7^{+} (2C), 153.6^{+} (2C), 88.8*, 62.2, 61.9*, 50.1, 42.8, 42.1, 41.9*, 35.7*, 31.2*, 31.1, 26.1*, 22.9, 22.3, 22.3*, 13.8*, 13.8. HRMS: Calculated for $[C_{11}H_{17}NNaO_4]^{+}$: 250.1050; found: 250.1057. M.p. (pentane/EtOAc): 44 °C.

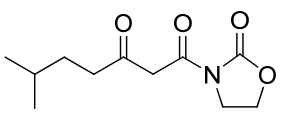


1-(2-Oxooxazolidin-3-yl)nonane-1,3-dione (1g). Following the general procedure **1g** was isolated by FC (pentane/EtOAc 2:1) in 76% yield. ^{1}H NMR (400 MHz, $CDCl_3$). Keto/enol ratio: >20:1; δ ppm 6.48* (s, 1H), 4.44^{+} (t, ***J*** = 8.11 Hz, 4H), 4.07^{+} (t, ***J*** = 8.31 Hz, 4H), 4.03 (s, 2H), 2.55 (t, ***J*** = 7.40 Hz, 2H), 2.28* (t, ***J*** = 7.29 Hz, 2H), 1.65-1.54^{+} (m, 4H), 1.36-1.22^{+} (m, 12H), 0.87^{+} (t, ***J*** = 6.44 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.4, 166.6^{+} (2C), 153.6^{+} (2C), 88.7*, 62.1, 61.8*, 50.1, 42.7, 42.0, 41.9*, 35.7*, 31.4, 31.3*, 28.6*, 28.5, 26.7*, 23.1, 22.3^{+} (2C), 13.9^{+} (2C). HRMS: Calculated for $[C_{12}H_{19}NNaO_4]^{+}$: 264.1206; found: 264.1207. M.p. (pentane/EtOAc): 50 °C.

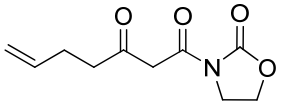


1-(2-Oxooxazolidin-3-yl)decane-1,3-dione (1h). Following the general procedure 1**h** was isolated by

FC (pentane/EtOAc 2:1) in 51% yield. ^{1}H NMR (400 MHz, $CDCl_3$). Keto/enol ratio: 1.2:1; δ ppm 5.98* (s, 1H), 4.41 (t, ***J*** = 8.10 Hz, 2H), 4.04 (d, ***J*** = 8.12 Hz, 2H), 4.00 (s, 2H), 3.63-3.55* (m, 4H), 2.52 (t, ***J*** = 7.44 Hz, 2H), 2.18* (t, ***J*** = 7.61 Hz, 2H), 1.68-1.50^{+} (m, 4H), 1.35-1.19^{+} (m, 16H), 0.90-0.80^{+} (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) (Individual assignment of the two forms, keto and enol, not possible due to discrimination difficulties) δ 203.4, 173.3, 166.7, 153.6, 88.8, 62.2, 50.2, 44.1, 42.9, 42.1, 41.0, 36.6, 31.6, 29.1, 29.0, 29.0, 28.9, 25.6, 23.3, 22.5, 14.0. HRMS: Calculated for $[C_{13}H_{21}NNaO_4]^{+}$: 278.1363; found: 278.1359. M.p. (pentane/EtOAc): 46 °C.



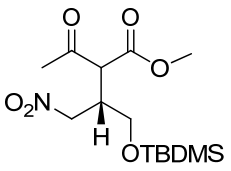
6-Methyl-1-(2-oxooxazolidin-3-yl)heptane-1,3-dione (1i). Following the general procedure **1i** was isolated by FC (pentane/EtOAc 2:1) in 41% yield. ^{1}H NMR (400 MHz, $CDCl_3$). Keto/enol ratio: 12:1; δ ppm 6.49* (s, 1H), 4.44^{+} (t, ***J*** = 8.12 Hz, 4H), 4.07^{+} (t, ***J*** = 8.15 Hz, 4H), 4.04 (s, 2H), 2.55 (t, ***J*** = 7.62 Hz, 2H), 2.29* (t, ***J*** = 7.90 Hz, 2H), 1.61-1.44^{+} (m, 6H), 0.91* (d, ***J*** = 6.49 Hz, 6H), 0.89 (d, ***J*** = 6.39 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.5, 166.6, 153.6, 62.2, 50.1, 42.0, 40.8, 31.9, 27.4, 22.2 (2C). HRMS: Calculated for $[C_{11}H_{17}NNaO_4]^{+}$: 250.1050; found: 250.1048. M.p. (pentane/EtOAc): 61 °C.



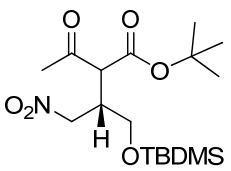
1-(2-Oxooxazolidin-3-yl)hept-6-ene-1,3-dione (1j). Following the general procedure **1j** was isolated by FC (pentane/EtOAc 2:1) in 65% yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$). Keto/enol ratio: 11:1; δ ppm 6.50* (s, 1H), 5.89-5.73^{+} (m, 2H), 5.13-4.95^{+} (m, 4H), 4.44^{+} (t, ***J*** = 8.13 Hz, 4H), 4.07^{+} (t, ***J*** = 8.10 Hz, 4H), 4.03 (s, 2H), 3.03* (t, ***J*** = 7.38 Hz, 2H), 2.66 (t, ***J*** = 7.40 Hz, 2H), 2.46-2.29^{+} (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.4, 166.5^{+} (2C), 153.7^{+} (2C), 136.5^{+} (2C), 115.4^{+} (2C), 89.0*, 62.2, 62.0*, 50.2, 42.4*, 42.1, 41.9*, 41.7, 27.1^{+} (2C). HRMS: Calculated for $[C_{10}H_{13}NNaO_4]^{+}$: 234.0737; found: 234.0744.

5. General procedure for the conjugate addition

An ordinary vial equipped with a magnetic stirring bar was charged with the nitroalkene **2** (0.2 mmol, 43.5 mg, 1 equiv), the nucleophile **1** (0.6 mmol, 3 equiv) and toluene (0.2 mL for [**2**] = 1 M; 0.4 mL for [**2**] = 0.5 M). After stirring at the given temperature for 5 min., the catalyst **3** (0.02 mmol, 10 mol%) was added to the mixture. The stirring was maintained until completion of the reaction (monitored by thin layer chromatography; usually 24-48 h). The crude reaction mixture was directly charged on Iatrobeads and subjected to FC. (Note: In some of the screening entries, solvents other than toluene were used.)

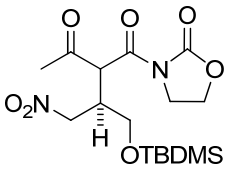


(3*S*)-Methyl 2-acetyl-4-(*tert*-butyldimethylsilyloxy)-3-(nitromethyl)butanoate (4a). Following the general procedure **4a** was isolated by FC (pentane/EtOAc 4:1) in 62% (CH_2Cl_2 as solvent) or 88% (toluene as solvent) yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) (d.r.: 1:1; No individual assignment of the two diastereomers is made) δ ppm 4.63-4.56 (m, 4H), 3.94-3.83 (m, 2H), 3.77 (s, 3H), 3.75 (s, 3H), 3.70-3.61 (m, 4H), 3.16-3.01 (m, 2H), 2.32 (s, 3H), 2.31 (s, 3H), 0.88-0.85 (m, 18H), 0.04-0.02 (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.7, 201.2, 168.4, 168.4, 74.1, 74.1, 61.5, 61.3, 57.3, 57.1, 52.8, 52.8, 39.0, 38.7, 30.6, 30.3, 25.7 (3C), 25.7 (3C), 18.2 (2C; Note: overlap of signals from the two diastereomers), -5.8 (2C), -5.8 (2C). HRMS: Calculated for $[C_{14}H_{27}NNaO_6Si]^+$: 356.1500; found: 356.1504. $[\alpha]_D^{rt}$: +2.6 (c = 0.39, $CHCl_3$).

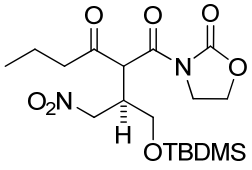


(3*S*)-*tert*-Butyl 2-acetyl-4-(*tert*-butyldimethylsilyloxy)-3-(nitromethyl)butanoate (4b). Following the general procedure **4b** was isolated by FC (pentane/EtOAc 4:1) in 37% yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) (d.r.: 1:1; No individual assignment of the two diastereomers was made) δ ppm 4.62-4.54 (m, 4H), 3.78 (dd, ***J*** = 14.71, 7.99 Hz, 2H), 3.71-3.57 (m, 4H), 3.11-2.96 (m, 2H), 2.30 (s, 6H), 1.47-1.46$^+$ (m, 18H), 0.89-0.87$^+$ (m, 18H), 0.05-0.01$^+$ (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.1, 201.7, 166.9, 166.9, 83.1, 83.1, 74.3, 74.1, 61.5, 61.0, 58.5, 58.2, 39.0,

38.7, 30.4, 30.3, 27.8 (3C), 27.8 (3C), 25.7 (3C), 25.7 (3C), 18.2 (2C; Note: Overlap of signals from both diastereomers), -5.7 (4C; Note: Overlap of signals from both diastereomers). HRMS: Calculated for $[C_{17}H_{33}NNaO_6Si]^+$: 398.1969; found: 398.1970. $[\alpha]_D^{rt}$: +4.0 (c = 0.58, $CHCl_3$).

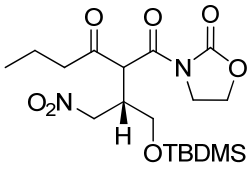


2-((*R*)-1-(*tert*-Butyldimethylsilyloxy)-3-nitropropan-2-yl)-1-(2-oxooxazolidin-3-yl)butane-1,3-dione (4d). Following the general procedure **4d** was isolated by FC (pentane/EtOAc 2:1) in 84% yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$). d.r.: 4:1; δ ppm 5.10 (d, ***J*** = 4.04 Hz, 1H), 5.03* (d, ***J*** = 4.77 Hz, 1H), 4.72 (dd, ***J*** = 14.20, 8.13 Hz, 1H), 4.64-4.57* (m, 1H), 4.55-4.38$^+$ (m, 6H), 4.15-3.97$^+$ (m, 4H), 3.83* (dd, ***J*** = 10.56, 7.26 Hz, 1H), 3.79 (dd, ***J*** = 10.06, 5.90 Hz, 1H), 3.71-3.64$^+$ (m, 2H), 3.21-3.12$^+$ (m, 2H), 2.39 (s, 3H), 2.32* (s, 3H), 0.91-0.82$^+$ (m, 18H), 0.07-(-0.01)$^+$ (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.2, 202.3*, 168.0*, 167.9, 153.5, 153.4*, 74.5*, 74.3, 62.4, 62.2$^+$ (2C), 61.4*, 56.9, 56.4*, 42.5*, 42.4, 39.7*, 39.2, 30.0*, 29.5, 25.7* (3C), 25.6 (3C), 18.1$^+$ (2C), -5.7, -5.7*, -5.7*, -5.8. HRMS: Calculated for $[C_{16}H_{28}N_2NaO_7Si]^+$: 411.1558; found: 411.1563. $[\alpha]_D^{rt}$: +34.0 (c = 1.11, $CHCl_3$).

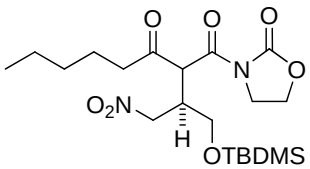


2-((*R*)-1-(*tert*-Butyldimethylsilyloxy)-3-nitropropan-2-yl)-1-(2-oxooxazolidin-3-yl)hexane-1,3-dione (4e). Following the general procedure **4e** was isolated by FC (pentane/EtOAc 2:1) in 89% yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$). d.r.: 4:1; δ ppm 5.11 (d, ***J*** = 4.11 Hz, 1H), 5.04* (d, ***J*** = 4.92 Hz, 1H), 4.71 (dd, ***J*** = 14.20, 8.29 Hz, 1H), 4.60* (dd, ***J*** = 6.40, 1.14 Hz, 1H), 4.52-4.36$^+$ (m, 6H), 4.10-3.95$^+$ (m, 4H), 3.82* (dd, ***J*** = 10.45, 7.41 Hz, 1H), 3.76 (dd, ***J*** = 10.06, 5.82 Hz, 1H), 3.69-3.59$^+$ (m, 2H), 3.20-3.09$^+$ (m, 2H), 2.78-2.47$^+$ (m, 4H), 1.61$^+$ (tq, ***J*** = 7.42, 7.42 Hz, 4H),0.95-0.82$^+$ (m, 24H), 0.04-0.00$^+$ (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.3, 204.2*, 168.1*, 168.0, 153.4, 153.3*, 74.6*, 74.3, 62.5, 62.2$^+$ (2C), 61.4*, 56.4, 55.8*, 44.3*, 43.8, 42.5*, 42.4, 39.8*, 39.5, 25.7*(3 C), 25.6 (3 C), 18.1*, 18.1, 16.6$^+$ (2C), 13.5$^+$ (2C), -5.7, -

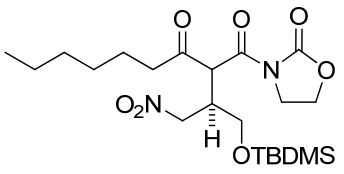
5.7*, -5.7*, -5.8. HRMS: Calculated for $[C_{18}H_{32}N_2NaO_7Si]^+$: 439.1871; found: 439.1877. $[\alpha]_D^{rt}$: +32.7 (c = 1.48, $CHCl_3$).



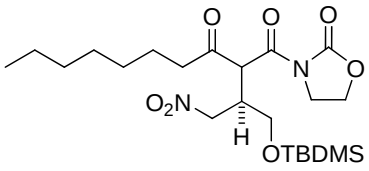
2-((*S*)-1-(*tert*-Butyldimethylsilyloxy)-3-nitropropan-2-yl)-1-(2-oxooxazolidin-3-yl)hexane-1,3-dione (*ent*-4e). Following the general procedure ***ent*-4e** was isolated by FC (pentane/EtOAc 2:1) in 92% yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$). d.r.: 4:1; δ ppm 5.11 (d, ***J*** = 4.11 Hz, 1H), 5.04* (d, ***J*** = 4.92 Hz, 1H), 4.71 (dd, ***J*** = 14.20, 8.29 Hz, 1H), 4.60* (dd, ***J*** = 6.40, 1.14 Hz, 1H), 4.52-4.36$^+$ (m, 6H), 4.10-3.95$^+$ (m, 4H), 3.82* (dd, ***J*** = 10.45, 7.41 Hz, 1H), 3.76 (dd, ***J*** = 10.06, 5.82 Hz, 1H), 3.69-3.59$^+$ (m, 2H), 3.20-3.09$^+$ (m, 2H), 2.78-2.47$^+$ (m, 4H), 1.61$^+$ (tq, ***J*** = 7.42, 7.42 Hz, 4H),0.95-0.82$^+$ (m, 24H), 0.04-0.00$^+$ (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.3, 204.2*, 168.1*, 168.0, 153.4, 153.3*, 74.6*, 74.3, 62.5, 62.2$^+$ (2C), 61.4*, 56.4, 55.8*, 44.3*, 43.8, 42.5*, 42.4, 39.8*, 39.5, 25.7*(3 C), 25.6 (3 C), 18.1*, 18.1, 16.6$^+$ (2C), 13.5$^+$ (2C), -5.7, -5.7*, -5.7*, -5.8. HRMS: Calculated for $[C_{18}H_{32}N_2NaO_7Si]^+$: 439.1871; found: 439.1877. $[\alpha]_D^{rt}$: -30.5 (c = 1.47, $CHCl_3$).



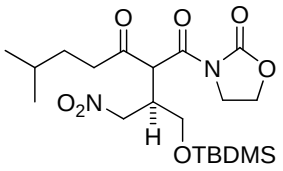
2-((*R*)-1-(*tert*-Butyldimethylsilyloxy)-3-nitropropan-2-yl)-1-(2-oxooxazolidin-3-yl)octane-1,3-dione (4f) Following the general procedure **4f** was isolated by FC (pentane/EtOAc 3:1) in 62% yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$). d.r.: 3:1; δ ppm 5.12 (d, ***J*** = 4.16 Hz, 1H), 5.04* (d, ***J*** = 4.94 Hz, 1H), 4.70 (dd, ***J*** = 14.19, 8.28 Hz, 1H), 4.60* (dd, ***J*** = 6.41, 1.84 Hz, 1H), 4.52-4.38$^+$ (m, 6H), 4.09-3.96$^+$ (m, 4H), 3.86-3.59$^+$ (m, 4H), 3.19-3.09$^+$ (m, 2H), 2.79-2.47$^+$ (m, 4H), 1.58$^+$ (tq, ***J*** = 7.37, 7.37 Hz, 4H), 1.36-1.20$^+$ (m, 8H), 0.91-0.82$^+$ (m, 24H), 0.05-(-0.01)$^+$ (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.4, 204.4*, 168.1*, 168.0, 153.4, 153.3*, 74.6*, 74.3, 62.5, 62.2$^+$ (2C), 61.4*, 56.4, 55.8*, 42.5*, 42.4*, 42.4, 41.9, 39.9*, 39.5, 31.0$^+$ (2C), 25.7* (3C), 25.6 (3C), 22.8$^+$ (2C), 22.4$^+$ (2C), 18.1*, 18.1, 13.8$^+$ (2C), -5.7, -5.7*, -5.7*, -5.8. HRMS: Calculated for $[C_{20}H_{36}N_2NaO_7Si]^+$: 467.2184; found: 467.2174. $[\alpha]_D^{rt}$: +30.7 (c = 2.50, $CHCl_3$).



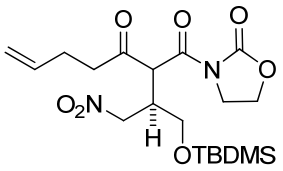
2-((*R*)-1-(*tert*-Butyldimethylsilyloxy)-3-nitropropan-2-yl)-1-(2-oxooxazolidin-3-yl)nonane-1,3-dio-ne (4g). Following the general procedure **4g** was isolated by FC (pentane/EtOAc 3:1) in 77% yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$). d.r.: 3.5:1; δ ppm 5.12 (d, ***J*** = 4.05 Hz, 1H), 5.04* (d, ***J*** = 4.77 Hz, 1H), 4.71 (dd, ***J*** = 14.20, 8.25 Hz, 1H), 4.60* (dd, ***J*** = 6.34, 1.20 Hz, 1H), 4.52-4.36^{+} (m, 6H), 4.15-3.95^{+} (m, 4H), 3.82* (dd, ***J*** = 10.3, 7.4 Hz, 1H), 3.76 (dd, ***J*** = 10.07, 5.81 Hz, 1H), 3.70-3.58^{+} (m, 2H), 3.19-3.09^{+} (m, 2H), 2.79-2.48^{+} (m, 4H), 1.66-1.50^{+} (m, 4H), 1.36-1.20^{+} (m, 12H), 0.93-0.80^{+} (m, 24H), 0.08-(-0.02)$^{+}$ (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.5, 204.4*, 168.1*, 168.0, 153.4, 153.3*, 74.6*, 74.3, 62.5, 62.2^{+} (2C), 61.4*, 56.4, 55.8*, 42.5*, 42.5*, 42.4, 42.0, 39.9*, 39.5, 31.5, 31.4*, 28.7*, 28.6, 25.7* (3C), 25.6 (3C), 23.1^{+} (2C), 22.4^{+} (2C), 18.1^{+} (2C), 14.2*, 14.0, -5.7, -5.7*, -5.7*, -5.8. HRMS: Calculated for $[C_{21}H_{38}N_2NaO_7Si]^{+}$: 481.2340; found: 481.2346. $[\alpha]_D^{rt}$: +26.5 (c = 1.20, $CHCl_3$).



2-((*R*)-1-(*tert*-Butyldimethylsilyloxy)-3-nitropropan-2-yl)-1-(2-oxooxazolidin-3-yl)decane-1,3-dione (4h). Following the general procedure **4h** was isolated by FC (pentane/EtOAc 3:1) in 72% yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$). d.r.: 3:1; δ ppm 5.13 (d, ***J*** = 4.13 Hz, 1H), 5.05* (d, ***J*** = 4.91 Hz, 1H), 4.71 (dd, ***J*** = 14.19, 8.30 Hz, 1H), 4.61* (dd, ***J*** = 6.41, 2.19 Hz, 1H), 4.53-4.38^{+} (m, 6H), 4.09-3.97^{+} (m, 4H), 3.86-3.59^{+} (m, 4H), 3.21-3.08^{+} (m, 2H), 2.78-2.48^{+} (m, 4H), 1.66-1.51^{+} (m, 4H), 1.33-1.21^{+} (m, 16H), 0.89-0.83^{+} (m, 24H), 0.04-0.01^{+} (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.4, 204.4*, 168.1*, 168.0, 153.4, 153.3*, 74.7*, 74.3, 62.5, 62.2^{+} (2C), 61.4*, 56.4, 55.8*, 42.5*, 42.5*, 42.4, 42.0, 39.9*, 39.5, 31.6^{+} (2C), 29.0^{+} (2C), 28.9^{+} (2C), 25.7* (3C), 25.7 (3C), 23.2^{+} (2C), 22.6^{+} (2C), 18.1*, 18.1, 14.0^{+} (2C), -5.7, -5.7*, -5.7*, -5.8. HRMS: Calculated for $[C_{22}H_{40}N_2NaO_7Si]^{+}$: 495.2497 found: 495.2493. $[\alpha]_D^{rt}$: +31.0 (c = 2.50, $CHCl_3$).



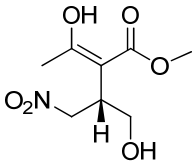
2-((*R*)-1-(*tert*-Butyldimethylsilyloxy)-3-nitropropan-2-yl)-6-methyl-1-(2-oxooxazolidin-3-yl)heptane-1,3-dione (4i). Following the general procedure **4i** was isolated by FC (pentane/EtOAc 2:1) in 66% yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$). d.r.: 2.5:1; δ ppm 5.14 (d, ***J*** = 4.04 Hz, 1H), 5.06* (d, ***J*** = 4.50 Hz, 1H), 4.72 (dd, ***J*** = 14.21, 8.24 Hz, 1H), 4.62* (dd, ***J*** = 6.20, 1.82 Hz, 1H), 4.54-4.37^{+} (m, 6H), 4.08-3.98^{+} (m, 4H), 3.83* (dd, ***J*** = 10.33, 7.00 Hz, 1H), 3.77 (dd, ***J*** = 10.08, 5.99 Hz, 1H), 3.70-3.59^{+} (m, 2H), 3.20-3.11^{+} (m, 2H), 2.80-2.49^{+} (m, 4H), 1.61-1.41^{+} (m, 6H), 0.94-0.84^{+} (m, 30H), 0.07-0.01^{+} (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.7, 204.6*, 168.2*, 168.0, 153.4, 153.3*, 74.7*, 74.3, 62.6, 62.2^{+} (2C), 61.4*, 56.5, 55.9*, 42.5*, 42.4, 40.5*, 40.0, 39.9*, 39.5, 32.0*, 32.0, 27.4^{+} (2C), 25.7* (3C), 25.7 (3C), 22.3* (2C), 22.3 (2C), 18.1*, 18.1, -5.6, -5.7*, -5.7*, -5.7. HRMS: Calculated for $[C_{20}H_{36}N_2NaO_7Si]^{+}$: 467.2184; found: 467.2192. $[\alpha]_D^{rt}$: +31.2 (c = 1.30, $CHCl_3$).



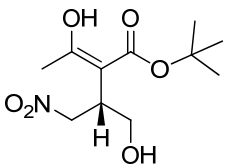
2-((*R*)-1-(*tert*-Butyldimethylsilyloxy)-3-nitropropan-2-yl)-1-(2-oxooxazolidin-3-yl)hept-6-ene-1,3-dione (4j). Following the general procedure **4j** was isolated by FC (hexane/EtOAc 2:1) in 84% yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$). d.r.: 2.5:1; δ ppm 5.84-5.72^{+} (m, 2H), 5.12 (d, ***J*** = 4.17 Hz, 1H), 5.06* (d, ***J*** = 4.99 Hz, 1H), 5.08-4.96^{+} (m, 4H), 4.71 (dd, ***J*** = 14.25, 8.23 Hz, 1H), 4.61* (t, ***J*** = 5.92 Hz, 1H), 4.52-4.39^{+} (m, 6H), 4.11-3.97^{+} (m, 4H), 3.82* (dd, ***J*** = 10.46, 7.23 Hz, 1H), 3.77 (dd, ***J*** = 10.08, 5.76 Hz, 1H), 3.69-3.61^{+} (m, 2H), 3.21-3.11^{+} (m, 2H), 2.91-2.63^{+} (m, 4H), 2.41-2.27^{+} (m, 4H), 0.89-0.84^{+} (m, 18H), 0.04-0.01^{+} (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) 204.5, 203.5*, 168.0*, 167.9, 153.5, 153.3*, 136.5, 136.6*, 115.7, 115.7*, 74.6*, 74.2, 62.5, 62.2^{+} (2C), 61.4*, 56.4, 55.8*, 42.5*, 42.4, 41.6*, 41.1, 39.9*, 39.4, 27.2^{+} (2C), 25.7* (3C), 25.7 (3C), 18.1*, 18.1, -5.6, -5.7*, -5.7*, -5.8. HRMS: Calculated for $[C_{19}H_{32}N_2NaO_7Si]^{+}$: 451.1871; found: 451.1887. $[\alpha]_D^{rt}$: +34.1 (c = 0.52, $CHCl_3$).

6. General procedure for the deprotection/cyclization

An ordinary vial equipped with a magnetic stirring bar was charged with the Michael adducts **4** (0.1 mmol). 2 M HCl in EtOAc (0.2 mL), freshly prepared by slow addition of dry MeOH (0.4 mmol) to a stirring solution of AcCl (0.4 mmol) in dry EtOAc (0.2 mL), was then added to the vial followed by the addition of H_2O (0.5 mmol, 9 µL). The reaction was monitored by TLC. Upon completion (usually 90 to 150 min), the mixture was diluted with H_2O (0.4 mL) and neutralized by careful addition of $NaHCO_3$ until no more gas evolution occurred. The pH of the mixture was controlled by universal pH-paper before extracting with EtOAc (3 x 1 mL). The combined organic layers were dried over $MgSO_4$, concentrated ***in vacuo*** and subjected to FC on Iatrobeads.

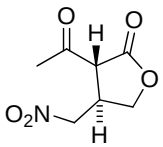


(*S,Z*)-Methyl 3-hydroxy-2-(1-hydroxy-3-nitropropan-2-yl)but-2-enoate (4'a). Following the general procedure **4'a** was isolated by FC (pentane/EtOAc 2:1) in 84% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 4.84 (dd, ***J*** = 13.29, 3.16 Hz, 1H), 4.58 (t, ***J*** = 10.00 Hz 1H), 4.43 (ddd, ***J*** = 10.25, 4.62, 1.89 Hz, 1H), 4.37-4.29 (m, 1H), 4.00-3.87 (m, 1H), 3.74 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 165.3, 100.7, 76.7, 74.1, 51.2, 41.2, 14.5. HRMS: Calculated for $[C_8H_{11}NNaO_5]^+$ ($M+Na^+-H_2O$): 224.0531; found: 224.0529. The ee was determined by HPLC using a Chiralcel OD column [hexane/***i***-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 9.9 min, τ_{minor} = 10.7 min (81% ee). $[\alpha]_D^{rt}$: +74.6 (c = 0.30, $CHCl_3$).

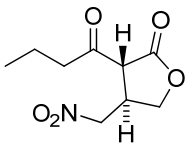


(*S,Z*)-*tert*-Butyl 3-hydroxy-2-(1-hydroxy-3-nitropropan-2-yl)but-2-enoate (4'b). Following the general procedure **4'b** was isolated by FC (pentane/EtOAc 2:1) in 61% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 4.83 (dd, ***J*** = 13.14, 3.27 Hz, 1H), 4.53 (t, ***J*** = 9.89 Hz, 1H), 4.39 (dd, ***J*** = 10.24, 4.71 Hz, 1H), 4.33 (dd, ***J*** = 13.14, 10.07 Hz, 1H), 3.92-3.83 (m, 1H), 2.20-2.16 (m, 3H), 1.50 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 164.3, 102.2, 80.6, 76.9, 73.7, 41.7, 28.351 (3C), 14.429. HRMS: Calculated for $[C_{11}H_{17}NNaO_5]^+$ ($M+Na^+-H_2O$): 266.0999; found: 266.1002. The ee

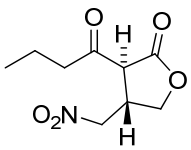
was determined by HPLC using a Chiralcel OD column [hexane/***i***-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major} = 6.4 min, τ_{minor} = 6.8 min (76% ee). $[\alpha]_D^{rt}$: +85.3 (c = 0.30, $CHCl_3$).



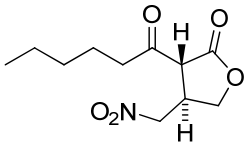
(3*R*,4*R*)-3-Acetyl-4-(nitromethyl)dihydrofuran-2(3H)-one (5a). Following the general procedure **5a** was isolated by FC (Pentane/EtOAc 2:1) in 70% yield. ^{1}H NMR (400 MHz, $CDCl_3$). Keto/enol ratio: 2.5:1; δ ppm 11.25* (bs, 1H), 4.66-4.43$^+$ (m, 6H),4.38* (dd, ***J*** = 10.38, 2.20 Hz, 1H), 4.14 (dd, ***J*** = 9.62, 7.41 Hz, 1H), 3.88-3.73$^+$ (m, 2H), 3.63 (d, ***J*** = 8.11 Hz, 1H), 2.50 (s, 3H), 2.08* (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.2, 174.8*, 171.5*, 169.9, 94.2*, 76.6*, 75.0, 69.9*, 68.7, 55.7, 35.8*, 34.7, 29.4, 19.0*. HRMS: Calculated for $[C_7H_9NO_5Na]^+$: 210.0373; found: 210.0367. The ee was determined by GC using a chiral Chrompack CP Chiralsil-Dex Cβ column. Temperature program: from 70 °C to 160 °C at a rate of 10 °C/min, maintaining the temperature for 20 minutes, then to 180 °C at a rate of 10 °C/min. τ_{major} = 19.1 min, τ_{minor} = 18.4 min (84% ee). $[\alpha]_D^{rt}$: -24.7 (c = 0.45, $CHCl_3$).



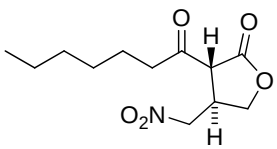
(3*R*,4*R*)-3-Butyryl-4-(nitromethyl)dihydrofuran-2(3H)-one (5b). Following the general procedure **5b** was isolated by FC (pentane/EtOAc 2:1) in 71% yield. ^{1}H NMR (400 MHz, $CDCl_3$). Keto/enol ratio: 15:1; only the keto form is characterized; δ ppm 4.62 (dd, ***J*** = 9.54, 8.03 Hz, 1H), 4.59-4.46 (m, 2H), 4.13 (dd, ***J*** = 9.59, 7.13 Hz, 1H), 3.86-3.76 (m, 1H), 3.61 (d, ***J*** = 7.70 Hz, 1H), 3.01 (dt, ***J*** = 18.16, 7.32 Hz, 1H), 2.67-2.57 (m, 1H), 1.66 (tq, ***J*** = 7.50, 7.50 Hz, 2H), 0.95 (t, ***J*** = 7.42 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.6, 170.1, 75.1, 68.8, 55.1, 44.1, 34.9, 16.6, 13.4. HRMS: Calculated for $[C_9H_{13}NO_5Na]^+$: 238.0686; found: 238.0679. The ee was determined by HPLC using a Chiralcel OD column [hexane/***i***-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 47.5 min, τ_{minor} = 39.6 min (90% ee). $[\alpha]_D^{rt}$: -11.7 (c = 0.26, $CHCl_3$).



(3*R*,4*R*)-3-Butyryl-4-(nitromethyl)dihydrofuran-2(3H)-one (*ent*-5b). Following the general procedure ***ent*-5b** was isolated by FC (pentane/EtOAc 2:1) in 68% yield. ^{1}H NMR (400 MHz, $CDCl_3$). Keto/enol ratio: 15:1; only the keto form is characterized; δ ppm 4.62 (dd, ***J*** = 9.54, 8.03 Hz, 1H), 4.59-4.46 (m, 2H), 4.13 (dd, ***J*** = 9.59, 7.13 Hz, 1H), 3.86-3.76 (m, 1H), 3.61 (d, ***J*** = 7.70 Hz, 1H), 3.01 (dt, ***J*** = 18.16, 7.32 Hz, 1H), 2.67-2.57 (m, 1H), 1.66 (tq, ***J*** = 7.50, 7.50 Hz, 2H), 0.95 (t, ***J*** = 7.42 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.6, 170.1, 75.1, 68.8, 55.1, 44.1, 34.9, 16.6, 13.4. HRMS: Calculated for $[C_9H_{13}NO_5Na]^+$: 238.0686; found: 238.0679. The ee was determined by HPLC using a Chiralcel OD column [hexane/***i***-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 39.6 min, τ_{minor} = 47.5 min (86% ee). $[\alpha]_D^{rt}$: +12.2 (c = 0.29, $CHCl_3$).

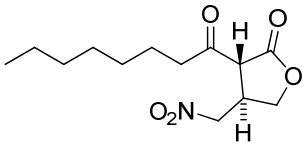


(3*R*,4*R*)-3-Hexanoyl-4-(nitromethyl)dihydrofuran-2(3H)-one (5c). Following the general procedure **5c** was isolated by FC (pentane/EtOAc 3:1) in 76% yield. ^{1}H NMR (400 MHz, $CDCl_3$). Keto/enol ratio: >10:1; only the keto form is characterized; δ ppm 4.62 (dd, ***J*** = 9.58, 8.01 Hz, 1H), 4.58-4.44 (m, 2H), 4.13 (dd, ***J*** = 9.61, 7.10 Hz, 1H), 3.86-3.75 (m, 1H), 3.61 (d, ***J*** = 7.71 Hz, 1H), 3.02 (dt, ***J*** = 18.10, 7.37 Hz, 1H), 2.64 (dt, ***J*** = 18.08, 7.29 Hz, 1H), 1.67-1.57 (m, 2H), 1.39-1.22 (m, 4H), 0.89 (t, ***J*** = 6.89 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.7, 170.1, 75.1, 68.8, 55.1, 42.2, 34.9, 31.0, 22.8, 22.4, 13.9. HRMS: Calculated for $[C_{11}H_{17}NO_5Na]^+$: 266.1004; found: 266.0996. The ee was determined by HPLC using a Chiralcel OD column [hexane/***i***-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 45.3 min, τ_{minor} = 40.4 min (83% ee). $[\alpha]_D^{rt}$: -14.3 (c = 0.78, $CHCl_3$).

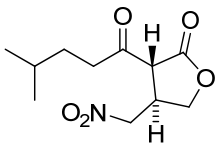


(3*R*,4*R*)-3-heptanoyl-4-(nitromethyl)dihydrofuran-2(3H) -one (5d). Following the general procedure **5d** was isolated by FC (pentane/EtOAc 3:1) in 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$). Keto/enol ratio: >20:1; only the keto form is characterized; δ ppm 4.62 (dd, ***J*** = 9.59, 7.99 Hz, 1H), 4.57-4.47 (m, 2H), 4.13 (dd, ***J*** = 9.61, 7.11 Hz, 1H), 3.87-3.76 (m, 1H), 3.61 (d, ***J*** = 7.71 Hz, 1H), 3.02 (dt, J = 18.11, 7.49 Hz, 1H), 2.64 (dt, ***J*** = 18.07, 7.10

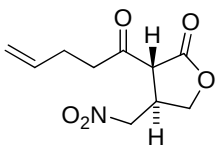
Hz, 1H), 1.68-1.55 (m, 2H), 1.38-1.23 (m, 6H), 0.88 (t, ***J*** = 6.73 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.7, 170.1, 75.1, 68.8, 55.1, 42.3, 34.9, 31.5, 28.5, 23.1, 22.4, 14.0. HRMS: Calculated for $[C_{12}H_{19}NO_5Na]^+$: 280.1155; found: 280.1154. The ee was determined by HPLC using a Chiralcel OD column [hexane/***i***-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 54.3 min, τ_{minor} = 48.6 min (85% ee). $[\alpha]_D^{rt}$: -13.3 (c = 0.15, $CHCl_3$).



(3*R*,4*R*)-4-(Nitromethyl)-3-octanoyldihydrofuran-2(3H)-one (5e). Following the general procedure **5e** was isolated by FC (pentane/EtOAc 3:1) in 75% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 4.67-4.37 (m, 3H), 4.13 (dd, ***J*** = 9.60, 7.11 Hz, 1H), 3.87-3.76 (m, 1H), 3.61 (d, ***J*** = 7.72 Hz, 1H), 3.02 (dt, ***J*** = 18.09, 7.38 Hz, 1H), 2.64 (dt, ***J*** = 18.08, 7.37 Hz, 1H), 1.69-1.56 (m, 2H), 1.35-1.24 (m, 8H), 0.88 (t, ***J*** = 5.80 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.7, 170.1, 75.1, 68.8, 55.1, 42.3, 34.9, 31.6, 29.0, 28.8, 23.2, 22.6, 14.1. HRMS: Calculated for $[C_{13}H_{21}NO_5Na]^+$: 294.1312; found: 294.1316. The ee was determined by HPLC using a Chiralcel OD column [hexane/***i***-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 43.3 min, τ_{minor} = 38.8 min (84% ee). $[\alpha]_D^{rt}$: -20.8 (c = 0.60, $CHCl_3$).

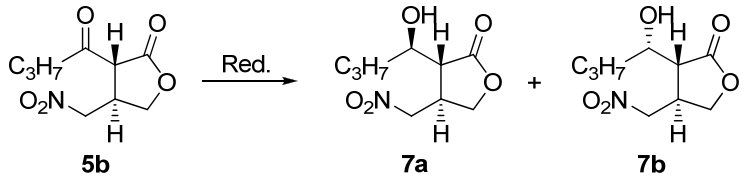


(3*R*,4*R*)-3-(4-Methylpentanoyl)-4-(nitromethyl)dihydrofuran-2(3H)-one (5f). Following the general procedure **5f** was isolated by FC (pentane/EtOAc 2:1) in 55% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 4.62 (dd, ***J*** = 9.49, 8.07 Hz, 1H), 4.58-4.46 (m, 2H), 4.13 (dd, ***J*** = 9.56, 7.11 Hz, 1H), 3.88-3.75 (m, 1H), 3.63 (d, ***J*** = 7.69 Hz, 1H), 3.08-2.98 (m, 1H), 2.71-2.59 (m, 1H), 1.67-1.45 (m, 3H), 0.91 (d, ***J*** = 6.12 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.9, 170.2, 75.1, 68.8, 55.1, 40.4, 34.9, 31.9, 27.5, 22.4, 22.2. HRMS: Calculated for $[C_{11}H_{17}NO_5Na]^+$: 266.0999; found: 266.0994. The ee was determined by HPLC using Chiralcel OD column [hexane/***i***-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 55.5 min, τ_{minor} = 48.4 min (82% ee). $[\alpha]_D^{rt}$: -11.3 (c = 0.53, $CHCl_3$).



(3*R*,4*R*)-4-(Nitromethyl)-3-pent-4-enoyldihydrofuran-2(3H) -one (5g). Following the general procedure **5g** was isolated by FC (pentane/EtOAc 3:1) in 68% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 5.88-5.72 (m, 1H), 5.12-4.99 (m, 2H), 4.68-4.45 (m, 3H), 4.14 (dd, ***J*** = 9.62, 7.29 Hz, 1H), 3.87-3.76 (m, 1H), 3.62 (d, ***J*** = 7.92 Hz, 1H), 3.16 (dt, ***J*** = 18.03, 7.28 Hz, 1H), 2.75 (dt, ***J*** = 18.18, 7.20 Hz, 1H), 2.44-2.36 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.9, 170.0, 136.1, 115.9, 75.0, 68.8, 55.1, 41.2, 34.9, 27.2. HRMS: Calculated for $[C_{10}H_{13}NO_5Na]^+$: 250.0686; found: 250.0694. The ee was determined by HPLC using a Chiralpak AD column [hexane/***i***-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 33.0 min, τ_{minor} = 29.1 min (88% ee). $[\alpha]_D^{rt}$: -14.4 (c = 0.30, $CHCl_3$).

7. Preliminary results for the reduction of 5b



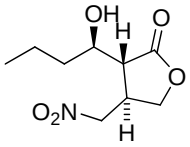
Entry	Reduction conditions	Temp. (°C)	Combi yield (%)[a]	**7a**:**7b**[b]	ee (%)[c]
1[d]	$NaBH_4$ (1 equiv), MeOH	-78	67	63:37	nd
2[d]	$NaBH_4/CaCl_2$ (1 equiv), MeOH	-78	82	75:25	nd
3[e]	(*S*,*S*)-**6** (5 mol%), Et_3N (5 equiv), HCO_2H (2 equiv), CH_2Cl_2	rt	93	77:23	99/66
4[e]	(*R*,*R*)-**6** (5 mol%), Et_3N (5 equiv), HCO_2H (2 equiv), CH_2Cl_2	rt	87	13:87	96/65

[a] Isolated yield after column chromatography. [b] Determined by ^{1}H NMR spectroscopy. [c] Determined by chiral stationary phase HPLC. [d] Reaction time was 1 h. [e] Reaction time was 24 h.

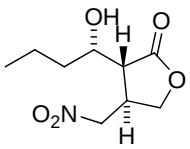
8. The synthesis of IM-2

The lactone **5b** (93.4 mg, 0.43 mmol) was dissolved in CH_2Cl_2 (0.9 mL) together with the catalyst (*S*,*S*)-**6** (13.2 mg, 5 mol%). A premixed solution of HCO_2H (79 μl, 5 equiv.) and Et_3N (114 μl, 2 equiv.) in CH_2Cl_2 (0.4 mL) was then added to the reaction mixture. After stirring at rt

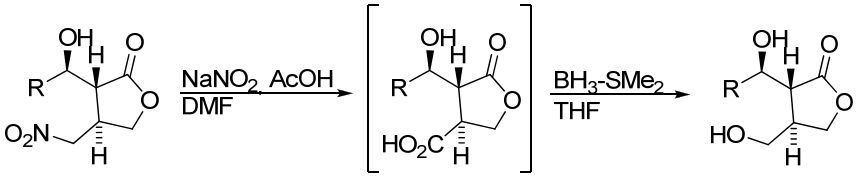
for 24 h, the reaction was quenched by addition of $NaHCO_3$ (sat.) The aq. phase is extracted with EtOAc (3 x 5 mL) and the combined organic layers were dried, concentrated *in vacuo* and subjected to FC on silica-gel yielding the diastereomers **7a** and **7b** in 72% (66.9 mg, 0.31 mmol) and 21% (20.0 mg, 0.09 mmol) yield, respectively.



(3*R*,4*R*)-3-((*R*)-1-Hydroxybutyl)-4-(nitromethyl)dihydrofuran-2(3H)-one (7a). Compound **7a** was isolated by FC (pentane/EtOAc 2:1) in 72% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 4.72 (dd, ***J*** = 13.97, 5.28 Hz, 1H), 4.62 (dd, ***J*** = 9.57, 8.10 Hz, 1H), 4.51 (dd, ***J*** = 13.96, 9.14 Hz, 1H), 4.08 (dd, ***J*** = 9.64, 7.22 Hz, 1H), 3.99-3.93 (m, 1H), 3.37-3.26 (m, 1H), 2.61 (bs, 1H), 2.53 (dd, ***J*** = 8.28, 3.95 Hz, 1H), 1.76-1.63 (m, 1H), 1.61-1.45 (m, 2H), 1.45-1.31 (m, 1H), 0.95 (t, ***J*** = 7.12 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 76.4, 70.9, 69.6, 47.8, 36.2, 35.8, 19.0, 13.7. HRMS: Calculated for $[C_9H_{15}NO_5Na]^+$: 240.0842; found: 240.0848. The ee was determined by HPLC using a Chiralpak OD column [hexane/***i***-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 29.5 min, τ_{minor} = 27.0 min (99% ee). $[\alpha]_D^{rt}$: -39.0 (c = 1.62, $CHCl_3$).

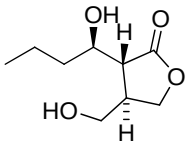


(3*R*,4*R*)-3-((*S*)-1-Hydroxybutyl)-4-(nitromethyl)dihydrofuran-2(3H)-one (7b). Compound **7b** was isolated by FC (pentane/EtOAc 2:1) in 21% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 4.67 (dd, ***J*** = 13.61, 5.45 Hz, 1H), 4.61 (dd, ***J*** = 9.58, 8.19 Hz, 1H), 4.51 (dd, ***J*** = 13.61, 9.07 Hz, 1H), 4.22-4.14 (m, 1H), 4.12 (dd, ***J*** = 9.62, 6.34 Hz, 1H), 3.51-3.39 (m, 1H), 2.45 (dd, ***J*** = 7.13, 3.57 Hz, 1H), 2.27 (bs, 1H), 1.64-1.48 (m, 3H), 1.43-1.29 (m, 1H), 0.97 (t, ***J*** = 7.07 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.4, 77.0, 70.4, 69.9, 48.3, 37.0, 34.2, 19.0, 13.7. HRMS: Calculated for $[C_9H_{15}NO_5Na]^+$: 240.0842; found: 240.0846. The ee was determined by HPLC using a Chiralpak OD column [hexane/***i***-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 29.1 min, τ_{minor} = 34.0 min (66% ee). $[\alpha]_D^{rt}$: -47.0 (c = 1.29, $CHCl_3$)



Not purified

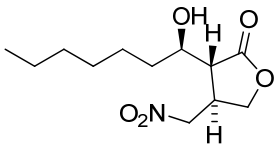
To a solution of the hydroxylactone **7a** (66.0 mg, 0.30 mmol) in DMF (0.6 mL) at 35°C were added $NaNO_2$ (62.1 mg, 0.90 mmol) and AcOH (0.17 mL, 3.0 mmol). The reaction mixture was kept at this temperature under stirring for 6 h and then acidified with 1 M HCl (pH below 3). The aqueous phase was extracted with EtOAc (8 x 2 mL), the organic layers were combined, dried over $MgSO_4$ and concentrated ***in vacuo***. Toluene (1 mL) was then added and the mixture was again concentrated. This process was repeated twice. Finally, remaining DMF was removed by Kugelrohr distillation (0.25 mbar, 40 °C). The afforded crude carboxylic acid intermediate was dissolved in dry THF (1.0 mL) at 0°C and $BH_3 \cdot SMe_2$ (114 µl, 1.20 mmol) was added dropwise. The reaction was allowed to stir at 0°C for 3 h and MeOH (1 mL) was slowly added. The volatiles were removed ***in vacuo*** (below 30 °C!). More MeOH was then added and the mixture was again concentrated (below 30°C). This was repeated 2 times and subsequent FC on silica gel (CH_2Cl_2/MeOH 20:1) afforded the pure γ-butyrolactone IM-2 (**8**) in 62% yield over 2 steps as a colorless oil.



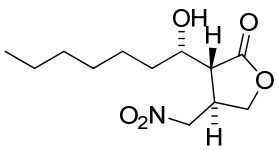
(3*R*,4*R*)-3-((R)-1-hydroxybutyl)-4-(hydroxymethyl)dihydrofuran-2(3H)-one (8). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 4.42 (t, ***J*** = 8.69 Hz, 1H), 4.06-4.00 (m, 1H), 3.98 (t, ***J*** = 8.85 Hz, 1H), 3.75 (dd, ***J*** = 10.68, 5.14 Hz, 1H), 3.67 (dd, ***J*** = 10.69, 6.62 Hz, 1H), 2.83-2.72 (m, 1H), 2.65 (dd, ***J*** = 9.38, 4.69 Hz, 1H), 1.68-1.32 (m, 4H), 0.95 (t, ***J*** = 7.11 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.3, 70.5, 68.3, 62.9, 49.2, 40.1, 36.0, 19.0, 13.9. HRMS: Calculated for $[C_9H_{16}O_4Na]^+$: 211.0941; found: 211.0942. $[\alpha]_D^{rt}$: -6.7 (c = 0.89, $CHCl_3$).

9. The synthesis of VB-D.

The lactone **5d** (90.8 mg, 0.35 mmol) was dissolved in CH_2Cl_2 (1.0 mL) together with the catalyst (*R,R*)-**6** (11.0 mg, 5 mol%). A premixed solution of HCO_2H (67 μl, 1.765 mmol, 5 equiv.) and Et_3N (100 μl, 0.71 mmol, 2 equiv.) in CH_2Cl_2 (0.5 mL) was then added to the reaction mixture. After stirring at rt for 24 h, the reaction was quenched by addition of $NaHCO_3$ (sat.). The aq. phase was extracted with EtOAc (3 x 5 mL) and the combined organic layers were dried, concentrated *in vacuo* and subjected to FC yielding diastereomers **9b** and **9a** in 86% (78.4 mg, 0.30 mmol) and 11% (9.8 mg, 0.04 mmol) yield, respectively.



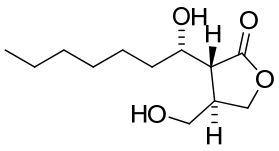
(3*R*,4R)-3-((*R*)-1-Hydroxyheptyl)-4-(nitromethyl)dihydrofuran-2(3H)-one (9a). Compound **9a** was isolated by FC (pentane/EtOAc 3:1) in 11% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 4.72 (dd, ***J*** = 13.87, 5.27 Hz, 1H), 4.64 (dd, ***J*** = 9.56, 8.10 Hz, 1H), 4.50 (dd, ***J*** = 13.89, 9.16 Hz, 1H), 4.09 (dd, ***J*** = 9.63, 7.31 Hz, 1H), 4.00-3.93 (m, 1H), 3.38-3.27 (m, 1H), 2.54 (dd, ***J*** = 8.40, 4.06 Hz, 1H), 2.38 (bs, 1H), 1.78-1.23 (m, 10H), 0.88 (t, ***J*** = 6.73, 6.73 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 76.4, 71.3, 69.5, 47.8, 36.3, 33.9, 31.7, 29.0, 25.8, 22.5, 14.0. HRMS: Calculated for $[C_{12}H_{21}NO_5Na]^+$: 282.1312; found: 282.1307. The ee was determined by HPLC using a Chiralpak OD column [hexane/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 29.6 min, τ_{minor} = 25.6 min (52% ee). $[\alpha]_D^{rt}$: -26.5 (c = 1.24, $CHCl_3$).



(3*R*,4*R*)-3-((S)-1-Hydroxyheptyl)-4-(nitromethyl)dihydrofuran-2(3H)-one (9b). Compound **9b** was isolated by FC (pentane/EtOAc 3:1) in 86% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 4.69-4.47 (m, 3H), 4.16-4.08 (m, 2H), 3.49-3.37 (m, 1H), 2.56 (d, ***J*** = 5.12 Hz, 1H; Note: OH), 2.44 (dd, ***J*** = 6.97, 3.49 Hz, 1H), 1.59-1.43 (m, 2H), 1.38-1.23 (m, 8H), 0.87 (t, ***J*** = 6.72 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 77.0, 70.6, 70.0, 48.3, 34.9, 34.1, 31.6, 28.9, 25.7, 22.5, 14.0. HRMS: Calculated

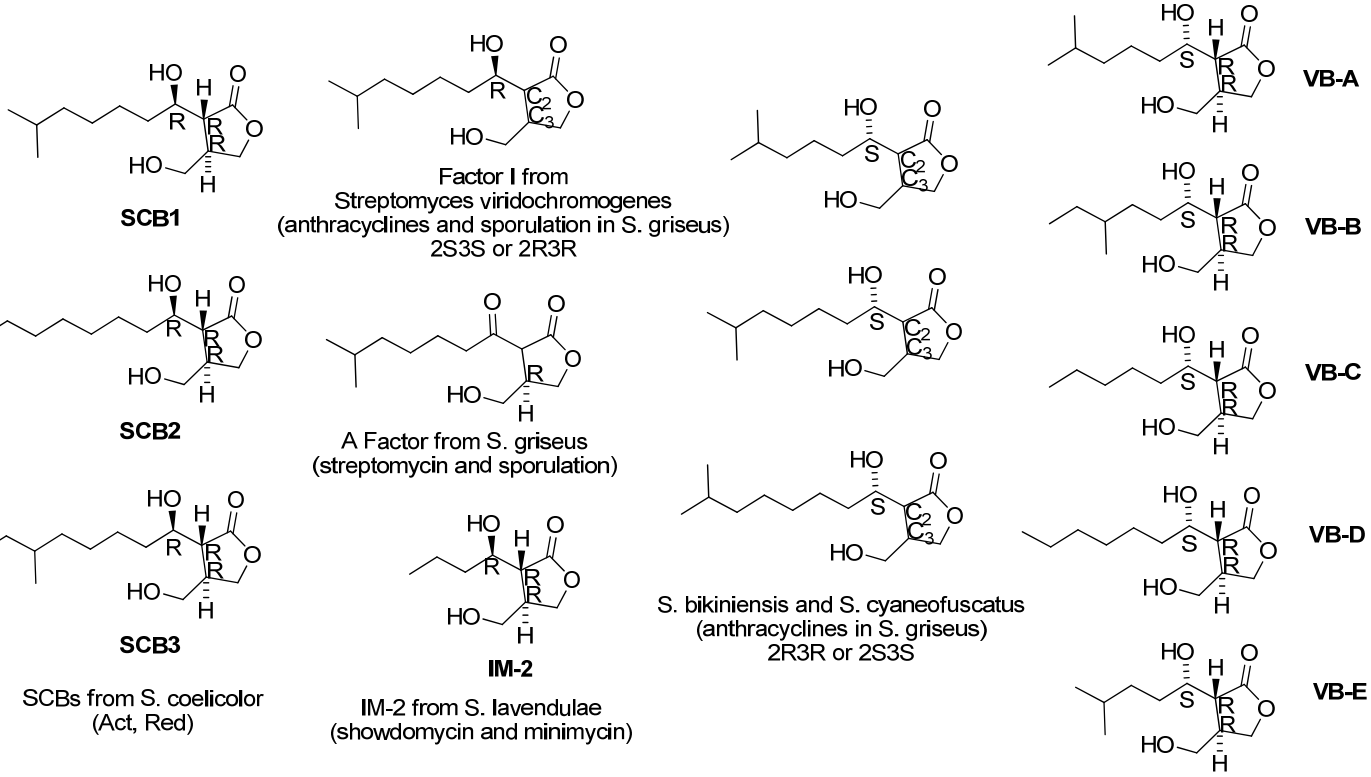
for $[C_{12}H_{21}NO_5Na]^+$: 282.1312; found: 282.1306. The ee was determined by HPLC using a Chiralpak OD column [hexane/***i***-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 23.3 min, τ_{minor} = 30.6 min (>98% ee). $[\alpha]_D^{rt}$: -45.5 (c = 1.04, $CHCl_3$).

To a solution of the hydroxylactone **9b** (71.6 mg, 0.28 mmol) in DMF (0.5 mL) at 35 °C were added $NaNO_2$ (57.1 mg, 0.83 mmol) and AcOH (0.16 mL, 2.76 mmol). The reaction mixture was stirred at this temperature for 6 h and acidified with 1 M HCl (pH below 3). This mixture was extracted with EtOAc (8 x 2 mL), the organic layers were combined, dried over $MgSO_4$ and concentrated ***in vacuo***. Toluene (1 mL) was then added and the mixture was again concentrated ***in vacuo***. This process was repeated twice. Finally, remaining DMF was removed by Kugelrohr distillation (0.25 mbar, 40 °C). The obtained crude carboxylic acid intermediate was dissolved in dry THF (1.0 mL) at 0 °C and $BH_3 \cdot SMe_2$ (110 µl, 1.10 mmol) was dropwise added. The reaction was allowed to stir at 0 °C for 2.5 h and then quenched by slow addition of MeOH (1 mL). The excess solvents were removed ***in vacuo*** (below 30°C!). More MeOH was then added and the mixture was again concentrated ***in vacuo*** (below 30 °C). This was repeated twice and subsequent FC on Silica gel afforded the pure γ-butyrolactone VB-D (**10**) in 43% yield over 2 steps as a colorless oil.



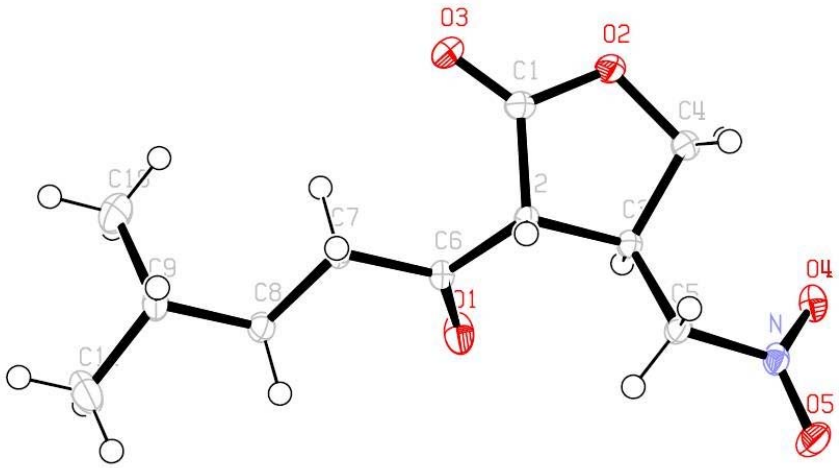
(3*R*,4*R*)-3-((*S*)-1-Hydroxyheptyl)-4-(hydroxymethyl)dihydrofuran-2(3H)-one (10). Compound **10** was isolated by FC (CH_2Cl_2/MeOH 20:1) in 43% yield over 2 steps. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 4.41 (t, ***J*** = 8.73 Hz, 1H), 4.10 (dd, ***J*** = 9.04, 6.57 Hz, 1H), 4.12-4.08 (m, 1H), 3.72 (dd, ***J*** = 10.67, 5.54 Hz, 1H), 3.67 (dd, ***J*** = 10.63, 6.14 Hz, 1H), 2.89-2.77 (m, 1H), 2.54 (dd, ***J*** = 7.08, 3.64 Hz, 1H), 1.64-1.23 (m, 10H), 0.88 (t, ***J*** = 6.76 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.0, 70.7, 69.7, 63.3, 48.2, 38.0, 34.8, 31.7, 29.1, 25.8, 22.6, 14.0. HRMS: Calculated for $[C_{12}H_{22}O_4Na]^+$: 253.1410; found: 253.1410. $[\alpha]_D^{rt}$: -34.3 (c = 1.69, $CHCl_3$).

10. Overview of γ-Butyrolactone autoregulators[6]



[6] E. Takano, *Curr. Opin. Microbiol.* **2006**,*9*, 287.

11. X-Ray of compound 5f



Crystal data for [**5f**]: $C_{11}H_{17}NO_5$, M = 243.26, orthorhombic, Space group P2(1)2(1)2(1), a = 5.6073(6) Å, b = 10.3774(11) Å, c = 20.890(2) Å, V = 1215.6(2) $Å^3$, T = 100 K, Z = 4, D_c = 1.329 g cm^{-3}, μ(Mo Kα, λ = 0.71073 Å) = 1.789 mm^{-1}, 9977 reflections collected, 2106 unique [R_{int} = 0.034], which were used in all calculations. Refinement on F2, final R(F) = 0.036, Rw(F2) = 0.0846. Flack parameter x = -0.3(10).

12. Representative NMR spectra

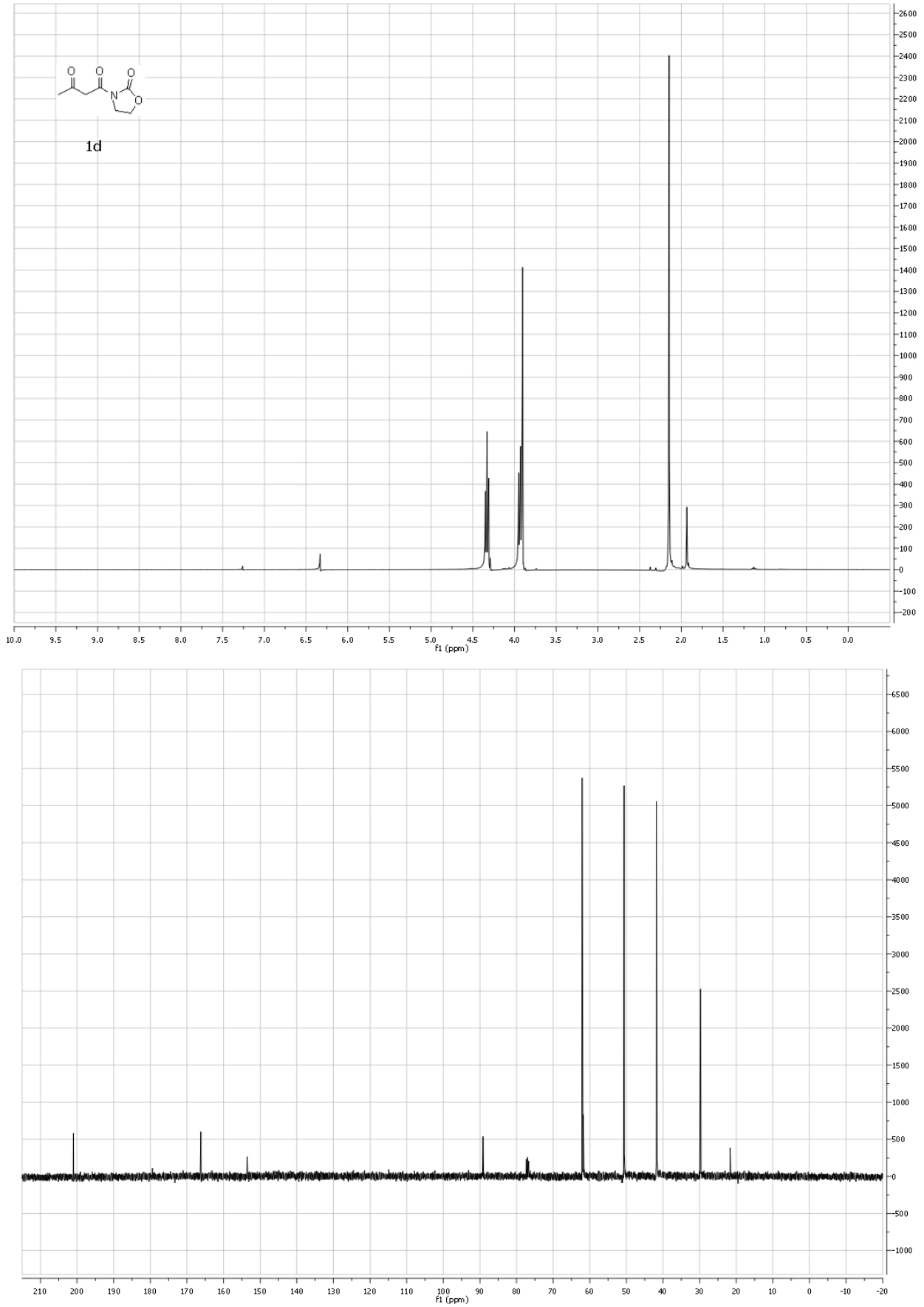


Figure 1: ^{1}H and ^{13}C NMR spectra of compound **1d.**

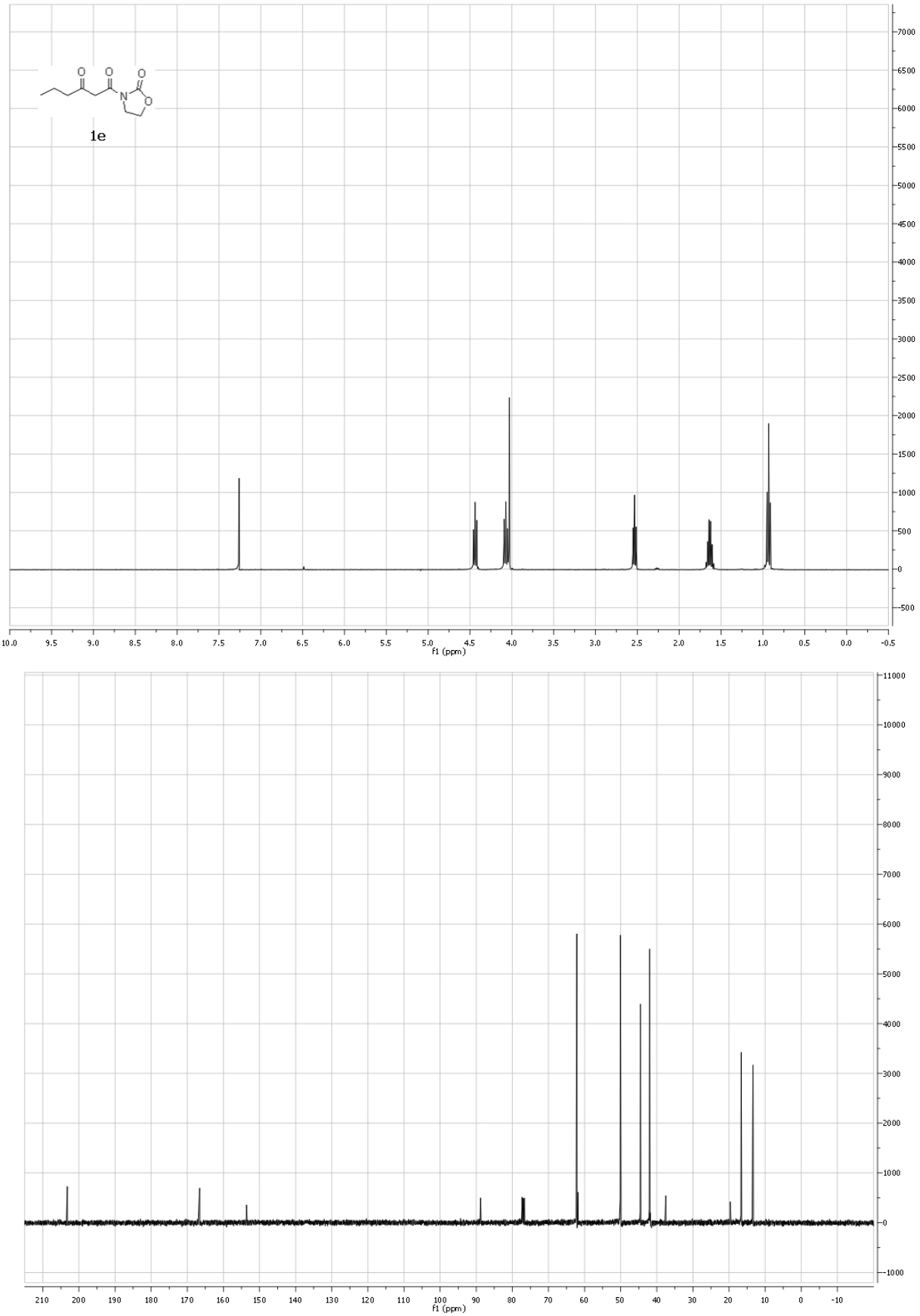
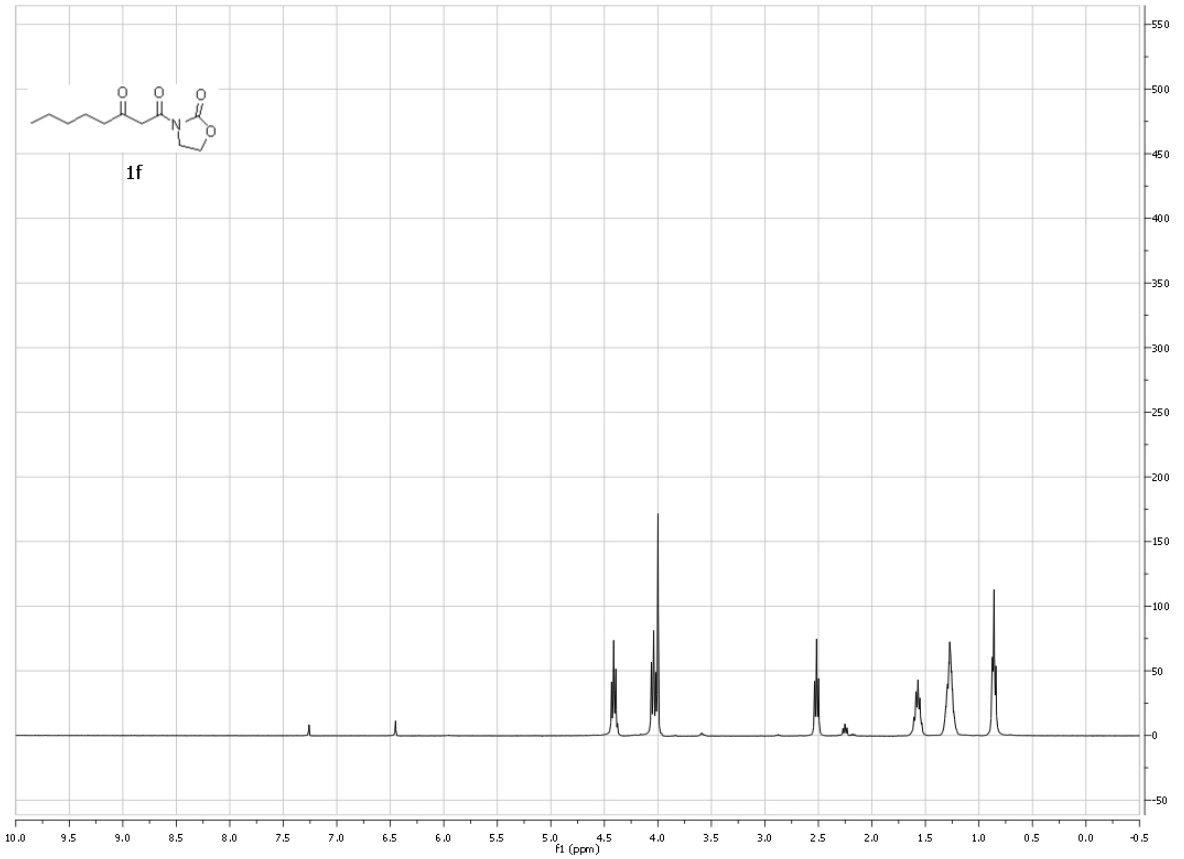


Figure 2: ^{1}H and ^{13}C NMR spectra of compound **1e.**



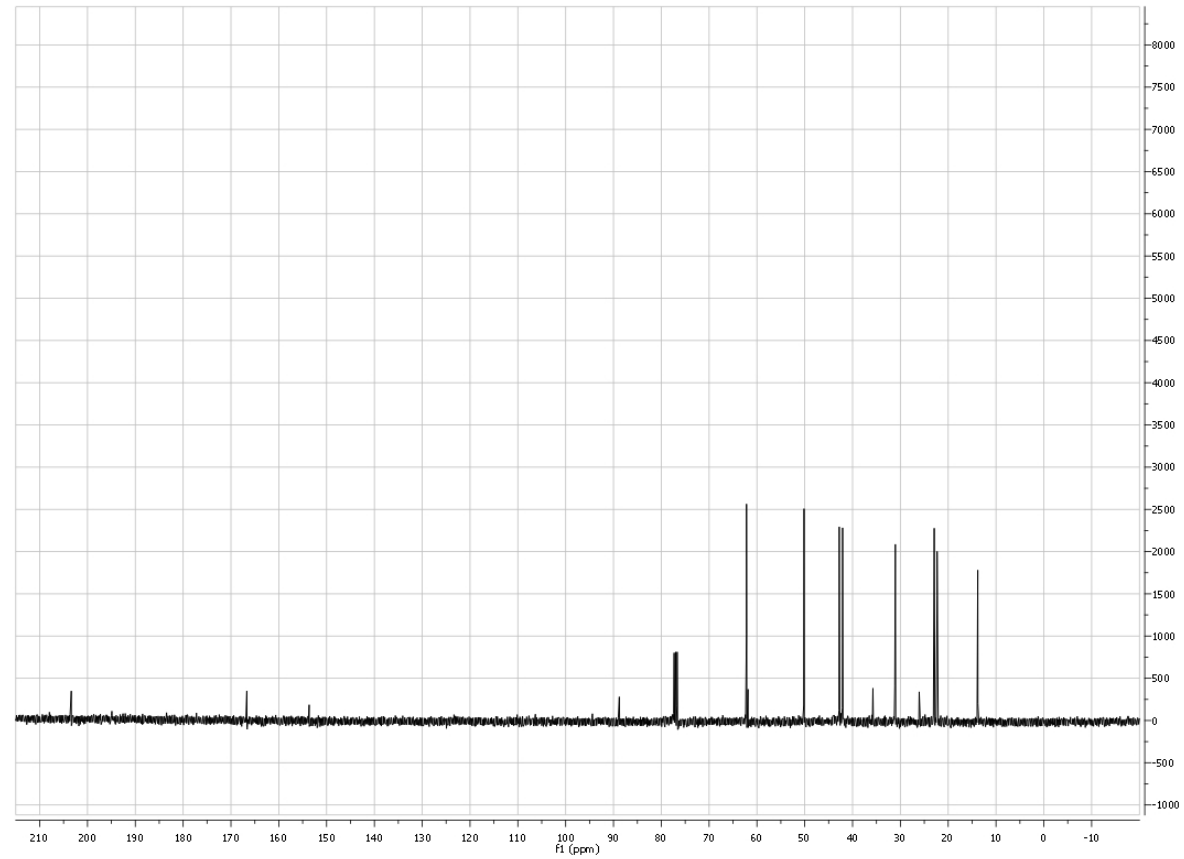


Figure 3: ^{1}H and ^{13}C NMR spectra of compound **1f**.

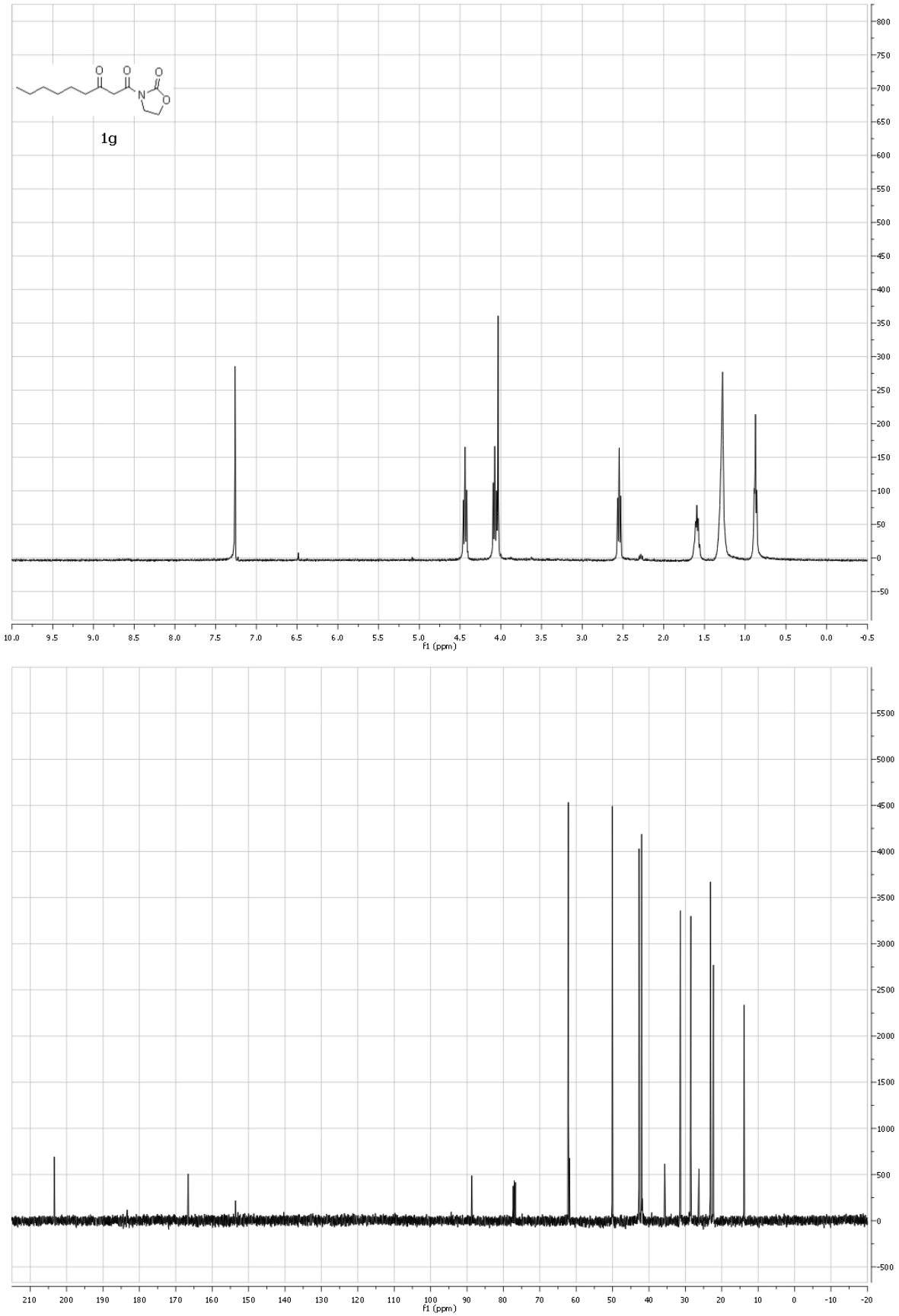


Figure 4: ^{1}H and ^{13}C NMR spectra of compound **1g**.

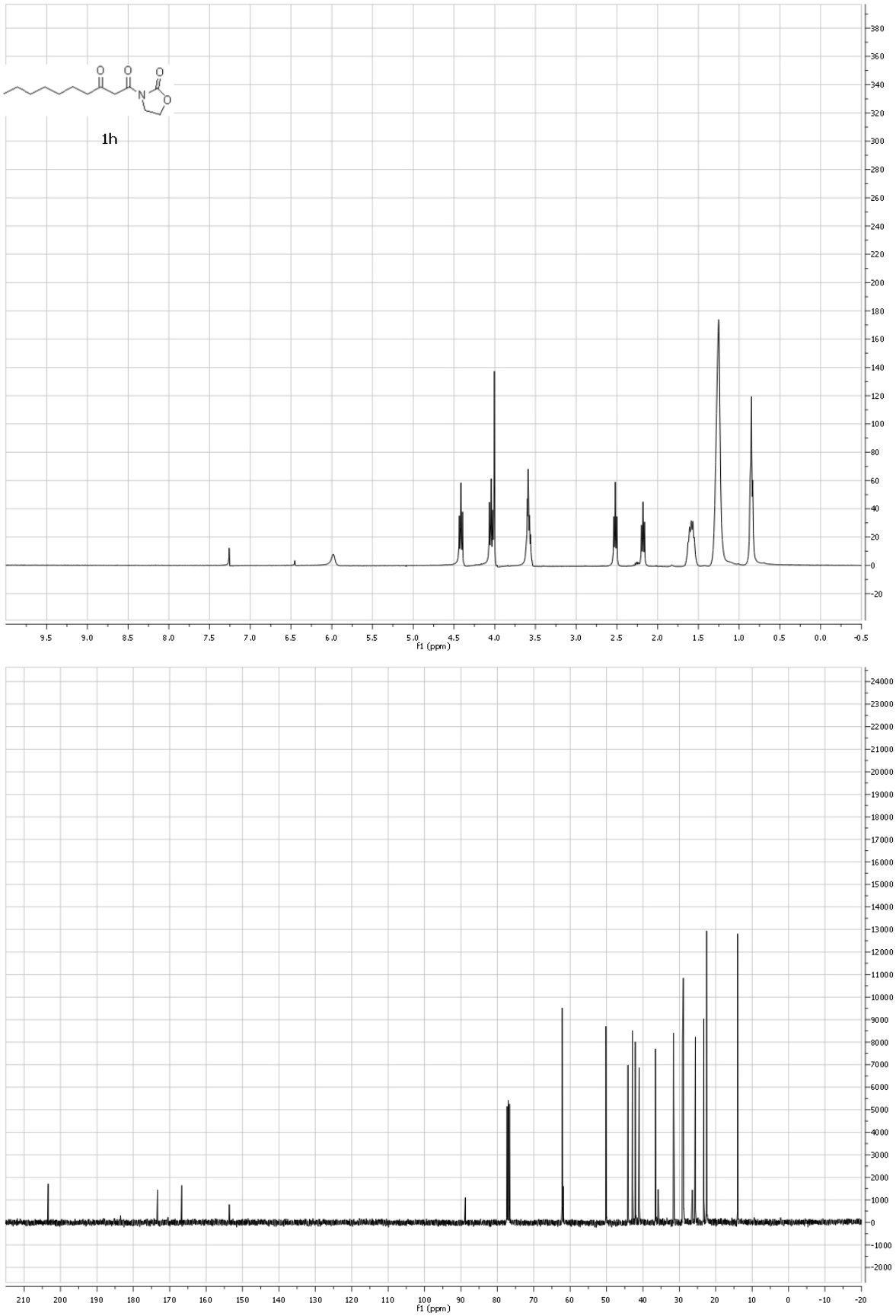


Figure 5: ^{1}H and ^{13}C NMR spectra of compound **1h**.

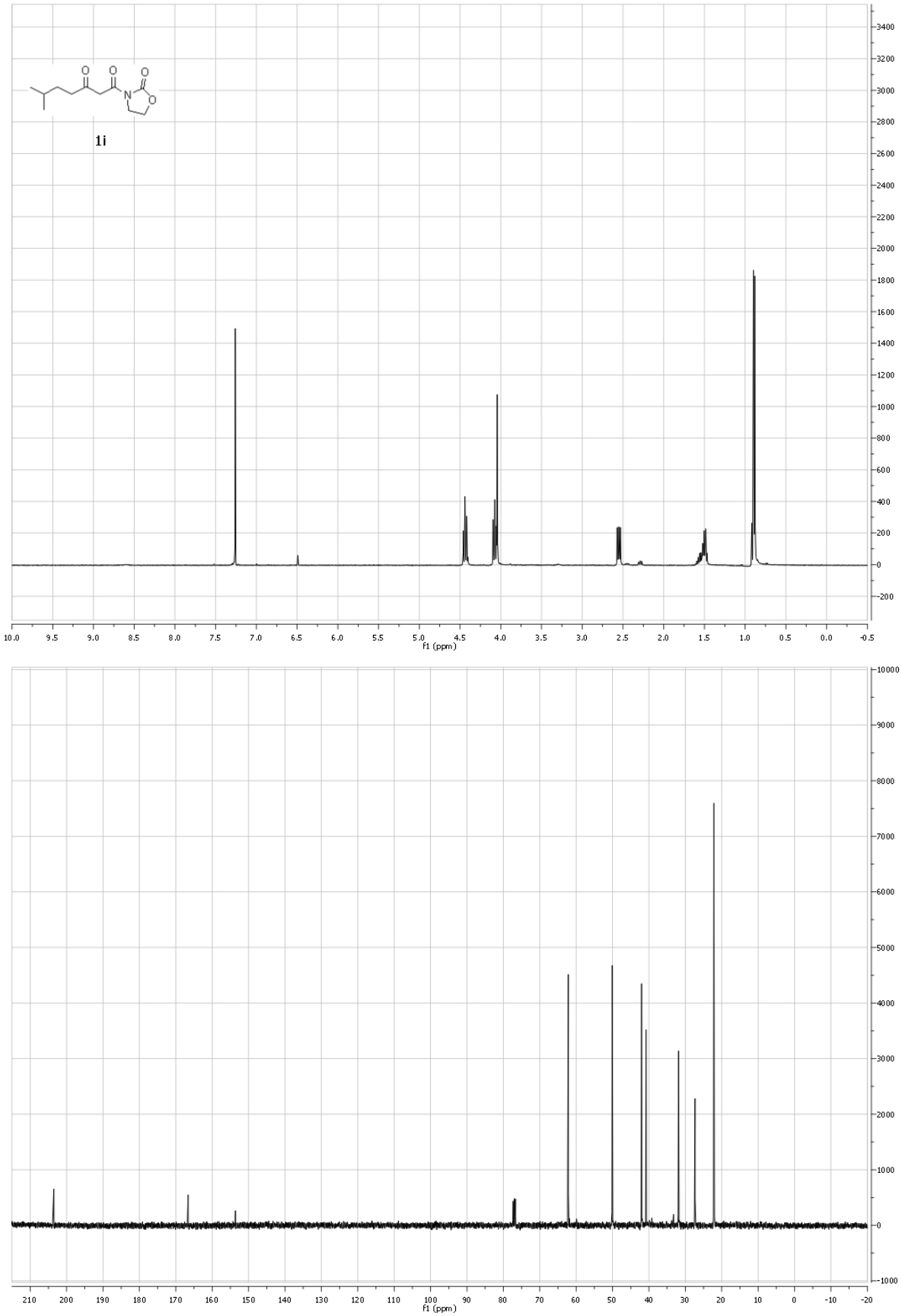


Figure 6: ^{1}H and ^{13}C NMR spectra of compound **1i**.

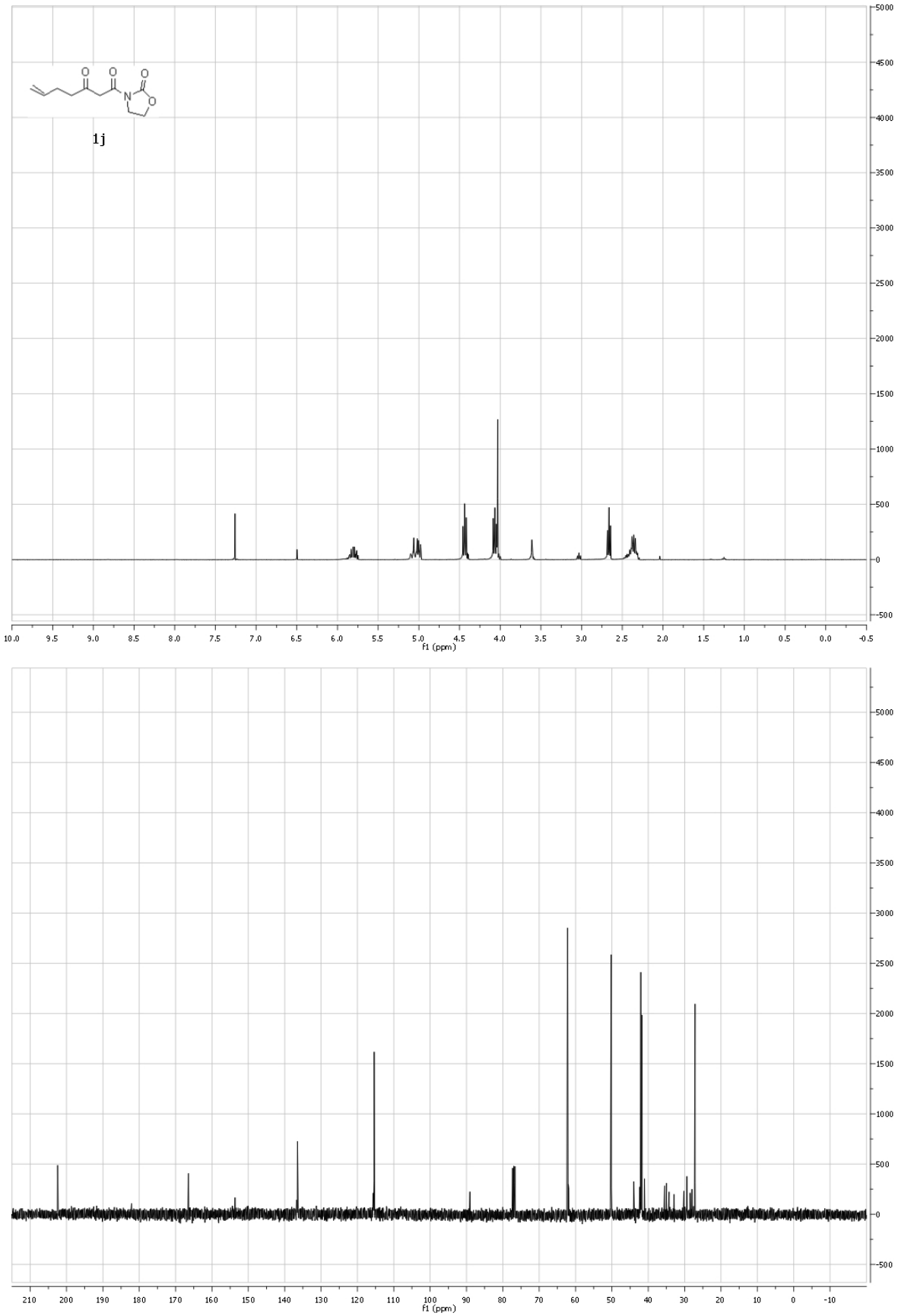


Figure 7: ^{1}H and ^{13}C NMR spectra of compound **1j**.

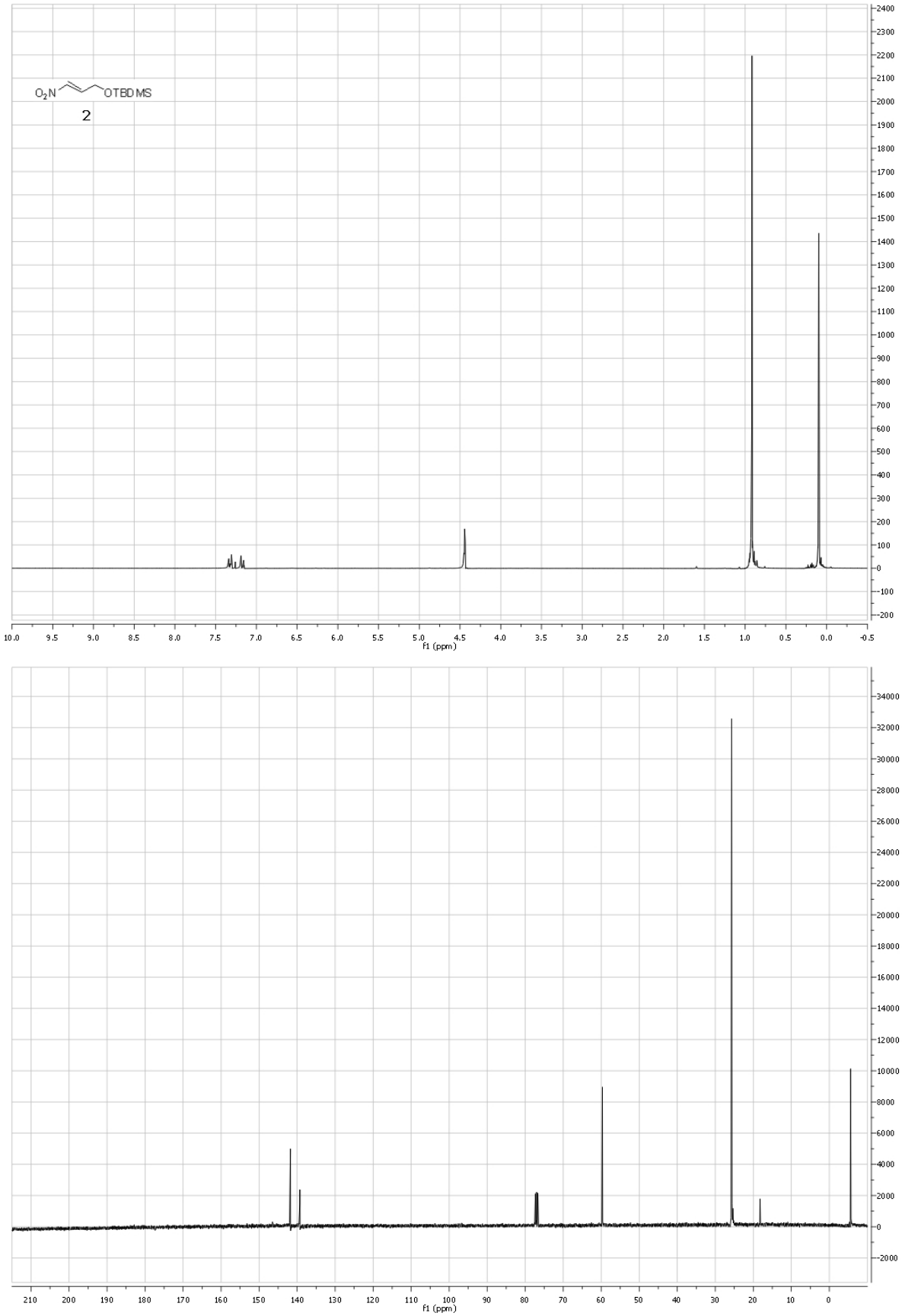


Figure 8: ^{1}H and ^{13}C NMR spectra of compound **2.**

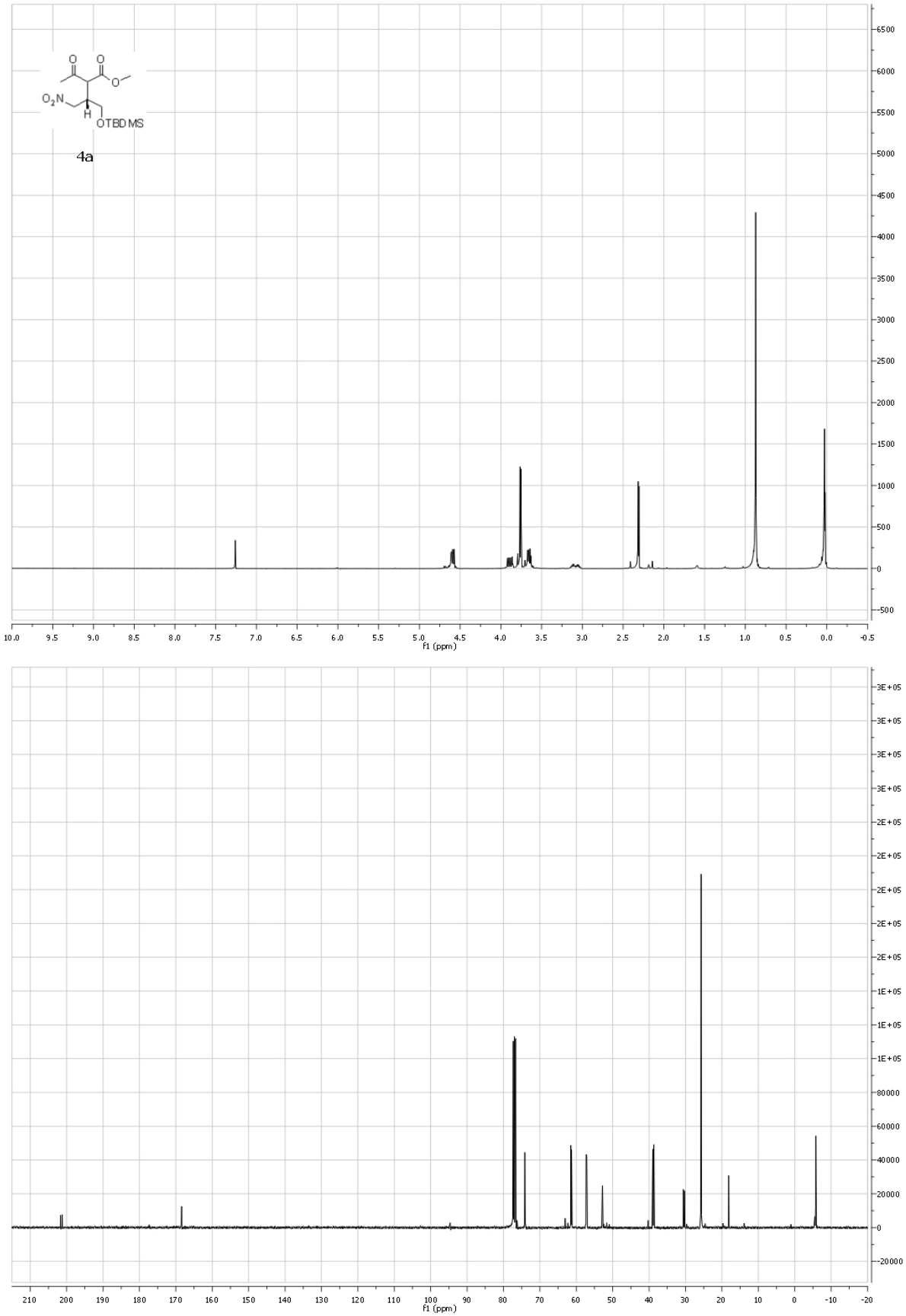


Figure 9: ^{1}H and ^{13}C NMR spectra of compound **4a.**

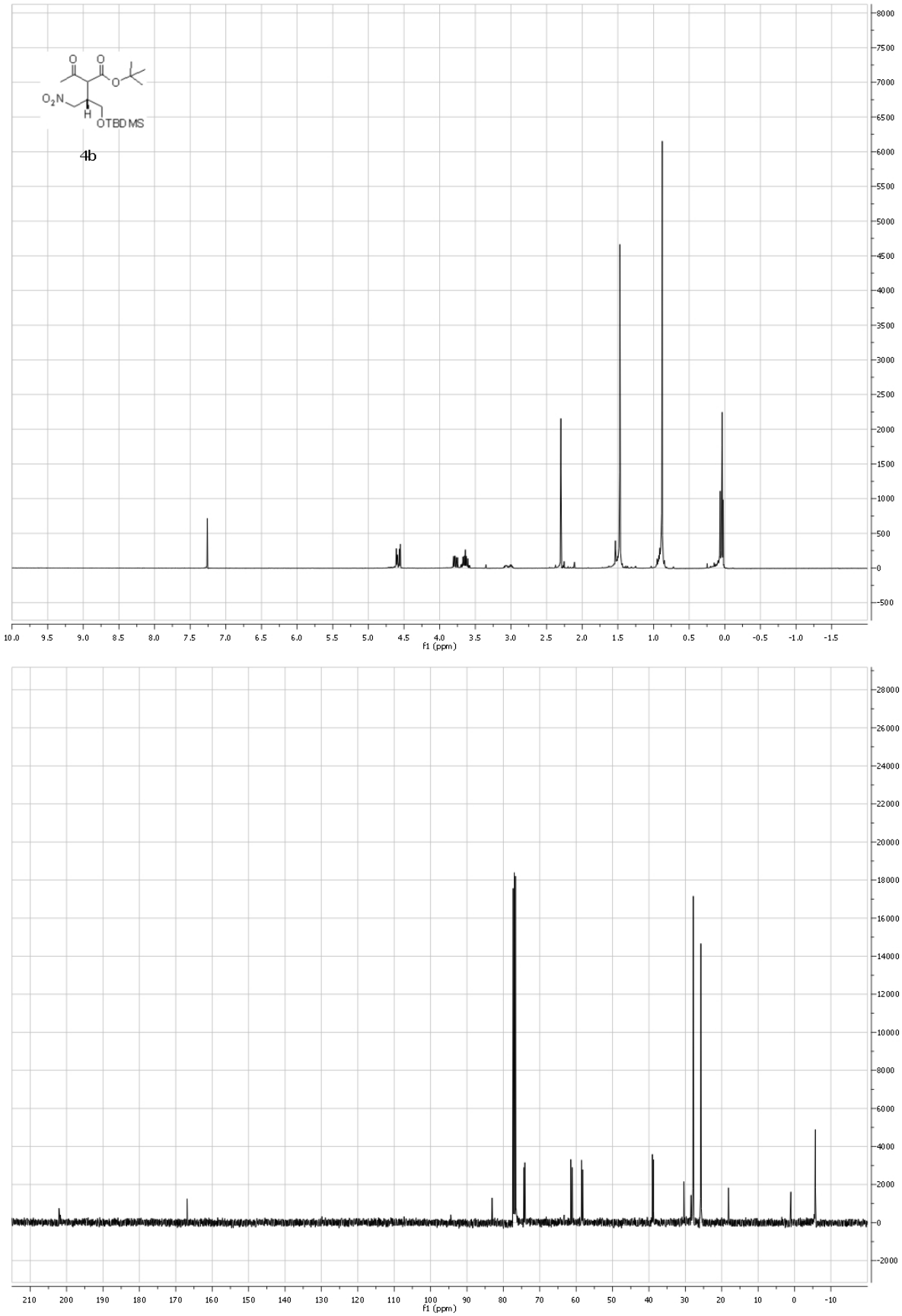


Figure 10: ^{1}H and ^{13}C NMR spectra of compound **4b**.

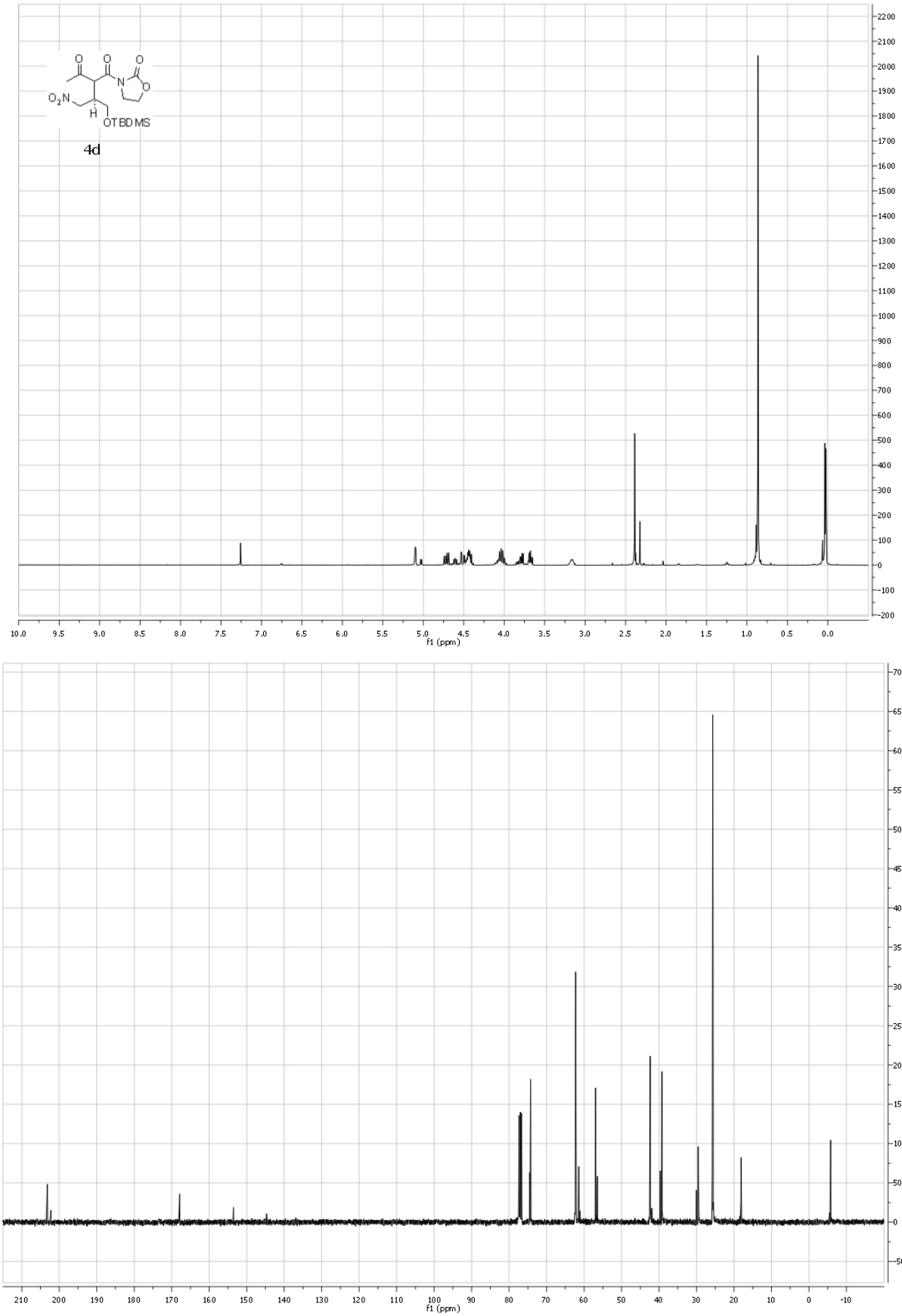


Figure 11: ^{1}H and ^{13}C NMR spectra of compound **4d**.

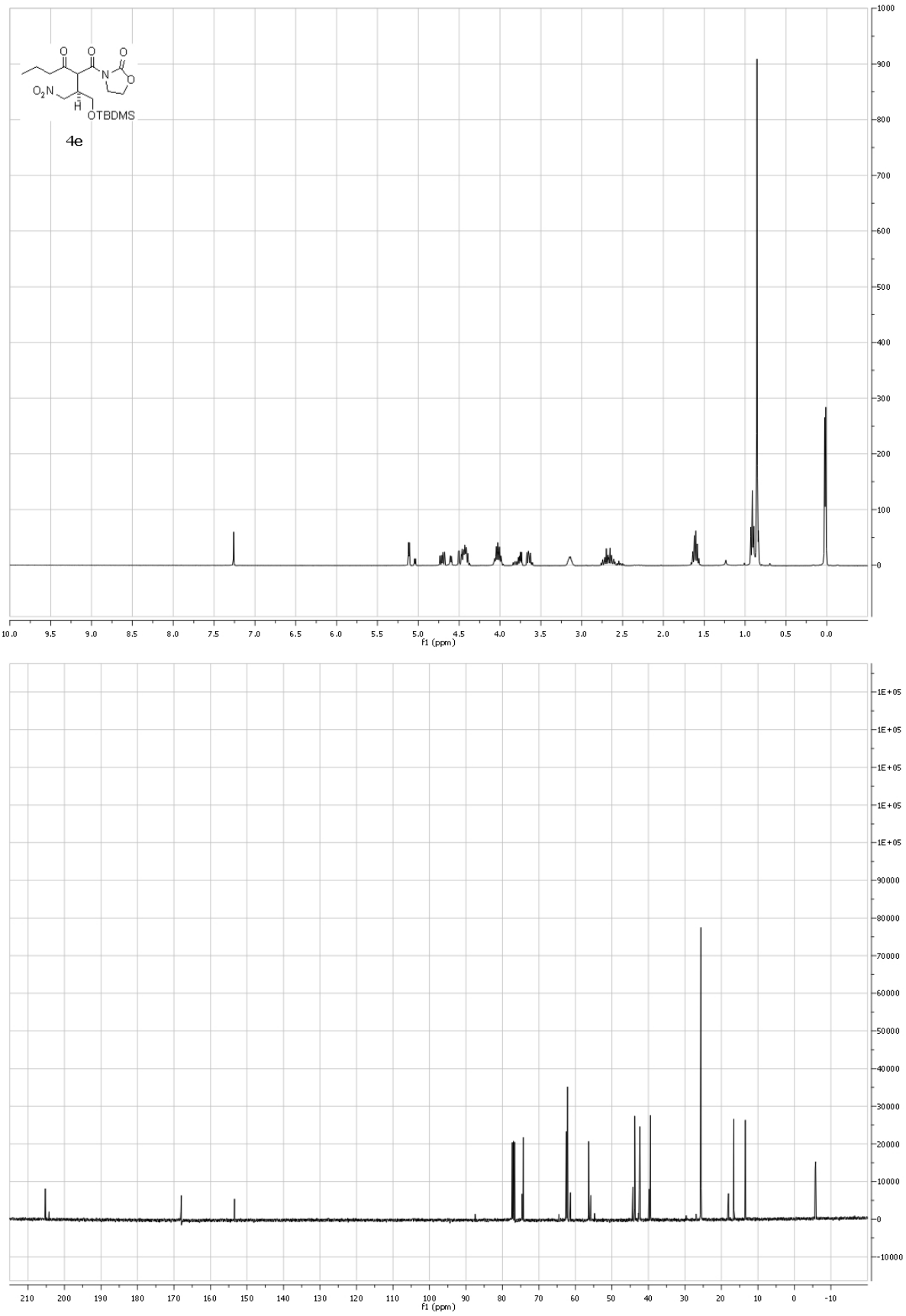


Figure 12: ^{1}H and ^{13}C NMR spectra of compound **4e**.

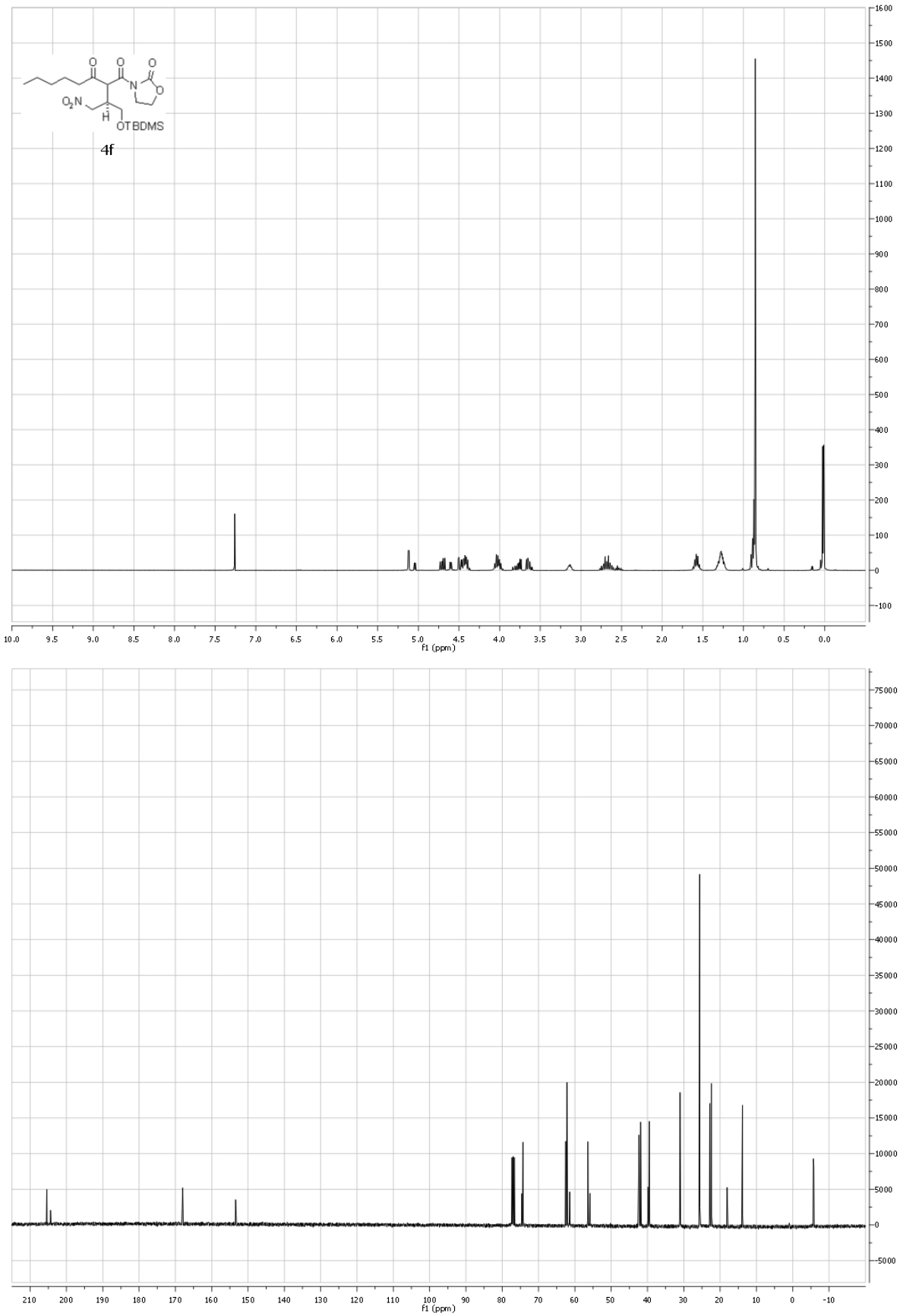


Figure 13: ^{1}H and ^{13}C NMR spectra of compound **4f**.

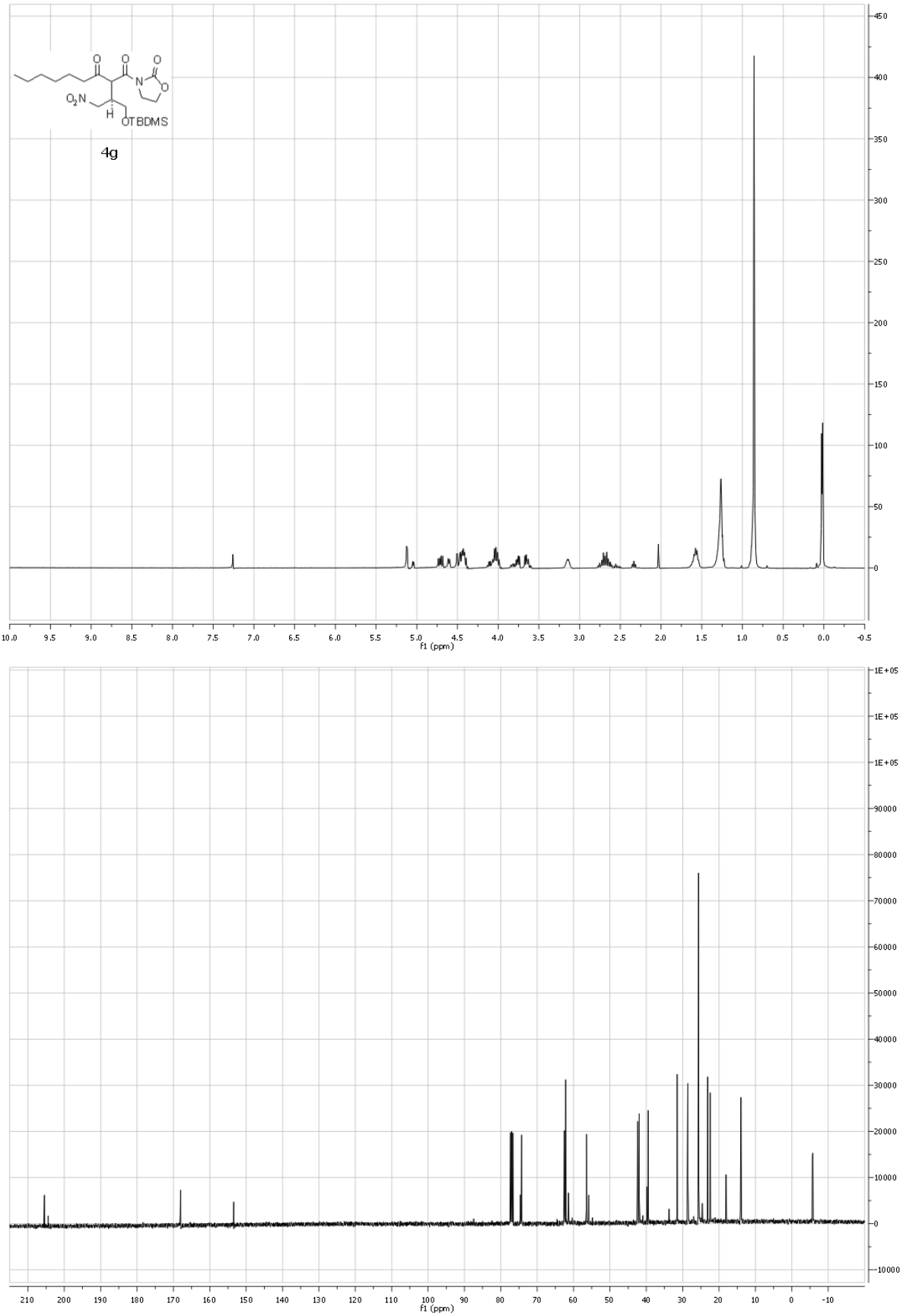


Figure 14: ^{1}H and ^{13}C NMR spectra of compound **4g**.

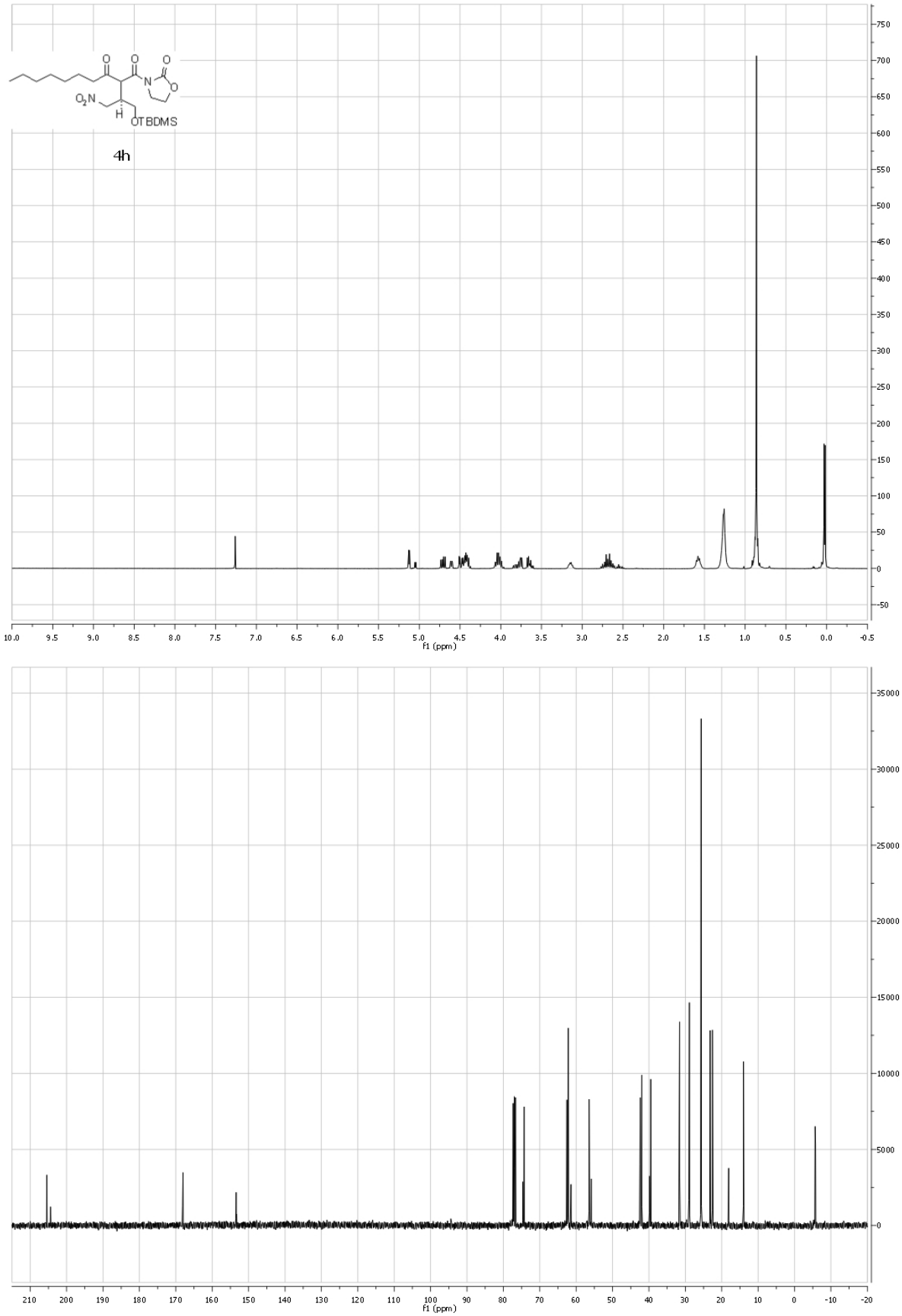


Figure 15: ^{1}H and ^{13}C NMR spectra of compound **4h**.

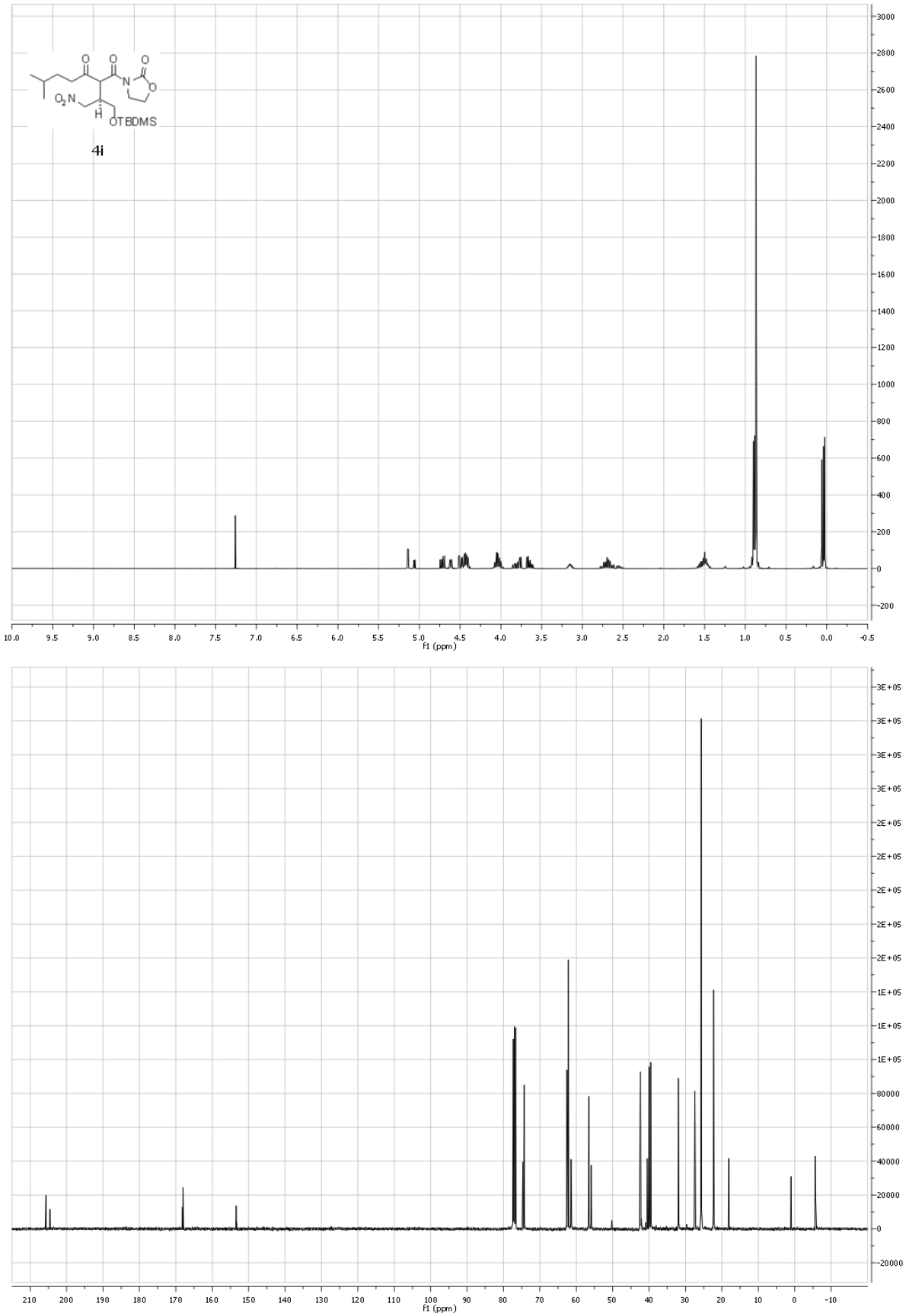
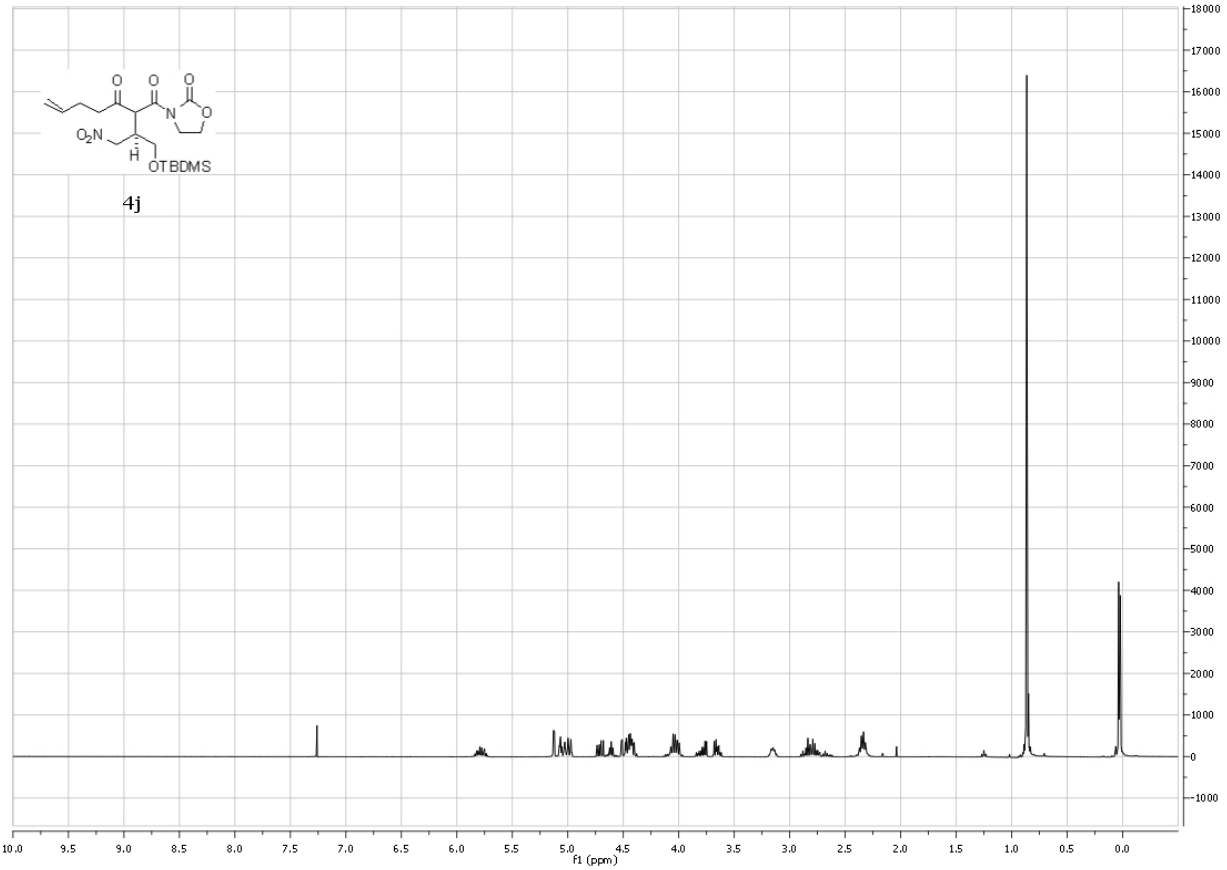


Figure 16: ^{1}H and ^{13}C NMR spectra of compound **4i**.



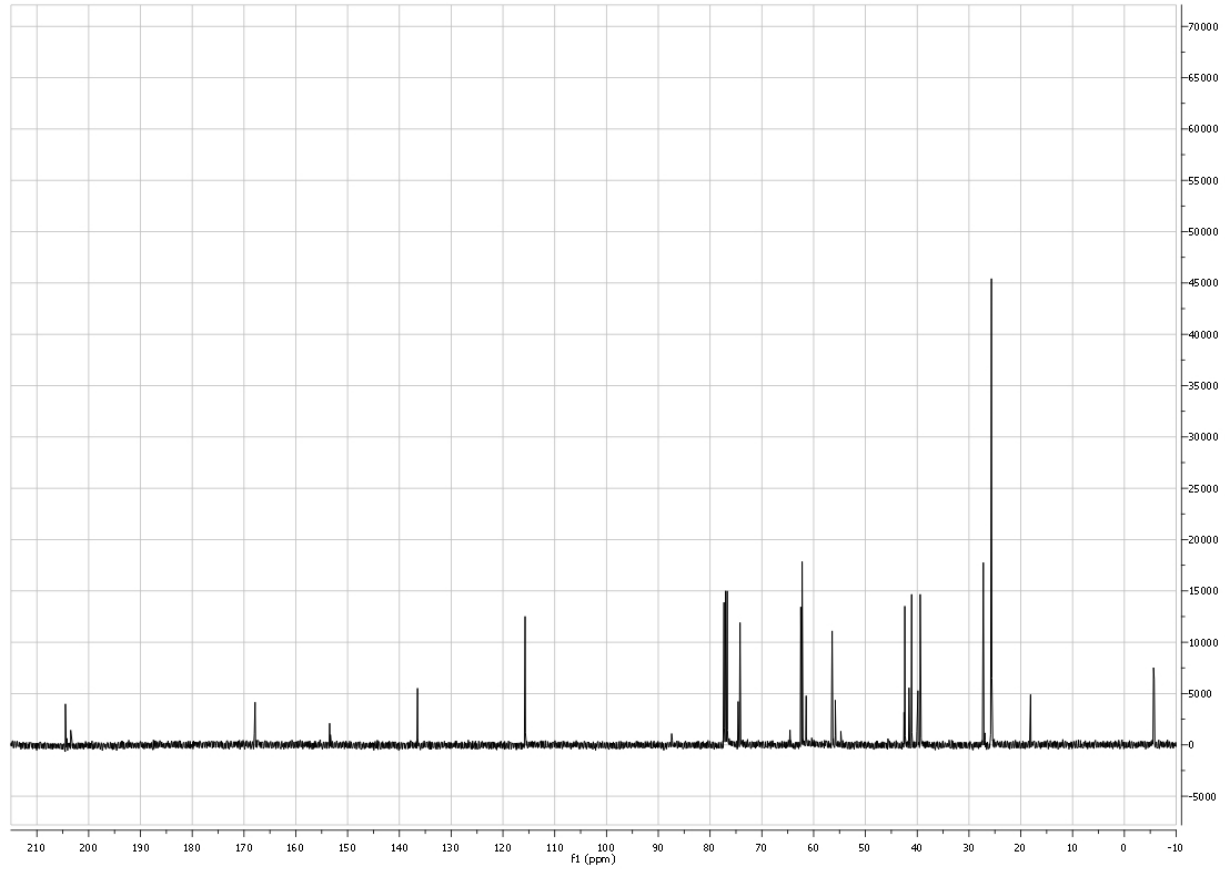


Figure 17: ^{1}H and ^{13}C NMR spectra of compound **4j**.

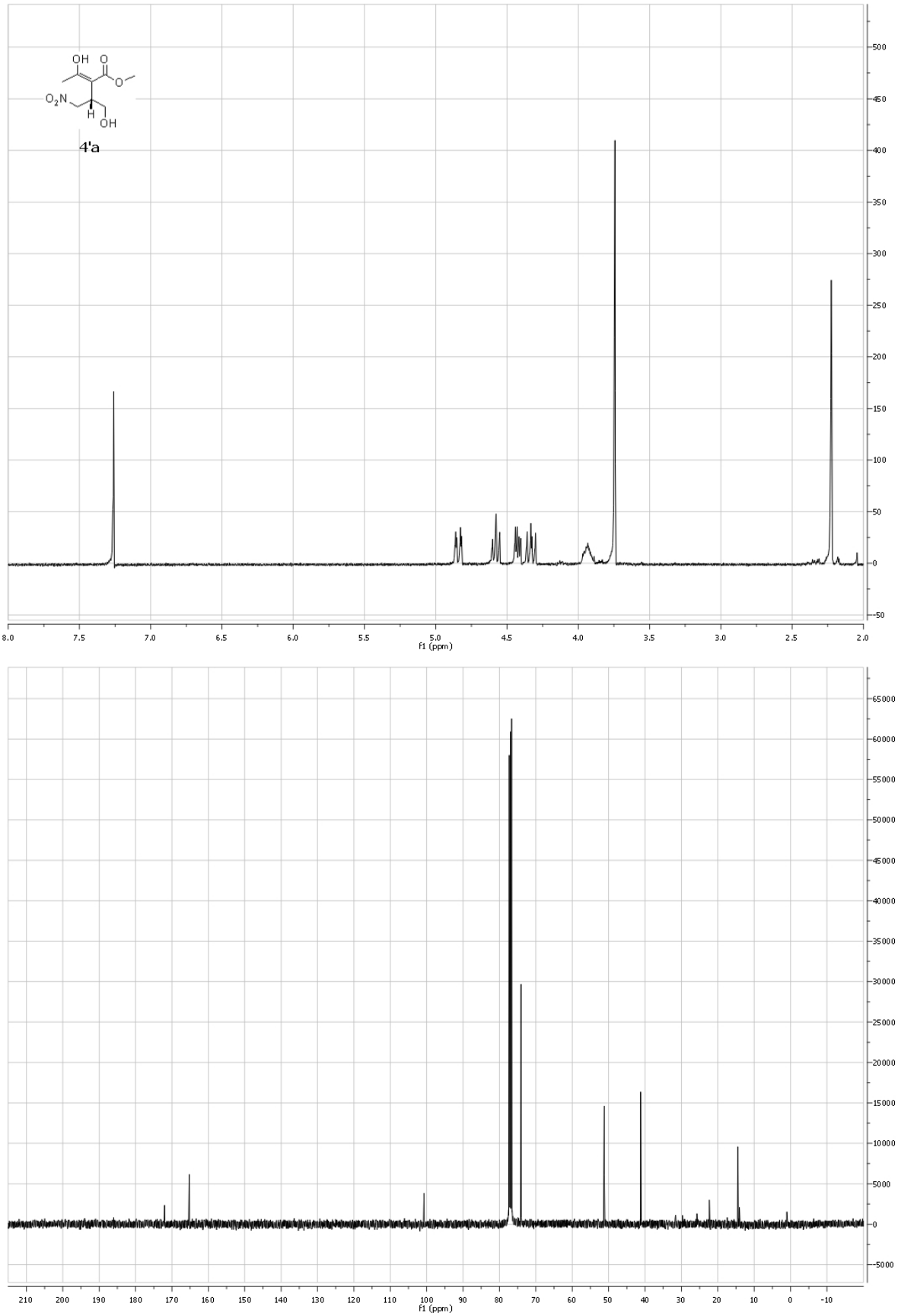


Figure 18: ^{1}H and ^{13}C NMR spectra of compound **4'a.**

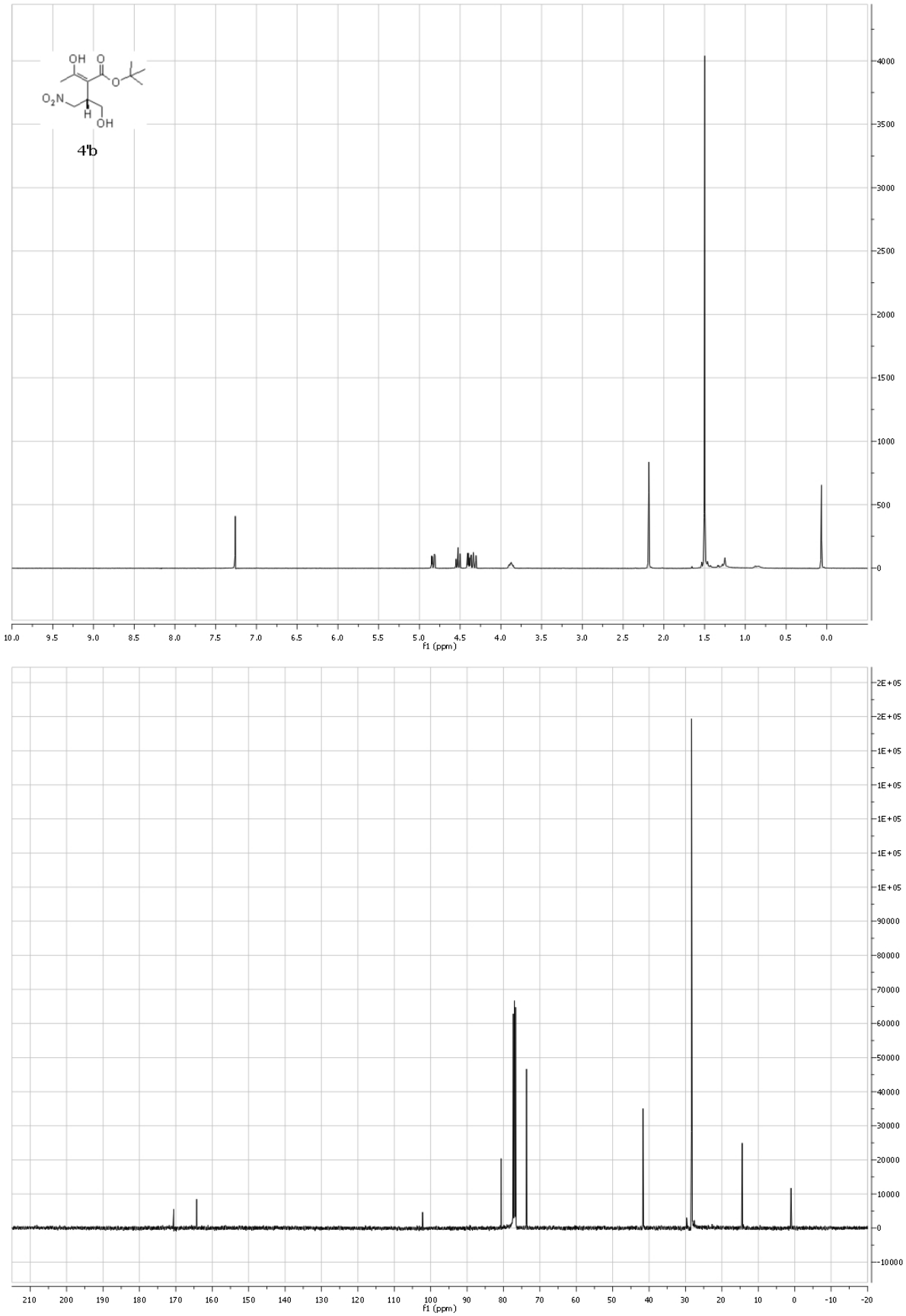


Figure 19: ^{1}H and ^{13}C NMR spectra of compound **4'b.**

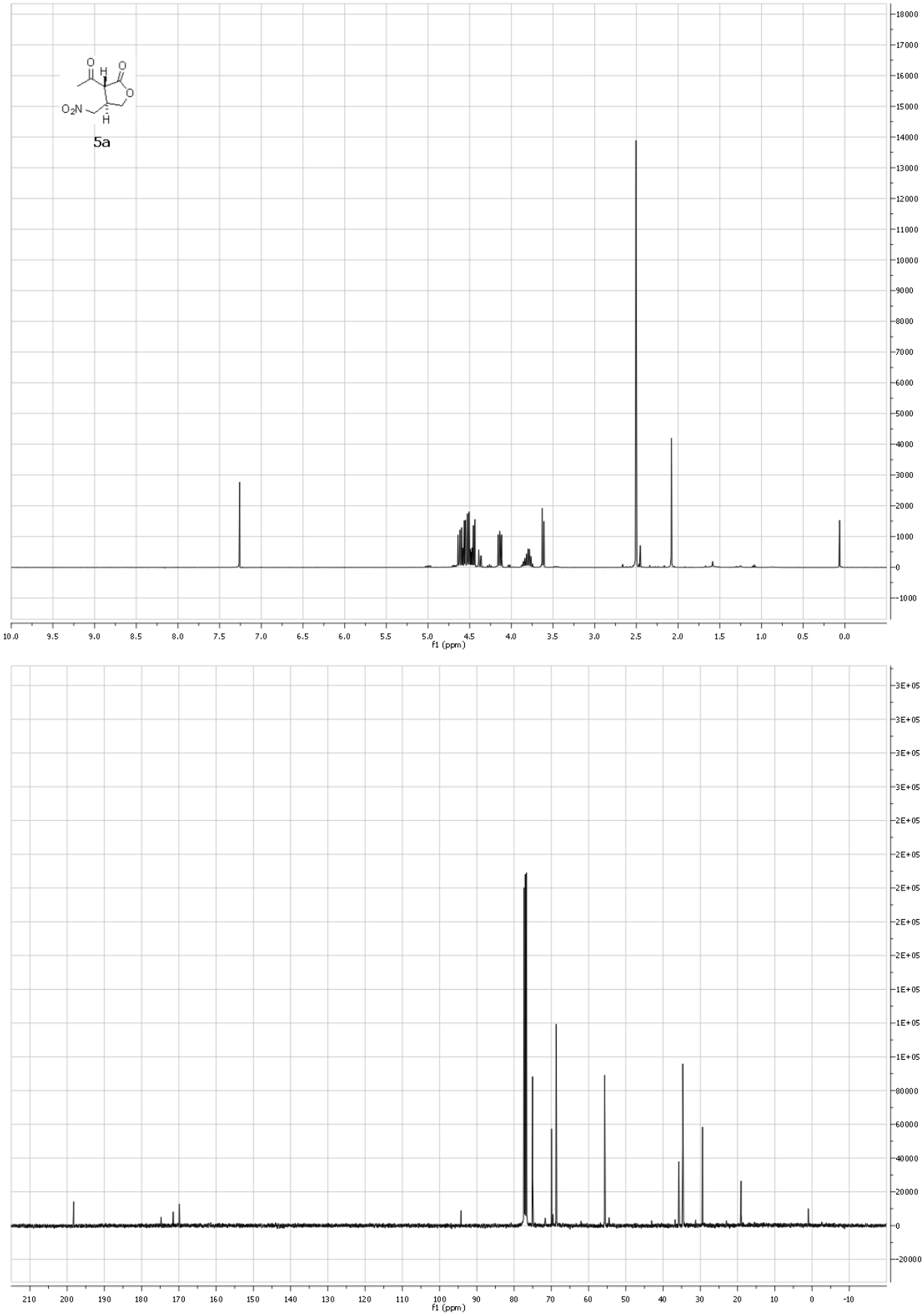
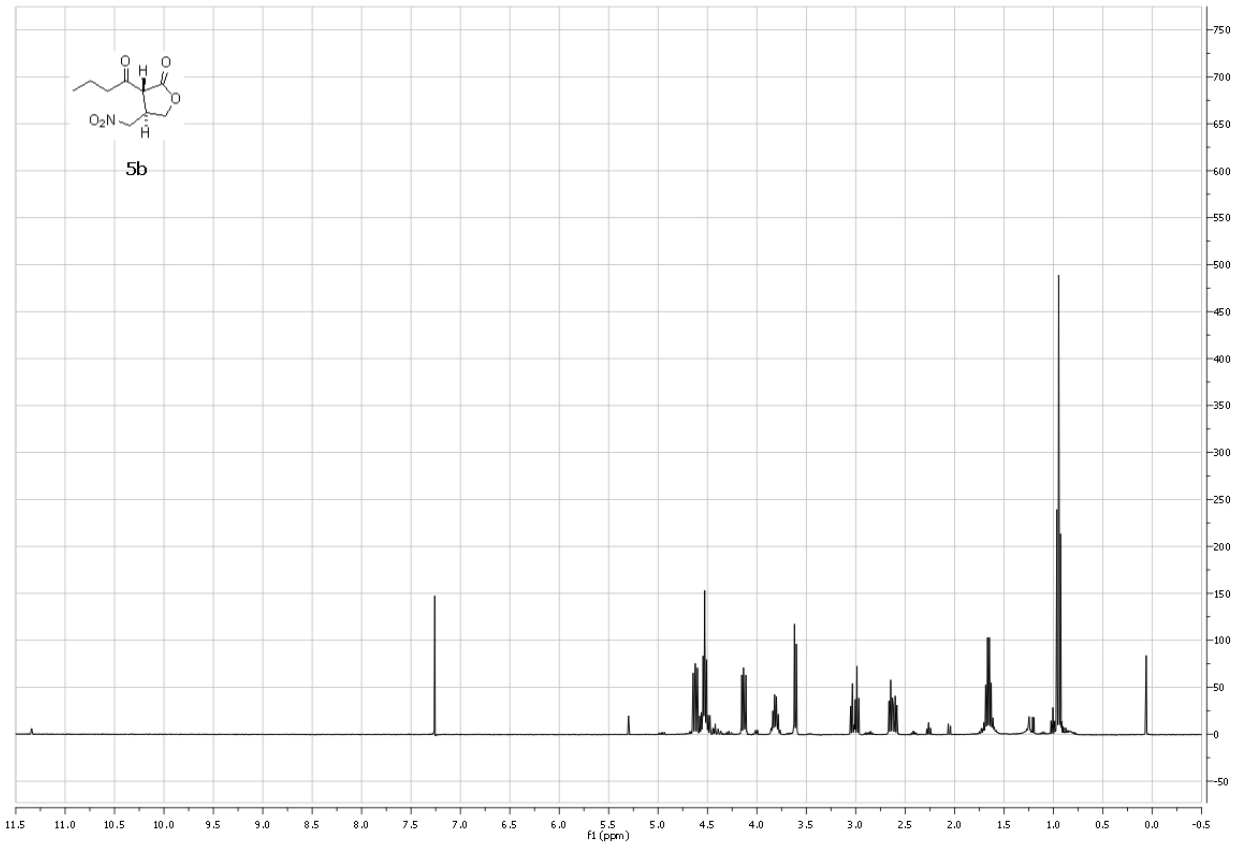


Figure 20: ^{1}H and ^{13}C NMR spectra of compound **5a**.



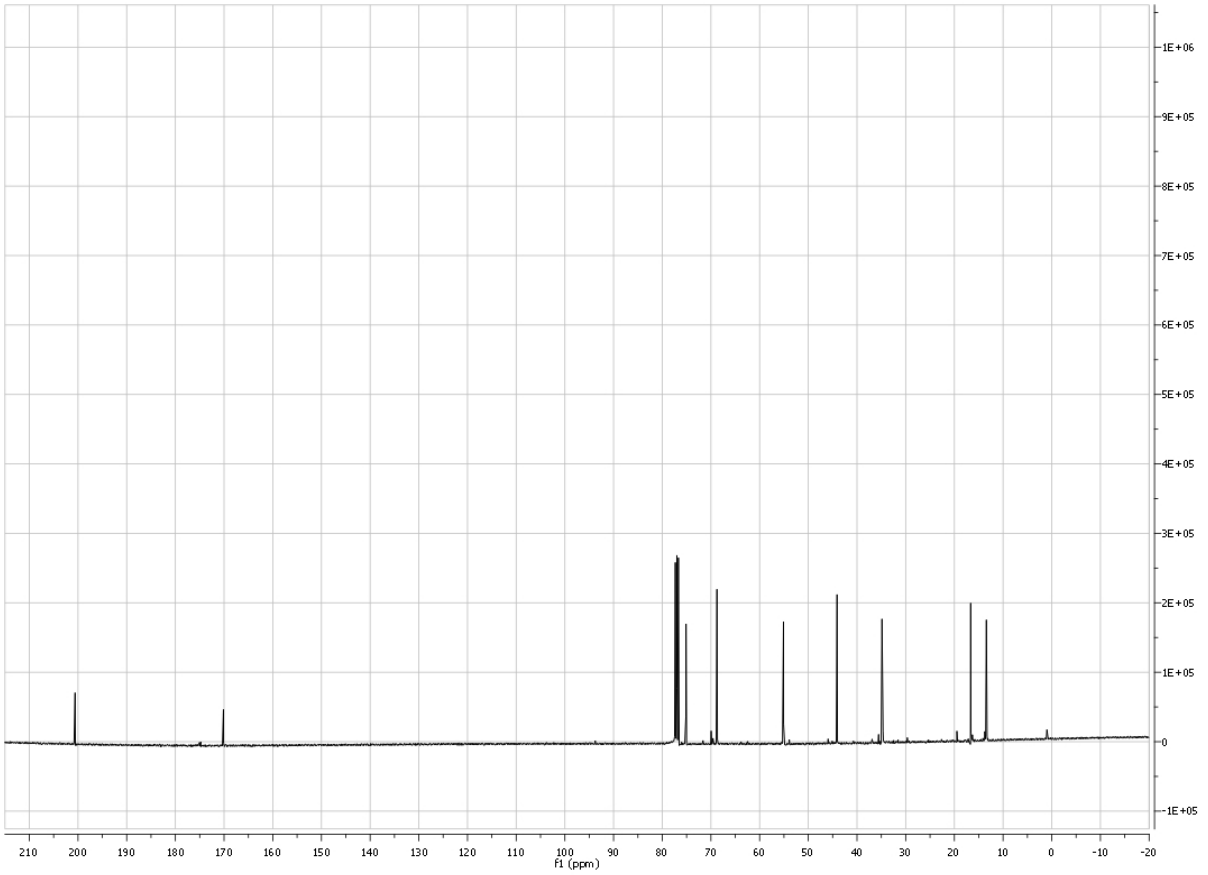


Figure 21: ^{1}H and ^{13}C NMR spectra of compound **5b**.

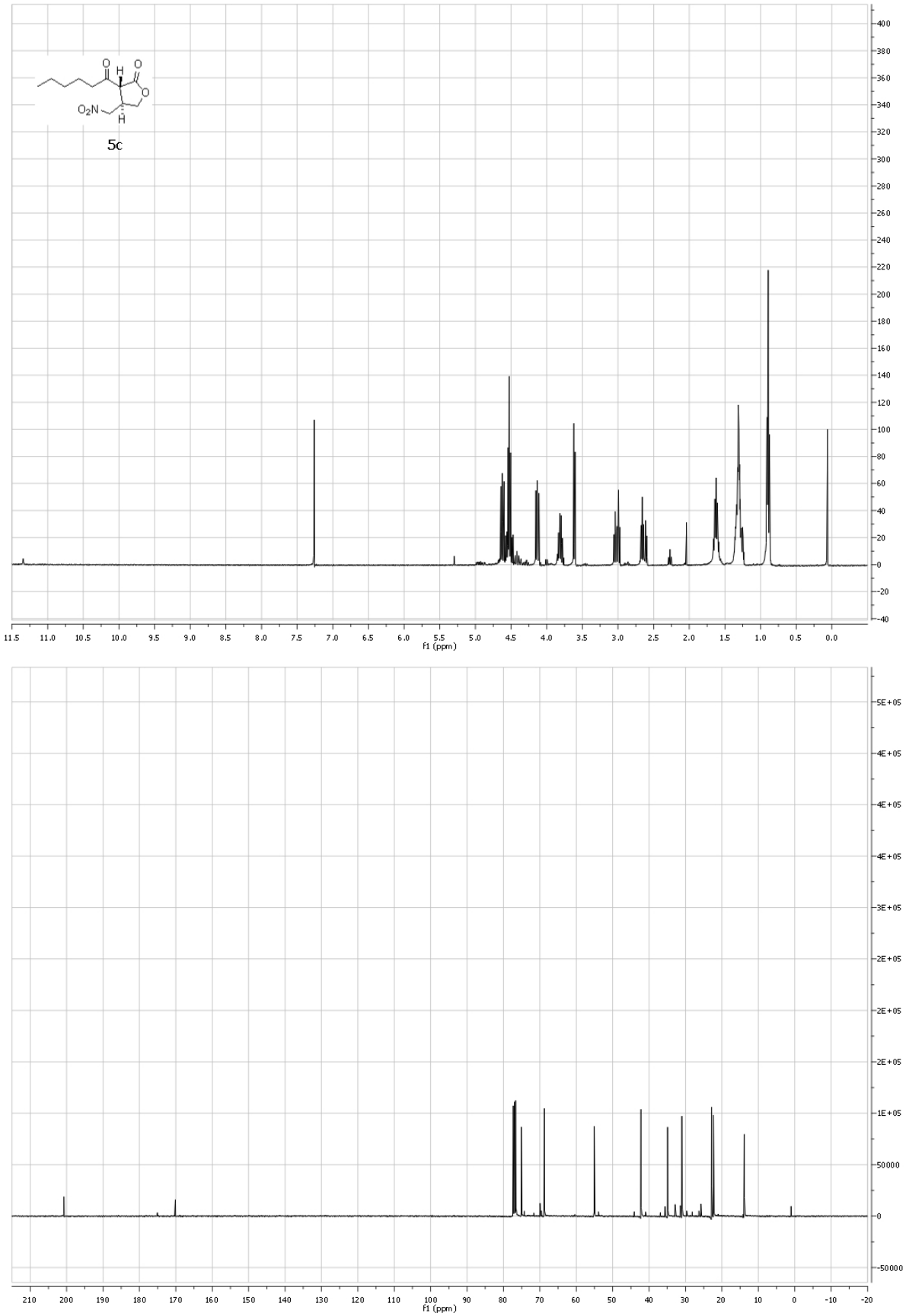


Figure 22: ^{1}H and ^{13}C NMR spectra of compound **5c**.

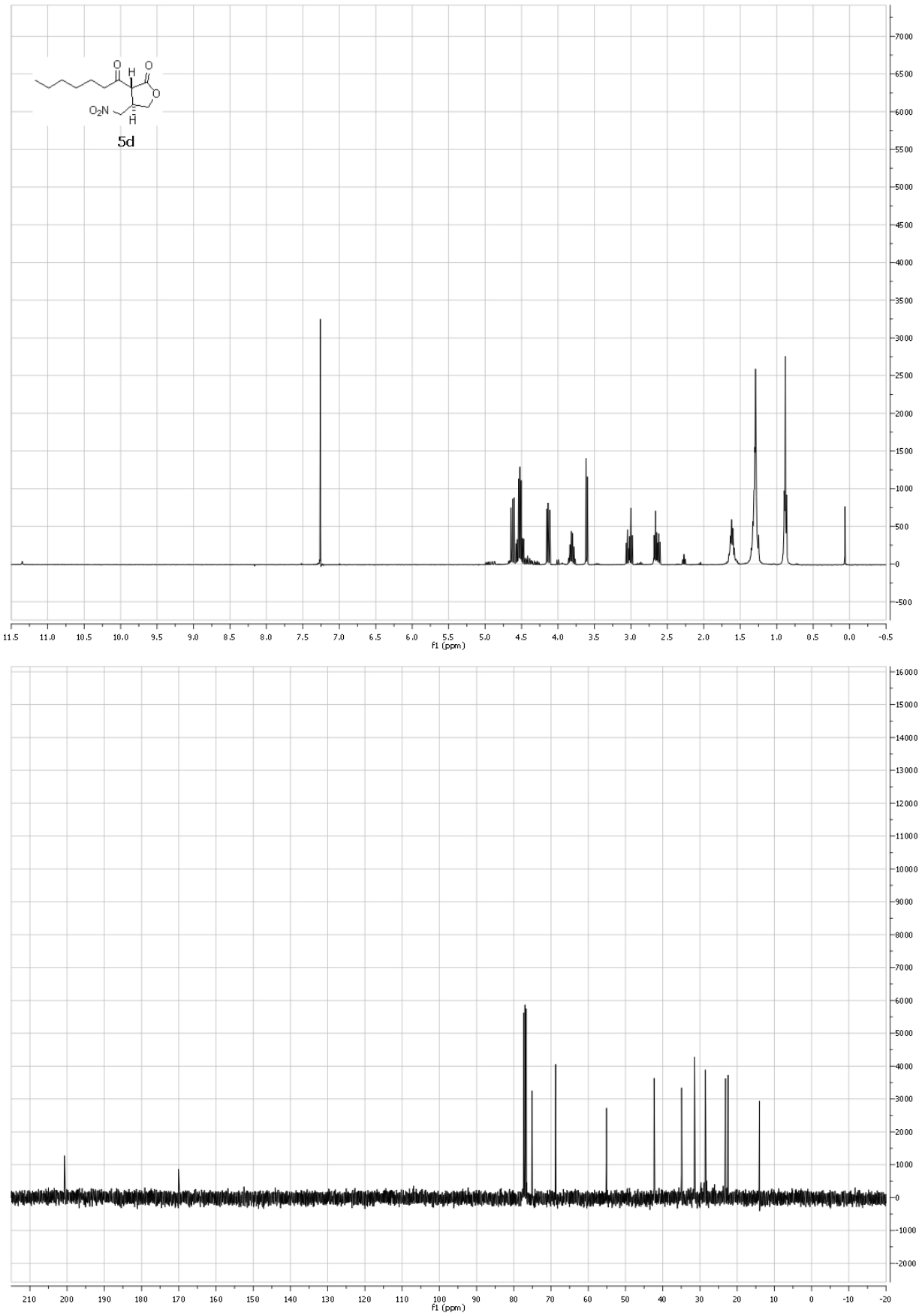


Figure 23: ^{1}H and ^{13}C NMR spectra of compound **5d**.

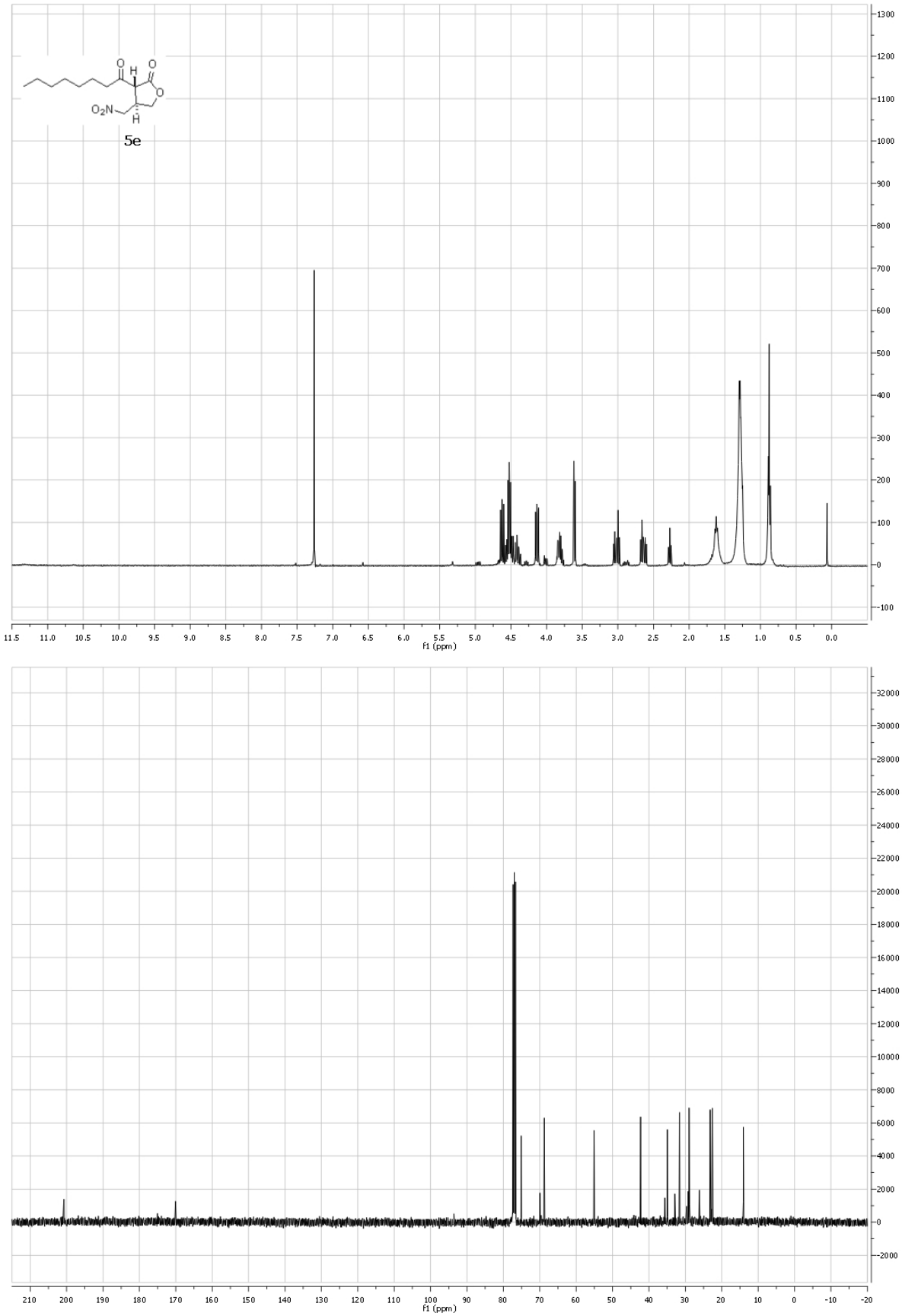


Figure 24: ^{1}H and ^{13}C NMR spectra of compound **5e**.

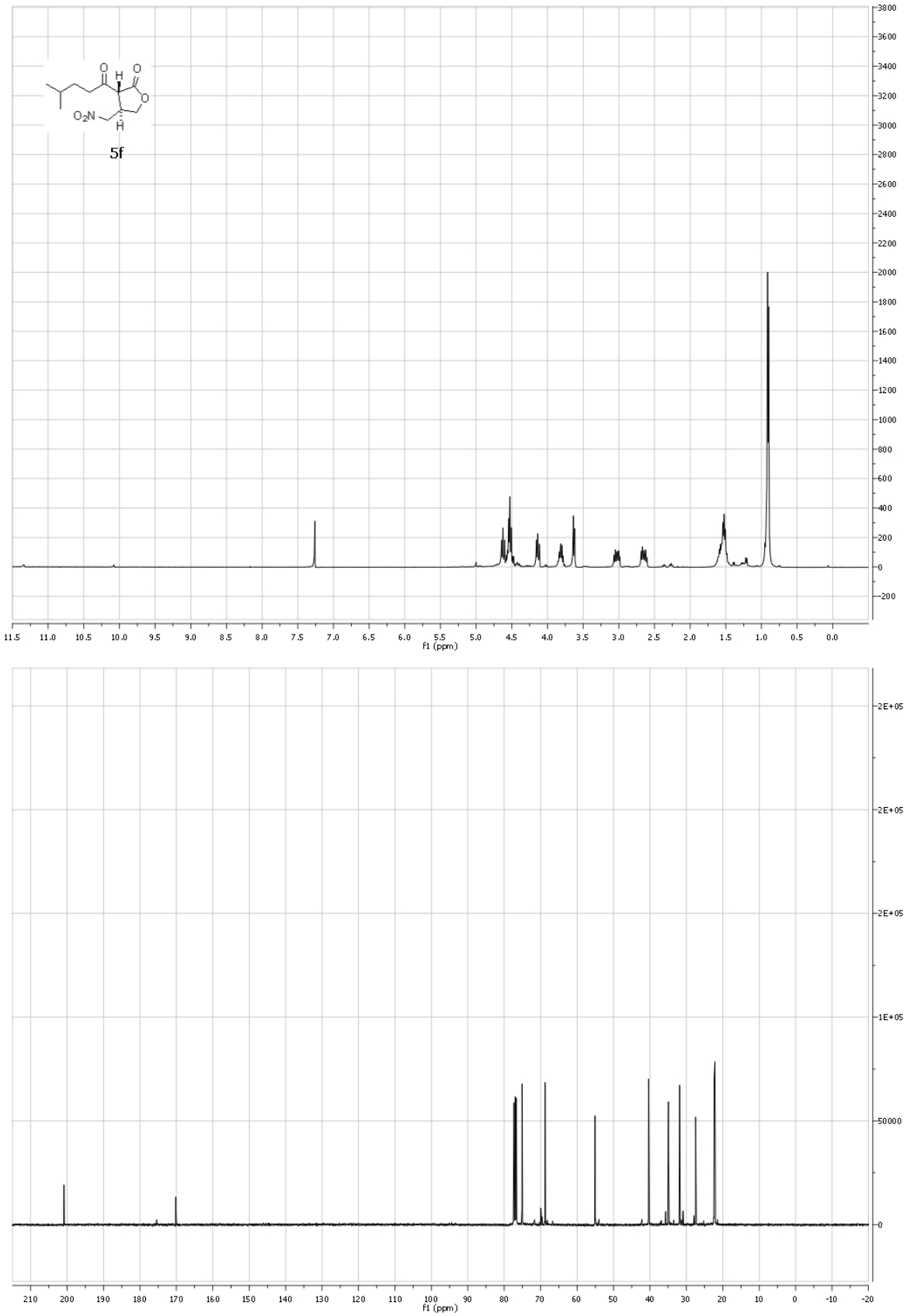


Figure 25: ^{1}H and ^{13}C NMR spectra of compound **5f**.

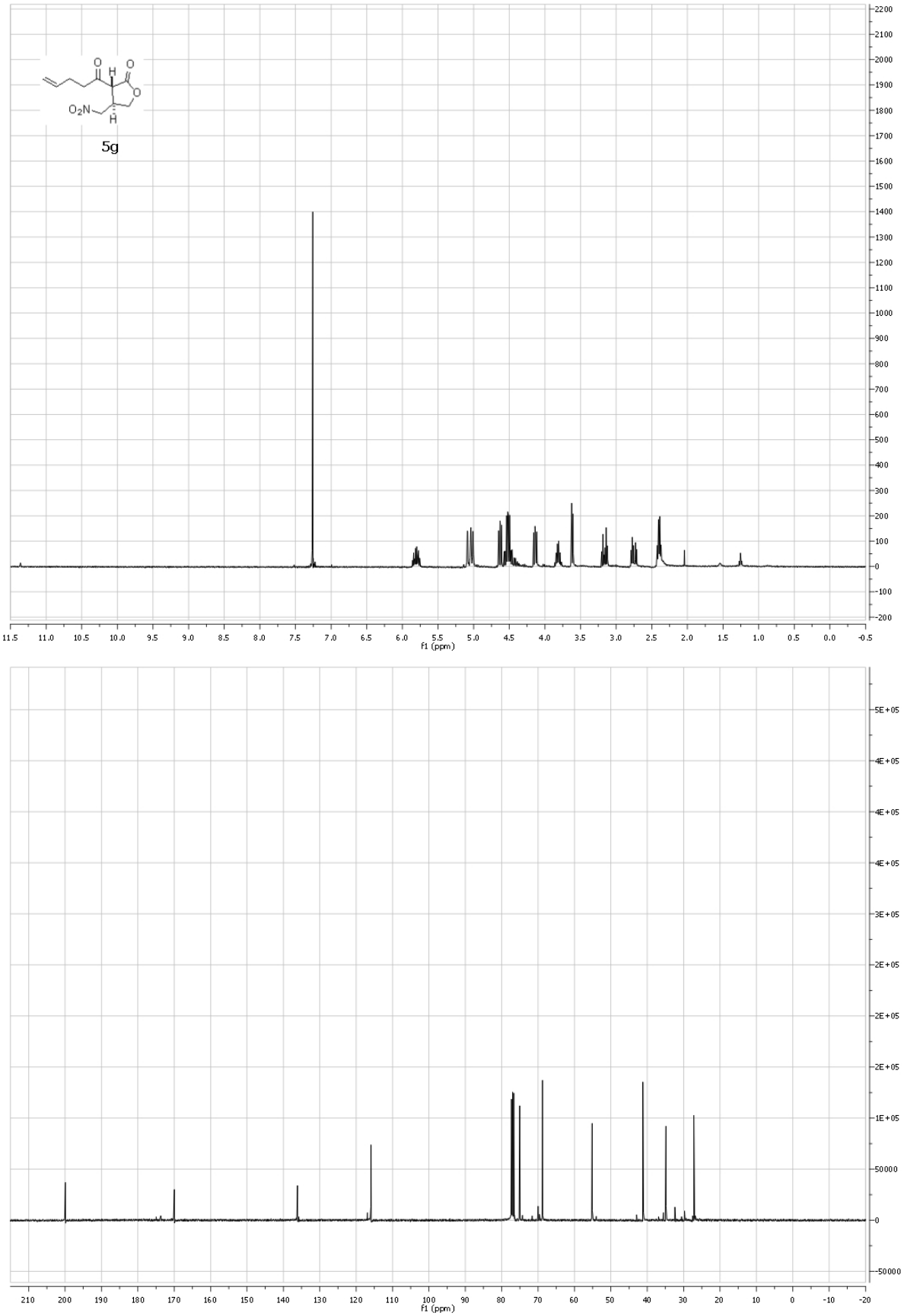


Figure 26: ^{1}H and ^{13}C NMR spectra of compound **5g**.

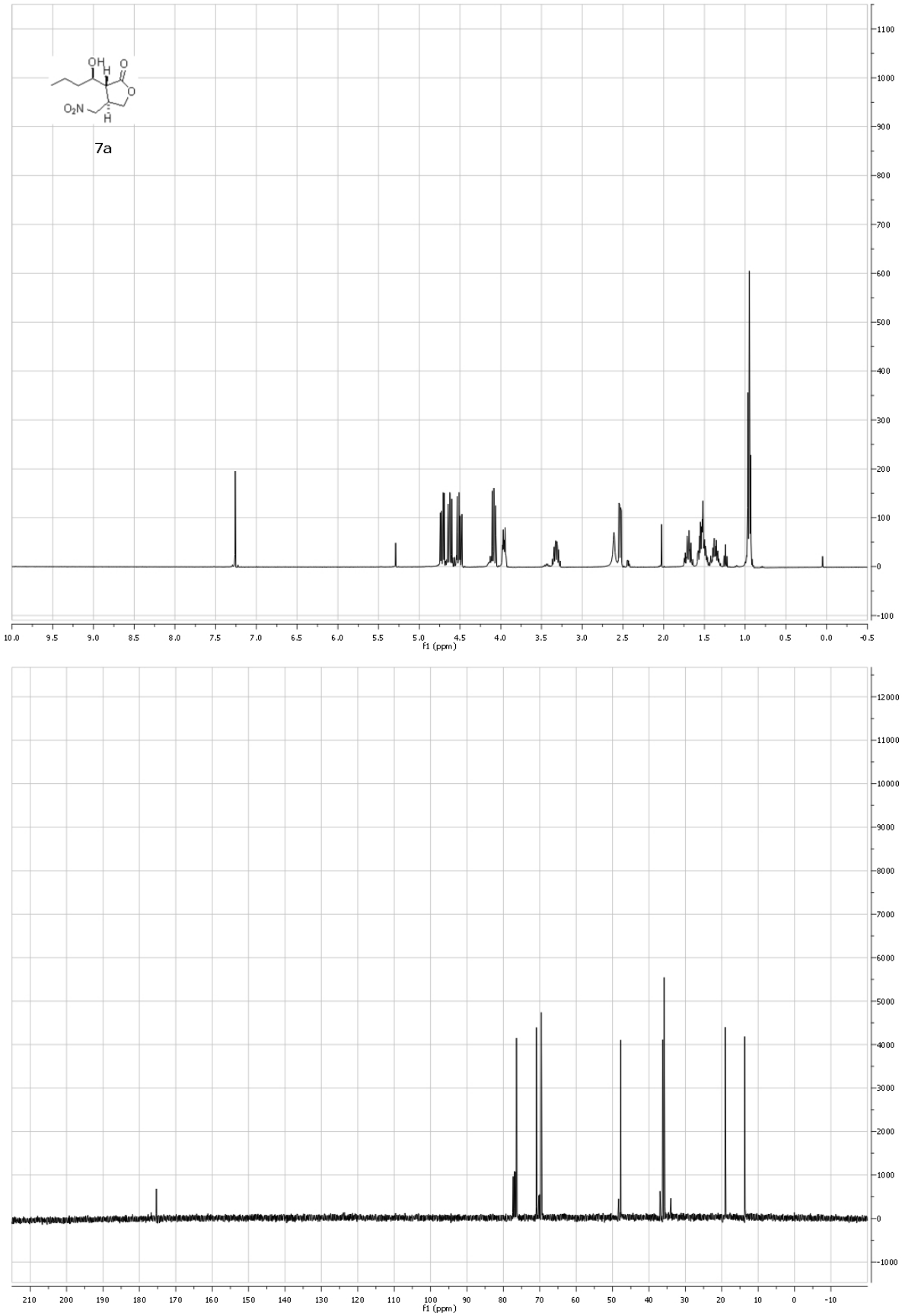


Figure 27: ^{1}H and ^{13}C NMR spectra of compound **7a**.

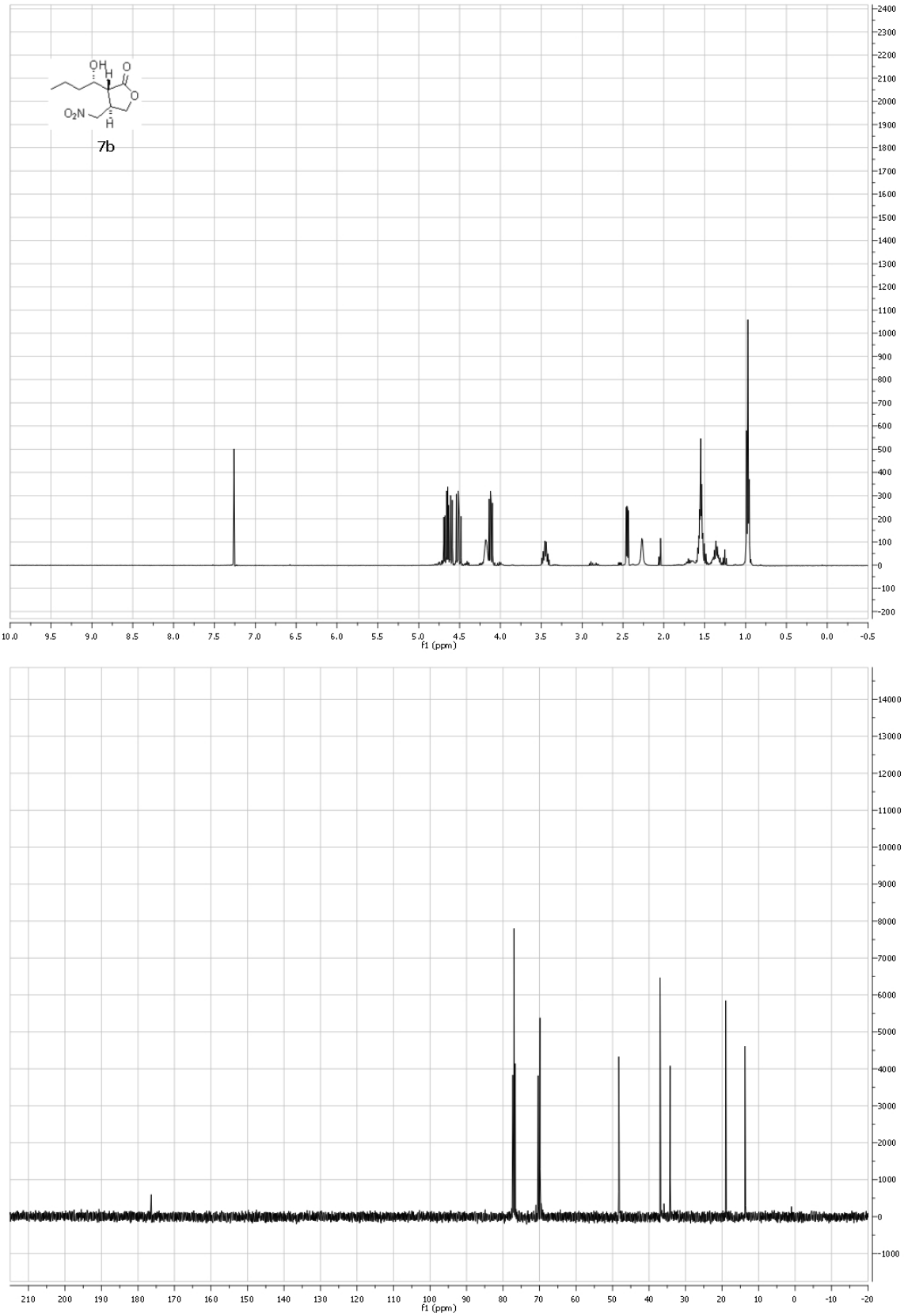


Figure 28: ^{1}H and ^{13}C NMR spectra of compound **7b**.

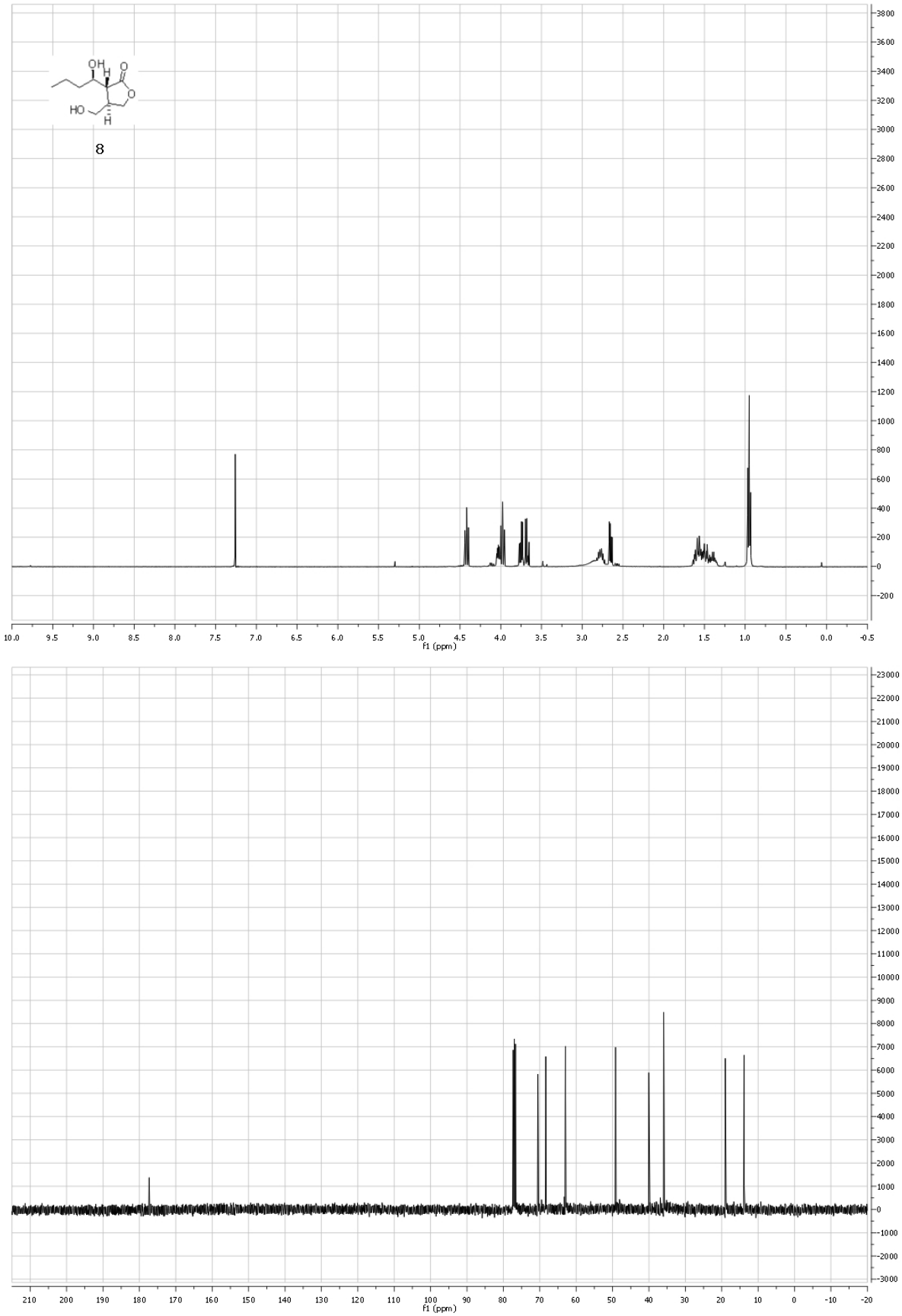


Figure 29: ^{1}H and ^{13}C NMR spectra of compound **8.**

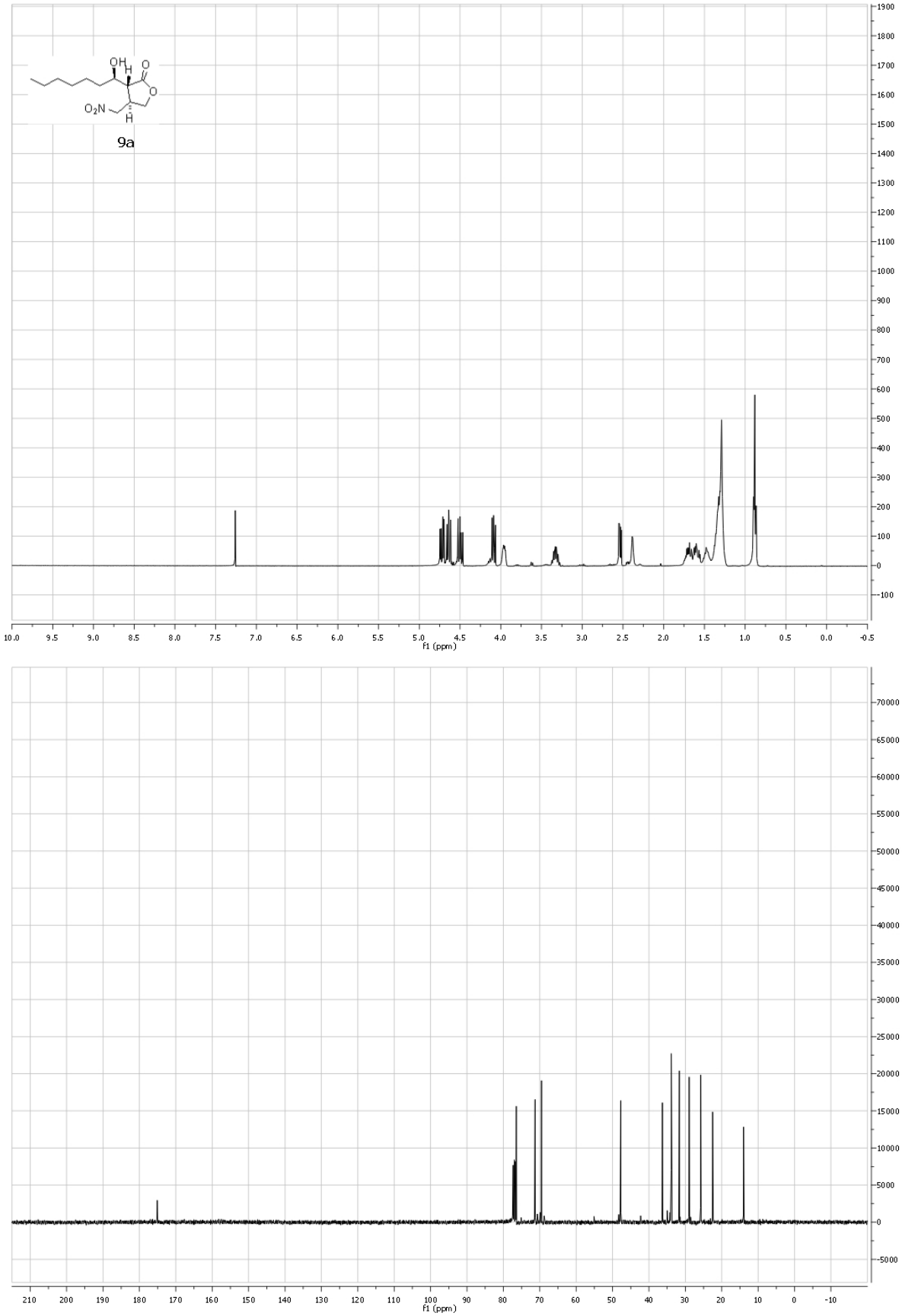


Figure 30: ^{1}H and ^{13}C NMR spectra of compound **9a**.

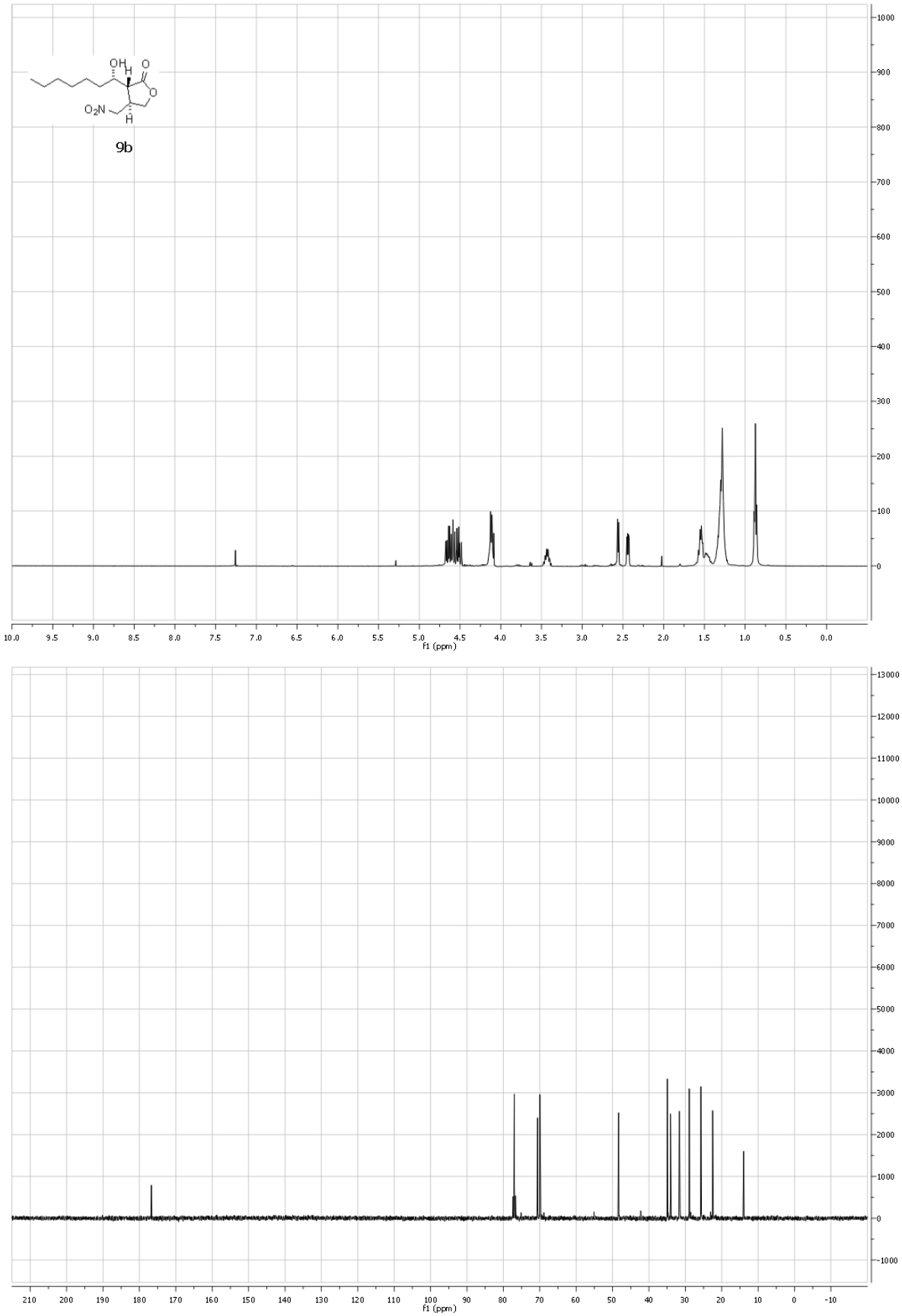


Figure 31: ^{1}H and ^{13}C NMR spectra of compound **9b**.

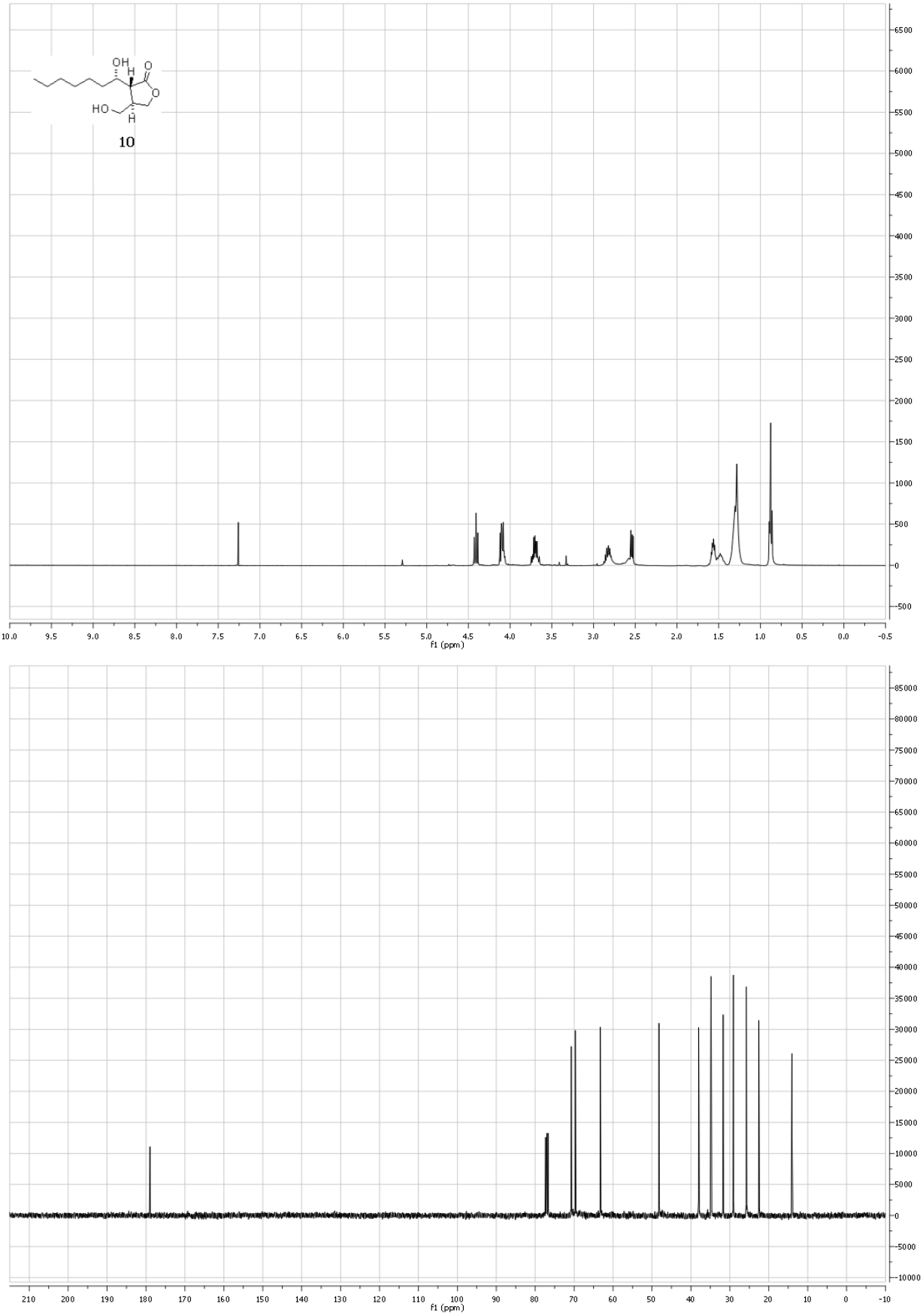


Figure 32: ^{1}H and ^{13}C NMR spectra of compound **10**.