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Supporting Information

Organocatalyzed Michael addition to nitroalkenes via masked acetaldehyde

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1. General information

All commercially available reagents were used as received and they were purchased by Sigma-Aldrich. Analytical grade solvents and silica gel (35-70 μm) were purchased by Sigma-Aldrich and Carlo Erba. HPLC solvents were purchased by Sigma-Aldrich. $MgSO_4$ was purchased by Carlo Erba. The starting materials **1b-h** were prepared according to the literature.[1,2]

^{1}H-NMR and ^{13}C-NMR spectra were measured respectively at 400 and 101 MHz using a Bruker Advance III 400 MHz spectrophotometer. Chemical shifts (δ) are reported in ppm relative to residual solvent signals for ^{1}H and ^{13}C NMR (^{1}H NMR: 7.26 ppm for $CDCl_3$; ^{13}C NMR: 77.0 ppm for $CDCl_3$). Optical rotations values were measured with a Perkin-Elmer 241 polarimeter.

Enantiomeric ratios were determined by chiral HPLC on an Agilent 1220 Infinity II liquid chromatographer. The chiral columns used for the determination of enantiomeric excesses by chiral HPLC were Phenomenex Lux 3μm-cellulose 1 and Lux 3μm-cellulose 5, and Chiralpak OJ-H. The high-resolution mass spectra (HRMS) were obtained with an ESI-QTOF (Agilent Technologies, model G6520A) instrument, and the m/z values are referred to the mono isotopic mass.

2. Determination of absolute configuration

The absolute configurations of previously reported optically active compounds were determined on the basis of the measured optical rotations that were compared with literature values. All other absolute configurations were assigned by analogy.

3. General procedure for aromatics nitroalkenes[1]

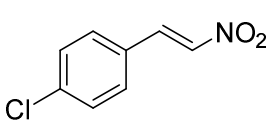
To a solution of MeOH (11 mL), water (0.026 eq.) and 2 M NaOH (1.2 eq.) at 5 °C in a 50mL one-neck round bottom flask equipped with a magnetic bar was added dropwise a solution of aldehyde (1 eq.) and $MeNO_2$ (1.2 eq.) in 2 mL of MeOH. The internal temperature was maintained between 5 and 10 °C for about 15-30 min. The reaction solution was stirred for an additional 30 min maintaining the temperature between 0 and

5 °C. It was then added dropwise to a 250mL beaker containing a solution of $ZnCl_2$ (5 eq.), HCl_{conc} (2.5 eq.) and H_2O (0.016 eq.) at 0-10 °C under vigorous agitation and stirred for 2-3 h. In order to achieve the best conversion on a small scale, a flanged beaker was used. The product precipitated during the addition was filtered and it was then washed with a solution of H_2O/MeOH 3:2.

NMR spectra of previously reported compounds were in agreement with those of the authentic samples and/or available literature data.

2.1 Synthesis and spectral characterization of aromatics nitroalkenes

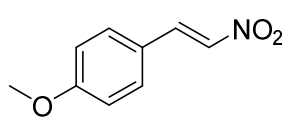
Synthesis of (E)-1-chloro-4-(2-nitrovinyl)benzene (**1b**)*:*[3]



Synthesized in accordance with *general procedure for aromatics nitroalkenes* using 4-chlorobenzaldehyde (1.5 g, 10.67 mmol), $MeNO_2$ (781.6 µL, 12.81 mmol) diluted in 2 mL of MeOH, water (5 mL, 0.28 mmol), NaOH (6.40 mL, 12.81 mmol) and MeOH (11 mL). Then the mixture was added to a solution of $ZnCl_2$ (7.5 g, 55 mmol), HCl (2.3 mL, 28 mmol) and H_2O (3 mL, 0.17 mmol). The desired product was obtained as a yellow solid (1.4 g, 8.1 mmol, yield = 72 %).

^{1}H-NMR (400 MHz, $CDCl_3$, 298 K) δ 7.96 (d, *J* = 13.7 Hz, 1H), 7.56 (d, *J* = 13.7 Hz, 1H), 7.52 – 7.47 (m, 2H), 7.46 – 7.40 (m, 2H).

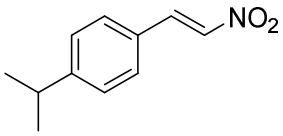
Synthesis of (E)-1-methoxy-4-(2-nitrovinyl)benzene (**1c**)*:*[3]



Synthesized in accordance with *general procedure for aromatics nitroalkenes* using 4-methoxybenzaldehyde (1.5 g, 11.02 mmol), $MeNO_2$ (708 µL, 13.22 mmol) diluted in 2 mL of MeOH, water (5.2 mL, 0.29 mmol), NaOH (6.6 mL, 13.22 mmol) and MeOH (11 mL). Then the mixture was added to a solution of $ZnCl_2$ (7.5 g, 55.1 mmol), HCl (2.3 mL, 28 mmol) and H_2O (3.2 mL, 0.18 mmol). The desired product was obtained as a yellow solid (1.3 g, 7.6 mmol, yield = 66 %).

^{1}H-NMR (400 MHz, $CDCl_3$, 298 K) δ 7.98 (d, *J* = 13.6 Hz, 1H), 7.57 – 7.47 (m, 3H), 7.02 – 6.90 (m, 2H), 3.87 (s, 3H).

Synthesis (E)-1-isopropyl-4-(2-nitrovinyl)benzene (**1d**)*:*



Synthesized in accordance with *general procedure for aromatics nitroalkenes* using 4-isopropylbenzaldehyde (1.5 mL, 10.12 mmol), $MeNO_2$ (650 µL, 12.14 mmol) diluted in 2 mL of MeOH, water (4.7 mL, 0.26 mmol), NaOH (6.07 mL, 12.14 mmol) and MeOH (11 mL). Then the mixture was added to a solution of $ZnCl_2$ (7 g, 50.6 mmol), HCl (2.12 mL, 25.3 mmol) and H_2O (2.9 mL, 0.16 mmol). The desired product was obtained as a yellow oil (1.1 g, 5.8 mmol, yield = 57 %).

^{1}H-NMR (400 MHz, $CDCl_3$, 298 K) δ 8.02 (d, *J* = 13.7 Hz, 1H), 7.60 (d, *J* = 13.6 Hz, 1H), 7.51 (d, *J* = 8.3 Hz, 2H), 7.34 (d, *J* = 8.3 Hz, 2H), 2.98 (dt, *J* = 13.8, 7.0 Hz, 1H), 1.29 (d, *J* = 6.9 Hz, 6H). HRMS calculated for $C_{11}H_{13}NO_2$: 192.1025, found: 192.1021.

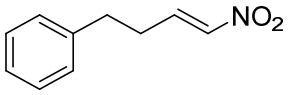
3. General procedure for aliphatics nitroalkenes[2]

To a mixture of aldehyde (1 eq.) and $MeNO_2$ (1 eq.) in MeOH (10 mL) at 0 °C in a 50mL one-neck round bottom flask equipped with a magnetic bar, a solution of NaOH (1.2 eq.) in H_2O (0.0024 eq.) was added dropwise. Then 2 mL of MeOH was added and the resulting yellow slurry was stirred at that temperature for 1 h. Water (30 mL) was added and the yellow solution was poured into a 250mL beaker containing a solution of HCl (20 mL) and H_2O (30 mL) under vigorous stirring and stirred for 15 min. In order to achieve the best conversion on a small scale, a flanged beaker was used. The aqueous mixture was then extracted with DCM (20 mL x 3) and the combined organic layers dried over $MgSO_4$ and concentrated *in vacuo* after filtration. The crude material was purified by flash chromatography on SiO_2 using a mixture of petroleum ether/ethyl acetate 9:1 v/v to give the desired product.

NMR spectra of previously reported compounds were in agreement with those of the authentic samples and/or available literature data.

3.1 Synthesis and spectral characterization of aliphatics nitroalkenes

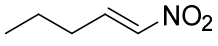
Synthesis of (E)-(4-nitrobut-3-en-1-yl)benzene (**1e**):[4]



Synthesized in accordance with *general procedure for aliphatics nitroalkenes* using 3-phenylpropanal (4 mL, 30 mmol), $MeNO_2$ (1.6 mL, 30 mmol) in MeOH (10 mL) at 0 °C and a solution of NaOH (1.44 g, 36 mmol) in H_2O (1.3 mL, 0.072 mmol) was added dropwise. The desired product was obtained as a yellow oil (1.8 g, 10.16 mmol, yield = 34%).

^{1}H-NMR (400 MHz, $CDCl_3$, 298 K) δ 7.34 (qd, J = 7.4, 6.9, 1.1 Hz, 3H), 7.30 – 7.24 (m, 1H), 7.23 – 7.17 (m, 2H), 6.99 (dt, J = 13.4, 1.5 Hz, 1H), 2.86 (t, J = 7.5 Hz, 2H), 2.62 (qd, J = 7.4, 1.2 Hz, 2H).

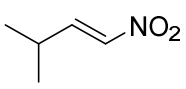
Synthesis of (E)-1-nitropent-1-ene (**1f**):[3]



Synthesized in accordance with *general procedure for aliphatics nitroalkenes* using butyraldehyde (4.09 mL, 45.3 mmol), $MeNO_2$ (2.42 mL, 45.3 mmol) in MeOH (10 mL) at 0 °C and a solution of NaOH (2.18 g, 54.4 mmol) in H_2O (2 mL, 0.11 mmol) was added dropwise. The desired product was obtained as a yellow oil (2.1 g, 18.3 mmol, yield = 40 %).

^{1}H-NMR (400 MHz, $CDCl_3$, 298 K) δ 7.41 – 7.14 (m, 1H), 6.99 (dt, J = 13.4, 1.4 Hz, 1H), 2.26 (qd, J = 7.4, 1.5 Hz, 2H), 1.55 (dt, J = 14.7, 7.4 Hz, 2H), 0.98 (t, J = 7.4 Hz, 3H).

Synthesis of (E)-3-methyl-1-nitrobut-1-ene (**1g**):[4]

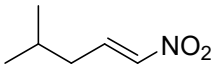


Synthesized in accordance with *general procedure for aliphatics nitroalkenes* using isobutyraldehyde (3.05 mg, 42.3 mmol), $MeNO_2$ (2.3 mL, 42.3 mmol) in MeOH (10 mL) at 0 °C and a solution of NaOH (2.03 g, 50.8

mmol) in H_2O (1.8 mL, 0.1 mmol) was added dropwise. The desired product was obtained as a yellow oil (2 g, 17.4 mmol, yield = 41%).

^{1}H-NMR (400 MHz, $CDCl_3$, 298 K) δ 7.38 – 7.15 (m, 1H), 6.94 (d, *J* = 13.9 Hz, 1H), 2.68 – 2.46 (m, 1H), 1.25 – 1.06 (m, 6H).

Synthesis of (E)-4-methyl-1-nitropent-1-ene (**1h**)*:*[3]



Synthesized in accordance with *general procedure for aliphatics nitroalkenes* using 3-methylbutanal (5 mL, 45.3 mmol), $MeNO_2$ (2.4 mL, 45.3 mmol) in MeOH (10 mL) at 0 °C and a solution of NaOH (2.18 g, 54.4 mmol) in H_2O (2 mL, 0.11 mmol) was added dropwise. The desired product was obtained as a yellow oil (1.9 g, 15 mmol, yield = 35 %).

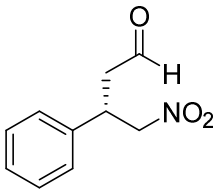
^{1}H-NMR (400 MHz, $CDCl_3$, 298 K) δ 7.21 (dt, *J* = 13.4, 8.0 Hz, 1H), 7.06 – 6.84 (m, 1H), 2.12 (ddd, *J* = 8.0, 6.9, 1.4 Hz, 2H), 1.80 (dt, *J* = 13.4, 6.7 Hz, 1H), 0.92 (d, *J* = 6.7 Hz, 6H).

4. General procedure for the asymmetric Michael addition of acetaldehyde dimethyl acetal

Acetaldehyde dimethyl acetal **5** (148 µL, 1.4 mmol, 2 eq.) was added to a 4ml scintillation vial equipped with a magnetic bar containing (*S*)-diphenyltrimethylsiloxymethylpyrrolidine **6** (0.05 eq.), nitroalkenes **1a-h** (1 eq.), Amberlyst-15 (25 mg, 10 mol%), water (76 µL, 4.2 mmol, 6 eq.) and chloroform (0.44 mL, 1.6 M) under stirring, and the reaction mixture was left under stirring at room temperature for the required time. The reaction was quenched with 2 mL of $HCl_{aq.}$ 1M. Then the aqueous mixture was extracted with ethyl acetate (3 x 3 mL) and the combined organic layers dried over $MgSO_4$ and concentrated *in vacuo* after filtration. The crude was purified by flash chromatography on SiO_2 using a mixture of petroleum ether/ethyl acetate 9:1 v/v to give the desired product.

NMR spectra of previously reported compounds were in agreement with those of the authentic samples and/or available literature data.

4.1 Synthesis and spectral characterization of asymmetric Michael addition of acetaldehyde dimethyl acetal

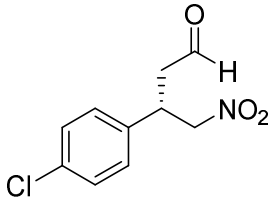


Synthesis of (S)-4-nitro-3-phenylbutanal (**3a**)*:*[5]

Synthesized in accordance with *general procedure of asymmetric Michael addition of acetaldehyde dimethyl acetal* using (*S*)-diphenyltrimethylsiloxymethylpyrrolidine (11.4 mg, 0.035 mmol), *trans*-β-nitrostyrene (105 mg, 0.7 mmol). The reaction mixture was stirred at room temperature for 24 h. The desired product was obtained as a pale-yellow oil (122 mg, 0.63 mmol, yield = 90 %).

^{1}H-NMR (400 MHz, $CDCl_3$, 298 K) δ 9.72 (s, 1H), 7.36 (q, *J* = 10.1, 8.5 Hz, 2H), 7.32 – 7.28 (m, 1H), 7.25 (d, *J* = 7.2 Hz, 2H), 4.67 (qd, *J* = 12.5, 7.4 Hz, 2H), 4.10 (p, *J* = 7.2 Hz, 1H), 2.99 – 2.93 (m, 2H). ^{13}C-NMR (101 MHz, $CDCl_3$, 298 K) δ 198.8, 138.2, 129.2, 128.1, 127.4, 79.4, 46.4, 38.0. HPLC (Lux-3µm-cellulose 1, Hexane/*i*-Propanol 90:10), flow rate: 0.5 mL/min, λ=210 nm), t_{minor}: 21.2 min; t_{major}: 26.5 min. $[\alpha]_D^{25}$ = - 4.04 (*c* = 0.053, $CHCl_3$)

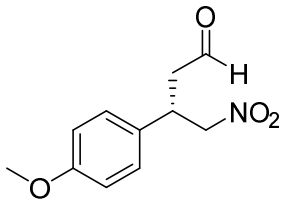
Synthesis of (S)-3-(4-chlorophenyl)-4-nitrobutanal (**3b**)*:*[5]



Synthesized in accordance with *general procedure of asymmetric Michael addition of acetaldehyde dimethyl acetal* using (*S*)-diphenyltrimethylsiloxymethylpyrrolidine (11.4 mg, 0.035 mmol), (*E*)-1-chloro-4-(2-nitrovinyl)benzene (129 mg, 0.7 mmol). The reaction mixture was stirred at room temperature for 72 h. The desired product was obtained as a pale-yellow oil (99 mg, 0.44 mmol, yield = 62 %).

^{1}H-NMR (400 MHz, $CDCl_3$, 298 K) δ 9.70 (s, 1H), 7.32 (d, J = 8.3 Hz, 2H), 7.17 (d, J = 8.3 Hz, 2H), 4.73 – 4.48 (m, 2H), 4.17 – 3.94 (m, 1H), 2.94 (d, J = 7.1 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$, 298 K) δ 198.4, 136.9, 134.2, 129.5, 128.9, 79.2, 46.5, 37.4. HPLC (Lux 3µm-cellulose 5, Hexane/*i*-Propanol 90:10), flow: 0.5 mL/min, λ=210 nm, t_{minor}: 20.4 min; t_{major}: 22.2 min. $[\alpha]_D^{25}$ = - 3.56 (*c* = 0.0082, $CHCl_3$).

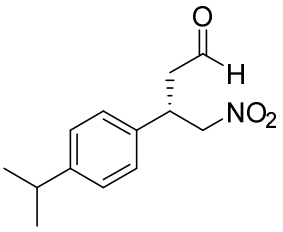
Synthesis of (S)-3-(4-methoxyphenyl)-4-nitrobutanal (**3c**)*:*[5]



Synthesized in accordance with *general procedure of asymmetric Michael addition of acetaldehyde dimethyl acetal* using (*S*)-diphenyltrimethylsiloxymethylpyrrolidine (11.4 mg, 0.035 mmol), (*E*)-1-methoxy-4-(2-nitrovinyl)benzene (125 mg, 0.7 mmol. The reaction mixture was stirred at room temperature for 72 h. The desired product was obtained as a pale-yellow oil (119 mg, 0.53 mmol, yield = 76 %).

^{1}H-NMR (400 MHz, $CDCl_3$, 298 K) δ 9.68 (s, 1H), 7.21 – 7.06 (m, 2H), 6.92 – 6.80 (m, 2H), 4.74 – 4.42 (m, 2H), 4.08 – 3.94 (m, 1H), 3.78 (s, 3H), 2.90 (d, *J* = 8.1 Hz, 2H). ^{13}C-NMR (101 MHz, $CDCl_3$, 298 K) δ 199.1, 159.4, 130.1, 128.6, 114.7, 79.8, 55.4, 46.7, 37.5. HPLC (Lux 3µm-cellulose 1, Hexane/*i*-Propanol 90:10), flow: 0.5 mL/min, λ=210 nm), t_{minor}: 23.3 min; t_{major}: 25.8 min. $[\alpha]_D^{25}$ = - 6 (*c* = 0.012, $CHCl_3$).

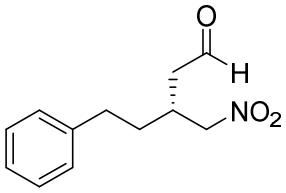
Synthesis of (S)-3-(4-isopropylphenyl)-4-nitrobutanal (**3d**)*:*



Synthesized in accordance with *general procedure of asymmetric Michael addition of acetaldehyde dimethyl acetal* using (*S*)-diphenyltrimethylsiloxymethylpyrrolidine (11.4 mg, 0.035 mmol), (*E*)-1-isopropyl-4-(2-nitrovinyl)benzene (134 mg, 0.7 mmol). The reaction mixture was stirred at room temperature for 48 h. The desired product was obtained as a pale-yellow oil (137 mg, 0.58 mmol, yield = 83 %).

^{1}H-NMR (400 MHz, $CDCl_3$, 298 K) δ 9.71 (s, 1H), 7.22 (d, *J* = 8.2 Hz, 2H), 7.19 – 7.12 (m, 2H), 4.65 (qd, *J* = 12.5, 7.4 Hz, 2H), 4.13 – 4.01 (m, 1H), 2.98 – 2.92 (m, 2H), 2.92 – 2.85 (m, 1H), 1.25 (d, *J* = 6.9 Hz, 6H). ^{13}C-NMR (101 MHz, $CDCl_3$, 298 K) δ 199.2, 148.9, 135.5, 127.4, 127.4, 79.6, 46.6, 37.8, 33.8, 24.0. HPLC (Lux 3µm-cellulose 5, Hexane/*i*-Propanol 95:5), flow: 0.4 mL/min, λ=210 nm, t_{minor}: 39.3 min; t_{major}: 42 min. $[\alpha]_D^{25}$ = - 3.2 (*c* = 0.019, $CHCl_3$). HRMS calculated for $C_{13}H_{18}NO_3$: 236.1287, found: 236.1282.

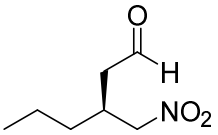
Synthesis of (R)-3-(nitromethyl)-5-phenylpentanal (**3e**)*:*[5]



Synthesized in accordance with *general procedure of asymmetric Michael addition of acetaldehyde dimethyl acetal* using (*S*)-diphenyltrimethylsiloxymethylpyrrolidine (11.4 mg, 0.035 mmol), (*E*)- (4-nitrobut-3-en-1-yl)benzene (124 mg, 0.7 mmol). The reaction mixture was stirred at room temperature for 48 h. The desired product was obtained as a pale-yellow oil (116 mg, 0.53 mmol, yield = 75 %).

^{1}H-NMR (400 MHz, $CDCl_3$, 298 K) δ 9.76 (s, 1H), 7.30 (t, *J* = 7.3 Hz, 2H), 7.24 – 7.19 (m, 1H), 7.18 – 7.14 (m, 2H), 4.49 (d, *J* = 5.7 Hz, 2H), 2.81 – 2.54 (m, 5H), 1.77 (dt, *J* = 6.7, 2.3 Hz, 2H). ^{13}C-NMR (101 MHz, $CDCl_3$, 298 K) δ 199.7, 140.5, 128.7, 128.3, 126.4, 78.1, 45.2, 33.1, 32.8, 31.6. HPLC (Chiralpak OJ-H, Hexane/*i*-Propanol 10:1), flow: 1 mL/min, λ=210 nm, t_{minor}: 36 min; t_{major}: 37 min. $[\alpha]_D^{25}$ = - 1.3 (*c* = 0.025, $CHCl_3$).

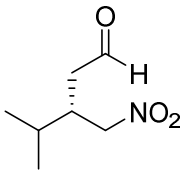
Synthesis of (S)-3-(nitromethyl)hexanal (**3f**)*:*[6]



Synthesized in accordance with *general procedure of asymmetric Michael addition of acetaldehyde dimethyl acetal* using (*R*)-diphenyltrimethylsiloxymethylpyrrolidine (11.4 mg, 0.035 mmol), (*E*)-1-nitropent-1-ene (81 mg, 0.7 mmol). The reaction mixture was stirred at room temperature for 48 h. The desired product was obtained as a pale-yellow oil (99 mg, 0.62 mmol, yield = 89 %).

^{1}H-NMR (400 MHz, $CDCl_3$, 298 K) δ 9.76 (s, 1H), 4.43 (d, *J* = 6.2 Hz, 2H), 2.78 – 2.65 (m, 1H), 2.65 – 2.53 (m, 2H), 1.46 – 1.27 (m, 4H), 0.91 (t, *J* = 6.8 Hz, 3H). ^{13}C-NMR (101 MHz, $CDCl_3$, 298 K) δ 200.1, 78.5, 45.4, 33.7, 31.9, 19.8, 13.9. HPLC (Lux 3µm-cellulose 5, Hexane/*i*-Propanol 95:5), flow: 0.4 mL/min, λ=210 nm, t_{minor}: 26.6 min; t_{major}: 28.1 min. $[\alpha]_D^{25}$ = + 5.24 (*c* = 0.0225, $CHCl_3$).

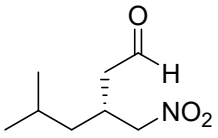
Synthesis of (S)-4-methyl-3-(nitromethyl)pentanal (**3g**).



Synthesized in accordance with *general procedure of asymmetric Michael addition of acetaldehyde dimethyl acetal* using (*S*)-diphenyltrimethylsiloxymethylpyrrolidine (11.4 mg, 0.035 mmol), (*E*)-3-methyl-1-nitrobut-1-ene (81 mg, 0.7 mmol). The reaction mixture was stirred at room temperature for 72 h. The desired product was obtained as a pale-yellow oil (104 mg, 0.65 mmol, yield = 93 %).

^{1}H-NMR (400 MHz, $CDCl_3$, 298 K) δ 9.77 (s, 1H), 4.41 (qd, *J* = 12.3, 6.6 Hz, 2H), 2.74 – 2.65 (m, 1H), 2.65 – 2.47 (m, 2H), 1.80 (dd, *J* = 6.8, 5.2 Hz, 1H), 0.93 (dd, *J* = 6.8, 3.8 Hz, 6H). ^{13}C-NMR (101 MHz, $CDCl_3$, 298 K) δ 200.1, 77.2, 42.9, 37.6, 29.0, 19.5, 19.0. HPLC (Lux 3µm-cellulose 5, Hexane/*i*-Propanol 95:5), flow: 0.5 mL/min, λ=210 nm, t_{minor}: 29.8 min; t_{major}: 33.4 min. $[\alpha]_D^{25}$ = - 8.4 (*c* = 0.019, $CHCl_3$). HRMS calculated for $C_7H_{14}NO_3$: 160.0974, found: 160.0975.

Synthesis of (R)-5-methyl-3-(nitromethyl)hexanal (**3h**)*:*[5]



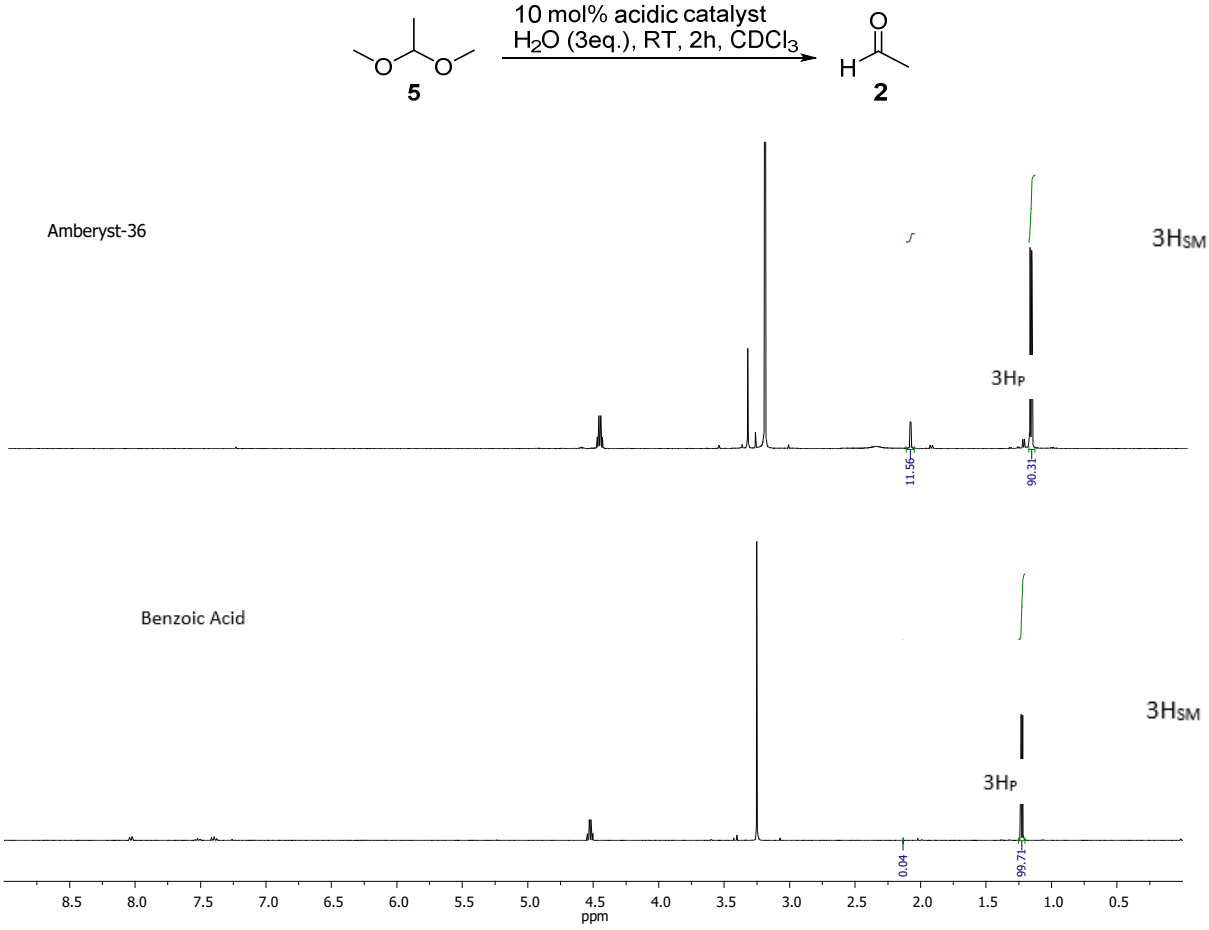
Synthesized in accordance with *general procedure of asymmetric Michael addition of acetaldehyde dimethyl acetal* using (*S*)-diphenyltrimethylsiloxymethylpyrrolidine (11.4 mg, 0.035 mmol), (*E*)-4-methyl-1-nitropent-1-ene (90 mg, 0.7 mmol). The reaction mixture was stirred at room temperature for 72 h. The desired product was obtained as a pale-yellow oil (75 mg, 0.43 mmol, yield = 83%).

^{1}H-NMR (400 MHz, $CDCl_3$, 298 K) δ 9.76 (s, 1H), 4.43 (dd, *J* = 6.0, 2.6 Hz, 2H), 2.82 – 2.70 (m, 1H), 2.70 – 2.50 (m, 2H), 1.62 (dp, *J* = 13.4, 6.8 Hz, 1H), 1.26 (td, *J* = 7.2, 2.0 Hz, 2H), 0.91 (dd, *J* = 12.2, 6.6 Hz, 6H). ^{13}C-NMR (101 MHz, $CDCl_3$, 298 K) δ 199.9, 78.6, 45.5, 40.7, 30.0, 25.1, 22.4., 22.3. HPLC (Lux 3µm-cellulose 1, Hexane/*i*-Propanol 95:5), flow: 0.5 mL/min, λ=210 nm, t_{minor}: 18.5 min; t_{major}: 21.3 min. $[\alpha]_D^{25}$ = - 3.7 (*c* = 1.3, $CHCl_3$).

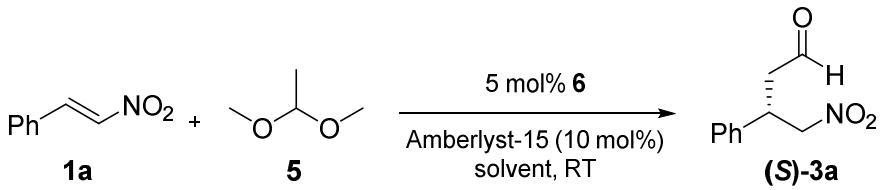
The same reaction was carried out using (*S*)-diphenyltrimethylsiloxymethylpyrrolidine (175 mg, 0.54 mmol), (*E*)-4-methyl-1-

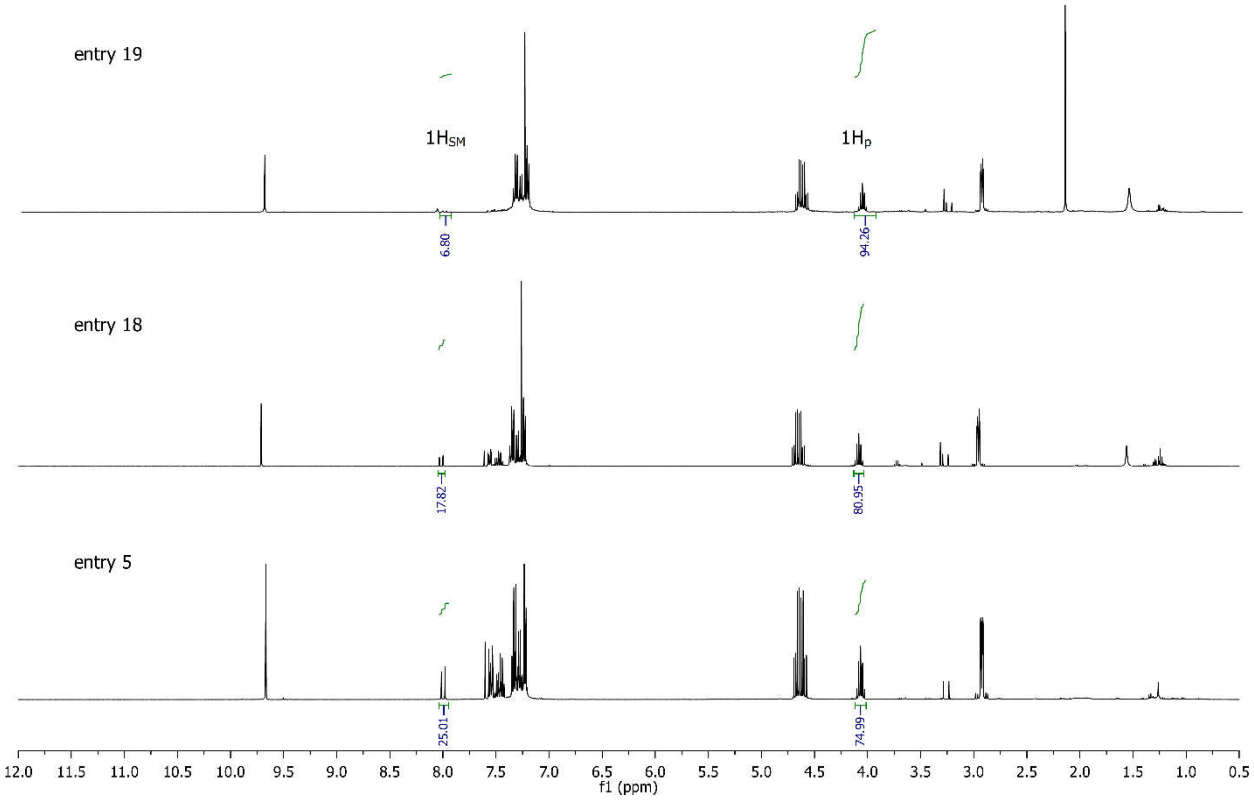
nitropent-1-ene (1.39 g, 10.77 mmol), Amberlyst-15 (385 mg), water (1.2 mL, 65 mmol), acetaldehyde dimethyl acetal (2.3 mL, 21.54 mmol) and $CHCl_3$ (6.7 mL). The reaction mixture was stirred at room temperature for 72 h. The desired product was obtained as a pale-yellow oil (1.8 g, 10.4 mmol, yield = 75%).

5. Representative NMR spectra of the acid-catalysed deprotection of acetaldehyde dimethyl 5 (Manuscript, Table 1)



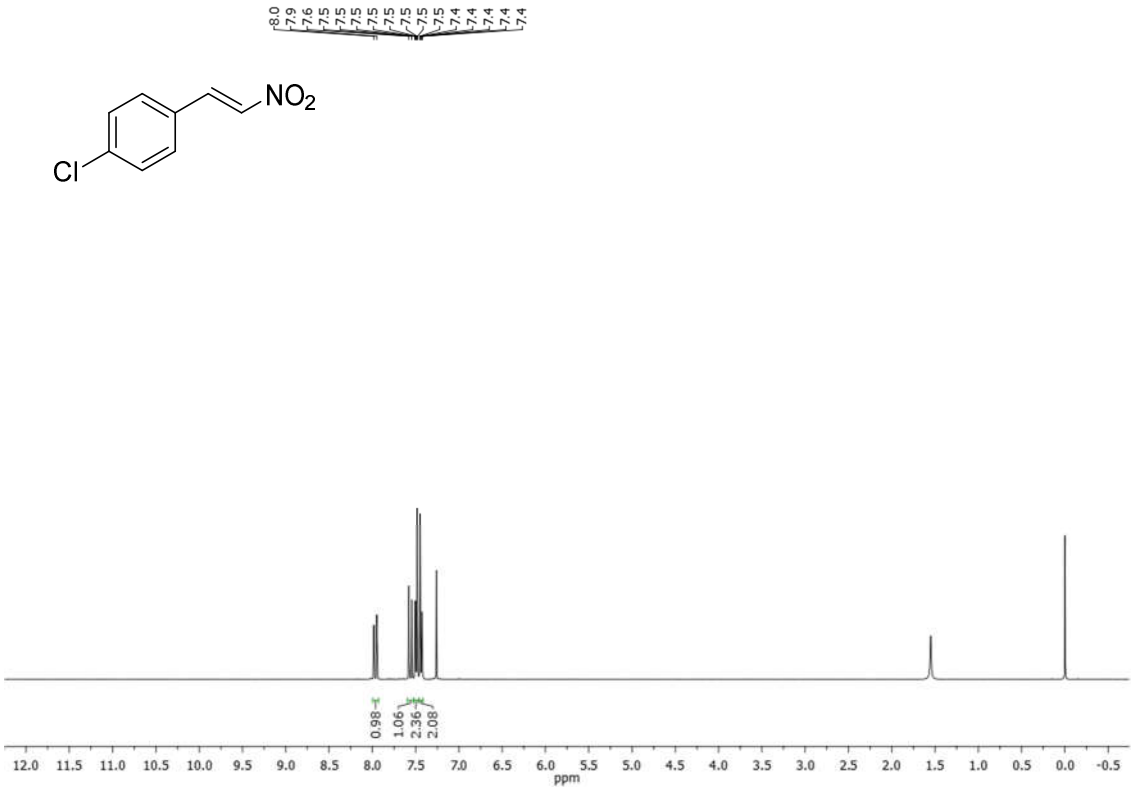
6. Representative NMR spectra of crude reaction mixture in the optimization of conditions for the Michael addition (Manuscript, Table 2)



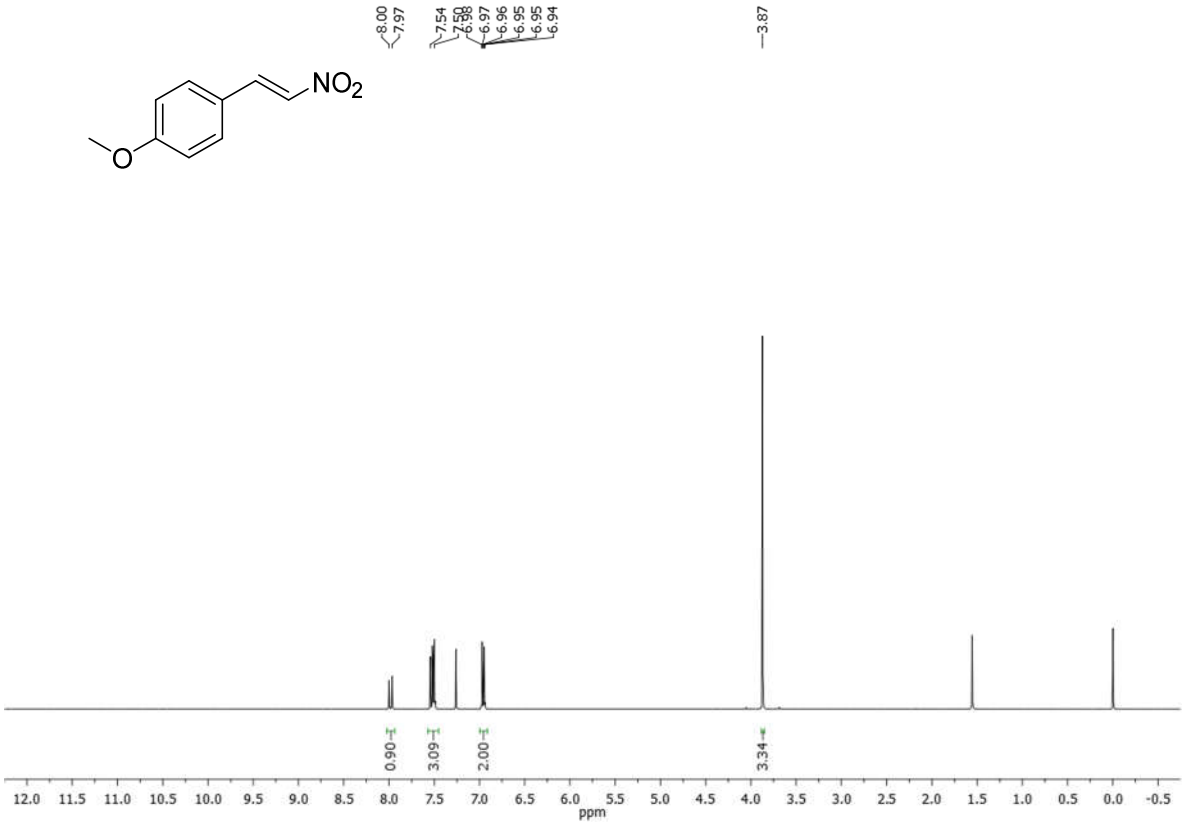


7. NMR spectra

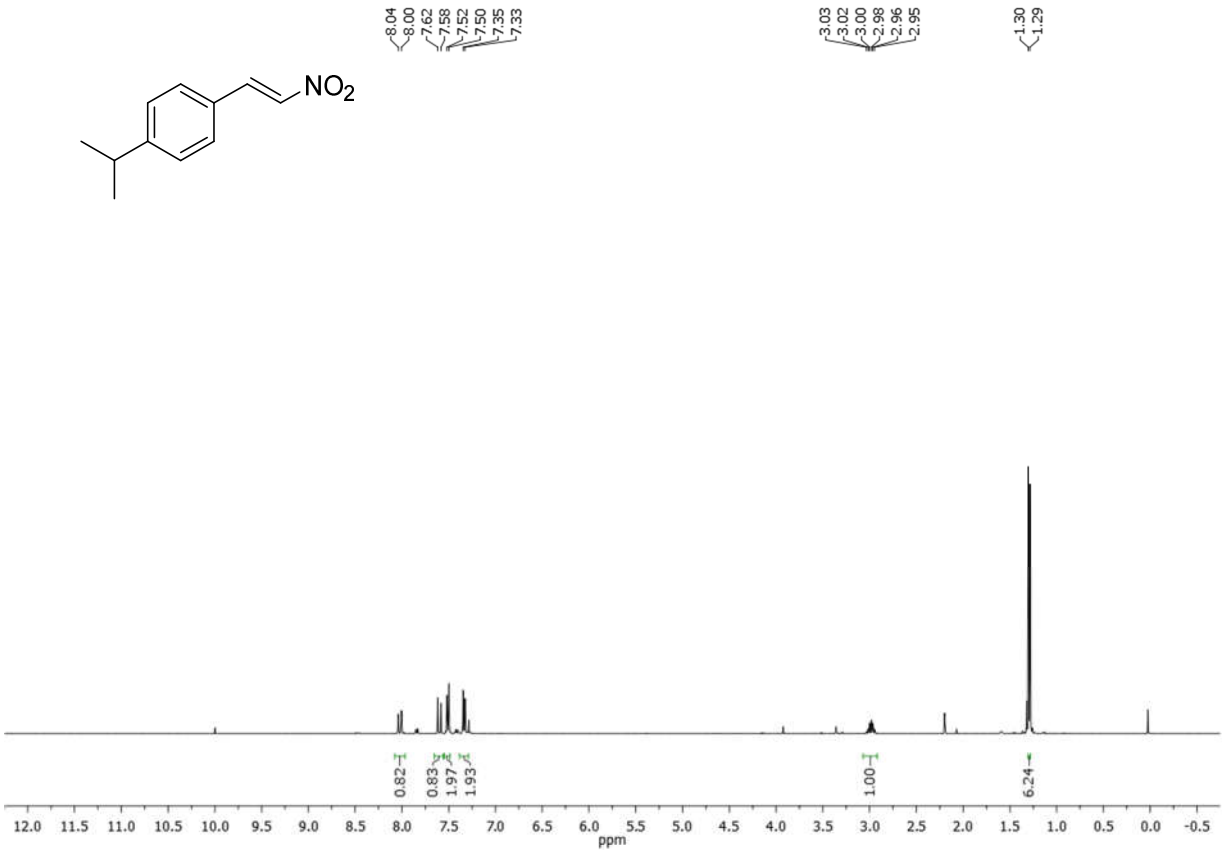
- **^{1}H-NMR spectrum of compound 1b in $CDCl_3$**



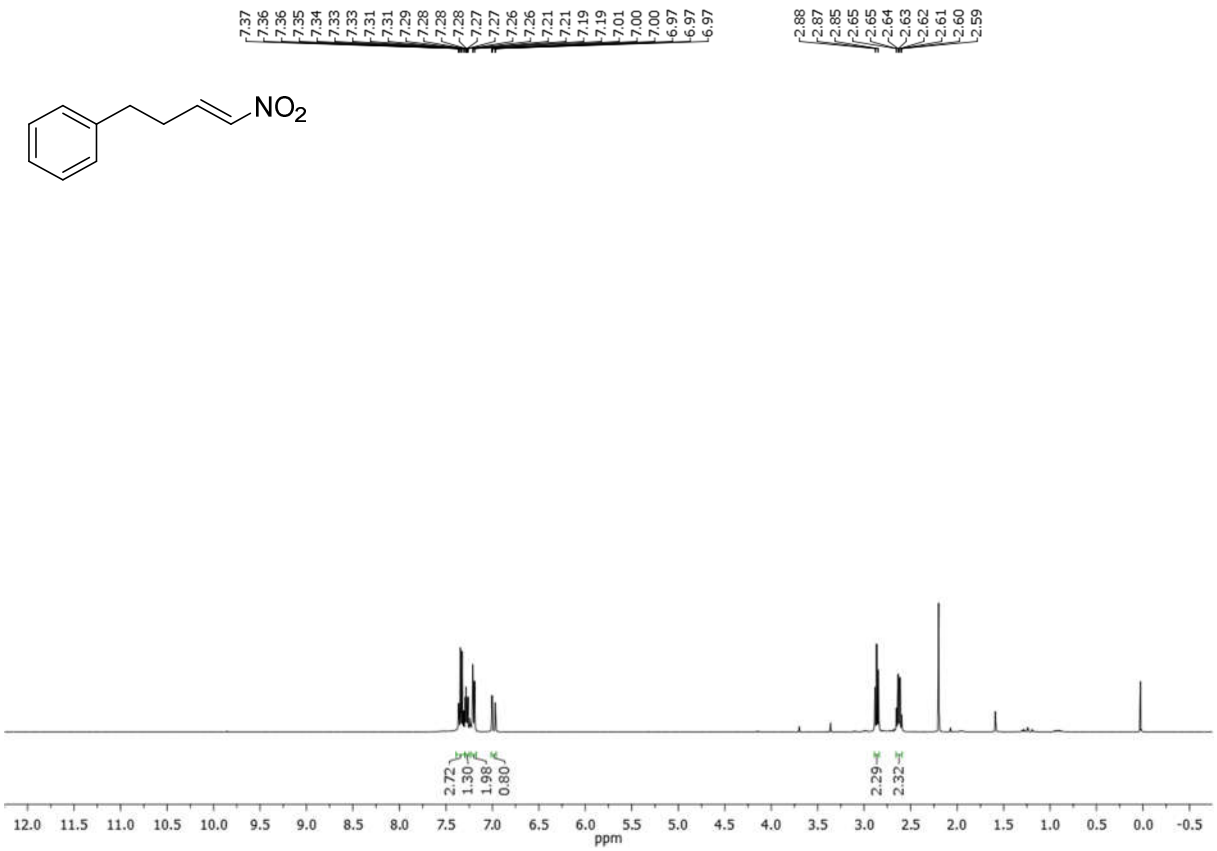
- **^{1}H-NMR spectrum of compound 1c in $CDCl_3$**



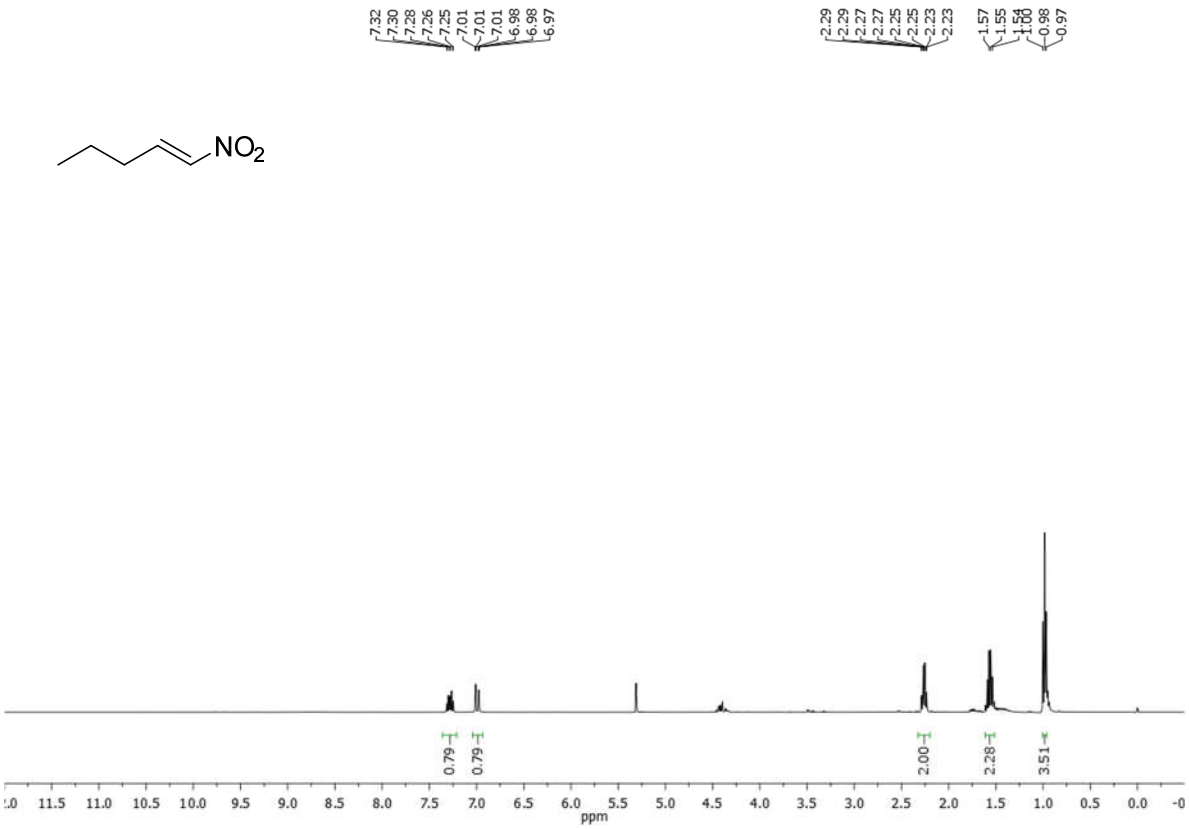
- **^{1}H-NMR spectrum of compound 1d in $CDCl_3$**



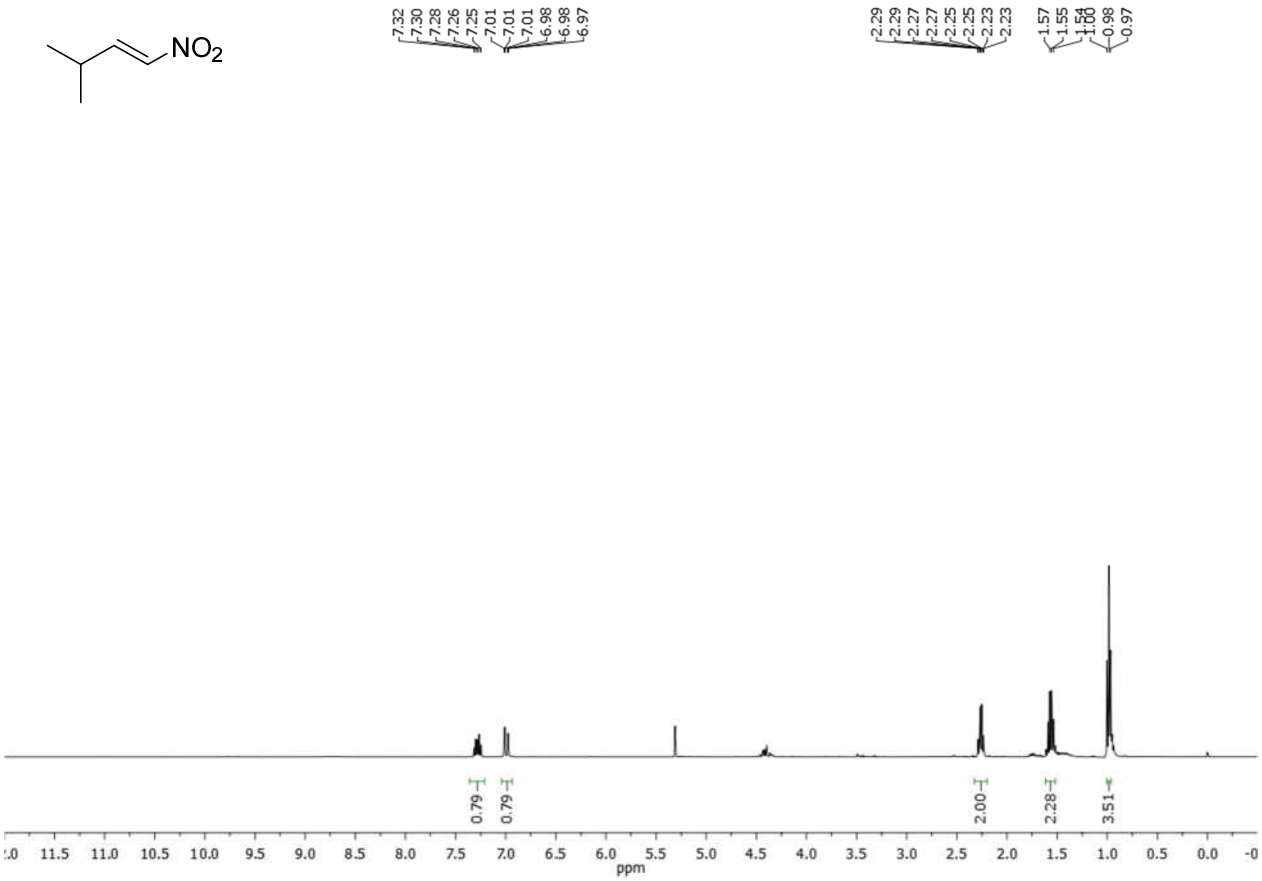
- **^{1}H-NMR spectrum of compound 1e in $CDCl_3$**



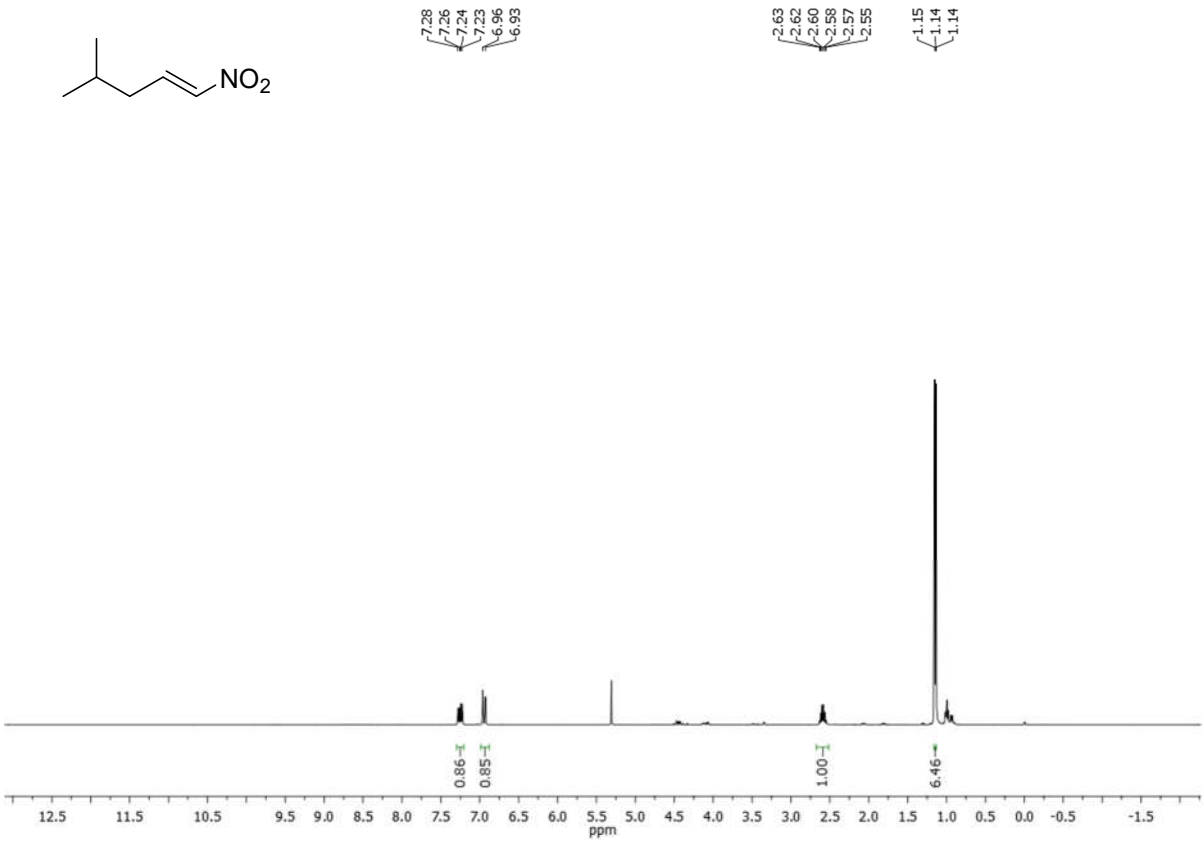
- **^{1}H-NMR spectrum of compound 1f in $CDCl_3$**



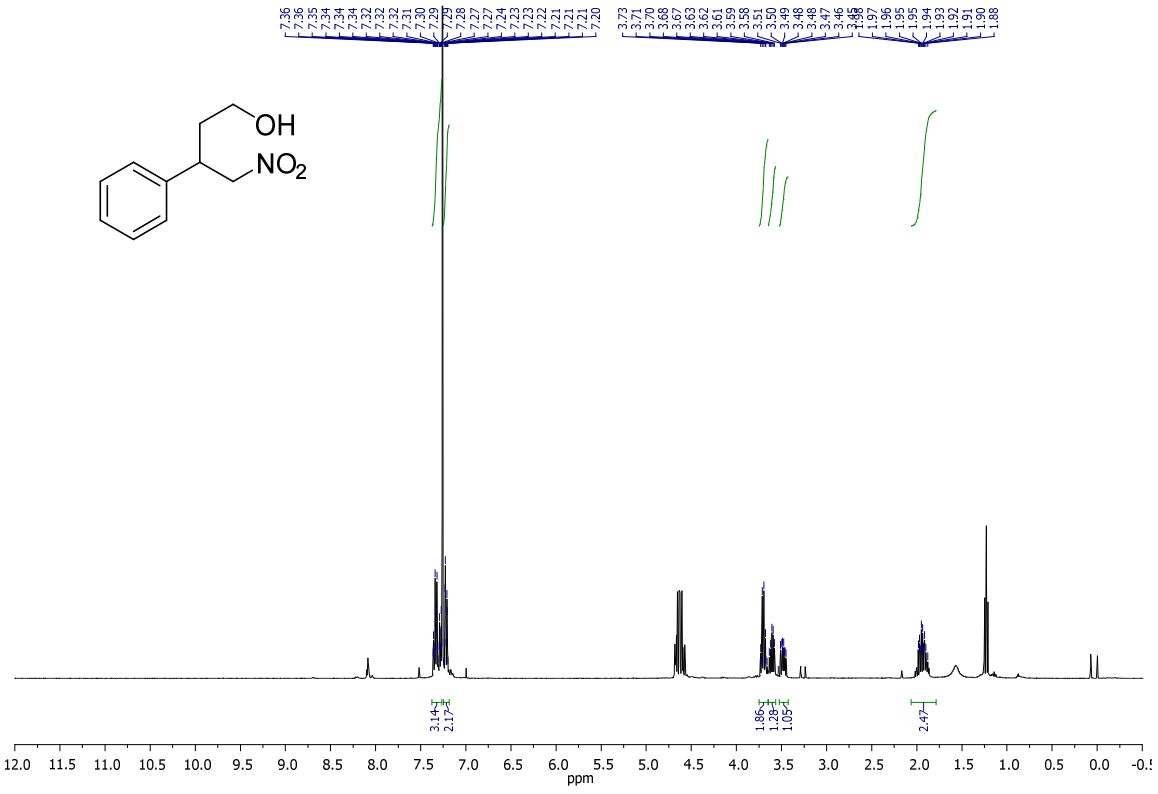
- **^{1}H-NMR spectrum of compound 1g in $CDCl_3$**



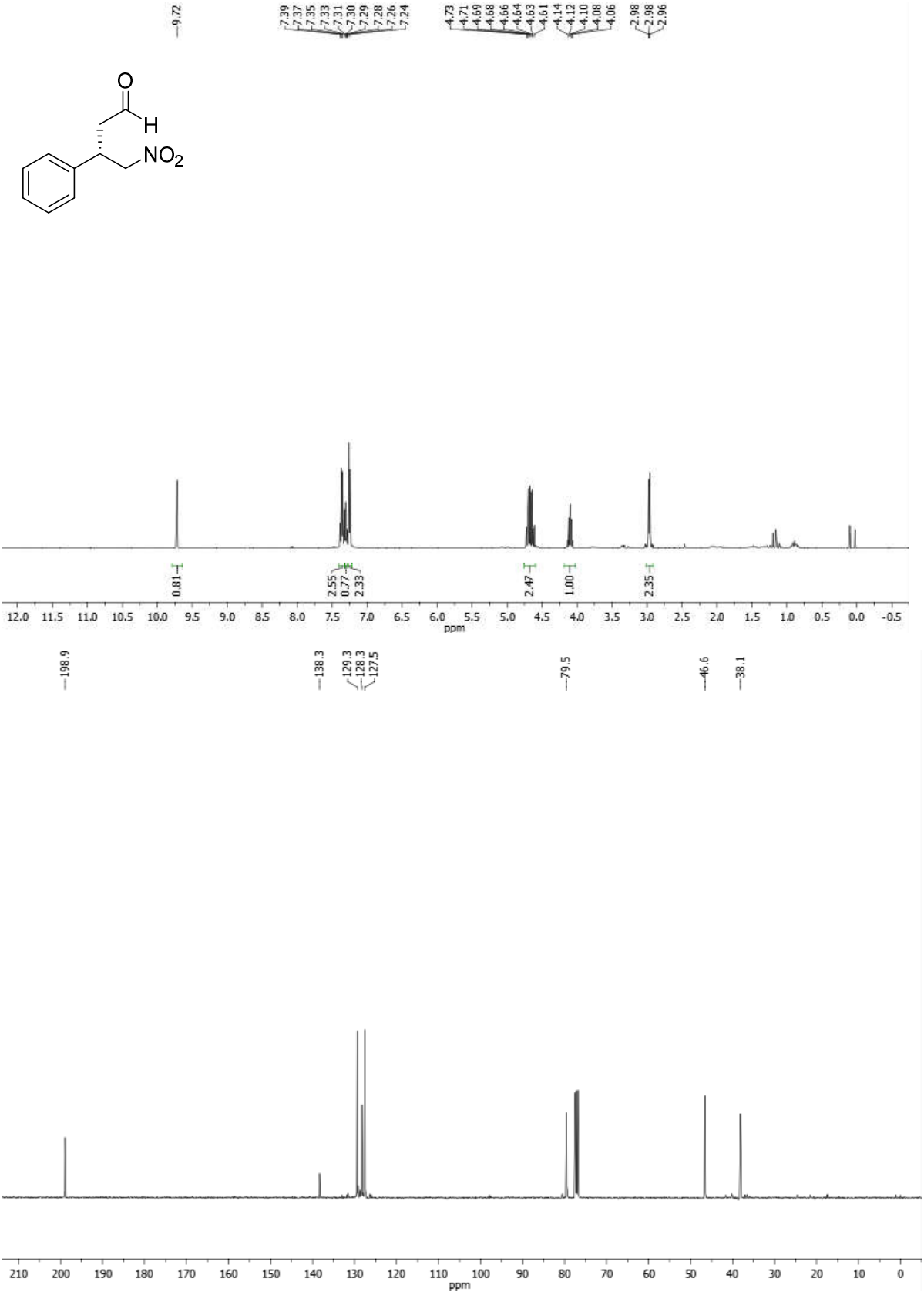
- **^{1}H-NMR spectrum of compound 1h in $CDCl_3$**



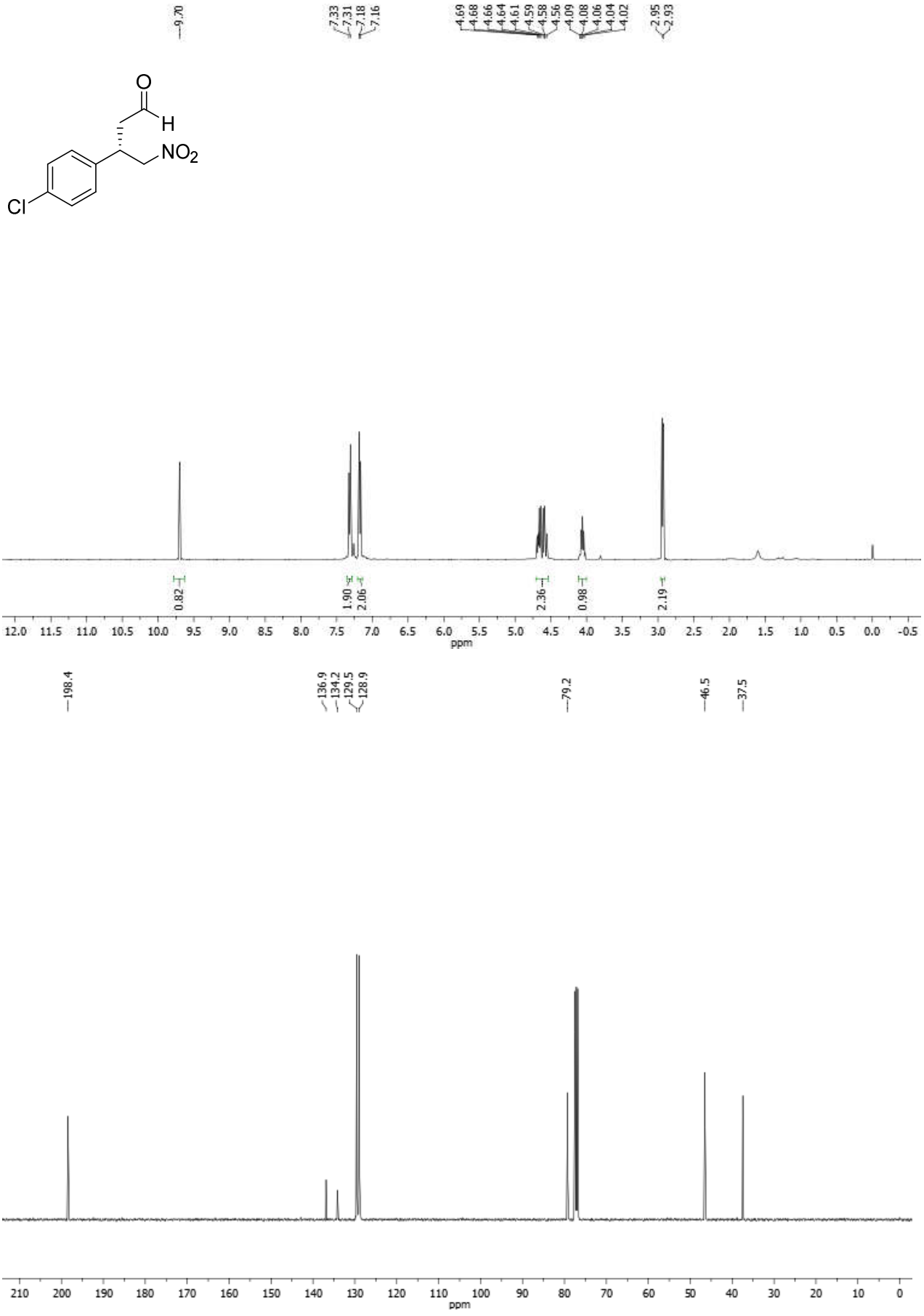
- **^{1}H-NMR spectrum of reduced 1a in $CDCl_3$**



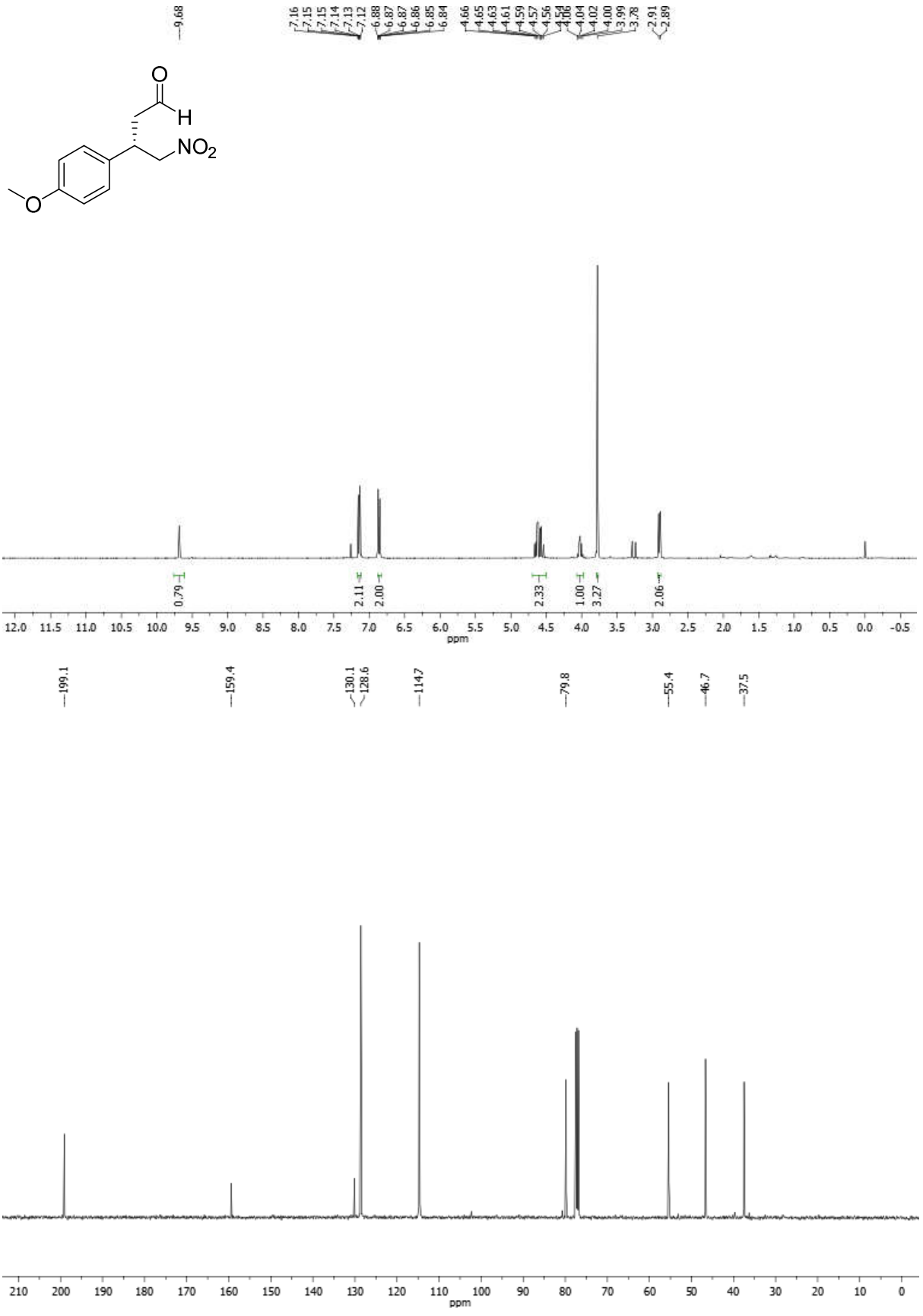
- **^{1}H-NMR and ^{13}C-NMR spectra of compound 3a in $CDCl_3$**



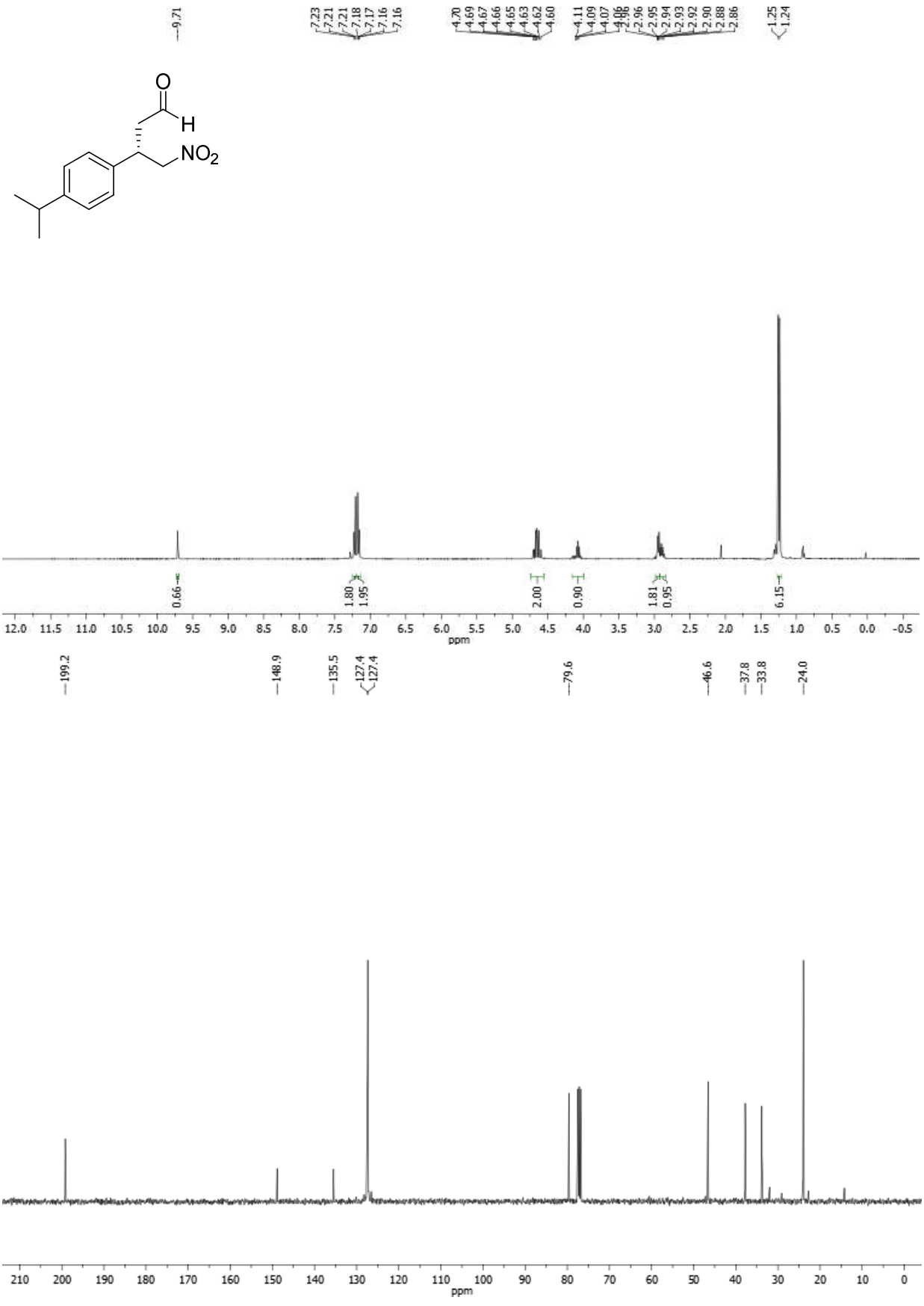
- **^{1}H-NMR and ^{13}C-NMR spectra of compound 3b in $CDCl_3$**



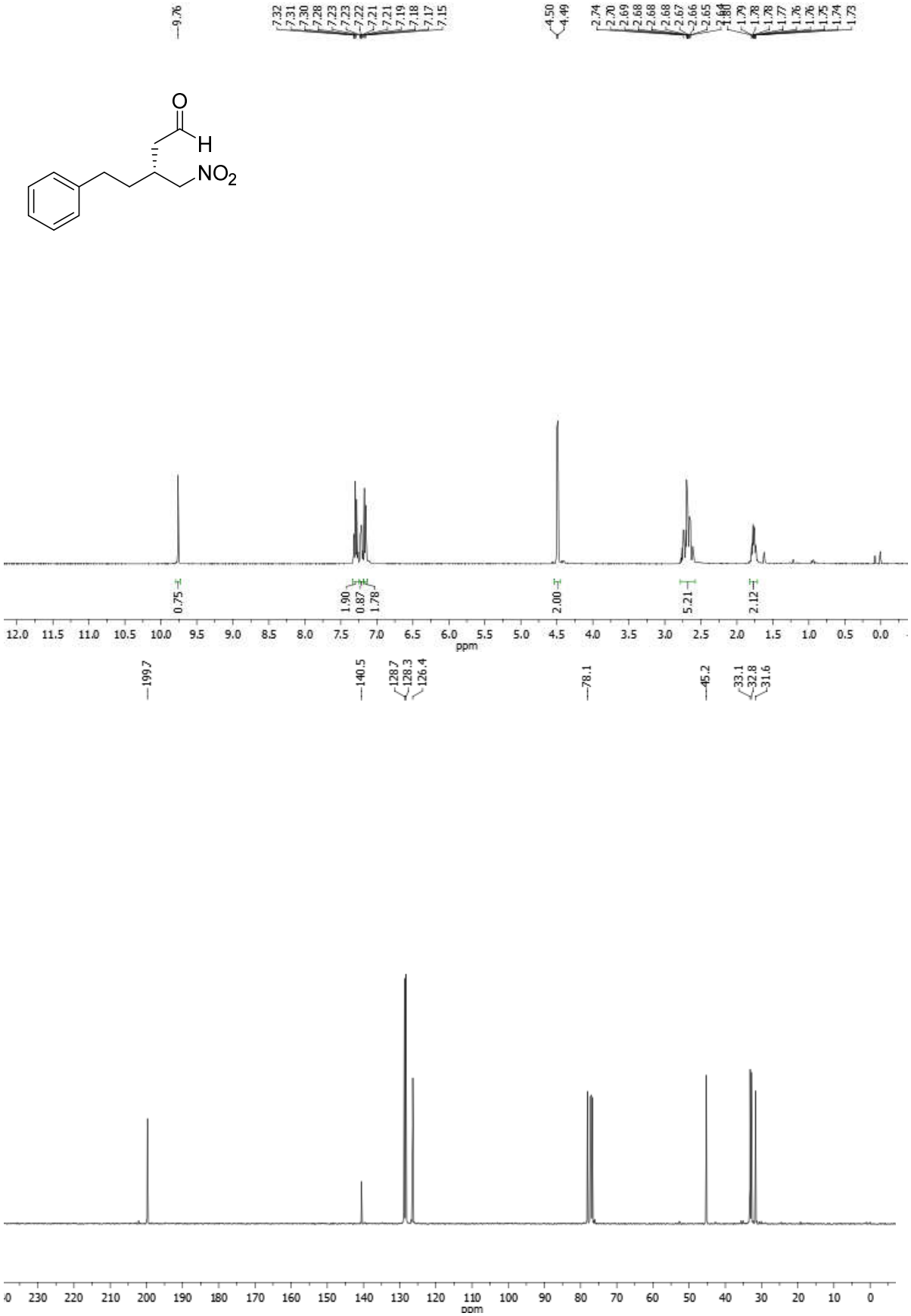
- **^{1}H-NMR and ^{13}C-NMR spectra of compound 3c in $CDCl_3$**



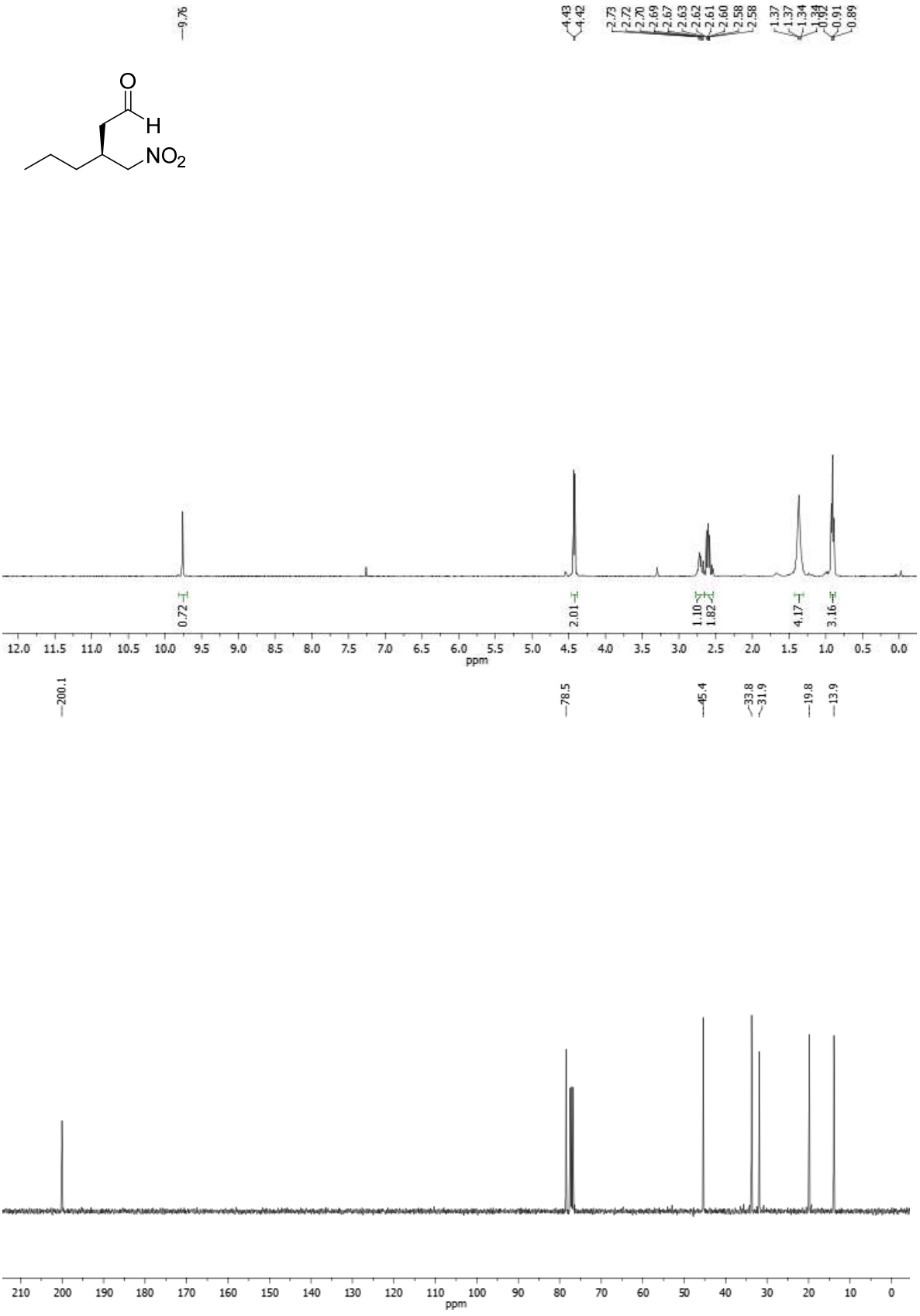
- **^{1}H-NMR and ^{13}C-NMR spectra of compound 3d in $CDCl_3$**



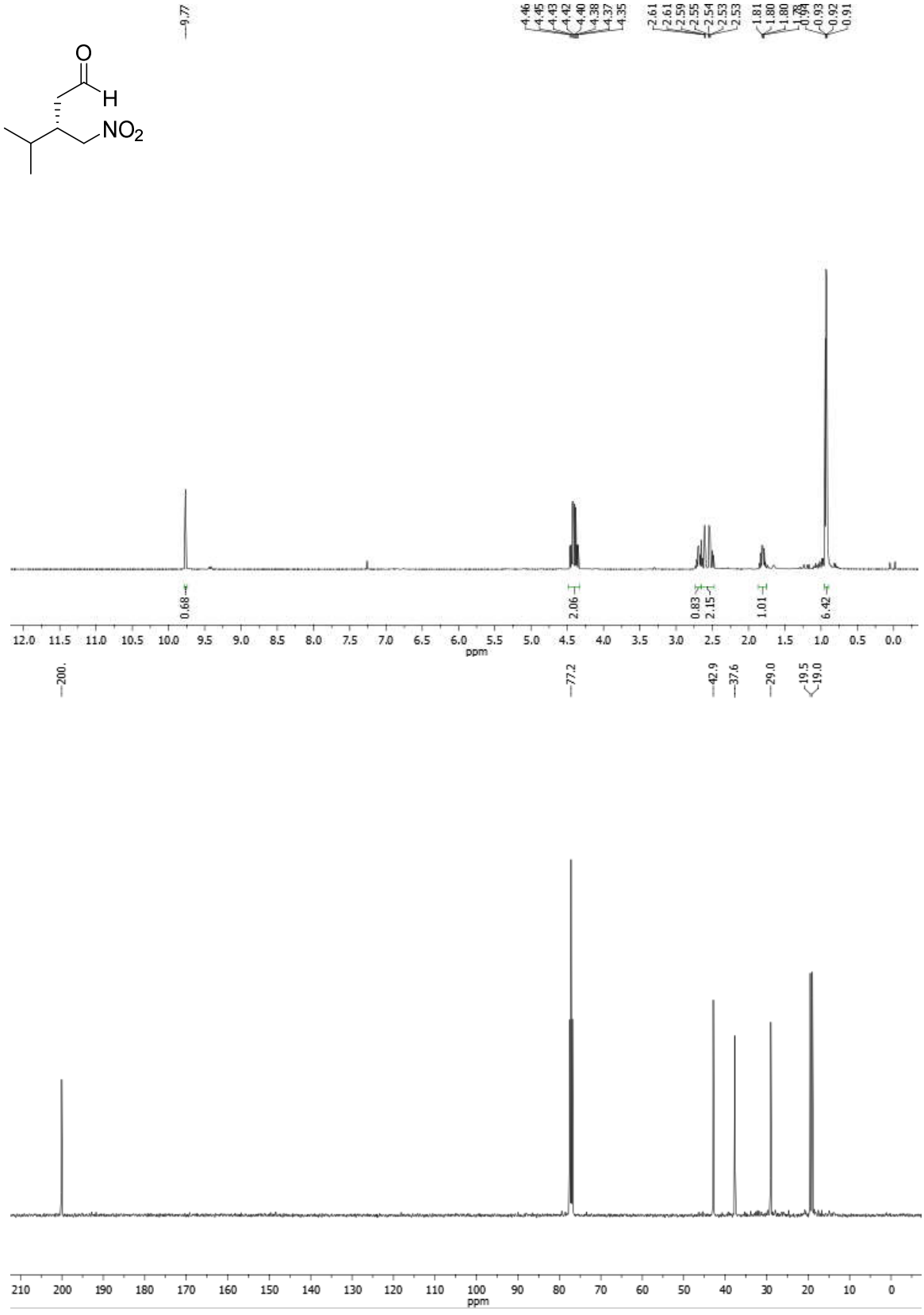
- **^{1}H-NMR and ^{13}C-NMR spectra of compound 3e in $CDCl_3$**



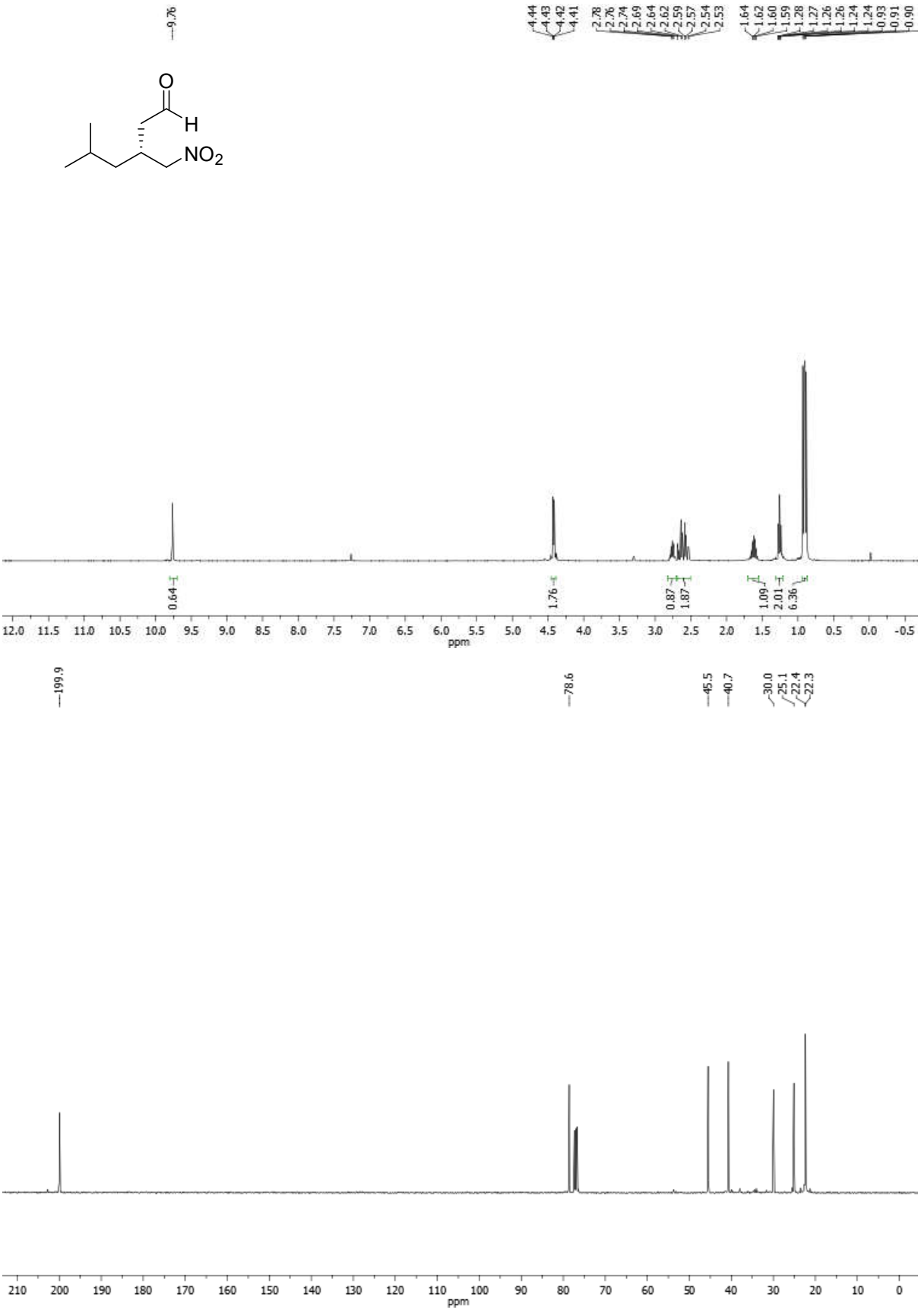
- **^{1}H-NMR and ^{13}C-NMR spectra of compound 3f in $CDCl_3$**



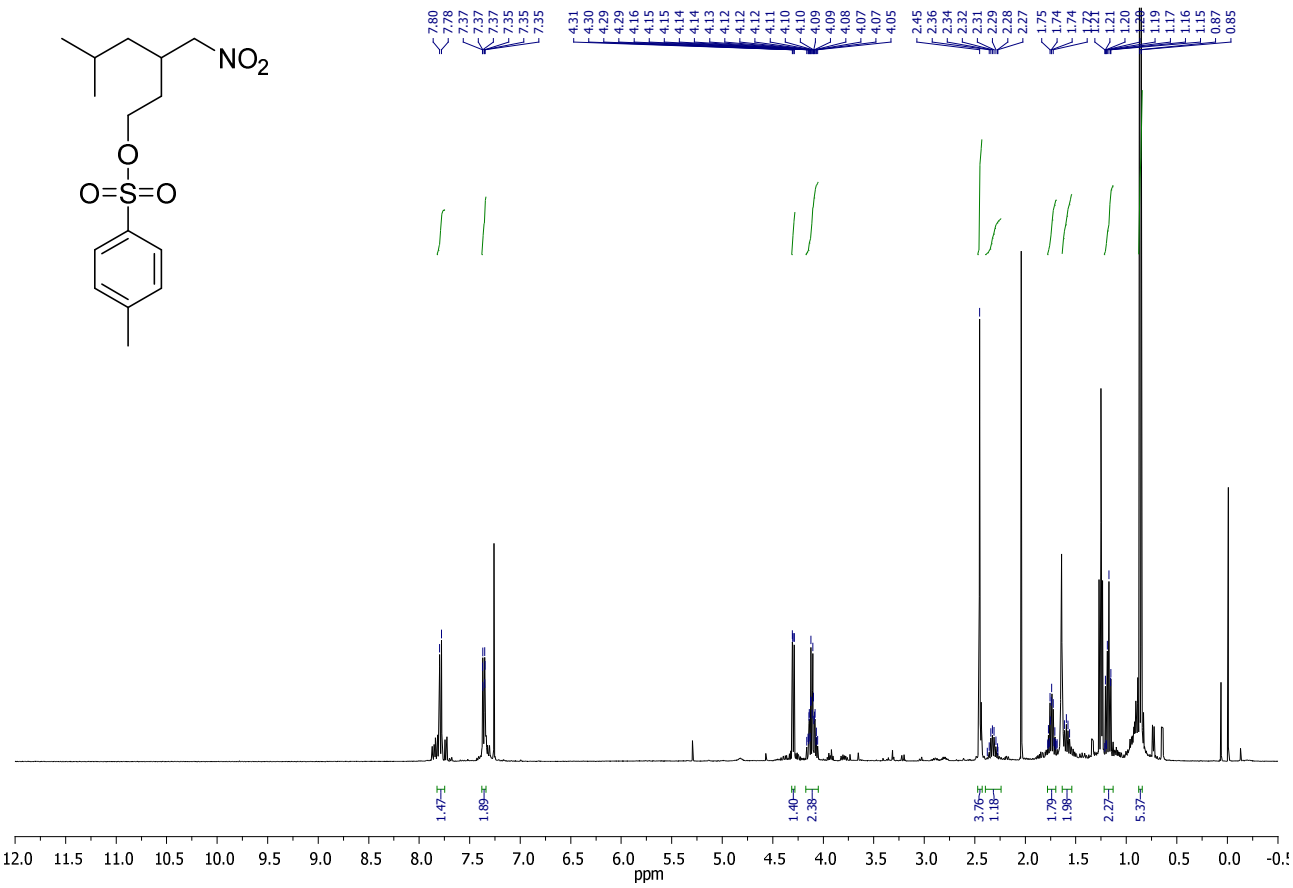
- **^{1}H-NMR and ^{13}C-NMR spectra of compound 3g in $CDCl_3$**



- **^{1}H-NMR and ^{13}C-NMR spectra of compound 3h in $CDCl_3$**



- **^{1}H-NMR spectrum of tosylate product of compound 3h in $CDCl_3$**



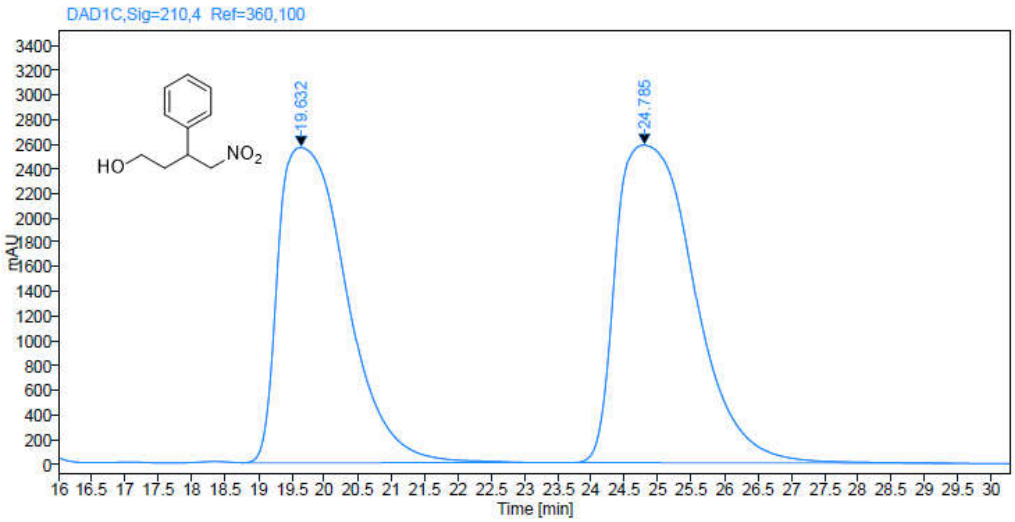
8. HPLC chromatograms

The products were converted to the corresponding alcohol with $NaBH_4$. The crude aldehyde product was dissolved in 0.7 mL MeOH. After that, this solution was slowly added into a $NaBH_4$ (1.5 mmol) solution in 0.3 mL MeOH under stirring at 0 ºC for 20 min.[7]

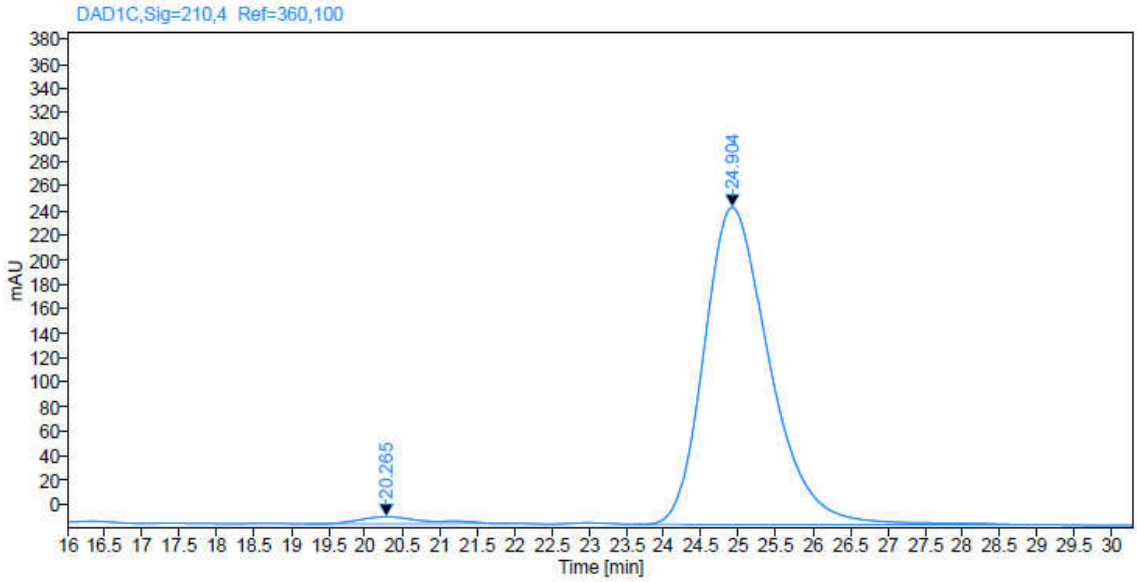
Compound **3h** was converted, after reduction, into the corresponding tosylate.

(*S*)-4-nitro-3-phenylbutan-1-ol (3a)

Lux 3µm-cellulose 1, Hexane/*i*-Propanol 90:10, flow: 0.5 mL/min, λ=210 nm.



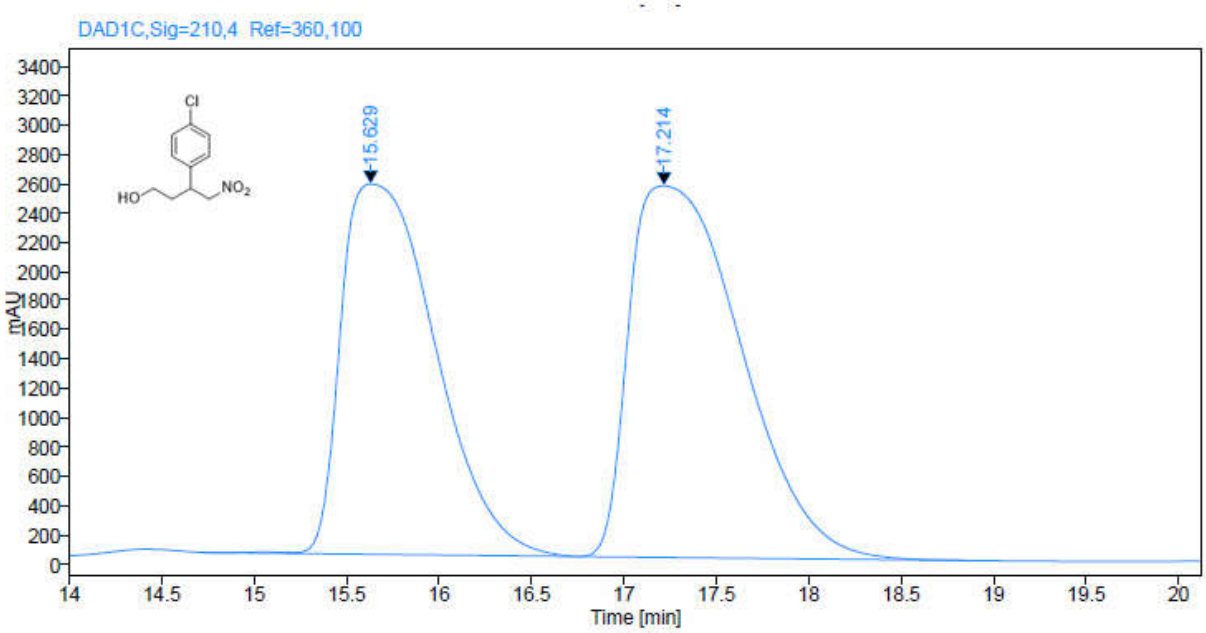
Peak #	RT [min]	Type	Width [min]	Area mAU	Height	Area %
1	19.632	VM m	0.8453	182174.1578	2556.7407	46.3296
2	24.785	MM m	0.9704	211039.5321	2574.3469	53.6704



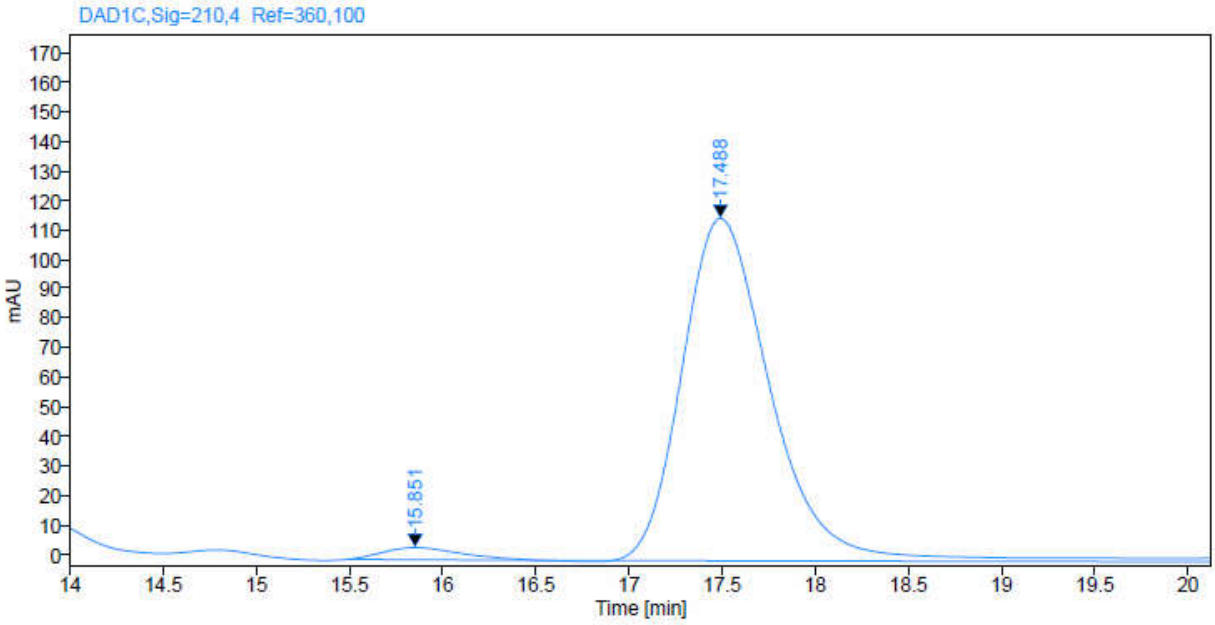
Peak #	RT [min]	Type	Width [min]	Area mAU	Height	Area %
1	20.265	MM m	0.8704	361.6719	5.7456	2.2392
2	24.904	BB	5.2727	15790.0885	259.3250	97.7608

(*S*)-3-(4-chlorophenyl)-4-nitrobutan-1-ol (3b)

Lux 3µm-cellulose 5, Hexane/*i*-Propanol 90:10, flow: 0.5 mL/min, λ=210 nm.



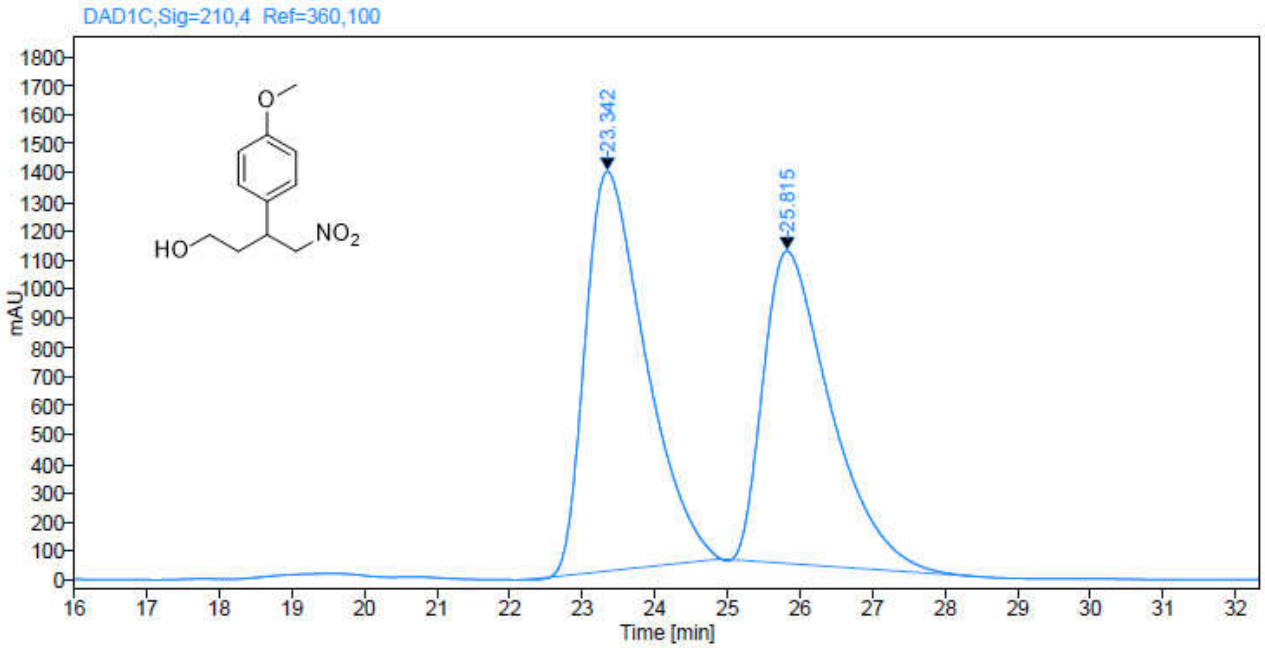
Peak #	RT [min]	Type	Width [min]	Area mAU	Height	Area %
1	15.629	MB m	0.5610	89347.1220	2523.9050	45.6053
2	17.214	BB	2.2510	106566.6913	2533.7013	54.3947



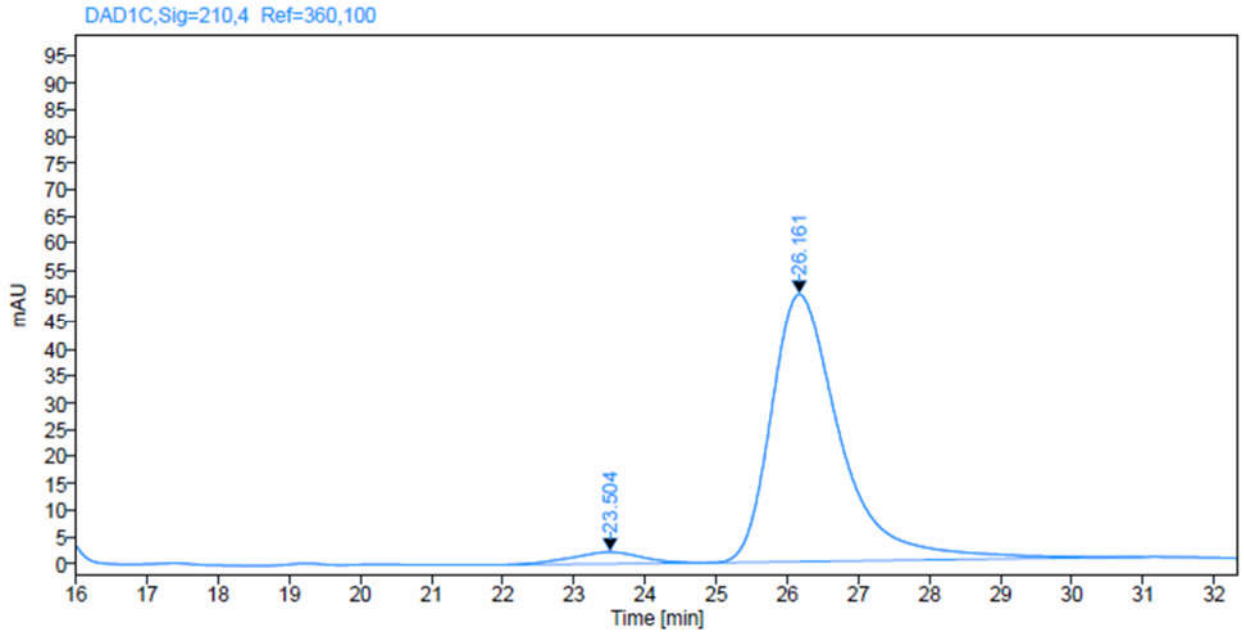
Peak #	RT [min]	Type	Width [min]	Area mAU	Height	Area %
1	15.851	MM m	0.4476	120.0760	4.0776	2.9528
2	17.488	MM m	0.5178	3946.4522	115.7285	97.0472

(*S*)-3-(4-methoxyphenyl)-4-nitrobutan-1-ol (3c)

Lux 3µm-cellulose 1, Hexane/*i*-Propanol 90:10, flow: 0.5 mL/min, λ=210 nm.



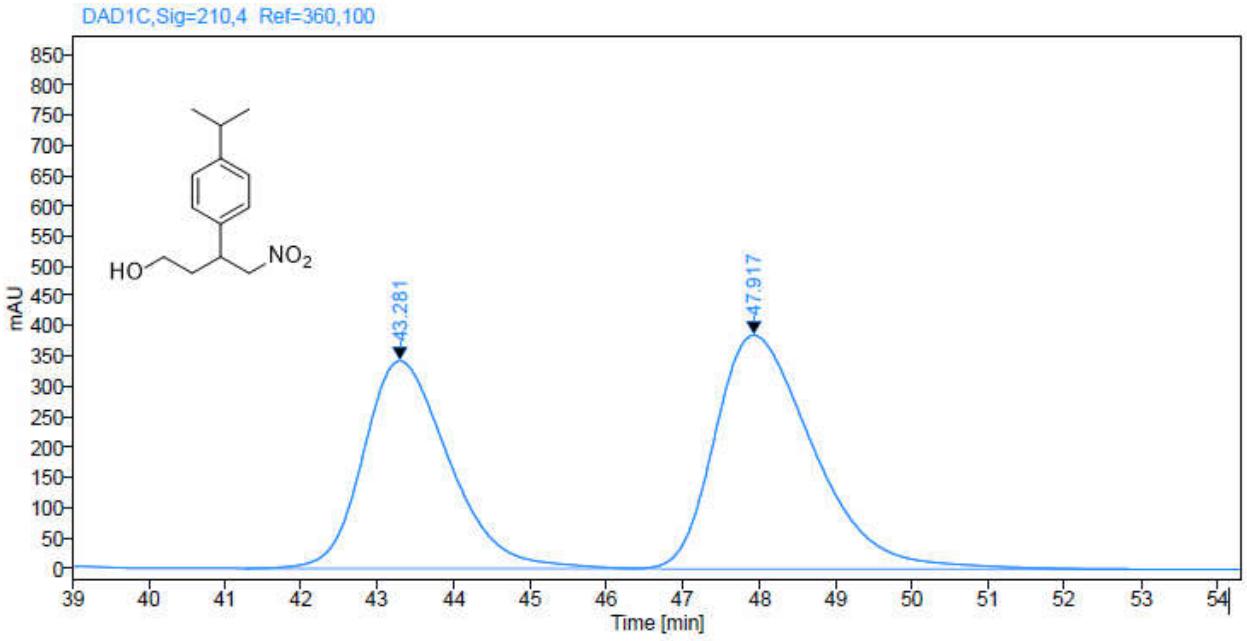
Peak #	RT [min]	Type	Width [min]	Area mAU	Height	Area %
1	23.342	MM m	0.8689	78931.9901	1372.5906	53.3125
2	25.815	MM m	0.9736	69123.2885	1073.0215	46.6875



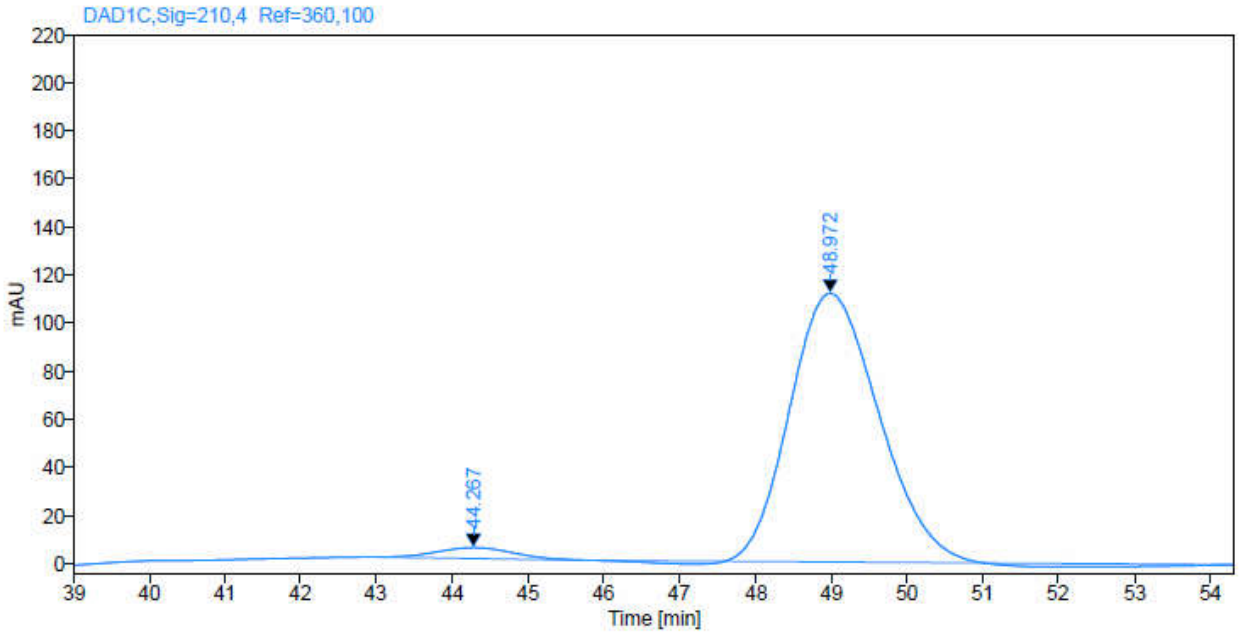
Peak #	RT [min]	Type	Width [min]	Area mAU	Height	Area %
1	23.504	MM m	0.8243	152.3772	2.1831	4.3332
2	26.161	MM m	0.9952	3364.1200	49.9818	95.6668

(*S*)-3-(4-isopropylphenyl)-4-nitrobutan-1-ol (3d)

Lux 3µm-cellulose 5, Hexane/*i*-Propanol 95:5, flow: 0.4 mL/min, λ=210 nm.



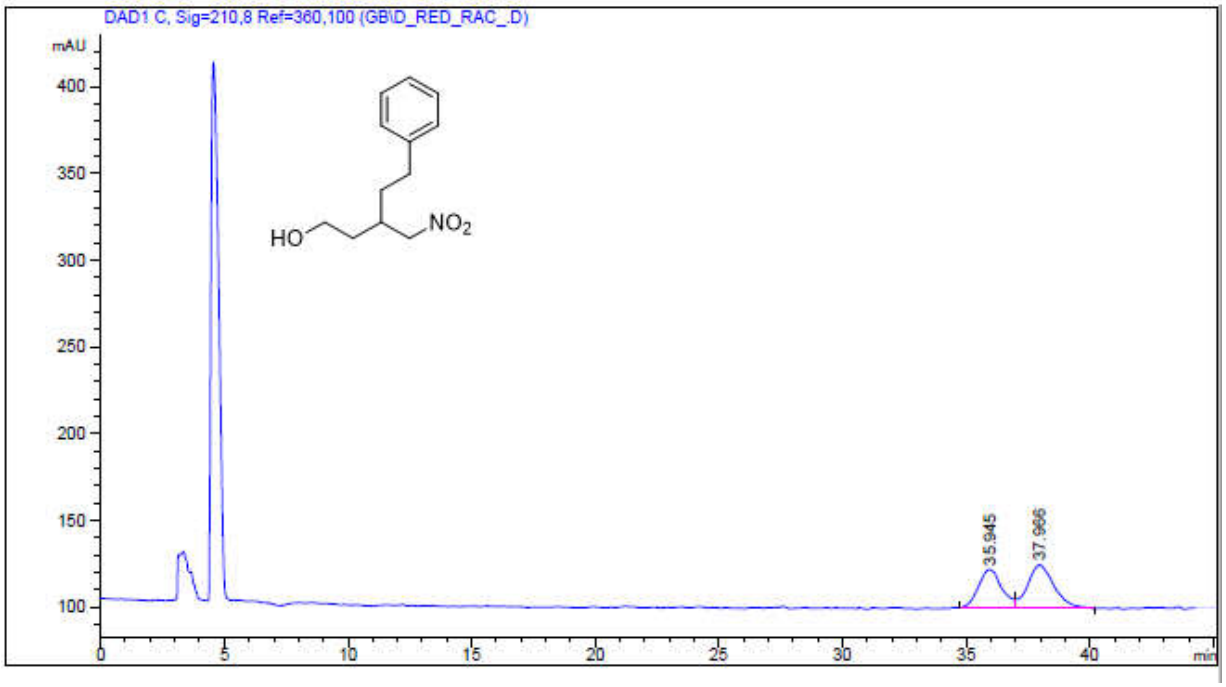
Peak #	RT [min]	Type	Width [min]	Area mAU	Height	Area %
1	43.281	BM m	1.1921	26803.2087	342.8562	43.6713
2	47.917	MM m	1.3794	34571.7143	385.8334	56.3287



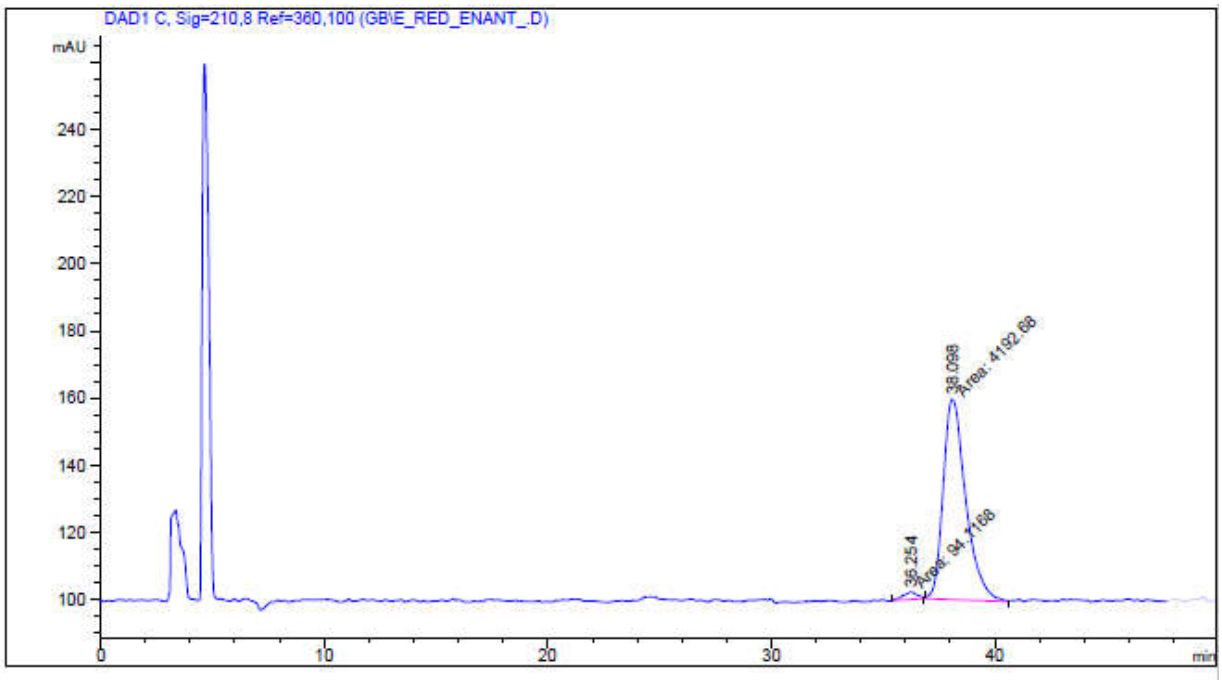
Peak #	RT [min]	Type	Width [min]	Area mAU	Height	Area %
1	44.267	BM m	0.8432	319.9457	4.5018	3.4872
2	48.972	MM m	1.2342	8854.9116	111.5408	96.5128

(*R*)-3-(nitromethyl)-5-phenylpentan-1-ol (3e)

Chiralpak OJ-H, Hexane/*i*-Propanol 10:1, flow: 1 mL/min, λ=210 nm.



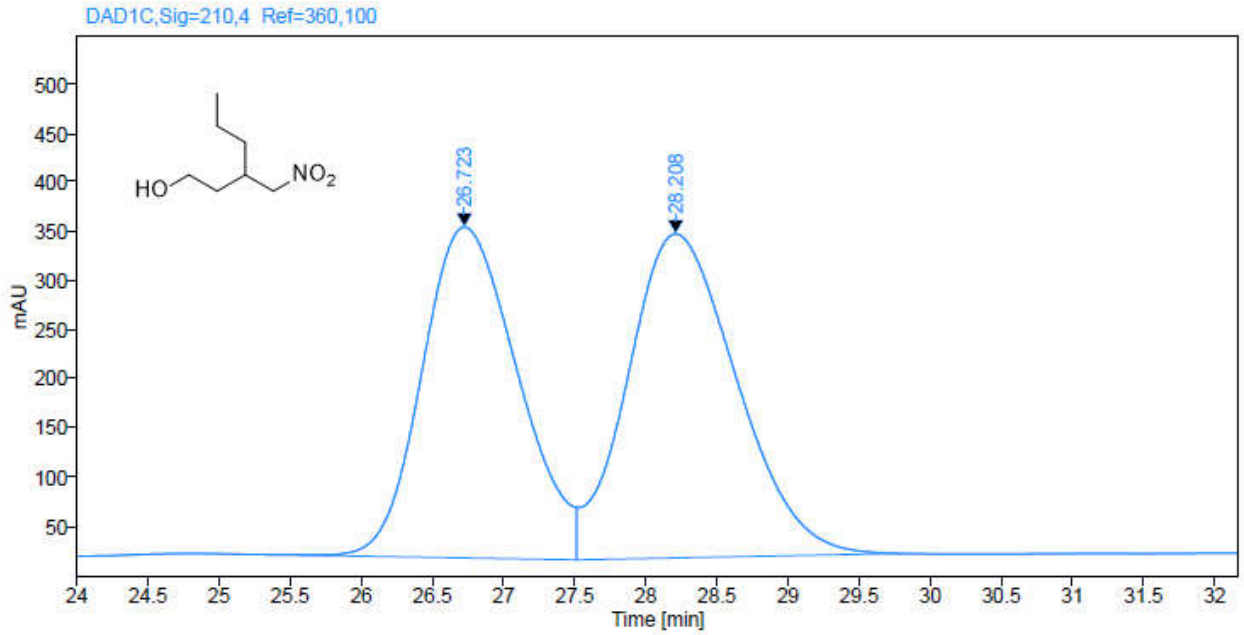
Peak #	RT [min]	Type	Width [min]	Area mAU	Height	Area %
1	35.945	VV	0.9326	1499.48364	22.41067	44.4131
2	37.966	VB	1.0802	1876.73804	25.10209	55.5869



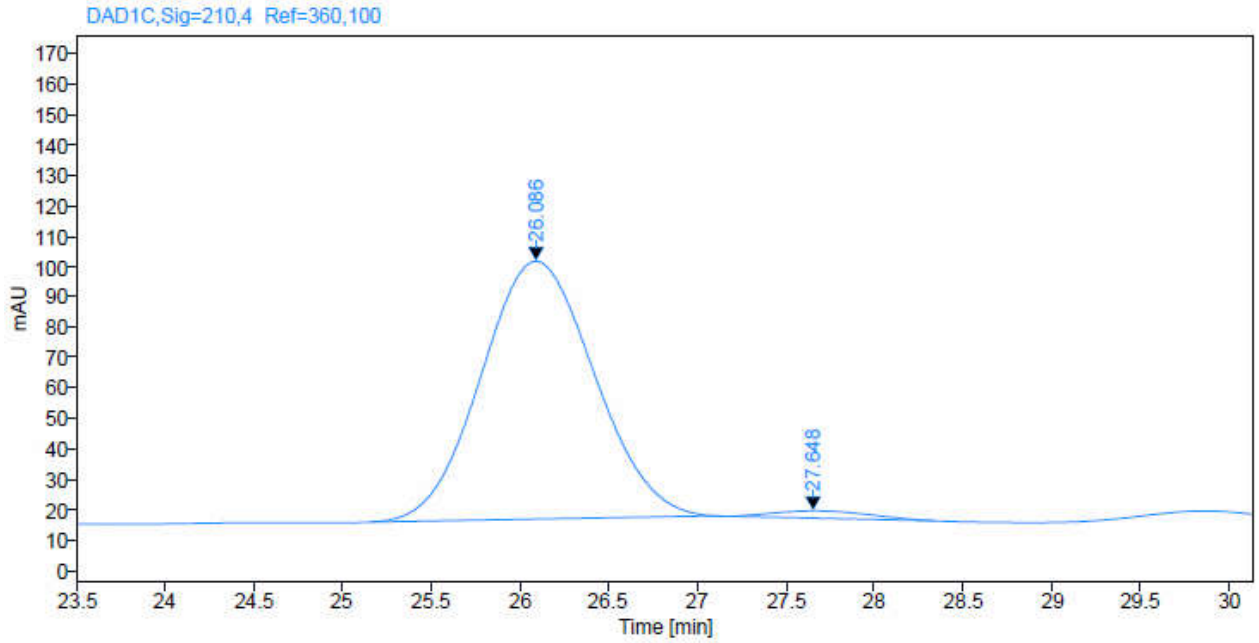
Peak #	RT [min]	Type	Width [min]	Area mAU	Height	Area %
1	36.254	MM	0.7380	94.11681	2.12546	2.1955
2	38.098	MM	1.1720	4192.69262	59.62528	97.8045

(*S*)-3-(nitromethyl)hexan-1-ol (3f)

Lux 3µm-cellulose 5, Hexane/*i*-Propanol 95:5, flow: 0.4 mL/min, λ=210 nm.



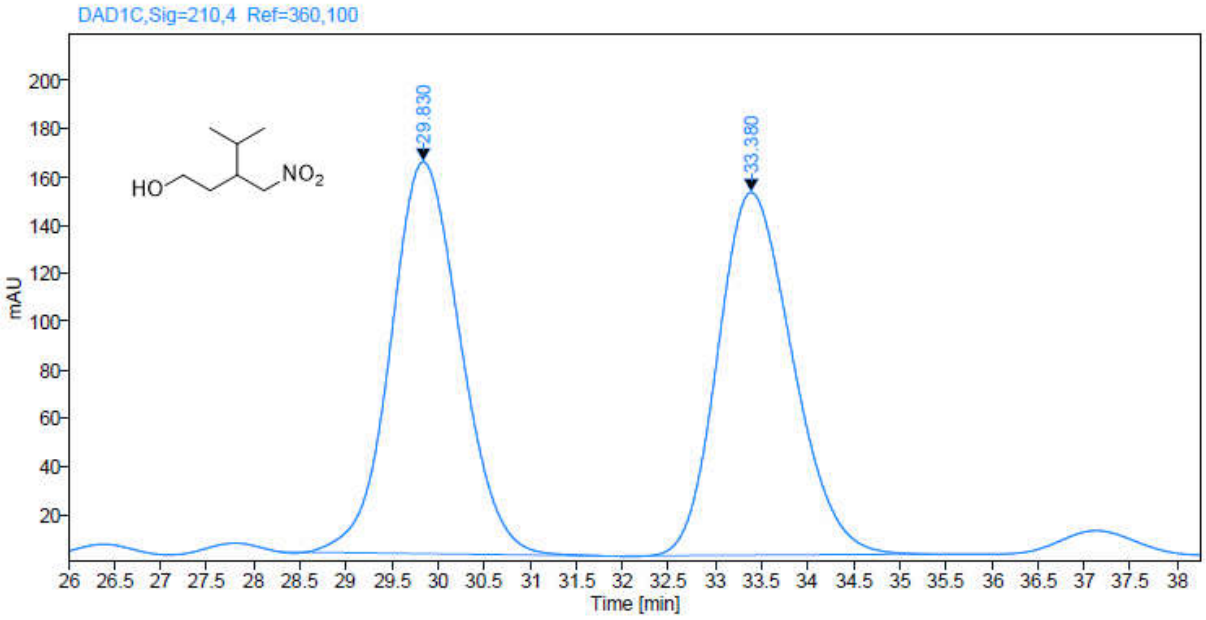
Peak #	RT [min]	Type	Width [min]	Area mAU	Height	Area %
1	26.574	MM m	0.6737	13041.9024	311.9882	47.7061
2	28.061	MM m	0.7648	14296.1051	298.4549	52.2939



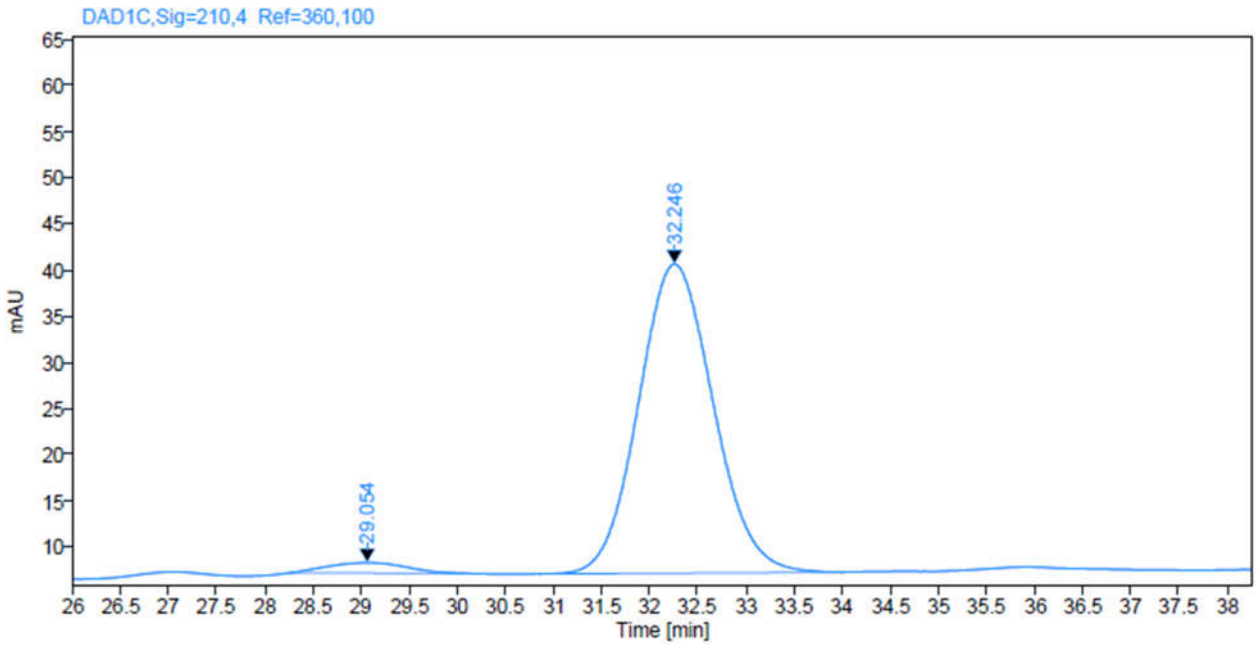
Peak #	RT [min]	Type	Width [min]	Area mAU	Height	Area %
1	26.086	MM m	0.6965	3742.9466	84.5534	97.6616
2	27.648	MM m	0.4593	89.6200	2.3803	2.3384

(*S*)-4-methyl-3-(nitromethyl)pentan-1-ol (3g)

Lux 3µm-cellulose 5, Hexane/*i*-Propanol 95:5, flow: 0.5 mL/min, λ=210 nm.



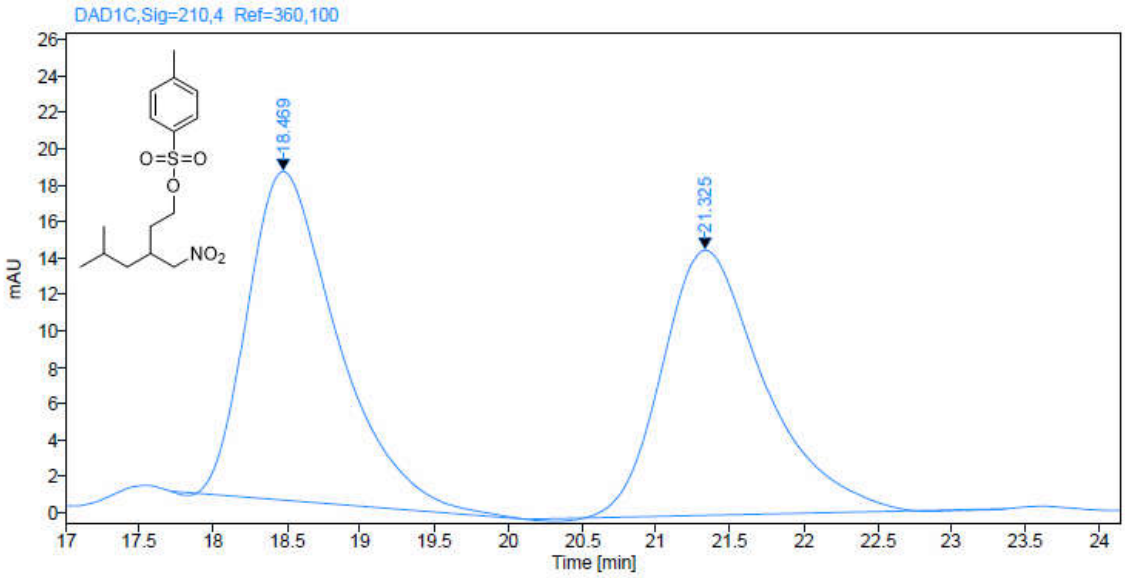
Peak #	RT [min]	Type	Width [min]	Area mAU	Height	Area %
1	29.830	MM m	0.8148	8533.6855	162.4687	50.2958
2	33.380	MB m	0.8744	8433.2944	150.3529	49.7042



Peak #	RT [min]	Type	Width [min]	Area mAU	Height	Area %
1	29.054	MM m	0.6690	63.0586	1.1198	3.3797
2	32.246	BB	3.1450	1802.7564	33.4665	96.6203

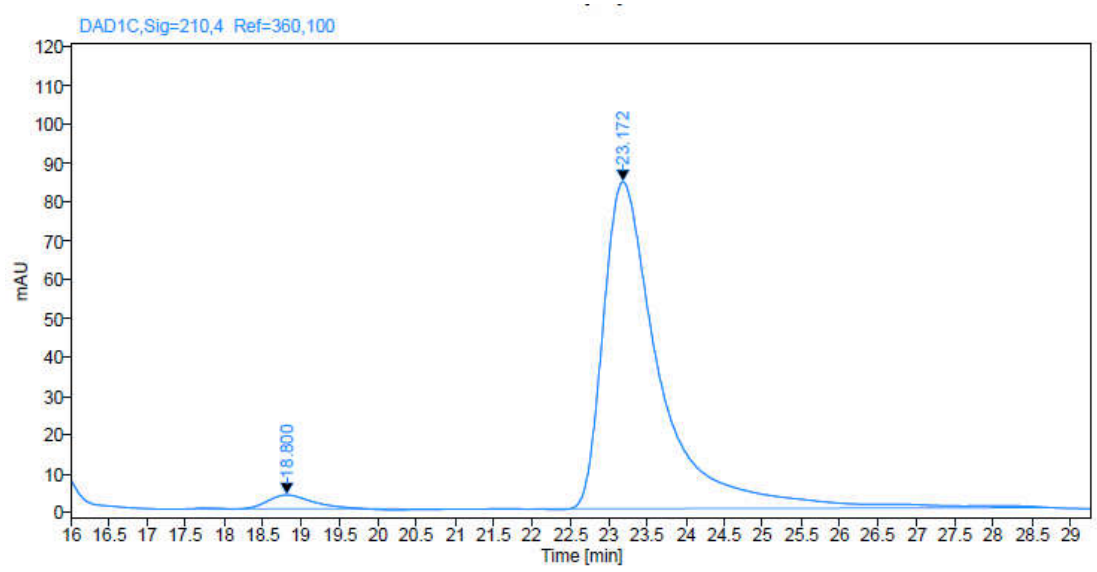
(*R*)-5-methyl-3-(nitromethyl)hexan-1-ol (3h)

Lux 3µm-cellulose 1, Hexane/*i*-Propanol 95:5, flow: 0.5 mL/min, λ=210 nm.



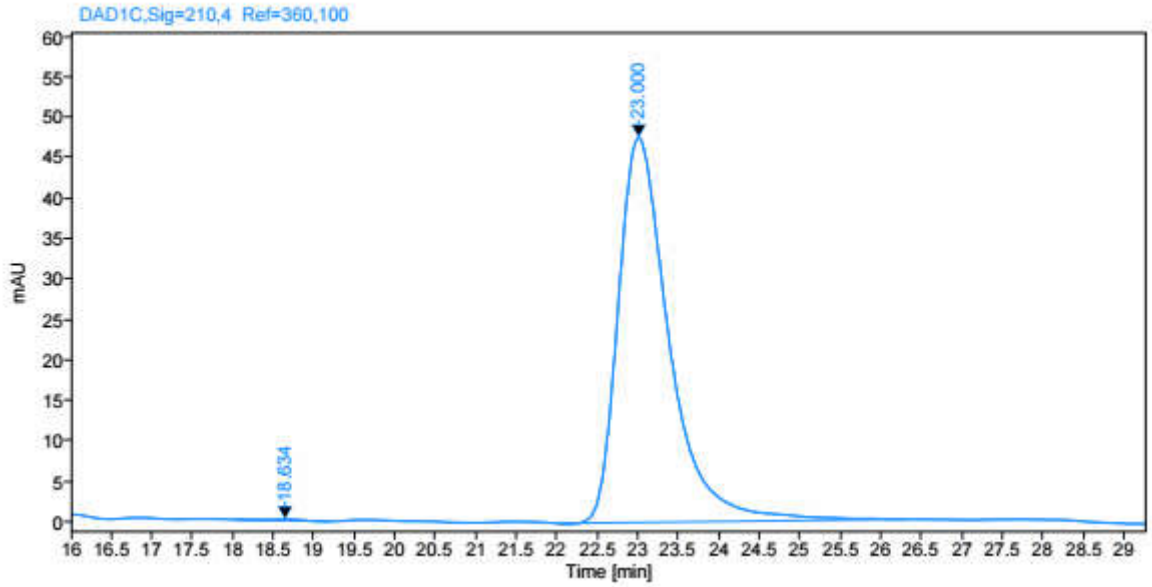
Peak #	RT [min]	Type	Width [min]	Area mAU	Height	Area %
1	18.469	MM m	0.6329	765.1859	18.0397	52.3450
2	21.325	MM m	0.7164	696.6274	14.5546	47.6550

ee for Table 2, entry 8



Peak #	RT [min]	Type	Width [min]	Area mAU	Height	Area %
1	18.800	MM m	0.5414	130.6467	3.5328	2.9162
2	23.172	MM m	0.7584	4349.3757	84.2401	97.0838

ee for the reaction carried out on 1.39g of **1h** (Scheme 2)



Peak #	RT [min]	Type	Width [min]	Area mAU	Height	Area %
1	18.634	MM m	0.1933	2.1340	0.1358	0.1026
2	23.000	MM m	0.6640	2078.0446	47.5348	99.8974

9. References

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