

# Synthesis of Nitrolipids: All Four Possible Diastereomers of Nitro-oleic acids: (*E*) and (*Z*), 9- and 10-Nitro-octadec-9-enoic acids.

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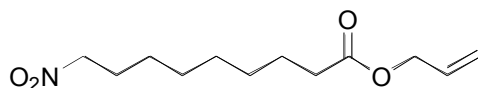
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## SUPPLEMENTAL INFORMATION

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**General methods.** Nonyl aldehyde (**1**), 9-bromononanol, 1-bromononane and oleic acid starting materials were purchased from Aldrich Chemical Company or TCI America Co. and used without further purification. All reagents were purchased from commercial sources and used as received. Diethyl ether, tetrahydrofuran, and dichloromethane reaction solvents were distilled once then used without further purification. Other reagent grade solvents are used as received.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a 300 MHz (75 MHz) or 500 MHz (125 MHz) instrument in  $\text{CDCl}_3$ . Chemical shifts are in  $\delta$  units (ppm) referenced to solvent residual proton or carbon signal (7.26 ppm, 77.0 ppm). Coupling constants ( $J$ ) are reported in Hertz (Hz). NMR splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; and br, broad. Brine refers to a saturated aqueous solution of NaCl. Analytical TLC was performed on Kieselgel 60 F254 aluminum sheets. Spots were observed by exposure to 254 nm UV light or phosphomolybdic acid dip (PMA). Column chromatography was performed on silica gel 40-64 mesh (Silicycle) using technical grade solvents according to the method of Still<sup>1</sup>. Mass spectrometry was performed by Jeff Morre of the Mass Spectrometry Facility, Oregon State University.



**9-Nitro-nonanoic acid, allyl ester (2).** 9-Bromononanol, 10.06 g, was charged<sup>2</sup> to a round bottom flask and dissolved in 25 mL acetone, then cooled in an ice bath to 0 °C. Jones' Reagent (25 mL, 1.5 eq., 1.4 M stock solution prepared from 13.36 g  $\text{CrO}_3$ /11.5 mL conc.  $\text{H}_2\text{SO}_4$ /  $\text{H}_2\text{O}$  added to fill to 50mL total volume) was added dropwise to the stirred solution over 1 h, then stirred for 4-5 h. Additional acetone and water were added to improve solubility if necessary. The solution was partitioned between 100 mL  $\text{Et}_2\text{O}$  and 50 mL water, separated, then the aq. layer extracted 3  $\times$  50 mL  $\text{Et}_2\text{O}$ . The organic layers were combined, then washed 2  $\times$  50 mL sat'd aq.  $\text{NH}_4\text{Cl}$ , 2  $\times$  50 mL water, and 2  $\times$  50 mL brine, dried over  $\text{Na}_2\text{SO}_4$ , filtered through silica/Celite plug, and the solvents removed under reduced pressure. The solids were then redissolved in 100mL  $\text{Et}_2\text{O}$  and extracted 3  $\times$  30mL 1M NaOH to extract the acid. The aqueous layers were combined, washed 2  $\times$   $\text{CH}_2\text{Cl}_2$  to remove nonpolar impurities, and reacidified with conc. HCl (10mL). The acidified layer was extracted 3  $\times$  50mL  $\text{Et}_2\text{O}$ , the organic layers combined, washed 1  $\times$  50 mL water and 1  $\times$  50 mL brine then dried over  $\text{Na}_2\text{SO}_4$  and filtered to yield 9-bromononanoic acid, 7.15 g (67%). mp = 33.0-34.5 °C (lit.<sup>2</sup> mp: 31.5-33.5 °C )  $^1\text{H}$  NMR (300MHz):  $\delta$  3.40 (t,  $J$  = 6.7 Hz, 2H); 2.35 (t,  $J$  = 7.5 Hz, 2H); 1.85 (m, 2H); 1.64 (m, 2H); 1.42 (m, 2H); 1.32 (br s, 6H). The crude product was used directly in the next step without further purification.

The crude 9-bromononanoic acid, 7.15 g, was transferred to a 100 mL round bottom flask and dissolved<sup>3</sup> in a solution of 20mL allyl alcohol and 20 mL toluene, with a catalytic amount of *p*-TsOH (5-10 mg). The flask was sealed with a condensor and Dean-stark trap, then refluxed, overnight (16-18 h). After cooling to rt the solution was

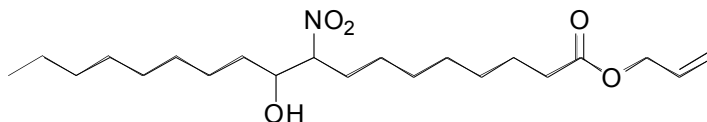
<sup>1</sup> Still, W.C.; Kahn, M.; Mitra, J.A. *J. Org. Chem.* **1978**, 48, 2923.

<sup>2</sup> Tranchepain, I.; Le Berre, F.; Dureault, A.; Le Merrer, Y.; Depezay, J. C. *Tetrahedron* **1989**, 45, 2057-2065. Buchanan, G. W.; Smits R.; Munteanu, E. *J. Fluorine Chem.* **2003**, 123(2), 255-259.

<sup>3</sup> Waldmann, H.; Kunz, H. *Liebigs Ann. Chem.* **1983**, 1712.

partitioned with Et<sub>2</sub>O and extracted 2 × 0.1 M NaOH (to remove unreacted acid). The combined aqueous fractions were back-extracted with Et<sub>2</sub>O, then the organic layers combined and washed 1 × water, 1 × brine. The solution was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered through silica/Celite plug, and the solvents removed under reduced pressure to yield 9-bromononanoic acid, allyl ester, 7.71 g (92%). <sup>1</sup>H NMR (300MHz): δ 5.92 (ddt, *J* = 17.3, 10.5, 5.9 Hz, 1H); 5.31 (dq, *J* = 17.3, 1.5 Hz, 1H); 5.23 (dq, *J* = 10.5, 1.5 Hz, 1H); 4.57 (dt, *J* = 5.9, 1.5 Hz, 2H); 3.40 (t, *J* = 6.7 Hz, 2H); 2.30 (t, *J* = 7.5 Hz, 2H); 1.84 (m, 2H); 1.62 (m, 2H); 1.31 (br s, 8H). <sup>13</sup>C NMR (75MHz): δ 173.2, 132.2, 117.9, 64.8, 34.1, 33.8, 32.6, 28.9, 28.8, 28.4, 28.0, 24.7. FTIR (KBr) ν<sub>max</sub> 2932, 2856, 1736, 1461, 1173 cm<sup>-1</sup>. The crude product was used in the next step directly without further purification.

Silver nitrite (6.42 g, 1.5 equiv.) was charged to a 100 mL round bottom flask and suspended in 50 mL Et<sub>2</sub>O purged with N<sub>2</sub>. The 9-bromononanoic acid, allyl ester, 7.71 g, was added to the stirred solution. The flask was stoppered and covered with aluminum foil to protect from light and stirred, rt, for 7 d. The resulting suspension was filtered through a plug of silica and Celite to remove solids, then purified via flash chromatography (EtOAc/hexanes, 1-2-5%) to yield 9-nitrononanoic acid, allyl ester<sup>4</sup> (**2**), 4.59 g (68%). <sup>1</sup>H NMR (300MHz): δ 5.87 (ddt, 1H); 5.27 (dq, 1H); 5.18 (dq, 1H); 4.53 (dt, 2H); 4.33 (t, *J* = 6.9 Hz, 2H); 2.29 (t, *J* = 7.6 Hz, 2H); 1.96 (q, 2H); 1.59 (q, 2H); 1.30 (s, 8H). <sup>13</sup>C NMR (75MHz): δ 173.2, 132.2, 117.9, 75.5, 64.8, 34.0, 28.7, 28.5, 27.2, 26.0, 24.7. FTIR (KBr) ν<sub>max</sub> 2931, 2856, 1736, 1553, 1461, 1173 cm<sup>-1</sup>.

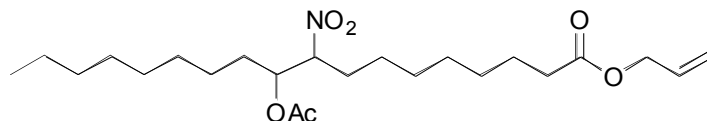


**10-Hydroxy-9-nitro-octadecanoic acid, allyl ester (3).** (General Nitro-Aldol Procedure): A 25 mL round bottom flask was cooled in an ice bath, then charged with the nonyl aldehyde (**1**, 1.75 mL) and nitroalkane **2** (2.43 g, 1.0 – 1.1 equiv.) under N<sub>2</sub>. To the stirred solution was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 0.15 mL, 0.1 equiv.) dropwise. The neat solution was stirred cold, 2 h, then allowed to warm to room temperature overnight, until <sup>1</sup>H-NMR monitoring indicated completion. The solution was partitioned with 10 mL Et<sub>2</sub>O and 10 mL 1M HCl, then the aqueous layer extracted 3 × 10 mL Et<sub>2</sub>O. The organic layers were combined, washed with 1 × 10mL water, 1 × 10mL brine, and dried over Na<sub>2</sub>SO<sub>4</sub>. After filtering off the drying agent the solvent was removed under reduced pressure, then upon purification by column chromatography (EtOAc/hexanes, 1-10%) 3.10 g **3** (81%) was isolated as a colorless oil. Mixture of diastereomers:<sup>5</sup> <sup>1</sup>H NMR (300 MHz): δ 5.87 (ddt, 1H); 5.26 (dq, 1H); 5.19 (dq, 1H); 4.53 (dt, 2H); 4.39 (m, 1H); 3.95, 3.83 (m, total of 1H); 2.44 (br s, 1H); 2.29 (t, *J* = 7.6 Hz, 2H); 1.95 (m, 1H); 1.74 (m, 1H); 1.58 (m, 2H); 1.46 (m, 4H); 1.26-1.23 (br m, 18H); 0.85 (t, *J* = 6.7 Hz, 3H). <sup>13</sup>C NMR (75 MHz): δ 173.4, 132.2, 118.0, 92.9, 92.3, 72.3,

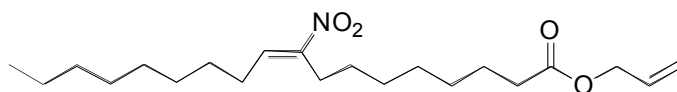
<sup>4</sup> For 9-nitrononanoic acid, see: Ballini, R.; Papa, F.; Abate, C. *Eur. J. Org. Chem.* **1999**, 1, 87-90

<sup>5</sup> The NMR signals are the result of a combination of diastereomers. Some peaks are coincident while others are distinct; this results in a variable number of carbon resonance signals and fractional proton integration.

72.0, 64.9, 34.1, 33.4, 33.2, 31.7, 30.2, 29.32, 29.28, 29.23, 29.1, 28.77, 28.75, 28.69, 28.64, 27.9, 25.8, 25.5, 25.2, 24.7, 22.5, 14.0. TLC (EtOAc/hexanes, 1:3)  $R_f$  = 0.38. FTIR (KBr)  $\nu_{\max}$  3470, 2928, 2856, 1738, 1549, 1463, 1378, 1175  $\text{cm}^{-1}$ . UV  $\lambda_{\max}$  (MeCN) 277 nm.



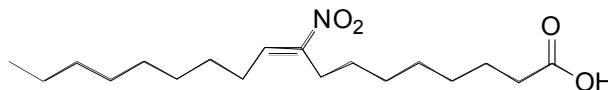
**10-Acetoxy-9-nitro-octadecanoic acid, allyl ester (4).** (General Acetylation Procedure): A 50mL round bottom flask was charged with  $\square$ -hydroxy-nitro **3** (3.10 g), acetic anhydride as solvent (15-20 mL), and a catalytic amount of *p*-toluenesulfonic acid (5 – 10 mg). The solution was stirred under  $\text{N}_2$ , overnight, rt. The solvent was removed by azeotropic removal with toluene (3  $\times$  20 mL) under reduced pressure, then redissolved in dichloromethane and filtered through a plug of silica/Celite to yield a quantitative amount of crude **4**. Upon purification by column chromatography (EtOAc/hexanes, 1-5%) 2.97 g **4** (86%) was isolated as a colorless oil. Mixture of diastereomers:<sup>5,6</sup>  $^1\text{H}$  NMR (300 MHz):  $\delta$  5.91 (ddt, 1H); 5.35-5.15 (m, total 3H); 4.60-4.55 (m, total 3H); 2.32 (t,  $J$  = 7.5 Hz, 2H); 2.09, 2.05 (s, total 3H); 1.95 (m, 1H); 1.62 (m, 4H); 1.30-1.26 (br m, 21H); 0.88 (t,  $J$  = 6.5 Hz, 3H).  $^{13}\text{C}$  NMR (75 MHz):  $\delta$  173.1, 170.0, 169.7, 132.2, 117.9, 90.0, 89.4, 72.7, 72.6, 64.8, 34.0, 31.6, 30.6, 29.6, 29.5, 29.2, 29.0, 28.76, 28.69, 28.67, 28.5, 28.52, 25.7, 25.4, 25.2, 24.6, 24.4, 22.5, 20.6, 20.5, 13.9. TLC (EtOAc/hexanes, 1:3)  $R_f$  = 0.51. FTIR (KBr)  $\nu_{\max}$  2929, 2857, 1747, 1556, 1464, 1374, 1228, 1174  $\text{cm}^{-1}$ . UV  $\lambda_{\max}$  (MeCN) 263 nm.



**(E)-9-Nitro-octadec-9-enoic acid (9-Nitro-oleic acid), allyl ester (5a).** (General Elimination Procedure): A 100 mL round bottom flask was charged with  $\square$ -acetoxy-nitro starting material **4** (3.20 g), sodium carbonate (0.47 g, 0.5 eq.), and benzene (30-40 mL). The solution was refluxed under  $\text{N}_2$  with vigorous stirring under a Dean-stark trap for azeotropic removal of water, 24 h, at 80-90  $^\circ\text{C}$  and monitored via TLC for completion. After completion the solution is cooled to rt, partitioned with 20-30mL sat'd  $\text{NH}_4\text{Cl}$  and 20mL  $\text{Et}_2\text{O}$ , extracted 3  $\times$  10mL  $\text{Et}_2\text{O}$ , the organic layers combined and washed 1  $\times$  20mL water, 1  $\times$  20mL brine, dried over  $\text{NaSO}_4$ , filtered through a plug of silica/Celite, and the solvent removed under reduced pressure. The nitroalkene product was isolated by column chromatography (EtOAc/hexanes, 1-5%) to yield 2.30 g **5a** (84%) as a pale yellow oil.  $^1\text{H}$  NMR (300 MHz):  $\delta$  7.08 (t,  $J$  = 7.9 Hz, 1 H); 5.92 (ddt,  $J$  = 17.3, 10.5, 5.9 Hz, 1H); 5.31 (dq,  $J$  = 17.3, 1.5 Hz, 1H); 5.23 (dq,  $J$  = 10.5, 1.5 Hz, 1H); 4.57 (dt,  $J$  = 5.9, 1.5 Hz, 2H); 2.56 (t,  $J$  = 7.6 Hz, 2H); 2.33 (t,  $J$  = 7.5 Hz, 2H); 2.20 (q,  $J$  = 7.6 Hz, 2H); 1.63 (m, 2H); 1.47 (m, 4H); 1.32-1.25 (br m, 16H); 0.88 (t,  $J$  = 6.7 Hz, 3H).  $^{13}\text{C}$  NMR (75 MHz):  $\delta$  173.3, 151.7, 136.5, 132.3, 118.1, 64.9, 34.1, 31.8, 29.28, 29.25, 29.1,

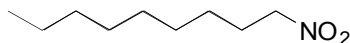
<sup>6</sup> Note that the  $^1\text{H}$  NMR signals for the  $\beta$ -nitro acetoxy compounds are obscured by the characteristic signals for the allyl group.

29.0, 28.99, 28.92, 28.85, 28.5, 28.0, 27.8, 26.3, 24.8, 22.6, 14.0. TLC (EtOAc/hexanes, 1:3)  $R_f$  = 0.60. FTIR (KBr)  $\nu_{\max}$  2928, 2856, 1738, 1521, 1462, 1336, 1244, 1171  $\text{cm}^{-1}$ . UV  $\lambda_{\max}$  (MeCN) 262 nm.

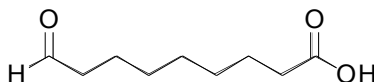


**(E)-9-Nitro-octadec-9-enoic acid (5).** (General Deprotection Procedure): A 50 mL round bottom flask was charged with allyl ester **5a** (0.51 g) and THF (20-25 mL). Formic acid (98%, 0.50 mL, 10 equiv.) and dry  $\text{Pd}(\text{PPh}_3)_4$  (85 mg, 5 mol%) were added and the solution sparged with  $\text{N}_2$  for 10 min, then sealed with a reflux condensor and refluxed for 24 h under  $\text{N}_2$ . After completion the solution was cooled to rt, filtered through a plug of silica/Celite, and the solvent removed under reduced pressure. The free acid was isolated by column chromatography (1% HOAc, 1-10% EtOAc/hexanes) to yield 0.433 g **5** (95%) as a pale yellow semisolid.  $^1\text{H}$  NMR (300 MHz):  $\delta$  11.1 (br s, 1H); 7.08 (t,  $J$  = 7.9 Hz, 1H); 2.56 (t,  $J$  = 7.6 Hz, 2H); 2.35 (t,  $J$  = 7.5 Hz, 2H); 2.20 (q,  $J$  = 7.6 Hz, 2H); 1.61 (m, 2H); 1.47 (m, 4H); 1.33-1.25 (br m, 16H); 0.88 (t,  $J$  = 6.7 Hz, 3H).  $^{13}\text{C}$  NMR (125 MHz):  $\delta$  180.3, 151.6, 136.3, 33.9, 31.7, 29.19, 29.17, 29.0, 28.87, 28.75, 28.4, 27.9, 27.7, 26.1, 24.4, 22.5, 13.9. TLC (5% MeOH/ $\text{CHCl}_3$ )  $R_f$  = 0.58. FTIR (KBr)  $\nu_{\max}$  2928, 2856, 1709, 1522, 1458, 1437, 1336, 1287  $\text{cm}^{-1}$ . UV  $\lambda_{\max}$  (MeCN) 261, 229 nm.

MS (CI)  $m/z$  (%) 328 (15), 310 (100), 281 (40), 263 (30), 168 (30). HRMS calc for  $\text{C}_{18}\text{H}_{34}\text{NO}_4$ : 328.2488 found 328.2480. See also pages S26 (MS/MS) and S30 (EI).

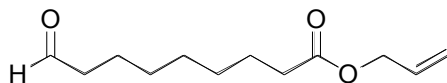


**1-Nitrononane (6).** Silver nitrite (24 g, 0.156 mol) was added to a flask protected from light with aluminum foil, suspended in  $\text{Et}_2\text{O}$ , and purged with  $\text{N}_2$ . 1-bromononane (21 g, 0.101 mol) was then added and the solution stirred at rt for 7 d. Solids were then removed by passing the solution through a plug of Celite. The solvent was removed under reduced pressure and purified by vacuum distillation (88  $^\circ\text{C}$ , 0.1 Torr) to yield **6** in 60% yield (10.5 g) as a pale yellow liquid.  $^1\text{H}$  NMR (300 MHz)  $\delta$  4.36 (t,  $J$  = 8 Hz, 2H), 1.98 (m, 2H), 1.32-1.25 (br m, 12H), 0.86 (t,  $J$  = 7.5 Hz, 3H).  $^{13}\text{C}$  NMR (75 MHz)  $\delta$  75.6, 31.7, 29.1, 29.0, 28.7, 27.3, 26.1, 22.5, 13.9. FTIR (KBr)  $\nu$  2927, 2857, 1555, 1466, 1436, 1382, 1136  $\text{cm}^{-1}$ .

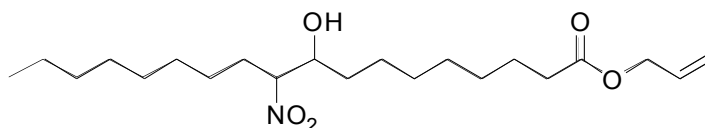


**9-Oxononanoic acid.** Oleic acid (20.0 g, 0.071 mol) dissolved in dry  $\text{CH}_2\text{Cl}_2$  (200 mL) in an oven-dried flask open to air was cooled to  $-78\text{ }^\circ\text{C}$  with stirring. Ozone was then bubbled into the solution until a faint blue color was observed (45 min), after which the solution was purged with  $\text{N}_2$  for 20 min and brought to rt. Dimethylsulfide (7.3 mL, 0.10 mol) was added via syringe and the solution stirred for 3 h. Excess  $\text{Me}_2\text{S}$  and solvent were then removed under reduced pressure and the mixture dissolved in

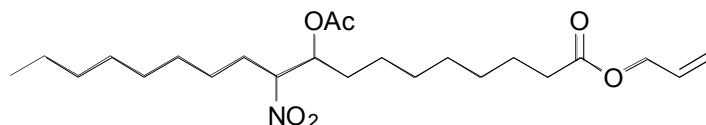
EtOAc (100 mL). The solution was then washed 3 × brine, dried over MgSO<sub>4</sub>, and the solvent removed under reduced pressure, yielding a 1:1 mixture of 9-oxononanoic acid<sup>7</sup> and nonanal (**1**), (21.5 g total, 96%) which was then purified by column chromatography (1:1 hexanes: ethyl acetate) for 7.0 g yield (90%) as a colorless liquid: <sup>1</sup>H NMR (300 MHz) δ 11.4 (br s, 1H), 9.68 (t, *J* = 1.8 Hz, 1H), 2.41 (t, *J* = 7.5 Hz, 2H), 2.35 (t, *J* = 7.5 Hz, 2H), 1.62 (m, 4H), 1.25 (m, 6H).



**9-Oxononanoic acid allyl ester (7).** A flask was charged with 9-oxononanoic acid (2.5 g, 15 mmol), N,N'-dicyclohexylcarbodiimide (DCC, 3.5 g, 17 mmol), and CH<sub>2</sub>Cl<sub>2</sub> (50 mL), and cooled to 0 °C under N<sub>2</sub>. N,N-dimethyl-4-aminopyridine (DMAP) (50 mg) was then added and the solution stirred for 30 min, after which allyl alcohol (1.5 g, 25 mmol) was added and the solution stirred for 2 h. The reaction was then warmed to rt and stirred overnight. The solution was passed through a plug of silica/Celite, and solvents removed under reduced pressure. Allyl ester **7** was purified by vacuum distillation (110 °C, 0.1 Torr) in 65% yield (2.0 g, colorless liquid): <sup>1</sup>H NMR (300 MHz) δ 9.74 (t, *J* = 1.8 Hz, 1H), 5.88 (ddt, 1H), 5.31 (dq, 1H), 5.22 (dq, 1H), 4.55 (dt, *J* = 9.6 Hz, 2H), 2.40 (t, *J* = 7.5 Hz, 2H), 2.30 (t, *J* = 7.5 Hz, 2H), 1.60 (m, 4H), 1.32 (m, 6H). <sup>13</sup>C NMR (75 MHz) δ 202.3, 172.9, 132.1, 117.7, 64.5, 43.5, 33.8, 28.7, 28.6, 28.5, 24.5, 21.6. FTIR (KBr) ν 2934, 2858, 2720, 1736, 1649, 1458, 1418, 1378, 1174, 1105 cm<sup>-1</sup>.

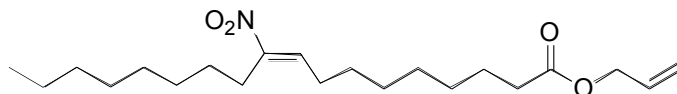


**9-Hydroxy-10-nitro-octadecanoic acid, allyl ester (8).** 1-Nitrononane (**6**) (1.03 g) and **7** (1.05 g) were condensed according to the general nitroaldol procedure, which upon purification by column chromatography (EtOAc/hexanes, 1-10%) yielded 1.53 g **8** (80%) as a colorless oil. Mixture of diastereomers:<sup>5</sup> <sup>1</sup>H NMR (300 MHz) δ 5.91 (ddt, 1H), 5.31 (dq, 1H), 5.22 (dq, 1H), 4.57 (dt, *J* = 9.6 Hz, 2H), 4.43 (m, 1H), 3.99, 3.86 (m, total 1H), 2.33 (t, *J* = 7.5 Hz, 2H), 2.05 (m, 1H), 1.76 (m, 1H), 1.63 (m, 2H), 1.49 (m, 4H), 1.32-1.25 (br m, 18H), 0.87 (t, *J* = 7.5 Hz, 3H). <sup>13</sup>C NMR (75 MHz) δ 173.4, 132.3, 118.1, 92.9, 92.3, 72.3, 72.0, 64.9, 34.1, 33.5, 33.1, 31.7, 30.5, 29.2, 29.1, 29.0, 28.9, 28.0, 25.9, 25.7, 25.5, 25.2, 24.8, 22.6, 14.0. FTIR (KBr) ν 3481, 2928, 2857, 1736, 1649, 1552, 1458, 1379, 1175, 1108 cm<sup>-1</sup>.

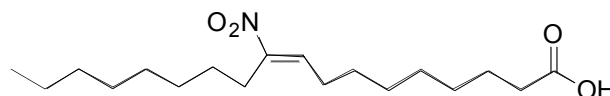


<sup>7</sup> see also Kharisov, R. Ya.; Botsman, O. V.; Botsman, L. P.; Ishmuratova, N. M.; Ishmuratov, G. Yu.; Tolstikov, G. A. *Chemistry of Natural Compounds* (Translation of *Khimiya Prirodnikh Soedinenii*) **2002**, 38(2), 145-148.

**9-Acetoxy-10-nitro-octadecanoic acid, allyl ester (9).** Compound **8** (2.00 g) was acetylated according to the general acetylation procedure, which upon purification by column chromatography (EtOAc/hexanes, 1-5%) yielded 2.20 g **9** (99%) as a colorless oil. Mixture of diastereomers:<sup>5,6</sup> <sup>1</sup>H NMR (300 MHz)  $\delta$  5.84 (ddt, 1H), 5.30-5.05 (m, total 3H); 4.60-4.50 (m, total 3H); 2.25 (t,  $J$  = 7.5 Hz, 2H), 2.02, 1.98 (s, total 3H), 1.90 (m, 1H), 1.60 (m, 4H), 1.36-1.19 (br m, 21H), 0.81 (t,  $J$  = 7.5 Hz, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  173.1, 170.0, 169.6, 132.2, 117.8, 89.9, 89.4, 72.6, 72.5, 64.7, 33.9, 31.6, 30.6, 29.6, 29.4, 29.0, 28.9, 28.87, 28.78, 28.72, 28.68, 25.7, 25.4, 25.1, 24.6, 24.3, 22.4, 20.6, 20.5, 13.9. FTIR (KBr)  $\nu$  3086, 2929, 2857, 1743, 1649, 1555, 1465, 1375, 1226, 1175, 1108 cm<sup>-1</sup>.

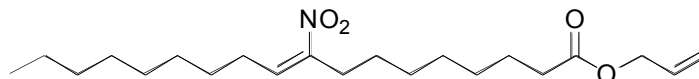


**(E)-10-Nitro-octadec-9-enoic acid, allyl ester (10a).** Compound **9** (1.50 g) was dehydrated according to the general elimination procedure, which upon purification by column chromatography (EtOAc/hexanes, 1-5%) yielded 0.95 g **10a** (74%) as a pale yellow oil. <sup>1</sup>H NMR (300 MHz)  $\delta$  7.03 (t,  $J$  = 7.8 Hz, 1H), 5.88 (ddt, 1H), 5.27 (dq, 1H), 5.20 (dq, 1H), 4.54 (dt,  $J$  = 9.6 Hz, 2H), 2.53 (t,  $J$  = 7.5 Hz, 2H), 2.30 (t,  $J$  = 7.5 Hz, 2H), 2.18 (q,  $J$  = 7.5 Hz, 2H), 1.61 (m, 2H), 1.45 (m, 4H), 1.30-1.26 (br m, 16H), 0.84 (t,  $J$  = 7.5 Hz, 3H). <sup>13</sup>C NMR (75 MHz)  $\delta$  173.2, 151.8, 136.1, 132.2, 117.9, 64.8, 34.0, 31.7, 29.1, 29.04, 29.02, 28.87, 28.82, 28.3, 27.84, 27.78, 26.2, 24.7, 22.5, 14.0. FTIR (KBr)  $\nu$  2928, 2857, 1739, 1667, 1521, 1459, 1336, 1171 cm<sup>-1</sup>.



**(E)-10-Nitro-octadec-9-enoic acid (10).** Compound **10a** (0.50 g) was deprotected according to the general deprotection procedure, which upon purification by column chromatography (1% HOAc, 1-10% EtOAc/hexanes) yielded 0.42 g **10** (95%) as a pale yellow waxy solid. <sup>1</sup>H NMR (300 MHz)  $\delta$  7.07 (t,  $J$  = 7.8 Hz, 1H), 2.56 (t,  $J$  = 7.8 Hz, 2H), 2.36 (t,  $J$  = 7.5 Hz, 2H), 2.21 (q,  $J$  = 7.5 Hz, 2H), 1.64 (m, 2H), 1.45 (m, 4H), 1.37-1.26 (br m, 16H), 0.88 (t,  $J$  = 7.5 Hz, 3H). <sup>13</sup>C NMR (75 MHz)  $\delta$  180.4, 151.8, 136.1, 33.9, 31.7, 29.12, 29.07, 29.00, 28.85, 28.74, 28.3, 27.84, 27.80, 26.2, 24.4, 22.5, 14.0. FTIR (KBr)  $\nu$  3500-2500, 2927, 2856, 1709, 1666, 1519, 1462, 1413, 1336, 1114 cm<sup>-1</sup>.

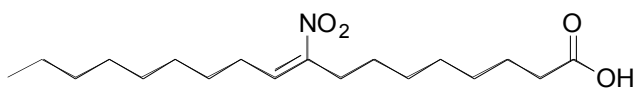
MS (CI)  $m/z$  (%) 328 (10), 310 (75), 156 (100). HRMS calc for C<sub>18</sub>H<sub>34</sub>NO<sub>4</sub>: 328.2488 found 328.2483. See also pages S27 (MS/MS) and S31 (EI).



**(Z)-9-Nitro-octadec-9-enoic acid (9-nitro-elaidic acid), allyl ester (11a).**

Compound **5a** (193 mg) was isomerized according to the general isomerization procedure, which yielded 179 mg crude **11a** (93%) as a pale yellow oil. Analysis by <sup>1</sup>H-

NMR showed (*Z*) isomer 73% of total. <sup>1</sup>H-NMR (300 MHz): δ 5.92 (ddt, 1H); 5.67 (t, *J* = 7.3 Hz, 1H); 5.31 (dq, 1H); 5.23 (dq, 1H); 4.57 (dt, 2H); 2.48 (t, *J* = 7.0 Hz, 2H); 2.33 (apparent t, *J* = 7.6 Hz, 4H); 1.62 (m, 2H); 1.44 (m, 4H); 1.31-1.27 (br m, 16H); 0.88 (t, *J* = 6.8 Hz, 3H). <sup>13</sup>C-NMR (75 MHz): δ 173.4, 151.1, 132.3, 132.0, 118.1, 64.9, 34.1, 32.7, 31.8, 29.25, 29.18, 29.15, 28.9, 28.8, 28.5, 28.2, 27.1, 24.8, 22.6, 14.1. TLC (EtOAc/hexanes, 1:3) *R<sub>f</sub>* = 0.61. FTIR (KBr)  $\nu_{\text{max}}$  2928, 2857, 1735, 1522, 1458, 1341, 1172 cm<sup>-1</sup>. UV  $\lambda_{\text{max}}$  (MeCN) 260 nm.



**(*Z*)-9-Nitro-octadec-9-enoic acid (11).** (General Isomerization Procedure): Diphenyl diselenide (81mg, 0.8 equiv.) was charged to a 25 mL round bottom flask and dissolved in 5-10 mL absolute ethanol at rt, sparged continuously with N<sub>2</sub>. To the bright yellow solution was added sodium borohydride in small portions (5-10 mg) until the solution turned clear (complete reduction to sodium phenylselenide).

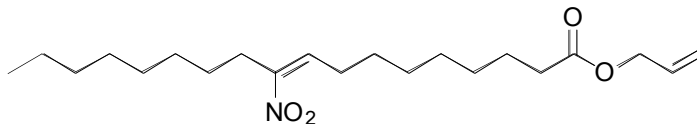
The nitroalkene **5** (103 mg) was dissolved in 1-2 mL absolute ethanol and added dropwise to the stirred and sparged solution of sodium phenylselenide. The solution was stirred, rt, 1 h, then cooled in a dry ice/acetone bath, and a precooled solution of glacial acetic acid (3-4 drops diluted in 1 mL ethanol; 10 equiv.) added dropwise. The solution was stirred, 2 h, -78 °C, then quenched by pouring into 20 mL water. The resulting biphasic solution was partitioned with 10mL EtOAc, separated, and the aqueous phase extracted twice more with 5-10 mL portions of EtOAc. The organic layers were combined, washed with 10-20 mL water and 10-20 mL brine, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered (Celite/silica plug) and the solvent removed under reduced pressure to yield the crude β-nitroselenide<sup>8</sup>. This intermediate can be purified, if desired, by column chromatography (0 – 5% EtOAc/hexanes).

The crude β-nitroselenide was redissolved in a solution of 3 mL chloroform/3 mL THF and cooled in an ice bath (0 °C). To the solution was added slowly H<sub>2</sub>O<sub>2</sub> (30% aq., 1 mL, 20-30 equiv.), then stirred cold 1 h. The solution was then quenched and partitioned with EtOAc (10 mL) and water (20 mL), the aqueous layer extracted 3 × 10 mL EtOAc, then the organic layers combined and washed 3 × 10-20 mL sat'd NaHCO<sub>3</sub>, 2 × 10 mL water, 1 × 20 mL brine, and dried over Na<sub>2</sub>SO<sub>4</sub>. The product was purified by column chromatography. (1% HOAc, 1-10% EtOAc/hexanes) to yield 79.6 mg **11** (77%) as a pale yellow waxy semisolid. Analysis by <sup>1</sup>H-NMR showed the (*E*:*Z*) ratio to be 18:82. An analytical sample (32 mg, 10% yield) of pure **11** was isolated by chromatography (1% MeOH/CHCl<sub>3</sub>). <sup>1</sup>H-NMR (300 MHz): δ 5.66 (t, *J* = 7.3 Hz, 1H); 2.49 (t, *J* = 7.0 Hz, 2H); 2.35 (apparent t, *J* = 7.5 Hz, 4H); 1.62 (m, 2H); 1.45 (m, 4H); 1.32-1.27 (br m, 16H); 0.87 (t, 3H). <sup>13</sup>C-NMR (125 MHz): δ 180.0, 151.2, 131.9, 33.9, 32.7, 31.8, 29.24, 29.18, 29.15, 28.90, 28.82, 28.79, 28.5, 28.2, 27.1, 24.5, 22.6, 14.1. TLC (5% MeOH/CHCl<sub>3</sub>) *R<sub>f</sub>*

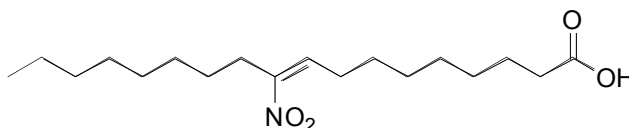
<sup>8</sup> The characteristic <sup>1</sup>H NMR of the □-nitroselenide intermediate is □ 4.45 ppm (td, 1H, *J* = 10.4, 2.7 Hz; HCNO<sub>2</sub>) and 3.30 ppm (dt, 1H, *J* = 9.0, 3.5 Hz; HCSePh, anti) or 3.41 ppm (m, HCSePh, syn) corresponding to the respective diastereomer. The *anti/syn* ratio of the □-nitroselenide corresponds to the *E/-Z*- ratio of the final product. See p.S21 for typical <sup>1</sup>H NMR.



= 0.52. FTIR (KBr)  $\nu_{\text{max}}$  2928, 2857, 2676, 1709, 1522, 1458, 1431, 1338, 1287  $\text{cm}^{-1}$ . UV  $\lambda_{\text{max}}$  (MeCN) 259 nm. MS: See pages S28 (MS/MS) and S32 (EI).

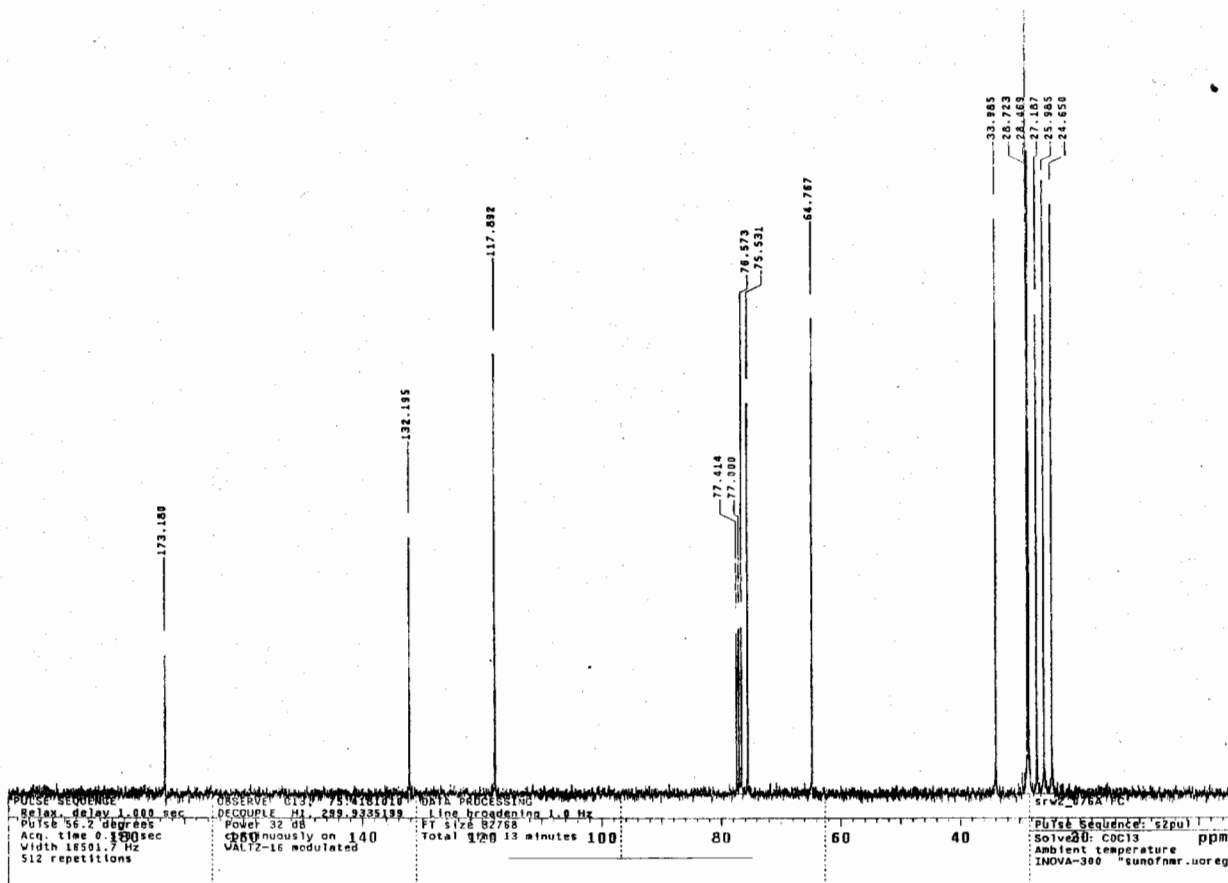
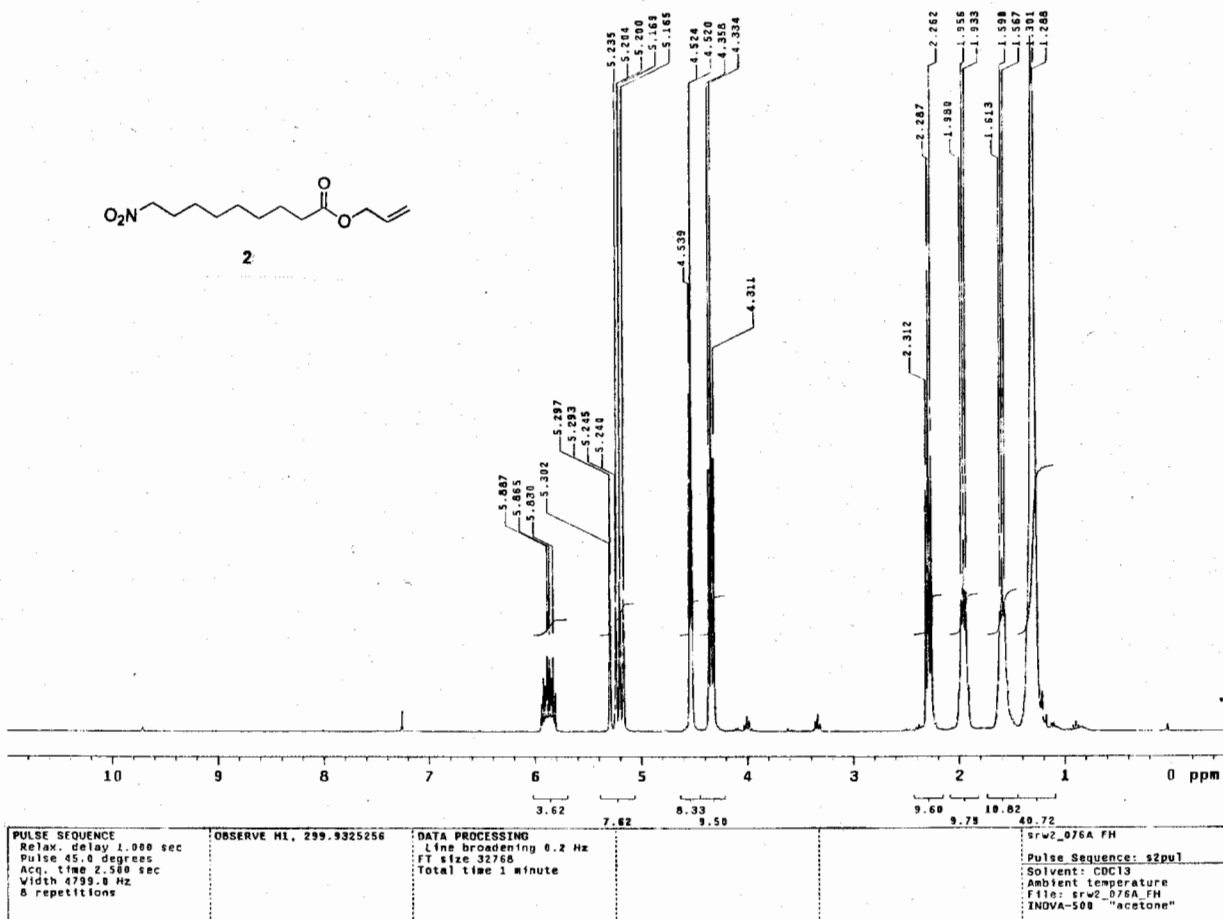
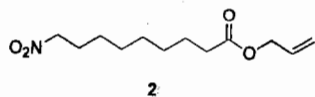


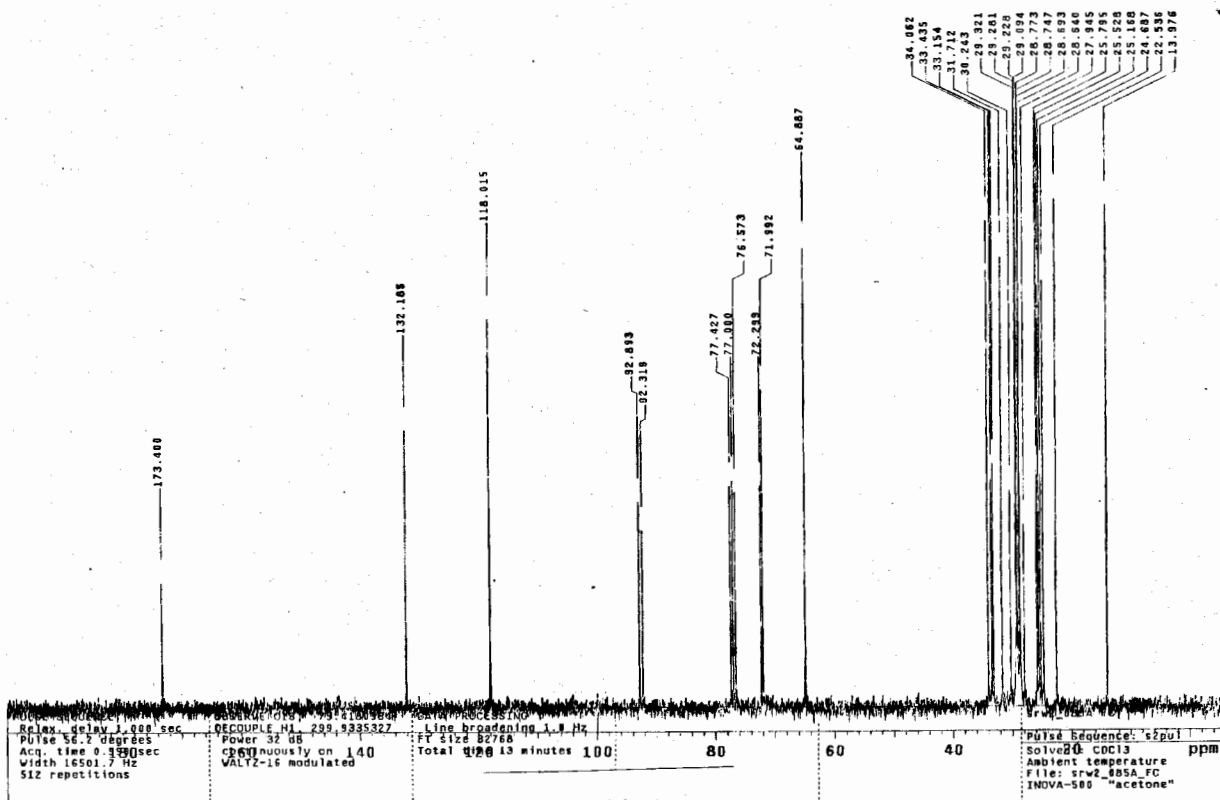
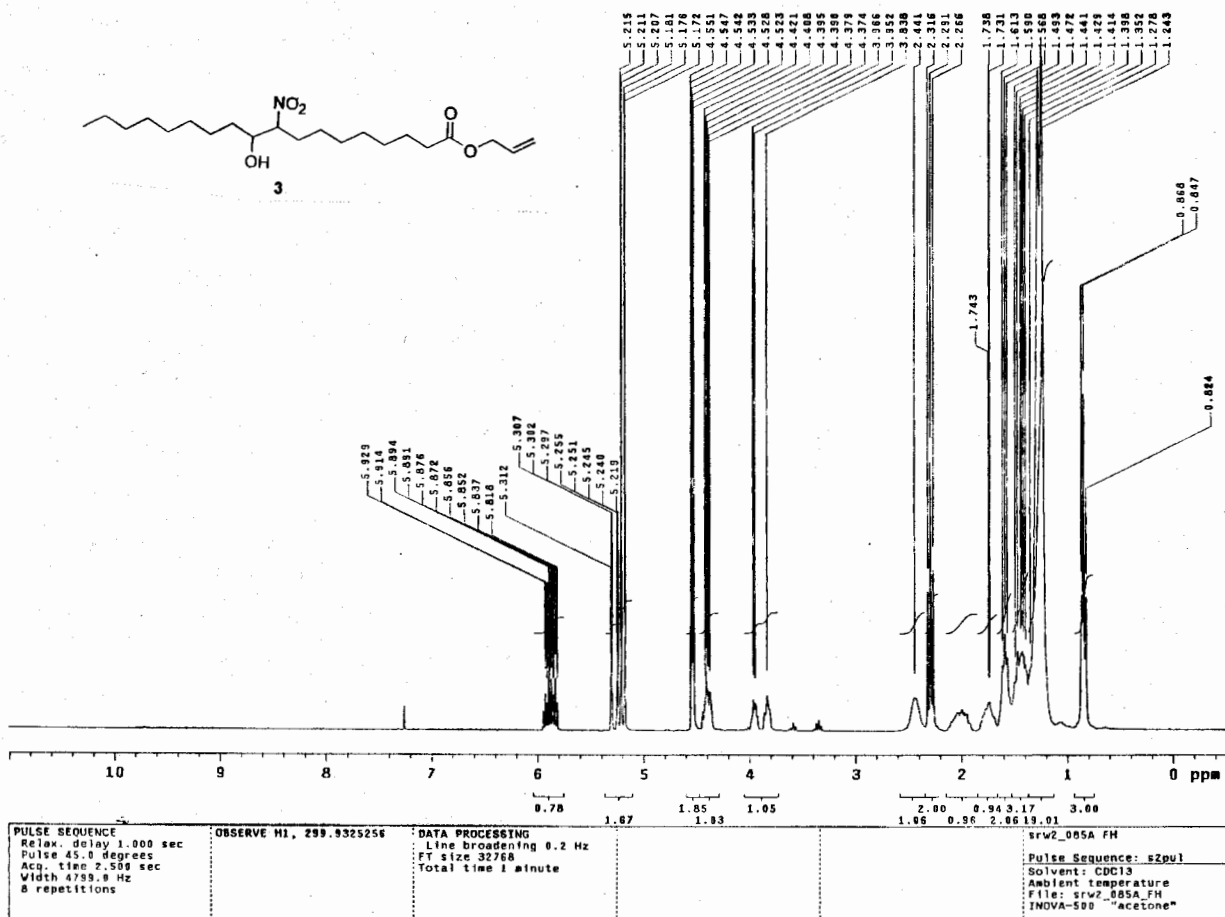
**(Z)-10-Nitro-octadec-9-enoic acid, allyl ester (13a).** Compound **10a** (0.25 g) was isomerized according to the general isomerization procedure, which upon purification yielded 0.19 g **13a** (75%) as a pale yellow oil.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  5.92 (ddt, 1H), 5.67 (t,  $J = 7.5$  Hz, 1H), 5.32 (dq, 1H), 5.24 (dq, 1H), 4.59 (dt,  $J = 9.6$  Hz, 2H), 2.51 (t,  $J = 7.5$  Hz, 2H), 2.35 (apparent t, 4H), 1.64 (m, 2H), 1.45 (m, 4H), 1.32-1.27 (br m, 16H), 0.89 (t,  $J = 7.5$  Hz, 3H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  173.3, 151.3, 132.2, 131.5, 118.0, 64.8, 34.1, 32.6, 31.7, 29.07, 29.04, 28.87, 28.72, 28.63, 28.1, 27.1, 24.8, 22.5, 14.0. FTIR (KBr)  $\nu$  2928, 2857, 1739, 1649, 1522, 1464, 1345, 1171  $\text{cm}^{-1}$ .

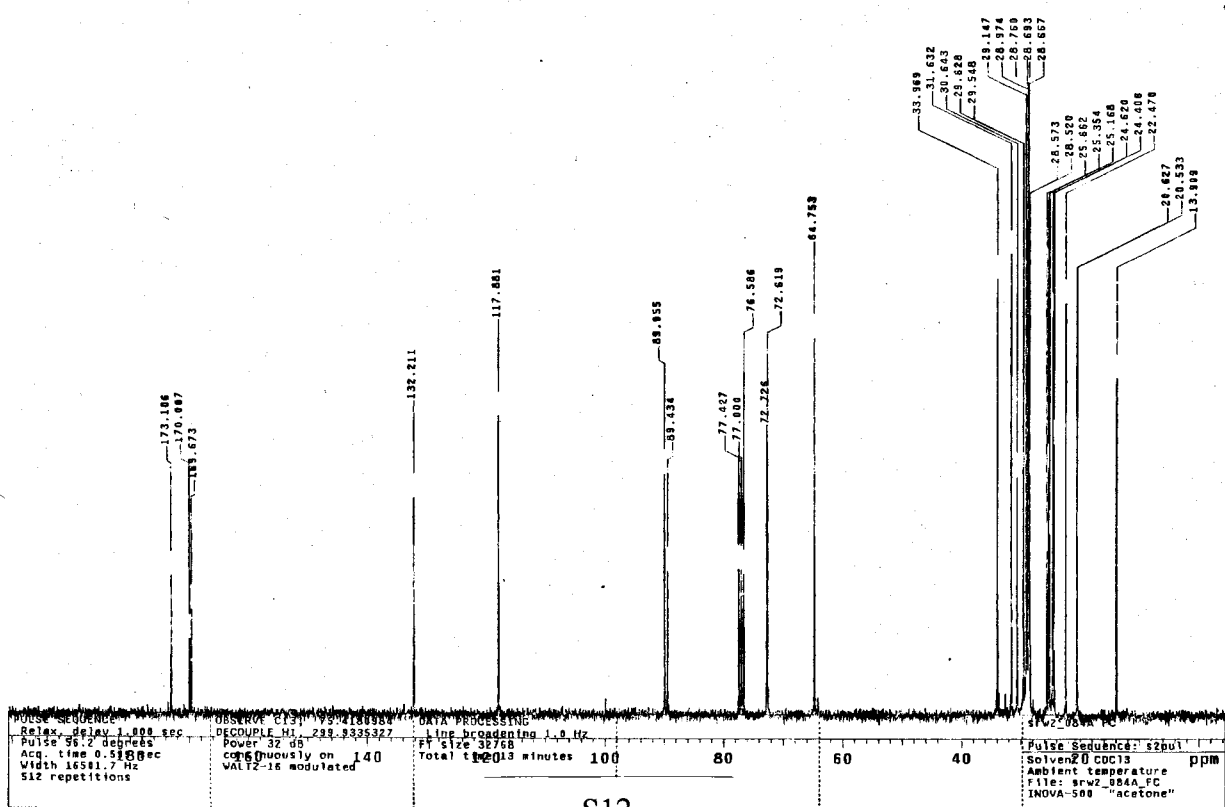
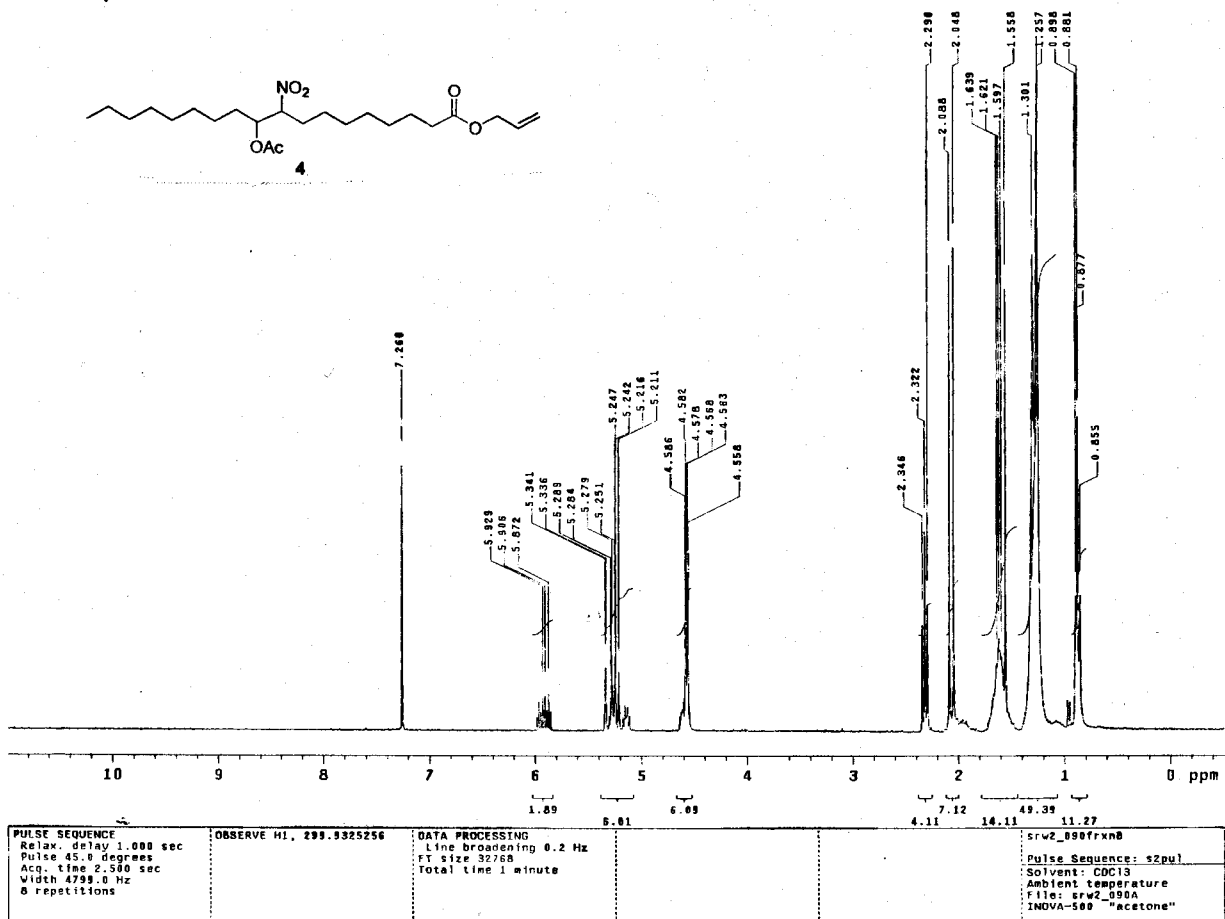


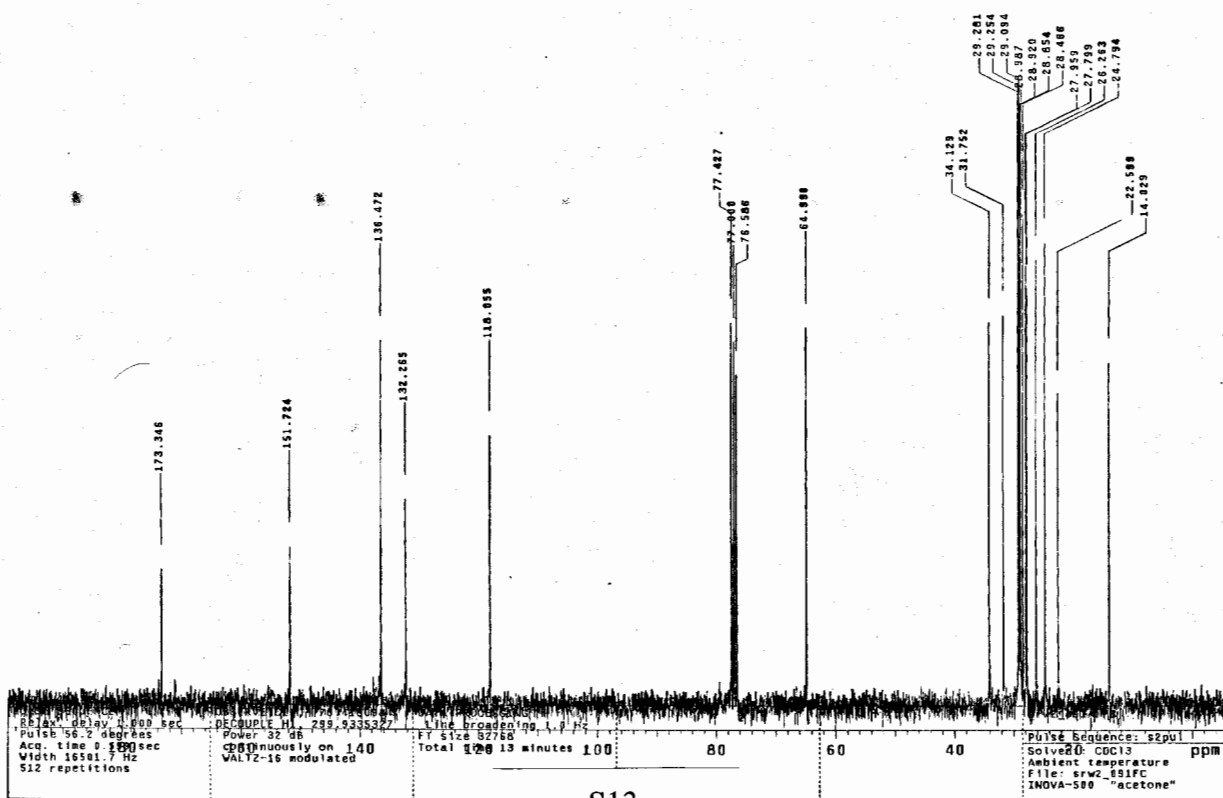
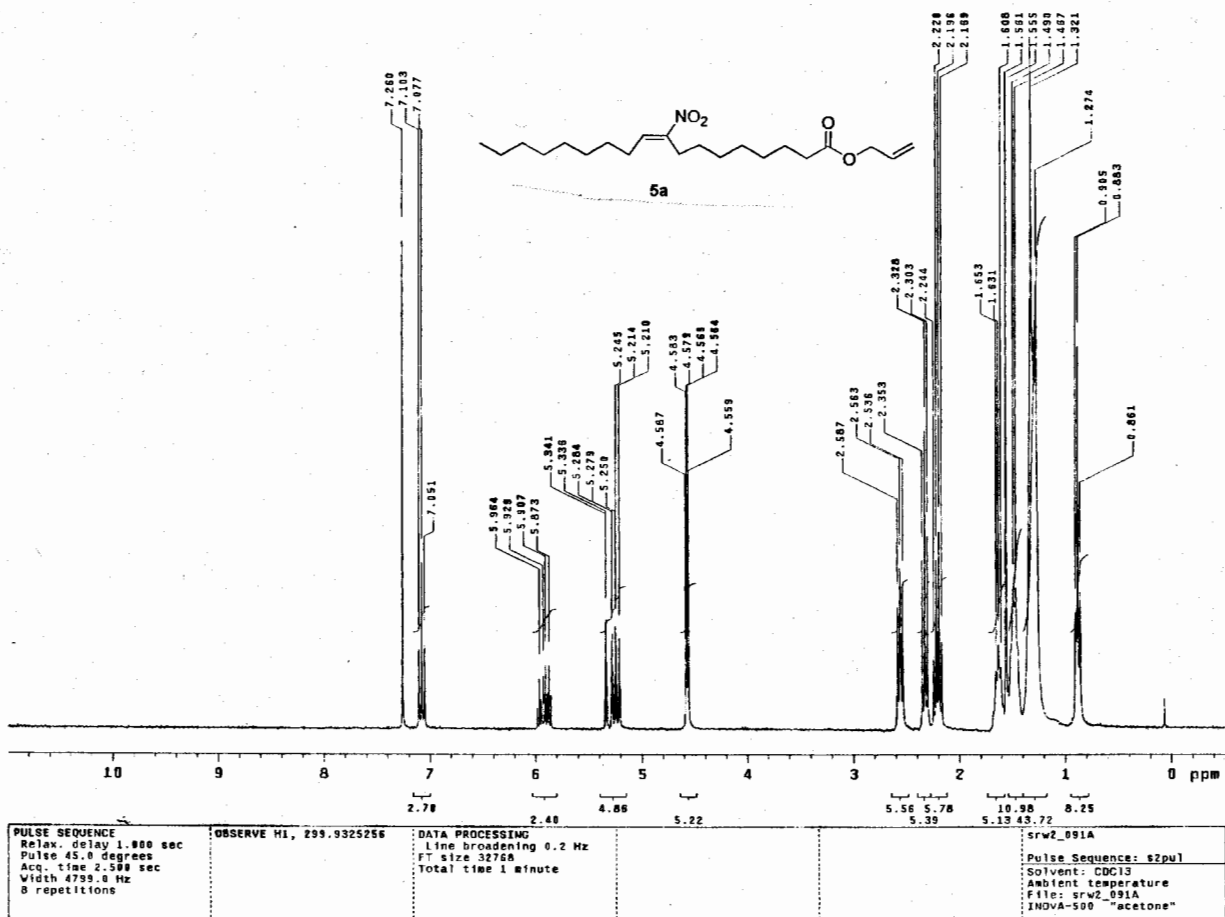
**(Z)-10-Nitro-octadec-9-enoic acid (13).** Compound **10** (0.30 g) was isomerized according to the general isomerization procedure, which yielded 0.23 g crude **13** (76%) as a pale yellow waxy solid.  $^1\text{H}$  NMR showed the (Z) isomer to be 85% of total. An analytical amount of pure **13** was isolated by chromatography (1% MeOH/ $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (300 MHz)  $\delta$  5.65 (t,  $J = 7.5$  Hz, 1H), 2.49 (t,  $J = 6.9$  Hz, 2H), 2.33 (apparent t, 4H), 1.62 (m, 2H), 1.45 (m, 4H), 1.331-1.26 (br m, 16H), 0.87 (t,  $J = 6.6$  Hz, 3H).  $^{13}\text{C}$  NMR (75 MHz)  $\delta$  180.0, 151.4, 131.5, 34.0, 32.7, 31.8, 29.14, 28.94, 28.86, 28.80, 28.71, 28.2, 27.2, 24.5, 22.6, 14.1. FTIR (KBr)  $\nu$  3500-2500, 2928, 2857, 1709, 1551, 1522, 1465, 1340, 1285  $\text{cm}^{-1}$ . MS: See pages S29 (MS/MS) and S33 (EI).

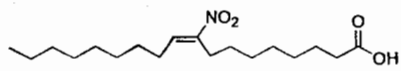
CAS Registry numbers: 9-bromononanoic acid: 41059-02-3, 9-bromononanoic acid allyl ester: 109849-93-6, (*E*)-9-nitrooctadec-9-enoic acid (**5**): 875685-44-2; 1-nitrononane (**6**): 2216-21-9, 9-oxononanoic acid: 2553-17-5, (*E*)-10-nitrooctadec-9-enoic acid (**10**): 875685-46-4.



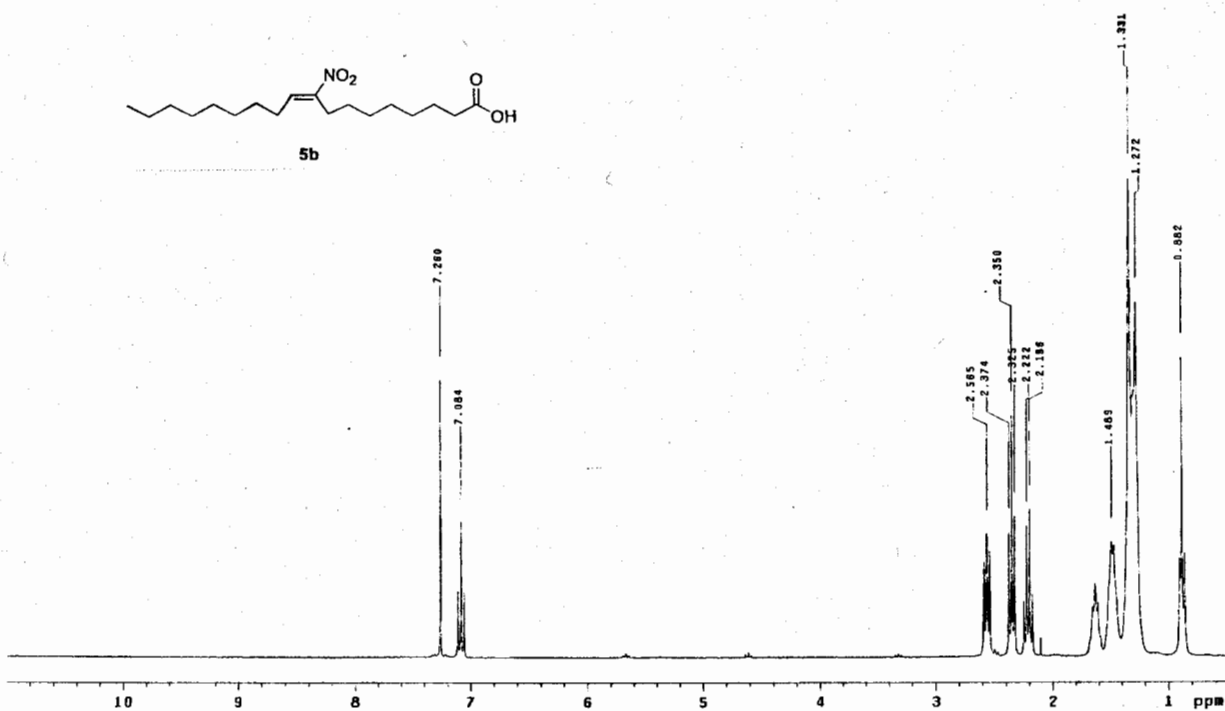




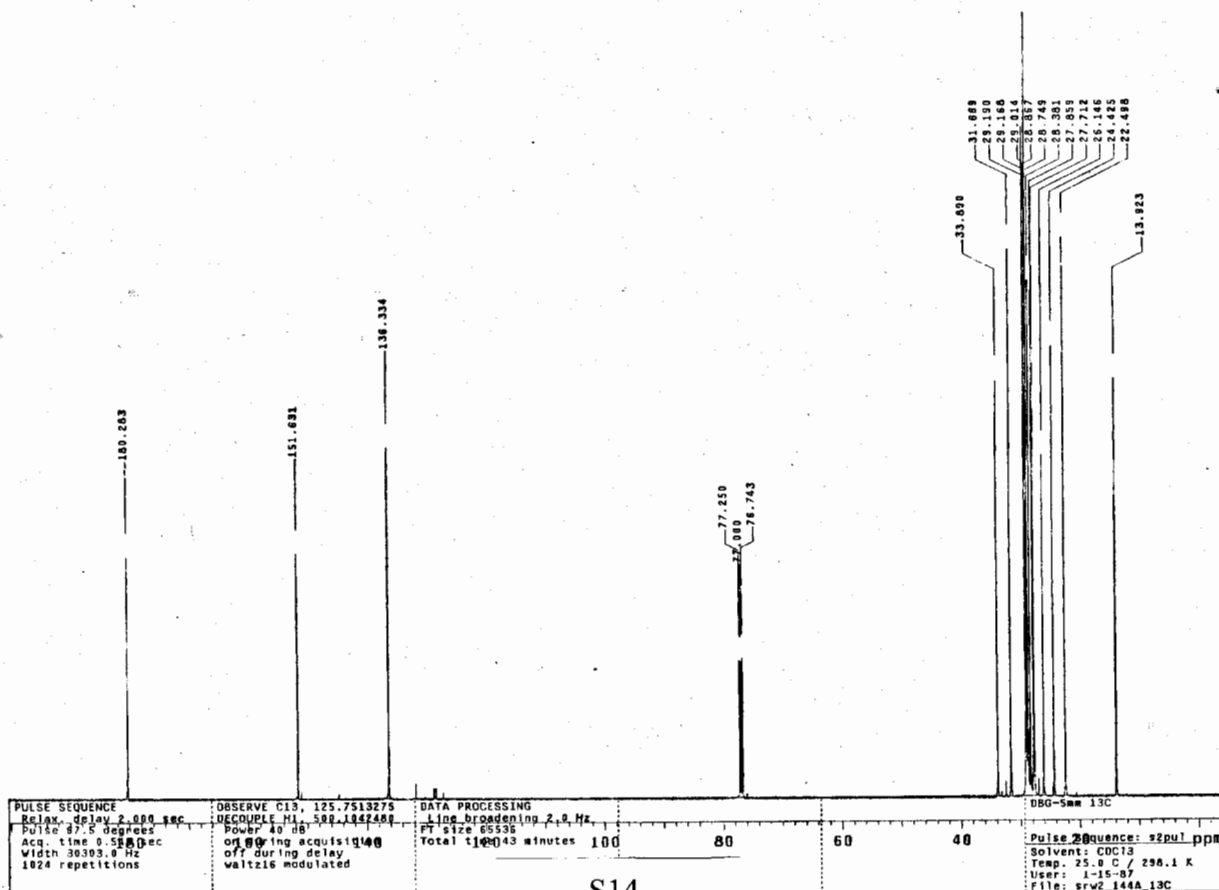




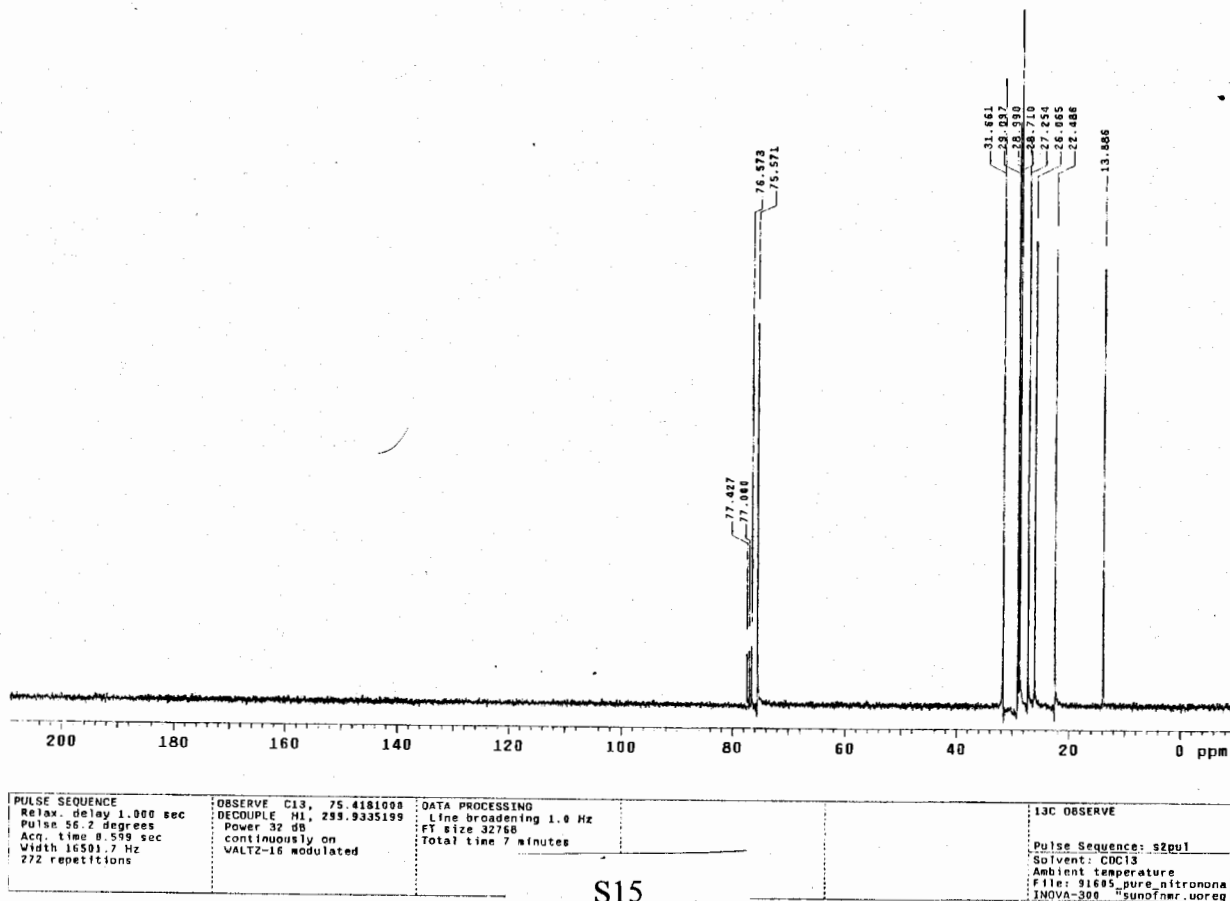
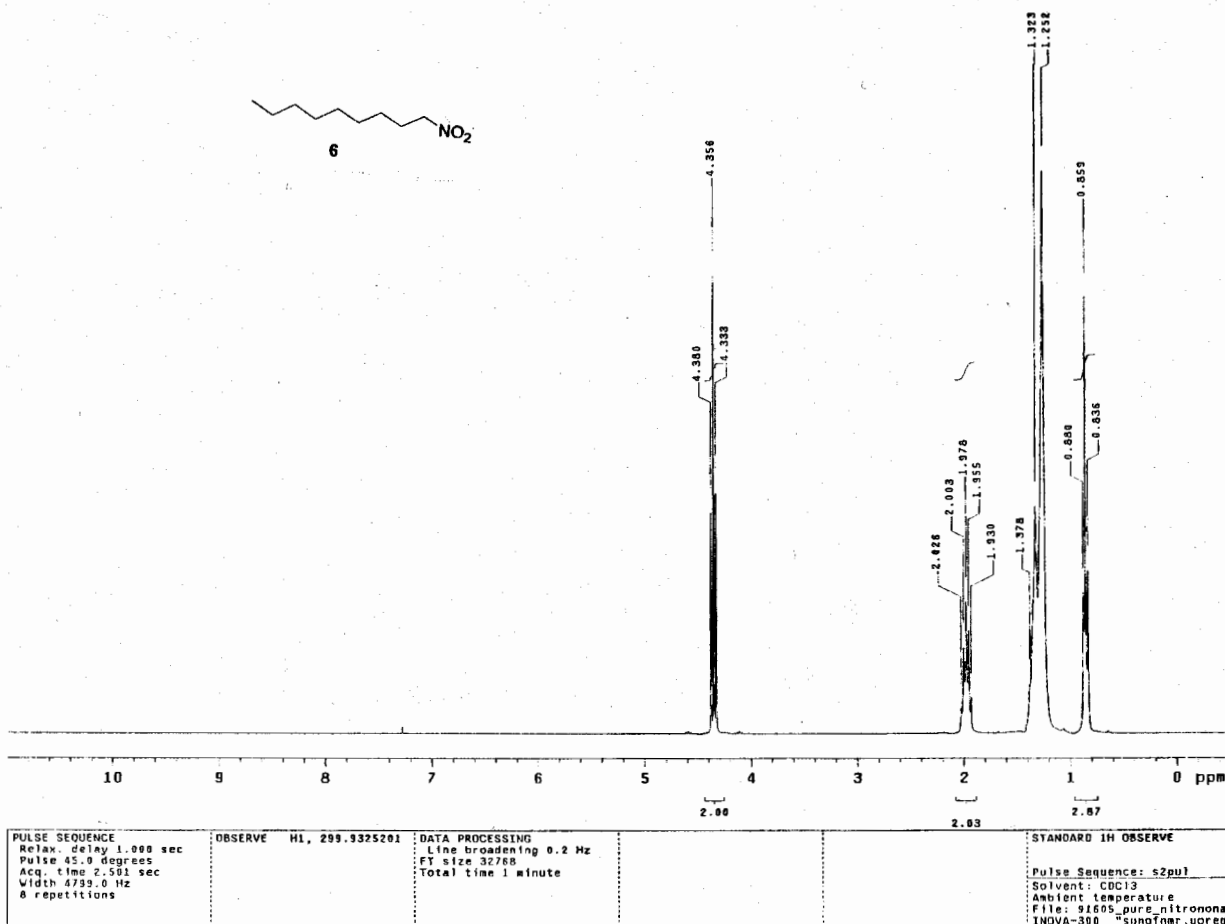
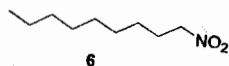
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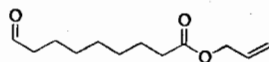


<b>PULSE SEQUENCE</b> Relax. delay 1.000 sec Pulse 45.0 degrees Acq. time 2.581 sec Width 4798.0 Hz 16 repetitions	<b>OBSERVE</b> H1, 299.9325259	<b>DATA PROCESSING</b> Line broadening 0.2 Hz FT size 32768 Total time 1 minute	srw2_144A 9-nitrooleic acid Pulse Sequence: s2pu1 Solvent: CDCl3 Ambient temperature INOVA-300 "sunofmr.uoreg"
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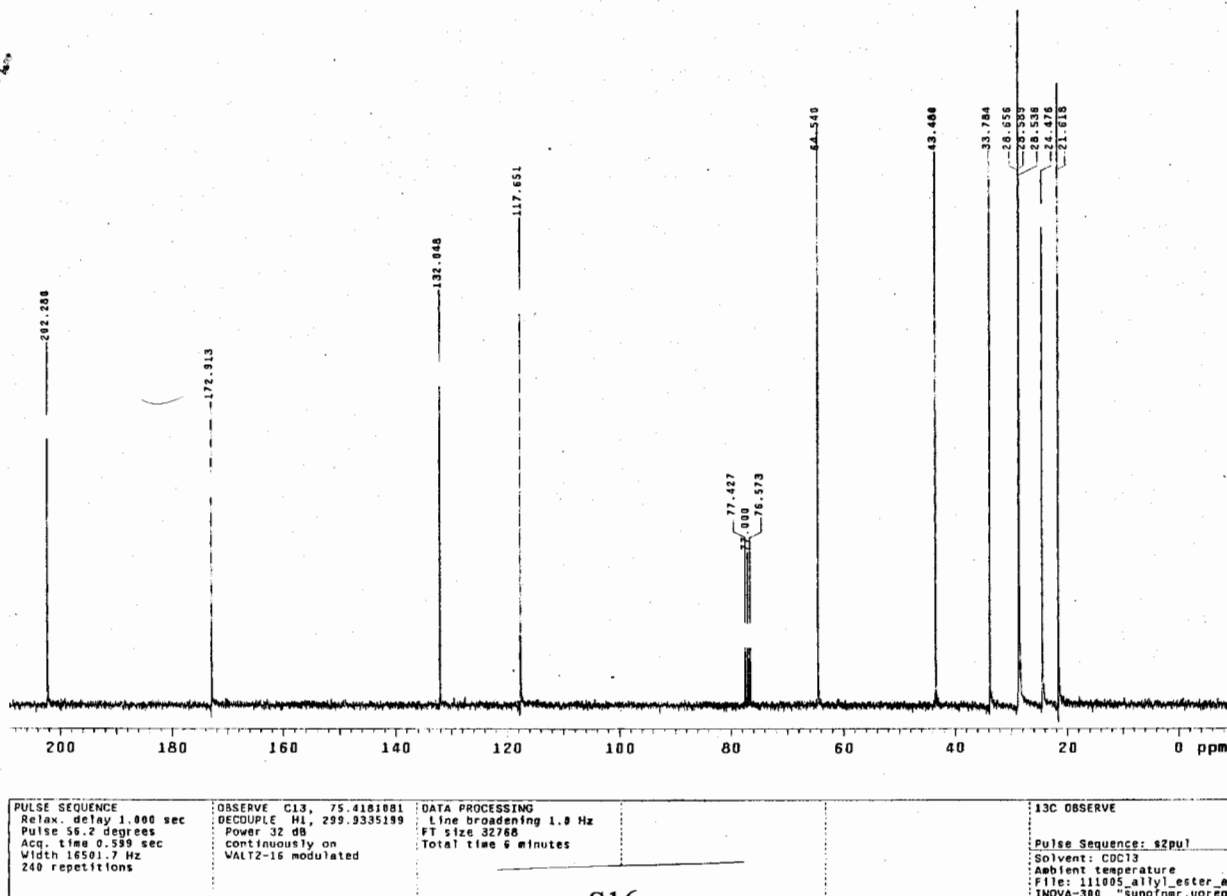
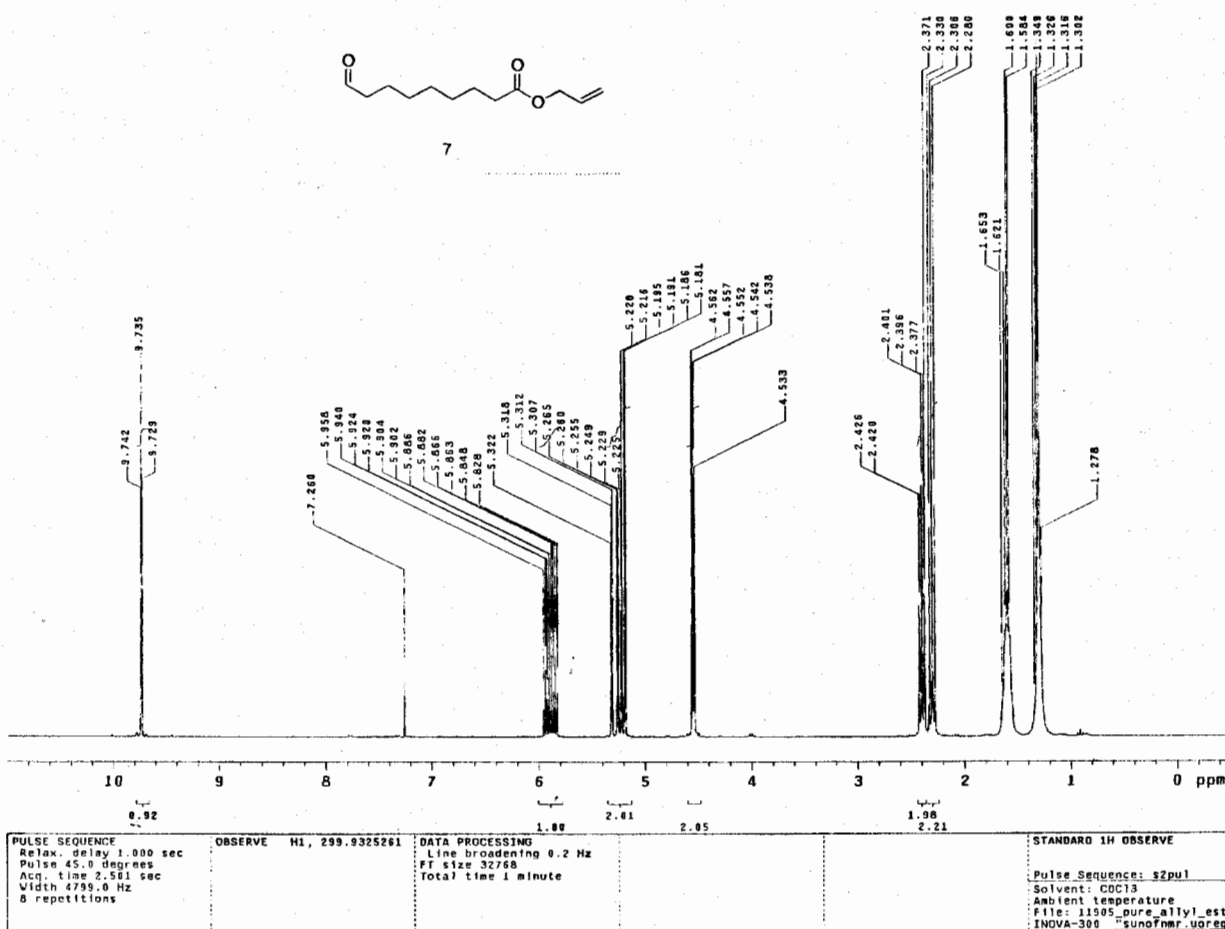


<b>PULSE SEQUENCE</b> Relax. delay 2.000 sec Pulse 87.5 degrees Acq. time 0.580 sec Width 30393.0 Hz 1824 repetitions	<b>OBSERVE</b> C13, 125.7513275 <b>DECOUPLE</b> H1, 500.1347400 Power 40 dB on during acquisition off during delay waltz16 modulated	<b>DATA PROCESSING</b> Line broadening 2.0 Hz FT size 65536 Total time 43 minutes	080-Sm 13C Pulse Sequence: s2pu1 ppm Solvent: CDCl3 Temp: 25.0 C / 298.1 K User: j-15-07 File: srw2_144A_13C
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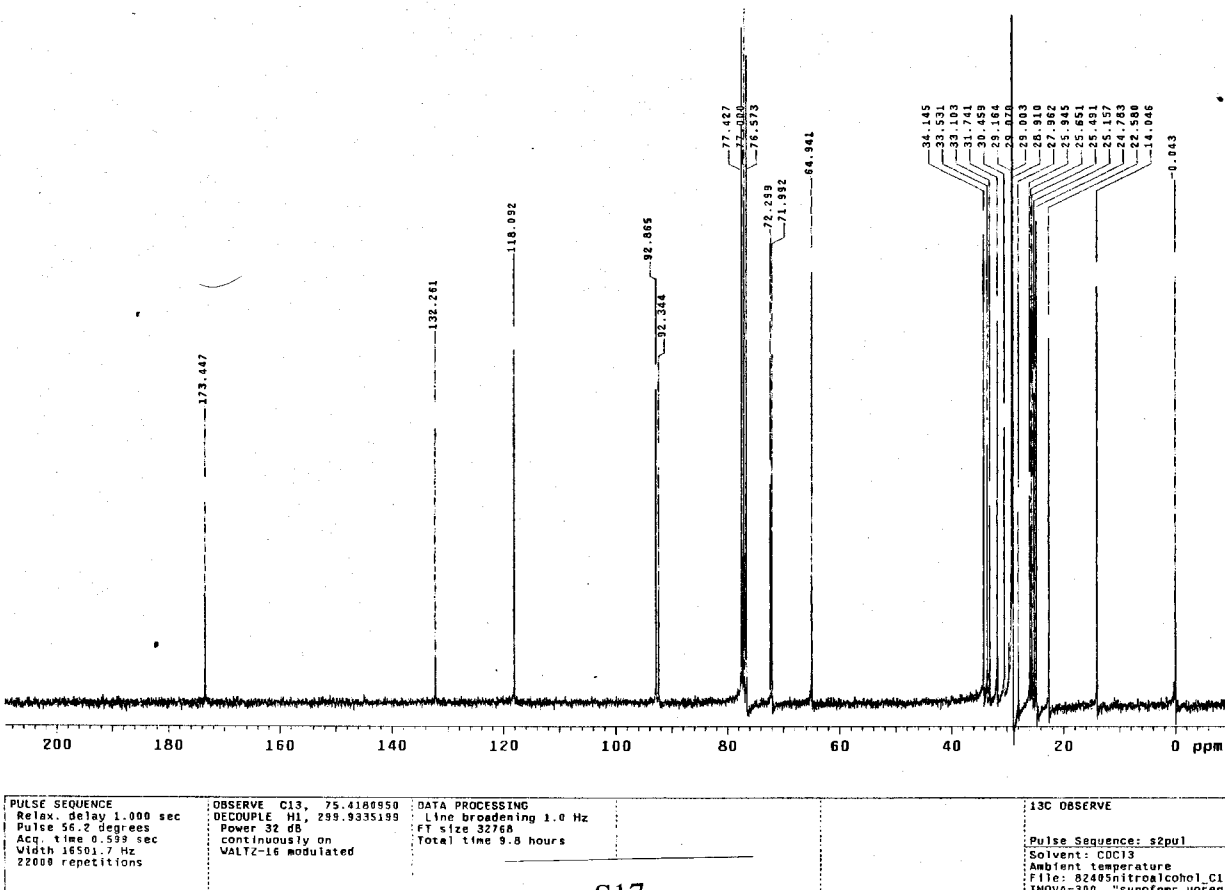


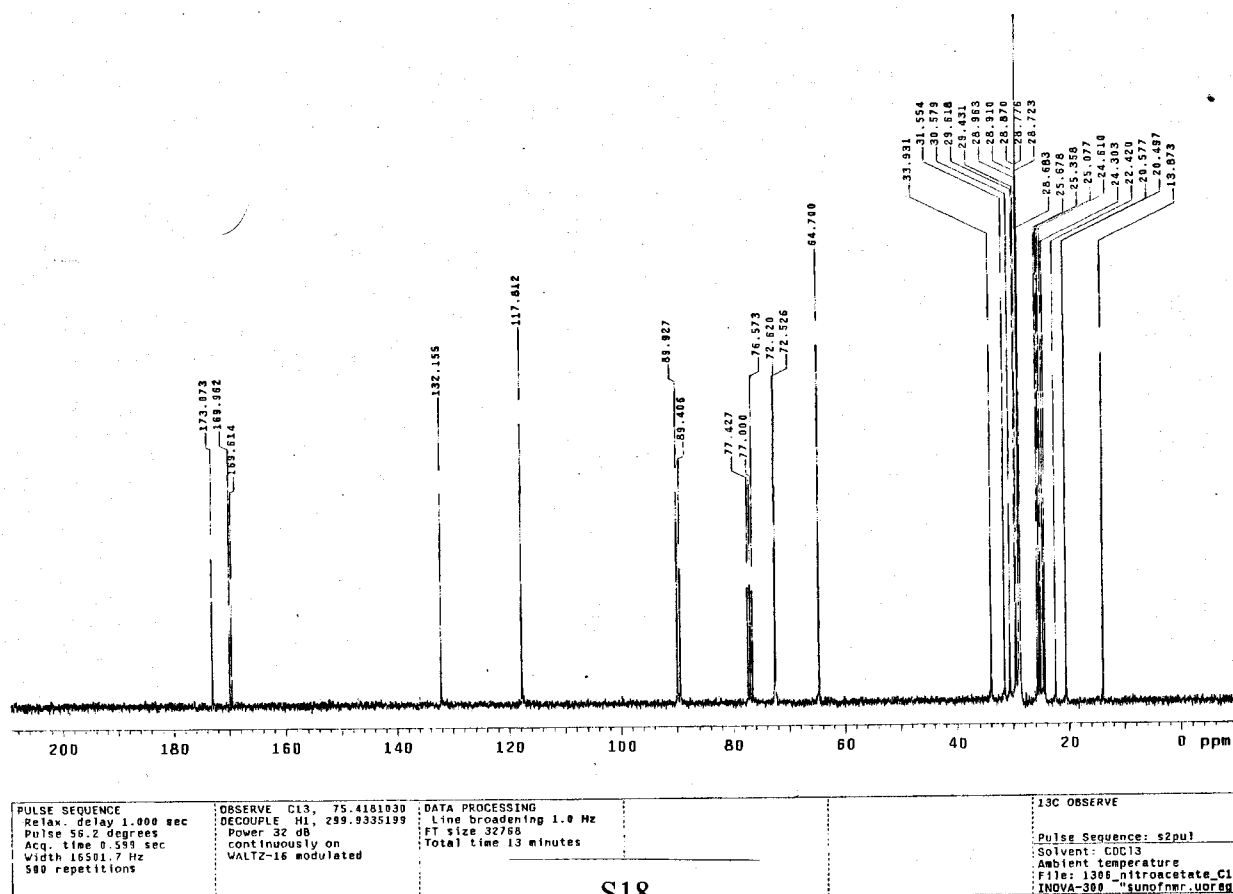
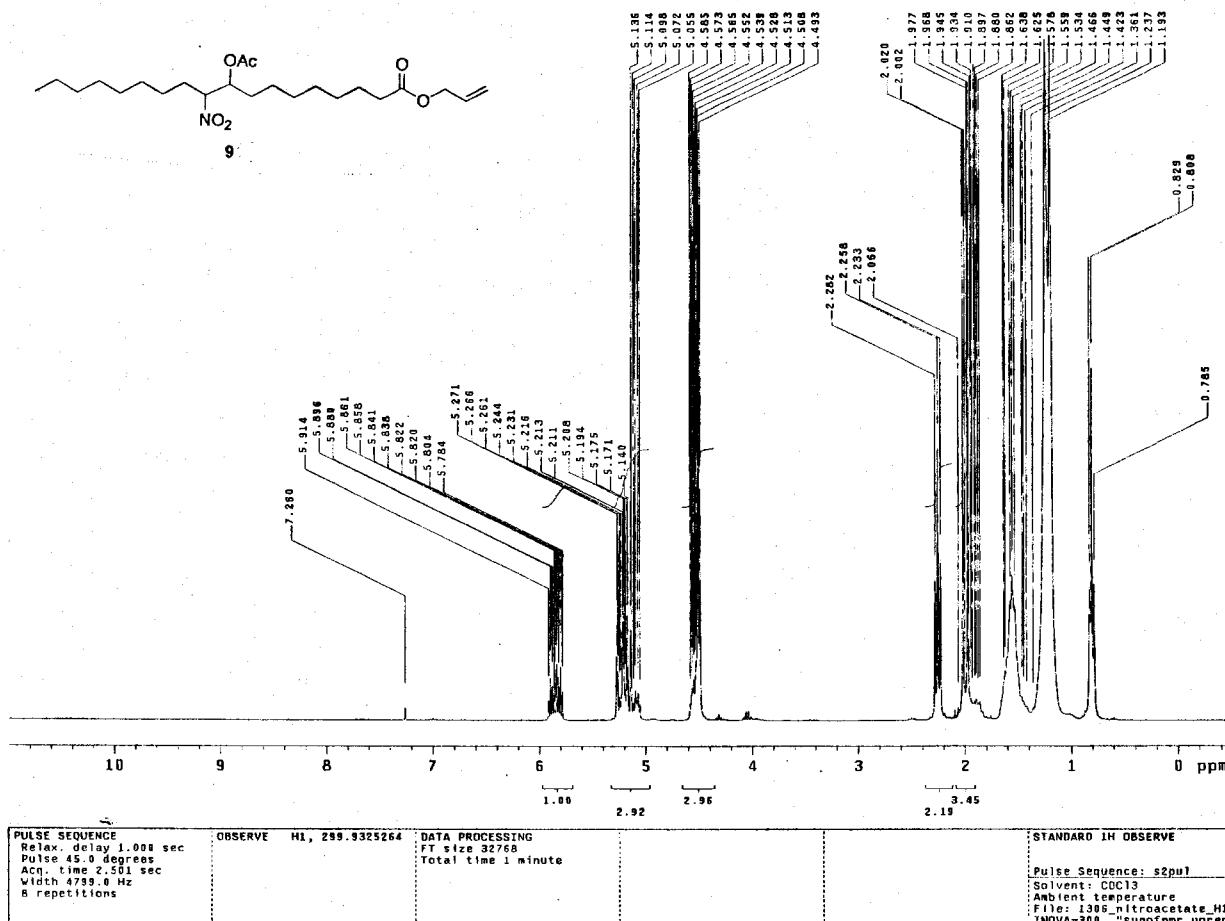


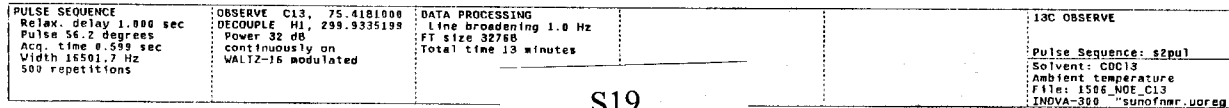
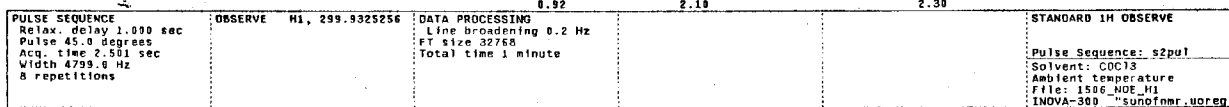
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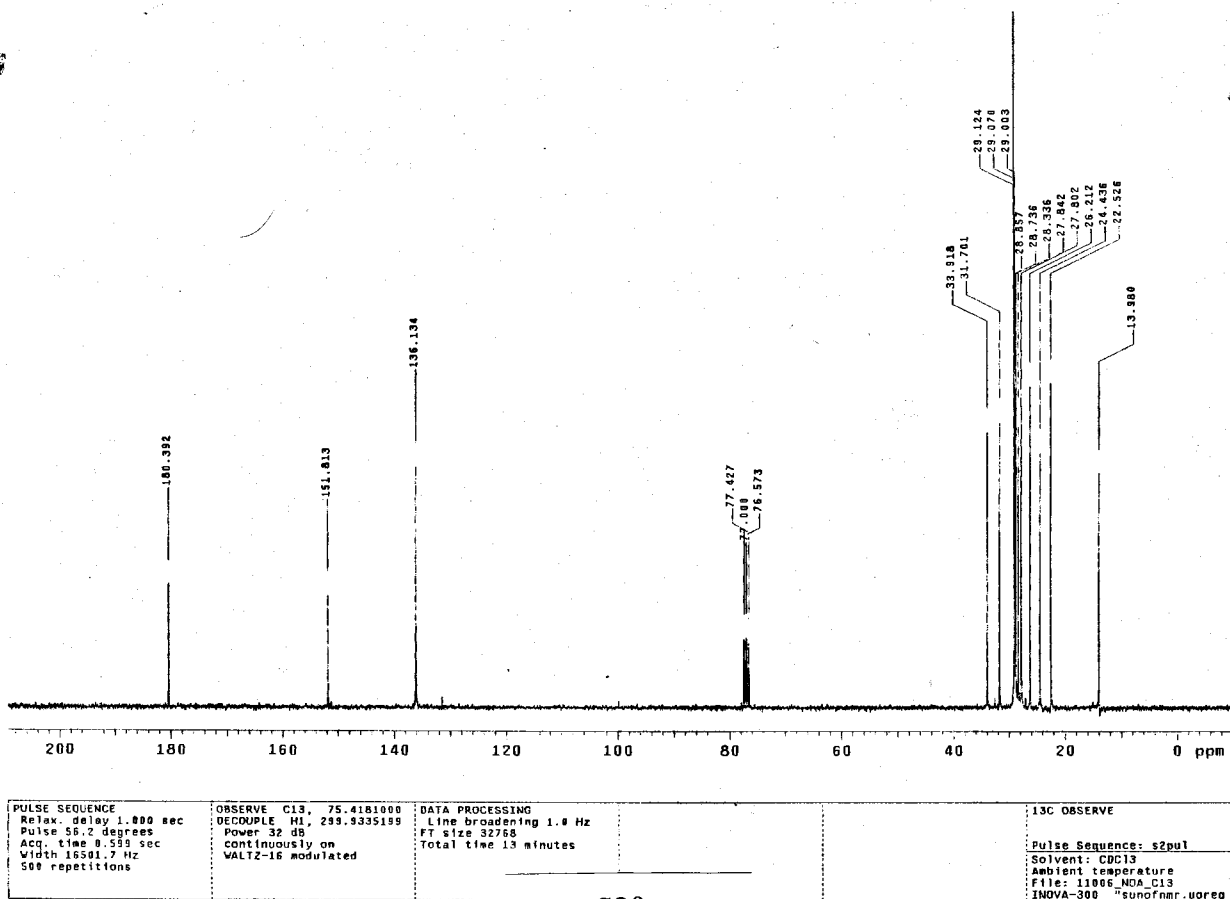
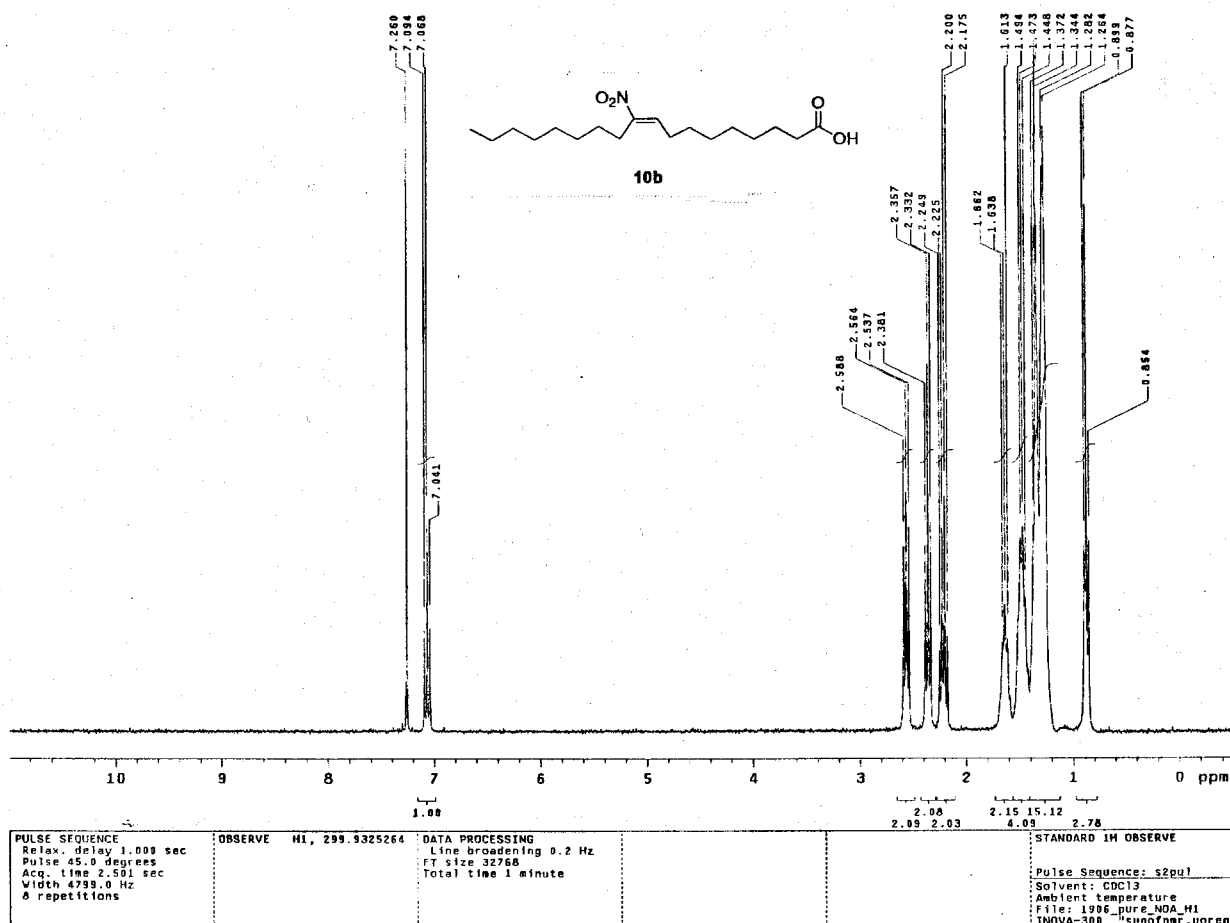


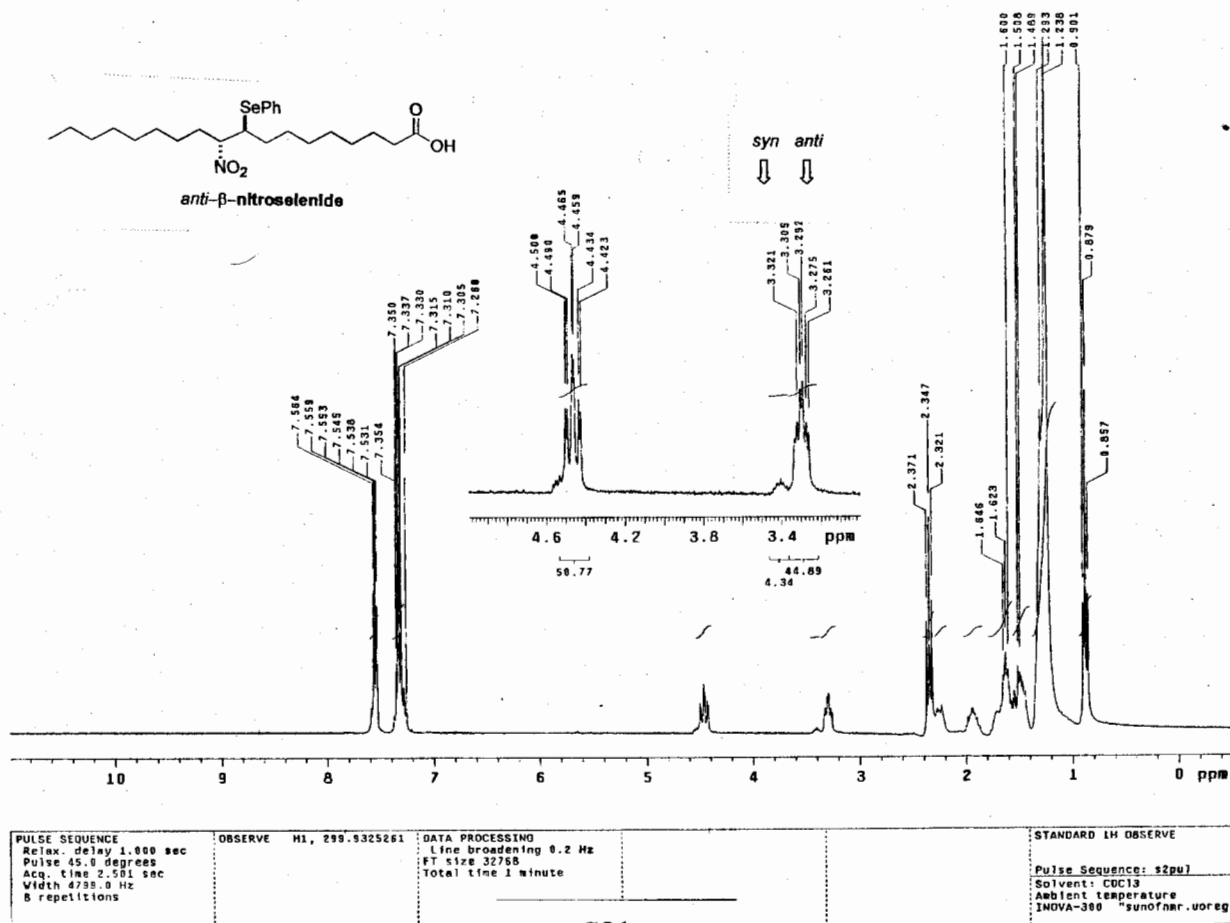
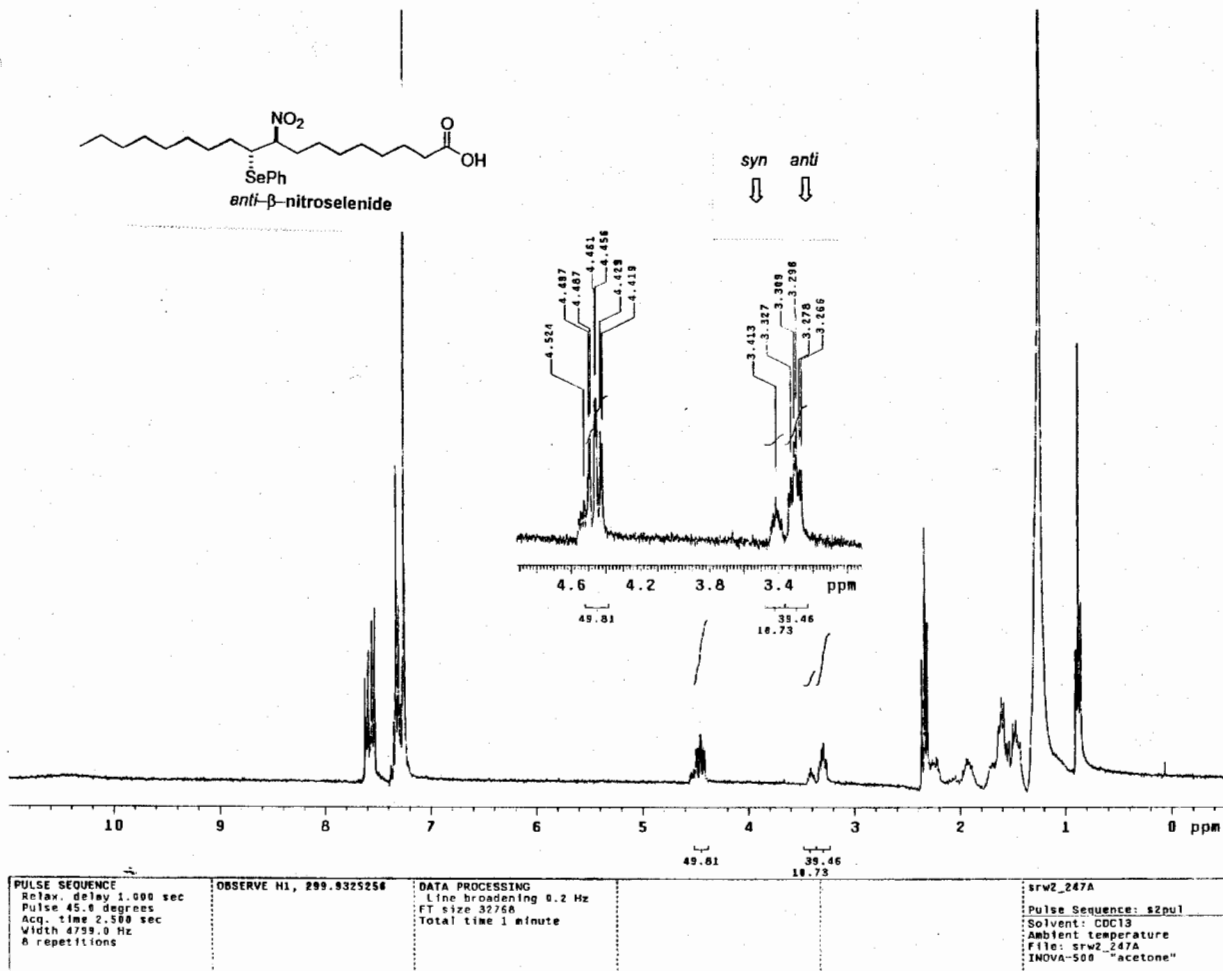


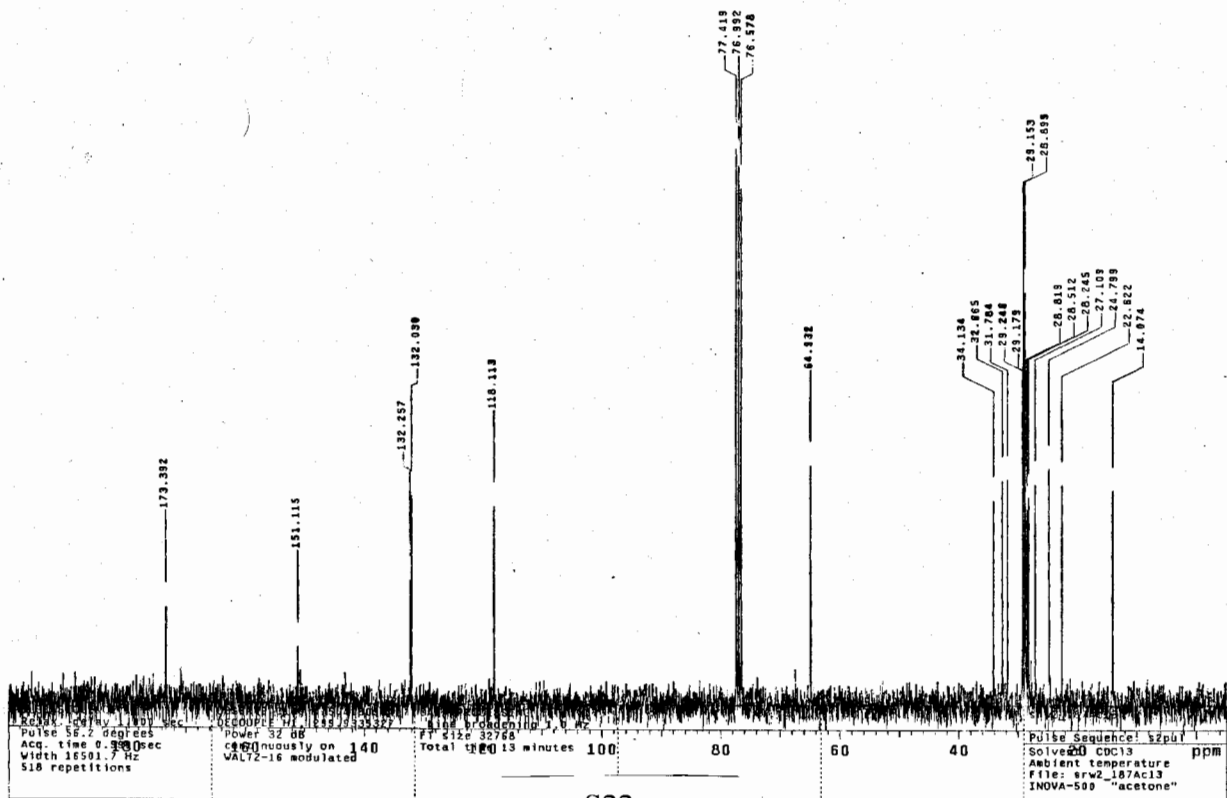
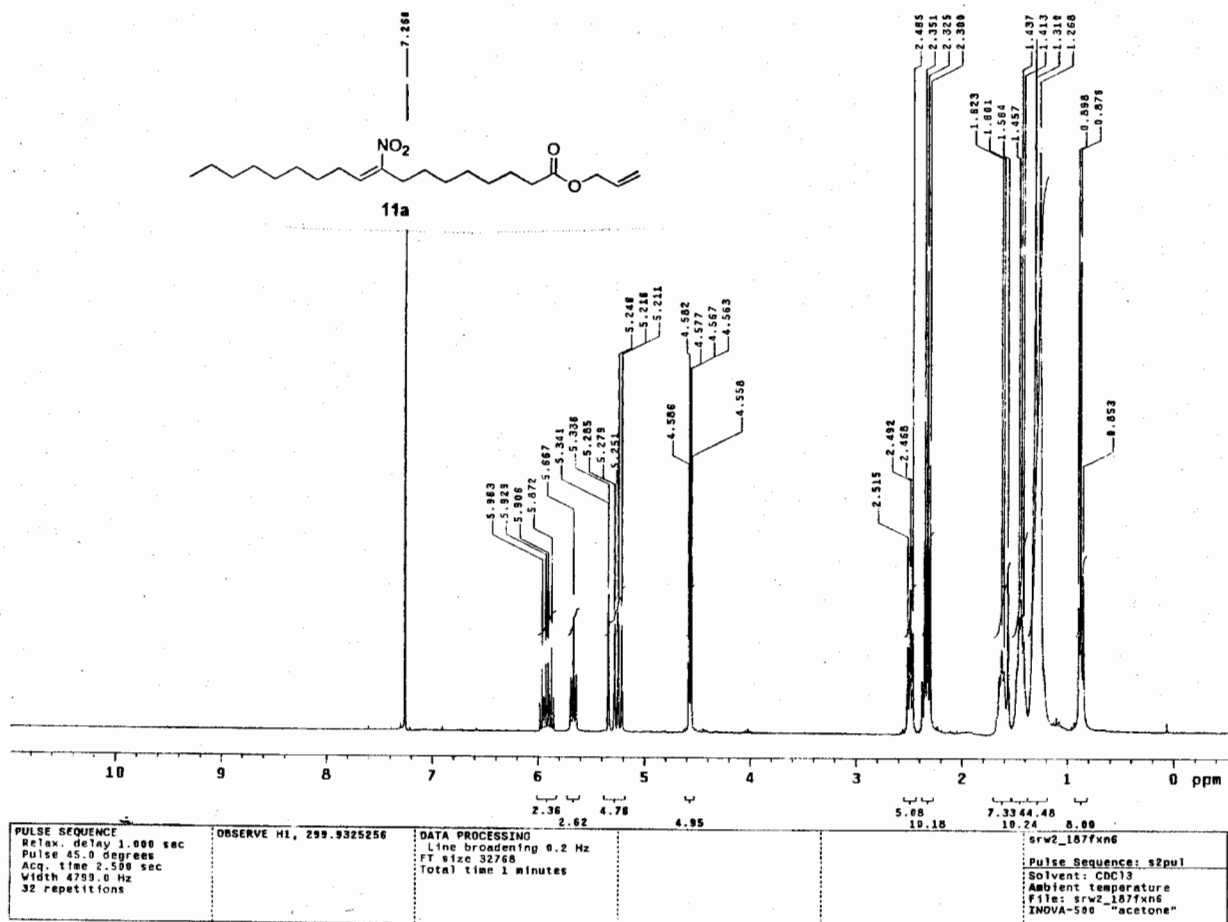


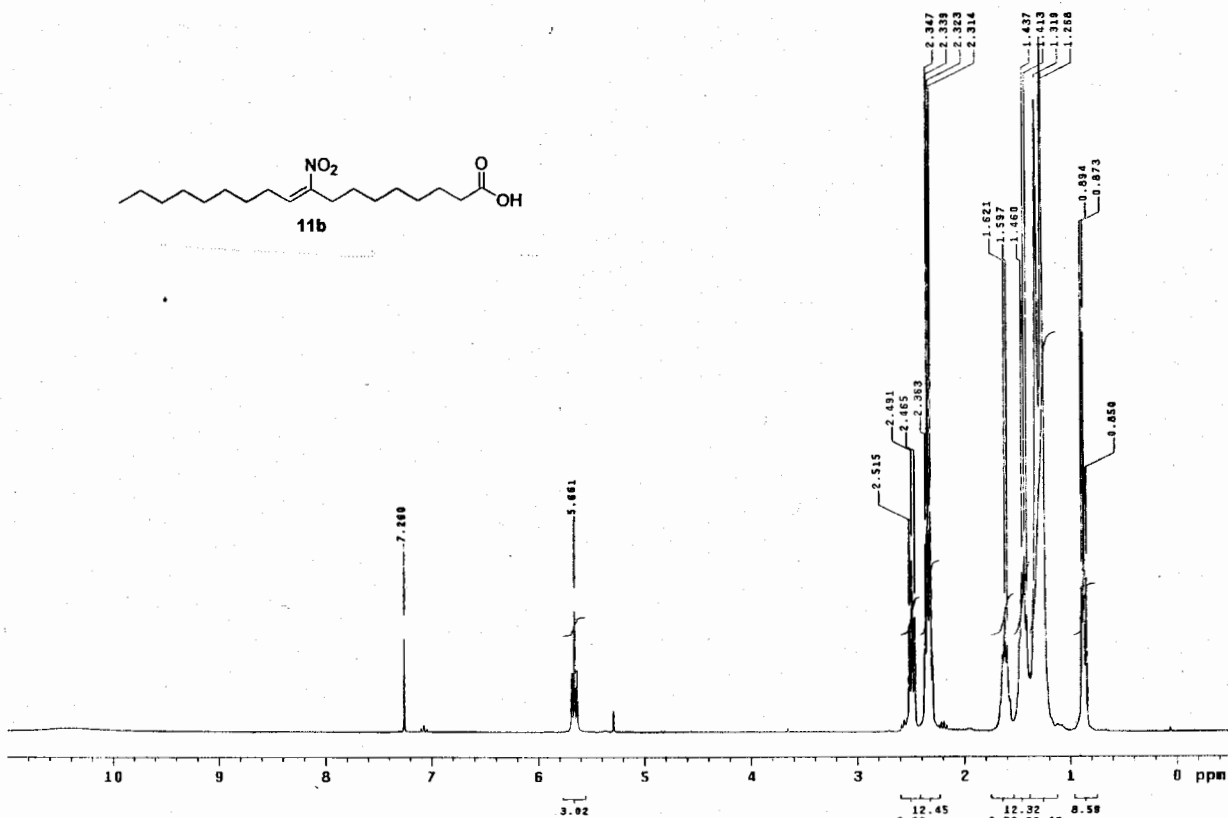




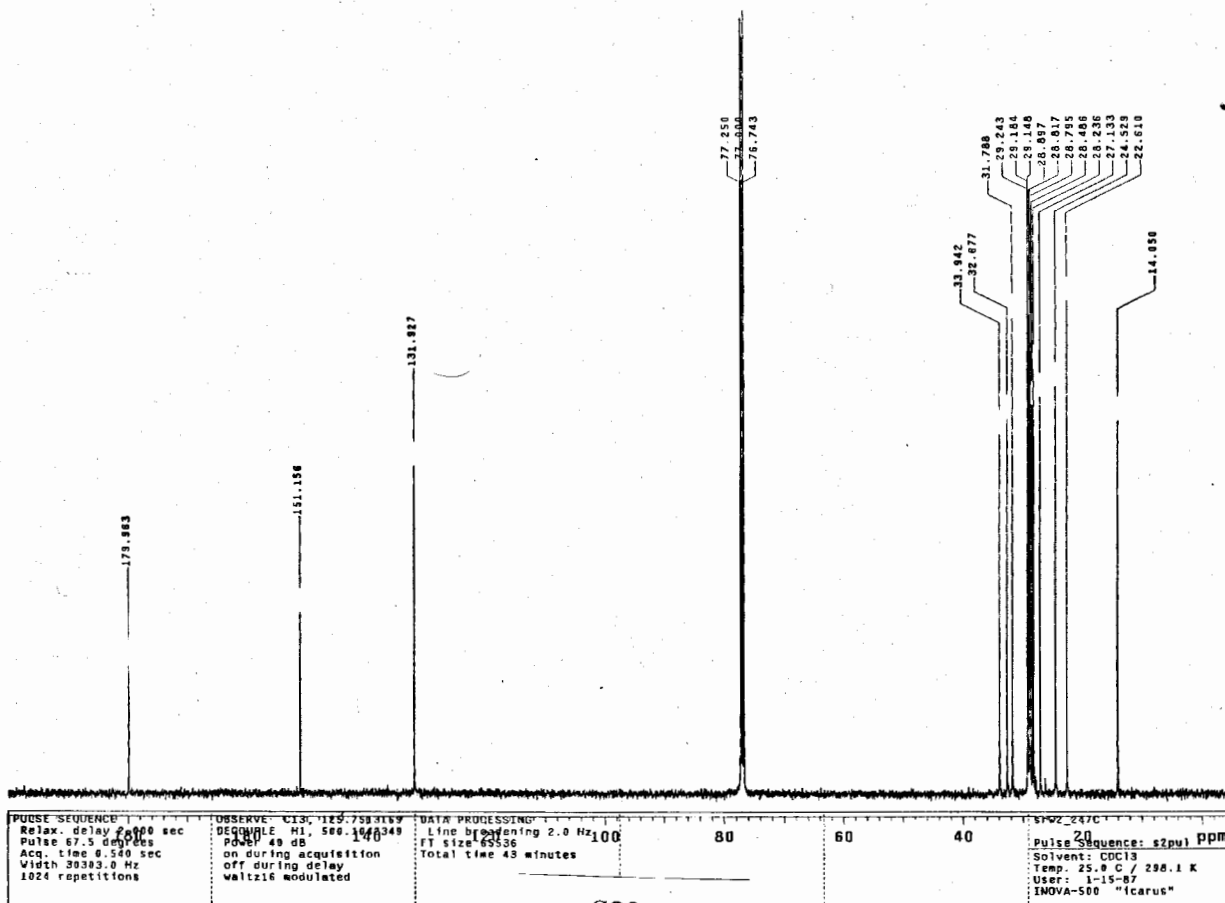


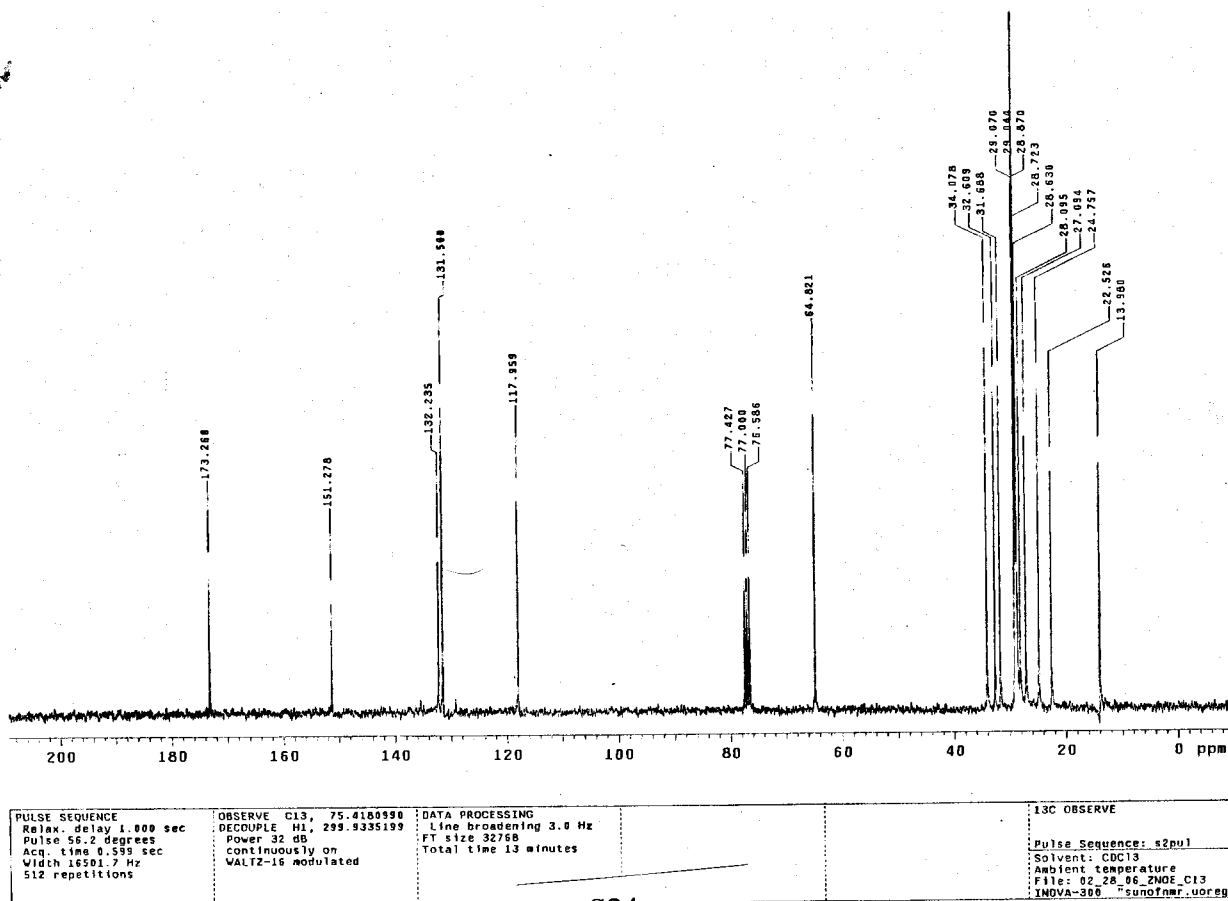
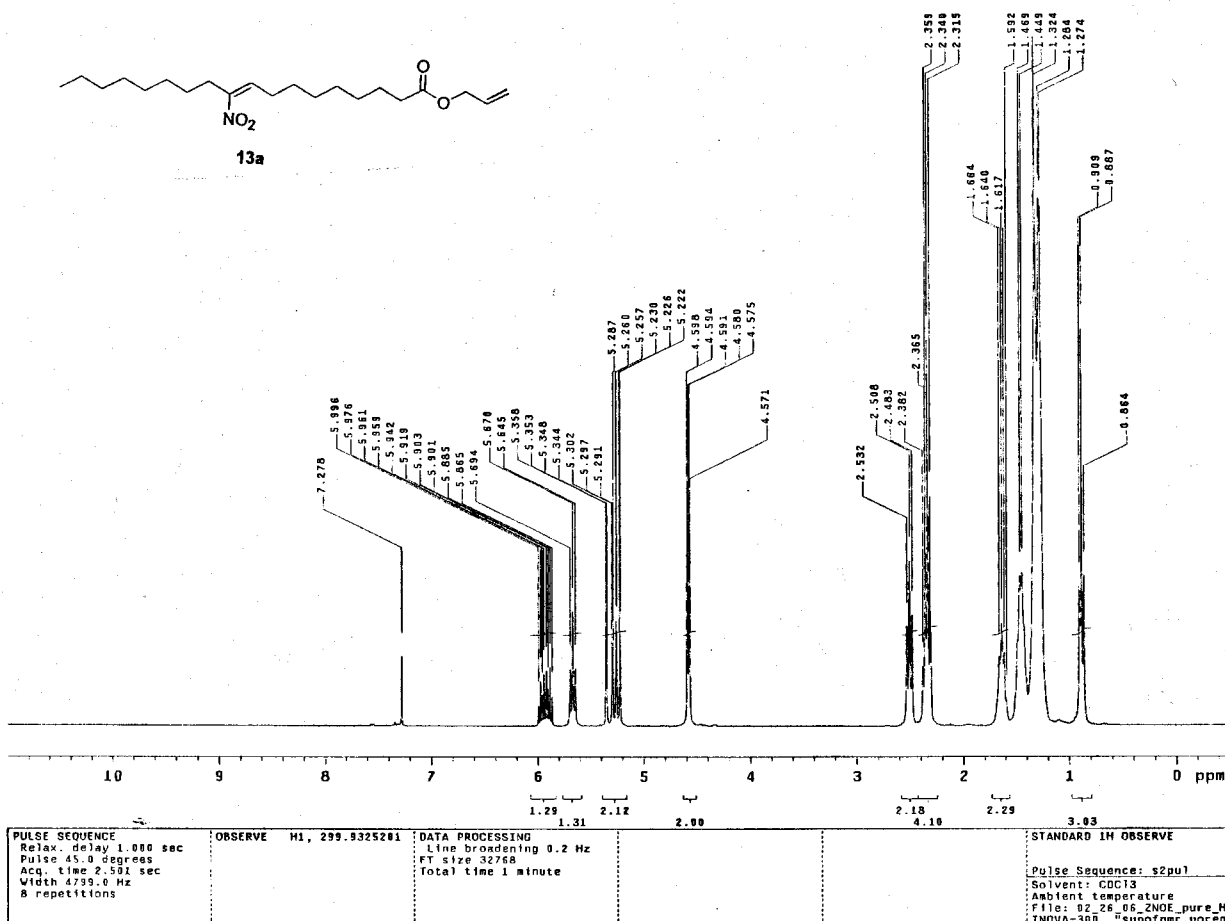
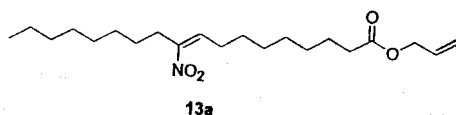




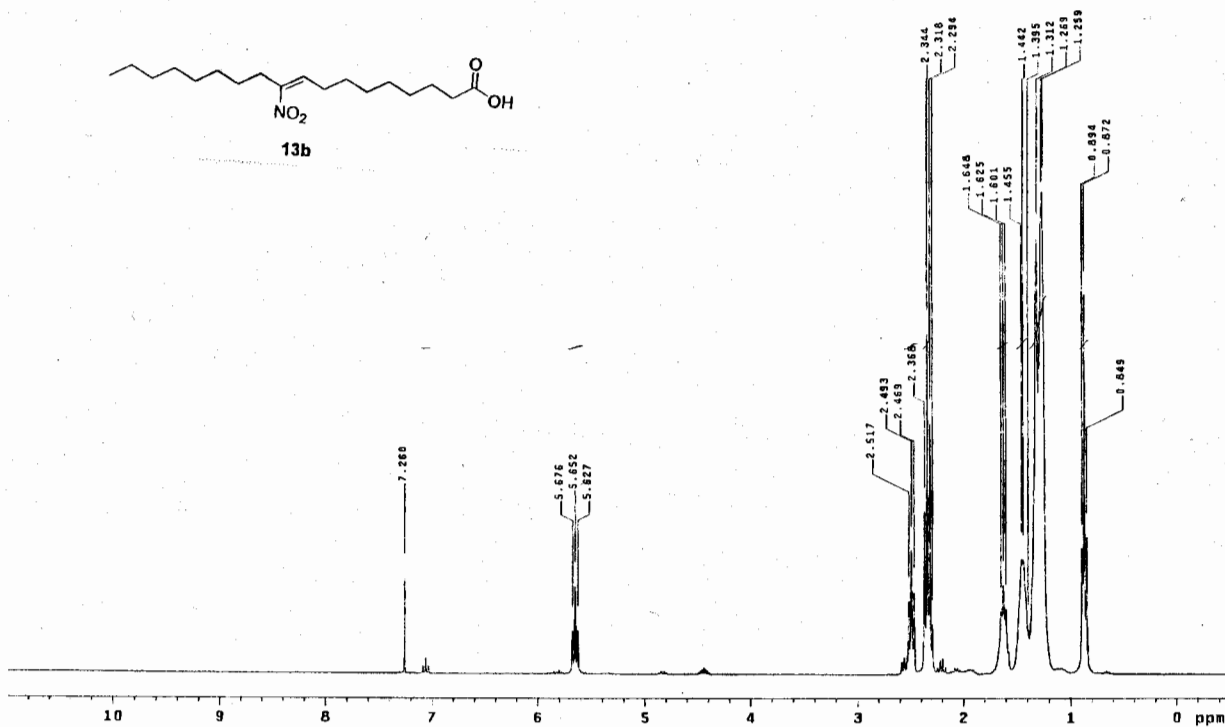
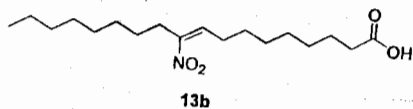


PULSE SEQUENCE Relax. delay 1.000 sec Pulse 45.0 degrees Acq. time 2.501 sec Width 4795.0 Hz 8 repetitions	OBSERVE H1, 299.9325259	DATA PROCESSING Line broadening 0.2 Hz FT size 32768 Total time 1 minute	6.32 6.86 50.43	srw2_247fxn4 Pulse Sequence: s2py1 Solvent: CDCl3 Ambient temperature INOVA-300 "sunofmr.uoreg
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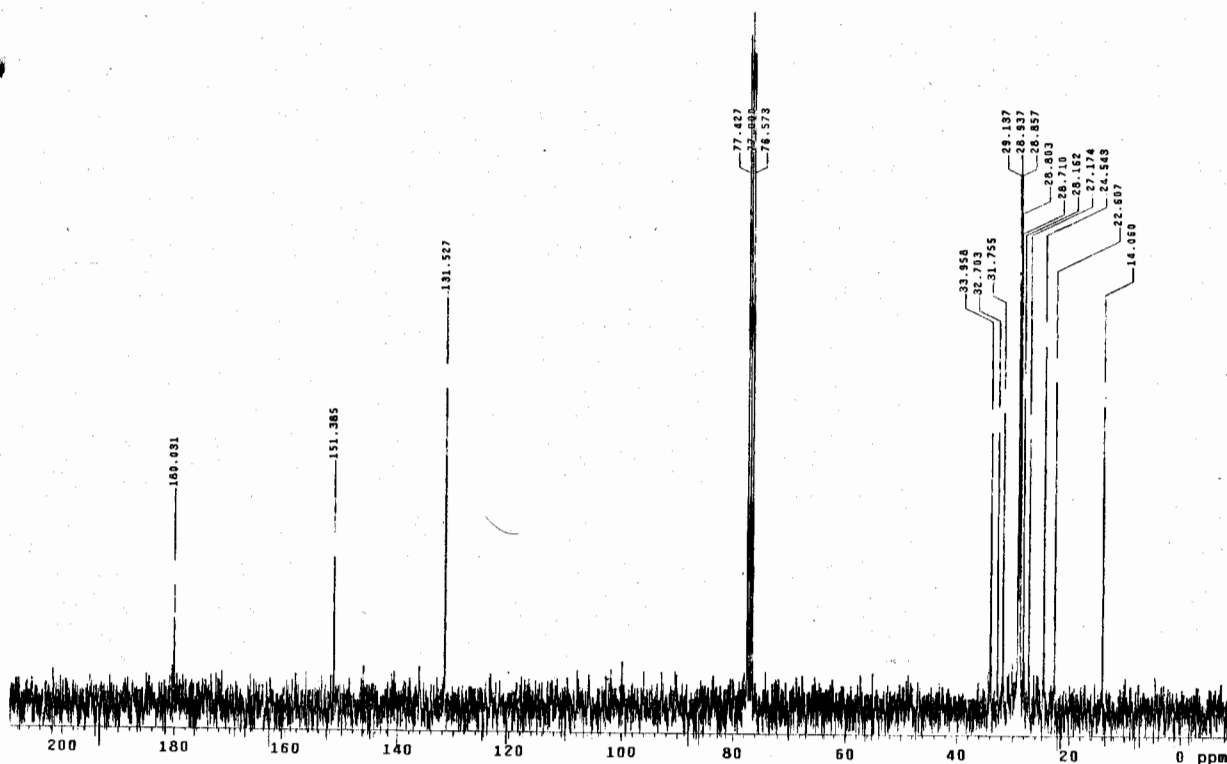




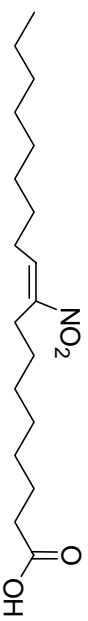




<b>PULSE SEQUENCE</b> Relax. delay 1.000 sec Pulse 45.0 degrees Acq. time 2.501 sec Width 4799.0 Hz 8 repetitions	<b>OBSERVE</b> H1, 299.9325264	<b>DATA PROCESSING</b> Line broadening 0.2 Hz FT size 32768 Total time 1 minute			<b>STANDARD 1H OBSERVE</b> Pulse Sequence: s2pul Solvent: CDCl3 Ambient temperature INOVA-300 sunofmr.uoreg
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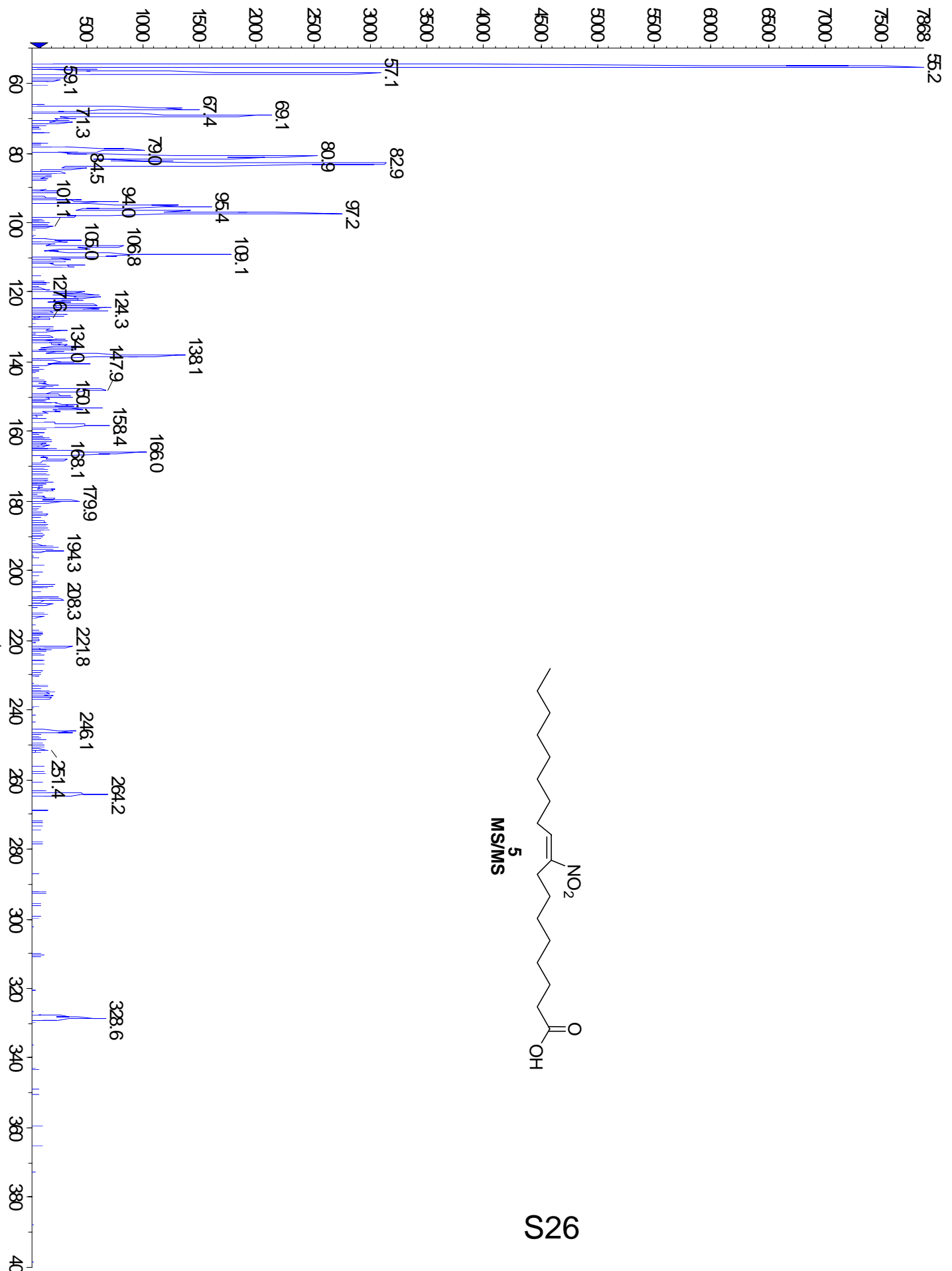


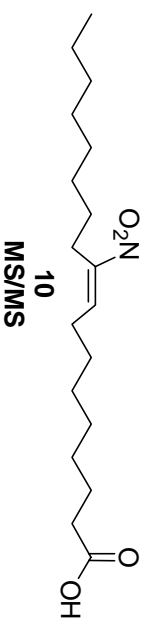
<b>PULSE SEQUENCE</b> Relax. delay 1.000 sec Pulse 56.2 degrees Acq. time 0.599 sec Width 16501.7 Hz 500 repetitions	<b>OBSERVE</b> C13, 75.4180950 <b>DECOUPLE</b> H1, 299.9335199 Power 32 dB continuously on WALTZ-16 modulated	<b>DATA PROCESSING</b> Line broadening 2.0 Hz FT size 32768 Total time 13 minutes			<b>13C OBSERVE</b> Pulse Sequence: s2pul Solvent: CDCl3 Ambient temperature INOVA-300 sunofmr.uoreg
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5  
MS/MS

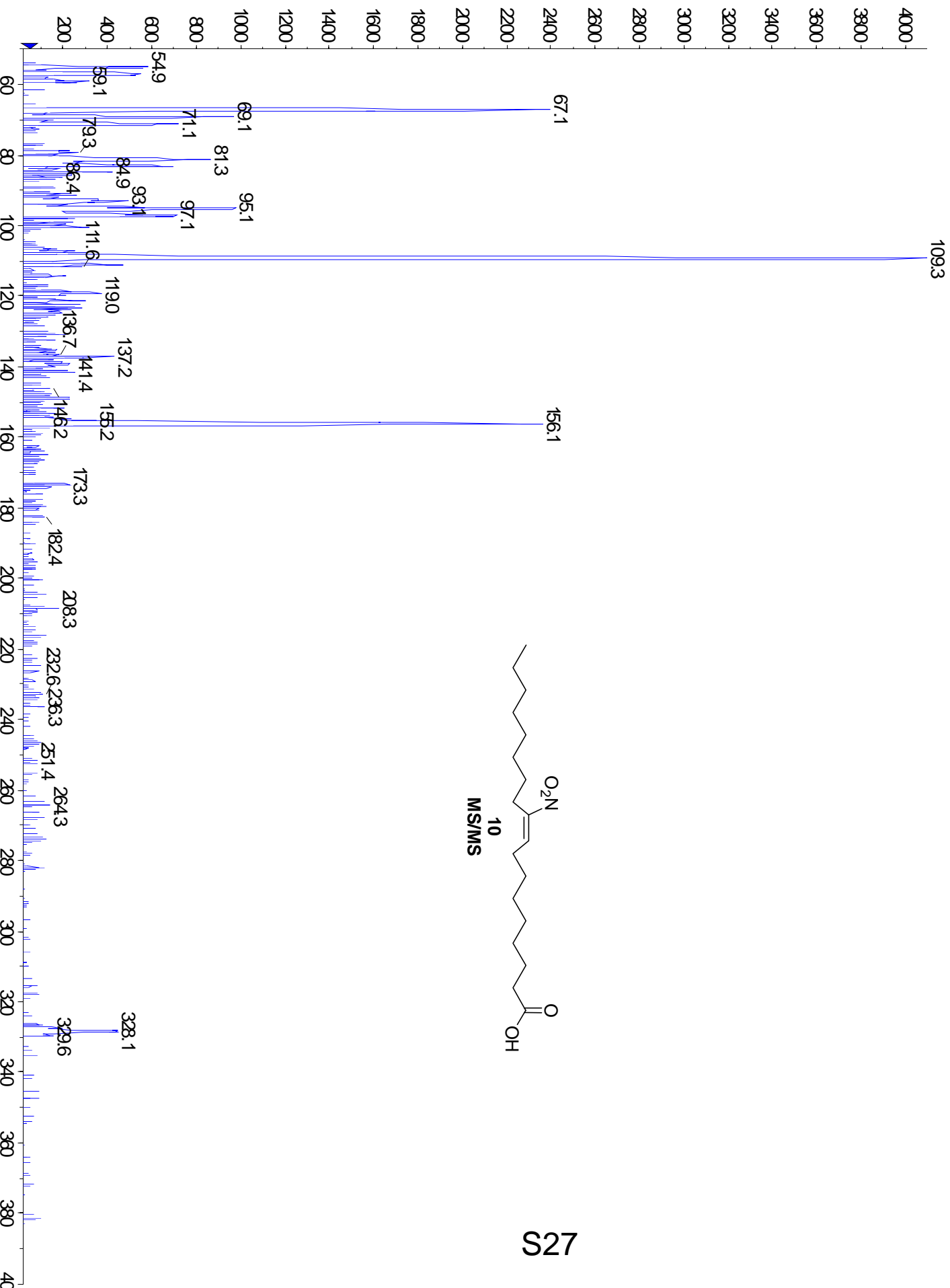
S26

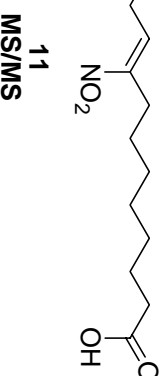




MS/MS

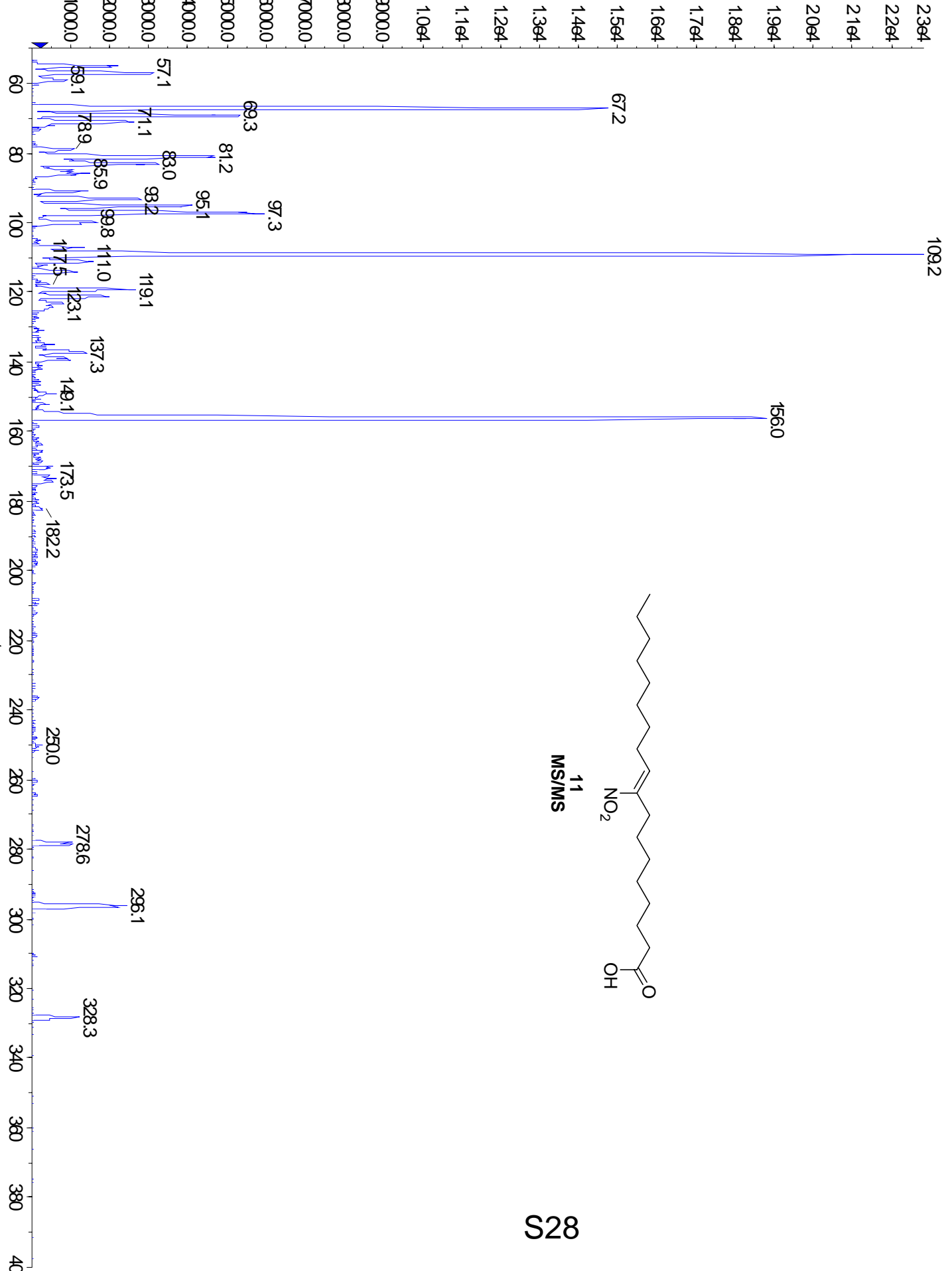
S27

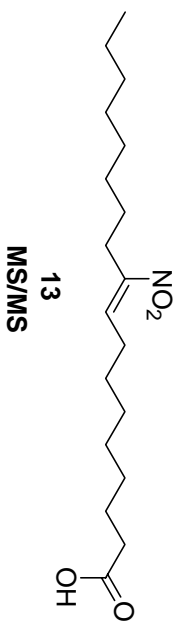




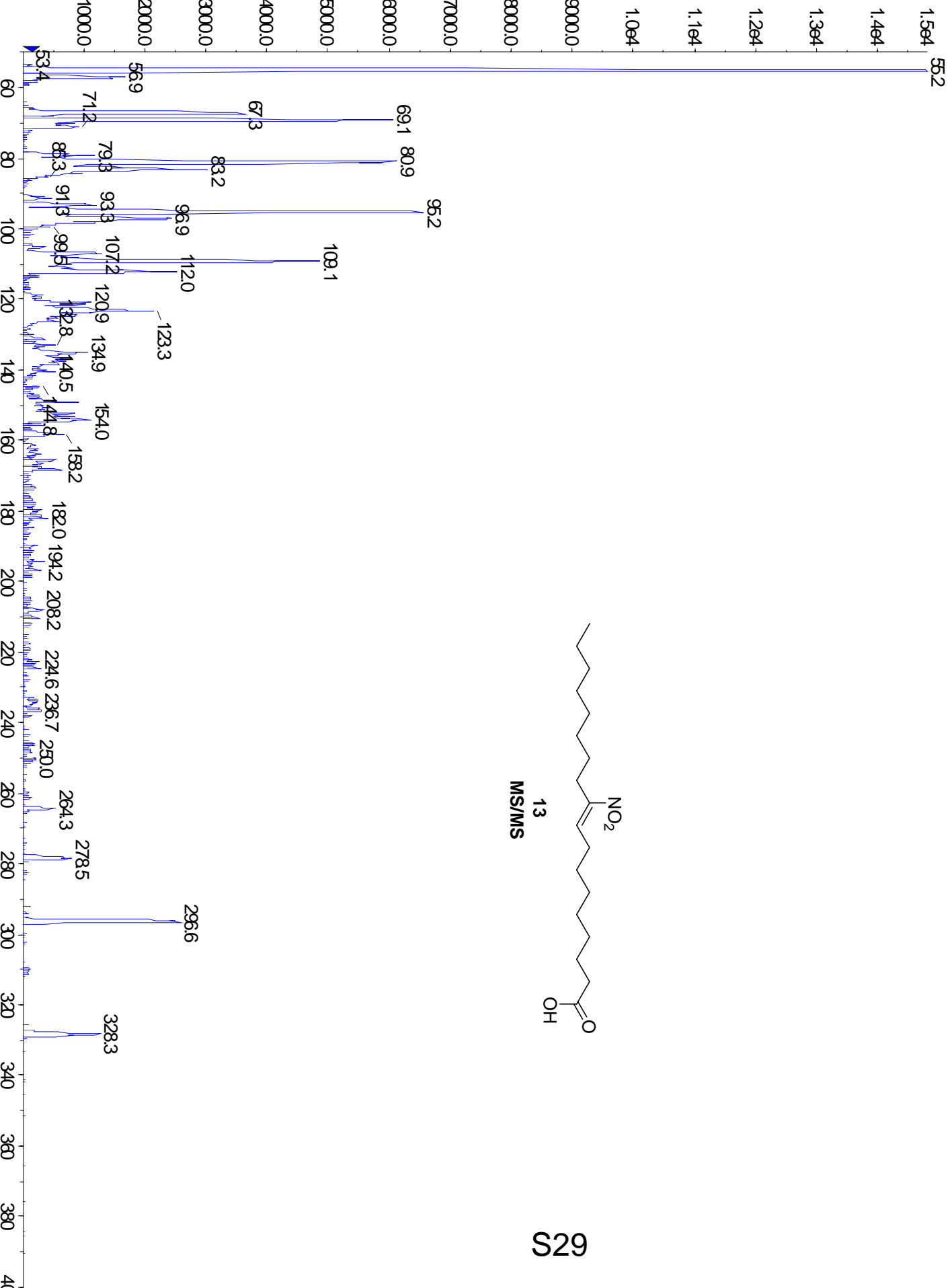
11  
MS/MS

S28





13  
MS/MS



7/11/2006 1:00:41 PM

File: 0711061r-05

Date Run: 07-11-2006 (Time Run: 12:19:07)

Sample: Steven Woodcock, SRW 246, very dil. EI pos, MW = 327.46

Instrument: JEOL MSRoute

Ionization mode: EI+

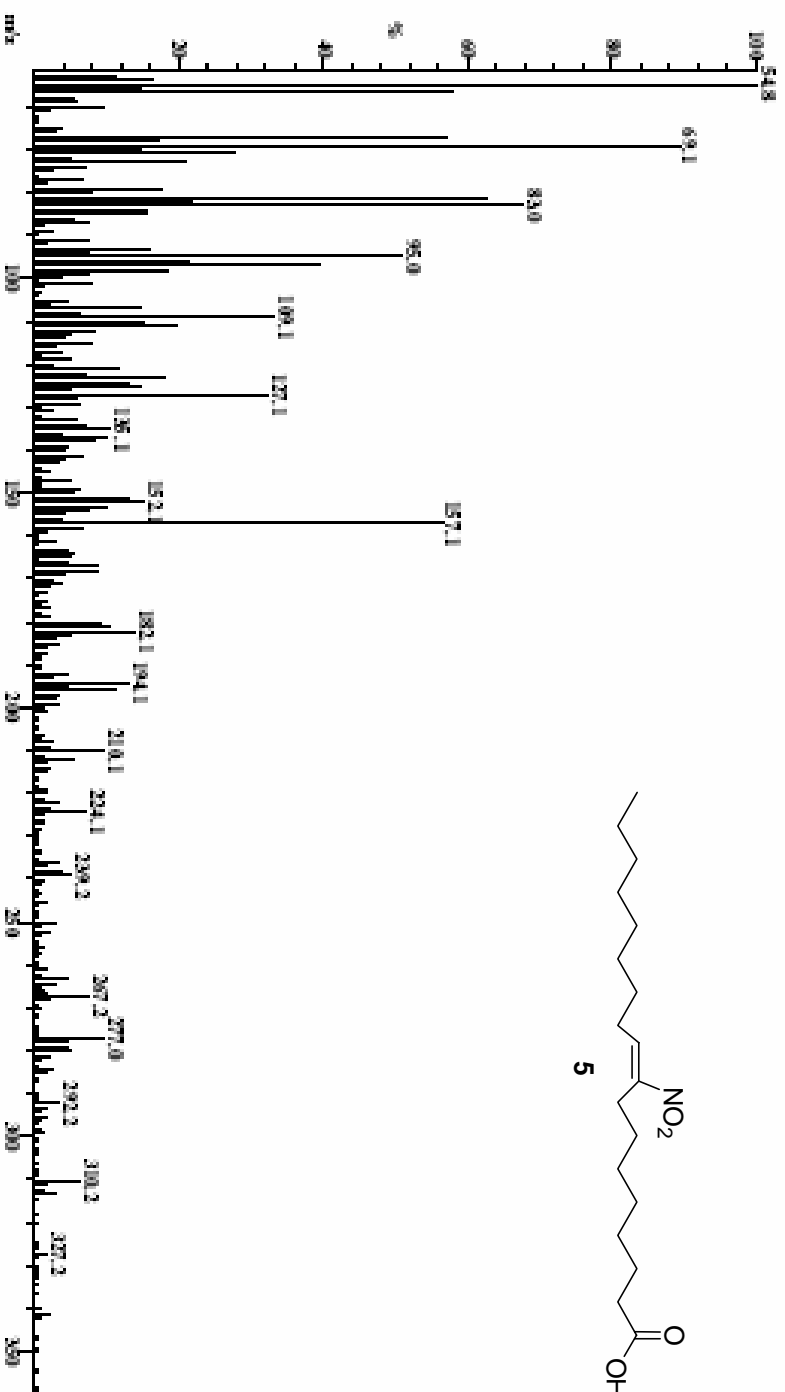
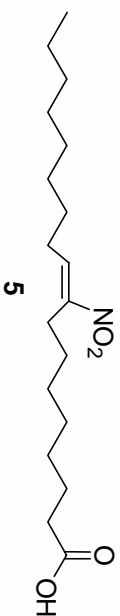
Run By: Morte

Scan: 42-107

R.T.: 1.48

Base: m/z 55; 24.2% FS TIC: 4910707

#Ions: 5675



7/11/2006 12:44:02 PM

File: 0711061c-07

Date Run: 07-11-2006 (Time Run: 12:41:28)

Sample: Steven Woodcock, AJM 070, very dil EI pos, MW = 327.46

Instrument: JEOL MSRoute

Ionization mode: EI+

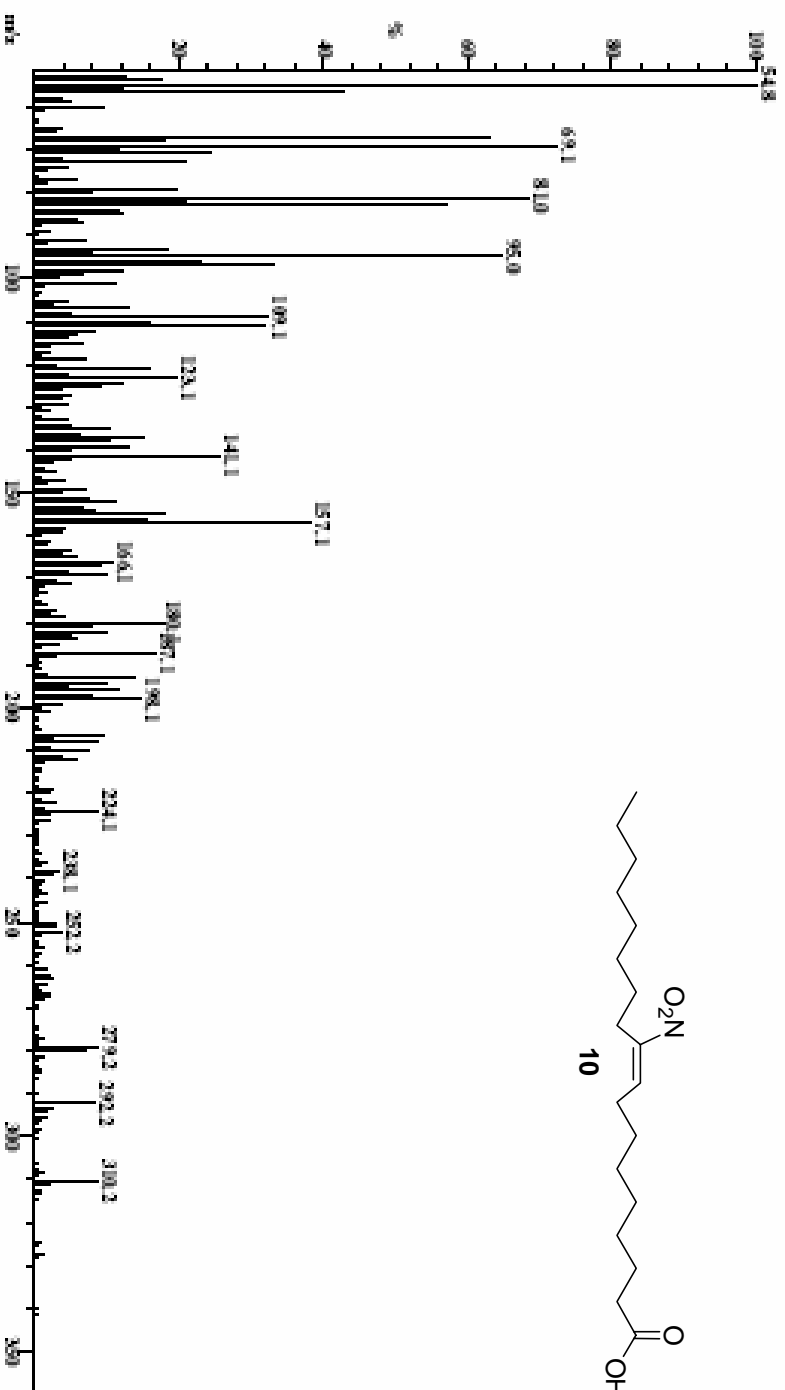
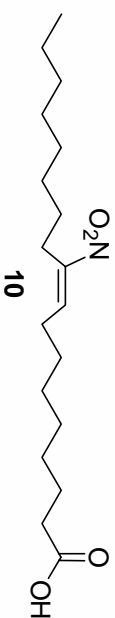
Run By: Morte

Scan: 9.36

R.T.: .44

Base: m/z 55; 57.6% FS TIC: 10996725

#Ions: 4061



OSU

7/11/2006 12:59:33 PM

File: 0711061r-08

Date Run: 07-11-2006 (Time Run: 12:56:52)

Sample: Steven Woodcock, SRW 247c, very dil. EI pos, MW= 327.46

Instrument: JEOL MSRoute

Ionization mode: EI+

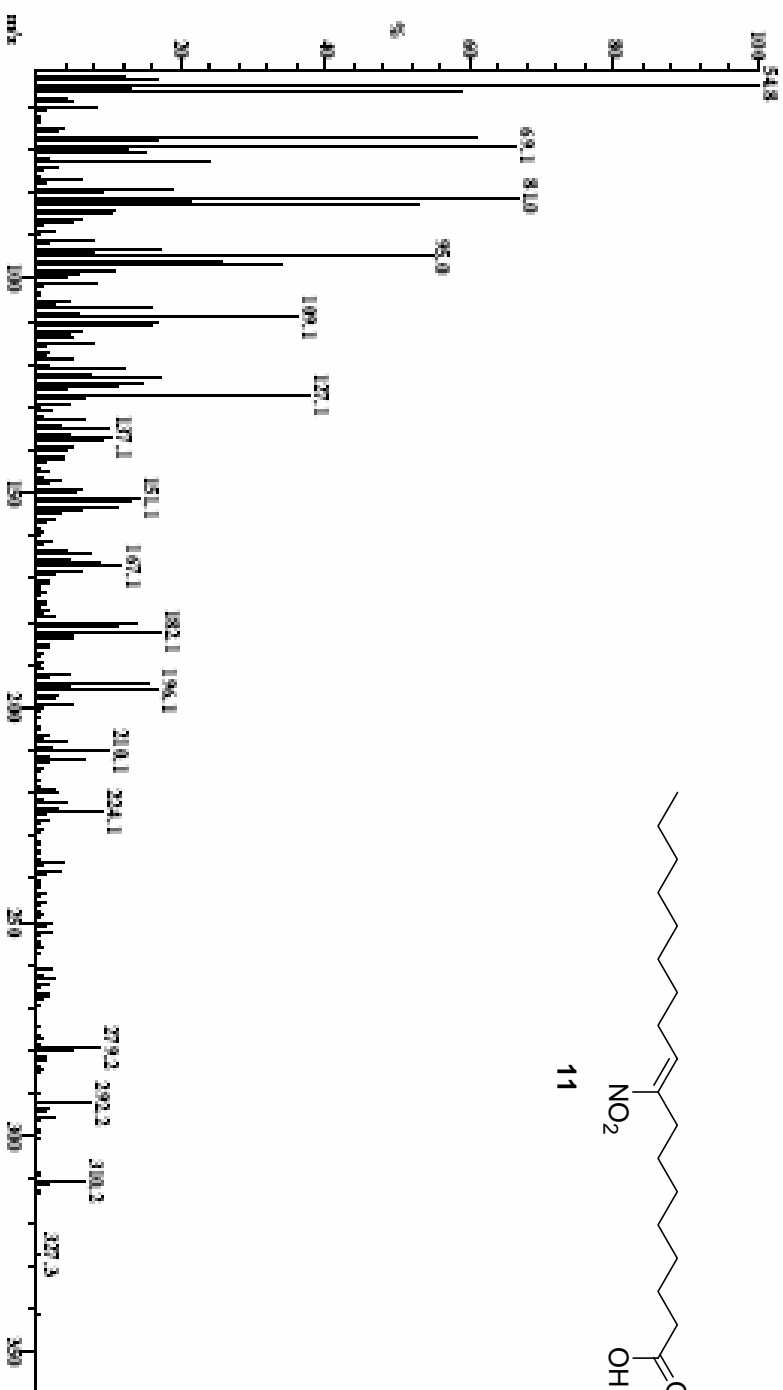
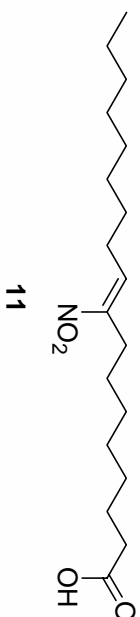
Run By: Morte

Scan: 15-69

R.T.: .83

Base: m/z 55; 40.6%FS TIC: 6906476

#Ions: 4246





7/11/2006 12:37:21 PM

File: 0711061r-06

Date Run: 07-11-2006 (Time Run: 12:28:43)

Sample: Steven Woodcock, AJM125, very dil. EI pos, MW= 327.46

Instrument: JEOL MSRoute

Ionization mode: EI+

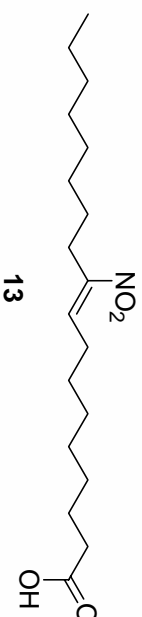
Run By: Morte

Scan: 8-21

R.T.: .28

Base: m/z 55; 4.6% FS TIC: 1420057

#Ions: 1745



S33

