Electronic Supplementary Material (ESI) for Chemical Communications

Highly Enantioselective Synthesis of Chiral 7-Ring O- and N-Heterocycles by a One-pot Nitro-Michael/Cyclization Tandem Reaction

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Supporting Information

Contents

General information and materials. NMR spectra were acquired on a Bruker ARX-300 and a Varian AV-300 or AV-400 MHz. Chemical shifts (δ) are reported in ppm relative to residual solvent signals ($CHCl_3$, 7.26 ppm for ^1H NMR and 77.16 ppm for ^{13}C NMR) and spin-spin coupling constants (*J*) are given in Hz. ^{13}C NMR spectra were acquired on a broad band decoupled mode. Mass spectra were recorded on a Micromass LCT spectrometer using electrospray ionisation (ESI^+) techniques. Analytical thin layer chromatography (TLC) was performed using pre-coated aluminium-backed plates (Merck Kieselgel 60 F254) and visualised by ultraviolet irradiation or $KMnO_4$ dip. Infrared spectra were recorded on a Varian Associated FT-IR 3100

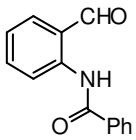
Excalibur. The wave numbers (ν) of recorded IR-signals are quoted in cm^{-1}. Optical rotations, $[\alpha]^{20}_D$, were measured on a Perkin-Elmer 241 polarimeter. The enantiomeric excess (*ee*) of the products was determined by chiral stationary phase HPLC (Daicel Chiralpak IA, IC and AD-H or Daicel Chiralcel OD-H columns). Catalysts **1a-d**,[1] **1e**[2] and **1f**[3] were prepared according to reported procedures in the literature.

X-Ray diffraction: Data sets were collected with a Nonius KappaCCD diffractometer. Programs used: data collection, COLLECT (Nonius B.V., 1998); data reduction Denzo-SMN (Z. Otwinowski, W. Minor, *Methods Enzymol.* **1997**, *276*, 307-326); absorption correction, Denzo (Z. Otwinowski, D. Borek, W. Majewski, W. Minor, *Acta Crystallogr.* **2003**, *A59*, 228-234); structure solution SHELXS-97 (G. M. Sheldrick, *Acta Crystallogr.* **1990**, *A46*, 467-473); structure refinement SHELXL-97 (G. M. Sheldrick, *Acta Crystallogr.* **2008**, *A64*, 112-122) and graphics, XP (BrukerAXS, 2000). Thermals ellipsoids are shown with 30% probability, *R*-values are given for observed reflections, and wR^2 values are given for all reflections.

Experimental procedures and characterization:

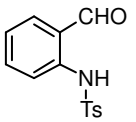
Synthesis of the aldehyde precursors 9a and 9b[4]

N-(2-Formylphenyl)benzamide (9a)[5]



2-Aminobenzyl alcohol (2.00 g, 16.24 mmol, 1.0 equiv.) and Et_3N (2.7 mL, 19.45 mmol, 1.2 equiv.) was dissolved in 50 mL of dry THF. Benzoyl chloride (2.1 mL, 17.86 mmol, 1.1 equiv.) was slowly added. After stirring the reaction mixture for 12 h at room temperature, the solvent was removed in vacuo and the residue was dissolved in ethylacetate, washed with saturated $NaHCO_3$ (aq.) and dried over $MgSO_4$. Without further purification the alcohol was dissolved in 250 mL CH_2Cl_2 and treated with pyridinium chlorochromate (4.20 g, 19.45 mmol, 1.2 equiv.). After full oxidation to the aldehyde, the reaction mixture was filtrated over a celite pad and the solvent removed in vacuo. The residue was purified by column chromatography (pentane-EtOAc: 15:1→ 9:1) affording *N*-(2-formylphenyl)benzamide (**9a**) (3.25 g, 14.45 mmol, 89%) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 12.07 (s, 1H), 9.96 (d, *J* = 0.8 Hz, 1H), 8.94 (d, *J* = 8.5 Hz, 1H), 8.08 – 8.03 (m, 2H), 7.69 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.64 (ddd, *J* = 8.8, 7.4, 1.7 Hz, 1H), 7.59 – 7.48 (m, 3H), 7.28 – 7.19 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 196.0, 166.1, 141.3, 136.4, 136.3, 134.4, 132.3, 129.0 (2C), 127.6 (2C), 123.1, 122.0, 120.0; **HRMS** (ESI^+): calculated for $C_{14}H_{11}NO_2$+Na^+ $[M+Na]^+$: m/z = 248.0682, found 248.0685.

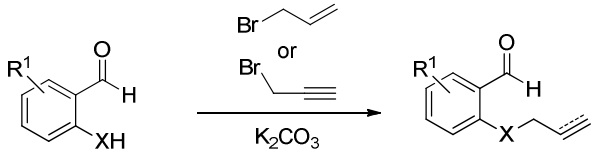
N-(2-Formylphenyl)-4-methylbenzenesulfonamide (9b)[4]



2-Aminobenzyl alcohol (2.00 g, 16.24 mmol, 1.0 equiv.) and pyridine (1.6 mL, 19.81 mmol, 1.2 equiv.) was dissolved in 60 mL of dry $CHCl_3$. 4-Toluenesulfonyl chloride (3.44 g, 17.86 mmol, 1.1 equiv.) was dissolved in 60 mL $CHCl_3$ and slowly added. After stirring the

reaction mixture for 12 h at room temperature, the solvent was removed in vacuo and the residue was dissolved in ethylacetate, washed with saturated $NaHCO_3$ (aq.) and dried over $MgSO_4$. Without further purification the alcohol was dissolved in 250 mL CH_2Cl_2 and treated with pyridinium chlorochromate (4.20 g, 19.45 mmol, 1.2 equiv.). After full oxidation to the aldehyde, the reaction mixture was filtrated over a celite pad and the solvent removed in vacuo. The residue was purified by column chromatography (pentane-EtOAc: 15:1→9:1) affording *N*-(2-formylphenyl)-4-methylbenzenesulfonamide (**9b**) (4.24 g, 15.43 mmol, 95%) as a white solid. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 10.79 (s, 1H), 9.82 (d, *J* = 0.7 Hz, 1H), 7.80 – 7.72 (m, 2H), 7.68 (d, *J* = 8.4 Hz, 1H), 7.59 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.50 (ddd, *J* = 8.6, 7.4, 1.6 Hz, 1H), 7.23 (dd, *J* = 8.2, 0.9 Hz, 2H), 7.16 (td, *J* = 7.5, 1.0 Hz, 1H), 2.36 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 195.1, 144.3, 140.0, 136.4, 136.2, 135.9, 129.9, 127.4, 123.1, 122.0, 117.8, 21.7; **HRMS** (ESI^+) calculated for $C_{14}H_{13}NO_3S+Na^+$ $[M+Na]^+$: m/z = 298.0508, found 298.0508.

General procedure for the O- and N-allylation or propargylation[5]

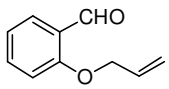


9 **10**

X = O or NR

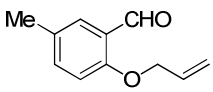
An ordinary vial equipped with a magnetic stirring bar was charged with aldehyde **9** (1 equiv.) and K_2CO_3 (1.1 equiv.) in DMF (0.6 M). To the stirring solution allyl bromide or propargyl bromide (1.1 equiv.) was added dropwise. After stirring the solution for 2 days water was added and extracted 3 times with Et_2O. The combined organic phases was dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography.

2-Allyloxy benzaldehyde (10a)[5]



Following the general procedure, salicylaldehyde (3.00 g, 24.56 mmol, 1.0 equiv.) was treated with K_2CO_3 (3.73 g, 27.02 mmol, 1.1 equiv.) and allyl bromide (2.40 mL, 27.02 mmol, 1.1 equiv.) in 30 mL DMF. The 2-allyloxy benzaldehyde (**10a**) was isolated by destillation (1 Torr, 90 °C) as colorless oil (3.82 g, 23.53 mmol, 96%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 10.53 (d, *J* = 0.8 Hz, 1H), 7.83 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.52 (ddd, *J* = 8.4, 7.3, 1.9 Hz, 1H), 7.13 – 6.88 (m, 2H), 6.20 – 5.94 (m, 1H), 5.44 (dq, *J* = 17.3, 1.6 Hz, 1H), 5.33 (dq, *J* = 10.6, 1.4 Hz, 1H), 4.65 (dt, *J* = 5.1, 1.6 Hz, 2H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 189.8, 161.0, 136.0, 132.5, 128.5, 125.1, 120.9, 118.1, 112.9, 69.2; **HRMS** (ESI^+) calculated for $C_{10}H_{10}O_2+Na^+$ $[M+Na]^+$: m/z = 85.0573, found 185.0571.

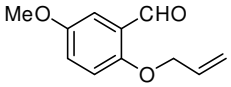
2-(Allyloxy)-5-methylbenzaldehyde (10e)[6]



Following the general procedure, 5-methylsalicylaldehyde (855 mg, 6.28 mmol, 1.0 equiv.) was treated with K_2CO_3 (927 mg, 6.71 mmol, 1.1 equiv.) and allyl bromide

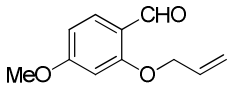
(530 µL, 6.71 mmol, 1.1 equiv.) in DMF (10 mL). The 2-(allyloxy)-5-methylbenzaldehyde (**10e**) was isolated by column chromatography (petane-EtOAc 400:3) as colorless oil (916 mg, 5.20 mmol, 83%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 10.50 (s, 1H), 7.64 (dd, *J* = 2.5, 1.0 Hz, 1H), 7.33 (ddd, *J* = 8.5, 2.1, 1.0 Hz, 1H), 6.88 (d, *J* = 8.5 Hz, 1H), 6.07 (ddt, *J* = 17.2, 10.4, 5.1 Hz, 1H), 5.44 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.32 (dq, *J* = 10.6, 1.4 Hz, 1H), 4.63 (dt, *J* = 5.0, 1.4 Hz, 2H), 2.31 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 190.1, 159.2, 136.6, 132.7, 130.4, 128.6, 124.9, 118.1, 113.0, 69.4, 20.4. **HRMS** (ESI^+): calculated for $C_{11}H_{12}O_2$+Na^+ $[M+Na]^+$: m/z = 199.0730, found 199.0732.

2-(Allyloxy)-5-methoxybenzaldehyde (10f)



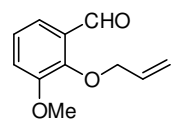
Following the general procedure, 5-methoxysalicylaldehyde (1.12 g, 7.35 mmol, 1.0 equiv.) was treated with K_2CO_3 (1.10 g, 7.85 mmol, 1.1 equiv.) and allyl bromide (670 µL, 7.85 mmol, 1.1 equiv.) in DMF (10 mL). The 2-(allyloxy)-5-methoxybenzaldehyde (**10f**) was isolated by column chromatography (petane-EtOAc 400:3) as colorless oil (1.41 mg, 7.34 mmol, 99%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 10.47 (s, 1H), 7.30 (d, *J* = 3.3 Hz, 1H), 7.08 (dd, *J* = 9.1, 3.3 Hz, 1H), 6.91 (d, *J* = 9.1 Hz, 1H), 6.03 (ddt, *J* = 17.3, 10.4, 5.2 Hz, 1H), 5.40 (dq, *J* = 17.3, 1.6 Hz, 1H), 5.29 (dq, *J* = 10.6, 1.4 Hz, 1H), 4.58 (dt, *J* = 5.2, 1.6 Hz, 2H), 3.77 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 189.5, 155.8, 153.8, 132.7, 125.4, 123.5, 118.0, 114.9, 110.3, 70.0, 55.8; **HRMS** (ESI^+) calculated for $C_{11}H_{12}O_3$+Na^+ $[M+Na]^+$: m/z = 215.0679, found 215.0686.

2-(Allyloxy)-4-methoxybenzaldehyde (10g)[6]



Following the general procedure, 4-methoxysalicylaldehyde (500 mg, 3.29 mmol, 1.0 equiv.) was treated with K_2CO_3 (499 mg, 3.61 mmol, 1.1 equiv.) and allyl bromide (313 µL, 3.61 mmol, 1.1 equiv.) in DMF (5 mL). The 2-(allyloxy)-4-methoxybenzaldehyde (**10g**) was isolated by column chromatography (petane-EtOAc 9:1) as colorless oil (620 mg, 3.23 mmol, 98%).**^{1}H NMR** (300 MHz, $CDCl_3$): δ = 10.35 (d, *J* = 0.8 Hz, 1H), 7.82 (d, *J* = 8.7 Hz, 1H), 6.55 (ddd, *J* = 8.7, 2.2, 0.8 Hz, 1H), 6.43 (d, *J* = 2.2 Hz, 1H), 6.07 (ddt, *J* = 17.3, 10.4, 5.1 Hz, 1H), 5.45 (dq, *J* = 17.3, 1.6 Hz, 1H), 5.33 (dq, *J* = 10.5, 1.4 Hz, 1H), 4.62 (dt, *J* = 5.1, 1.6 Hz, 2H), 3.86 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 188.3, 166.0, 162.6, 132.3, 130.5, 119.2, 118.1, 106.0, 99.0, 69.1, 55.6; **HRMS** (ESI^+) calculated for $C_{11}H_{12}O_3$+Na^+ $[M+Na]^+$: m/z = 215.0679, found 215.0688.

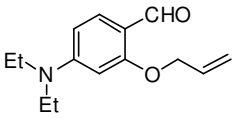
2-(Allyloxy)-5-methoxybenzaldehyde (10h)[5]



Following the general procedure, 3-methoxysalicylaldehyde (1.09 g, 7.14 mmol, 1.0 equiv.) was treated with K_2CO_3 (1.10 g, 7.85 mmol, 1.1 equiv.) and allyl bromide (670 µL, 7.85 mmol, 1.1 equiv.) in DMF (10 mL). The 2-(allyloxy)-5-methoxybenzaldehyde (**10h**) was isolated by column chromatography (petane-EtOAc 400:3→400:14) as colorless oil (1.31 g, 6.82 mmol, 95%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 10.42 (d, *J* = 0.8 Hz, 1H), 7.39 (dd, *J* = 6.9, 2.5 Hz, 1H), 7.17 – 7.04 (m,

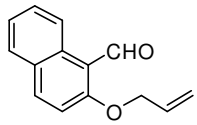
2H), 6.05 (ddt, *J* = 17.1, 10.3, 6.1 Hz, 1H), 5.33 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.24 (dq, *J* = 10.3, 1.2 Hz, 1H), 4.64 (dt, *J* = 6.1, 1.3 Hz, 2H), 3.88 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 190.5, 153.1, 151.3, 133.2, 130.2, 124.2, 119.1, 119.0, 118.0, 75.2, 56.1; **HRMS** (ESI^+): calculated for $C_{11}H_{12}O_3$+Na^+ $[M+Na]^+$: m/z = 215.0679, found 215.0689.

2-(Allyloxy)-4-diethylaminobenzaldehyde (10i)



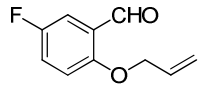
Following the general procedure, 4-diethylaminosalicylaldehyde (1.00 g, 5.17 mmol, 1.0 equiv.) was treated with K_2CO_3 (786 mg, 5.69 mmol, 1.1 equiv.) and allyl bromide (490 µL, 5.69 mmol, 1.1 equiv.) in DMF (8 mL). The 2-(allyloxy)-4-diethylaminobenzaldehyde (**10i**) was isolated by column chromatography (petane-EtOAc 9:1) as a yellow solid (1.20 g, 5.14 mmol, 99%).**^{1}H NMR** (300 MHz, $CDCl_3$): δ = 10.20 (s, 1H), 7.72 (d, *J* = 8.9 Hz, 1H), 6.37 – 6.22 (m, 1H), 6.07 (ddt, *J* = 17.5, 10.4, 5.1 Hz, 2H), 5.45 (dq, *J* = 17.3, 1.6 Hz, 1H), 5.32 (dq, *J* = 10.4, 1.4 Hz, 1H), 4.63 (dt, *J* = 5.2, 1.6 Hz, 2H), 3.41 (q, *J* = 7.1 Hz, 4H), 1.21 (t, *J* = 7.1 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 187.2, 163.3, 133.1 (2C), 130.5 (2C), 117.8 (2C), 104.8, 69.1, 45.2 (2C), 12.7 (2C); **HRMS** (ESI^+) calculated for $C_{14}H_{19}NO_2$+Na^+ $[M+Na]^+$: m/z = 256.1208, found 256.1309.

2-(Allyloxy)-1-naphthaldehyde (10j)[5]



Following the general procedure, 2-hydroxy-1-naphthaldehyde (2.00 g, 11.62 mmol, 1.0 equiv.) was treated with K_2CO_3 (1.77 g, 12.78 mmol, 1.1 equiv.) and allyl bromide (1.10 mL, 142.78 mmol, 1.1 equiv.) in DMF (18 mL). 2-(allyloxy)-1-naphthaldehyde (**10j**) was isolated by column chromatography (petane-EtOAc 9:1) as a white solid (2.44 g, 11.50 mmol, 99%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 10.95 (s, 1H), 9.28 (dd, *J* = 8.8, 1.0 Hz, 1H), 8.03 (dt, *J* = 9.1, 0.6 Hz, 1H), 7.77 (ddt, *J* = 8.2, 1.4, 0.6 Hz, 1H), 7.62 (ddd, *J* = 8.6, 6.9, 1.5 Hz, 1H), 7.42 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 7.26 (d, *J* = 9.1 Hz, 1H), 6.10 (ddt, *J* = 17.3, 10.4, 5.1 Hz, 1H), 5.48 (dtd, *J* = 17.2, 1.7, 1.2 Hz, 1H), 5.36 (dq, *J* = 10.6, 1.4 Hz, 1H), 4.79 (dt, *J* = 5.1, 1.6 Hz, 2H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 192.2, 163.2, 137.6, 132.4, 131.7, 130.0, 128.7, 128.3, 125.1, 125.0, 118.5, 117.2, 113.9, 70.3; **HRMS** (ESI^+) calculated for $C_{14}H_{12}O_2$+Na^+ $[M+Na]^+$: m/z = 235.0730, found 235.0737.

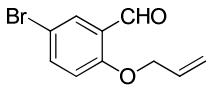
2-(Allyloxy)-5-fluorobenzaldehyde (10k)[5]



Following the general procedure, 5-fluorobenzaldehyde (1.00 g, 7.14 mmol, 1.0 equiv.) was treated with K_2CO_3 (1.10 g, 7.85 mmol, 1.1 equiv.) and allyl bromide (670 µL, 7.85 mmol, 1.1 equiv.) in DMF (10 mL). The 2-(allyloxy)-5-fluorobenzaldehyde (**10k**) was isolated by column chromatography (petane-EtOAc 400:5) as colorless oil (1.89 g, 6.60 mmol, 93%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 10.48 (d, *J* = 3.2 Hz, 1H), 7.51 (dd, *J* = 8.3, 3.3 Hz, 1H), 7.23 (ddd, *J* = 9.1, 7.6, 3.3 Hz, 1H), 6.95 (dd, *J* = 9.1, 3.9 Hz, 1H), 6.06 (ddt, *J* = 17.1, 10.5, 5.2 Hz, 1H), 5.44 (dq, *J* = 17.3, 1.6 Hz, 1H), 5.35 (dq, *J* = 10.5, 1.4 Hz, 1H), 4.64 (dt, *J* = 5.3, 1.5 Hz, 2H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 188.8 (d, ^4J = 1.8 Hz),

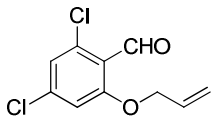
157.4 (d, ^4J = 1.5 Hz), 157.1 (d, ^1J = 241.5 Hz), 132.3 , 126.0 (d, ^3J = 6.1 Hz), 122. 6 (d, ^2J = 23.9 Hz), 118.5, 114.7 (d, ^3J = 7.2 Hz), 114.2 (d, ^2J = 23.4 Hz), 70.0; **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -122.33; **HRMS** (ESI^+) calculated for $C_{10}H_9FO_2$+Na^+ $[M+Na]^+$: m/z = 203.0479, found 203.0483.

2-(Allyloxy)-5-bromobenzaldehyde (10l)[5]



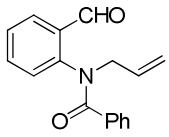
Following the general procedure, 5-bromosalicylaldehyde (1.44 g, 7.14 mmol, 1.0 equiv.) was treated with K_2CO_3 (1.10 g, 7.85 mmol, 1.1 equiv.) and allyl bromide (670 µL, 7.85 mmol, 1.1 equiv.) in DMF (10 mL). The 2-(allyloxy)-5-bromobenzaldehyde (**10l**) was isolated by column chromatography (petane-EtOAc 400:3) as a yellow solid (1.67 g, 6.93 mmol, 97%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 10.41 (s, 1H), 7.89 (d, *J* = 2.7 Hz, 1H), 7.57 (dd, *J* = 8.9, 2.6 Hz, 1H), 6.86 (d, *J* = 8.9 Hz, 1H), 6.04 (ddt, *J* = 17.3, 10.4, 5.2 Hz, 1H), 5.42 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.33 (dq, *J* = 10.6, 1.4 Hz, 1H), 4.63 (dt, *J* = 5.2, 1.6 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 188.3, 159.9, 138.3, 132.0, 131.0, 126.4, 118.6, 115.0, 113.7, 69.6; **HRMS** (ESI^+) calculated for $C_{10}H_9BrO_2$+Na^+ $[M+Na]^+$: m/z = 262.9678, found 262.9677.

2-(Allyloxy)-4,6-dichlorobenzaldehyde (10m)[5]



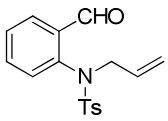
Following the general procedure, 4,6-dichlorosalicylaldehyde (701 mg, 3.67 mmol, 1.0 equiv.) was treated with K_2CO_3 (558 mg, 4.04 mmol, 1.1 equiv.) and allyl bromide (350 µL, 4.04 mmol, 1.1 equiv.) in DMF (6 mL). The 2-(allyloxy)-4,6-dichlorobenzaldehyde (**10m**) was isolated by column chromatography (petane-EtOAc 400:3) as colorless oil (796 mg, 3.44 mmol, 94%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 10.47 (s, 1H), 7.06 (dd, *J* = 1.9, 0.5 Hz, 1H), 6.89 (d, *J* = 1.8 Hz, 1H), 6.03 (ddt, *J* = 17.3, 10.6, 5.1 Hz, 1H), 5.48 (dtd, *J* = 17.3, 1.7, 1.1 Hz, 1H), 5.37 (dq, *J* = 10.6, 1.4 Hz, 1H), 4.64 (dt, *J* = 5.1, 1.6 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 188.0, 161.5, 140.4, 137.3, 131.4, 123.5, 121.2, 119.0, 112.5, 70.2; **HRMS** (ESI^+) calculated for $C_{10}H_8Cl_2O_2$+Na^+ $[M+Na]^+$: m/z = 252.9794, found 252.9800.

***N*-Allyl-*N*-(2-formylphenyl)benzamide (10n)**[5]



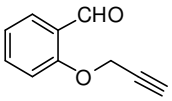
Following the general procedure, *N*-(2-formylphenyl)benzamide **8a** (1.00 g, 4.44 mmol, 1.0 equiv.) was treated with K_2CO_3 (675 mg, 4.88 mmol, 1.1 equiv.) and allyl bromide (420 µL, 4.88 mmol, 1.1 equiv.) in DMF (7.5 mL). The *N*-allyl-*N*-(2-formylphenyl)benzamide (**10n**) was isolated by column chromatography (petane-DCM-EtOAc 2:1:0.1) as colorless oil (1.11 g, 4.17 mmol, 94%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 10.05 (s, 1H), 7.70 (d, *J* = 7.8 Hz, 1H), 7.54 (t, *J* = 7.8 Hz, 1H), 7.34 (d, *J* =7.8 Hz, 1H), 7.28 – 7.07 (m, 6H), 6.00 (dd, *J* = 16.9, 8.8 Hz, 1H), 5.14 (t, *J* = 14.6 Hz, 2H), 4.55 (ddd, *J* = 69.0, 14.0, 6.4 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 189.4, 170.5, 145.0, 135.3, 134.9 (2C), 132.4, 132.0, 130.3, 130.1 (2C), 129.9, 128.6, 128.1, 128.0, 119.7, 54.2; **HRMS** (ESI^+) calculated for $C_{17}H_{15}NO_2$+Na^+ $[M+Na]^+$: m/z = 288.0995, found 288.0993.

_N_-Allyl-_N_-(2-formylphenyl)-4-methylbenzenesulfonamide (10o)[5]



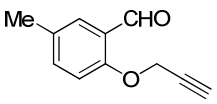
Following the general procedure, salicylaldehyde (1.30 g, 4.72 mmol, 1.0 equiv.) was treated with K_2CO_3 (717 mg, 5.19 mmol, 1.1 equiv.) and allyl bromide (500 µL, 5.19 mmol, 1.1 equiv.) in DMF (7.5 mL). The *N*-allyl-*N*-(2-formylphenyl)-4-methylbenzenesulfonamide (**10o**) was isolated by column chromatography (petane-DCM-EtOAc 2:1:0.1) as a white solid (1.44 g, 4.57 mmol, 97%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 10.40 (s, 1H), 8.04 – 7.77 (m, 1H), 7.51 – 7.33 (m, 4H), 7.34 – 7.14 (m, 2H), 6.67 (dd, *J* = 7.7, 1.4 Hz, 1H), 5.70 (ddt, *J* = 16.9, 10.2, 6.8 Hz, 1H), 5.20 – 4.88 (m, 2H), 4.56 (br.s, 1H), 3.81 (br.s, 1H), 2.41 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 190.2, 144.3, 141.3, 136.0, 134.2, 134.1, 131.6, 129.7 (2C), 128.6, 128.3, 127.9 (2C), 127.8, 120.5, 54.3, 21.6; **HRMS** (ESI^+) calculated for $C_{17}H_{17}NO_3S+Na^+$ $[M+Na]^+$: m/z = 338.0821, found 338.0817.

2-(Prop-2-yn-1-yloxy)benzaldehyde (10p)[7]



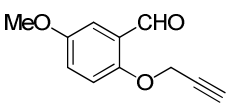
Following the general procedure, salicylaldehyde (1.00 g, 8.19 mmol, 1.0 equiv.) was treated with K_2CO_3 (1.00 mL, 9.01 mmol, 1.1 equiv.) and propargyl bromide (80% in toluene; 1.00 mL, 9.01 mmol, 1.1 equiv.) in DMF (13 mL). The 2-(prop-2-yn-1-yloxy)benzaldehyde (**7l**) was isolated by column chromatography (petane-DCM 5:3) as colorless oil (1.28 g, 7.99 mmol, 98%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 10.47 (s, 1H), 7.85 (dd, *J* = 7.7, 1.9 Hz, 1H), 7.56 (ddd, *J* = 8.4, 7.3, 1.9 Hz, 1H), 7.08 (ddt, *J* = 14.2, 7.5, 1.0 Hz, 2H), 4.82 (d, *J* = 2.4 Hz, 2H), 2.57 (t, *J* = 2.4 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 189.6, 159.8, 135.8, 128.6, 125.5, 121.8, 113.3, 77.8, 76.6, 56.4; **HRMS** (ESI^+) calculated for $C_{10}H_8O_2+Na^+$ $[M+Na]^+$: m/z = 183.0417, found 183.0420.

5-Methyl-2-(prop-2-yn-1-yloxy)benzaldehyde (10q)[6]



Following the general procedure, 5-methylsalicylaldehyde (739 mg, 5.43 mmol, 1.0 equiv.) was treated with K_2CO_3 (825 mg, 5.97 mmol, 1.1 equiv.) and and propargyl bromide (80% in toluene; 0.67 mL, 5.97 mmol, 1.1 equiv.) in DMF (4.7 mL). The 2-(allyloxy)-5-methylbenzaldehyde (**10q**) was isolated by column chromatography (petane-EtOAc 20:1) as a yellow solid (696 mg, 4.00 mmol, 74%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 10.44 (s, 1H), 7.71 – 7.57 (m, 1H), 7.36 (ddd, *J* = 8.5, 2.4, 0.8 Hz, 1H), 7.01 (d, *J* = 8.5 Hz, 1H), 4.79 (d, *J* = 2.4 Hz, 2H), 2.55 (t, *J* = 2.4 Hz, 1H), 2.31 (t, *J* = 0.7 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 189.8, 158.0, 136.5, 131.3, 128.7, 125.3, 113.4, 78.0, 76.5, 56.6, 20.4; **HRMS** (ESI^+): calculated for $C_{11}H_{10}O_2+Na^+$ $[M+Na]^+$: m/z = 197.0573, found 197.0586.

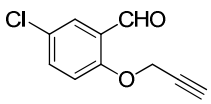
5-Methoxy-2-(prop-2-yn-1-yloxy)benzaldehyde (10r)[6]



Following the general procedure, 5-methoxysalicylaldehyde (974mg, 6.40mmol, 1.0 equiv.) was treated with K_2CO_3 (973 mg, 7.04 mmol, 1.1 equiv.) and and propargyl bromide (80% in toluene; 0.82 mL, 7.04 mmol, 1.1 equiv.) in DMF (5 mL). The 2-

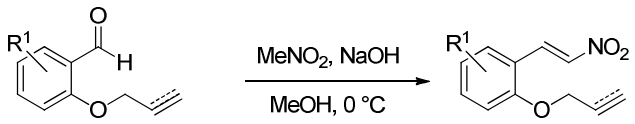
(allyloxy)-5-methylbenzaldehyde (**10r**) was isolated by column chromatography (petane-EtOAc 20:1) as a yellow solid (1.14 g, 6.01 mmol, 64%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 10.44 (s, 1H), 7.34 (d, *J* = 3.2 Hz, 1H), 7.14 (dd, *J* = 9.1, 3.1 Hz, 1H), 7.07 (d, *J* = 9.0 Hz, 1H), 4.78 (d, *J* = 2.4 Hz, 2H), 3.80 (s, 3H), 2.55 (t, *J* = 2.4 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 189.5, 154.6, 154.5, 126.2, 123.4, 115.7, 110.5, 78.0, 76.5, 57.5, 55.9; **HRMS** (ESI^+) calculated for $C_{11}H_{10}O_2$+Na^+ $[M+Na]^+$: m/z = 213.0522, found 213.0532.

5-Chloro-2-(prop-2-yn-1-yloxy)benzaldehyde (10s)[6]

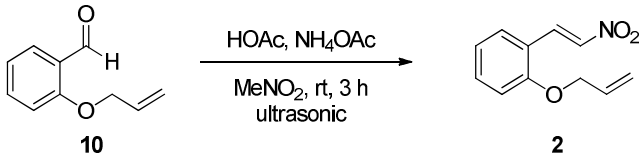


Following the general procedure, 5-clorosalicylaldehyde (1.00 g, 6.40mmol, 1.0 equiv.) was treated with K_2CO_3 (973 mg, 7.04 mmol, 1.1 equiv.) and and propargyl bromide (80% in toluene; 0.82 mL, 7.04 mmol, 1.1 equiv.) in DMF (5 mL). The 2-(allyloxy)-5-methylbenzaldehyde (**7b**) was isolated by column chromatography (petane-EtOAc 20:1) as a yellow solid (1.14 g, 6.01 mmol, 64%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 10.39 (s, 1H), 7.79 (d, *J* = 2.8 Hz, 1H), 7.50 (dd, *J* = 8.9, 2.8 Hz, 1H), 7.08 (d, *J* = 8.9 Hz, 1H), 4.82 (d, *J* = 2.4 Hz, 2H), 2.59 (t, *J* = 2.4 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 188.3, 158.2, 135.3, 128.2, 127.5, 126.4, 115.1, 77.3, 77.1, 56.8; **HRMS** (ESI^+) calculated for $C_{10}H_7O_2$+Na^+ $[M+Na]^+$: m/z = 217.0027, found 217.0027.

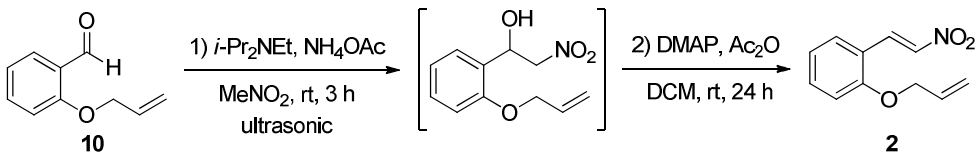
General procedures for the synthesis of nitroolefins 2



Method A:[8] Aldehyde **10** (1.0 equiv.) was treated with $MeNO_2$ (1 equiv.) and 10 M NaOH aq. solution (1.1 equiv.) in MeOH (4 M) at 0 °C for 15 min. Nitroolefin **2** was then isolated by column chromatography.

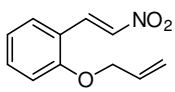


Method B:[9] Aldehyde **10** (1.0 equiv.) was treated with $MeNO_2$ (12.1 equiv.), AcOH (2.9 equiv.) and NH_4OAc (2.2 equiv.) at rt under ultrasound irradiation for 3 h. The nitroolefin **2** was then isolated by column chromatography.



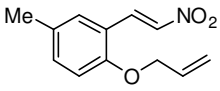
Method C:[9] Aldehyde **10** (1.0 equiv.) was treated with nitromethane (18.7 equiv.), diisopropylethylamine (0.1 equiv.) and NH_4OAc (2.5 equiv.) at rt under ultrasound irradiation for 3 h. The generated crude alcohol was treated in CH_2Cl_2 (0.1 M) with Ac_2O (1.1 equiv.) in the presence of 4-dimethylaminopyridine (0.05 equiv.) for 24 h. The nitroolefin **2** was then isolated by column chromatography.

(*E*)-1-(Allyloxy)-2-(2-nitrovinyl)benzene (2a)[10]



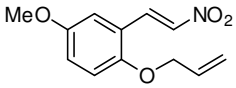
Following the general procedure **A**, aldehyde **10a** (3.80 g, 23.42 mmol, 1.0 equiv.) was treated with nitromethane (1.26 mL, 23.42 mmol, 1.0 equiv.) and 10 M NaOH aq. solution (2.6 mL, 25.76 mmol, 1.1 equiv.) in MeOH (6 mL). The corresponding nitroolefin **2a** was isolated by column chromatography (petane-DCM 4:1) as a yellow solid (2.80 g, 13.60 mmol, 58%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.17 (d, *J* = 13.6 Hz, 1H), 7.88 (d, *J* = 13.6 Hz, 1H), 7.54 – 7.35 (m, 2H), 7.07 – 6.90 (m, 2H), 6.10 (ddt, *J* = 17.1, 10.6, 5.4 Hz, 1H), 5.44 (dq, *J* = 17.3, 1.5 Hz, 1H), 5.37 (dq, *J* = 10.5, 1.3 Hz, 1H), 4.68 (dt, *J* = 5.5, 1.5 Hz, 2H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 158.6, 138.4, 135.6, 133.5, 132.5, 132.3, 121.4, 119.4, 119.0, 112.6, 69.5; **HRMS** (ESI^+) calculated for $C_{11}H_{11}NO_3$+Na^+ $[M+Na]^+$: m/z = 228.0631, found 228.0636.

(*E*)-1-(Allyloxy)-4-methyl-2-(2-nitrovinyl)benzene (2e)



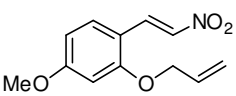
Following the general procedure **B**, aldehyde **10e** (916 mg, 5.20 mmol, 1.0 equiv.) was treated with nitromethane (3.40 mL, 63.00 mmol, 12.1 equiv.), acetic acid (0.86 mL, 15.08 mmol, 2.9 equiv.) and NH_4OAc (882 mg, 11.44 mmol, 2.2 equiv.). The corresponding nitroolefin **2e** was isolated by column chromatography (petane-EtOAc 98:2→7:1) as a yellow solid (990 mg, 4.52 mmol, 87%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.14 (d, *J* = 13.6 Hz, 1H), 7.87 (d, *J* = 13.6 Hz, 1H), 7.26 – 7.19 (m, 2H), 6.86 (d, *J* = 8.3 Hz, 1H), 6.08 (ddt, *J* = 17.3, 10.6, 5.4 Hz, 1H), 5.42 (dq, *J* = 17.3, 1.5 Hz, 1H), 5.35 (dq, *J* = 10.5, 1.3 Hz, 1H), 4.64 (dt, *J* = 5.4, 1.5 Hz, 2H), 2.31 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 156.6, 138.2, 135.8, 134.1, 132.7, 132.5, 130.7, 119.1, 118.7, 112.6, 69.6, 20.4; **HRMS** (ESI^+) calculated for $C_{12}H_{13}NO_3$+Na^+ $[M+Na]^+$: m/z = 242.0788, found 242.0785.

(*E*)-1-(Allyloxy)-4-methoxy-2-(2-nitrovinyl)benzene (2f)



Following the general procedure **B**, aldehyde **10f** (1.41 g, 7.34 mmol, 1.0 equiv.) was treated with nitromethane (4.80 mL, 88.78 mmol, 12.1 equiv.), acetic acid (1.20 mL, 21.28, 2.9 equiv.) and NH_4OAc (1.24 g, 16.14 mmol, 2.2 equiv.). The corresponding nitroolefin **2f** was isolated by column chromatography (petane-DCM 4:1→3:1) as a yellow solid (1.46 mg, 6.20 mmol, 85%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.14 (d, *J* = 13.6 Hz, 1H), 7.85 (d, *J* = 13.6 Hz, 1H), 7.02 – 6.86 (m, 3H), 6.08 (ddt, *J* = 17.3, 10.6, 5.4 Hz, 1H), 5.42 (dq, *J* = 17.3, 1.5 Hz, 1H), 5.34 (dq, *J* = 10.5, 1.3 Hz, 1H), 4.62 (dt, *J* = 5.4, 1.5 Hz, 2H), 3.80 (s, 3H); **^{13}C NMR** (75MHz, $CDCl_3$): δ = 153.8, 153.0, 138.6, 135.4, 132.6, 120.0, 119.3, 118.7, 116.1, 114.0, 70.1, 56.0; **HRMS** (ESI) calculated for $C_{12}H_{13}NO_4$+Na^+ $[M+Na]^+$: m/z = 258.0737, found 258.0739.

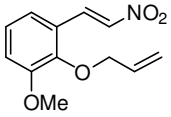
(*E*)-1-(Allyloxy)-5-methoxy-2-(2-nitrovinyl)benzene (2g)



Following the general procedure **B**, aldehyde **10g** (620 mg, 3.20 mmol, 1.0 equiv.) was treated with nitromethane (2.10 mL, 39.03 mmol, 12.1 equiv.), acetic acid (0.53 mL, 9.28 mmol, 2.9 equiv.) and NH_4OAc (543 mg, 7.04 mmol, 2.2 equiv.). The

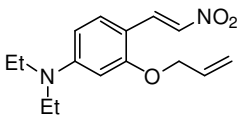
corresponding nitroolefin **2g** was isolated by column chromatography (petane-DCM 5:1→3:1→1:1) as a yellow solid (685 mg, 2.91 mmol, 91%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.12 (d, *J* = 13.5 Hz, 1H), 7.84 (d, *J* = 13.5 Hz, 1H), 7.39 (d, *J* = 8.6 Hz, 1H), 6.56 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.48 (d, *J* = 2.3 Hz, 1H), 6.10 (ddt, *J* = 17.3, 10.7, 5.4 Hz, 1H), 5.44 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.38 (dq, *J* = 10.5, 1.3 Hz, 1H), 4.65 (dt, *J* = 5.4, 1.4 Hz, 2H), 3.86 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 164.4, 160.3, 136.2, 135.9, 134.4, 132.2, 119.1, 112.7, 106.3, 99.9, 69.7, 55.8; **HRMS** (ESI^+) calculated for $C_{12}H_{13}NO_4$+Na^+ $[M+Na]^+$: m/z = 258.0737, found 258.0742.

(*E*)-1-(Allyloxy)-6-methoxy-2-(2-nitrovinyl)benzene (2h)



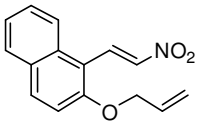
Following the general procedure **B**, aldehyde **10h** (1.31 g, 6.80 mmol, 1.0 equiv.) was treated with nitromethane (4.45 mL, 82.28 mmol, 12.1 equiv.), acetic acid (1.11 mL, 19.72 mmol, 2.9 equiv.) and NH_4OAc (1.15 mg, 14.96 mmol, 2.2 equiv.). The corresponding nitroolefin **2h** was isolated by column chromatography (petane-DCM 4:1) as a yellow solid (1.17 mg, 4.97 mmol, 73%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.22 (d, *J* = 13.7 Hz, 1H), 7.75 (d, *J* = 13.7 Hz, 1H), 7.14 – 6.98 (m, 3H), 6.07 (ddt, *J* = 17.1, 10.3, 6.1 Hz, 1H), 5.37 (dq, *J* = 17.1, 1.5 Hz, 1H), 5.27 (dq, *J* = 10.3, 1.1 Hz, 1H), 4.60 (dt, *J* = 6.1, 1.3 Hz, 2H), 3.89 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 153.3, 148.1, 138.5, 135.0, 133.3, 124.6, 124.6, 121.3, 119.1, 115.8, 74.5, 56.0; **HRMS** (ESI^+) calculated for $C_{12}H_{13}NO_4$+Na^+ $[M+Na]^+$: m/z = 258.0737, found 258.0738.

(*E*)-1-(Allyloxy)-5-diethylamino-2-(2-nitrovinyl)benzene (2i)



Following the general procedure **B**, aldehyde **10i** (933 mg, 4.00 mmol, 1.0 equiv.) was treated with nitromethane (2.62 mL, 48.40 mmol, 12.1 equiv.), acetic acid (0.66 mL, 11.60 mmol, 2.9 equiv.) and NH_4OAc (678 mg, 8.80 mmol, 2.2 equiv.). The corresponding nitroolefin **2i** was isolated by column chromatography (petane-DCM 7:3→1:1) as a yellow solid (1.02 mg, 3.68 mmol, 92%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 13.2 Hz, 1H), 7.77 (d, *J* = 13.2 Hz, 1H), 7.25 (d, *J* = 9.0 Hz, 1H), 6.29 (dd, *J* = 8.9, 2.4 Hz, 1H), 6.18 – 6.00 (m, 2H), 5.44 (dq, *J* = 17.3, 1.5 Hz, 1H), 5.35 (dq, *J* = 10.5, 1.3 Hz, 1H), 4.65 (dt, *J* = 5.5, 1.5 Hz, 2H), 3.41 (q, *J* = 7.1 Hz, 4H), 1.21 (t, *J* = 7.1 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 161.1, 152.3, 137.0, 134.8, 132.8, 132.7, 118.6, 107.3, 105.1, 94.9, 69.3, 45.0, 12.7; **HRMS** (ESI^+) calculated for $C_{15}H_{20}N_2O_3$+Na^+ $[M+Na]^+$: m/z = 299.1366, found 299.1367.

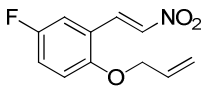
(*E*)-2-(Allyloxy)-1-(2-nitrovinyl)naphthalene (2j)



Following the general procedure **B**, aldehyde **10j** (620 mg, 3.20 mmol, 1.0 equiv.) was treated with nitromethane (2.62 mL, 48.40 mmol, 12.1 equiv.), acetic acid (0.66 mL, 11.60 mmol, 2.9 equiv.) and NH_4OAc (678 mg, 8.80 mmol, 2.2 equiv.). The corresponding nitroolefin **2j** was isolated by column chromatography (petane-DCM 7:1) as a yellow solid (932 mg,

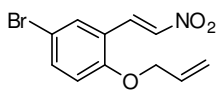
3.65 mmol, 91%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.84 (d, *J* = 13.3 Hz, 1H), 8.24 – 8.10 (m, 2H), 7.94 (d, *J* = 9.1 Hz, 1H), 7.90 – 7.76 (m, 1H), 7.61 (ddd, *J* = 8.5, 6.9, 1.4 Hz, 1H), 7.44 (ddd, *J* = 8.0, 6.9, 1.0 Hz, 1H), 7.28 (d, *J* = 9.2 Hz, 1H), 6.14 (ddt, *J* = 17.3, 10.6, 5.4 Hz, 1H), 5.47 (dq, *J* = 17.3, 1.5 Hz, 1H), 5.40 (dq, *J* = 10.5, 1.3 Hz, 1H), 4.84 (dt, *J* = 5.4, 1.5 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 158.1, 140.5, 134.3, 133.5, 132.3, 131.0, 129.1, 129.1, 128.6, 124.7, 122.4, 119.3, 113.5, 112.0, 70.2; **HRMS** (ESI^+) calculated for $C_{15}H_{13}NO_3$+Na^+ $[M+Na]^+$: m/z = 278.0788, found 278.0790.

(*E*)-1-(Allyloxy)-4-fluoro-2-(2-nitrovinyl)benzene (2k)



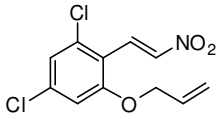
Following the general procedure **C**, aldehyde **10k** (1.19 g, 6.59 mmol, 1.0 equiv.) was treated with nitromethane (6.60 mL, 123 mmol, 18.7 equiv.), diisopropylethylamine (113 µL, 0.66 mmol, 0.1 equiv.) and NH_4OAc (1.27 g, 16.5 mmol, 2.5 equiv.). The generated alcohol was treated with Ac_2O (0.69 mL, 7.25 mmol, 1.1 equiv.) in the presence of 4-dimethylaminopyridine (40.3 mg, 0.33 mmol, 0.05 equiv.). The corresponding nitroolefin **2k** was isolated by column chromatography (petane-DCM 8:2) as a yellow solid (366 mg, 1.58 mmol, 24%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.10 (d, *J* = 13.6 Hz, 1H), 7.81 (d, *J* = 13.6 Hz, 1H), 7.21 – 7.06 (m, 2H), 6.96 – 6.86 (m, 1H), 6.07 (ddt, *J* = 17.3, 10.6, 5.4 Hz, 1H), 5.43 (dq, *J* = 17.3, 1.5 Hz, 1H) 5.36 (dq, *J* = 10.5, 1.3 Hz, 1H), 4.64 (dt, *J* = 5.5, 1.5 Hz, 2H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 156.8 (d, ^1J = 240.7 Hz), 154.7 (d, ^4J = 2.1 Hz), 139.2 , 134.2 (d, ^4J = 2.4 Hz), 132.1 , 120.4 (d, ^3J = 7.7 Hz), 119.7 (d, ^2J = 23.1 Hz), 119.1, 117.6 (d, ^2J = 23.6 Hz), 113.9 (d, ^3J = 8.0 Hz), 70.1; **^{19}F NMR** (282 MHz, Chloroform-*d*): δ = -122.56; **HRMS** (ESI^+) calculated for $C_{11}H_{10}FNO_3$+Na^+ $[M+Na]^+$: m/z = 246.0537, found 246.0539.

(*E*)-1-(Allyloxy)-4-bromo-2-(2-nitrovinyl)benzene (2l)[10]



Following the general procedure **C**, aldehyde **10l** (1.67 g, 6.91 mmol, 1.0 equiv.) was treated with nitromethane (6.92 mL, 129.18 mmol, 18.7 equiv.), diisopropylethylamine (118 µL, 0.69 mmol, 0.1 equiv.) and NH_4OAc (1.33 g, 17.27 mmol, 2.5 equiv.). The generated alcohol was treated with Ac_2O (0.72 mL, 7.60 mmol, 1.1 equiv.) in the presence of 4-dimethylaminopyridine (42.2 mg, 0.35 mmol, 0.05 equiv.). The corresponding nitroolefin **2l** was isolated by column chromatography (petane-DCM 8:2) as a yellow solid (1.10 g, 3.85 mmol, 56%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.00 (d, *J* = 13.6 Hz, 1H), 7.75 (d, *J* = 13.7 Hz, 1H), 7.50 (d, *J* = 2.5 Hz, 1H), 7.43 (dd, *J* = 8.9, 2.5 Hz, 1H), 6.78 (d, *J* = 8.9 Hz, 1H), 6.00 (ddt, *J* = 17.3, 10.7, 5.4 Hz, 1H), 5.40 – 5.28 (m, 2H), 4.59 (dt, *J* = 5.4, 1.5 Hz, 2H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 157.4, 139.2, 135.7, 134.3, 133.9, 131.8, 121.3, 119.3, 114.4, 113.4, 69.9; **HRMS** (ESI^+)calculated for $C_{11}H_{10}BrNO_3$+Na^+ $[M+Na]^+$: m/z = 305.9736, found 305.9729.

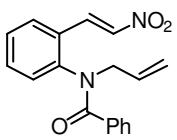
(*E*)-1-(allyloxy)-3,5-dichloro-2-(2-nitrovinyl)benzene (2m)



Following the general procedure **B**, aldehyde **10m** (749 mg, 3.24 mmol, 1.0 equiv.) was treated with nitromethane (2.1 mL, 39.2 mmol, 12.1 equiv.), acetic acid (0.54 mL,

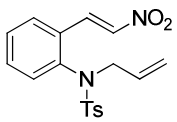
9.40 mmol, 2.9 equiv.) and NH_4OAc (549 mg, 7.13 mmol, 2.2 equiv.). The corresponding nitroolefin **2m** was isolated by column chromatography (petane-DCM 8:1) as a yellow solid (533 mg, 1.94 mmol, 60%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.42 (d, *J* = 13.6 Hz, 1H), 8.05 (d, *J* = 13.6 Hz, 1H), 7.16 (d, *J* = 1.9 Hz, 1H), 6.89 (d, *J* = 1.9 Hz, 1H), 6.08 (ddt, *J* = 17.2, 10.4, 5.5 Hz, 1H), 5.47 (dq, *J* = 10.0, 1.2 Hz, 1H), 5.42 (dq, *J* = 3.3, 1.2 Hz, 1H), 4.69 (dt, *J* = 5.5, 1.4 Hz, 2H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 159.3, 140.9, 138.2, 138.1, 130.6, 130.0, 122.7, 119.9, 116.3, 111.6, 70.6; **HRMS** (ESI^+) calculated for $C_{11}H_9Cl_2NO_3$+Na^+ $[M+Na]^+$: m/z = 295.9852, found 295.9858.

(E)-*N*-Allyl-*N*-(2-(2-nitrovinyl)phenyl)benzamide (2n)



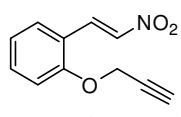
Following the general procedure **A**, aldehyde **10n** (660 mg, 2.48 mmol, 1.0 equiv.) was treated with nitromethane (140 µL, 2.48 mmol, 1.0 equiv.) and 10 M NaOH aq. solution (0.27 mL, 2.73 mmol, 1.1 equiv.) in MeOH (1 mL). The corresponding nitroolefine **2n** was isolated by column chromatography (petane-EtOAc 6:1→3:1) as a yellow solid (534 mg, 1.73 mmol, 80%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.04 (d, *J* = 13.6 Hz, 1H), 7.56 – 7.00 (m, 10H), 6.02 (dq, *J* = 16.5, 7.5 Hz, 1H), 5.23 – 5.09 (m, 2H), 4.64 (dd, *J* = 14.3, 6.5 Hz, 1H), 4.34 (dd, *J* = 14.2, 7.0 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 138.6, 135.3, 134.4, 132.8, 131.9 (2C), 130.3 (2C), 128.5 (2C), 128.5 (2C), 128.4, 128.2, 128.0 (2C), 119.9, 54.0; **HRMS** (ESI^+) calculated for $C_{18}H_{16}N_2O_3$+Na^+ $[M+Na]^+$: m/z = 331.1053, found 331.1054.

(E)-*N*-Allyl-4-Methyl-N-(2-(2-nitrovinyl)phenyl)benzenesulfonamide (2o)



Following the general procedure **A**, aldehyde **10o** (1.00 g, 3.17 mmol, 1.0 equiv.) was treated with nitromethane (178 µL, 3.33 mmol, 1.05 equiv.) and 10 M NaOH aq. solution (0.35 mL, 3.49 mmol, 1.1 equiv.) in MeOH (0.78 mL). The corresponding nitroolefin **2o** was isolated by column chromatography (petane-DCM-EtOAc 4:1:0.1) as a yellow solid (357 mg, 1.00 mmol, 31%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.21 (d, *J* = 13.8 Hz, 1H), 7.64 – 7.58 (m, 1H), 7.54 (d, *J* = 8.3 Hz, 2H), 7.48 (d, *J* = 13.8 Hz, 1H), 7.42 – 7.36 (m, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 6.94 – 6.83 (m, 1H), 5.74 (ddt, *J* = 16.9, 10.0, 6.8 Hz, 1H), 5.13 – 4.85 (m, 2H), 4.44 (br.s, 1H), 3.94 (br.s, 1H), 2.44 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 144.5, 139.7, 138.4, 135.2, 134.9, 132.3, 132.0, 131.8, 130.1, 129.9 (2C), 129.2, 128.2 (2C), 128.0, 120.6, 55.0, 21.7; **HRMS** (ESI^+) calculated for $C_{18}H_{18}N_2O_4S$+Na^+ $[M+Na]^+$: m/z = 381.0879, found 381.0878.

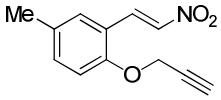
(*E*)-1-(2-Nitrovinyl)-2-(prop-2-yn-1-yloxy)benzene (2p)[7]



Following the general procedure **B**, aldehyde **10p** (1.00 g, 6.24 mmol, 1.0 equiv.) was treated with nitromethane (4.04 mL, 75.5 mmol, 12.1 equiv.), acetic acid (1.03 mL, 18.10 mmol, 2.9 equiv.) and NH_4OAc (1.06 g, 13.73 mmol, 2.2 equiv.). The corresponding nitroolefin **2p** was isolated by column chromatography (petane-DCM 8:2) as a yellow solid (938 mg, 4.62 mmol, 74%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.15 (d, *J* = 13.6 Hz, 1H), 7.85 (d, *J* = 13.6 Hz, 1H), 7.54 – 7.40 (m, 2H), 7.16 – 7.00 (m, 2H),

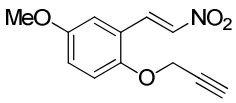
4.84 (d, J = 2.4 Hz, 2H), 2.59 (t, J = 2.4 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 157.3, 138.6, 135.18, 133.4, 132.4, 122.1, 119.7, 112.8, 77.5, 76.8, 56.3; **HRMS** (ESI^+): calculated for $C_{11}H_9NO_3$+Na^+ $[M+Na]^+$: m/z = 226.0475, found 226.0476.

(*E*)-4-Methyl-2-(2-nitrovinyl)-1-(prop-2-yn-1-yloxy)benzene (2q)



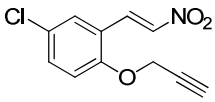
Following the general procedure **B**, aldehyde **10q** (650 mg, 3.73 mmol, 1.0 equiv.) was treated with nitromethane (2.42 mL, 45.13 mmol, 12.1 equiv.), acetic acid (0.62 mL, 10.82 mmol, 2.9 equiv.) and NH_4OAc (633 mg, 8.21 mmol, 2.2 equiv.). The corresponding nitroolefin **2q** was isolated by column chromatography (petane-DCM 3:1) as a yellow solid (651 mg, 2.99 mmol, 80%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.13 (d, J = 13.7 Hz, 1H), 7.84 (d, J = 13.6 Hz, 1H), 7.34 – 7.18 (m, 2H), 6.99 (d, J = 8.9 Hz, 1H), 4.81 (d, J = 2.4 Hz, 2H), 2.56 (t, J = 2.4 Hz, 1H), 2.32 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 155.4, 138.5, 135.4, 134.0, 132.6, 131.5, 119.5, 112.9, 76.6, 56.4, 20.4; **HRMS** (ESI^+): calculated for $C_{12}H_{11}NO_3$+Na^+ $[M+Na]^+$: m/z = 240.0631, found 240.0639.

(*E*)-4-Methoxy-2-(2-nitrovinyl)-1-(prop-2-yn-1-yloxy)benzene (2r)



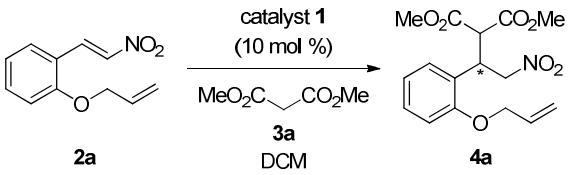
Following the general procedure **B**, aldehyde **10r** (1.12 g, 5.89 mmol, 1.0 equiv.) was treated with nitromethane (3.82 mL, 71.25 mmol, 12.1 equiv.), acetic acid (0.98 mL, 17.08 mmol, 2.9 equiv.) and NH_4OAc (999 mg, 12.96 mmol, 2.2 equiv.). The corresponding nitroolefin **2r** was isolated by column chromatography (petane-DCM 2:1) as a yellow solid (1.14 g, 4.90 mmol, 83%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.13 (d, J = 13.6 Hz, 1H), 7.82 (d, J = 13.6 Hz, 1H), 7.16 – 6.86 (m, 3H), 4.78 (d, J = 2.4 Hz, 2H), 3.81 (s, 3H), 2.56 (t, J = 2.4 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 154.3, 151.7, 138.8, 135.0, 120.5, 119.0, 116.1, 114.4, 77.9, 76.6, 56.9, 56.0; 20.4; **HRMS** (ESI^+): calculated for $C_{12}H_{11}NO_4$+Na^+ $[M+Na]^+$: m/z = 256.0580, found 256.0580.

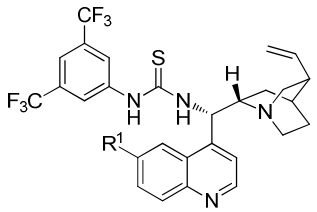
(*E*)-4-Chloro-2-(2-nitrovinyl)-1-(prop-2-yn-1-yloxy)benzene (2s)



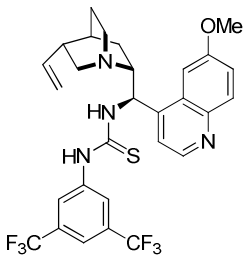
Following the general procedure **A**, aldehyde **10s** (1.18 g, 6.06 mmol, 1.0 equiv.) was treated with nitromethane (341 µL, 6.36 mmol, 1.05 equiv.) and 10 M NaOH aq. solution (666 µL, 6.67 mmol, 1.1 equiv.) in MeOH (1.38 mL). The corresponding nitroolefin **2s** was isolated by column chromatography (petane-DCM 4:1) as a yellow solid (1.08 g, 4.55 mmol, 75%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.08 (d, J = 13.7 Hz, 1H), 7.81 (d, J = 13.7 Hz, 1H), 7.49 – 7.38 (m, 2H), 7.05 (d, J = 8.8 Hz, 1H), 4.83 (d, J = 2.4 Hz, 2H), 2.59 (t, J = 2.4 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 155.7, 139.4, 133.6, 132.7, 131.2, 127.1, 121.2, 114.3, 77.2, 77.1, 56.7; **HRMS** (ESI^+): calculated for $C_{11}H_8ClNO_3$+Na^+ $[M+Na]^+$: m/z = 260.0085, found 260.0086.

Optimization of the model organocatalyzed asymmetric reaction[a]

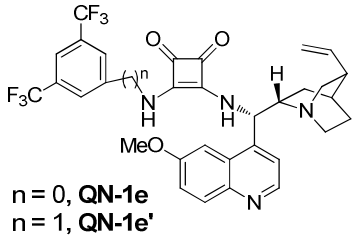




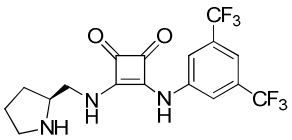
QN-1a, R^1 = OMe
CD-1c, R^1 = H



QD-1b, R^1 = OMe
CN-1d, R^1 = H



n = 0, **QN-1e**
n = 1, **QN-1e'**



1f

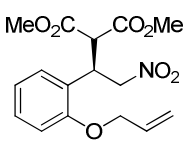
entry	1	Temp. (°C)	time (d)	yield (%)[b]	Ee (%)[c]	(Conf.)
1	**QN-1a**	30	3	99	-90	(*S*)
2	**QD-1b**	30	3	99	92	(*R*)
3	**CD-1c**	30	3	99	-92	(*S*)
4	**CN-1d**	30	3	99	91	(*R*)
5	**QN-1e**	30	3	99	-74	(*S*)
6	**1f**	30	3	<10	0	0
7	**QD-1b**	10	4	99	95	(*R*)
8	**QD-1b**	10[d]	7	99	96	(*R*)
9	**QD-1b**	10[d],[e]	7	99	96	(*R*)

[a] Catalyst **1** (10 mol %), **2a** (0.1 mmol) and **3** (0.12 mmol) in DCM (0.5 mL, 0.2 M). [b] GC-yield. [c] Ee determined by chiral HPLC. [d] Reaction in *o*-xylene. [e] Same results for the reactions in 1 mL *o*-xylene (0.1 M) and 0.2 mL (0.5 M).

An ordinary vial equipped with a magnetic stirring bar was charged with catalyst **1** (10 mol%), malonate **3** (0.24 mmol), nitroolefin **2** (0.20 mmol) and *o*-xylene (1.0 mL) at 10 ºC. The stirring was maintained at 10 ºC for 7 d. The crude reaction mixture was directly charged onto silica-gel and purified by column chromatography.

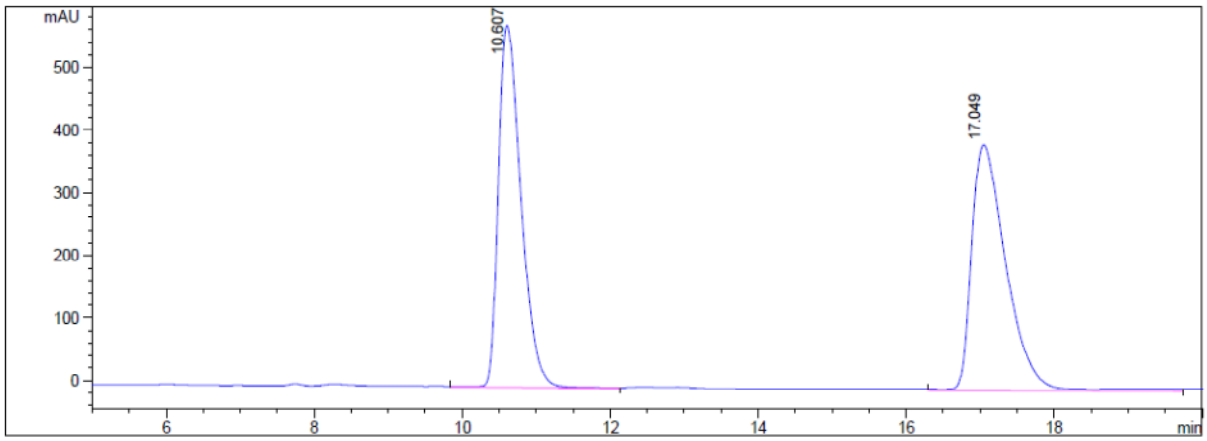
The corresponding racemic products were prepared using DABCO (leading to very low yields) or a 1:1 mixture of pseudoenantiomers of the thiourea-chincona derivatives in CH_2Cl_2 at 40 °C for 3 d.

(*R*)-Dimethyl 2-(1-(2-(allyloxy)phenyl)-2-nitroethyl)malonate (4a)

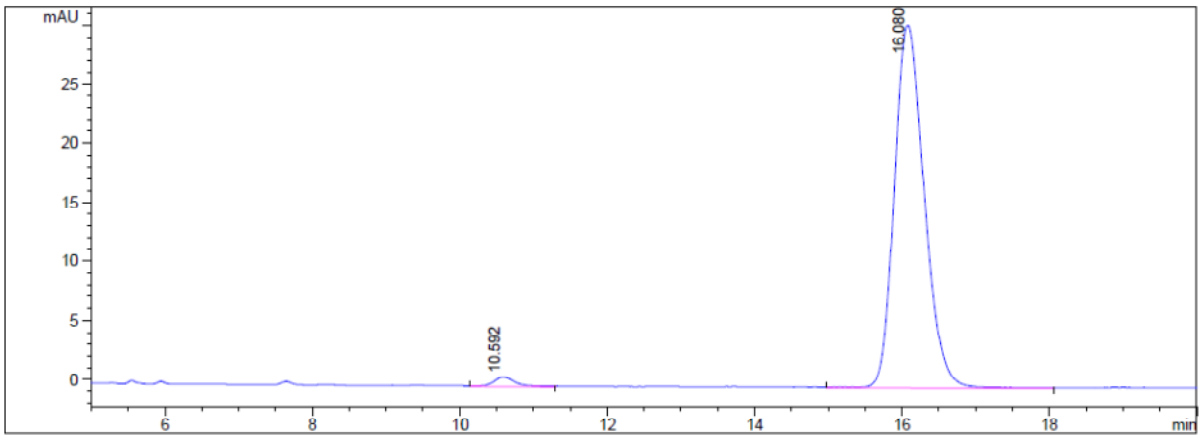


According to the general procedure using 10 mol% of catalyst **1b**, the title compound **4a** was obtained after FC (petane-EtOAc 6:1) as a white solid (99%, 96% ee). $[\alpha]^{20}_D$ = -21.7 (*c* 1.05 $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.22 (ddd, *J* = 8.1, 7.5, 1.7 Hz, 1H), 7.15 (dd, *J* = 7.6, 1.7 Hz, 1H), 6.92 – 6.81 (m, 2H), 6.08 (ddt, *J* = 17.3, 10.5, 5.2 Hz, 1H), 5.43 (dq, *J* = 17.3, 1.6 Hz, 1H), 5.32 (dq, *J* = 10.6, 1.4 Hz, 1H), 5.06 (dd, *J* = 13.0, 9.1 Hz, 1H), 4.89 (dd, *J* = 13.0, 4.6 Hz, 1H),

4.65 – 4.54 (m, 2H), 4.42 (td, J = 9.5, 4.6 Hz, 1H), 4.21 (d, J = 9.9 Hz, 1H), 3.75 (s, 3H), 3.50 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 168.4, 167.7, 156.4, 132.9, 130.8, 129.7, 123.9, 121.1, 118.1, 112.4, 76.1, 69.2, 53.0, 52.7, 52.7, 40.5; **HRMS** (ESI^+) calculated for $C_{16}H_{19}NO_7$+Na^+ $[M+Na]^+$: m/z = 360.1054, found 360.1051. **IR**: ν_{max} 3027, 2960, 2875, 2360, 2337, 1757, 1723, 1600, 1587, 1552, 1495, 1457, 1433, 1379, 1365, 1348, 1332, 1307, 1288, 1229, 1197, 1170, 1121, 1084, 1067, 1011, 999, 984, 937, 924, 851, 837, 762; HPLC: OD-H, Pentane:*i*-PrOH 90:10, F = 1.0 mL/min, λ = 230 nm, t_R minor (*S*) = 10.3 min, t_R major (*R*) = 15.1 min.

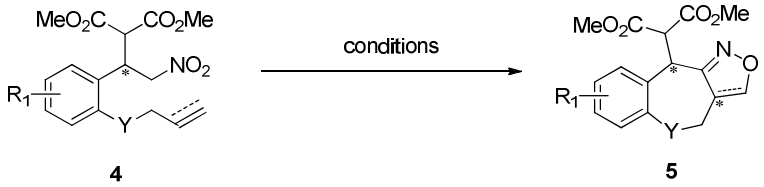


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	10.607	577.765	59.559	12287.461	49.099
2	17.049	392.306	40.441	12738.391	50.901



#	Meas. Ret. Time	Height	Height %	Area	Area %
1	10.592	0.828	2.622	17.675	1.999
2	16.080	30.742	97.378	866.649	98.001

Optimization and general procedure for the nitrile cycloaddition reaction

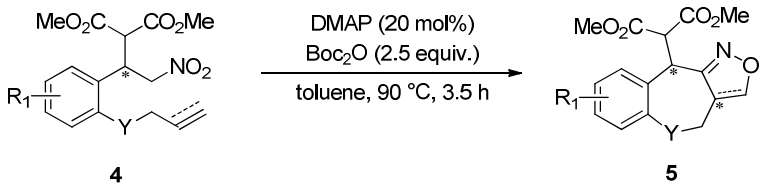


4 **5**

Entry	reagent (equiv.)	additive	Solvent	time (h)	Temp.	Yield (%)[a]	Ee (%)[d]
1	$ClCO_2Et$ (2)	Et_3N	Benzene	6 h	90 °C	30	Nd
2	$PhSO_2Cl$ (2)	Et_3N	$CHCl_3$	15 h	0 °C à rt	40	Nd
3	PhNCO (1.8)	Et_3N	Benzene	4 h	rt à 90 °C	72[b]	Nd
4	Boc_2O (2.5)	DMAP	MeCN	3.5 h	60 °C	32	Nd
5	Boc_2O (2.5)	DMAP	DCM	3.5 h	60 °C	traces	Nd
6	Boc_2O (2.5)	DMAP	Toluene	3.5 h	90 °C	60(75)[c]	96[e]
7	Boc_2O (2.5)	DMAP	Toluene	24 h	90 °C	40%	Nd
8	Ac_2O (2.5)	DMAP	Toluene	3.5 h	90 °C	57%	Nd

[a] Isolated yields. [b] **5a** together with inseparable byproducts. [c] NMR yield in brackets. [d] Ee determined by HPLC. [e] Starting from **4a** with 96% ee. N.d. = not determined.

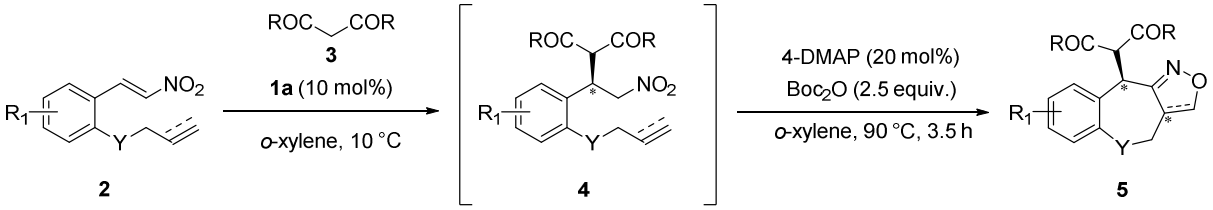
General Procedure with Boc_2O and DMAP:



4 **5**

Nitro compound **4** (0.2 mmol, 1.0 equiv.) and DMAP (0.04 mmol, 0.2 equiv.) were dissolved in freshly distilled toluene and heated to 90 °C. To the hot reaction mixture, a solution of Boc_2O in toluene (0.5 M, 1.0 mL, 2.5 equiv.) was added over 20 min. The reaction was then allowed to proceed for further 3.5 h at 90 °C. After cooling to room temperature, the crude reaction mixture was directly charged onto silica-gel and purified by column chromatography.

General procedure for the one-pot reaction

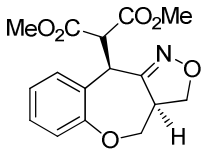


2 **4** **5**

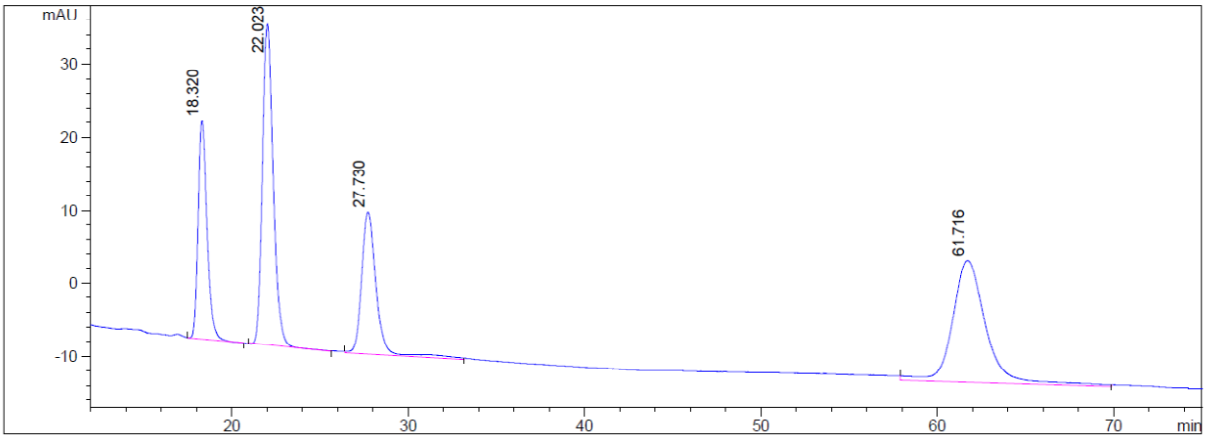
A schlenk tube was charged with catalyst **1** (10 mol%), malonate or diketone **3** (0.24 mmol), nitroolefin **2** (0.20 mmol) and dry *o*-xylene (1.0 mL) at 10 ºC. The stirring was maintained at 10 ºC for 7 d. Then, 0.1 mL of

a solution of 4-DMAP (4.9 mg, 0.04 mmol, 0.2 equiv.) and Boc_2O (109.1 mg, 0.5 mmol, 2.5 equiv.) in dry *o*-xylene (1.0 mL) was added at room temperature and the mixture stirred for 5 min. The reaction mixture was then heated at 90 °C and the rest of the solution (0.9 mL) added dropwise. (Alternatively, the reaction mixture was added dropwise to a mixture of DMAP and Boc_2O in *o*-xylene heated at 90 °C). The reaction was then allowed to proceed for further 3.5 h at 90 °C. After cooling to room temperature the crude reaction mixture was directly charged onto silica-gel and purified by column chromatography.

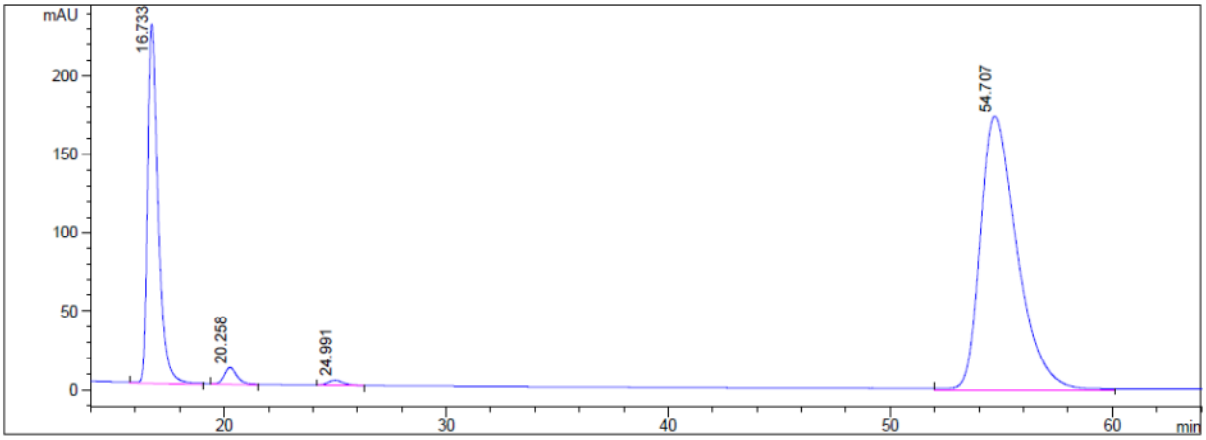
Dimethyl 2-((3a*R*,10*R*)-3,3a,4,10-tetrahydrobenzo[6,7]oxepino[4,3-c]isoxazol-10-yl)malonate (5a)



Following the general procedure, the title compound **5a** was obtained after FC (petane-EtOAc 8:1) as a white solid (61%) and a 3:1 mixture of diastereoisomers (96% ee each). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.36 – 6.94 (m, 4H major + 4H minor), 4.88 (d, *J* = 11.8 Hz, 1H major), 4.67 (d, *J* = 11.8 Hz, 1H minor), 4.56 – 4.41 (m, 2H major + 2H minor), 4.40 – 4.28 (m, 1H major + 1H minor), 3.79 (s, 3H major), 3.76 (s, 3H minor), 3.62 (s, 3H major), 3.50 (s, 3H minor) 3.92-3.50 (m, 3H major + 2H minor); **^{13}C NMR** (75 MHz, $CDCl_3$): Major isomer: δ = 168.1, 167.8, 158.1, 132.0, 130.1, 129.6, 126.8, 125.5, 122.7, 74.1, 70.5, 53.3, 53.1, 53.1, 51.6, 39.5; Minor isomer: δ = 167.4, 167.2, 156.7, 131.9, 131.2, 130.0, 128.8, 125.2, 122.8, 74.5, 70.4, 53.8, 53.2, 52.7, 50.2, 44.0; **HRMS** (ESI$^+$) calculated for $C_{16}H_{17}NO_6$+Na^+ $[M+Na]^+$: m/z = 342.0948, found 342.0950; **IR**: ν_{max} 3075, 2957, 2889, 2360, 1738, 1718, 1635, 1603, 1579, 1488, 1453, 1438, 1431, 1352, 1325, 1312, 1294, 1282, 1267, 1240, 1223, 1199, 1178, 1148, 1008, 890, 875, 788, 774; **HPLC**: IC, Pentane:*i*-PrOH 65:35, F = 1.0 mL/min, λ = 230 nm: Major isomer: t_R minor = 20.3 min, t_R major = 54.7 min; Minor isomer: t_R major = 16.7 min, t_R minor = 25.0 min.

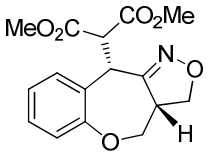


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	18.320	29.879	27.203	1051.312	16.893
2	22.023	43.883	39.953	1864.406	29.958
3	27.730	19.500	17.754	1131.214	18.177
4	61.716	16.573	15.089	2176.367	34.971

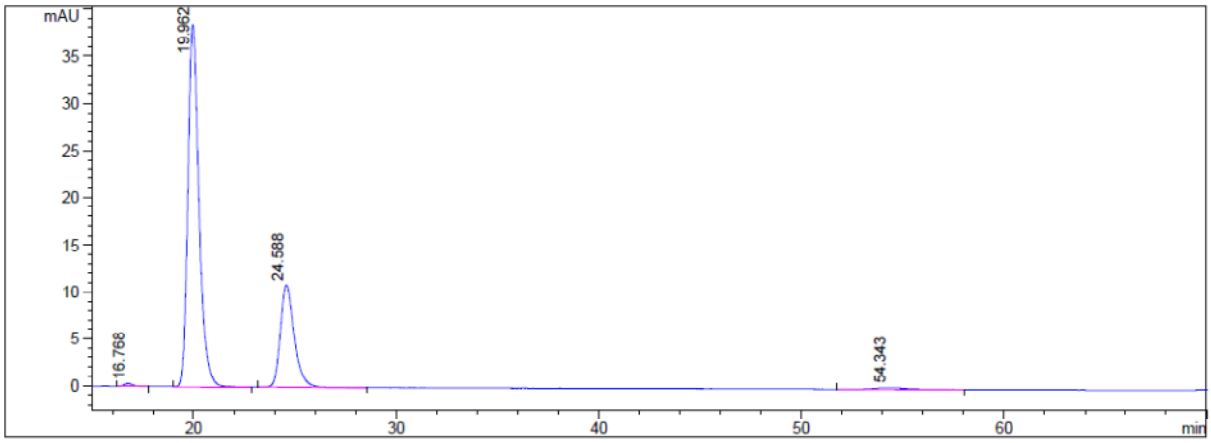


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	16.733	229.440	54.983	7617.737	26.924
2	20.258	10.606	2.542	444.362	1.571
3	24.991	3.128	0.750	152.615	0.539
4	54.707	174.116	41.725	20078.742	70.966

Dimethyl 2-((3a*S*,10*S*)-3,3a,4,10-tetrahydrobenzo[6,7]oxepino[4,3-c]isoxazol-10-yl)malonate (*ent*-5a)

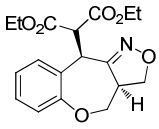


Following the general procedure, the title compound ***ent-5a*** was obtained after FC (petane-EtOAc 8:1) as a white solid (75%) and a 2.8:1 mixture of diastereoisomers (97% ee each). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.32 (dd, *J* = 7.6, 1.7 Hz, 1H, minor), 7.30 – 7.19 (m, 2H major + 2H minor), 7.19 (dd, *J* = 7.8, 2.1 Hz, 1H, major), 7.12 (dd, *J* = 7.5, 1.4 Hz, 1H, major), 7.12 – 7.03 (m, 1H major + 1H minor), 7.01 (dd, *J* = 8.0, 1.3 Hz, 1H, minor), 4.89 (d, *J* = 11.8 Hz, 1H, major), 4.68 (d, *J* = 11.8 Hz, 1H, minor), 4.56 – 4.43 (m, 2H major + 2H minor), 4.40 – 4.29 (m, 1H major + 1H minor), 3.95 – 3.79 (m, 2H major +2H minor), 3.80 (s, 3H major), 3.77 (s, 3H minor), 3.72 – 3.65 (m, 1H major), 3.63 (s, 3H), 3.58 – 3.53 (m, 1H minor), 3.51 (s, 3H minor); **^{13}C NMR** (100 MHz, $CDCl_3$): Major isomer: δ = 168.1, 167.8, 158.2, 132.1, 130.1, 129.6, 126.8, 125.6, 122.8, 74.1, 70.5, 53.3, 53.1, 53.1, 51.6, 39.5; Minor isomer: δ = 167.5, 167.2, 159.3, 156.7, 132.1, 130.1, 128.8, 125.2, 122.8, 74.5, 70.4, 53.8, 53.2, 52.7, 50.2, 44.0; **HRMS** (ESI^+) calculated for $C_{16}H_{17}NO_6$+Na^+ $[M+Na]^+$: m/z = 342.0948, found 342.0951; **IR**: ν_{max} 3075, 2957, 2889, 2360, 1738, 1718, 1635, 1603, 1579, 1488, 1453, 1438, 1431, 1352, 1325, 1312, 1294, 1282, 1267, 1240, 1223, 1199, 1178, 1148, 1008, 890, 875, 788, 774; **HPLC**: IC, Pentane:*i*-PrOH 65:35, F = 1.0 mL/min, λ = 230 nm: Major isomer: t_R major = 20.0 min, t_R minor = 54.3 min; Minor isomer: t_R minor = 16.8 min, t_R major = 24.6 min.

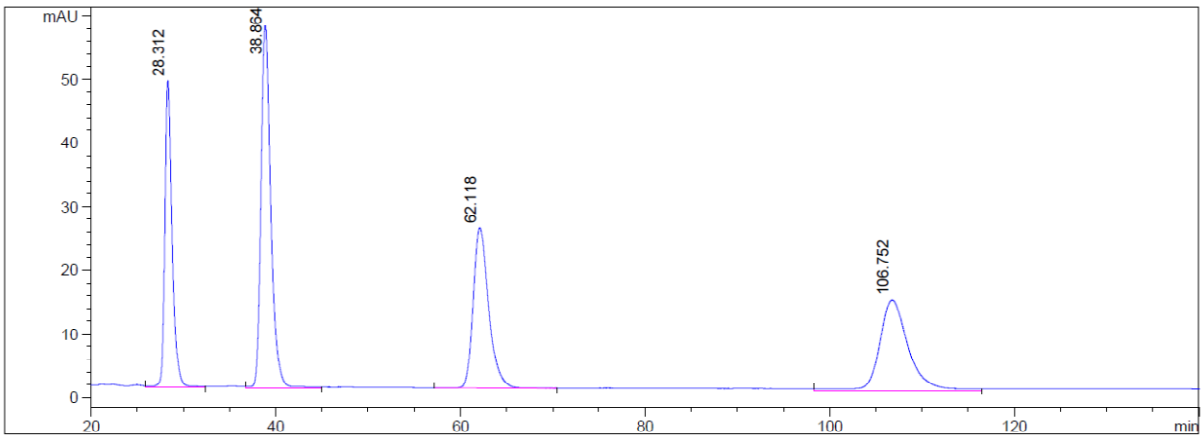


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	16.768	0.319	0.639	10.174	0.501
2	19.962	38.500	77.096	1474.819	72.615
3	24.588	10.928	21.883	522.855	25.744
4	54.343	0.190	0.381	23.160	1.140

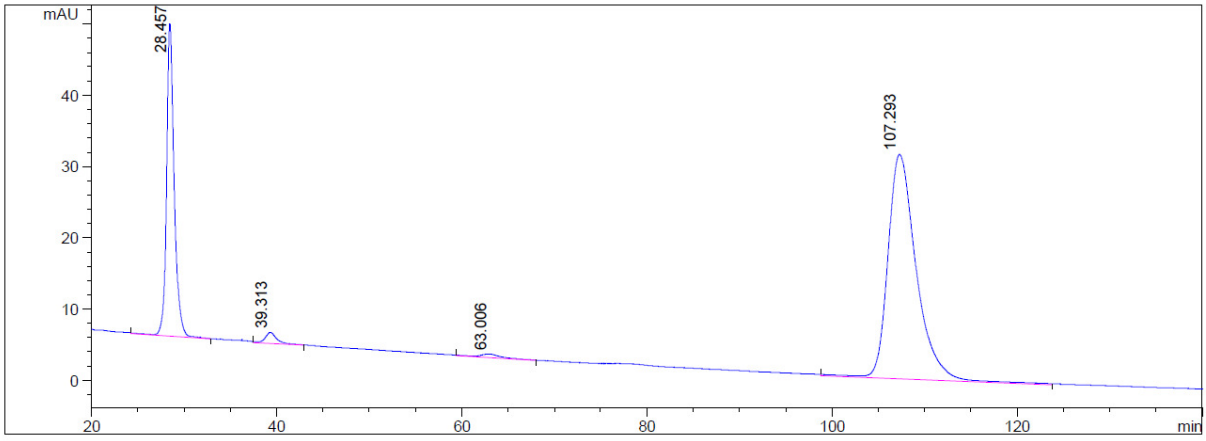
Diethyl 2-((3a*R*,10*R*)-3a-methyl-3,3a,4,10-tetrahydrobenzo[6,7]oxepino[4,3-c]isoxazol-10-yl)malonate (5b)



Following the general procedure, the title compound **5b** was obtained after FC (petane-EtOAc 8:1) as a white solid (69%) and a 2.5:1 mixture of diastereoisomers (96% ee each). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.32 (dd, *J* = 7.6, 1.7 Hz, 1H minor), 7.26 – 7.18 (m, 2H major + 1H minor), 7.13 – 6.96 (m, 2H major + 2H minor), 4.88 (d, *J* = 11.9 Hz, 1H major), 4.66 (d, *J* = 11.8 Hz, 1H minor), 4.55 – 4.40 (m, 2H major + 2H minor), 4.37 – 4.29 (m, 1H major + 1H minor), 4.29 – 4.16 (m, 2H major + 1H minor), 4.08 (q, *J* = 7.1 Hz, 2H major), 4.00 – 3.77 (m, 2H major + 3 H minor), 3.65 (t, *J* = 11.0 Hz, 1H major), 3.53 (t, *J* = 11.6 Hz, 1H minor), 1.27 (td, *J* = 7.1, 6.4 Hz, 3H major + 3H minor), 1.11 (t, *J* = 7.1 Hz, 3H major), 1.02 (t, *J* = 7.1 Hz, 3H minor); **^{13}C NMR** (100 MHz, $CDCl_3$): Major isomer: δ = 167.6, 167.4, 158.2, 158.1, 130.2, 129.5, 126.8, 125.4, 122.6, 74.1, 70.4, 62.2, 62.0, 53.4, 51.8, 39.3, 14.1, 14.0; Minor isomer: δ = 167.1, 166.7, 159.3, 156.7, 132.1, 129.9, 129.0, 125.1, 122.7, 74.6, 70.3, 62.2, 61.6, 53.9, 50.2, 44.0, 14.1, 13.9; **HRMS** (ESI^+) calculated for $C_{18}H_{21}NO_6$+Na^+ $[M+Na]^+$: m/z = 370.1261, found 370.1263; **IR**: ν_{max} 3065, 2982, 2895, 1739, 1717, 1602, 1489, 1447, 1374, 1344, 1276, 1267, 1217, 1192, 1145, 1105, 1059, 1040, 1015, 1000, 948, 916, 885, 857, 826, 786, 775, 625; **HPLC**: IC, Pentane:*i*-PrOH 80:20, F = 1.0 mL/min, λ = 230 nm: Major isomer: t_R major = 107.3 min, t_R minor = 39.3 min; Minor isomer: t_R minor = 63.0 min, t_R major = 28.5 min.

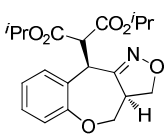


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	28.312	48.170	33.308	2623.927	20.242
2	30.064	56.957	39.304	4213.660	32.505
3	62.118	25.213	17.434	2955.840	22.802
4	106.752	14.281	9.875	3169.610	24.451



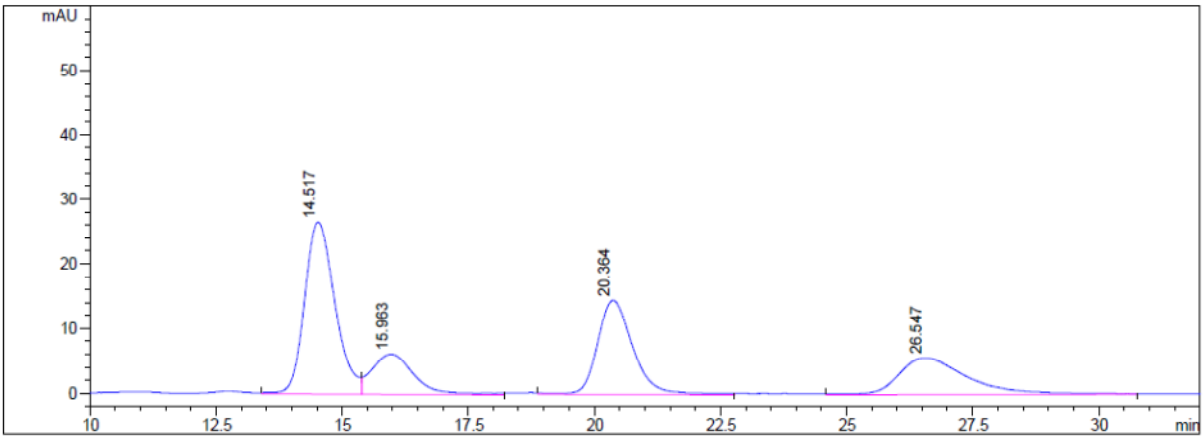
#	Meas. Ret. Time	Height	Height %	Area	Area %
1	28.457	43.908	56.707	2531.797	26.756
2	39.313	1.539	1.988	132.692	1.402
3	63.006	0.510	0.658	81.709	0.864
4	107.293	31.473	40.647	6716.169	70.978

Diisopropyl 2-((3a*R*,10*R*)-3,3a,4,10-tetrahydrobenzo[6,7]oxepino[4,3-c]isoxazol-10-yl)malonate (5c)

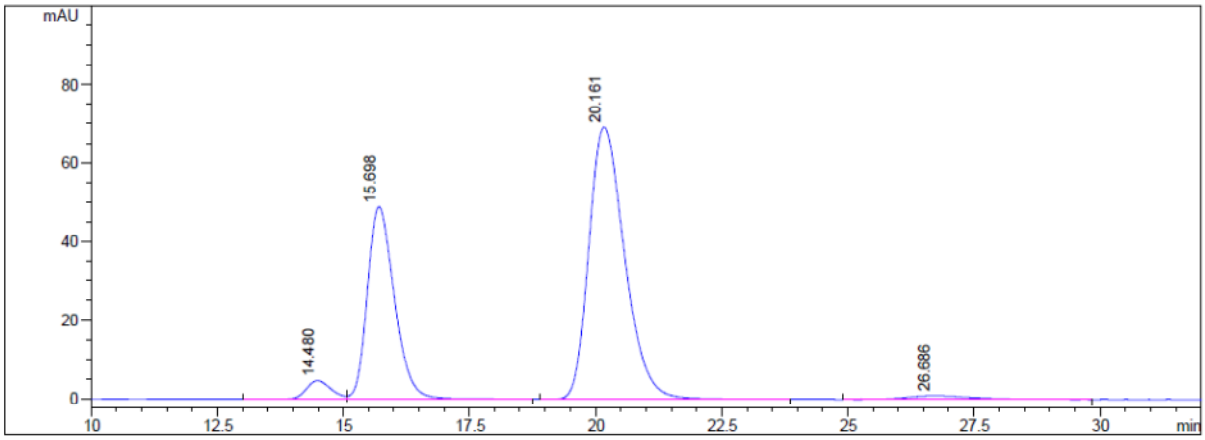


Following the general procedure, the title compound **5c** was obtained after FC (petane-EtOAc 8:1) as a white solid (75%) and a 2.2:1 mixture of diastereoisomers (90% ee each). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.33 (dd, *J* = 7.6, 1.7 Hz, 1H minor), 7.25 – 7.17 (m, 2H major + 1H minor), 7.10 – 7.02 (m, 2H major), 7.00 (dd, *J* = 8.0, 1.3 Hz, 1H minor), 5.07 (hept, *J* = 6.3 Hz, 1H major), 5.07 (hept, *J* = 6.3 Hz, 1H minor), 4.94 (hept, *J* = 6.3 Hz, 1H major), 4.87 (d, *J* = 12.0 Hz, 1H major), 4.81 (hept, *J* = 6.3 Hz, 1H minor), 4.64 (d, *J* = 11.9 Hz, 1H minor), 4.52 (ddd, *J* = 11.8, 6.7, 5.1 Hz, 1H major + 1H minor), 4.43 (d, *J* = 12.0 Hz, 1H major), 4.43 (dd, *J* = 10.9, 8.4 Hz, 1H minor), 4.34 (dd, *J* = 10.3, 8.1 Hz, 1H major), 4.27 (d, *J* = 11.9 Hz, 1H minor), 4.21 (tdd, *J* = 11.3, 8.4, 6.4 Hz, 1H minor), 3.96 – 3.85 (m, 1H major + 1H minor), 3.81 (t, *J* = 8.1 Hz, 1H major), 3.61 (t, *J* = 11.2 Hz, 1H major), 3.53 (t, *J* = 11.6 Hz, 1H minor),

1.28 (d, *J* = 6.3 Hz, 3H major), 1.26 (d, *J* = 3.1 Hz, 3H minor), 1.24 (d, *J* = 6.1 Hz, 3H major), 1.24 (d, *J* = 3.1 Hz, 3H minor), 1.14 (d, *J* = 6.3 Hz, 3H major), 1.10 (d, *J* = 6.4 Hz, 3H major) 1.15 – 1.10 (m, 3H minor), 0.93 (d, *J* = 6.3 Hz, 3H minor); **^{13}C NMR** (100 MHz, $CDCl_3$): Major isomer: δ = 167.1, 167.0, 158.4, 158.1, 130.3, 129.3, 126.6, 125.3, 122.5, 74.2, 70.2, 69.7, 69.5, 53.5, 52.0, 39.0, 21.7, 21.6, 21.5, 21.4; Minor isomer: δ = 166.7, 166.3, 159.4, 156.8, 132.3, 129.9, 129.1, 125.0, 122.7, 74.6, 70.3, 69.9, 69.2, 54.2, 50.2, 43.8, 21.7 (2C), 21.5, 21.4; **HRMS** (ESI^+) calculated for $C_{20}H_{25}NO_6$+Na^+ $[M+Na]^+$: m/z = 398.1574, found 398.1579; **IR**: ν_{max} 3065, 2982, 2936, 2881, 2363, 2342, 1744, 1729, 1488, 1466, 1454, 1375, 1297, 1260, 1239, 1219, 1177, 1164, 1097, 1006, 8914, 824, 785, 773; **HPLC**: AS-H, Pentane:*i*-PrOH 95:05, F = 1.0 mL/min, λ = 230 nm: Major isomer: t_R major = 20.2 min, t_R minor = 14.5 min; Minor isomer: t_R minor = 26.7 min, t_R major = 15.7 min.

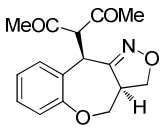


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	14.517	26.497	50.198	1106.497	40.683
2	15.963	6.154	11.659	359.559	13.220
3	20.364	14.508	27.485	712.522	26.197
4	26.547	5.626	10.659	541.254	19.900

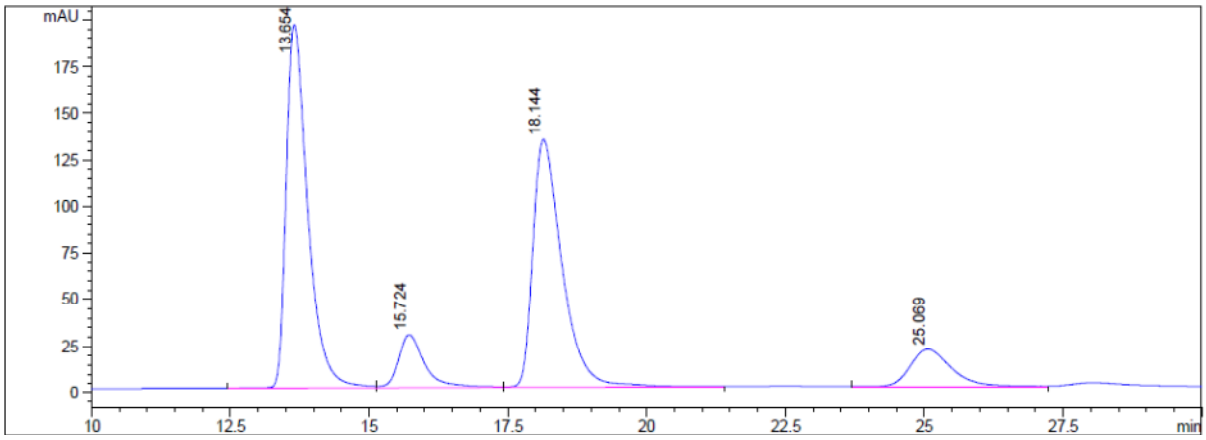


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	14.480	4.741	3.825	174.907	3.150
2	15.698	48.981	39.517	1843.588	33.201
3	20.161	69.215	55.842	3428.374	61.740
4	26.686	1.012	0.816	106.010	1.909

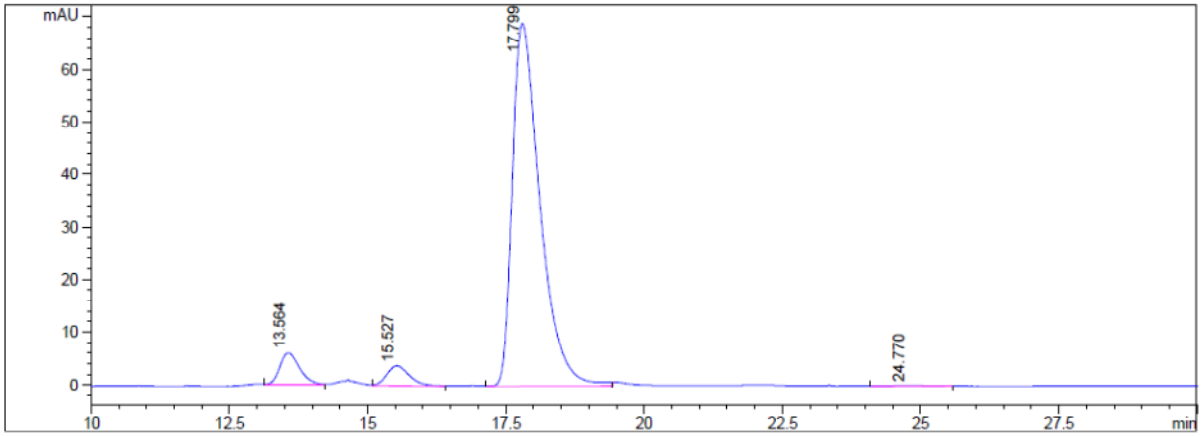
3-((3a*R*,10*R*)-3,3a,4,10-Tetrahydrobenzo[6,7]oxepino[4,3-c]isoxazol-10-yl)pentane-2,4-dione (5d)



Following the general procedure, the title compound **5d** was obtained after FC (petane-EtOAc 6:1) as a white solid (46%) and a 5.0:1 mixture of diastereoisomers (90% ee each). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 – 7.20 (m, 2H major + 2H minor), 7.11 – 7.05 (m, 1H major + 2H minor), 7.02 (dd, *J* = 7.9, 1.3 Hz, 1H major), 5.00 (d, *J* = 12.1 Hz, 1H minor), 4.93 (d, *J* = 12.1 Hz, 1H minor), 4.76 (d, *J* = 11.9 Hz, 1H major), 4.65 (d, *J* = 11. Hz, 1H major), 4.56 (dd, *J* = 11.3, 7.1 Hz, 1H minor), 4.52 (dd, *J* = 11.5, 6.3 Hz, 1H major), 4.43 (dd, *J* = 11.0, 8.4 Hz, 1H major), 4.36 (dd, *J* = 10.4, 8.2 Hz, 1H minor), 4.02 (tdd, *J* = 11.3, 8.9, 6.3 Hz, 1H major), 3.95 – 3.89 (m, 1H minor), 3.86 (t, *J* = 8.7 Hz, 1H major), 3.80 (t, *J* = 8.4 Hz, 1H minor), 3.58 (t, *J* = 11.3 Hz, 1H minor), 3.54 (t, *J* = 11.6 Hz, 1H major), 2.39 (s, 3H minor), 2.26 (s, 3H major), 2.02 (s, 3H minor), 1.86 (s, 3H major); **^{13}C NMR** (100 MHz, $CDCl_3$): Major isomer: δ = 202.5, 202.2, 159.1, 156.5, 132.0, 130.0, 128.6, 125.5, 123.0, 74.5, 70.8, 70.4, 50.0, 44.1, 32.1, 26.8; Minor isomer: δ = 202.4, 202.3, 159.1, 156.5, 132.0, 129.7, 126.7, 125.9, 122.8, 74.4, 70.5, 69.5, 52.1, 39.0, 30.8, 29.8; **HRMS** (ESI^+) calculated for $C_{16}H_{17}NO_4$+Na^+ $[M+Na]^+$: m/z = 310.1050, found 310.1058; **IR**: ν_{max} 3002, 2969, 2928, 2878, 2361, 2342, 1715, 1691, 1487, 1449, 1411, 1358, 1292, 1268, 1224,1199, 1187, 1154, 1103, 1011, 922, 866, 843, 774, 621, 612; **HPLC**: OD-H, Pentane:*i*-PrOH 90:10, F = 1.0 mL/min, λ = 230 nm: Major isomer: t_R major = 17.8 min, t_R minor = 13.6 min; Minor isomer: t_R minor = 24.8 min, t_R major = 15.5 min.

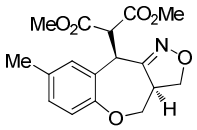


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	13.654	194.960	51.807	5268.562	43.472
2	15.724	28.457	7.562	944.606	7.794
3	18.144	132.879	35.310	4881.713	40.280
4	25.069	20.022	5.321	1024.559	8.454

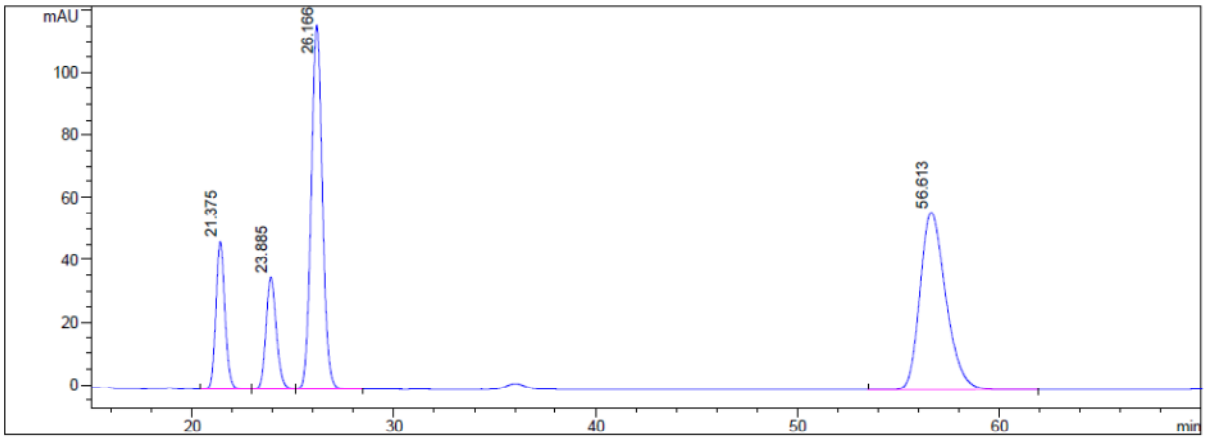


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	13.564	5.901	7.495	146.366	5.492
2	15.527	3.732	4.740	108.707	4.079
3	17.799	68.973	87.602	2403.640	90.197
4	24.770	0.128	0.162	6.179	0.232

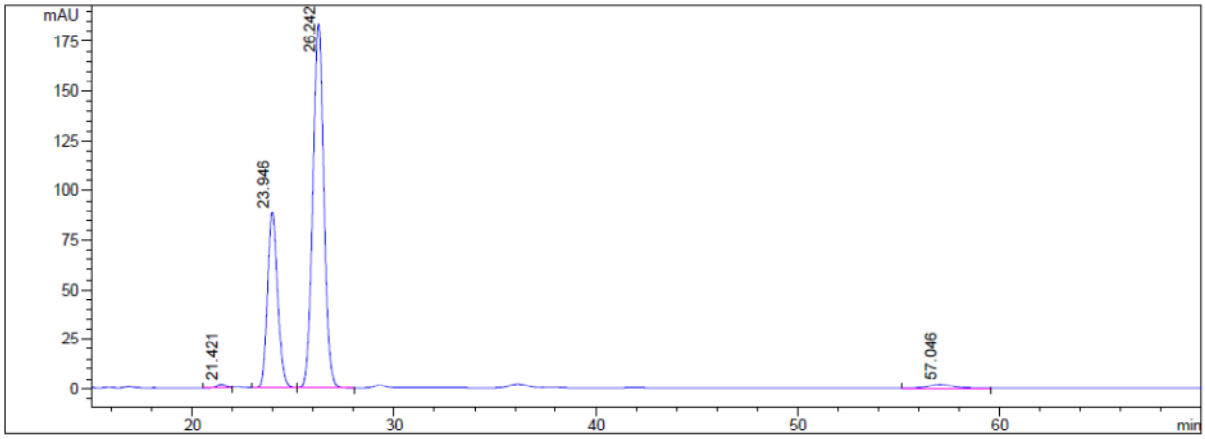
Dimethyl 2-((3a*R*,10*R*)-8-methyl-3,3a,4,10-tetrahydrobenzo[6,7]oxepino[4,3-c]isoxazol-10-yl)malonate (5e)



Following the general procedure, the title compound **5e** was obtained after FC (petane-EtOAc 8:1) as a white solid (72%) and a 2.7:1 mixture of diastereoisomers (95% ee each). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.13 – 6.85 (m, 3H major + 3H minor), 4.84 (d, *J* = 11.8 Hz, 1H major), 4.60 (d, *J* = 11.8 Hz, 1H minor), 4.55 – 4.24 (m, 3H major + 3 minor), 4.17 (qd, *J* = 11.2, 7.1 Hz, 1H minor), 3.95 – 3.72 (m, 6H major + 2H minor), 3.63 (s, 3H major + 3H minor), 3.51 (s, 3H minor), 2.28 (s, 3H major + 3H minor); **^{13}C NMR** (75 MHz, $CDCl_3$): Major isomer: δ = 168.1, 167.8, 158.3, 155.8, 135.1, 129.9, 129.6, 127.3, 122.3, 74.1, 70.5, 53.3, 53.1, 53.0, 51.6, 39.4, 21.1; Minor isomer: δ = 167.5, 167.2, 157.1, 156.8, 134.8, 132.3, 130.4, 128.3, 122.4, 74.7, 70.4, 53.8, 53.2, 52.6, 50.2, 44.0, 20.8; **HRMS** (ESI^+) calculated for $C_{17}H_{19}NO_6$+Na^+ $[M+Na]^+$: m/z = 356.1105, found 356.1104; **IR**: ν_{max} 2978, 2957, 2920, 2904, 2360, 2337, 1746, 1722, 1496, 1452, 1428, 1299, 1261, 1240, 1200, 1156, 1004, 975, 915, 887, 831, 801; **HPLC**: AD-H, Pentane:*i*-PrOH 90:10, F = 1.0 mL/min, λ = 230 nm: Major isomer: t_R major = 26.2 min, t_R minor = 57.0 min; Minor isomer: t_R minor = 21.4 min, t_R major = 23.9 min.

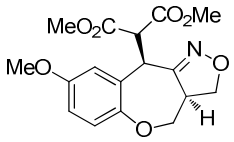


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	21.375	47.351	18.427	1476.363	11.971
2	23.885	35.850	13.951	1279.091	10.372
3	26.166	116.841	45.469	4494.651	36.445
4	56.613	56.928	22.154	5082.489	41.212



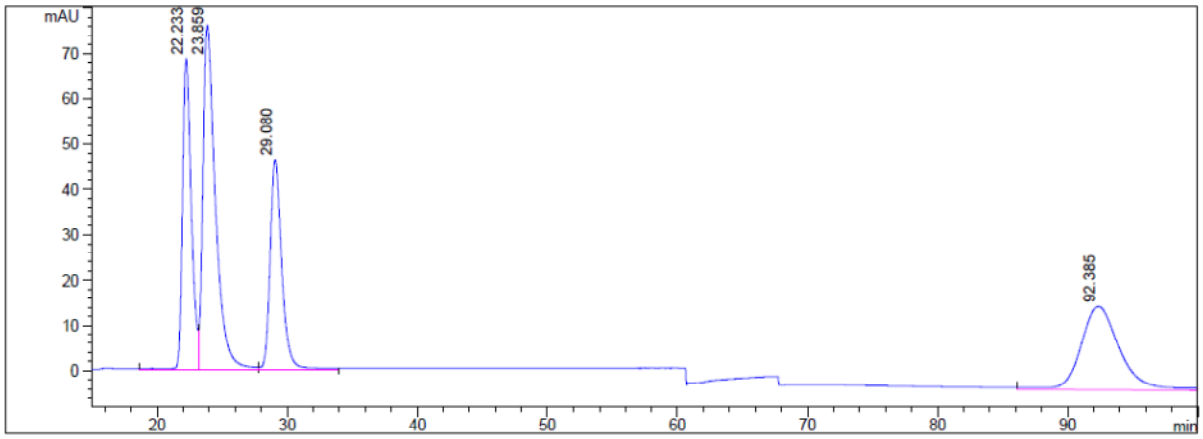
#	Meas. Ret. Time	Height	Height %	Area	Area %
1	21.421	2.131	0.769	70.461	0.678
2	23.946	88.943	32.104	3142.225	30.229
3	26.242	183.765	66.329	6973.131	67.083
4	57.046	2.212	0.798	208.962	2.010

Dimethyl 2-((3a*R*,10*R*)-8-methoxy-3,3a,4,10-tetrahydrobenzo[6,7]oxepino[4,3-c]isoxazol-10-yl)malonate (5f)

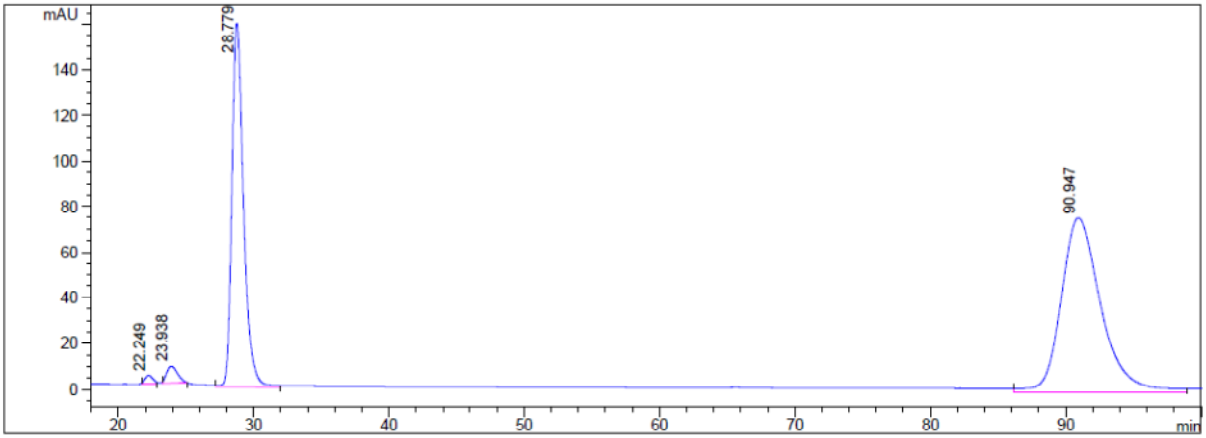


Following the general procedure, the title compound **5f** was obtained after FC (petane-EtOAc 5:1) as a white solid (63%) and a 3:1 mixture of diastereoisomers (95% ee each). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.02 – 6.95 (m, 1H major), 6.92 (d, *J* = 8.7 Hz, 1H minor), 6.83 (d, *J* = 3.0 Hz, 1H minor), 6.76 – 6.69 (m, 2H major + 1H minor), 4.85 (d, *J* = 11.8 Hz, 1H major), 4.60 (d, *J* = 11.8 Hz, 1H minor), 4.54 – 4.28 (m, 3H major + 3H minor), 3.94 – 3.77 (m, 2H major + 2H minor), 3.78 (s, 3H major), 3.76 (s, 3H minor), 3.75 (s, 3H minor), 3.74 (s, 3H major), 3.66 (s, 3H major), 3.60 (t, *J* = 10.9 Hz, 1H major), 3.54 (s, 3H minor), 3.49 (t, *J* = 11.6 Hz, 1H minor); **^{13}C NMR** (75 MHz, $CDCl_3$): Major isomer: δ = 168.0, 167.8, 158.1, 156.8, 151.8, 130.8, 123.3, 114.0, 112.1, 74.5, 70.5, 55.7,

53.3, 53.2, 53.0, 51.7, 39.5; Minor isomer: δ = 167.4, 167.1, 156.7, 156.4, 152.9, 129.5, 123.5, 116.4, 115.2, 74.9, 70.4, 55.8, 53.7, 53.2, 52.7, 50.1, 44.1; **HRMS** (ESI$^+$) calculated for $C_{17}H_{19}NO_7$+Na^+ $[M+Na]^+$: m/z = 372.1054, found 372.1061; **IR**: ν_{max} 3008, 2956, 2923, 2848, 2361, 1755; 1735, 1610, 1580, 1495, 1433, 1284, 1261, 1238, 1197, 1149, 1034, 1009, 993, 887, 831; **HPLC**: IC, Pentane:*i*-PrOH 65:35, F = 1.0 mL/min, λ = 230 nm: Major isomer: t_R minor = 23.9 min, t_R major = 90.9 min; Minor Isomer: t_R minor = 22.2 min, t_R major = 28.8 min.

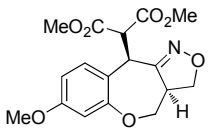


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	22.233	68.535	32.747	3216.556	21.494
2	23.859	76.053	36.339	5055.543	33.783
3	29.080	46.317	22.131	2864.073	19.139
4	92.385	18.382	8.783	3828.540	25.584

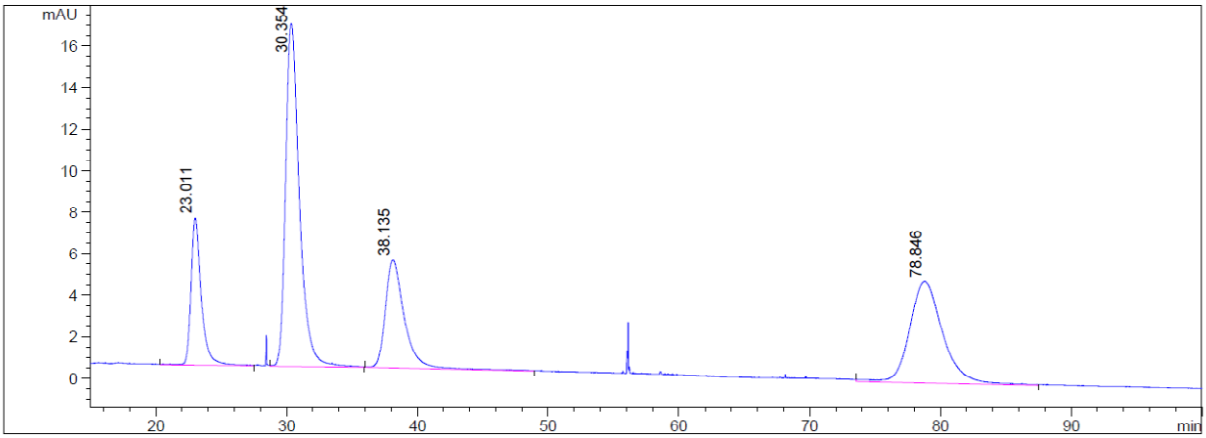


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	22.249	3.899	1.580	166.418	0.643
2	23.938	7.340	2.974	410.448	1.586
3	28.779	159.288	64.534	9530.808	36.827
4	90.947	76.303	30.913	15772.138	60.944

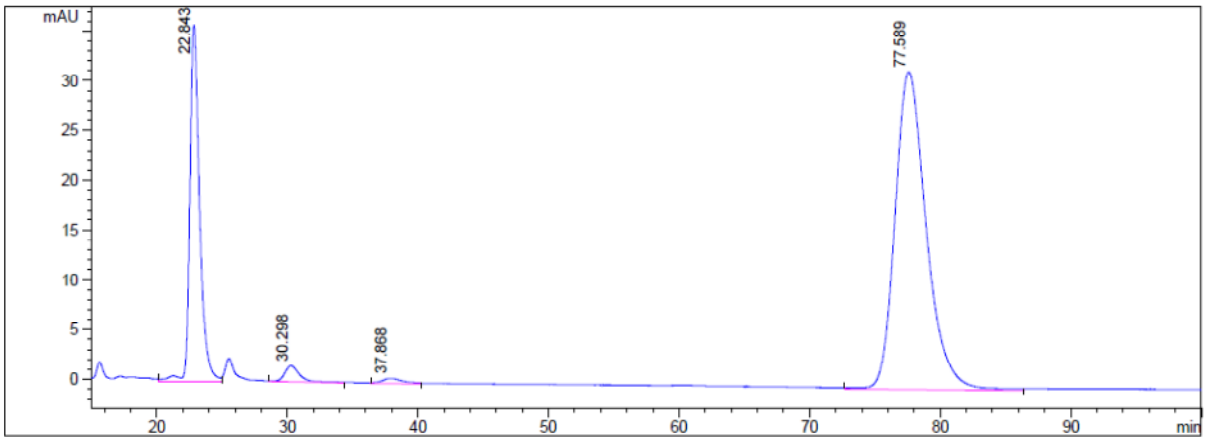
Dimethyl 2-((3a*R*,10*R*)-7-methoxy-3,3a,4,10-tetrahydrobenzo[6,7]oxepino[4,3-c]isoxazol-10-yl)malonate (5g)



Following the general procedure, the title compound **5g** was obtained after FC (petane-EtOAc 4:1) as a white solid (52%) and a 3:1 mixture of diastereoisomers (95% ee each). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.20 (d, *J* = 8.5 Hz, 1H), 7.11 – 7.05 (m, 1H major), 6.66 – 6.58 (m, 2H major + 1H minor), 6.55 (d, *J* = 2.6 Hz, 1H minor), 4.77 (d, *J* = 11.6 Hz, 1H major), 4.61 (d, *J* = 11.8Hz, 1H minor), 4.54 – 4.38 (m, 2H major + 2H minor), 4.35 – 4.25 (m, 1H major + 1H minor), 4.21 – 4.14 (m, 1H minor), 3.91 – 3.65 (m, 10H major + 8H minor), 3.61 (s, 3H major), 3.52 (s, 1H minor); **^{13}C NMR** (100 MHz, $CDCl_3$): Major isomer : δ = 168.1, 167.8, 160.5, 158.8, 158.4, 127.7, 121.9, 110.6, 108.9, 73.9, 70.5, 55.5, 53.4, 53.2, 53.0, 51.4, 39.1; Minor isomer: δ = 167.5, 167.2, 160.8, 160.2, 156.8, 132.6, 120.6, 110.6, 108.3, 74.6, 70.3, 55.5, 54.0, 53.1, 52.6, 50.2, 43.3; (ESI+) calculated for $C_{17}H_{19}NO_7$+Na^+ $[M+Na]^+$: m/z = 372.1054, found 372.1047; **IR**: ν_{max} 3006, 2978, 2959, 2923, 2837, 2360, 2325, 1744, 1722, 1611, 1574, 1500, 1450, 1438, 1374, 1350, 1311, 1295, 1281, 1259, 1196, 1178, 1149, 1126, 1106, 1085, 1034, 1018, 976, 936, 914, 884, 851, 835, 824, 794; **HPLC**: IC, Pentane:*i*-PrOH 65:35, F = 1.0 mL/min, λ = 230 nm: Major isomer: t_R major = 77.6 min, t_R minor = 30.3 min; Minor isomer: t_R minor = 37.9 min, t_R major = 22.8 min.

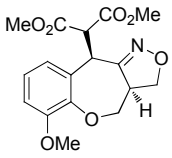


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	23.011	7.098	21.058	394.240	13.080
2	30.354	16.526	49.030	1218.567	40.429
3	38.135	5.195	15.414	530.667	17.606
4	78.846	4.887	14.499	870.610	28.885

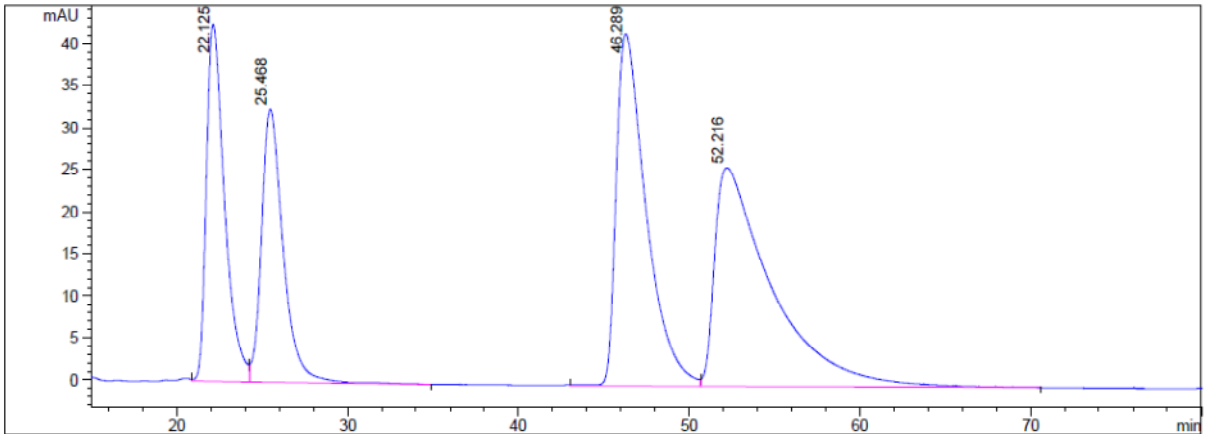


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	22.843	35.853	51.295	1874.868	25.396
2	30.298	1.628	2.330	132.543	1.795
3	37.868	0.498	0.712	53.141	0.720
4	77.589	31.917	45.663	5321.853	72.088

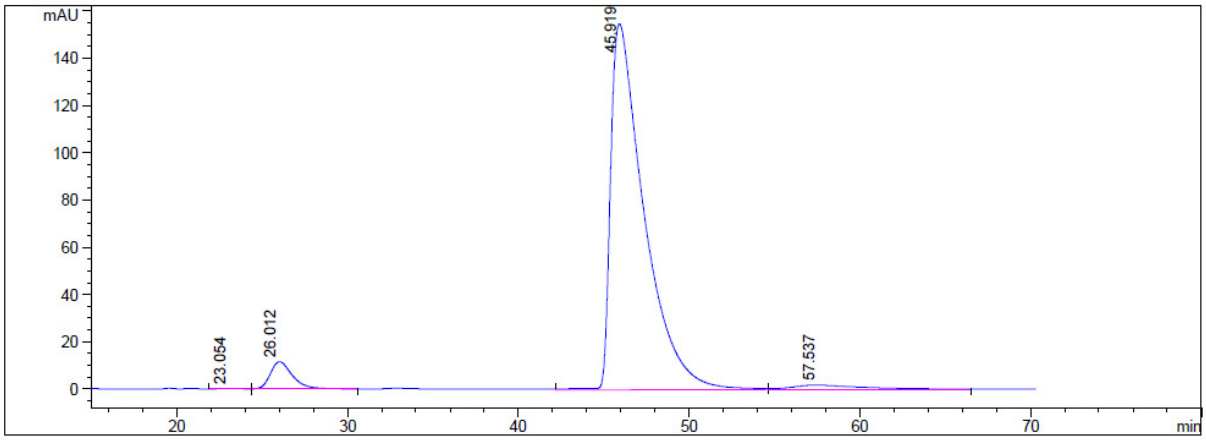
Dimethyl 2-((3a*R*,10*R*)-6-methoxy-3,3a,4,10-tetrahydrobenzo[6,7]oxepino[4,3-c]isoxazol-10-yl)malonate (5h)



Following the general procedure, the title compound **5h** was obtained after FC (petane-EtOAc 8:1) as a white solid (87%) and a 20:1 mixture of diastereoisomers (95% ee each). Only signals of the major diastereoisomer: **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.05 (t, *J* = 8.1 Hz, 1H), 6.87 (dd, *J* = 8.4, 1.4 Hz, 1H), 6.76 (ddd, *J* = 7.9, 1.3, 0.6 Hz, 1H), 4.92 (d, *J* = 11.9 Hz, 1H), 4.57 (dd, *J* = 11.0, 7.2 Hz, 1H), 4.51 (d, *J* = 11.9 Hz, 1H), 4.37 – 4.31 (m, 1H), 3.88 – 3.81 (m, 1H), 3.84 (s, 3H), 3.79 (s, 3H), 3.63 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 168.1, 167.8, 158.0, 152.6, 131.6, 125.7, 125.7, 118.0, 112.1, 73.6, 70.5, 56.1, 53.3, 53.1, 53.1, 51.8, 39.4; **HRMS** (ESI^+) calculated for $C_{17}H_{19}NO_7$+Na^+ $[M+Na]^+$: m/z = 372.1054, found 372.1056; **IR**: ν_{max} 3001, 2955, 2886, 2841, 2360, 2333, 1736, 1599, 1584, 1481, 1456, 1436, 1370, 1275, 1259, 1241, 1199, 1148, 1088, 1059, 1004, 915, 884, 753, 729; **HPLC**: OD-H, Pentane:*i*-PrOH 90:10, F = 1.0 mL/min, λ = 230 nm: Major isomer: t_R major = 45.9 min, t_R minor = 57.5 min; Minor isomer: t_R minor = 23.1min, t_R major = 26.0 min.

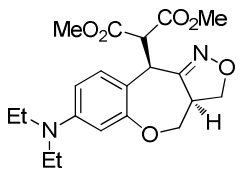


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	22.125	42.467	29.758	3148.434	18.425
2	25.468	32.434	22.727	2864.733	16.765
3	46.289	41.879	29.346	5102.828	29.863
4	52.216	25.928	18.169	5971.644	34.947



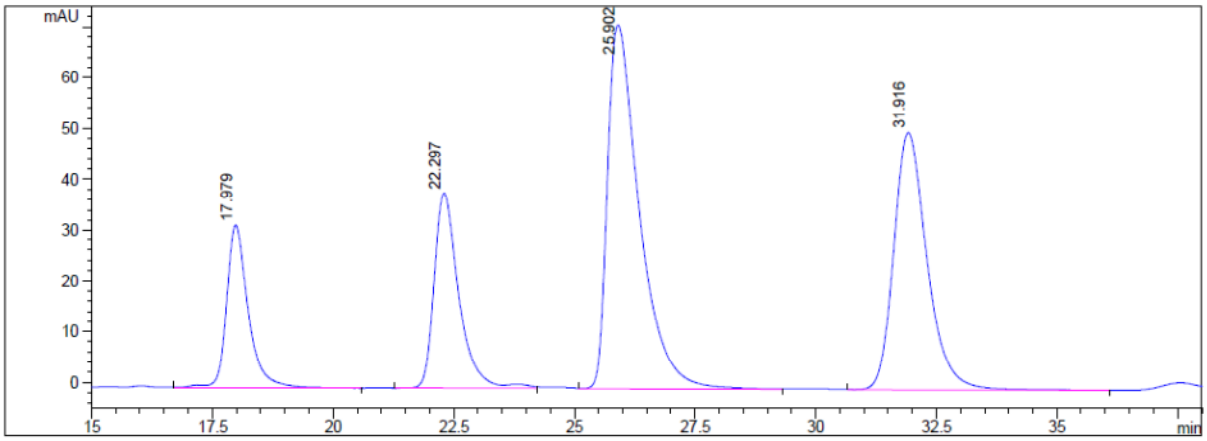
#	Meas. Ret. Time	Height	Height %	Area	Area %
1	23.054	0.269	0.160	22.191	0.097
2	26.012	11.596	6.873	1057.268	4.637
3	45.919	155.007	91.870	21139.598	92.722
4	57.537	1.851	1.097	579.850	2.543

Dimethyl 2-((3a*R*,10*R*)-7-(diethylamino)-3,3a,4,10-tetrahydrobenzo[6,7]oxepino[4,3-c]isoxazol-10-yl)malonate (5i)

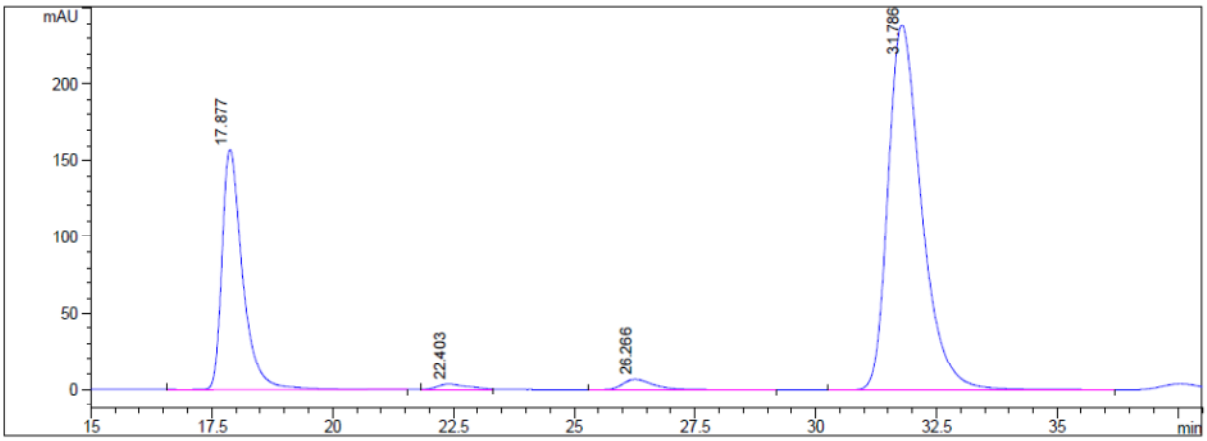


Following the general procedure, the title compound **5i** was obtained after FC (petane-EtOAc 5:1) as a white solid (66%) and a 2.5:1 mixture of diastereoisomers (95% ee each). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.09 (d, *J* = 8.5 Hz, 1H minor), 6.97 (d, *J* = 8.4 Hz, 1H major), 6.45 – 6.23 (m, 2H major + minor), 4.73 (d, *J* = 11.8 Hz, 1H major), 4.56 (d, *J* = 11.7 Hz, 1H minor), 4.51 – 4.38 (m, 2H major + 2 H minor), 4.37 – 4.24 (m, 1H major + 1H minor), 3.78 (s, 3H major), 3.74 (s, 1H minor), 3.64 (s, 3H major), 3.55 (s, 3H minor), 3.89 – 3.52 (m, 3H major + 3H minor), 3.30 (q, *J* = 7.1 Hz, 4H major +4H minor), 1.13 (t, *J* = 7.1 Hz, 6H major + 6H minor); **^{13}C NMR** (75 MHz, $CDCl_3$): Major isomer: δ = 168.3, 168.0, 159.1, 159.0, 149.0, 127.5, 115.5, 108.1, 105.4,

74.0, 70.4, 53.5, 53.2, 53.0, 51.7, 44.4 (2C), 38.9, 12.6 (2C); Minor isomer: δ = 167.7, 167.4, 160.4, 157.4, 149.3, 132.6, 114.0, 108.0, 105.0, 74.5, 70.2, 54.4, 53.1, 52.6, 50.3, 44.4 (2C), 43.2, 12.6 (2C); **HRMS** (ESI^+) calculated for $C_{20}H_{26}N_2O_6$+Na^+ $[M+Na]^+$: m/z = 413.1683, found 413.1681; **IR**: ν_{max} 2969, 2933, 2882, 1756, 1736, 1614, 1557, 1512, 1434, 1398, 1376, 1297, 1272, 1257, 1238, 1216, 1193, 1146, 1108, 1080, 1021, 916, 882, 729; **HPLC**: IA, Pentane:*i*-PrOH 90:10, F = 1.0 mL/min, λ = 230 nm: Major isomer: t_R minor = 26.3 min, t_R major = 31.8 min; Minor isomer: t_R major = 17.9 min, t_R minor = 22.4 min.

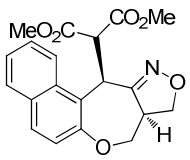


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	17.979	32.074	16.656	1005.206	12.424
2	22.297	38.321	19.900	1362.953	16.846
3	25.902	71.618	37.190	3287.861	40.637
4	31.916	50.558	26.254	2434.723	30.093

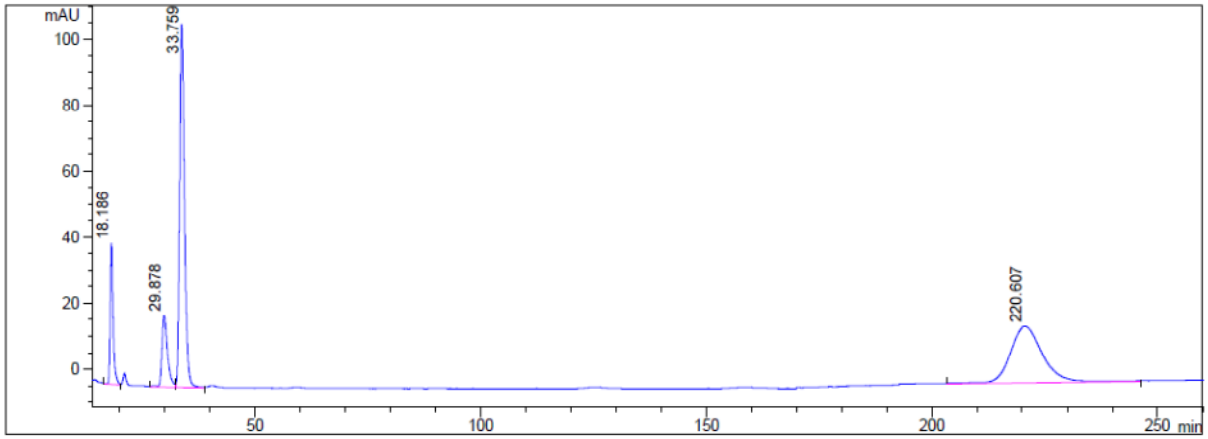


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	17.877	157.791	38.721	4692.175	28.028
2	22.403	3.458	0.849	143.628	0.858
3	26.266	6.840	1.678	321.446	1.920
4	31.786	239.418	58.752	11584.077	69.195

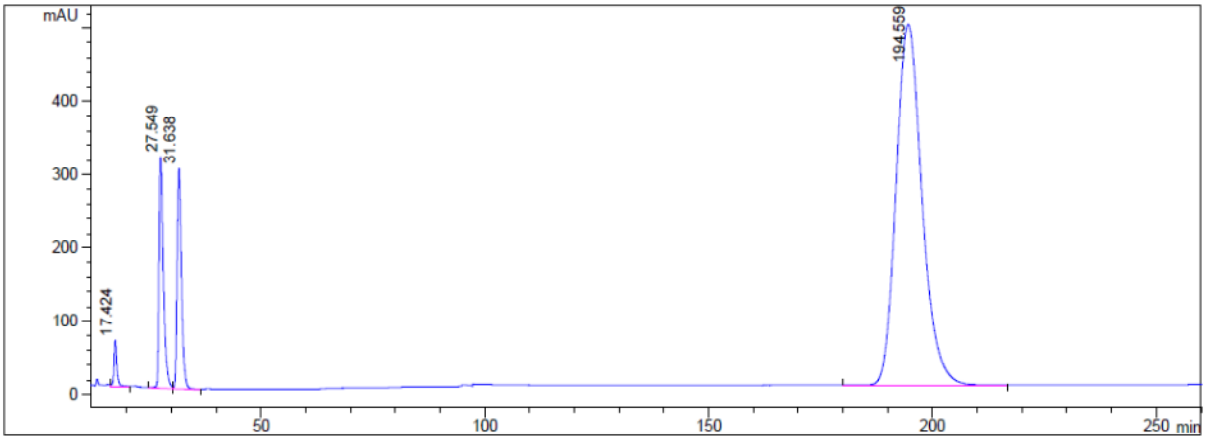
Dimethyl 2-((8a*R*,12*R*)-8,8a,9,12-tetrahydronaphtho[1',2':6,7]oxepino[4,3-c]isoxazol-12-yl)malonate (5j)



Following the general procedure, the title compound **5j** was obtained after FC (petane-EtOAc 5:1) as a white solid (63%) and a 3.8:1 mixture of diastereoisomers (81% ee each). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.36 (d, *J* = 8.7 Hz, 1H minor), 8.28 (d, *J* = 8.7 Hz, 2H major), 7.90 – 7.72 (m, 2H major + 2H minor), 7.66 – 7.53 (m, 1H major + 1H minor), 7.53 – 7.39 (m, 1H major + 1H minor), 7.26 (d, *J* = 8.7 Hz, 1H major), 7.20 (d, *J* = 8.8 Hz, 1H minor), 5.65 (d, *J* = 11.8 Hz, 1H minor), 5.63 (d, *J* = 9.8 Hz, 1H major), 4.76 (d, *J* = 11.7 Hz, 1H minor), 4.64 (dd, *J* = 11.3, 6.7 Hz, 1H minor), 4.54 (d, *J* = 9.8 Hz, 1H major), 4.49 (dd, *J* = 11.0, 8.3 Hz, 1H minor), 4.36 – 4.15 (m, 3H major + 1H minor), 4.08 (dd, *J* = 8.5, 6.3 Hz, 1H major), 3.86 (s, 3H major), 3.83 (s, 3H minor), 3.89 – 3.76 (m, 1H major) 3.66 – 3.55 (m, 2H minor), 3.45 – 3.29 (m, 1H major), 3.20 (s, 3H minor), 3.09 (s, 3H major); **^{13}C NMR** (75 MHz, $CDCl_3$): Major isomer: δ = 168.4, 167.2, 159.7, 153.4, 131.9, 131.7, 131.1, 128.6, 127.0, 125.3, 125.0, 123.9, 122.1, 71.9, 71.3, 55.6, 53.1, 52.2, 48.5, 35.6; Minor isomer: δ = 167.7, 167.0, 157.9, 156.4, 131.8, 131.6, 130.9, 130.8, 128.5, 125.0, 124.3, 123.6, 122.3, 74.8, 70.3, 53.3, 53.2, 52.4, 49.9, 36.7; **HRMS** (ESI^+) calculated for $C_{20}H_{19}NO_6$+Na^+ $[M+Na]^+$: m/z = 392.1105, found 392.1109; **IR**: ν_{max} 3059, 2953, 2884, 2361, 1735, 1622, 1594, 1512, 1434, 1376, 1332, 1297, 1242, 1219, 1150, 1079, 1008, 913, 885, 859, 830, 753, 730; **HPLC**: IC, Pentane:*i*-PrOH 75:25, F = 1.2 mL/min, λ = 230 nm: Major isomer: t_R minor = 31.6 min, t_R major = 194.6 min; Minor isomer: t_R minor = 17.4 min, t_R major = 27.5 min.

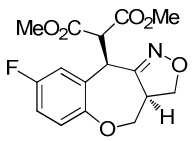


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	18.186	42.744	22.319	1937.726	9.349
2	29.878	21.545	11.250	1838.441	8.870
3	33.759	110.052	57.464	8273.394	39.916
4	220.607	17.175	8.968	8677.504	41.866

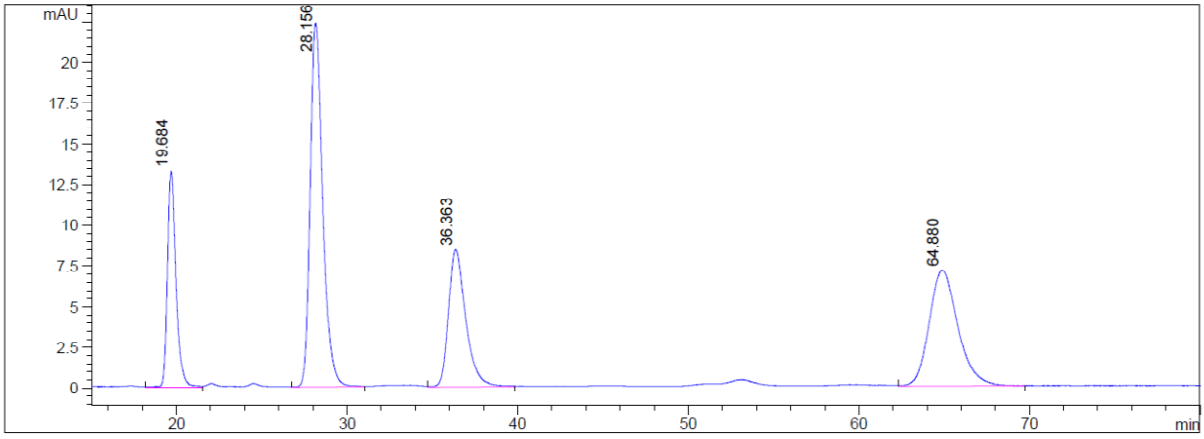


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	17.424	63.976	5.446	2916.449	1.198
2	27.549	316.444	26.937	21575.439	8.865
3	31.638	301.268	25.646	20394.070	8.379
4	194.559	493.049	41.971	198503.703	81.558

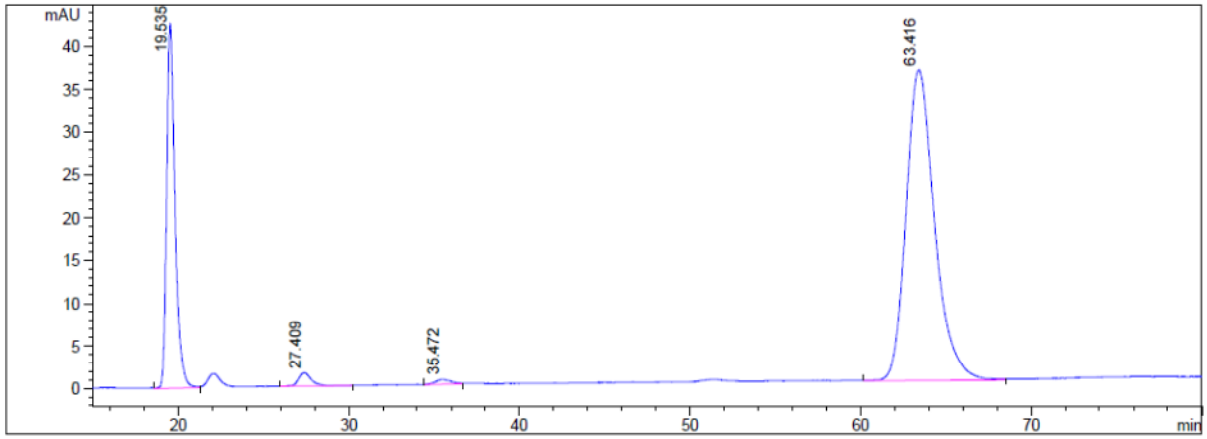
Dimethyl 2-((3a*R*,10*R*)-8-fluoro-3,3a,4,10-tetrahydrobenzo[6,7]oxepino[4,3-c]isoxazol-10-yl)malonate (5k)



Following the general procedure, the title compound **5k** was obtained after FC (petane-EtOAc 5:1) as a white solid (57%) and a 2.8:1 mixture of diastereoisomers (96% ee each). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.10 – 6.86 (m, 3H major + 3H minor), 4.87 (d, *J* = 11.7 Hz, 1H major), 4.62 (d, *J* = 11.8 Hz, 1H minor), 4.56 – 4.41 (m, 2H major + 2H minor), 4.41 – 4.30 (m, 1H major+ 1H minor), 3.96 – 3.80 (m, 2H major + 2H minor), 3.79 (s, 3H major), 3.77 (s, 3H minor), 3.69 (s, 3H major), 3.66 – 3.47 (m, 1H major + 1 H minor); 3.57 (s, 3H minor); **^{13}C NMR** (75 MHz, $CDCl_3$): Major isomer: δ = 167.8, 167.6, 159.7 (d, ^{1}J = 244.5 Hz), 157.6, 154.2 (d, ^{4}J = 2.9 Hz), 132.0 (d, ^{3}J = 7.9 Hz), 124.0 (d, ^{3}J = 8.7 Hz), 115.8 (d, ^{2}J = 22.7 Hz), 113.7 (d, ^{3}J = 25.0 Hz), 74.4 (d, ^{6}J = 1.5 Hz), 70.6, 53.4, 53.3, 52.8, 51.6, 39.3 (d, ^{4}J = 1.3 Hz); Minor Isomer: δ = 167.2, 167.0, 159.1 (d, ^{1}J = 244.6 Hz), 156.2; 155.3 (d, ^{4}J = 2.8 Hz), 130.6 (d, ^{3}J = 8.0 Hz), 124.2 (d, ^{3}J = 8.5 Hz), 118.5 (d, ^{2}J = 24.0 Hz), 116.5 (d, ^{2}J = 22.8 Hz), 74.8 (d, ^{6}J = 0.9 Hz), 70.5, 53.6, 53.3, 52.8, 50.1, 43.7 (d, ^{4}J = 1.4 Hz); **HRMS** (ESI^{+}) calculated for $C_{16}H_{16}FNO_6$+Na^{+} $[M+Na]^{+}$: m/z = 360.0854, found 360.0844; **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -115.99 (major), -117.14 (minor); **IR**: ν_{max} 3078, 3007, 2958,2923, 2852, 1754, 1736, 1590, 1489, 1430, 1383, 1350, 1305, 1262, 1239, 1184, 1145, 1014, 1005, 978, 962, 918, 887, 870, 842, 823; **HPLC**: IC, Pentane:*i*-PrOH 80:20, F = 1.0 mL/min, λ = 210 nm: Major isomer: t_R minor = 27.4 min, t_R major = 63.4 min; Minor isomer: t_R major = 19.5 min, t_R minor = 35.5 min.

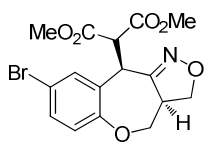


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	19.684	13.260	25.930	458.005	15.159
2	28.156	22.355	43.714	1138.294	37.674
3	36.363	8.413	16.451	590.932	19.558
4	64.880	7.111	13.905	834.202	27.609



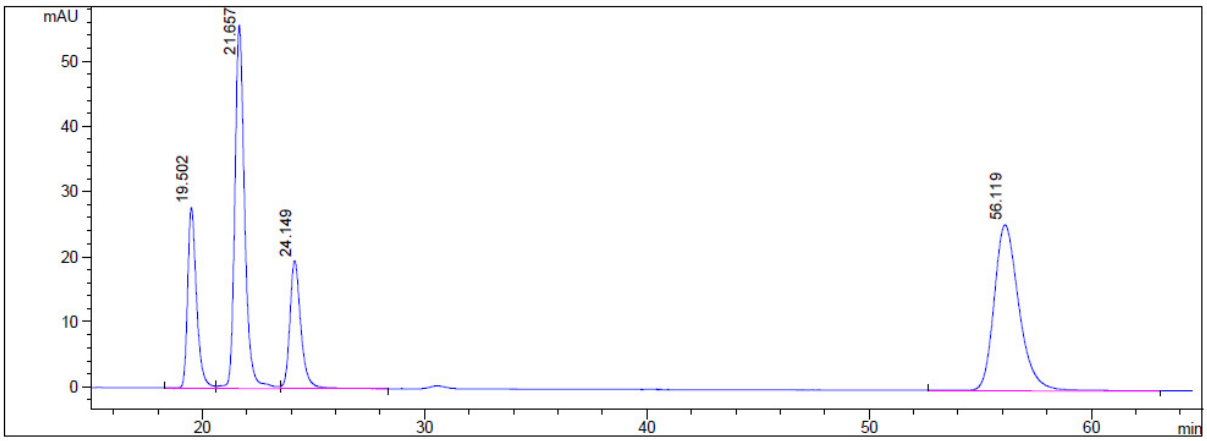
#	Meas. Ret. Time	Height	Height %	Area	Area %
1	19.535	42.675	52.608	1445.387	25.015
2	27.409	1.552	1.913	82.424	1.426
3	35.472	0.541	0.667	34.538	0.598
4	63.416	36.350	44.811	4215.808	72.961

Dimethyl 2-((3a*R*,10*R*)-8-bromo-3,3a,4,10-tetrahydrobenzo[6,7]oxepino[4,3-c]isoxazol-10-yl)malonate (5l)

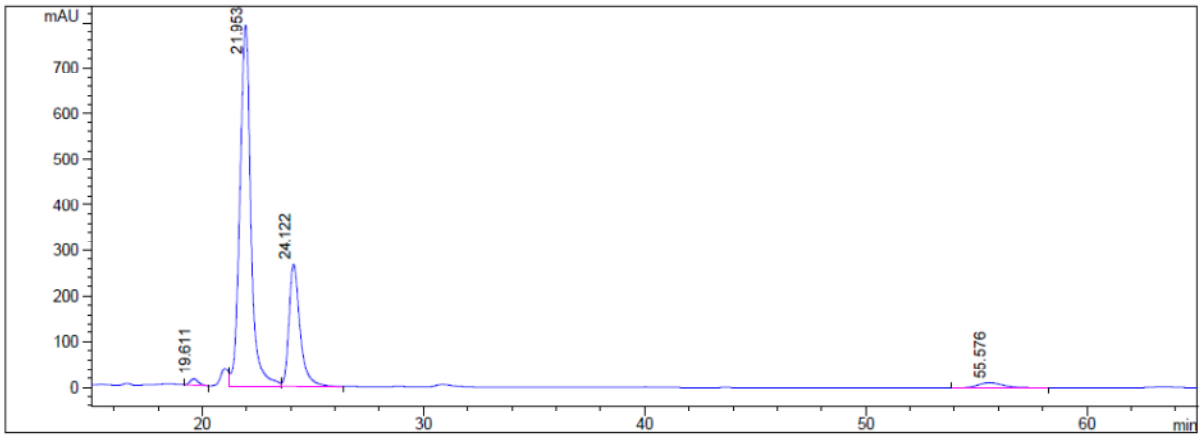


Following the general procedure, the title compound **5l** was obtained after FC (petane-EtOAc 5:1) as a white solid (50%) and a 3.6:1 mixture of diastereoisomers (92% ee each). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.47 (d, *J* = 2.4 Hz, 1H, minor), 7.40 – 7.31 (m, 2H, major + 2H, minor), 6.96 (d, *J* = 8.4 Hz, 1H, major), 6.90 (d, *J* = 8.5 Hz, 1H, minor), 4.84 (d, *J* = 11.6 Hz, 1H, major), 4.61 (d, *J* = 11.7 Hz, 1H, minor), 4.56 – 4.15 (m, 4H, major + 1 H, minor), 3.96 – 3.81 (m, 2H, major +2 H minor), 3.79 (s, 3H, major), 3.77 (s, 1H, minor), 3.70 (s, 3H, major), 3.65 (t, *J* = 9.0 Hz, 1H, major), 3.57 (s, 1H, minor), 3.56 – 3.43 (m, 2H, minor). **^{13}C NMR** (150 MHz, $CDCl_3$): Major isomer: δ = 167.8, 167.6, 157.5, 157.2, 132.5, 132.4, 130.1, 124.5, 118.2, 74.1, 70.6, 53.3, 53.2, 52.9, 51.4, 39.4; Minor isomer: δ = 167.2, 166.9, 158.4, 156.1, 134.6, 132.9, 131.0, 124.7, 117.7, 74.6, 70.4, 53.7, 53.3, 52.8,

50.0, 43.6; **HRMS** (ESI$^+$) calculated for $C_{16}H_{16}BrNO_6$+Na$^+$ [M+Na]$^+$: m/z = 420.0053, found 420.0056; **IR**: ν_{max} 2915, 2872, 1682, 1591, 1475, 1412, 1392, 1271, 1236, 1222, 1180, 1124, 1098, 1013, 993, 936, 901, 885, 876, 852, 810; **HPLC**: IA, Pentane:*i*-PrOH 90:10, F = 1.0 mL/min, λ = 230 nm: Major isomer: t_R major = 22.0 min, t_R minor = 55.6 min; Minor isomer: t_R minor = 19.6 min, t_R major = 24.1 min.

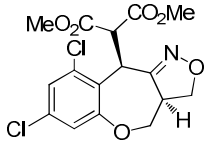


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	19.502	27.810	21.588	777.864	15.027
2	21.657	55.843	43.348	1709.710	33.028
3	24.149	19.679	15.276	686.547	13.263
4	56.119	25.492	19.788	2002.349	38.682



#	Meas. Ret. Time	Height	Height %	Area	Area %
1	19.611	14.304	1.314	379.654	0.989
2	21.953	794.109	72.950	27484.262	71.571
3	24.122	268.077	24.627	9395.403	24.466
4	55.576	12.074	1.109	1141.859	2.973

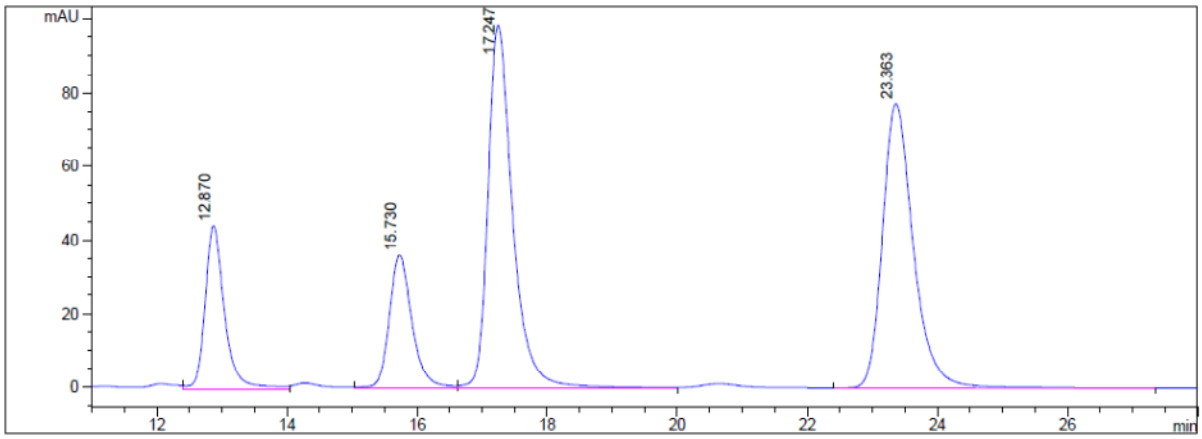
Dimethyl 2-((3a*R*,10*R*)-7,9-dichloro-3,3a,4,10-tetrahydrobenzo[6,7]oxepino[4,3-c]isoxazol-10-yl)malonate (5m)



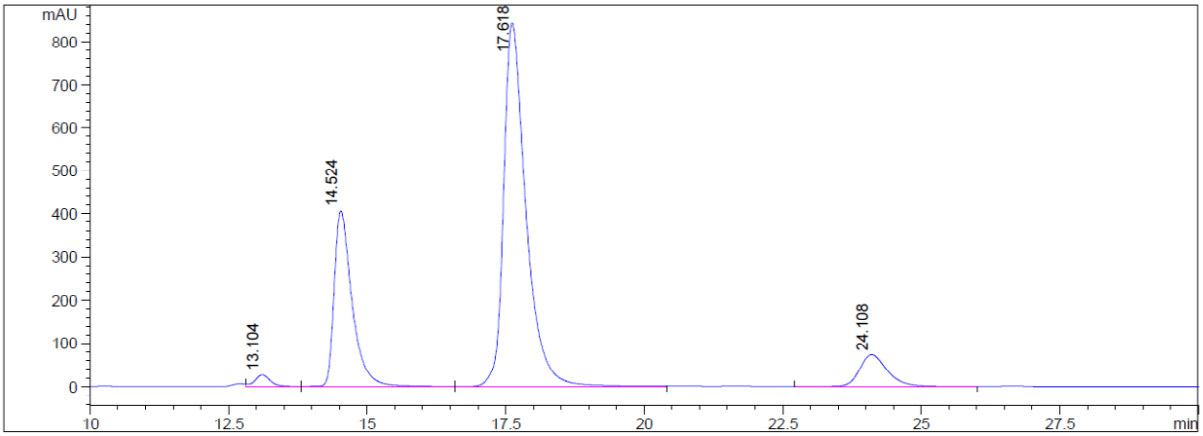
Following the general procedure, the title compound **5m** was obtained after FC (petane-EtOAc 6:1) as a white solid (58%) and a 2.9:1 mixture of diastereoisomers (80% ee each): **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.28 (d, *J* = 2.1 Hz, 1H, major), 7.25 (d, *J* = 2.2 Hz, 1H, minor), 7.04 (d, *J* = 2.1 Hz, 1H, major), 6.99 (d, *J* = 2.1 ´Hz, 1H, minor), 5.37 (d, *J* = 11.7 Hz, 1H, minor),

5.31 (d, *J* = 9.9 Hz, 1H, major), 4.58 (dd, *J* = 11.5, 6.6 Hz, 1H, minor), 4.47 (dd, *J* = 11.1, 8.6 Hz, 2H, minor), 4.35 – 4.21 (m, 2H, major), 4.21 (d, *J* = 9.0 Hz, 2H, major), 4.04 (dd, *J* = 8.6, 6.8 Hz, 1H, major), 3.90 (t, *J* = 8.5 Hz, 1H, minor), 3.81 (s, 3H, major), 3.78 (s, 1H, minor), 3.59 (s, 1H, minor), 3.54 (s, 3H, major), 3.50 – 3.29 (m, 1H, major + 1H, minor); **^{13}C NMR** (100 MHz, $CDCl_3$):Major isomer: δ = 167.7, 167.0, 157.6, 156.8, 135.8, 135.3, 128.7, 126.9, 122.6, 72.6, 71.2, 54.9, 53.2, 52.8, 48.2, 37.5; Minor isomer: δ = 166.3, 163.8, 156.4, 155.1, 137.0, 135.0, 129.4, 126.5, 122.2, 71.4, 71.3, 53.5, 53.3, 52.7, 48.5, 40.5.

The major diastereomer could be isolated: **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.28 (d, *J* = 2.1 Hz, 1H), 7.03 (dd, *J* = 2.1, 0.5 Hz, 1H), 5.30 (d, *J* = 9.7 Hz, 0H), 4.31 (d, *J* = 9.8 Hz, 1H), 4.27 (dd, *J* = 9.8, 8.6 Hz, 1H), 4.21 (d, *J* = 1.1 Hz, 1H), 4.19 (d, *J* = 2.6 Hz, 1H), 4.03 (dd, *J* = 8.6, 6.8 Hz, 1H), 3.80 (s, 3H), 3.54 (s, 3H), 3.46 – 3.32 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 167.7, 167.0, 157.6, 156.8, 135.8, 135.3, 128.6, 126.9, 122.6, 72.6, 71.2, 54.9, 53.2, 52.8, 48.2, 37.5; **HRMS** (ESI^+) calculated for $C_{16}H_{15}Cl_2NO_6$+Na^+ $[M+Na]^+$: m/z = 410.0169 found 410.0166; **IR**: ν_{max} 3081, 2954, 2888, 1736, 1586, 1558, 1435, 1406, 1370, 1334, 1297, 1258, 1238, 1194, 1151, 1089, 1011, 914, 882, 842, 803, 731, 650; **HPLC**: IA, Pentane:*i*-PrOH 90:10, F = 1.0 mL/min, λ = 230 nm: Major isomer: t_R major = 17.6 min, t_R minor = 24.1 min; Minor isomer: t_R minor = 13.1 min, t_R major = 14.5 min.

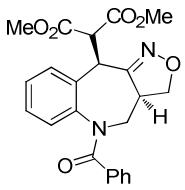


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	12.870	44.350	17.283	922.327	13.210
2	15.730	36.207	14.110	876.416	12.552
3	17.247	98.617	38.431	2604.405	37.300
4	23.363	77.433	30.176	2579.084	36.938

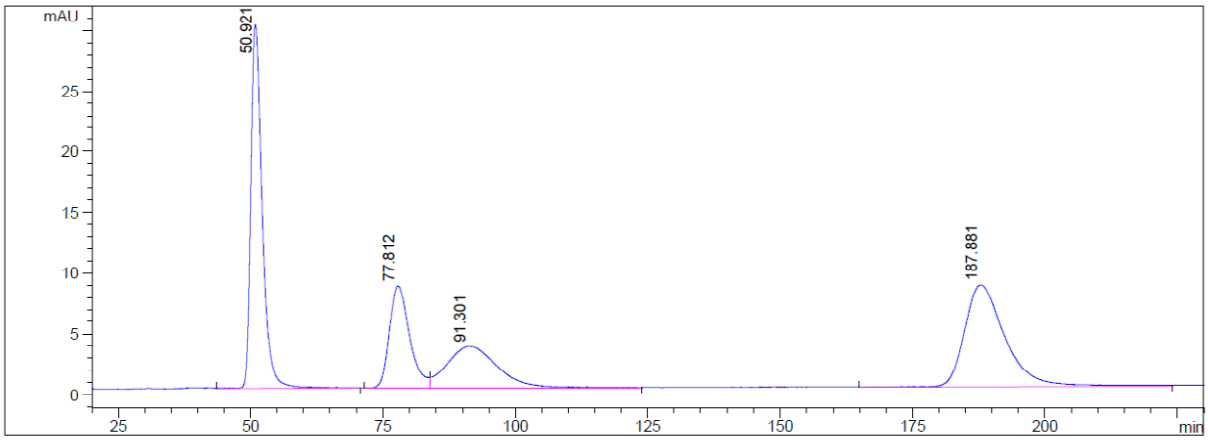


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	13.104	27.010	2.003	531.670	1.484
2	14.524	406.276	30.134	9144.719	25.525
3	17.618	841.724	62.432	23574.039	65.801
4	24.108	73.222	5.431	2575.984	7.190

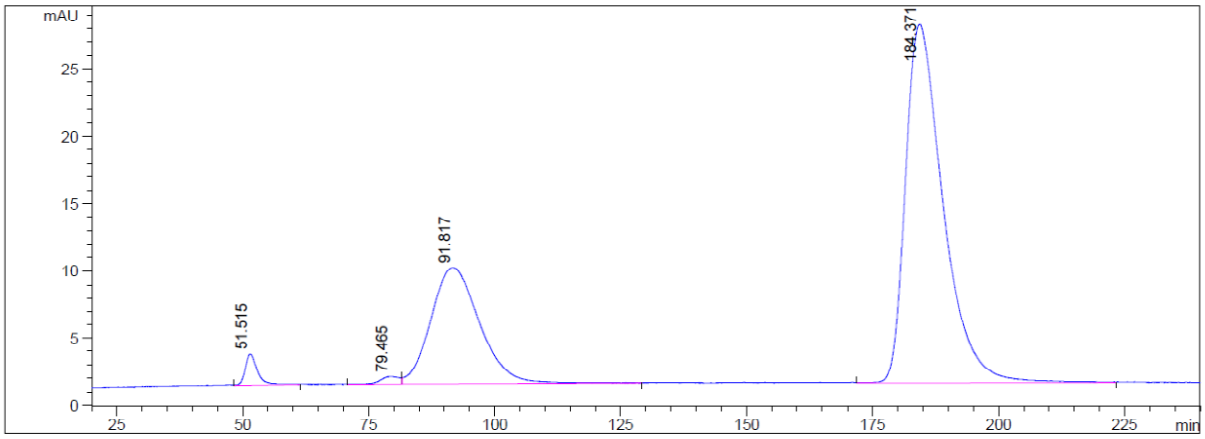
Dimethyl 2-((3a*S*,10*R*)-5-benzoyl-3a,4,5,10-tetrahydro-3*H*-benzo[b]isoxazolo[3,4-e]azepin-10-yl)malonate (5n)



Following the general procedure, the title compound **5n** was obtained after FC (petane-EtOAc 4:1→2:1) as a white solid (60%) and a 3.6:1 mixture of diastereoisomers (95% ee each). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.51 (d, *J* = 7.8 Hz, 2H, minor), 7.45 – 7.38 (m, 2H, major), 7.36 – 7.11 (m, 6H, major, +6 H, minor), 7.13 – 6.97 (m, 1H,major, + 1H, minor), 6.75 (d, *J* = 7.7 Hz, 1H, major), 6.66 (d, *J* = 7.8 Hz, 1H, minor), 5.36 (dd, *J* = 13.1, 6.5 Hz, 1H, major), 5.34 – 5.23 (m, 1H, minor), 5.05 (d, *J* = 12.6 Hz, 1H, major), 4.88 (d, *J* = 12.4 Hz, 1H, minor), 4.74 (d, *J* = 12.6 Hz, 1H, major), 4.52 (dd, *J* = 10.7, 8.2 Hz, 1H, major), 4.34 (d, *J* = 12.5 Hz, 1H, minor), 4.10 – 3.97 (m, 3H, minor), 3.92 – 3.84 (m, 1H, major), 3.82 (s, 3H, major), 3.76 (s, 3H, minor), 3.76 (s, 3H, major), 3.68 (s, 3H, minor), 2.82 (t, *J* = 12.3 Hz, 1H, minor), 2.71 (dd, *J* = 13.0, 11.6 Hz, 1H, major); **^{13}C NMR** (100 MHz, $CDCl_3$): Major isomer: δ = 169.7 (2C), 167.7, 167.7, 157.3, 143.9, 134.8, 133.8, 130.4, 129.4, 129.3, 128.9, 128.7, 128.5, 128.0, 125.1, 71.6, 53.6, 53.4, 52.1, 50.8, 49.9, 39.8; Minor isomer: δ = 166.9, 166.8, 158.4, 156.9, 143.1, 134.1, 131.7, 130.7, 130.0, 129.3, 128.9, 128.8, 128.6, 128.1, 128.1, 127.8, 72.2, 60.5, 53.9, 53.4, 52.9, 50.5, 48.6; **HRMS** (ESI^+) calculated for $C_{23}H_{22}NO_6$+Na^+ $[M+Na]^+$: m/z = 445.1370, found 445.1369; **IR**: ν_{max} 1745, 1725, 1649, 1602, 1579, 1490, 1449, 1435, 1395, 1345, 1320, 1294, 1275, 1264, 1199, 1151, 970, 926, 894, 875, 789, 777, 728, 708; **HPLC**: IC, Pentane:*i*-PrOH 80:20, F = 1.0 mL/min, λ = 230 nm: Major isomer: t_R minor = 51.9 min, t_R major = 184.4min; Minor isomer: t_R minor = 79.5 min, t_R major = 91.8 min.

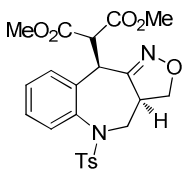


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	50.921	29.969	59.735	4485.035	33.094
2	77.812	8.404	16.752	2242.413	16.546
3	91.301	3.433	6.842	2336.524	17.241
4	187.881	8.364	16.671	4488.320	33.119



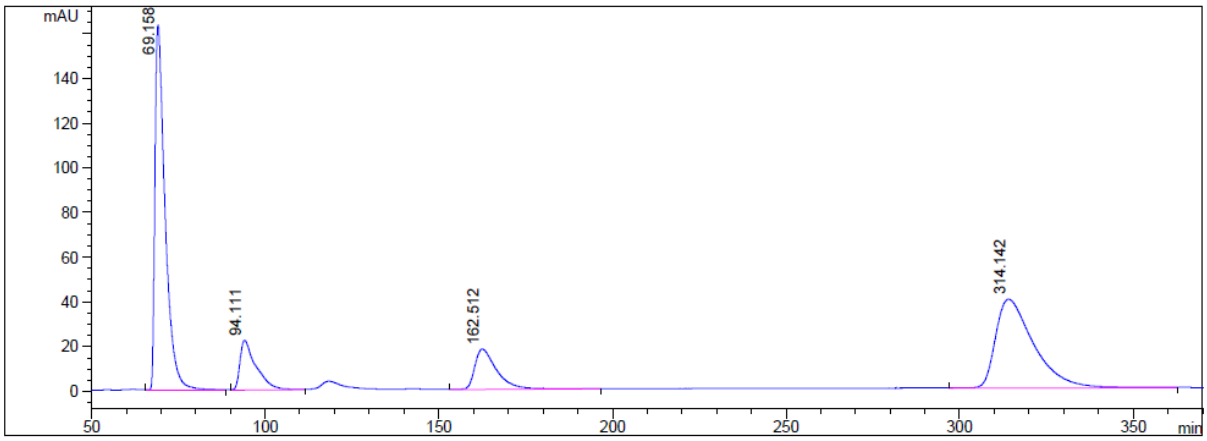
#	Meas. Ret. Time	Height	Height %	Area	Area %
1	51.515	2.323	6.069	386.970	1.905
2	79.465	0.587	1.533	155.437	0.765
3	91.817	8.708	22.750	5862.489	28.853
4	184.371	26.659	69.648	13913.712	68.478

Dimethyl 2-((3a*S*,10*R*)-5-(4-toluensulfonyl)-3a,4,5,10-tetrahydro-3H-benzo[b]isoxazolo[3,4-e]azepin-10-yl)malonate (5o)

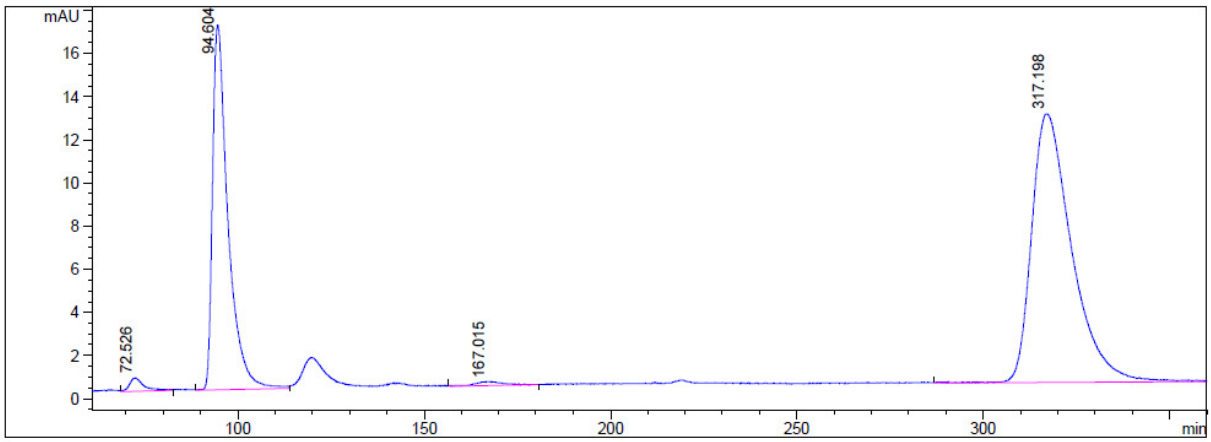


Following the general procedure, the title compound **5o** was obtained after FC (petane-EtOAc 2:1) as a white solid (57%) and a 2.3:1 mixture of diastereoisomers (97% ee each). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 8.3 Hz, 2H minor), 7.78 (d, 8.3 Hz, 2H major), 7.50 (dd, *J* = 7.6, 1.8 Hz, 1H minor), 7.44 – 7.10 (m, 6H major + 4H minor), 6.88 (dd, *J* = 7.8, 1.5 Hz, 1H minor), 4.83 – 4.53 (m, 3H major +2H minor), 4.51 – 4.22 (m, 2H major + 1H minor), 4.01 – 3.83 (m, 1H major + 2H minor), 3.79 (d, *J* = 3.2 Hz, 1H minor), 3.77 (s, 3H minor), 3.74 (s, 3H major), 3.67 (s, 3H major), 3.61 (s, 3H minor), 3.04 – 2.83 (m, 1H major + 1H minor), 2.48 (s, 3H minor), 2.44 (s, 3H major); **^{13}C NMR** (75 MHz, $CDCl_3$): Major isomer: δ = 167.6, 167.4, 157.6, 144.1, 140.1, 138.3, 136.0, 133.8,

130.2, 129.9, 129.6, 129.4, 128.7, 127.3, 125.1, 71.3, 53.3, 52.8, 52.2, 51.8, 50.5, 39.1, 21.8; Minor isomer: δ = 167.6, 167.3, 157.1, 144.4, 140.3, 138.5, 136.0, 134.7, 130.3, 129.9, 129.5, 129.4, 128.6, 127.4, 127.2, 71.7, 53.5, 53.2, 44.6, 21.8; **HRMS** (ESI$^+$) calculated for $C_{23}H_{24}N_2O_7S$+Na^+ $[M+Na]^+$: m/z = 495.1196, found 495.1190; **IR**: ν_{max} 3291; 2954, 2924, 2850, 2361, 2343, 2257, 1755, 1732, 1599, 1553, 1493, 1452, 1435, 1344, 1304, 1241, 1157, 1089, 1018, 912, 880; **HPLC**: IC, Pentane:*i*-PrOH 80:20, F = 1.0 mL/min, λ = 230 nm: Major isomer: t_R minor = 72.5 min, t_R major = 317.2 min; Minor isomer: t_R major = 94.6 min, t_R minor = 167.0 min.

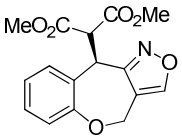


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	69.158	163.469	67.133	33431.914	42.198
2	94.111	22.210	9.121	7234.951	9.132
3	162.512	17.993	7.389	7972.649	10.063
4	314.142	39.828	16.356	30586.051	38.606

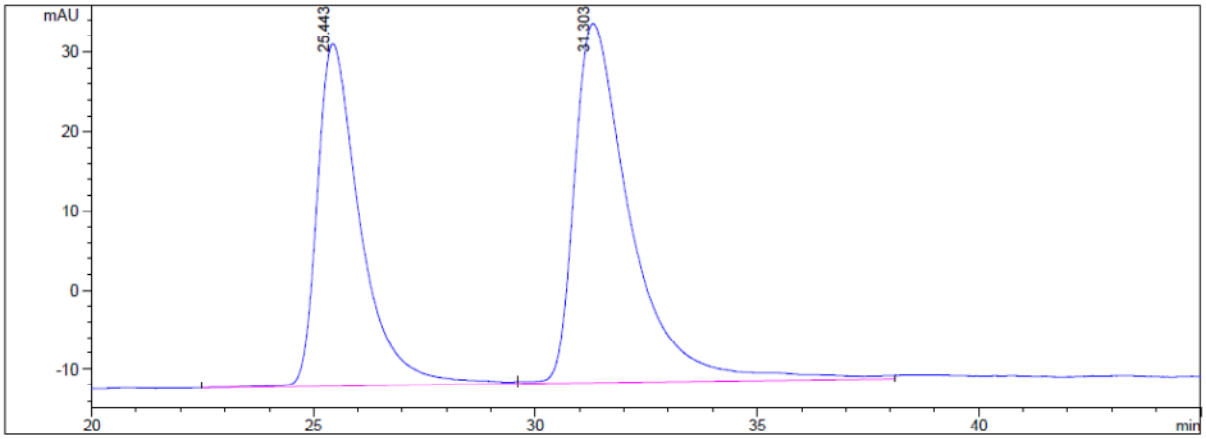


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	72.526	0.616	2.041	164.617	1.139
2	94.604	16.912	56.063	4883.356	33.799
3	167.015	0.191	0.633	96.068	0.665
4	317.198	12.447	41.263	9304.162	64.397

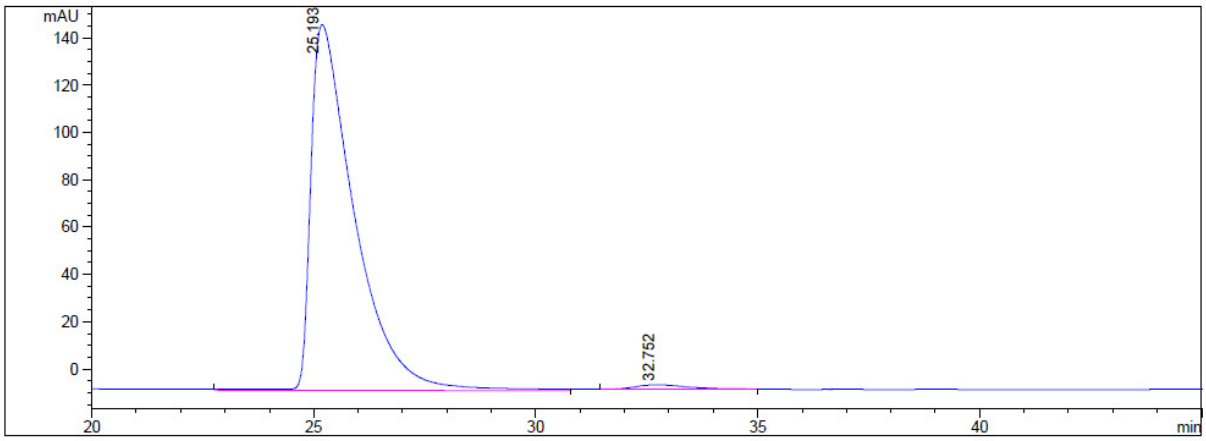
(*R*)-Dimethyl 2-(4,10-dihydrobenzo[6,7]oxepino[4,3-c]isoxazol-10-yl)malonate (5p)



Following the general procedure, the title compound **5p** was obtained after FC (petane-EtOAc 4:1) as a white solid (99%, 96% ee). $[\alpha]^{20}_{D}$ = +119 (*c* 2.27, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 1.1 Hz, 1H), 7.39 (dd, *J* = 7.1, 1.5 Hz, 1H), 7.30 (ddd, *J* = 8.1, 7.3, 1.7 Hz, 1H), 7.12 (td, *J* = 7.8, 7.4, 1.1 Hz, 2H), 5.40 (dd, *J* = 14.6, 1.2 Hz, 1H), 4.93 (dd, *J* = 11.2, 0.8 Hz, 1H), 4.81 (dd, *J* = 14.6, 1.4 Hz, 1H), 4.53 (d, *J* = 11.2 Hz, 1H), 3.67 (s, 3H), 3.54 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 167.5, 167.4, 158.9, 157.4, 153.3, 132.0, 131.3, 130.3, 125.5, 123.0, 116.1, 65.9, 56.2, 52.9, 52.6, 41.3; **HRMS** (ESI^+) calculated for $C_{16}H_{15}NO_6$+Na^+ $[M+Na]^+$: m/z = 340.0792, found 340.0788; **IR**: ν_{max} 3118, 3005, 2955, 2873, 1734, 1601, 1582, 1488, 1457, 1434, 1419, 1261, 1238, 1148, 1106, 1013, 894, 782; **HPLC**: OJ-H, Pentane:*i*-PrOH 85:15, F = 1.0 mL/min, λ = 230 nm, t_R major (*R*) = 25.2 min, t_R minor (*S*) = 32.8 min.

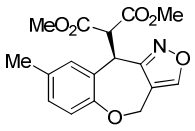


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	25.443	43.143	48.776	2928.793	42.181
2	31.303	45.308	51.224	4014.544	57.819

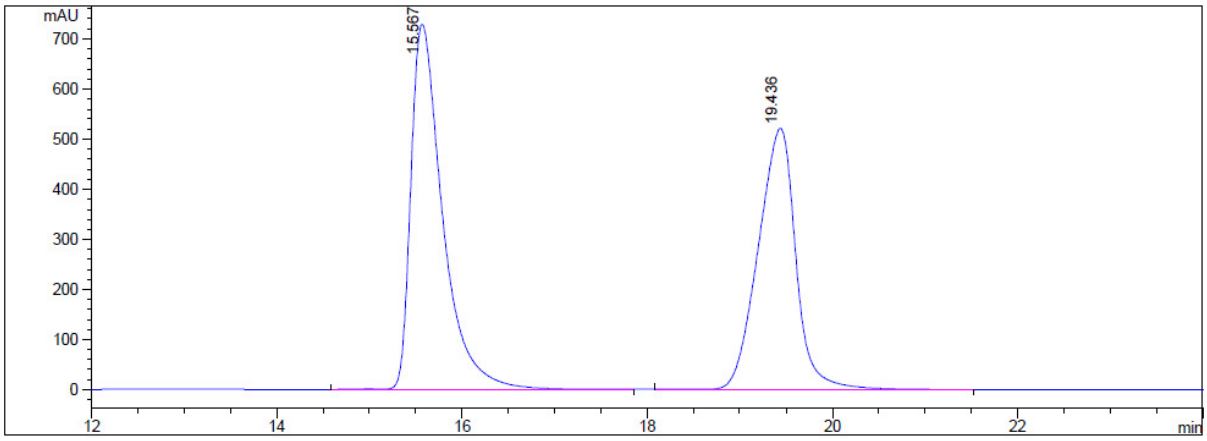


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	25.193	154.763	98.657	10558.085	98.114
2	32.752	2.107	1.343	202.923	1.886

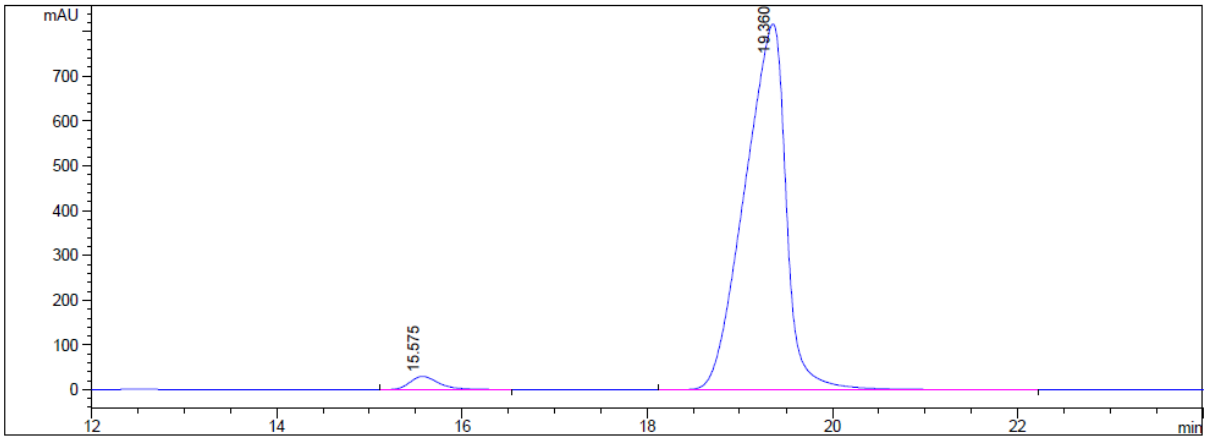
(*R*)-Dimethyl 2-(8-methyl-4,10-dihydrobenzo[6,7]oxepino[4,3-c]isoxazol-10-yl)malonate (5q)



Following the general procedure, the title compound **5q** was obtained after FC (petane-EtOAc 6:1) as a white solid (55%, 95% ee). $[\alpha]^{20}_{D}$ = +122 (*c* 1.24, $CHCl_3$); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.03 (q, *J* = 1.1 Hz, 1H), 7.12 (dd, *J* = 2.2, 0.9 Hz, 1H), 7.02 (ddd, *J* = 8.1, 2.2, 0.8 Hz, 1H), 6.94 (d, *J* = 8.1 Hz, 1H), 5.31 (dd, *J* = 14.6, 1.2 Hz, 1H), 4.81 (d, *J* = 10.8 Hz, 1H), 4.71 (dd, *J* = 14.6, 1.4 Hz, 1H), 4.46 (d, *J* = 11.2 Hz, 1H), 3.60 (s, 3H), 3.49 (s, 3H), 2.23 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 167.6, 167.5, 159.1, 155.1, 153.2, 135.1, 131.7, 131.6, 130.7, 122.6, 116.2, 65.9, 56.1, 52.8, 52.6, 41.3, 20.9; **HRMS** (ESI$^+$) calculated for $C_{17}H_{17}NO_6$+Na$^+$ $[M+Na]^+$: m/z = 354.0948, found 354.0948; **IR**: ν_{max} 3132, 3005, 2956, 2921, 2876, 2361, 2343, 1757, 1729, 1606, 1499, 1427, 1420, 1263, 1242, 1232, 1218, 1143, 1123, 1105, 1011, 881, 843, 828; **HPLC**: IA, Pentane:*i*-PrOH 90:10, F = 1.0 mL/min, λ = 230 nm: t_R major = 19.4 min, t_R minor = 15.6 min.

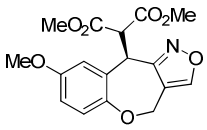


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	15.567	729.990	58.309	17552.102	54.124
2	19.436	521.950	41.691	14877.222	45.876

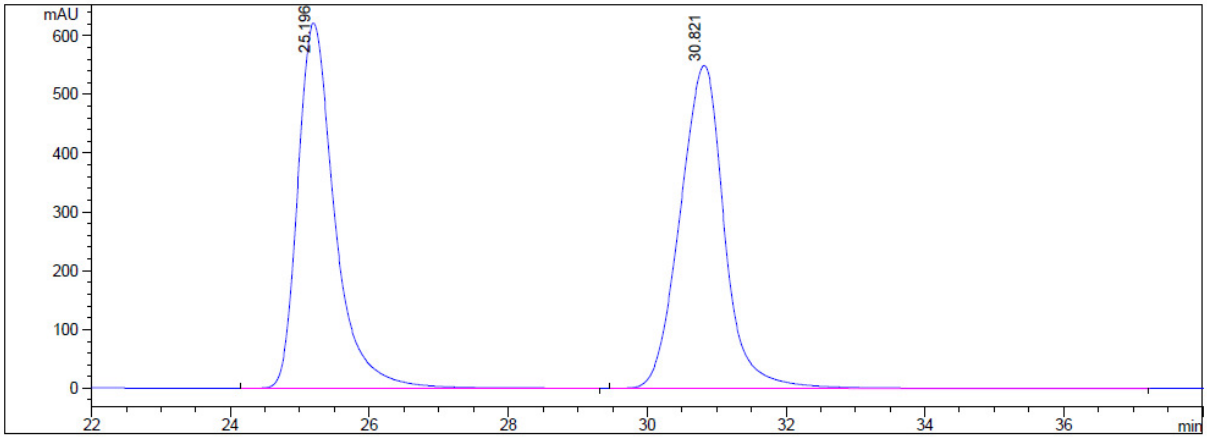


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	15.575	29.635	3.497	671.615	2.567
2	19.360	817.858	96.503	25488.770	97.433

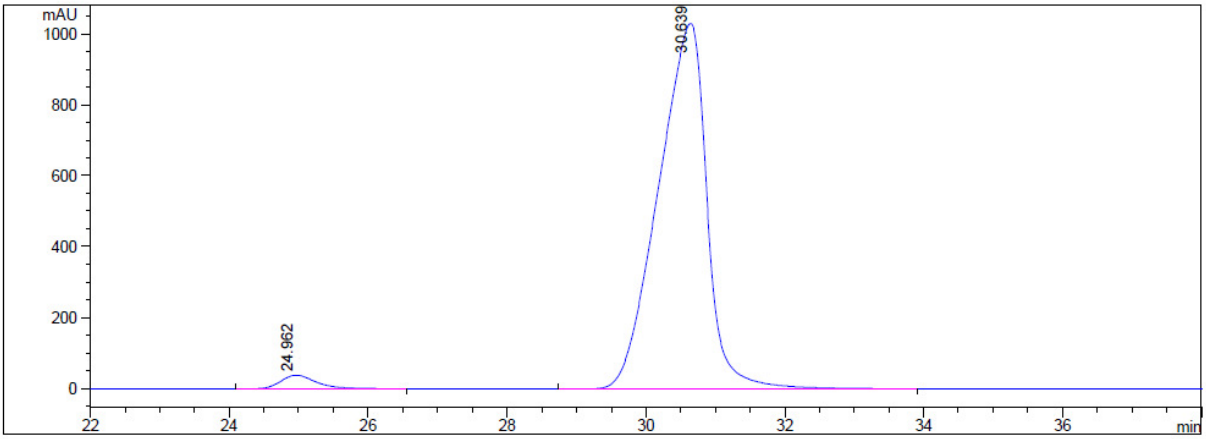
(*R*)-Dimethyl 2-(8-methoxy-4,10-dihydrobenzo[6,7]oxepino[4,3-c]isoxazol-10-yl)malonate (5r)



Following the general procedure, the title compound **5r** was obtained after FC (petane-EtOAc 6:1) as a white solid (56%, 94% ee). $[\alpha]^{20}_{D}$ = +109 (*c* 1.59, $CHCl_3$); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.10 (d, *J* = 1.0 Hz, 1H), 7.04 (d, *J* = 8.7 Hz, 1H), 6.91 (d, *J* = 3.0 Hz, 1H), 6.79 (dd, *J* = 8.7, 3.0 Hz, 1H), 5.34 (dd, *J* = 14.5, 1.1 Hz, 1H), 4.87 (dd, *J* = 11.2, 0.8 Hz, 1H), 4.76 (dd, *J* = 14.5, 1.4 Hz, 1H), 4.53 (d, *J* = 11.2 Hz, 1H), 3.76 (s, 3H), 3.66 (s, 3H), 3.57 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 167.5, 167.4, 158.9, 156.6, 153.3, 150.9, 132.7, 123.6, 116.2, 116.0, 115.2, 66.0, 56.1, 55.8, 52.9, 52.7, 41.4; **HRMS** (ESI^+) calculated for $C_{17}H_{17}NO_7$+Na^+ $[M+Na]^+$: m/z = 370.0897, found 370.0892; **IR**: ν_{max} 3017, 2958, 2833, 2362, 2343, 1761, 1740, 1615, 1601, 1583, 1495, 1431, 1419, 1291, 1236, 1221, 1204, 1193, 1167, 1150, 1118, 1108, 1038, 1028, 1014, 925, 892, 830, 674, 665; **HPLC**: IA, Pentane:*i*-PrOH 90:10, F = 1.0 mL/min, λ = 230 nm: t_R major = 30.6 min, t_R minor = 25.0 min.

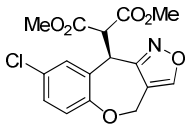


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	25.196	621.764	53.086	23019.363	48.477
2	30.821	549.474	46.914	24466.115	51.523

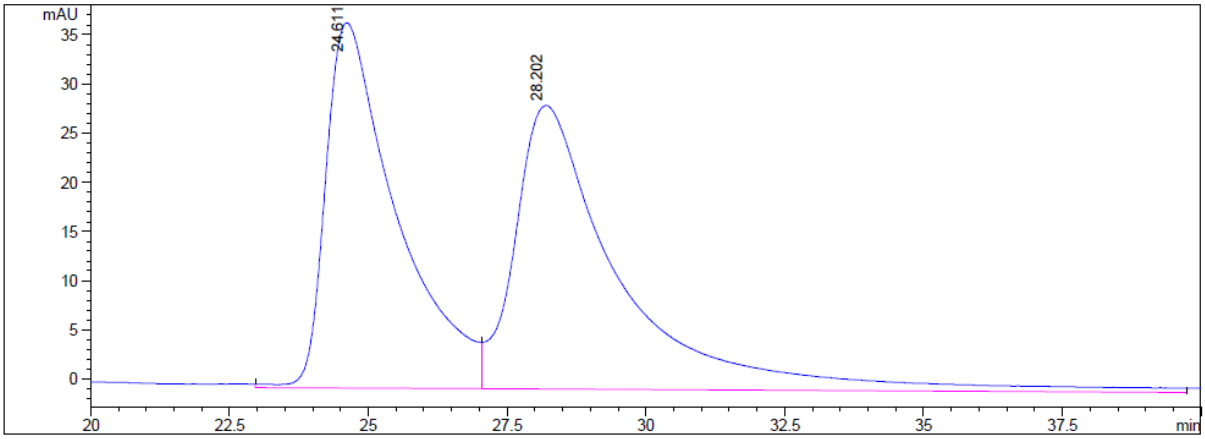


#	Meas. Ret. Time	Height	Height %	Area	Area %
1	24.962	38.728	3.614	1434.704	2.761
2	30.639	1032.837	96.386	50525.184	97.239

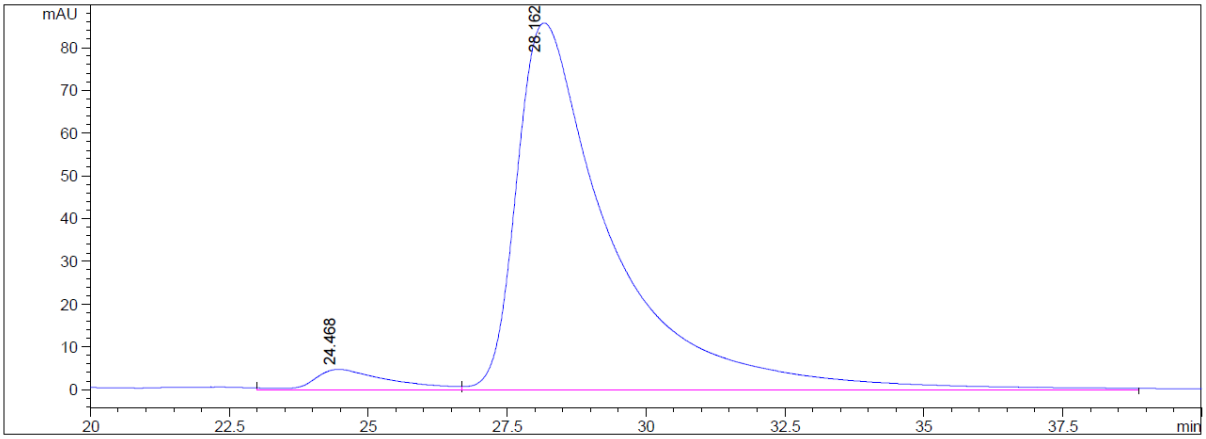
(*R*)-Dimethyl 2-(8-chloro-4,10-dihydrobenzo[6,7]oxepino[4,3-c]isoxazol-10-yl)malonate (5s)



Following the general procedure, the title compound **5s** was obtained after FC (petane-EtOAc 8:1) as a white solid (56%, 93% ee). $[\alpha]^{20}_{D}$ = +94 (*c* 0.76, $CHCl_3$); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 1.1 Hz, 1H), 7.40 (d, *J* = 2.6 Hz, 1H), 7.28 – 7.24 (m, 1H), 7.07 (d, *J* = 8.5 Hz, 1H), 5.40 (dd, *J* = 14.6, 1.2 Hz, 1H), 4.93 – 4.84 (m, 1H), 4.79 (dd, *J* = 14.6, 1.4 Hz, 1H), 4.48 (d, *J* = 11.1 Hz, 1H), 3.67 (s, 3H), 3.60 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 167.3, 167.2, 158.4, 155.9, 153.5, 133.7, 131.2, 130.6, 130.2, 124.4, 115.8, 66.1, 56.0, 53.0, 52.8, 41.0; **HRMS** (ESI^+) calculated for $C_{16}H_{14}ClNO_6$+Na^+ $[M+Na]^+$: m/z = 374.0402, found 374.0398; **IR**: ν_{max} 2978, 2958, 2923, 2852, 2358, 1756, 1733, 1601, 1487, 1458, 1443, 1435, 1417, 1326, 1300, 1262, 1175, 1153, 1116, 1102, 1007, 900, 890, 841, 681, 667, 608, 592; **HPLC**: IA, Pentane:*i*-PrOH 90:10, F = 1.0 mL/min, λ = 230 nm: t_R major = 28.2 min, t_R minor = 24.5 min.



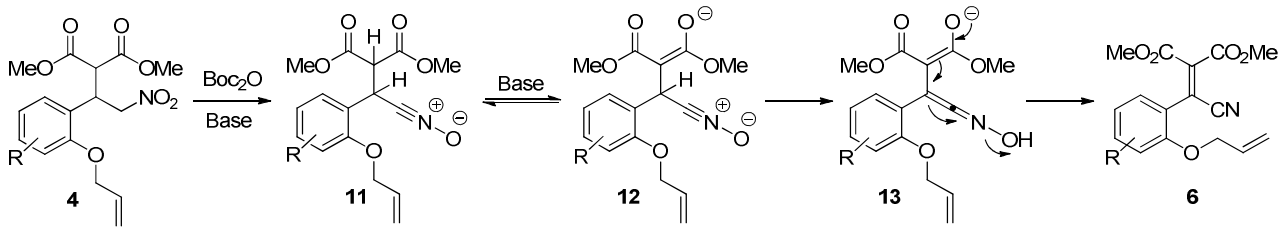
#	Meas. Ret. Time	Height	Height %	Area	Area %
1	24.611	37.108	56.290	3304.087	46.277
2	28.202	28.815	43.710	3835.777	53.723



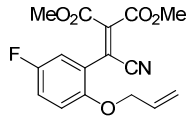
#	Meas. Ret. Time	Height	Height %	Area	Area %
1	24.468	4.865	5.362	471.713	4.372
2	28.162	85.863	94.638	10316.749	95.628

Proposed mechanism for the formation of conjugated nitriles 6 side-products

Only in the cases of the F, Br and Cl substituted derivatives **4**, nitriles **6** were formed and isolated as side-products. The formation of **6** can be rationalized by the relative higher acidity of the benzylic position in these compounds due to the electron-withdrawing nature of the halogen substituents. Subsequently, we propose that after the formation of the nitrile oxide **11**, under the basic conditions employed, the malonate moiety might also be deprotonated to form the corresponding enolate **12**. This could now undergo a proton shift in the cases that the benzylic proton has the appropriate acidity, leading to the ethenone oxime **13**. Finally, the expulsion of the hydroxyl group would lead to the observed unsaturated nitrile **6**.

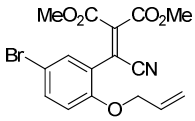


Dimethyl 2-((2-(allyloxy)-5-fluorophenyl)(cyano)methylene)malonate (6k)



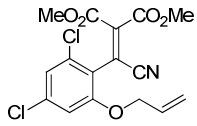
The title compound **6k** was obtained after FC (petane-EtOAc 5:1) as yellow oil (27%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.11 (ddd, *J* = 9.1, 7.8, 3.1 Hz, 1H), 7.01 (dd, *J* = 8.2, 3.1 Hz, 1H), 6.02 (ddt, *J* = 17.3, 10.5, 5.2 Hz, 1H), 5.40 (dq, *J* = 17.3, 1.5 Hz, 1H), 5.30 (dq, *J* = 10.6, 1.4 Hz, 1H), 4.59 (dt, *J* = 5.3, 1.6 Hz, 2H), 3.94 (s, 3H), 3.66 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 163.1, 161.9, 156.6 (d, ^1J = 242.6 Hz), 152.2 (d, ^3J = 2.8 Hz), 139.6, 132.2, 122.0 (d, ^4J = 1.3 Hz), 121.9 (d, ^4J = 1.5 Hz), 118.7 (d, ^2J = 22.9 Hz), 118.5, 116.6 (d, ^2J = 25.2 Hz), 114.8 , 114.3 (d, ^3J = 8.1 Hz), 70.5, 53.7, 53.1; **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -121.90; **HRMS** (ESI^+) calculated for $C_{16}H_{14}FNO_5$+Na^+ $[M+Na]^+$: m/z = 342.0748, found 342.0754; **IR**: ν_{max} 2363, 2343, 1736, 1612, 1590, 1493, 1456, 1436, 1426, 1371, 1303, 1256, 1194, 1180, 1152, 1126, 1083, 1028, 994, 935, 878, 843, 813, 750.

Dimethyl 2-((2-(allyloxy)-5-bromophenyl)(cyano)methylene)malonate (6l)



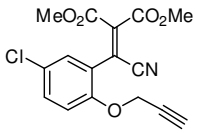
The title compound **6l** was obtained after FC (petane-EtOAc 5:1) as a yellow oil (34%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.49 (dd, *J* = 8.9, 2.4 Hz, 1H), 7.38 (d, *J* = 2.4 Hz, 1H), 6.82 (d, *J* = 8.9 Hz, 1H), 6.00 (ddt, *J* = 17.3, 10.4, 5.1 Hz, 1H), 5.40 (dq, *J* = 17.3, 1.6 Hz, 1H), 5.31 (dq, *J* = 10.6, 1.4 Hz, 1H), 4.60 (dt, *J* = 5.2, 1.6 Hz, 2H), 3.94 (s, 3H), 3.67 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 163.1, 161.8, 155.0, 139.6, 135.2, 132.3, 131.9, 122.7, 121.7, 118.6, 114.8, 114.6, 113.0, 70.1, 53.7, 53.1; **HRMS** (ESI^+) calculated for $C_{16}H_{14}BrNO_5$+Na^+ $[M+Na]^+$: m/z = 401.9948, found 401.9951; **IR**: ν_{max} 2951, 1779, 1735, 1615, 1591, 1483, 1455, 1435, 1400, 1371, 1264, 1242, 1146, 1121, 1093, 1026, 990, 931, 813, 764, 722.

Dimethyl 2-((2-(allyloxy)-4,6-dichlorophenyl)(cyano)methylene)malonate (6m)



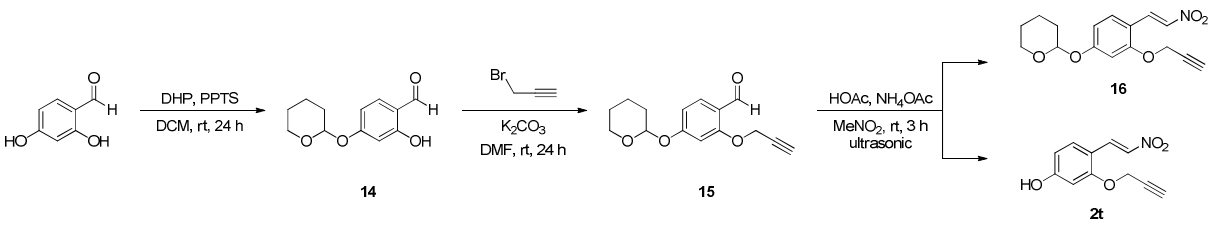
The title compound **6m** was obtained after FC (petane-EtOAc 4:1) as a white solid (25%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 6.95 (d, *J* = 2.0 Hz, 1H), 6.71 (d, *J* = 2.0 Hz, 1H), 5.99 (ddt, *J* = 17.2, 10.7, 5.4 Hz, 1H), 5.62 – 5.03 (m, 2H), 4.52 (dq, *J* = 5.5, 1.5 Hz, 2H), 3.71 (s, 3H), 3.42 (s, 3H); **HRMS** (ESI^+) calculated for $C_{16}H_{13}Cl_2NO_5$+Na^+ $[M+Na]^+$: m/z = 369.0171, found 369.01714.

Dimethyl 2-((2-(allyloxy)-5-chlorophenyl)(cyano)methylene)malonate (6s)

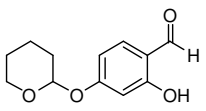


The title compound **6s** was obtained after FC (petane-EtOAc 8:1) as a yellow oil (26%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.40 (dd, *J* = 8.9, 2.6 Hz, 1H), 7.29 (d, *J* = 2.5 Hz, 1H), 7.06 (d, *J* = 8.9 Hz, 1H), 4.73 (d, *J* = 2.4 Hz, 2H), 3.94 (s, 3H), 3.69 (s, 3H), 2.57 (t, *J* = 2.4 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 163.0, 161.8, 153.4, 140.0, 132.2, 129.7, 127.0, 122.7, 121.2, 114.8, 114.6, 77.3, 77.1, 56.9, 53.7, 53.2; **HRMS** (ESI^+) calculated for $C_{16}H_{12}ClNO_5$+Na^+ $[M+Na]^+$: m/z = 356.0296, found 356.0297. **IR**: ν_{max} 3287, 2957, 1733, 1614, 1572, 1484, 1453, 1436, 1405, 1372, 1267, 1249, 1223, 1146, 1104, 1086, 1017, 990, 929, 891, 879, 813, 764, 675, 644, 612.

Synthesis of bioactive compound *ent*-8

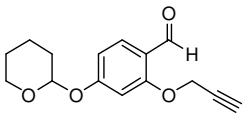


2-Hydroxy-4-((tetrahydro-2H-pyran-2-yl)oxy)benzaldehyde (14)



To a suspension of 2,4-dihydroxybenzalehyde (2.00 g, 14.48 mmol, 1.0 equiv.) and pyridinium-4-toluolsulfonate (35.7 mg, 0.14 mmol, 0.01 equiv.) in 70 mL DCM a solution of dihydropyran (1.45 mL, 15.93 mmol, 1.1 equiv.) in 24 mL DCM was slowly added. After stirring the reaction mixture for 1.5 h at room temperature, the reaction mixture was washed with saturated NaCl (aq.) and dried over Na_2SO_4 and the solvent removed in vacuo. The residue was purified by column chromatography (pentane-EtOAc: 20:1), affording **14** (2.32 g, 10.42 mmol, 72%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 11.35 (s, 1H), 9.71 (d, *J* = 0.7 Hz, 1H), 7.42 (d, *J* = 8.6 Hz, 1H), 6.64 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.61 (d, *J* = 2.3 Hz, 1H), 5.49 (t, *J* = 3.2 Hz, 1H), 3.81 (ddd, *J* = 11.3, 9.8, 3.1 Hz, 1H), 3.62 (dtd, *J* = 11.4, 4.1, 1.5 Hz, 1H), 1.97 (dddd, *J* = 13.7, 12.0, 6.9, 3.2 Hz, 1H), 1.86 (ddd, *J* = 6.7, 4.6, 3.2 Hz, 2H), 1.77 – 1.63 (m, 2H), 1.65 – 1.52 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 194.6, 164.4, 164.2, 135.4, 115.8, 109.5, 103.7, 96.3, 62.3, 30.0, 25.0, 18.5; **HRMS** (ESI^+): calculated for $C_{12}H_{14}O_4$+Na^+ $[M+Na]^+$: m/z = 245.0784, found 245.0790.

2-(Prop-2-yn-1-yloxy)-4-((tetrahydro-2H-pyran-2-yl)oxy)benzaldehyde (15)

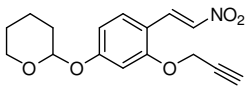


An ordinary vial equipped with a magnetic stirring bar was charged with **14** (2.23 g, 10.03 mmol, 1.0 equiv.), K_2CO_3 (1.53 g, 11.04 mmol, 1.1 equiv.) and DMF (15 mL, 0.6 M). To the stirring solution, propargyl bromide (80%, 1.23 mL, 11.04 mmol, 1.1 equiv.) was added dropwise. After stirring the solution for 5 h water was added and the mixture extracted 3 times with DCM. The combined organic phases were dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (pentane-EtOAc: 20:1) to obtain **15** (2.46 g, 9.44 mmol, 94%) as a light yellow oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 10.28 (d, *J* = 0.8 Hz, 1H), 7.76 (d, *J* = 8.5 Hz, 1H), 6.87 – 6.57 (m, 2H), 5.51 (t, *J* = 3.1 Hz, 1H), 4.82 (d, *J* = 2.4 Hz, 2H), 3.83 (ddd, *J* = 11.4, 9.6, 3.3 Hz, 1H), 3.61 (dtd, *J* = 11.5, 4.1, 1.4 Hz, 1H), 2.66 (t, *J* = 2.4 Hz, 1H), 2.06 – 1.92 (m, 1H), 1.92 – 1.79 (m, 2H), 1.77 – 1.43 (m, 4H); **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 188.3, 164.1, 161.9, 130.5, 120.4, 110.0, 101.8, 97.1, 78.2, 76.7, 62.7, 57.0, 30.6, 25.6, 19.1; **HRMS** (ESI^+): calculated for $C_{15}H_{16}O_4$+Na+ [M+Na]+: m/z = 283.0941, found 283.0944.

(E)-2-(4-(2-Nitrovinyl)-3-(prop-2-yn-1-yloxy)phenoxy)tetrahydro-2H-pyran (16) and **(E)-4-(2-nitrovinyl)-3-(prop-2-yn-1-yloxy)phenol (2t)**

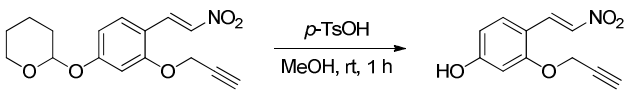
Aldehyde **15** (1.30 g, 4.99 mmol, 1.0 equiv.) was treated with nitromethane (3.23 mL, 60.34 mmol, 12.1 equiv.), acetic acid (828 µL, 14.47 mmol, 2.9 equiv.) and NH_4OAc (846 mg, 10.98 mmol, 2.2 equiv.) at rt under ultrasound irradiation for 3 h. The corresponding nitroolefins **16** (1.07 g, 3.54 mmol, 71%) and **2t** (0.31 g, 1.39 mmol, 28%) were then isolated by column chromatography (pentane-EtOAc: 10:1→4:1).

(E)-2-(4-(2-Nitrovinyl)-3-(prop-2-yn-1-yloxy)phenoxy)tetrahydro-2H-pyran (16)



Not stable under slightly acidic conditions! **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.04 (d, *J* = 13.6 Hz, 1H), 7.75 (d, *J* = 13.5 Hz, 1H), 7.32 (d, *J* = 8.3 Hz, 1H), 6.76 – 6.60 (m, 2H), 5.43 (t, *J* = 3.0 Hz, 1H), 4.74 (d, *J* = 2.5 Hz, 2H), 3.79 (ddd, *J* = 11.2, 9.7, 3.2 Hz, 1H), 3.57 (dtd, *J* = 11.4, 4.0, 1.6 Hz, 1H), 2.53 (t, *J* = 2.4 Hz, 1H), 2.01 – 1.87 (m, 1H), 1.82 (dt, *J* = 5.6, 3.6 Hz, 2H), 1.75 – 1.41 (m, 4H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 161.8, 159.0, 136.6, 135.5, 134..0, 113.3, 109.8, 101.7, 96.6, 77.4, 76.8, 62.3, 56.4, 30.2, 25.1, 18.6. **HRMS** (ESI^+) calculated for $C_{16}H_{17}NO_5$+Na^+ $[M+Na]^+$: m/z = 326.0999, found 326.0996.

(*E*)-4-(2-Nitrovinyl)-3-(prop-2-yn-1-yloxy)phenol (2t)

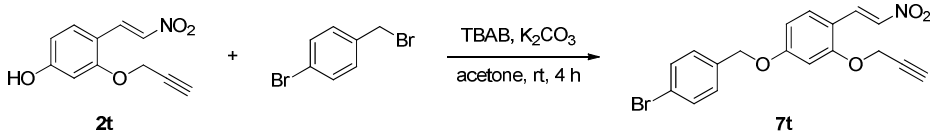


16 **2t**

To a solution of nitroolefin **16** (1.00 g, 3.30 mmol, 1.0 equiv.) in MeOH (83 mL, 0,04 M), *p*-TsOH (56.6 mg, 0.33 mmol, 0.1 equiv.) was added and stirred at rt for 1 h until completion of reaction (followed by TLC). The

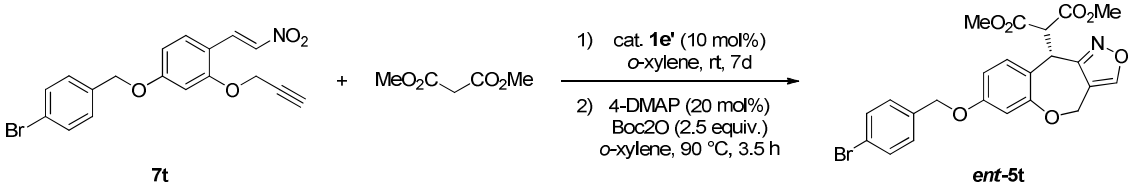
residue was purified by column chromatography (pentane-EtOAc: 4:1), affording **2t** as a yellow-orange solid (0.70 g, 3.20 mmol, 97%). **^{1}H NMR** (300 MHz, DMSO-d_6) δ = 10.65 (s, 1H), 8.12 (d, *J* = 13.4 Hz, 1H), 7.98 (d, *J* = 13.4 Hz, 1H), 7.66 (d, *J* = 8.5 Hz, 1H), 6.60 (d, *J* = 2.2 Hz, 1H), 6.51 (dd, *J* = 8.5, 2.2 Hz, 1H), 4.95 (d, *J* = 2.4 Hz, 2H), 3.70 (t, *J* = 2.3 Hz, 1H), 3.38 (br.s, 1H); **^{13}C NMR** (75 MHz, DMSO): δ = 163.4, 159.2, 135.4, 134.8, 134.0, 110.2, 109.6, 100.7, 79.1, 78.6, 56.2. **HRMS** (ESI$^+$): calculated for $C_{11}H_9NO_4$+Na^+ $[M+Na]^+$: m/z = 242.0424, found 242.0429.

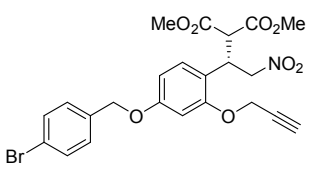
(*E*)-4-((4-Bromobenzyl)oxy)-1-(2-nitrovinyl)-2-(prop-2-yn-1-yloxy)benzene (7t)



To a solution of nitroolefin **2t** (600 mg, 2.74 mmol, 1.0 equiv.) and 4-bromobenzyl bromide (685 mg, 2.74 mmol, 1.0 eqiuv.) in acetone (8.5 mL, 0,33 M), K_2CO_3 (379 mg, 2.74 mmol, 1.0 eqiuv.) and TBAB (177 mg, 0.55 mmol, 0.2 equiv.) were added and stirred at rt for 4 h until completion of reaction (followed by TLC). The residue was purified by column chromatography (pentane-EtOAc: 4:1) affording **7t** as a yellow-orange solid (0.70 g, 3.20 mmol, 97%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.09 (d, *J* = 13.6 Hz, 1H), 7.80 (d, *J* = 13.5 Hz, 1H), 7.59 – 7.46 (m, 2H), 7.40 (d, *J* = 8.5 Hz, 1H), 7.35 – 7.27 (m, 2H), 6.70 – 6.60 (m, 2H), 5.08 (s, 2H), 4.79 (d, *J* = 2.4 Hz, 2H), 2.58 (t, *J* = 2.4 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 163.0, 159.0, 136.6, 135.3, 135.0, 134.2, 132.1 (2C), 129.3 (2C), 122.5, 113.2, 107.8, 100.8, 77.3, 77.0, 69.8, 56.4. **HRMS** (ESI$^+$) calculated for $C_{18}H_{14}BrNO_4$+Na^+ $[M+Na]^+$: m/z = 409.9998, found 410.0003.

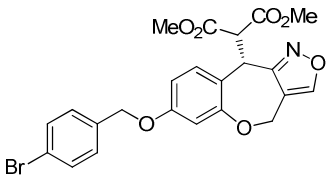
Dimethyl (*S*)-2-(7-((4-bromobenzyl)oxy)-4H,10H-benzo[6,7]oxepino[4,3-c]isoxazol-10-yl)malonate (*ent*-5t)



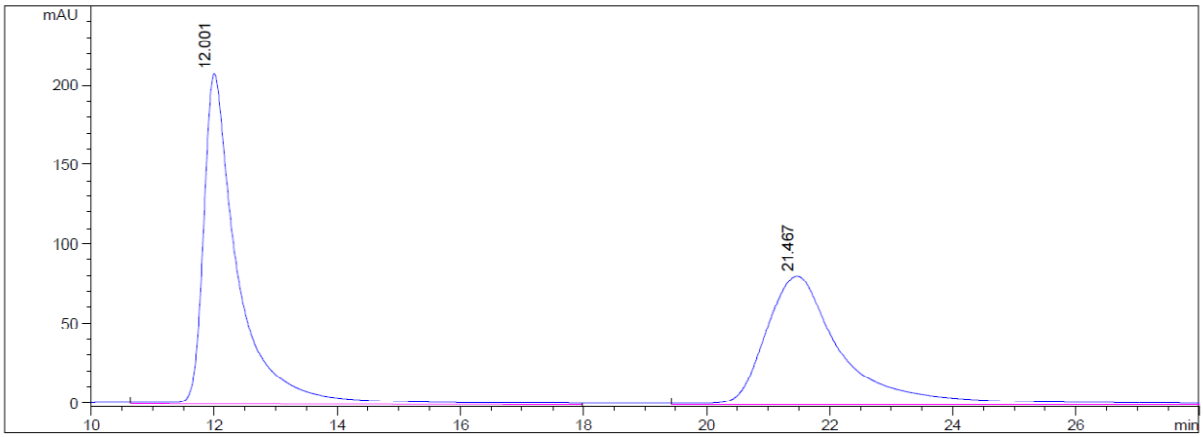


An ordinary vial equipped with a magnetic stirring bar was charged with catalyst **1e'** (10 mol%), malonate **3** (41.4 µL, 0.36 mmol, 1.2 equiv.), nitroolefin **7t** (77.6 mg, 0.30 mmol, 1.0 equiv.) and *o*-xylene (1.5 mL) at rt. The stirring was maintained at rt for 7 d. The crude reaction mixture was directly charged onto silica-gel and purified by column chromatography (pentane-EtOAc: 6:1) to afford compound ***ent*-4t** (93.4 mg, 0.18 mmol, 60%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.56 – 7.45 (m, 2H), 7.31 – 7.26 (m, 2H), 7.06 (d, *J* = 8.4 Hz, 1H), 6.60 (d, *J* = 2.3 Hz, 1H), 6.48 (dd, *J* = 8.5, 2.4 Hz, 1H), 5.00 (dd, *J* = 13.0, 9.2 Hz, 1H), 4.95 (s, 2H),

4.85 (dd, *J* = 13.0, 4.6 Hz, 1H), 4.71 (d, *J* = 2.4 Hz, 2H), 4.33 (td, *J* = 9.5, 4.6 Hz, 1H), 4.14 (d, *J* = 10.0 Hz, 1H), 3.75 (s, 3H), 3.51 (s, 3H), 2.55 (t, *J* = 2.4 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 168.4, 167.7, 159.7, 156.5, 135.7, 131.9 (2C), 131.6, 129.3 (2C), 122.2, 117.0, 106.5, 101.2, 77.9, 76.3, 76.3, 69.5, 56.3, 53.0, 52.8, 52.7, 39.9; **HRMS** (ESI^+) calculated for $C_{23}H_{22}BrNO_8$+Na+ [M+Na]+: m/z = 544.0402, found 544.0394.



The nitro compound ***ent*-4t** (104.1 mg, 0.2 mmol, 1.0 equiv.) and DMAP (4.9 mg, 0.04 mmol, 0.2 equiv.) were dissolved in freshly distilled toluene (1.0 mL) and heated to 90 °C. To the hot reaction mixture, a solution of Boc_2O in toluene (0.5 M, 1.0 mL, 2.5 equiv.) was added over 20 min. The reaction was then allowed to proceed for further 3.5 h at 90 °C. After cooling to room temperature, the crude reaction mixture was directly charged onto silica-gel and purified by column chromatography to afford the titled compound ***ent*-5t** (58.2 mg, 0.12 mmol, 58%, 97% ee). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 1.0 Hz, 1H), 7.50 (d, *J* = 8.4 Hz, 2H), 7.28 (dd, *J* = 8.4, 5.2 Hz, 3H), 6.86 – 6.62 (m, 2H), 5.39 (dd, *J* = 14.6, 1.2 Hz, 1H), 4.97 (s, 2H), 4.88 (d, *J* = 11.1 Hz, 1H), 4.79 (dd, *J* = 14.7, 1.4 Hz, 1H), 4.46 (d, *J* = 11.1 Hz, 1H), 3.67 (s, 3H), 3.56 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 167.6, 167.5, 159.9, 159.1, 158.4, 153.3, 135.6, 132.0, 131.9 (2C), 129.2 (2C), 124.4, 122.2, 116.1, 111.6, 109.7, 69.5, 66.0, 56.4, 52.9, 52.7, 40.6; **HRMS** (ESI^+) calculated for $C_{23}H_{20}BrNO_7$+Na+ [M+Na]+: m/z = 524.0315, found 524.0336; **IR** (ATR): ν_{max} 2954, 2875, 1736, 1611, 1580, 1495, 1456, 1434, 1415, 1287, 1260, 11,55, 1118, 1104, 1071, 1022, 1011, 946, 891, 805, 711, 559; **HPLC**: IA, Pentane:i-PrOH 70:30, F = 1.0 mL/min, λ = 230 nm, t_R major (*S*) = 12.3 min, t_R minor (*R*) = 22.2 min.



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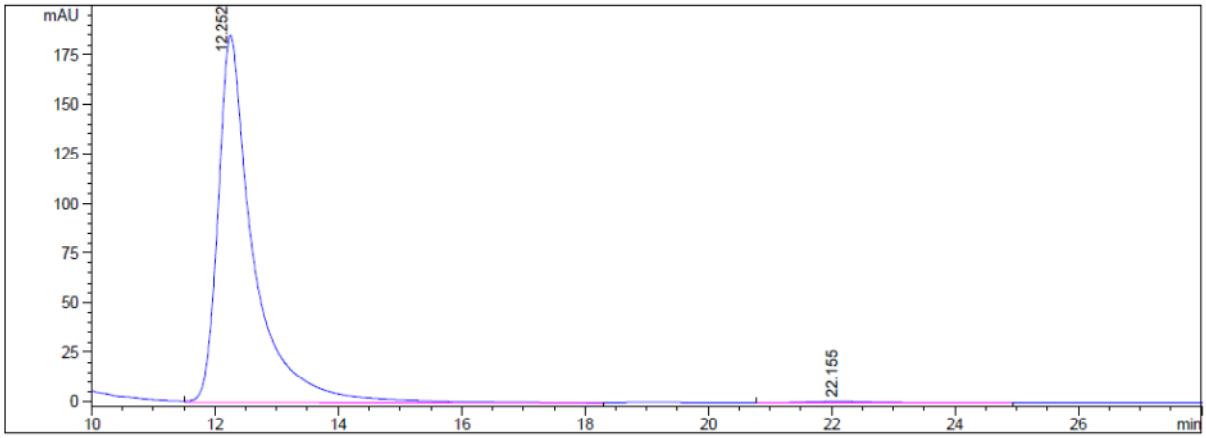
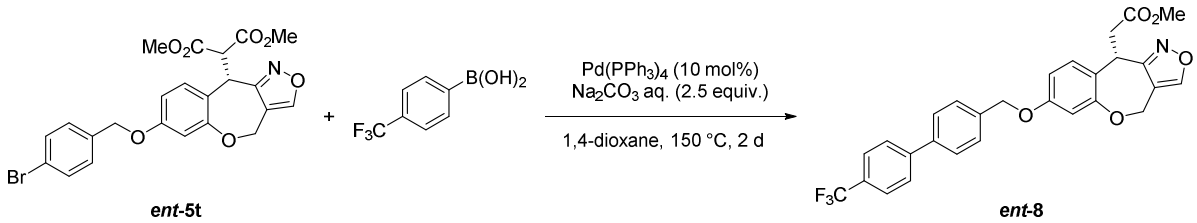


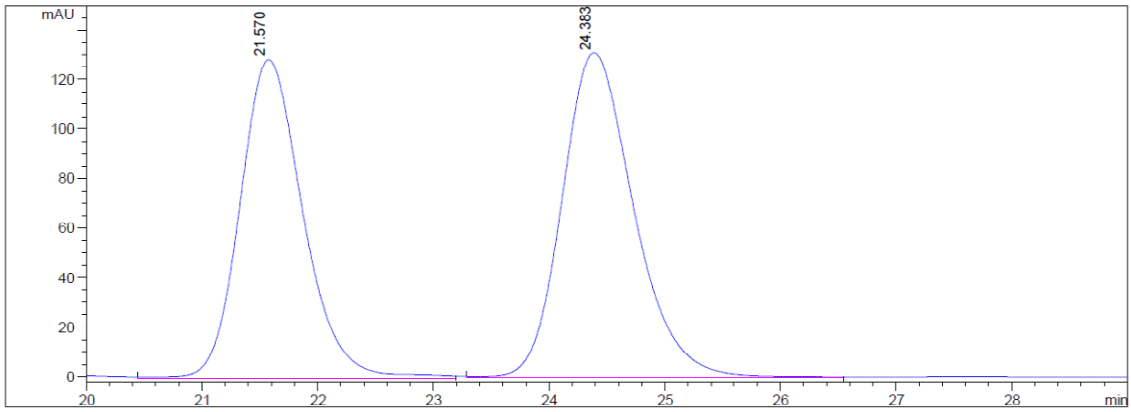
#	Meas. Ret. Time	Height	Height %	Area	Area %
1	12.252	184.942	99.519	7386.069	98.608
2	22.155	0.893	0.481	104.287	1.392

Methyl (*S*)-2-(7-((4'-(trifluoromethyl)-[1,1'-biphenyl]-4-yl)methoxy)-4H,10H-benzo[6,7]oxepino[4,3-c]isoxazol-10-yl)acetate (*ent*-8)



***ent*-5t** ***ent*-8**

To a solution of ***ent*-5t** (50.2 mg, 0.1 mmol, 1.0 equiv.), boronic acid (22.8 mg, 0.12 mmol, 1.2 equiv.) and Na_2CO_3 (26.5 mg, 0.25 mmol, 2.5 equiv.) in dry 1,4-dioxane (0.4 mL), $Pd(PPh_3)_4$ (11.6 mg, 0.01 mmol, 10 mol%) and dest. water (50 µL) were added. The reaction mixture was heated at 150 °C for 2d. The crude reaction mixture was directly charged onto silica-gel and purified by column chromatography (pentane-EtOAc: 4:1) to afford the titled compound ***ent*-8** as a white solid (50.4 mg, 0.99 mmol, 99%, 90% ee). $[\alpha]^{20}_D$ = -108 (*c* 0.98, $CHCl_3$); **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 8.10 (s, 1H), 7.70 (s, 4H), 7.65 – 7.59 (m, 2H), 7.55 – 7.50 (m, 1H), 7.23 (d, *J* = 8.5 Hz, 1H), 6.81 (d, *J* = 2.6 Hz, 1H), 6.76 (dd, *J* = 8.4, 2.6 Hz, 1H), 5.28 (dd, *J* = 14.5, 1.1 Hz, 1H), 5.09 (s, 2H), 4.89 (dd, *J* = 14.5, 1.4 Hz, 1H), 4.74 (dd, *J* = 9.0, 6.4 Hz, 1H), 3.63 (s, 3H), 3.18 (dd, *J* = 15.7, 9.0 Hz, 1H), 3.07 (dd, *J* = 15.7, 6.4 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 171.6, 161.2, 159.8, 158.6, 153.0, 144.3 (q, ^4J = 1.3 Hz, 2C), 139.7, 136.8, 130.3, 129.6 (q, ^2J = 32.6 Hz), 128.2 (2C), 127.7 (2C), 127.5 (2C), 126.3, 125.9 (q, ^3J = 3.7 Hz, 2C), 124.4 (d, ^1J = 272.0 Hz), 116.1, 111.5, 109.9, 70.0, 66.0, 51.9, 39.7, 37.1; **HRMS** (ESI^+) calculated for $C_{28}H_{22}F_3NO_5$+Na^+ $[M+Na]^+$: m/z = 532.1342, found 532.1341; **IR** (ATR): ν_{max} 3119, 2953, 2925, 2856, 2365, 2342, 1736, 1613, 1580, 1496, 1458, 1415, 1358, 1324, 1260, 1160, 1109, 1070, 1023, 1007, 909, 885, 850, 816, 732, 647, 621, 603. **HPLC**: AD-H, Pentane:*i*-PrOH 80:20, F = 1.0 mL/min, λ = 230 nm, t_R major (*S*) = 25.3 min, t_R minor (*R*) = 22.4 min.



#	Meas. Ret. Time	Height	Height %	Area	Area %
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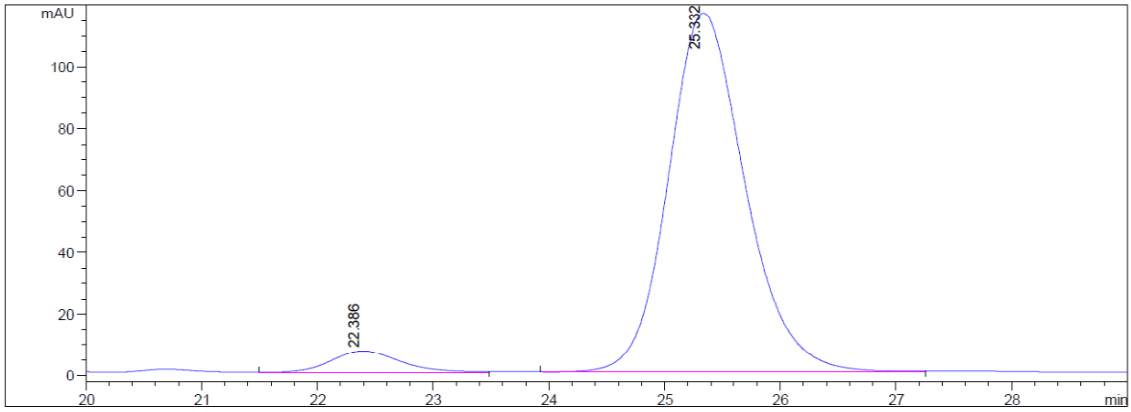
2	24.383	130.856	50.471	5607.558	53.554



#	Meas. Ret. Time	Height	Height %	Area	Area %
1	22.386	6.859	5.570	287.303	5.070
2	25.332	116.284	94.430	5378.982	94.930

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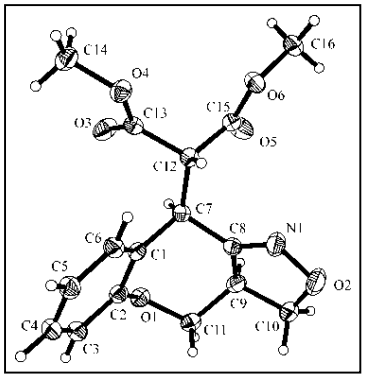
(12) H. R. Kim, H. J. Kim, J. L. Duffy, M. M. Olmstead, K. Ruhlandt-Senge, M. J. Kurth, *Tetrahedron Lett.* 1991, **32**, 4259.
(13) Y. Basel, A. Hassner, *Synthesis* 1997, 309.

X-Ray ORTEP and data of compound (3a*R*,10*R*)-5a



Formula $C_{16}H_{17}NO_6$, M = 319.31

Colourless crystal, 0.25 x 0.10 x 0.08 mm

a = 8.2054(1), b = 10.5740(1), c = 8.6556(1) Å, β = 95.960(1)

V = 746.9(1) $Å^3$, ρ_{calc} = 1.420 gcm^{-3}, μ = 0.923 mm^{-1}

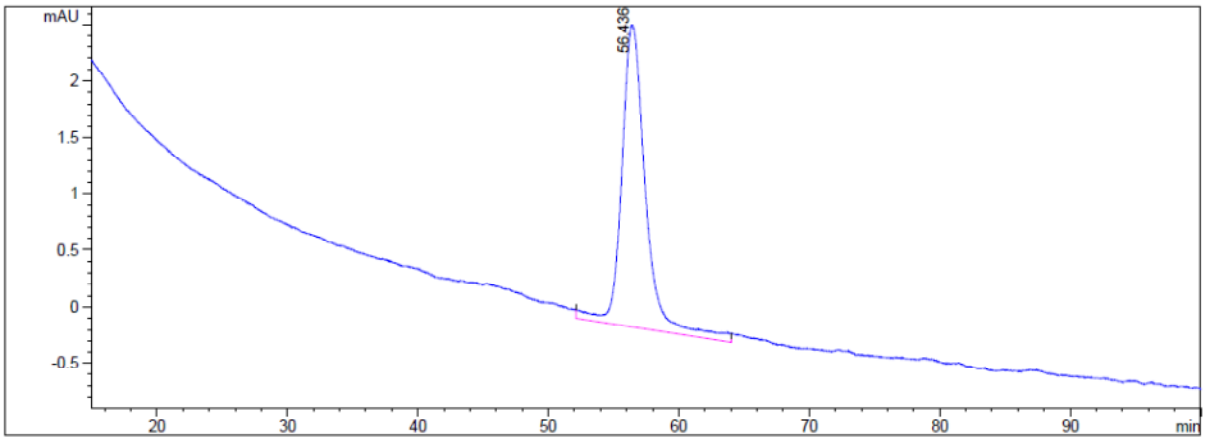
Empirical absorption correction ($0.802 \leq T \leq 0.929$)

Z = 2, monoclinic, space group $P2_1$ (No. 4)

λ = 1.54178 Å, T = 223(2) K

ω and φ scans, 3697 reflections collected ($\pm h$, $\pm k$, $\pm l$), [$(\sin\theta)/\lambda$] = 0.60 $Å^{-1}$, 2081 independent (R_{int} = 0.026) and 2077 observed reflections [$I>2\sigma(I)$], 210 refined parameters, R = 0.030, wR^2 = 0.07, max. (min.) residual electron density 0.09 (-0.10) e.$Å^{-3}$, the hydrogens were calculated and refined as riding atoms. Flack parameter was refined to 0.07(2).

It was possible to measure the crystal by HPLC, showing that the structure corresponds to the major enatiomer (*R*,*R*) of the major diastereomer pair (*R*,*R*)/(*S*,*S*).



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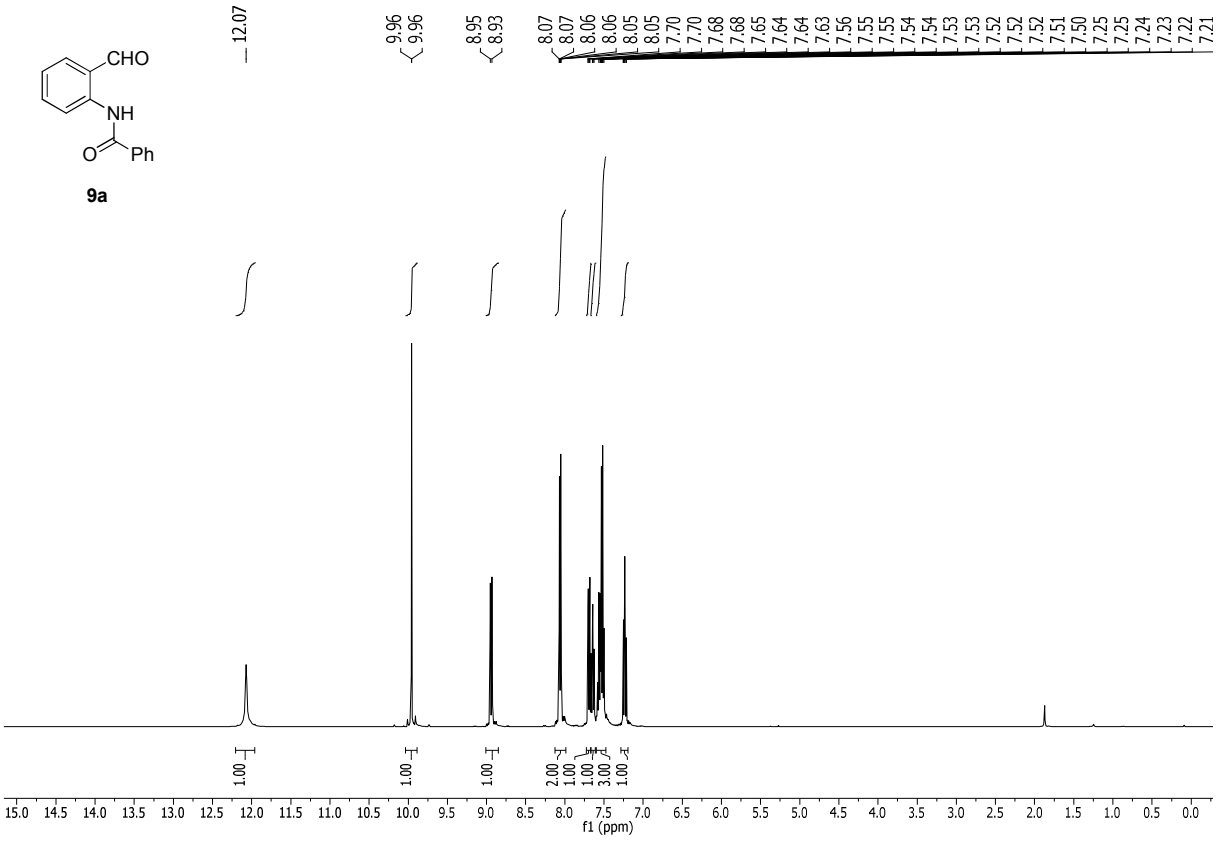
NMR Spectra: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Ph
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8.07
8.06
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8.05
8.05
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7.70
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7.68
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7.54
7.54
7.53
7.53
7.52
7.52
7.52
7.51
7.50
7.25
7.25
7.24
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1.00
2.00
1.00
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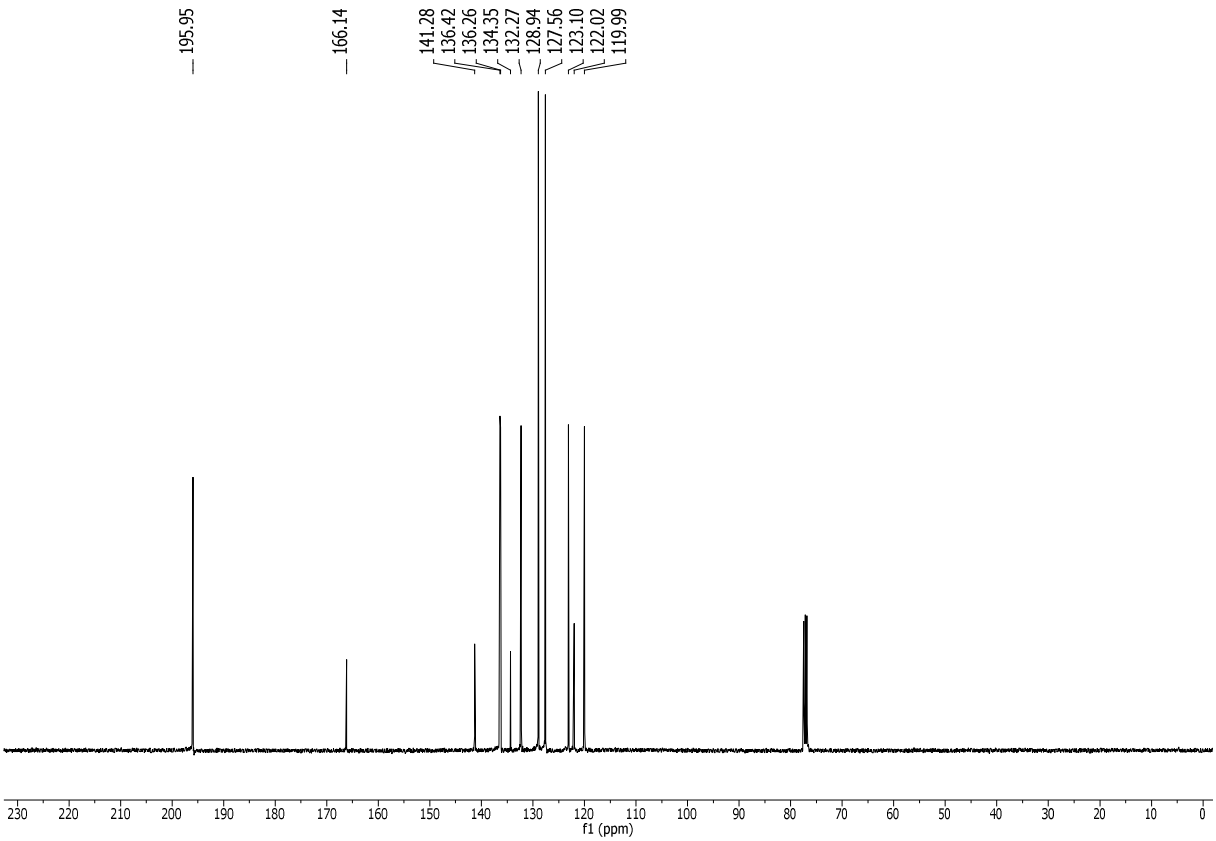
3.00
1.00
f1 (ppm)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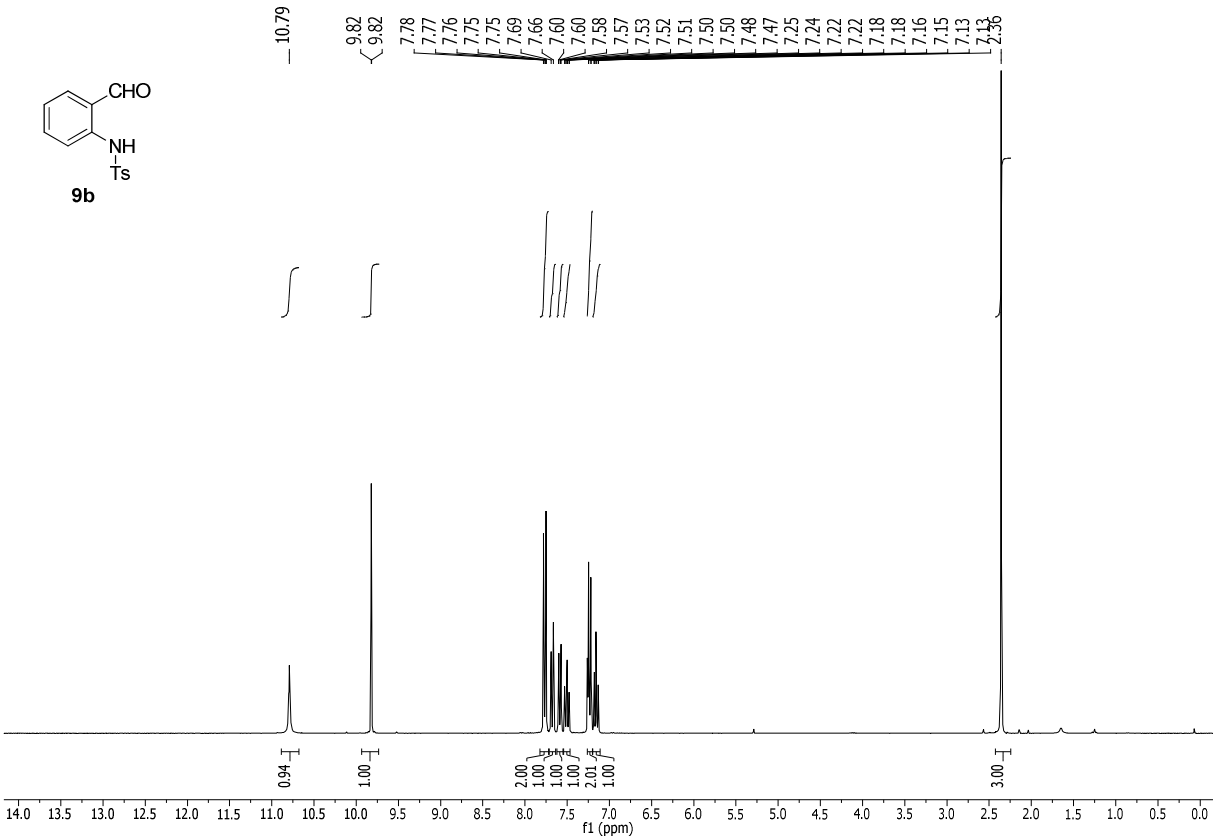
123.10
122.02
119.99
f1 (ppm)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7.58
7.57
7.53
7.52
7.51
7.50
7.50
7.48
7.47
7.25
7.24
7.22
7.22
7.18
7.18
7.16
7.15
7.13
7.13
2.36
CHO
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Ts
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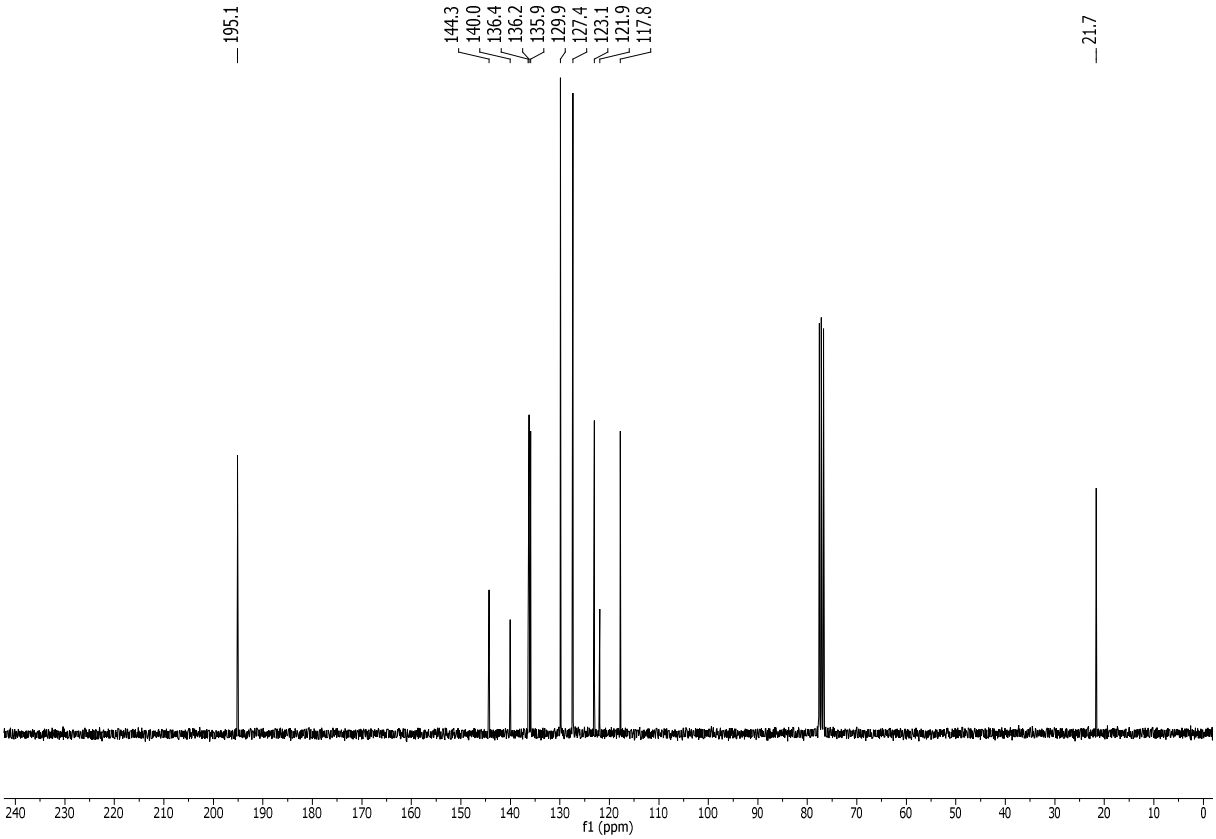
3.00
f1 (ppm)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127.4
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121.9
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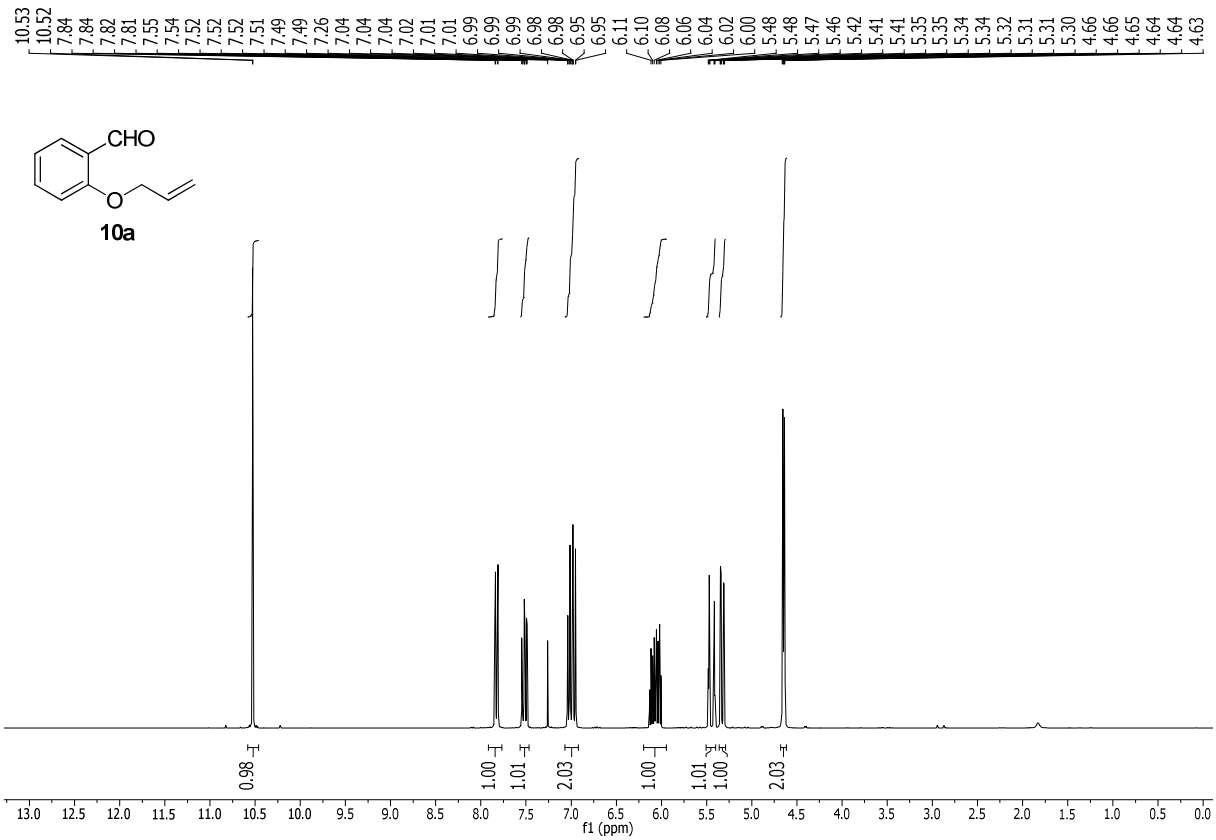
21.7
f1 (ppm)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7.04
7.04
7.02
7.01
7.01
6.99
6.99
6.99
6.98
6.98
6.95
6.95
6.11
6.10
6.08
6.06
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6.02
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5.48
5.47
5.46
5.42
5.41
5.41
5.35
5.35
5.34
5.34
5.32
5.31
5.31
5.30
4.66
4.66
4.65
4.64
4.64
4.63
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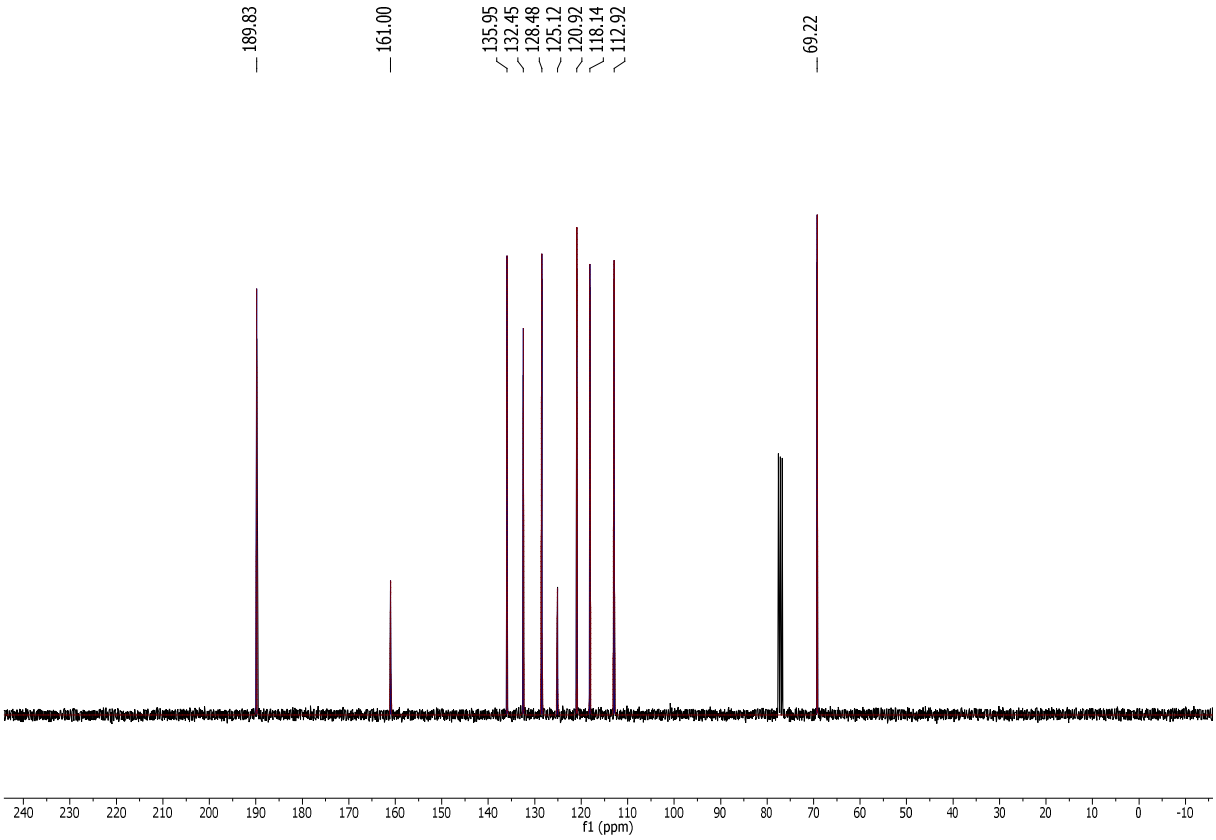
1.01
2.03
1.00
1.01
1.00
2.03
f1 (ppm)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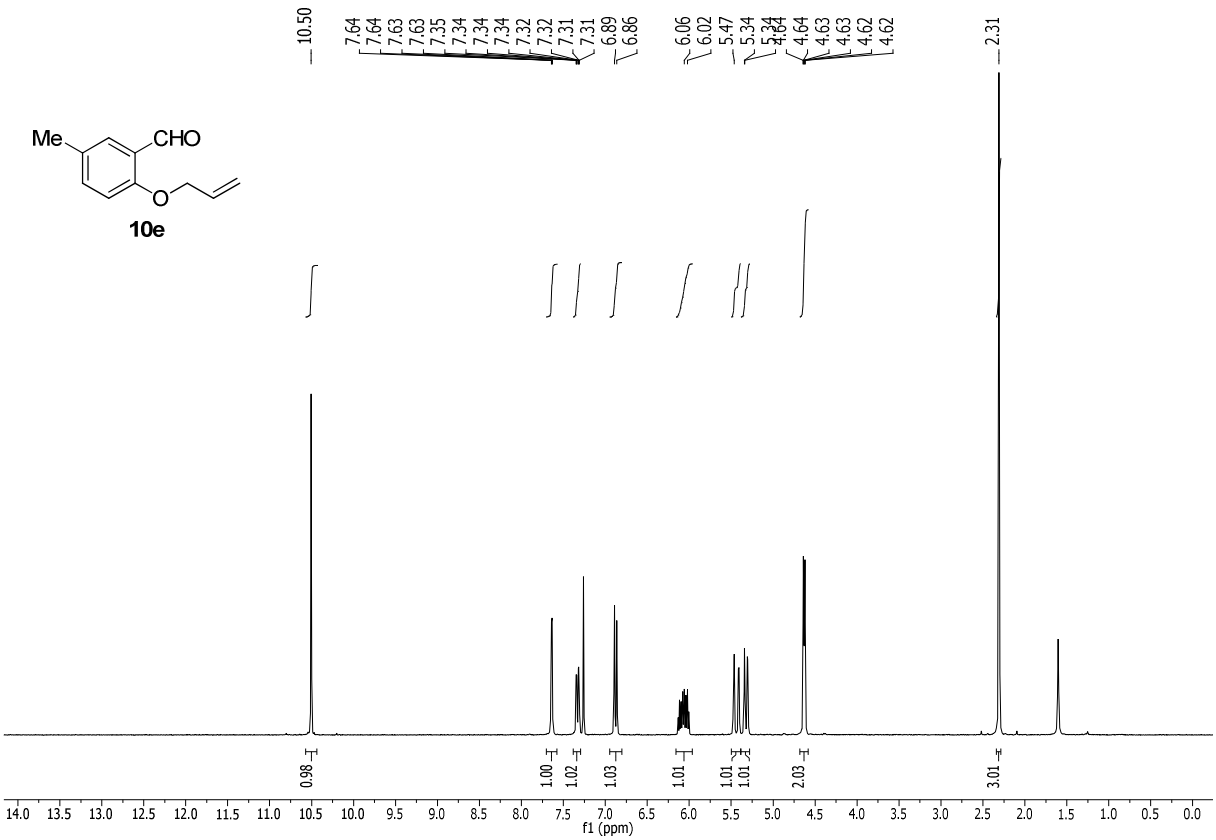
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7.34
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7.32
7.32
7.31
7.31
6.89
6.86
6.06
6.02
5.47
5.34
5.24
4.64
4.63
4.63
4.62
4.62
2.31
Me
CHO
O
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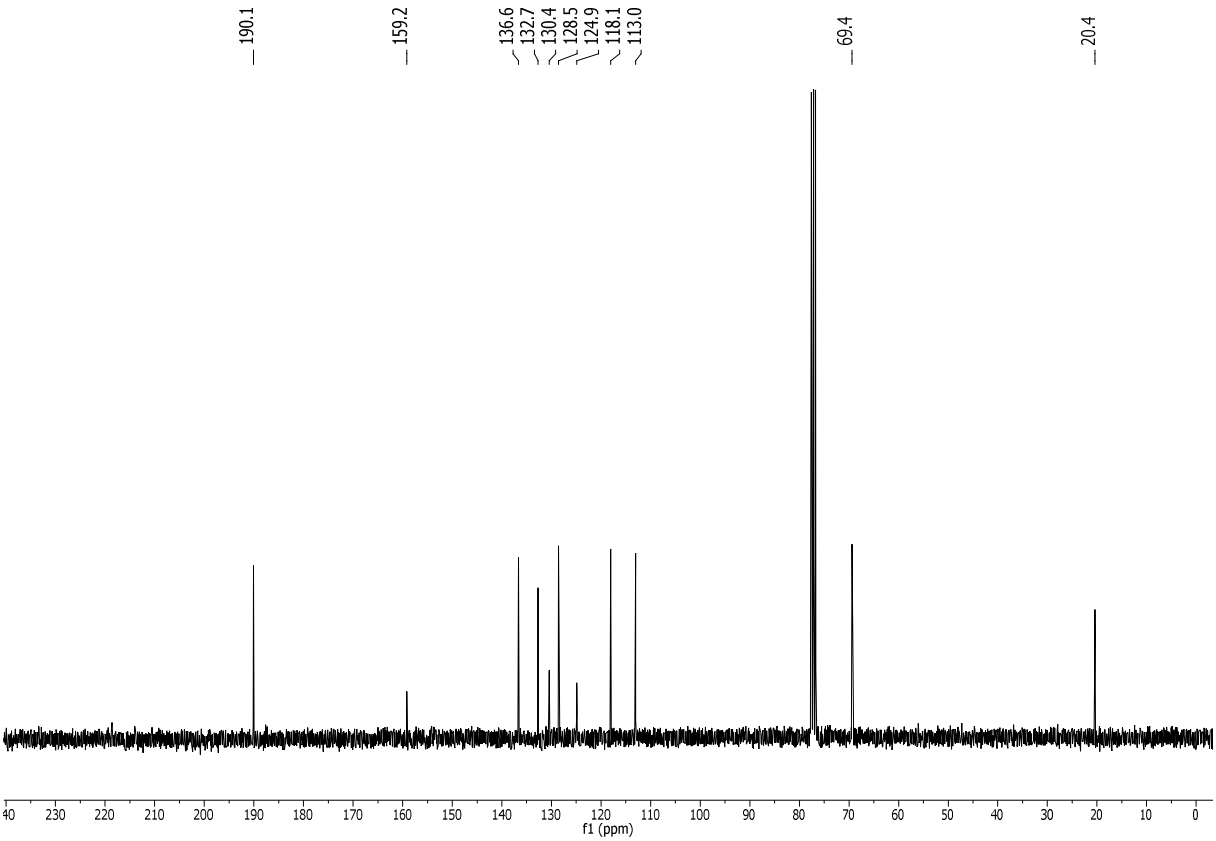
1.00
1.02
1.03
1.01
1.01
1.01
2.03
3.01
f1 (ppm)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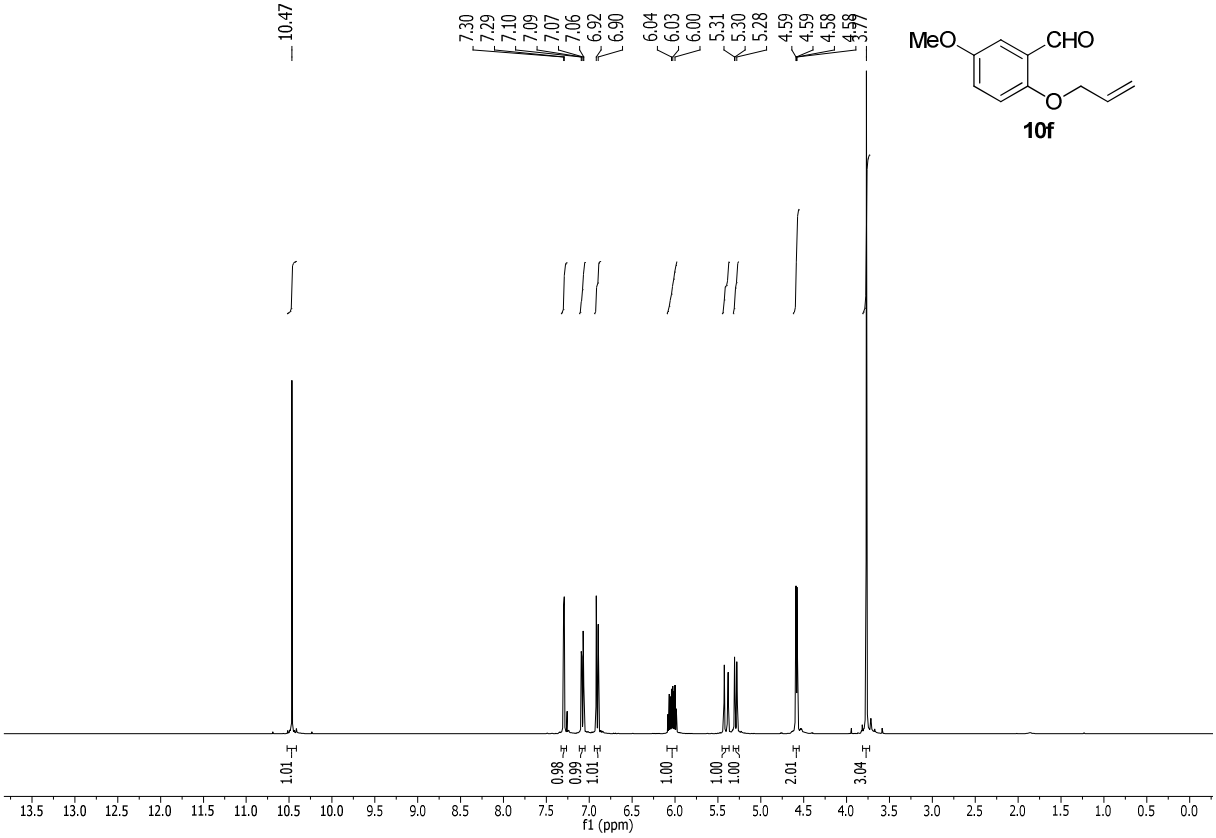
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6.04
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5.30
5.28
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4.59
4.58
4.58
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1.00
1.00
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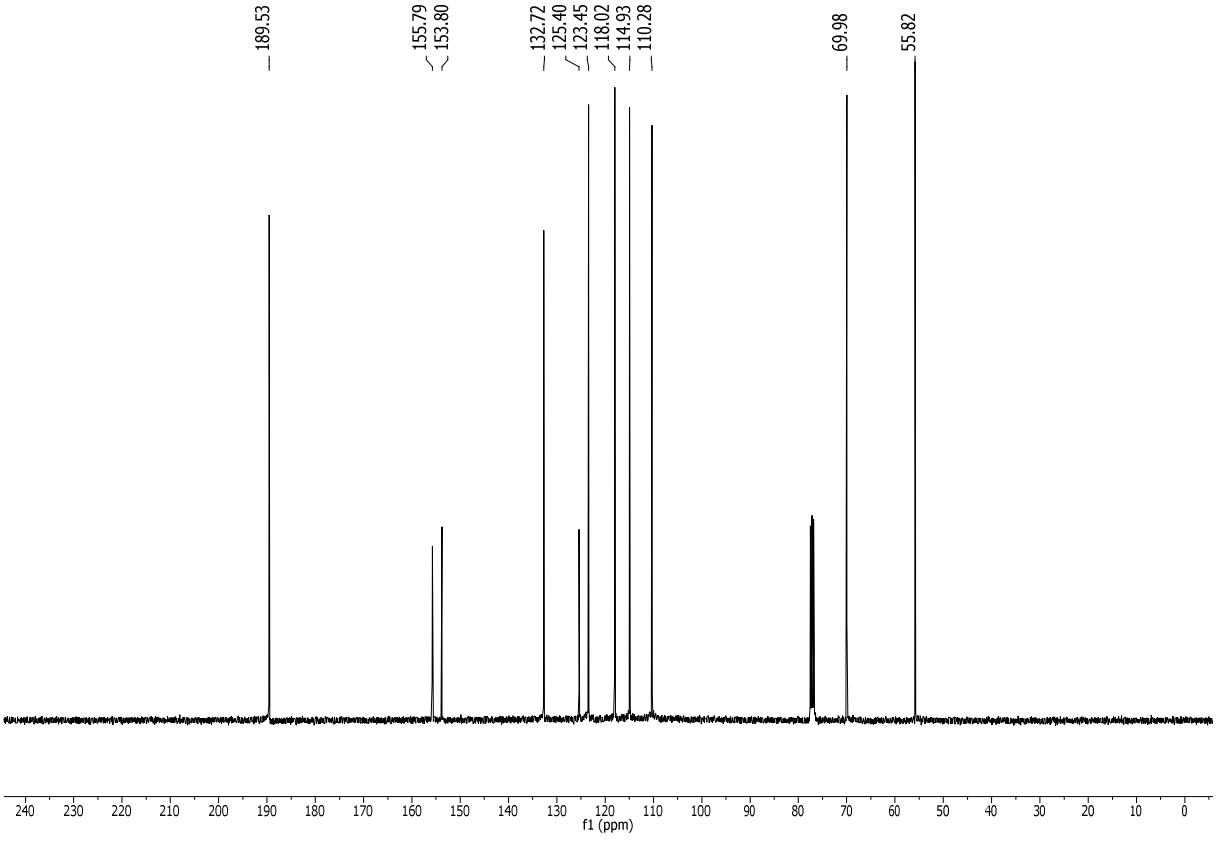
3.04
f1 (ppm)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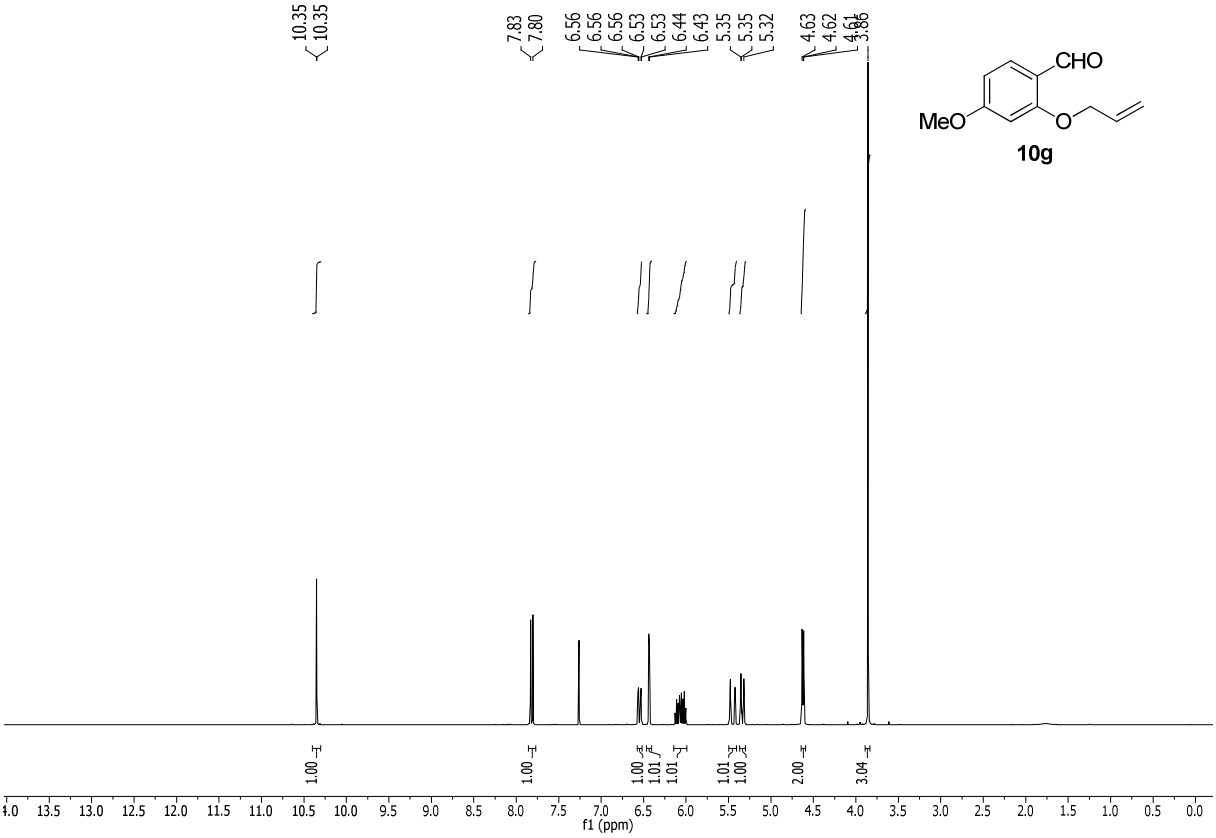
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4.62
4.61
3.86
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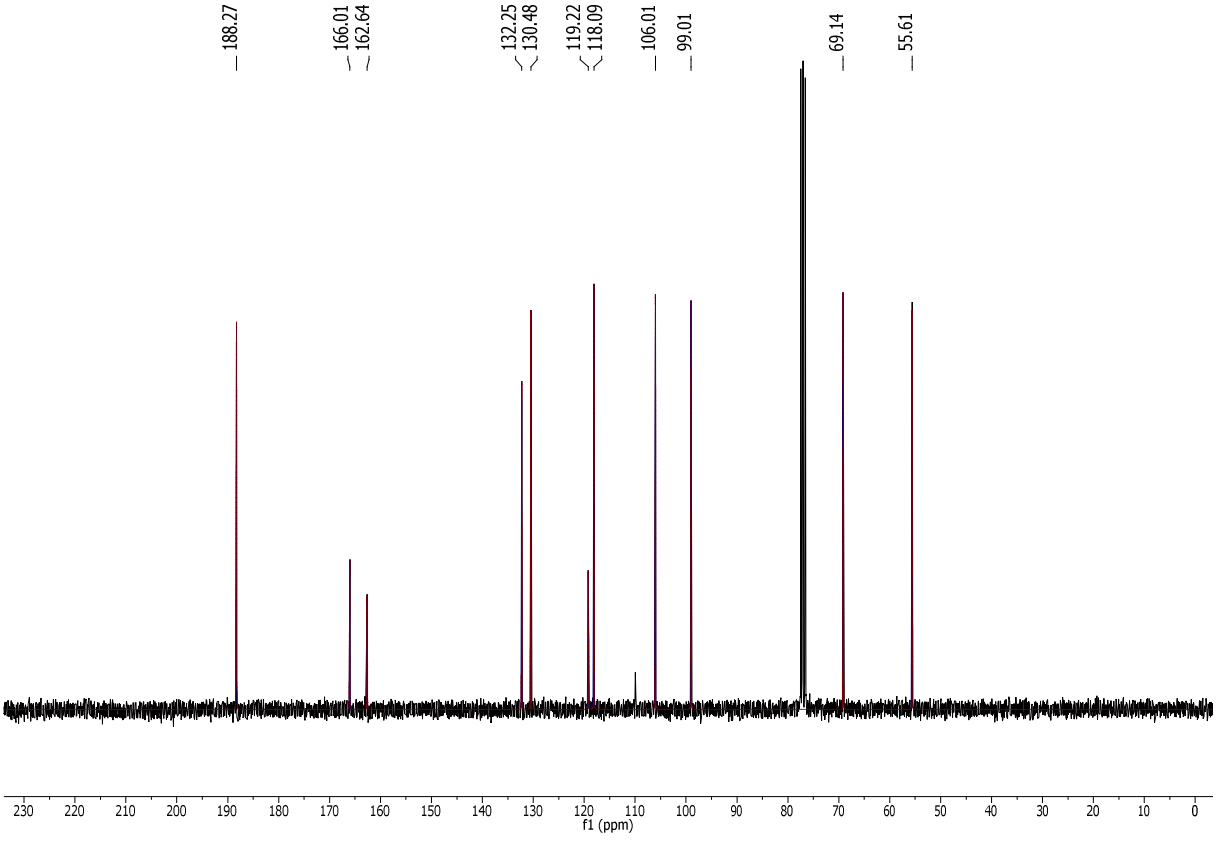
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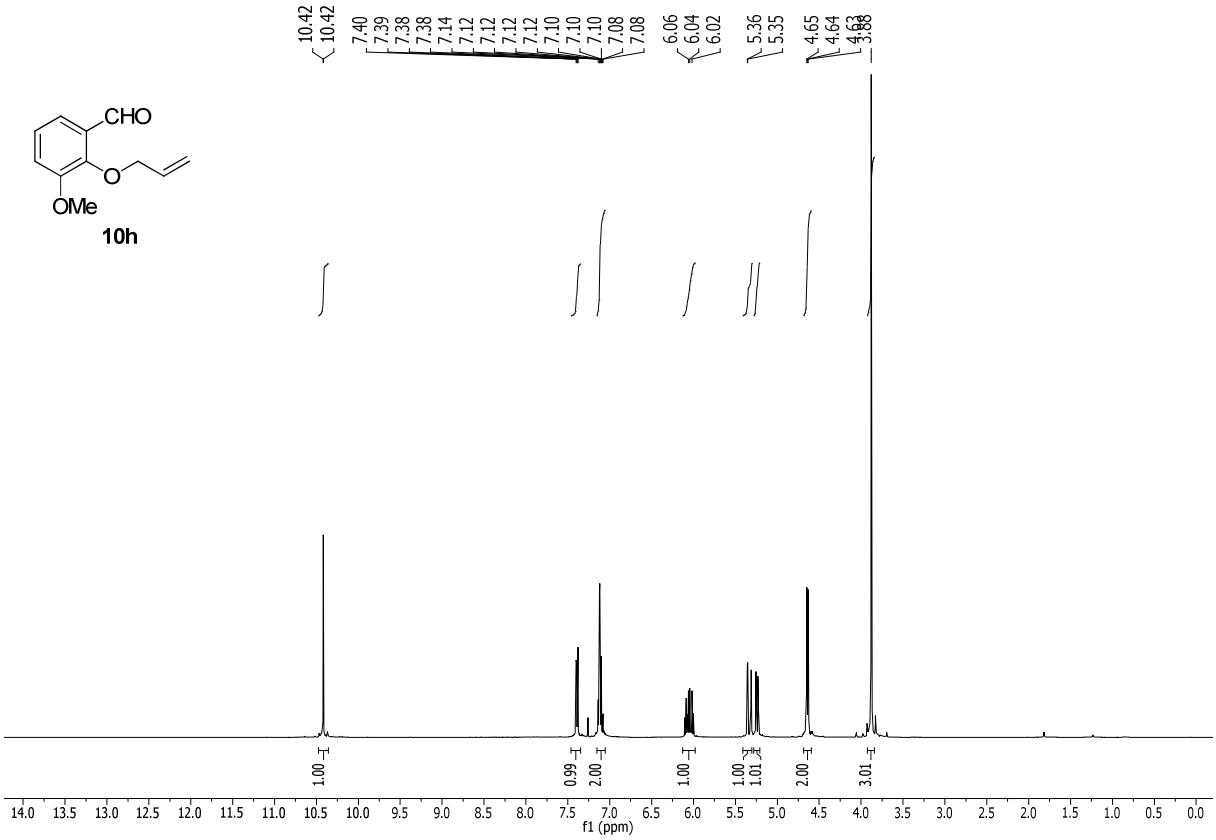
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7.10
7.08
7.08
6.06
6.04
6.02
5.36
5.35
4.65
4.64
4.63
3.88
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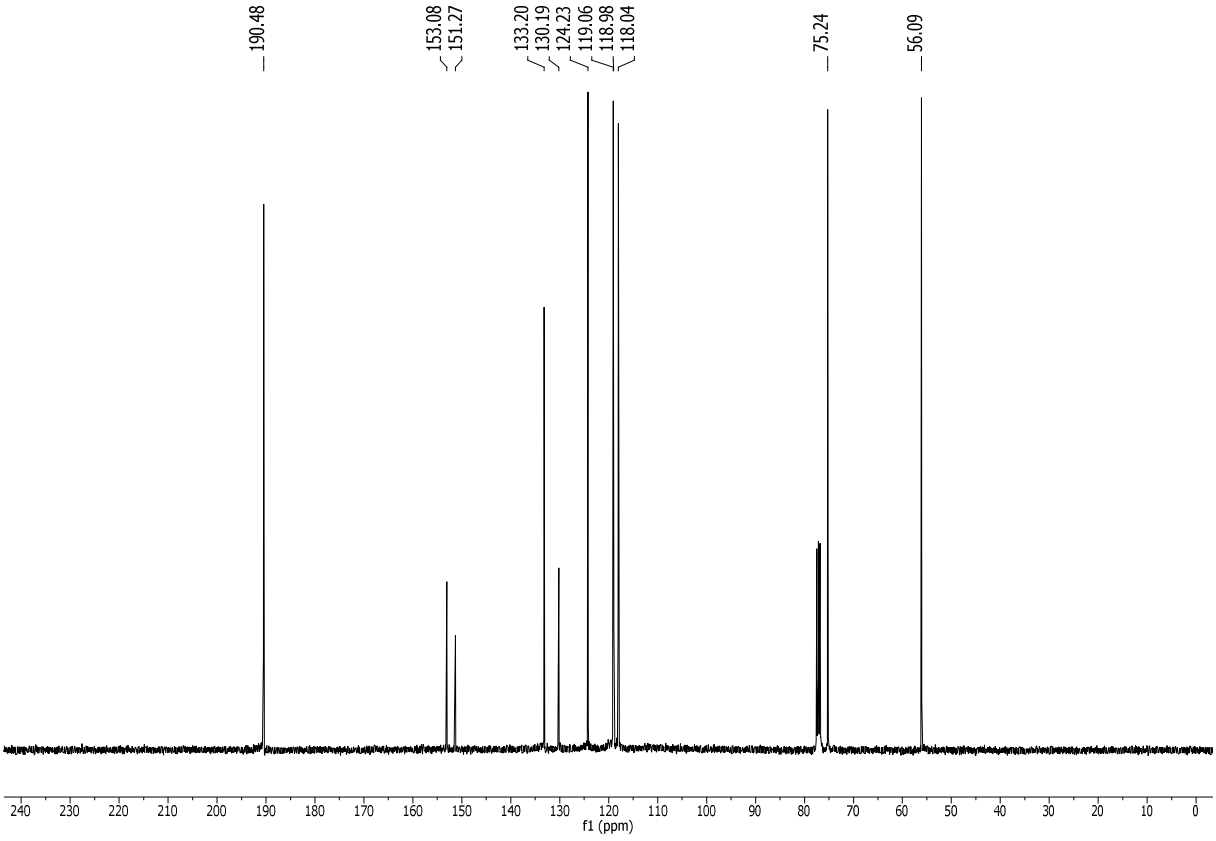
f1 (ppm)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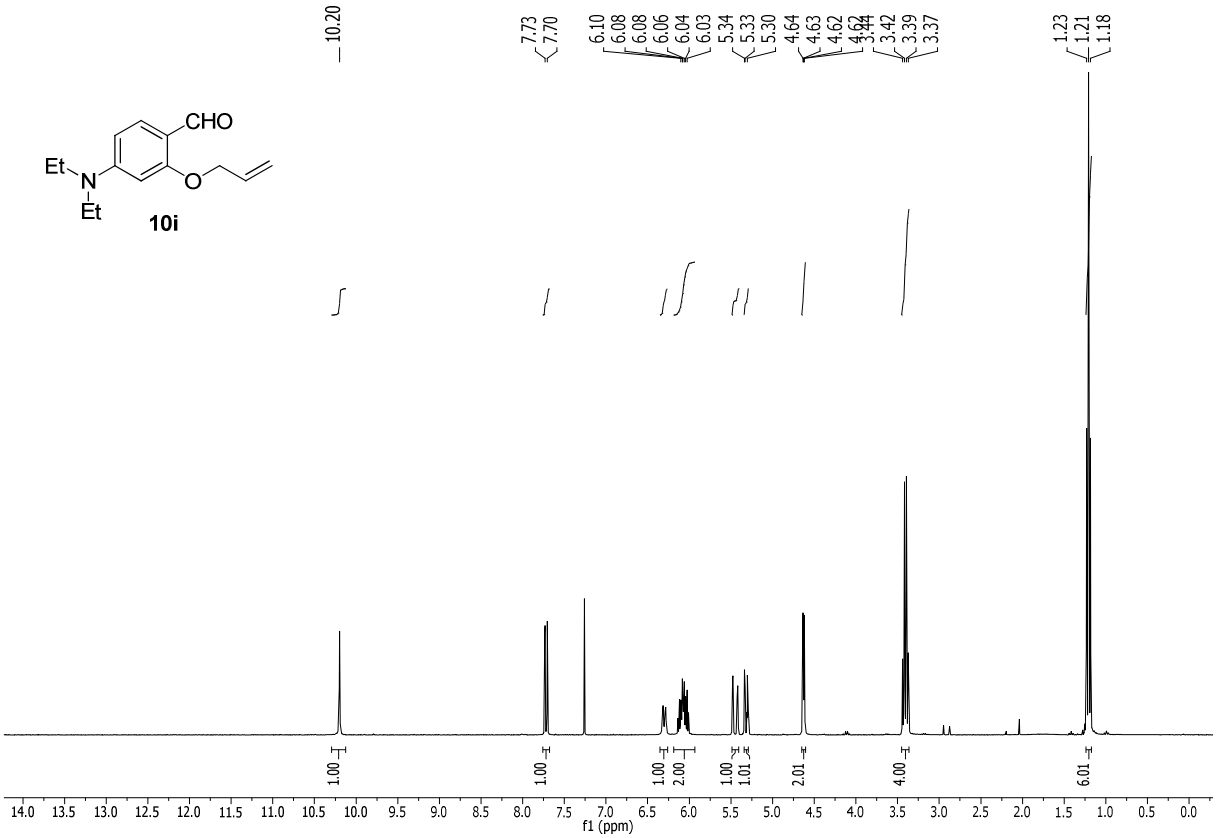
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4.63
4.62
3.42
3.39
3.37
1.23
1.21
1.18
CHO
Et
N
Et
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2.01
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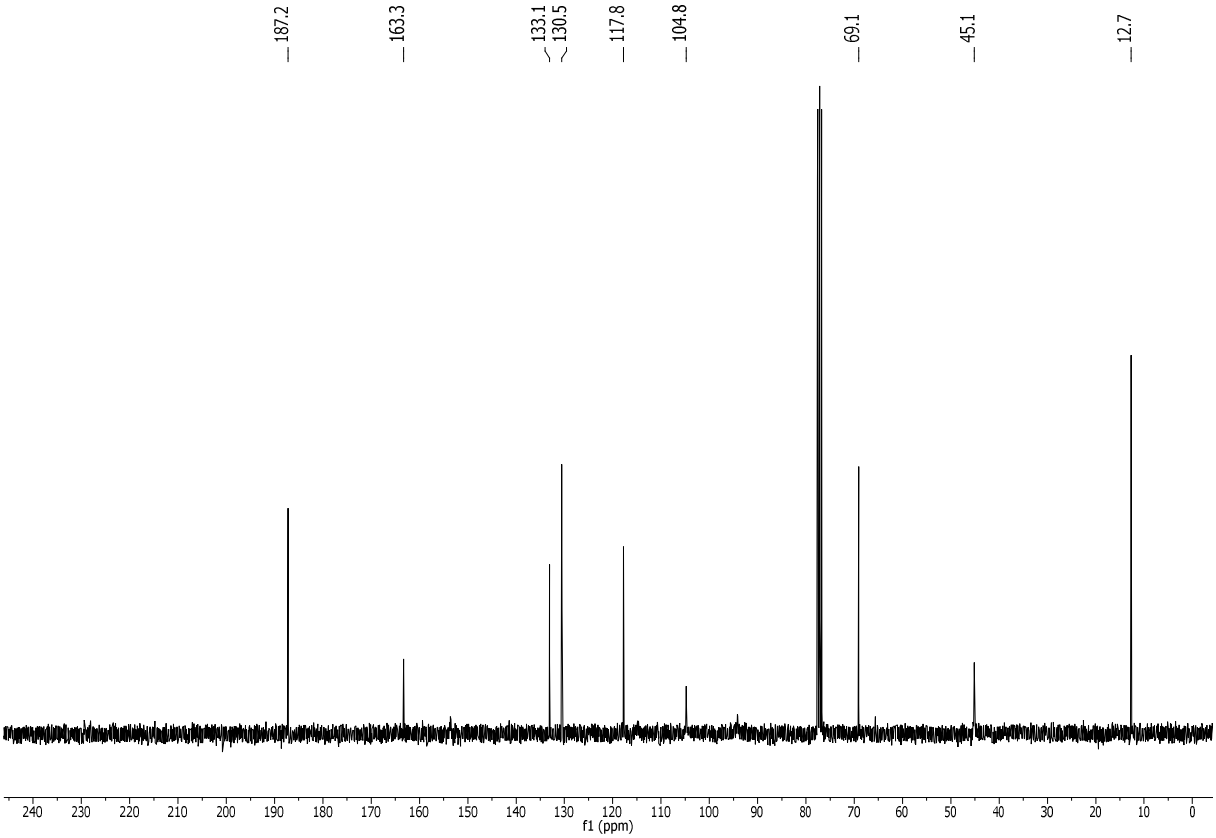
f1 (ppm)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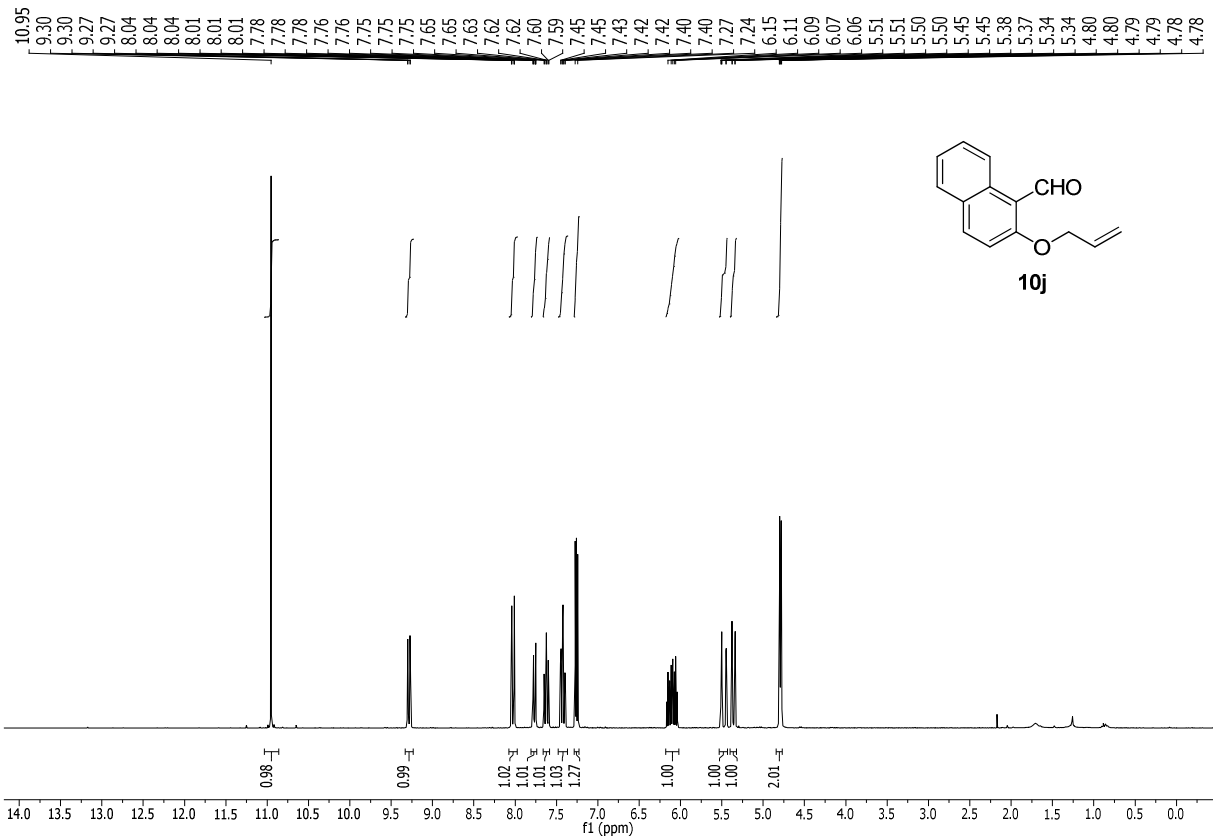
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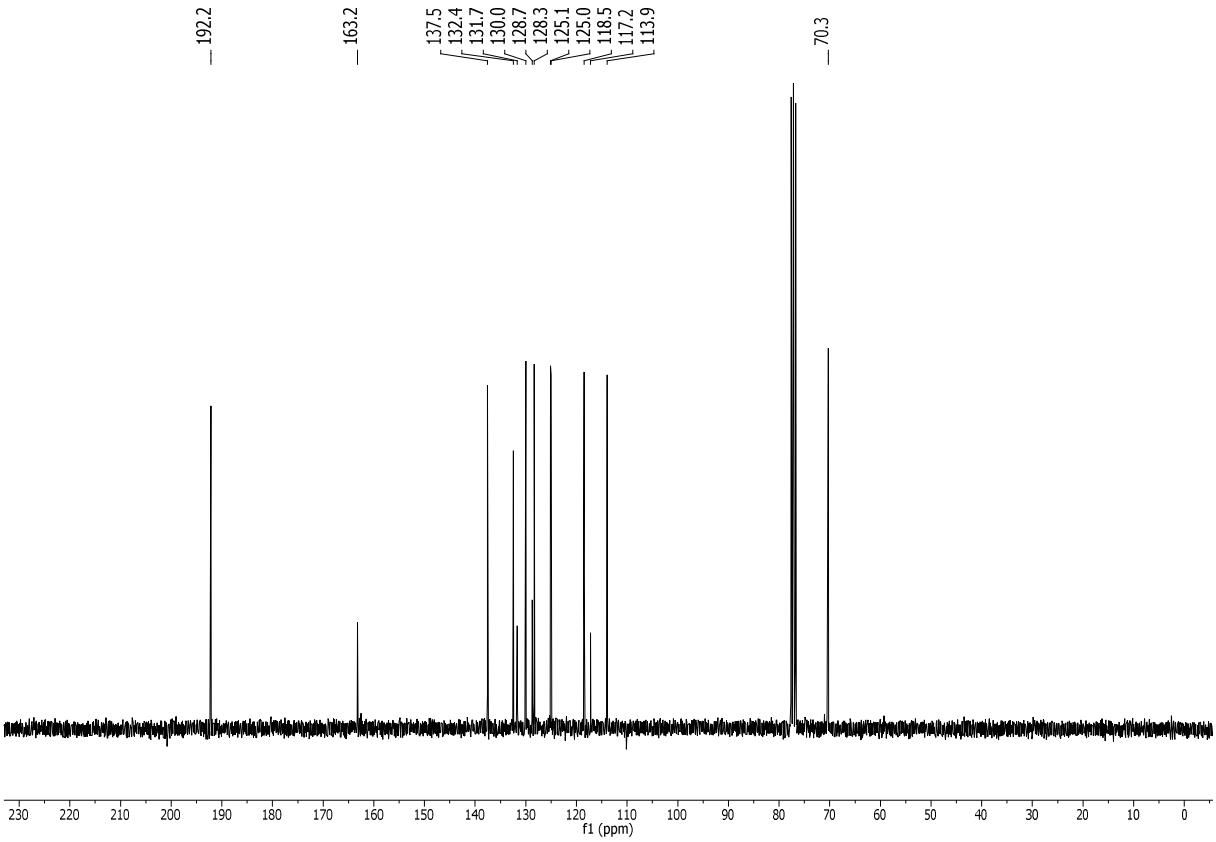
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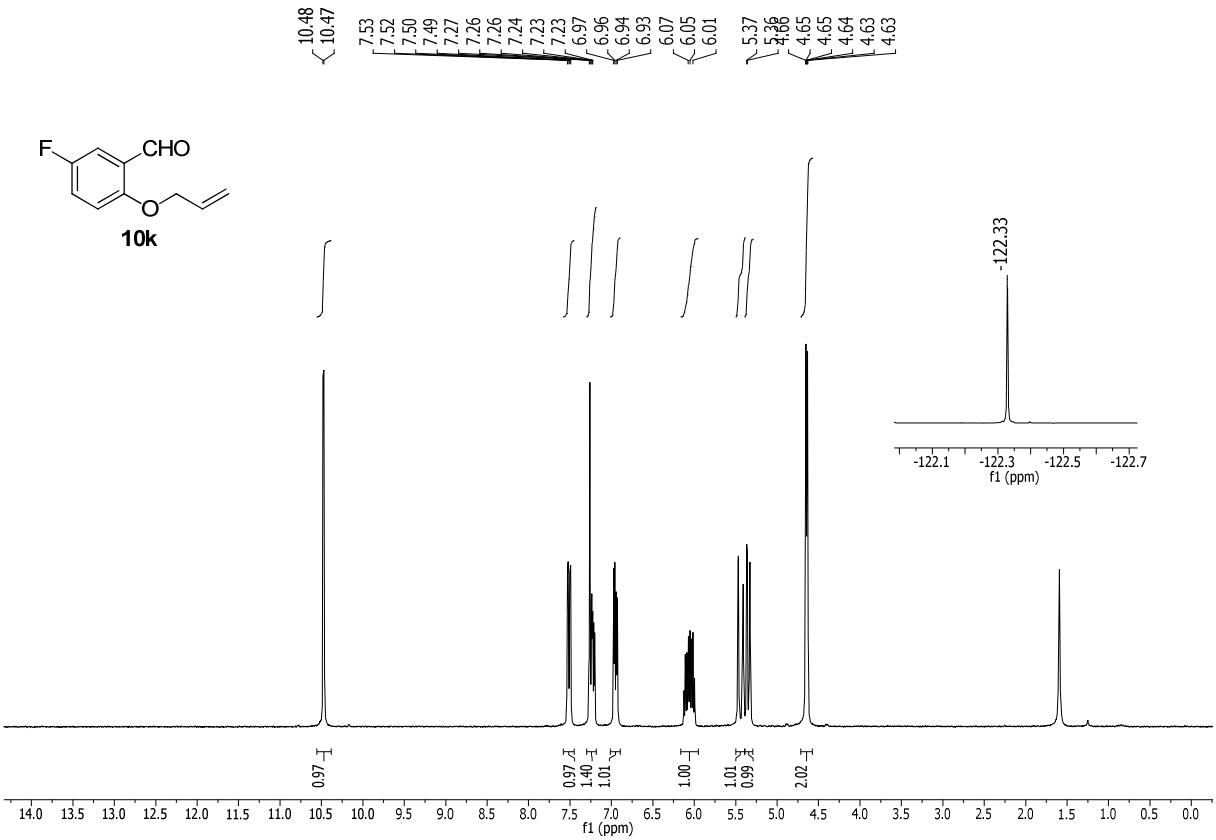
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6.93
6.07
6.05
6.01
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4.65
4.65
4.64
4.63
4.63
F
CHO
O
10k
-122.33
-122.1
-122.3
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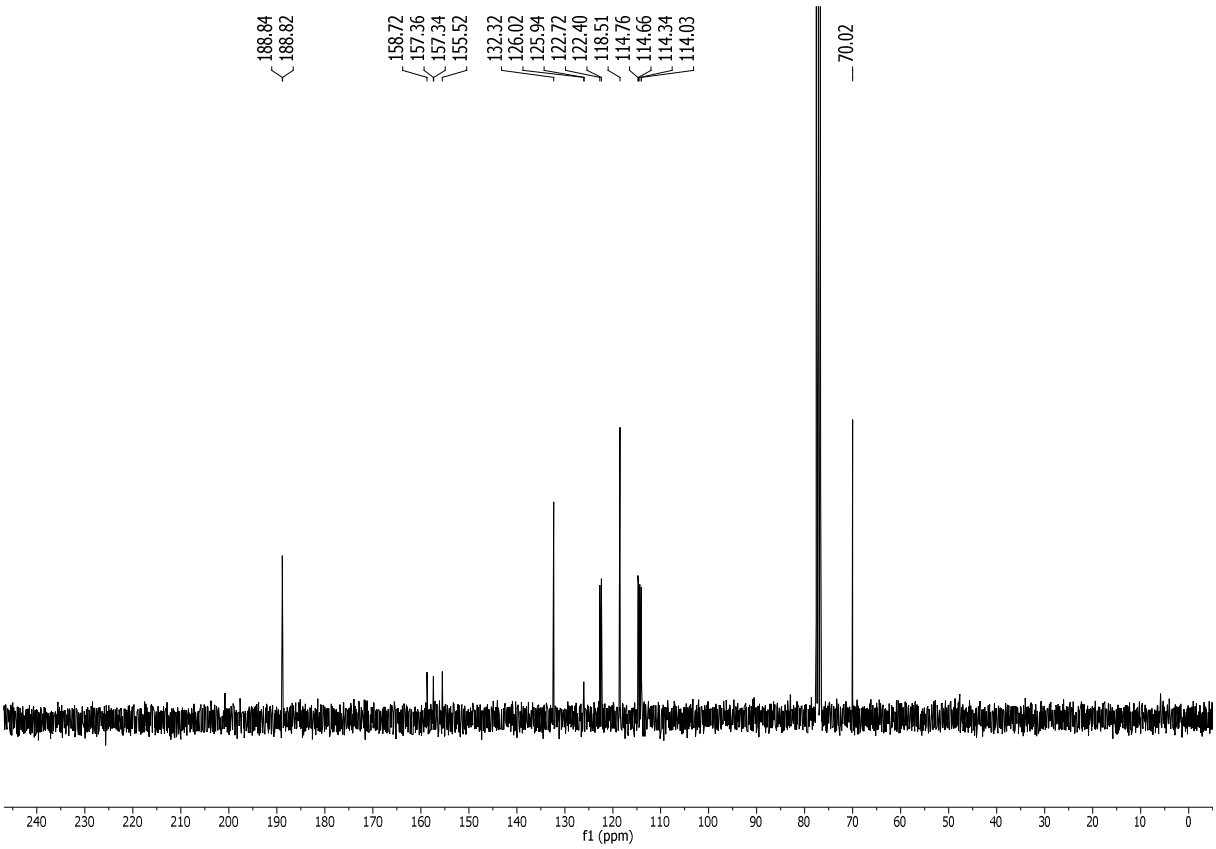
f1 (ppm)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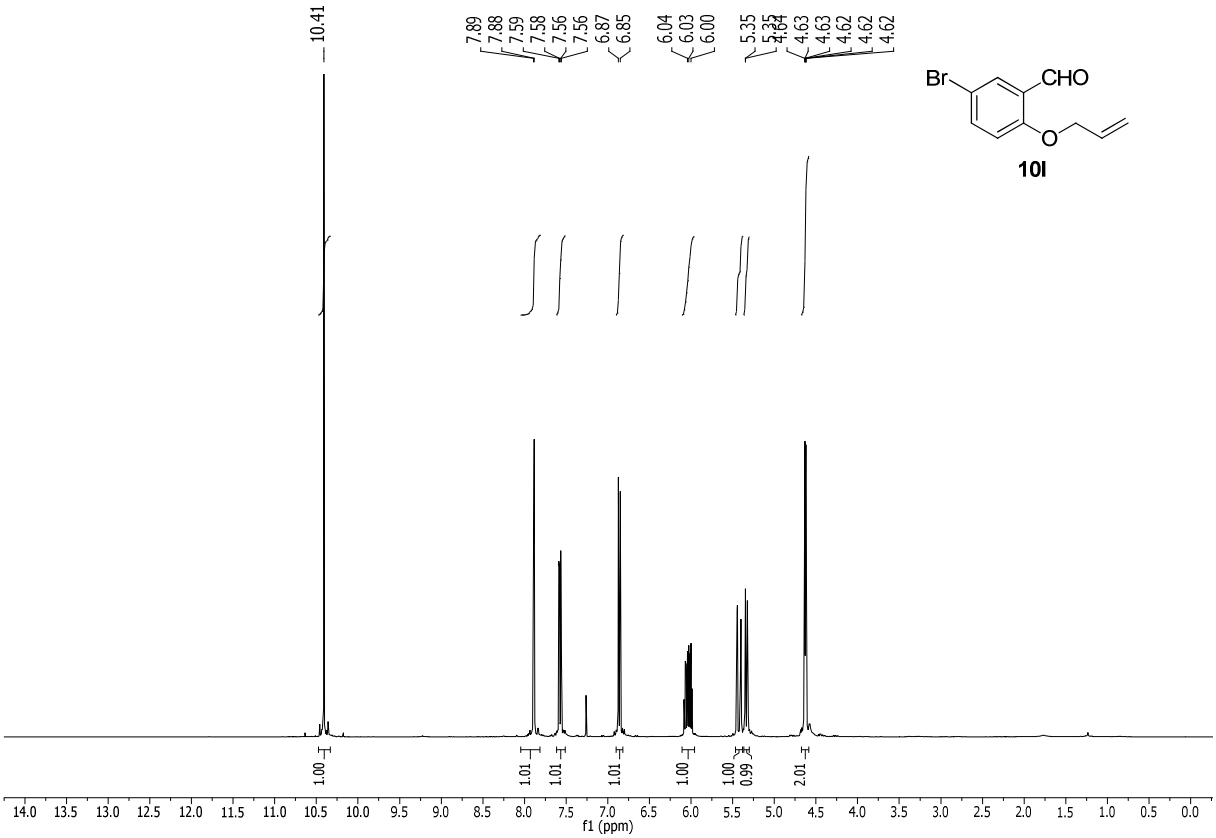
f1 (ppm)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4.62
4.62
4.62
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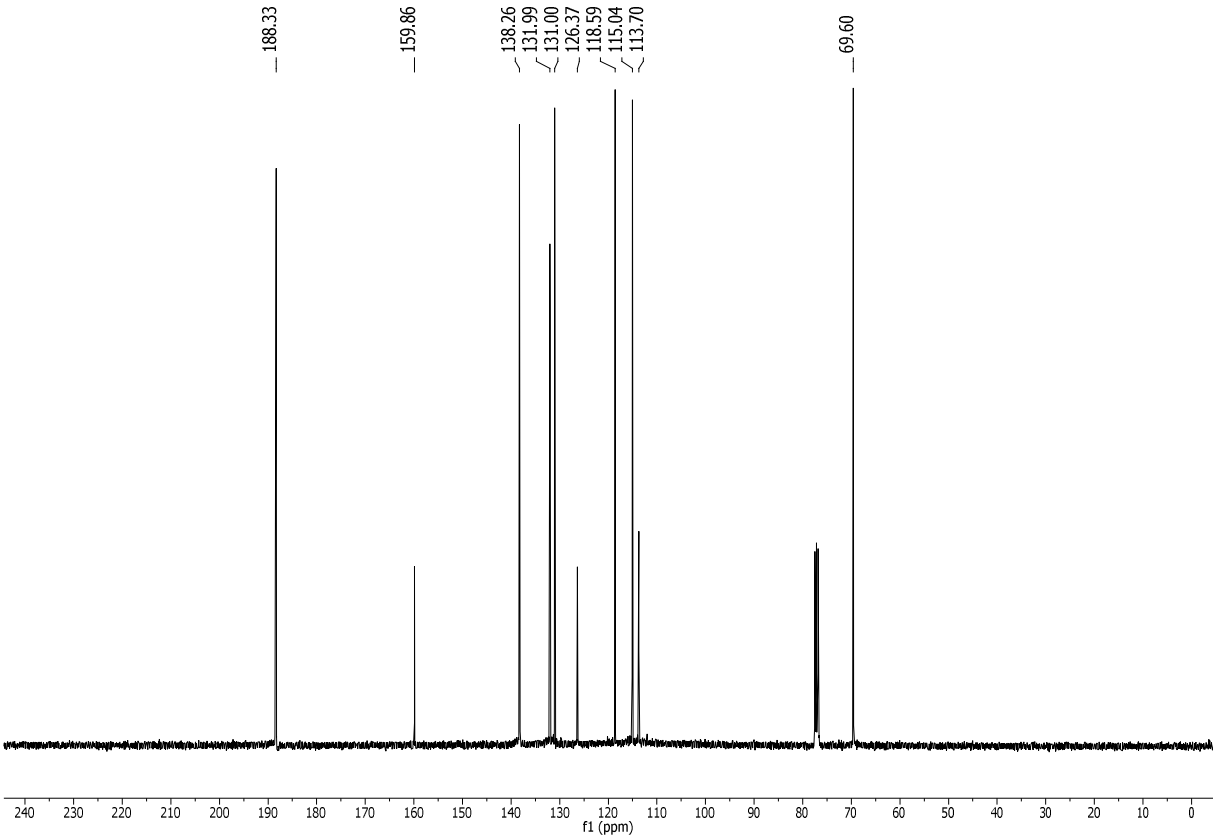
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69.60
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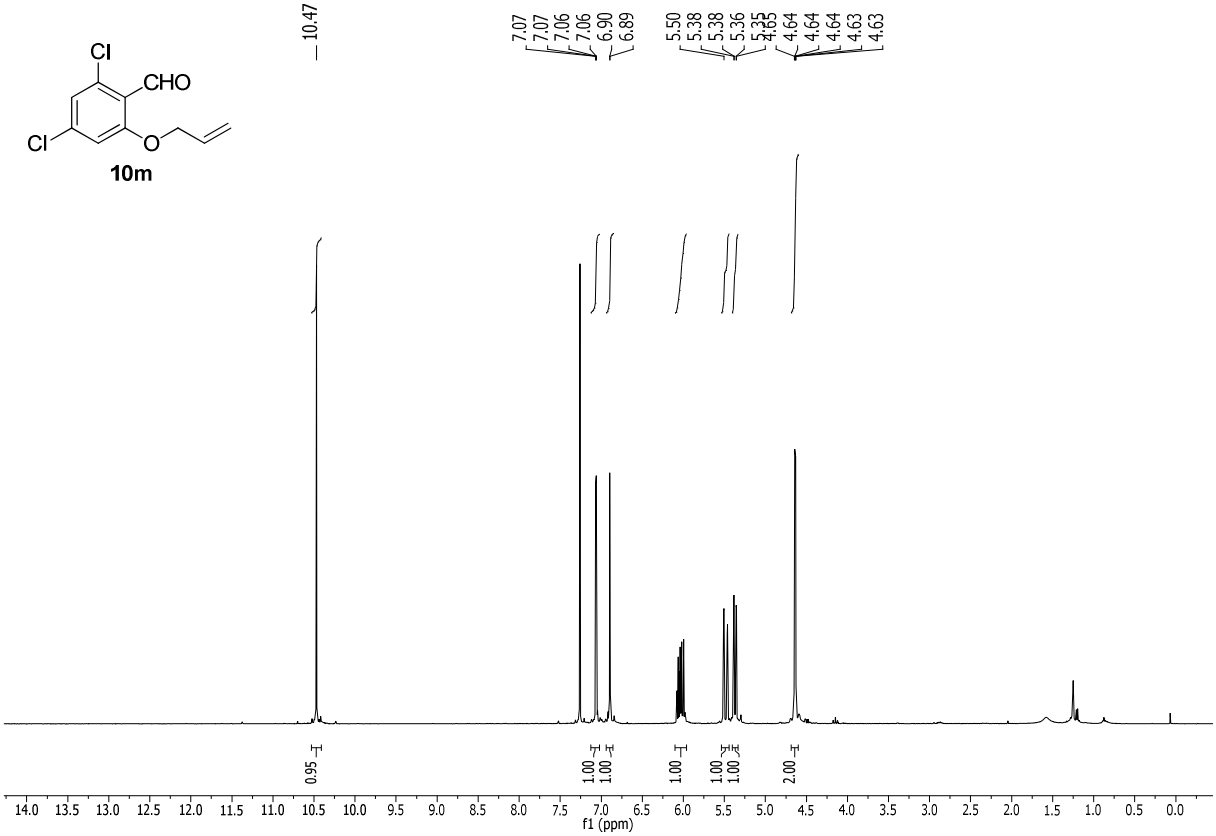
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5.38
5.36
5.35
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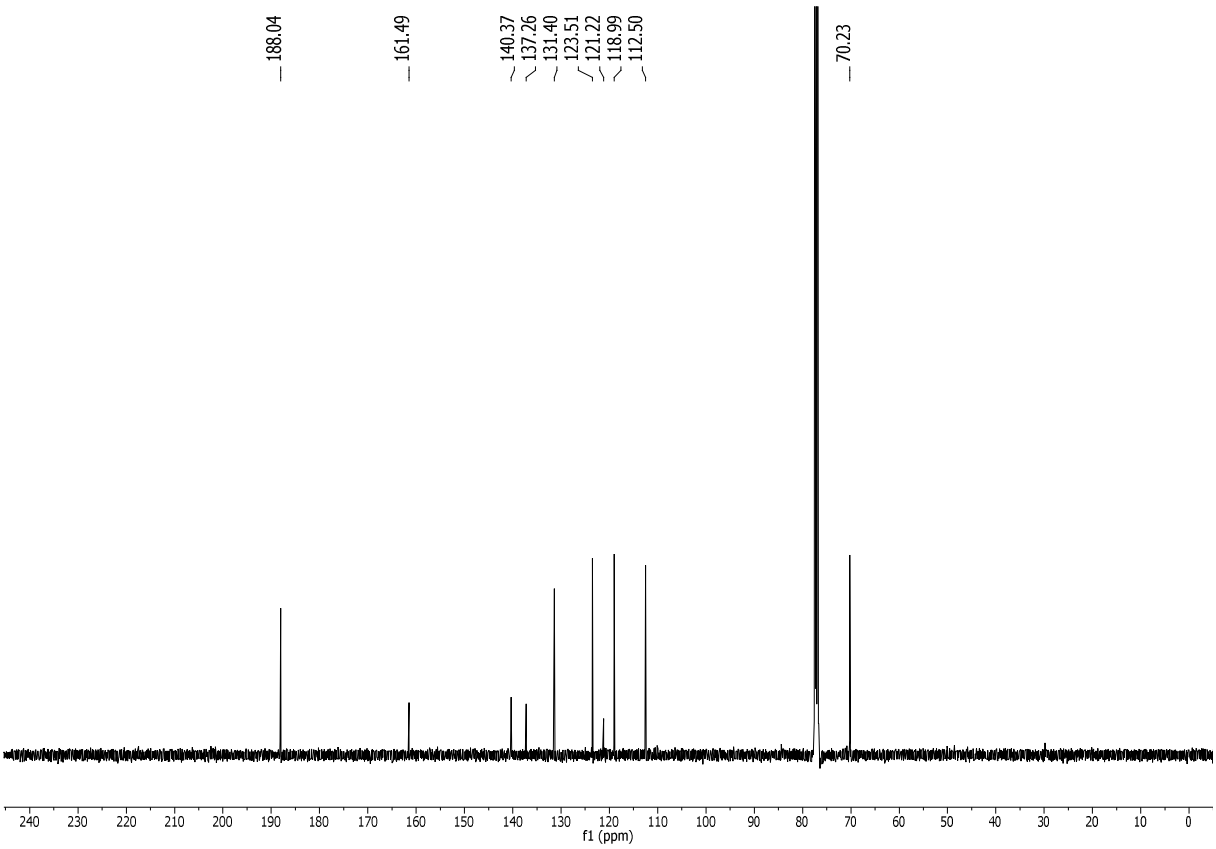
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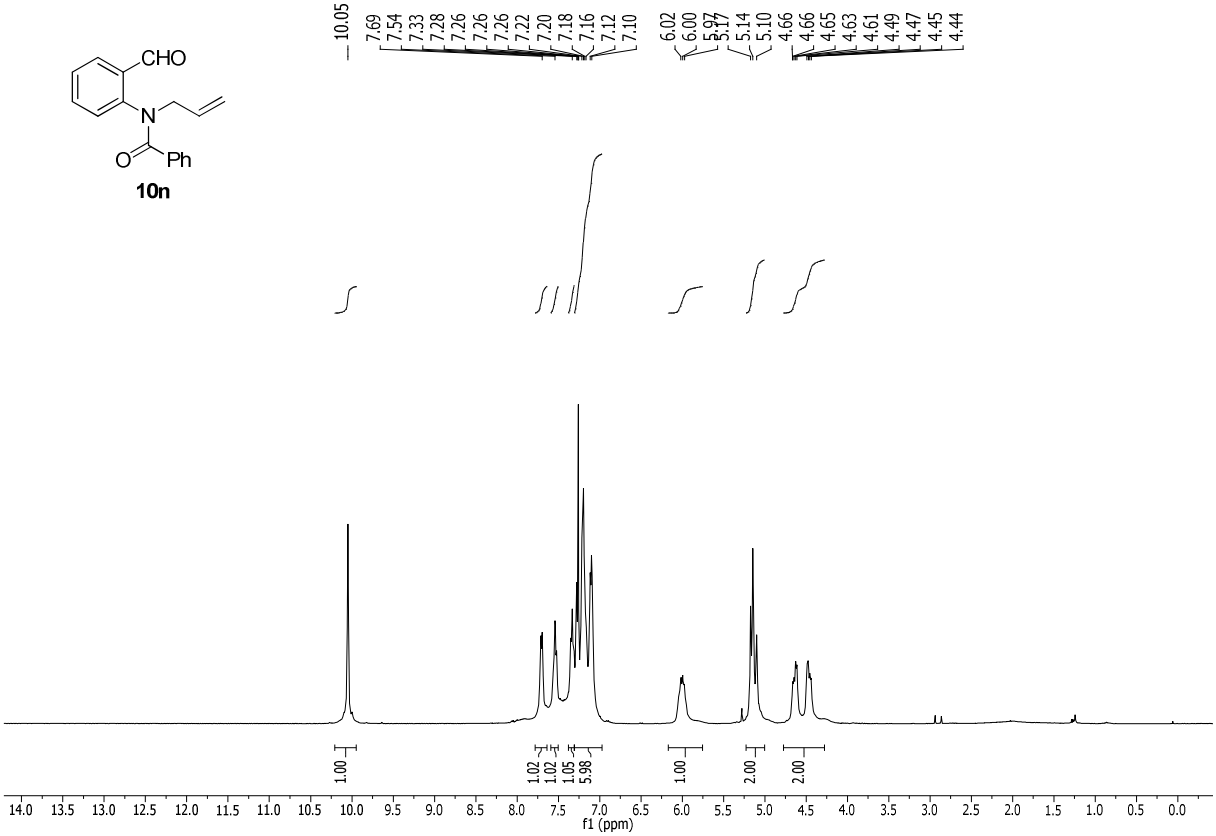
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7.18
7.16
7.12
7.10
6.02
6.00
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5.17
5.14
5.10
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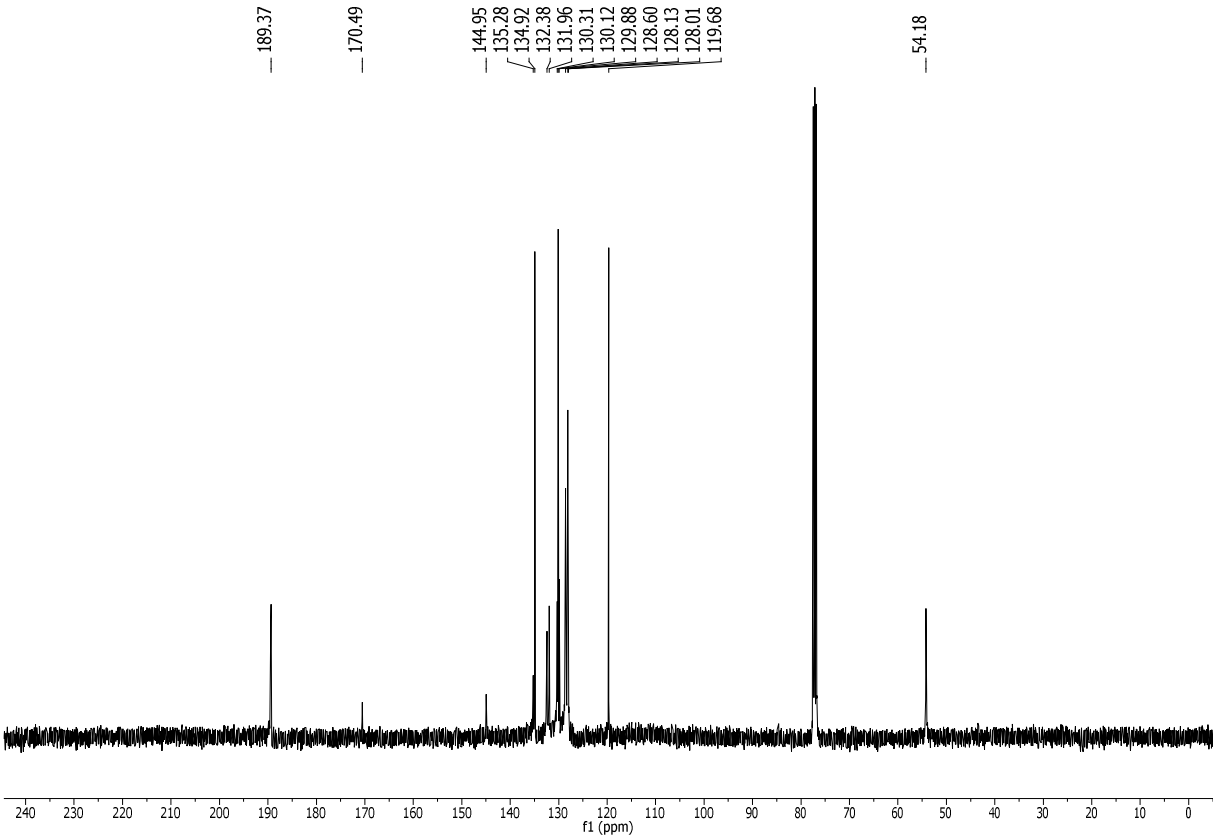
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128.01
119.68
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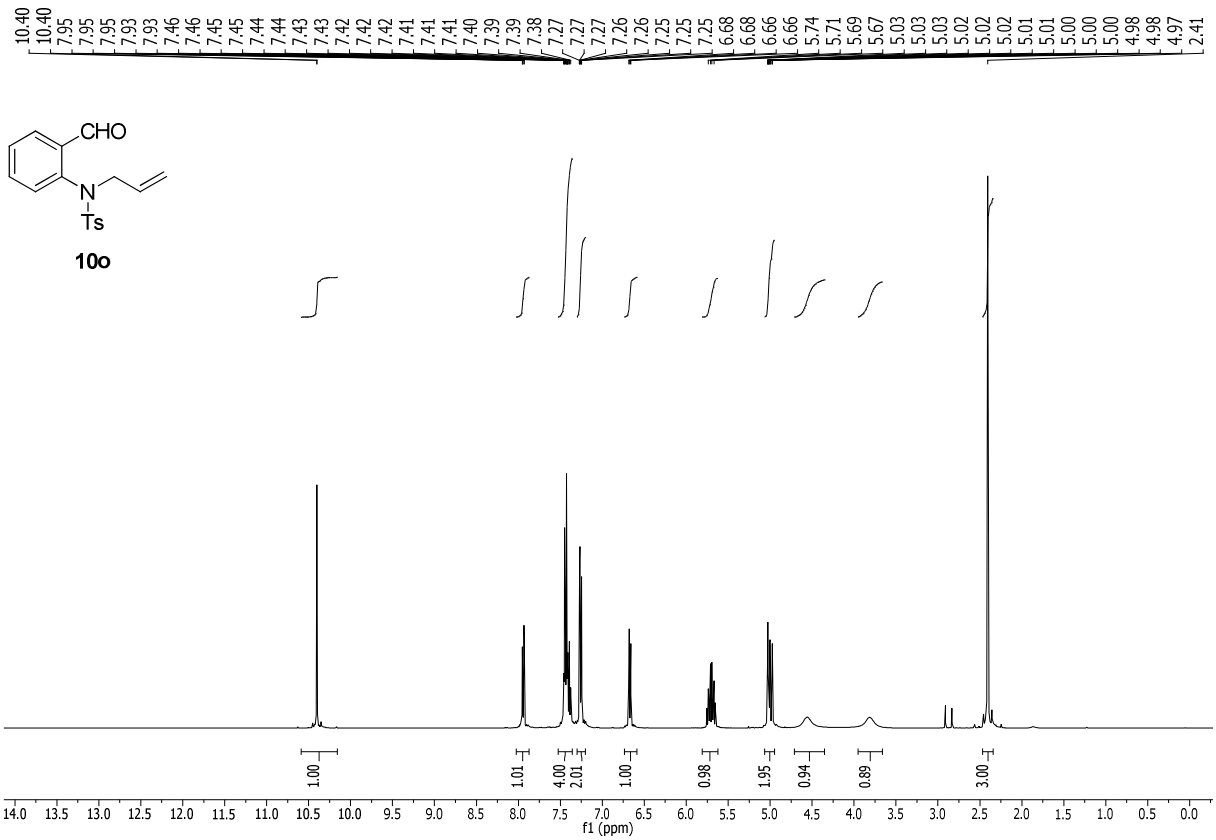
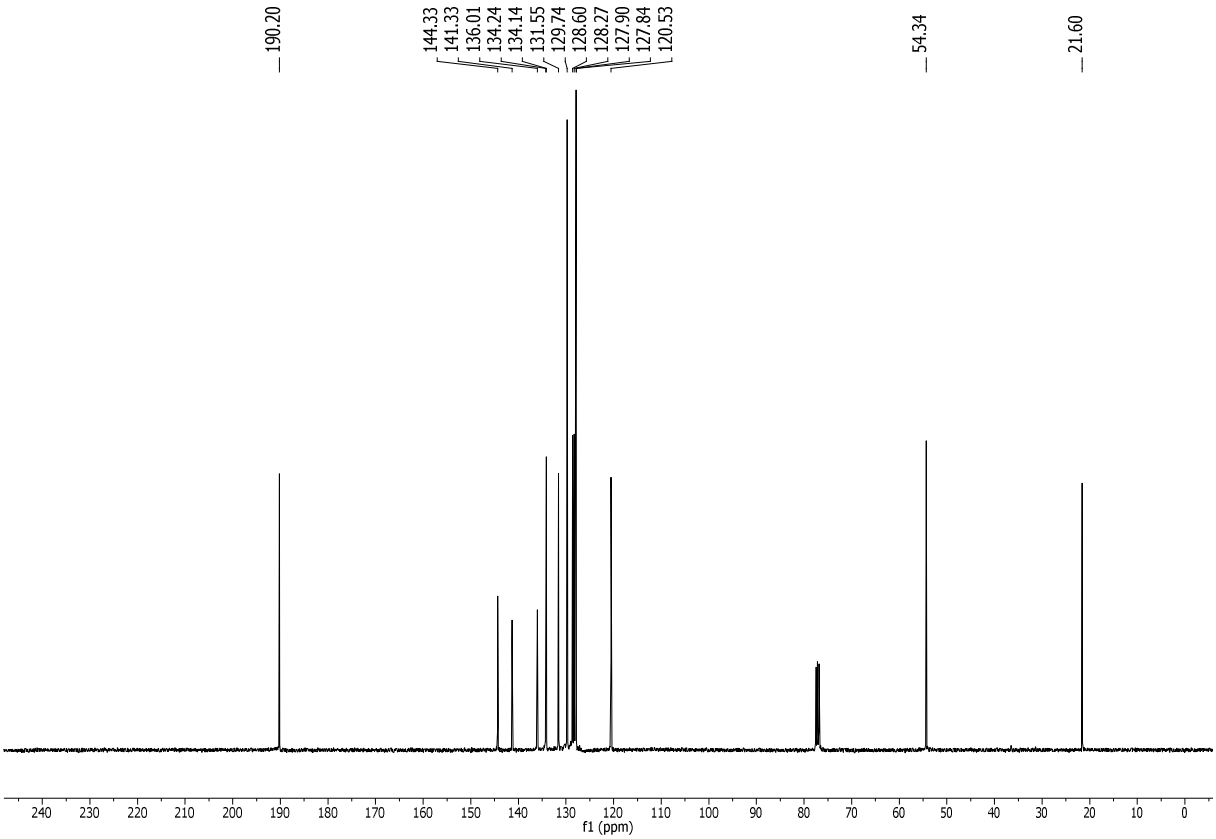
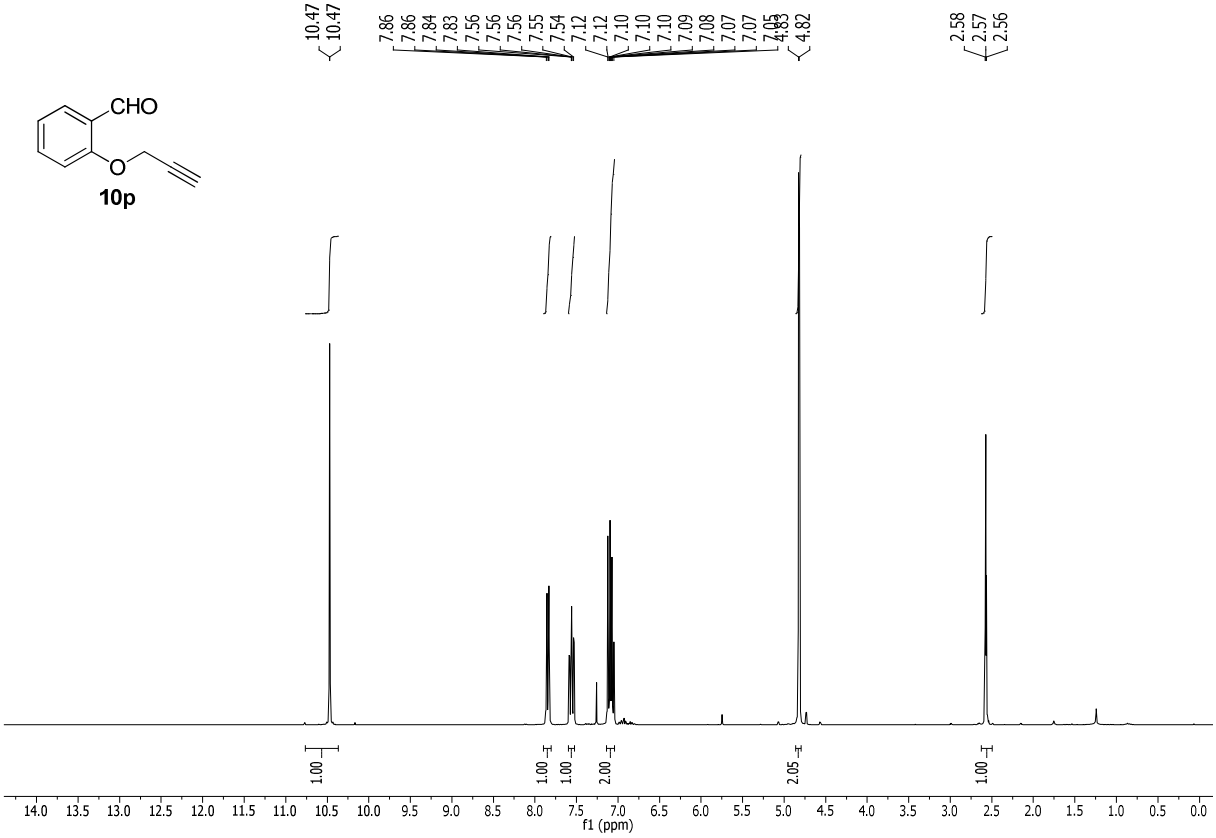
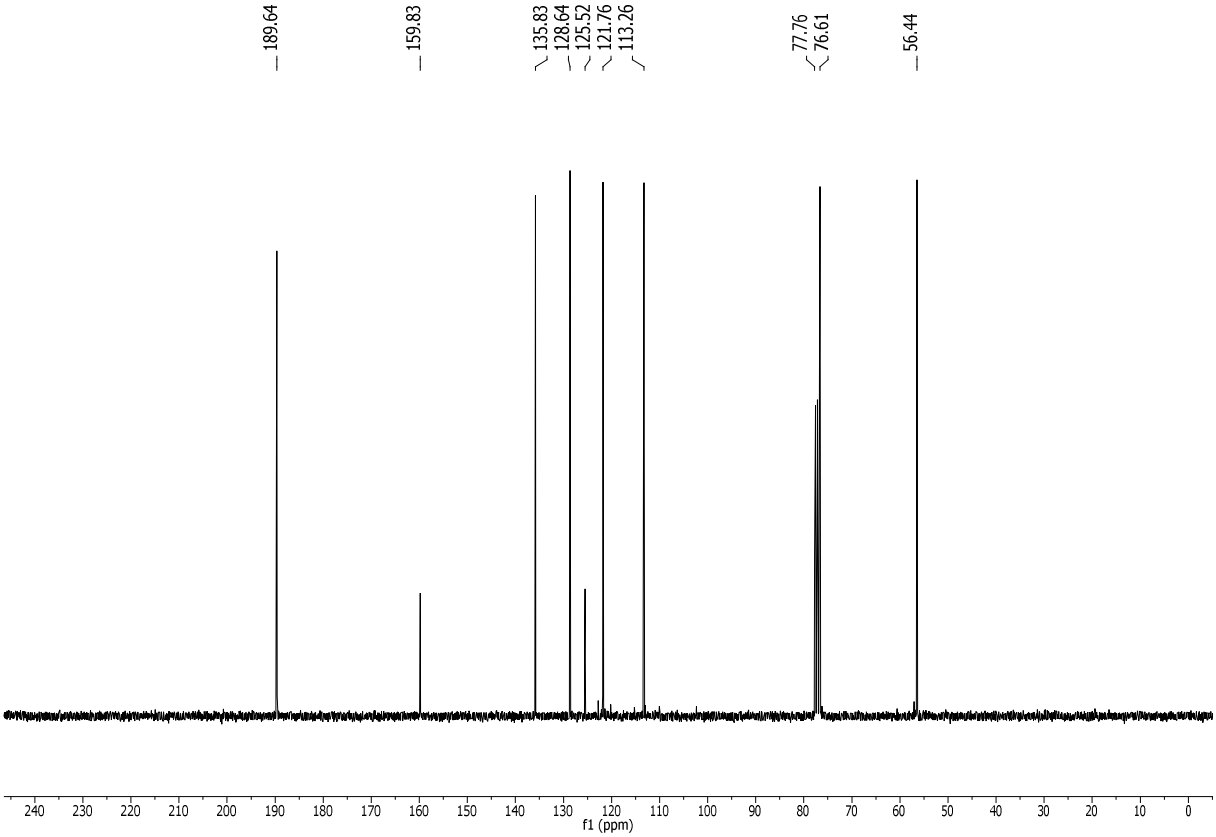
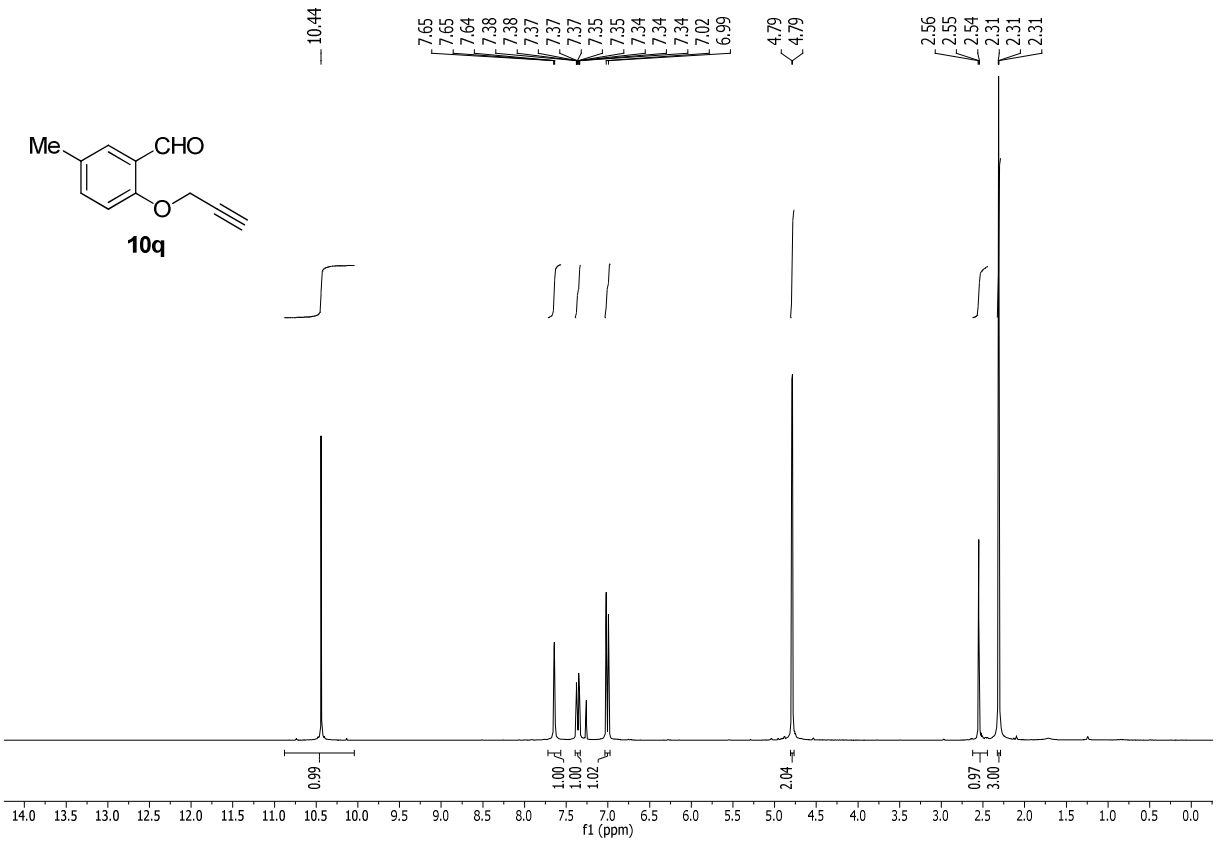
f1 (ppm)

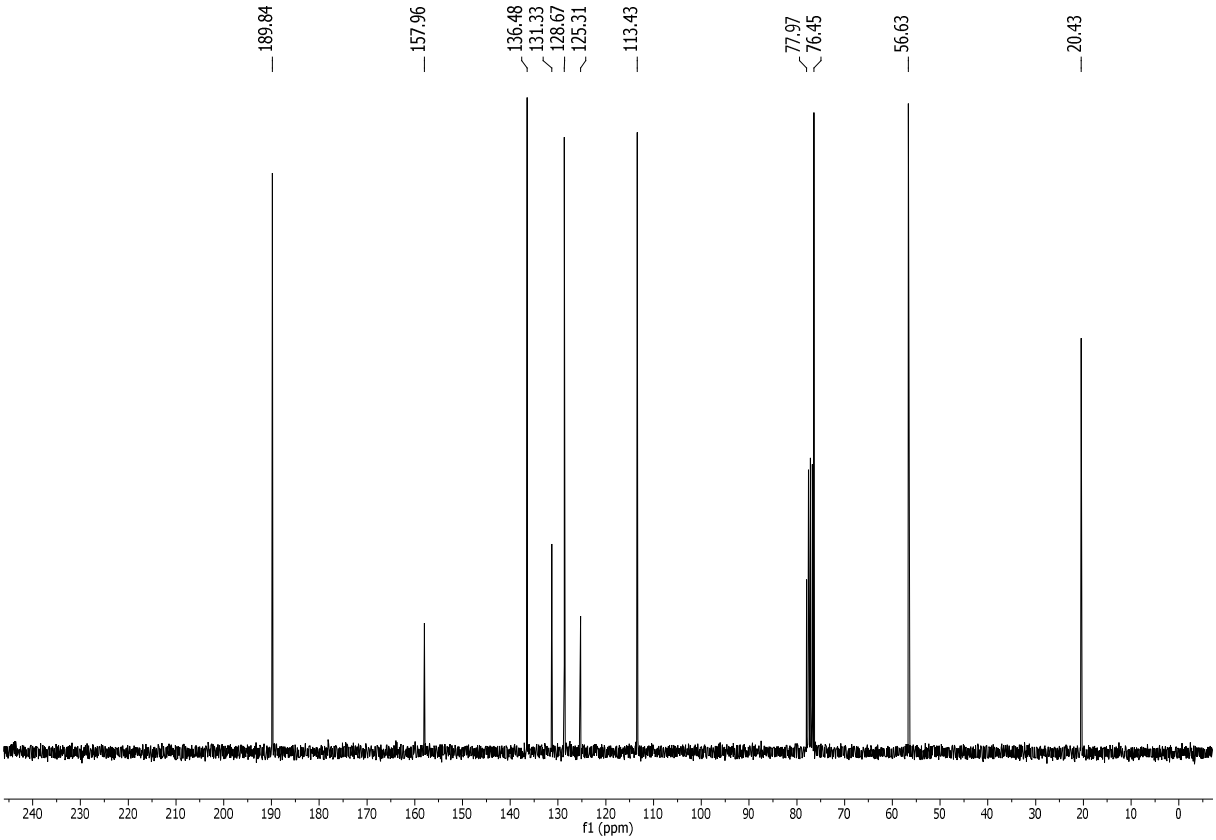

10.40 10.40 7.95 7.95 7.95 7.93 7.93 7.46 7.46 7.45 7.45 7.44 7.44 7.43 7.43 7.42 7.42 7.42 7.41 7.41 7.41 7.40 7.39 7.39 7.38 7.27 7.27 7.27 7.26 7.26 7.25 7.25 7.25 6.68 6.68 6.66 6.66 5.74 5.71 5.69 5.67 5.03 5.03 5.02 5.02 5.02 5.01 5.01 5.00 5.00 5.00 4.98 4.98 4.97 2.41
CHO
N
Ts
10o
1.00 1.01 4.00 2.01 1.00 0.98 1.95 0.94 0.89 3.00
14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

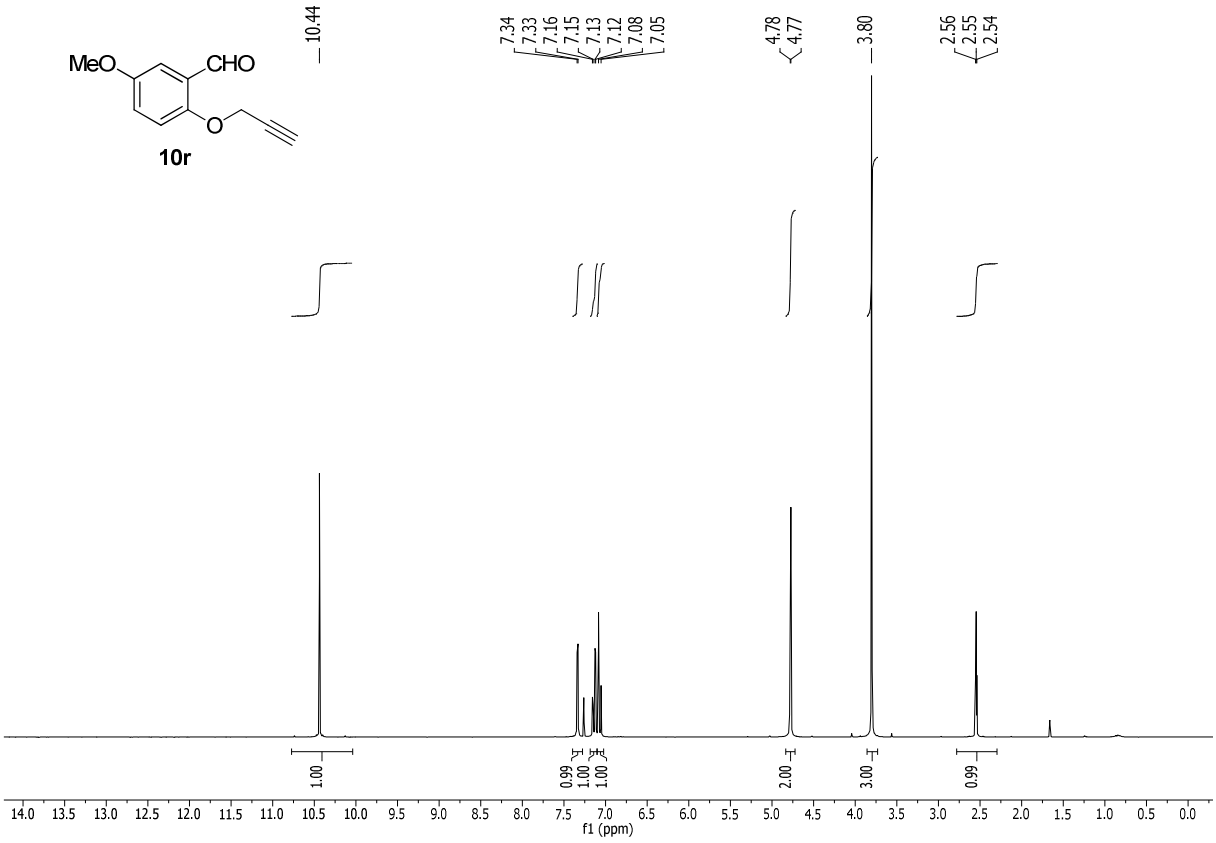

190.20
144.33 141.33 136.01 134.24 134.14 131.55 129.74 128.60 128.27 127.90 127.84 120.53
54.34
21.60
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

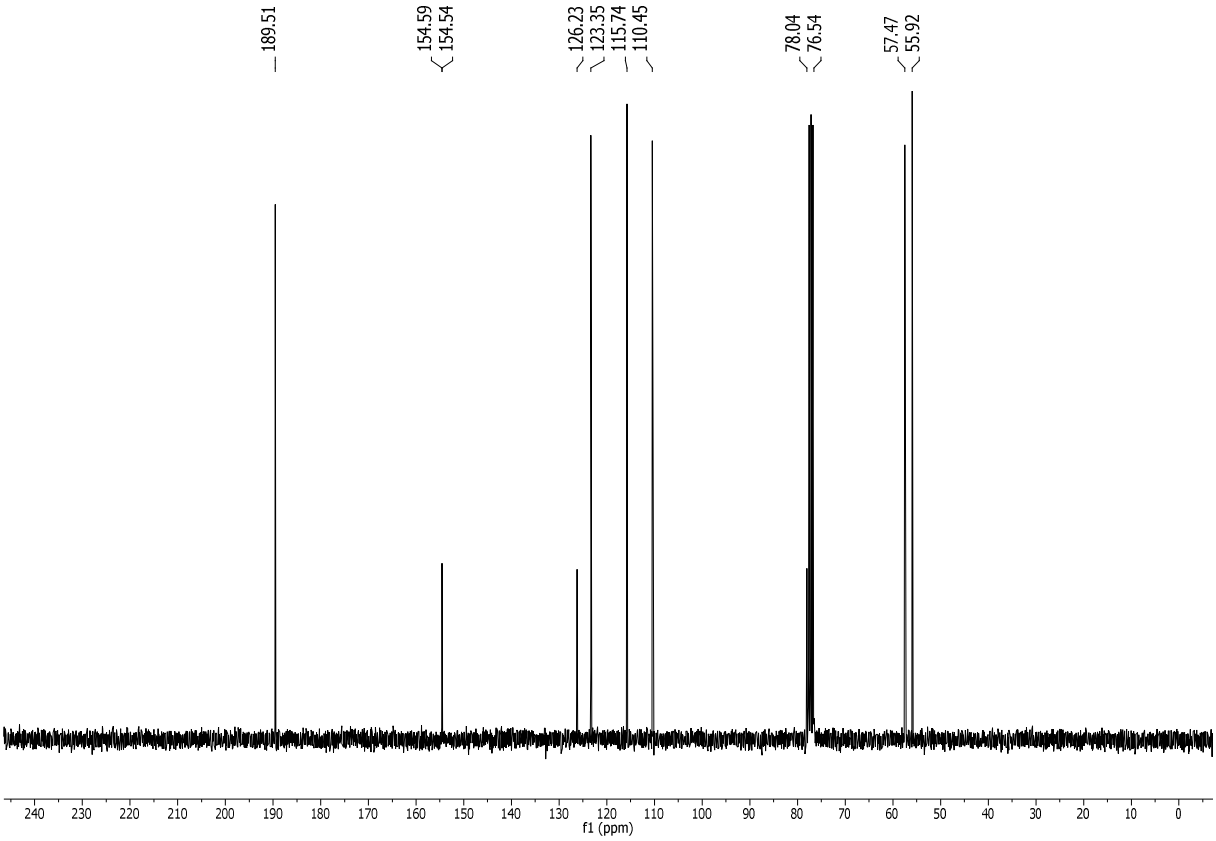

10.47
10.47
7.86
7.86
7.84
7.83
7.56
7.56
7.56
7.55
7.54
7.12
7.12
7.10
7.10
7.10
7.09
7.08
7.07
7.07
7.05
4.83
4.82
2.58
2.57
2.56
CHO
O
10p
1.00
1.00
1.00
2.00
2.05
1.00
f1 (ppm)

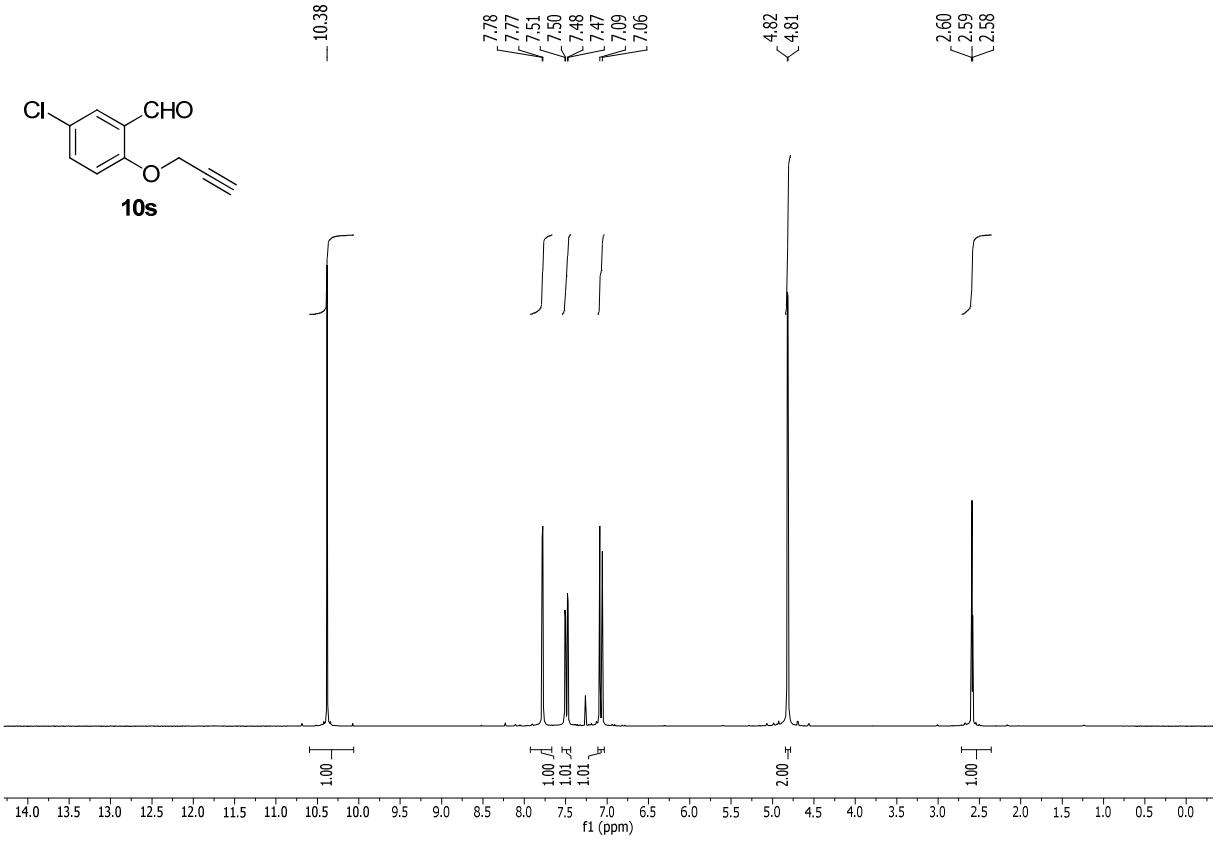

189.64
159.83
135.83
128.64
125.52
121.76
113.26
77.76
76.61
56.44
f1 (ppm)

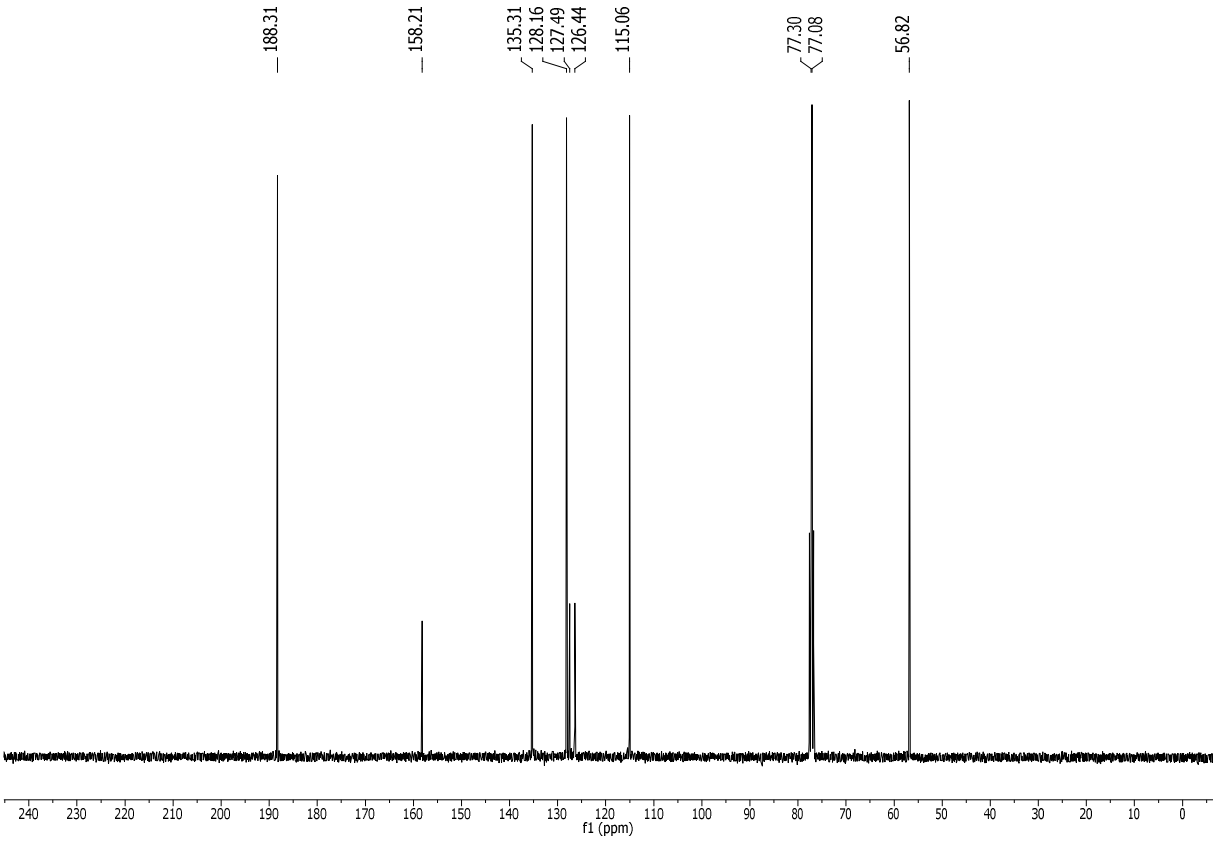

10.44
7.65
7.65
7.64
7.38
7.38
7.37
7.37
7.37
7.35
7.35
7.34
7.34
7.34
7.02
6.99
4.79
4.79
2.56
2.55
2.54
2.31
2.31
2.31
Me
CHO
O
10q
0.99
1.00
1.00
1.02
2.04
0.97
3.00
f1 (ppm)

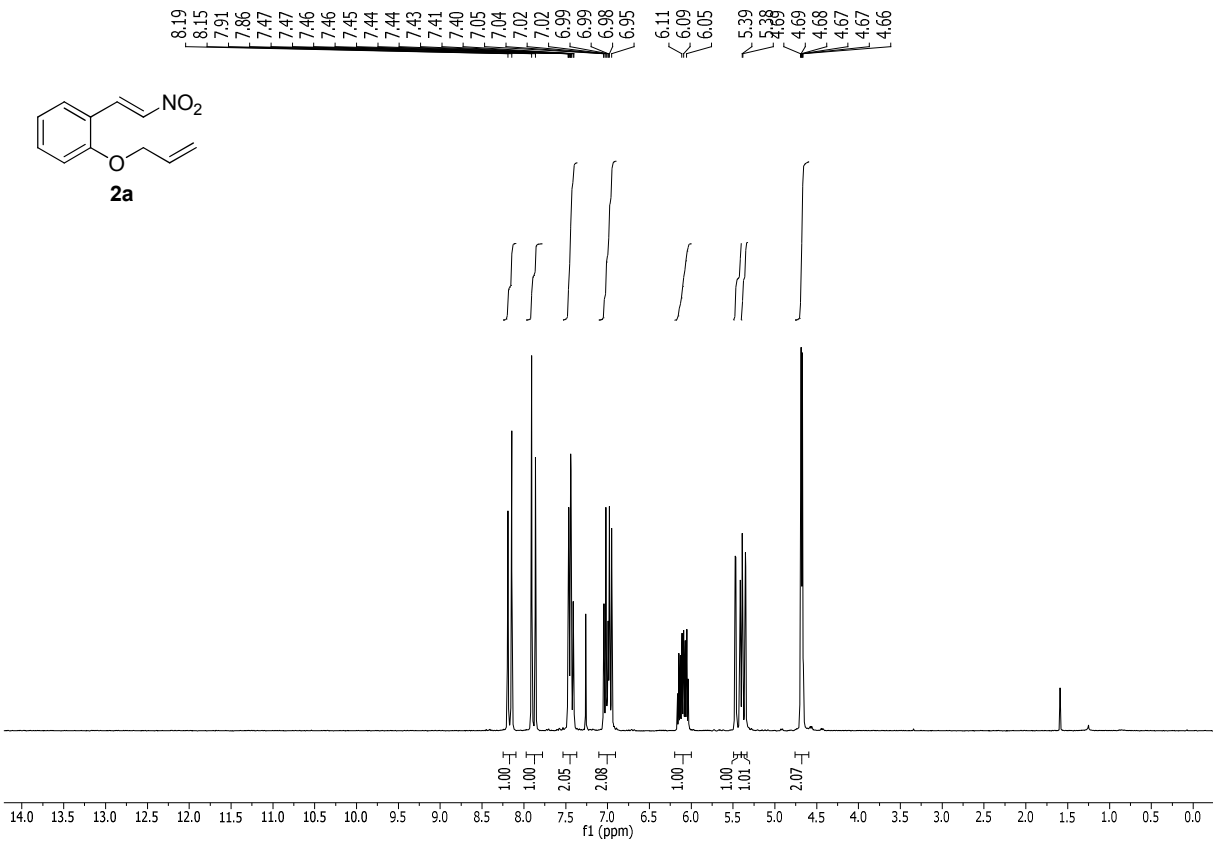

189.84
157.96
136.48
131.33
128.67
125.31
113.43
77.97
76.45
56.63
20.43
f1 (ppm)

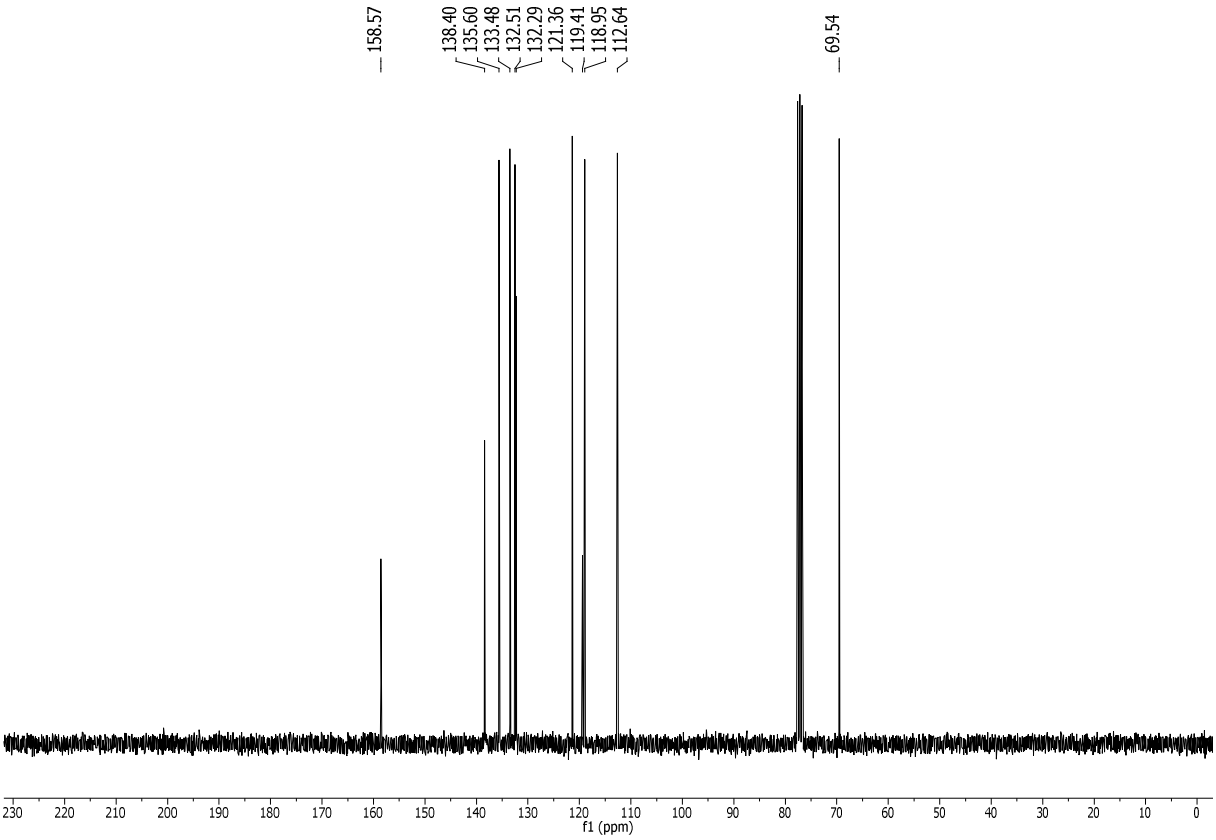

MeO
CHO
O
10r
10.44
7.34
7.33
7.16
7.15
7.13
7.12
7.08
7.05
4.78
4.77
3.80
2.56
2.55
2.54
1.00
0.99
1.00
1.00
2.00
3.00
0.99
f1 (ppm)

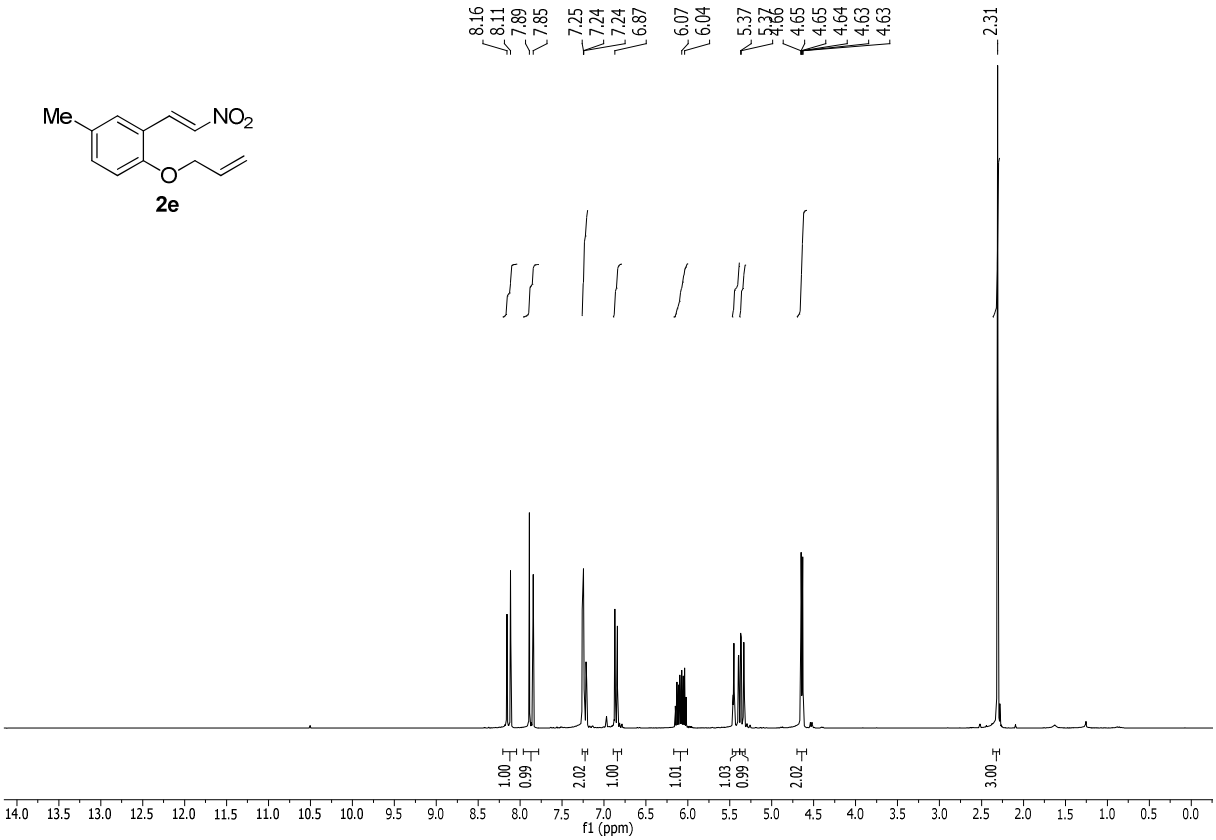

189.51
154.59
154.54
126.23
123.35
115.74
110.45
78.04
76.54
57.47
55.92
f1 (ppm)

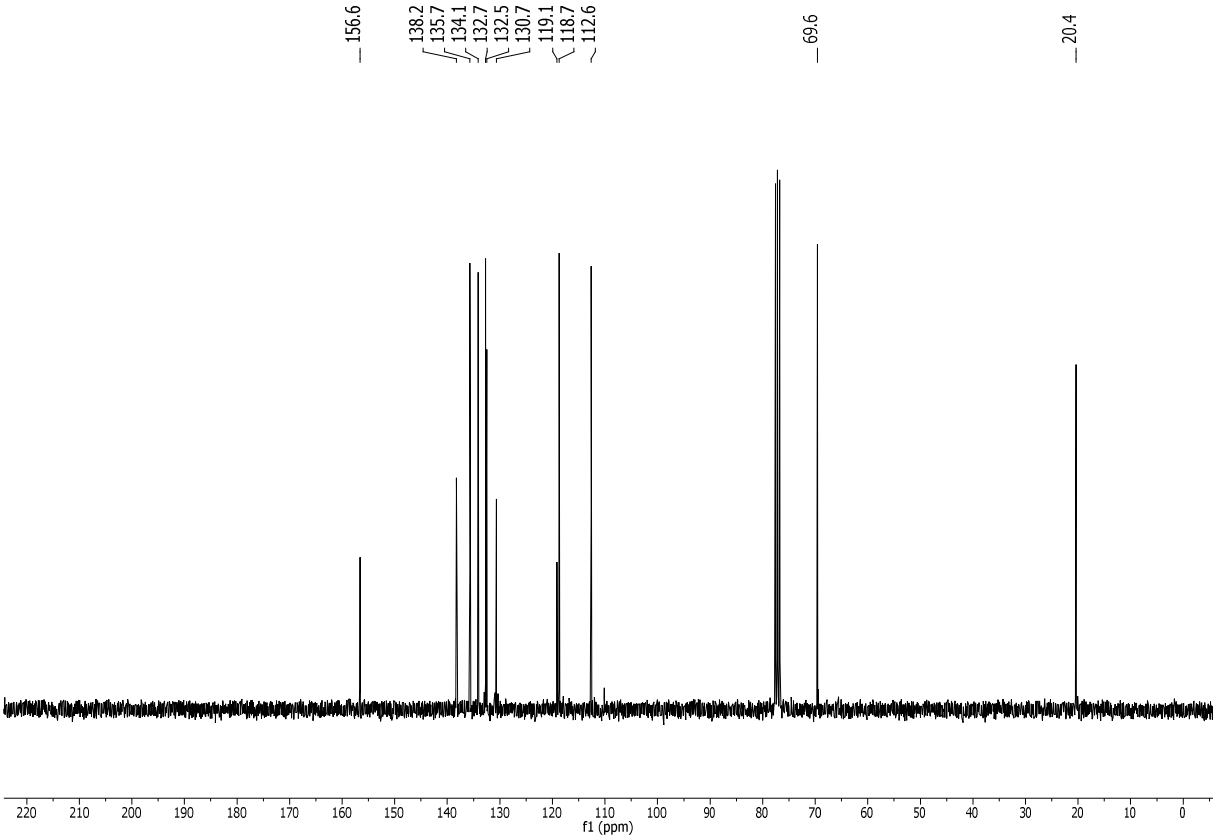

10.38
7.78
7.77
7.51
7.50
7.48
7.47
7.09
7.06
4.82
4.81
2.60
2.59
2.58
Cl
CHO
O
10s
1.00
1.00
1.01
1.01
2.00
1.00
f1 (ppm)

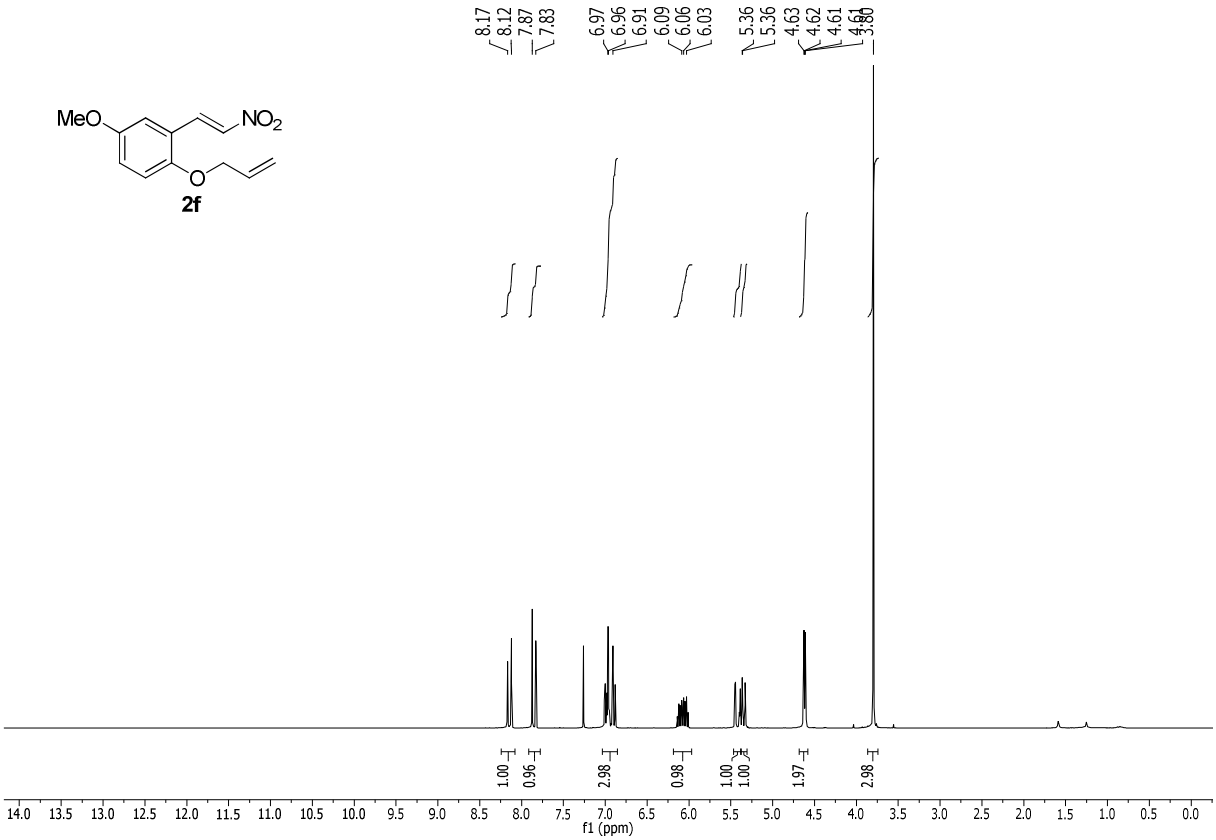

188.31
158.21
135.31
128.16
127.49
126.44
115.06
77.30
77.08
56.82
f1 (ppm)

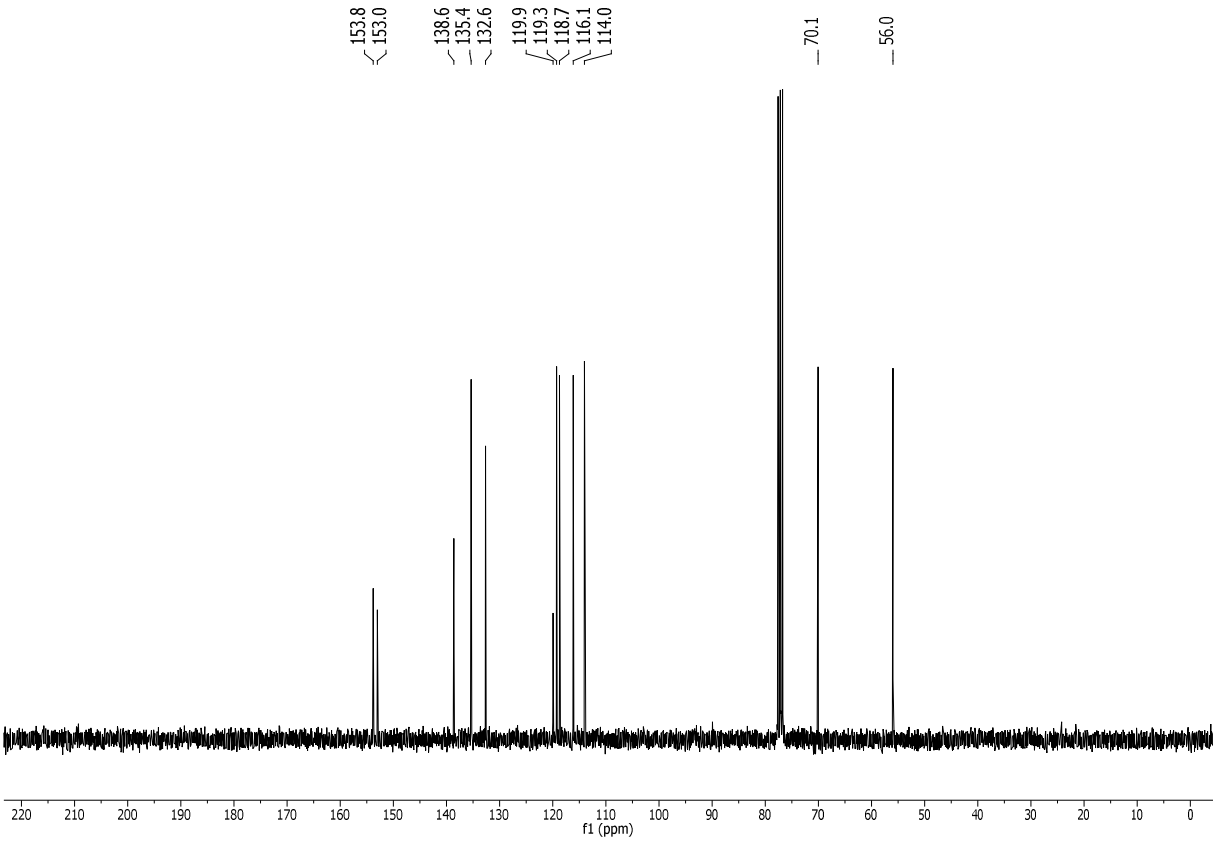

8.19
8.15
7.91
7.86
7.47
7.47
7.46
7.46
7.45
7.44
7.44
7.43
7.41
7.40
7.05
7.04
7.02
7.02
6.99
6.99
6.98
6.95
6.11
6.09
6.05
5.39
5.38
4.69
4.69
4.68
4.67
4.67
4.66
NO2
O
2a
1.00
1.00
2.05
2.08
1.00
1.00
1.01
2.07
f1 (ppm)

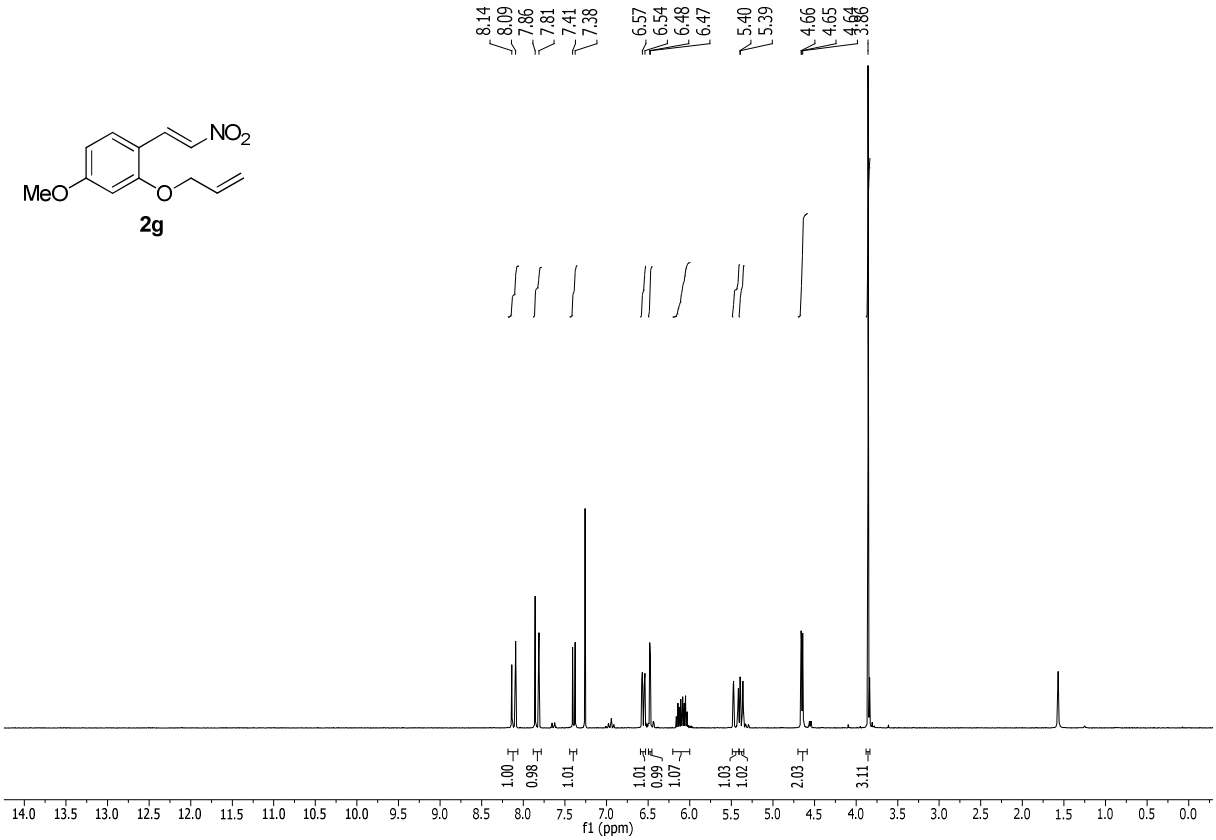

158.57
138.40
135.60
133.48
132.51
132.29
121.36
119.41
118.95
112.64
69.54
f1 (ppm)

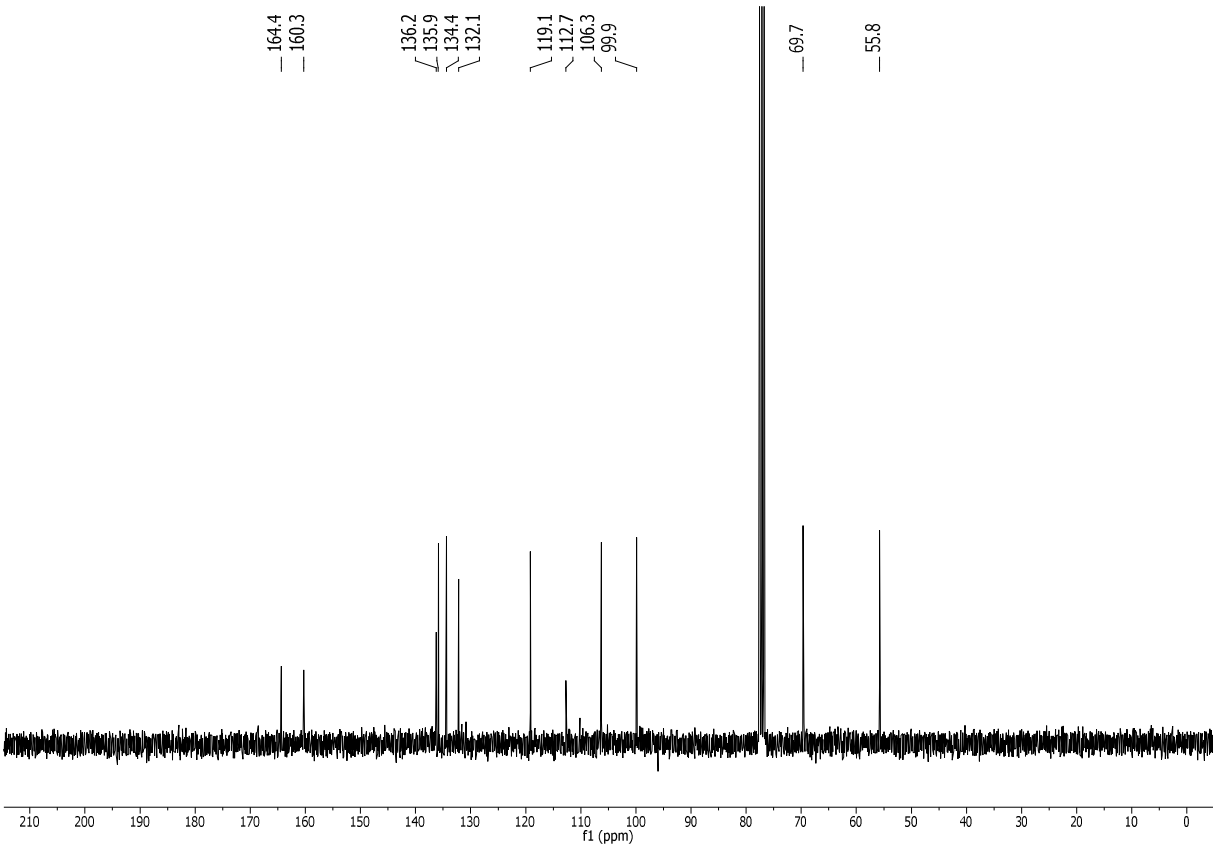

8.16
8.11
7.89
7.85
7.25
7.24
7.24
6.87
6.07
6.04
5.37
5.37
4.66
4.65
4.64
4.63
4.63
2.31
Me
NO2
O
2e
1.00
0.99
2.02
1.00
1.01
1.03
0.99
2.02
3.00
f1 (ppm)

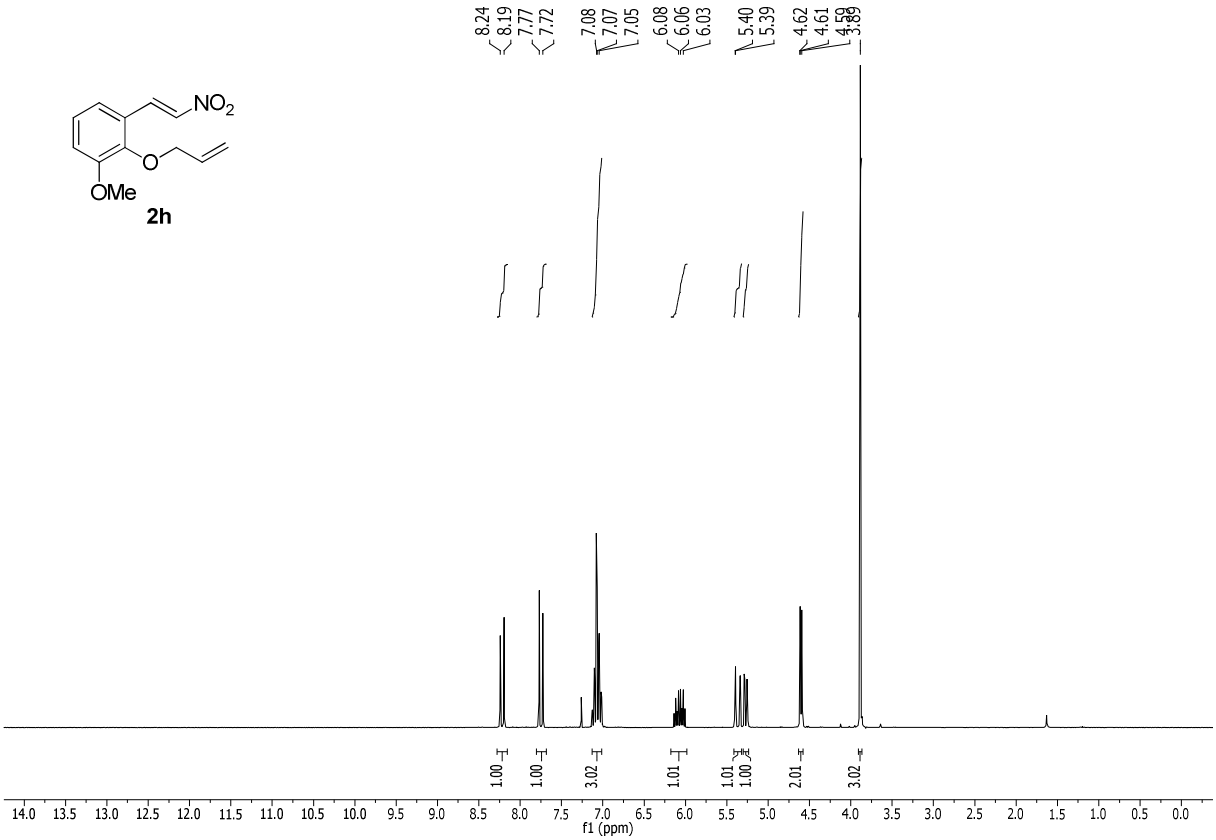

156.6
138.2
135.7
134.1
132.7
132.5
130.7
119.1
118.7
112.6
69.6
20.4
f1 (ppm)

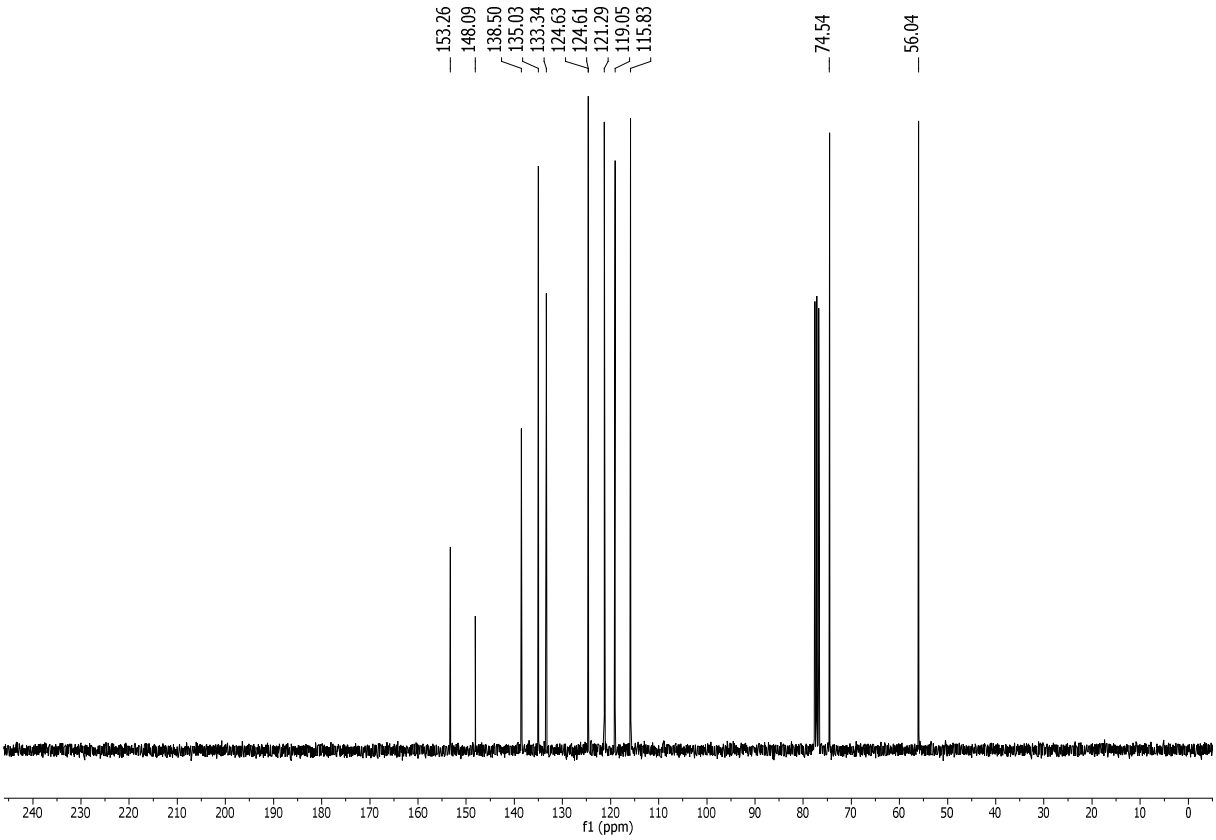

8.17
8.12
7.87
7.83
6.97
6.96
6.91
6.09
6.06
6.03
5.36
5.36
4.63
4.62
4.61
4.61
3.80
MeO
NO2
O
2f
1.00
0.96
2.98
0.98
1.00
1.00
1.97
2.98
f1 (ppm)

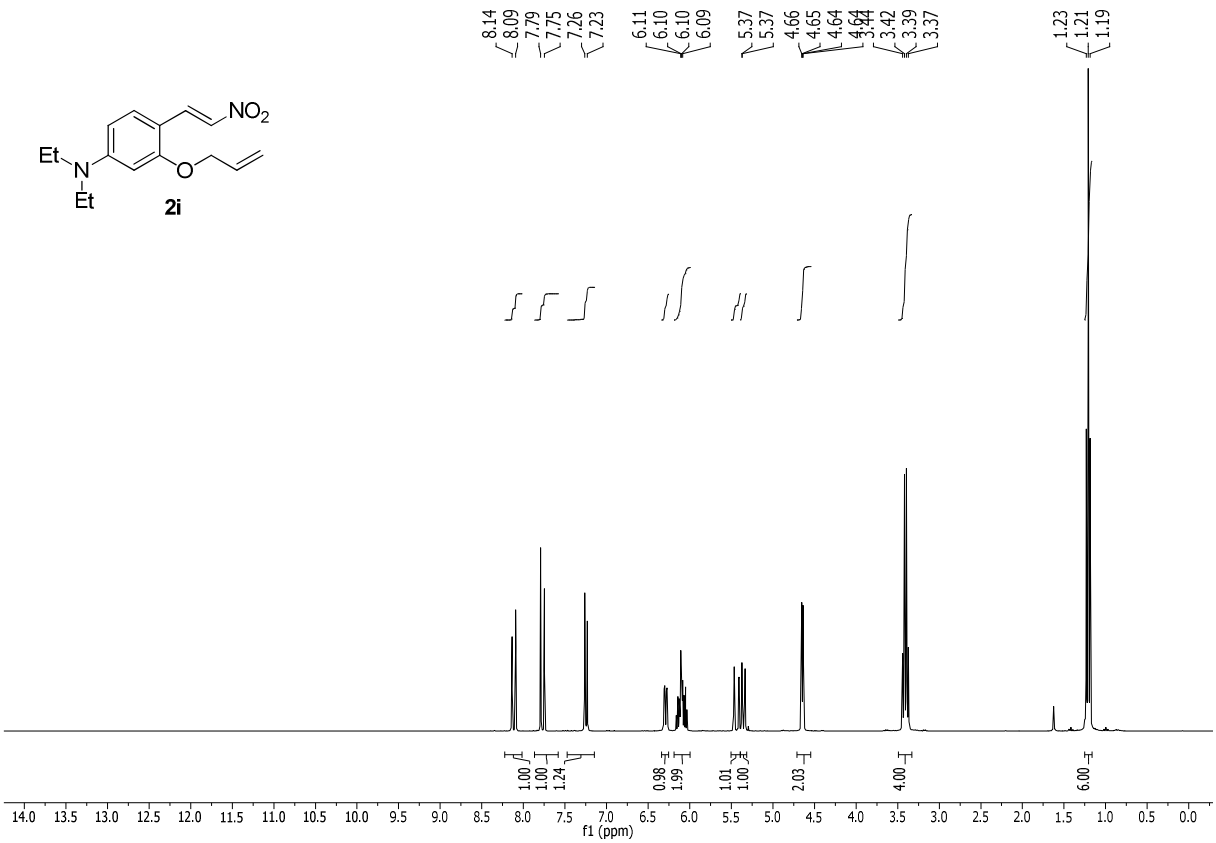

153.8
153.0
138.6
135.4
132.6
119.9
119.3
118.7
116.1
114.0
70.1
56.0
f1 (ppm)

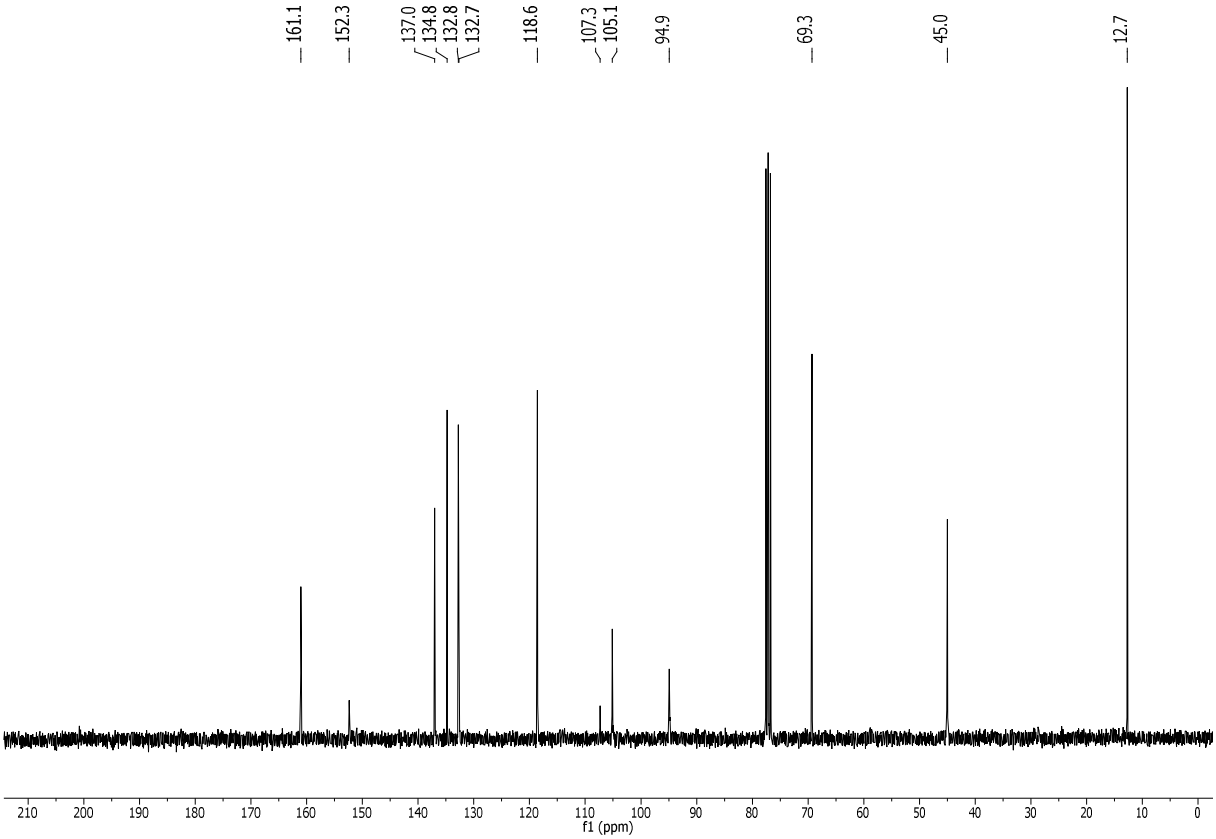

8.14
8.09
7.86
7.81
7.41
7.38
6.57
6.54
6.48
6.47
5.40
5.39
4.66
4.65
4.64
3.86
NO2
MeO
O
2g
1.00
0.98
1.01
1.01
0.99
1.07
1.03
1.02
2.03
3.11
f1 (ppm)

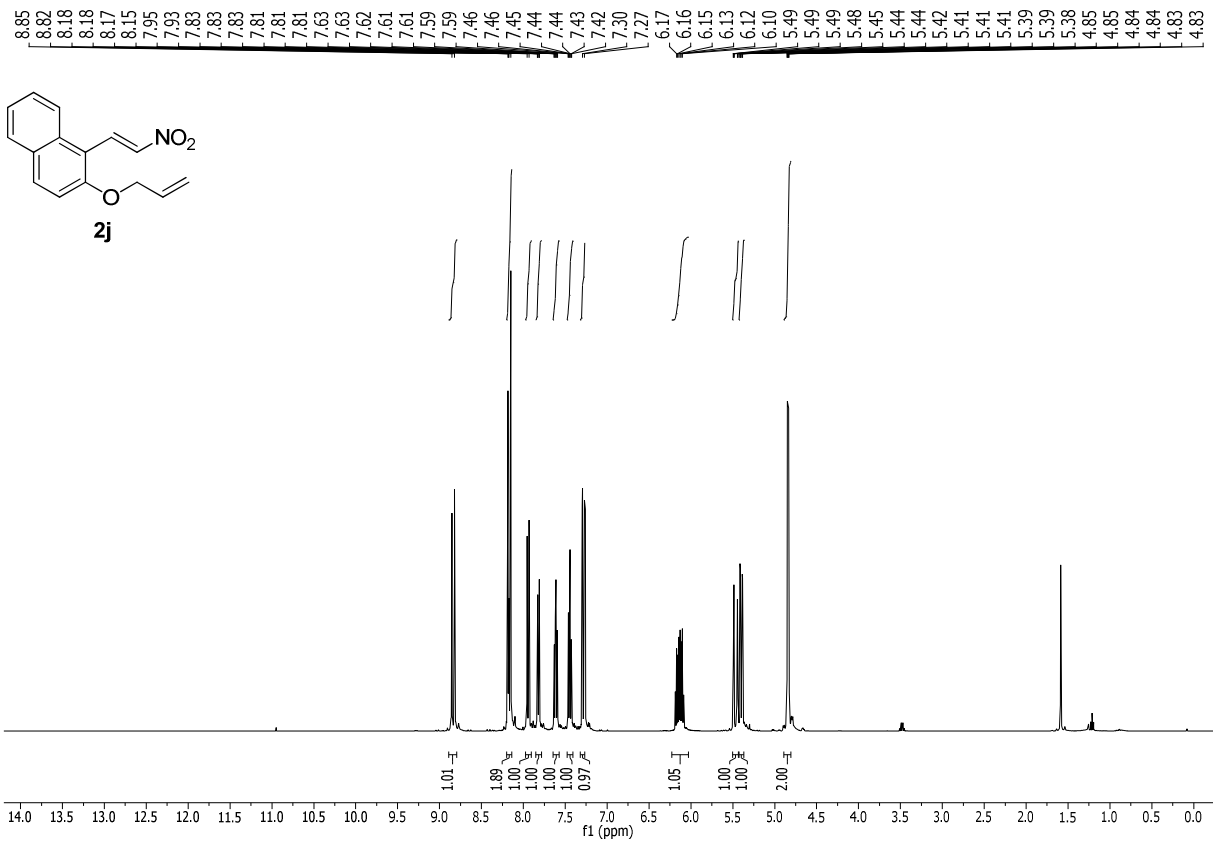

164.4
160.3
136.2
135.9
134.4
132.1
119.1
112.7
106.3
99.9
69.7
55.8
f1 (ppm)

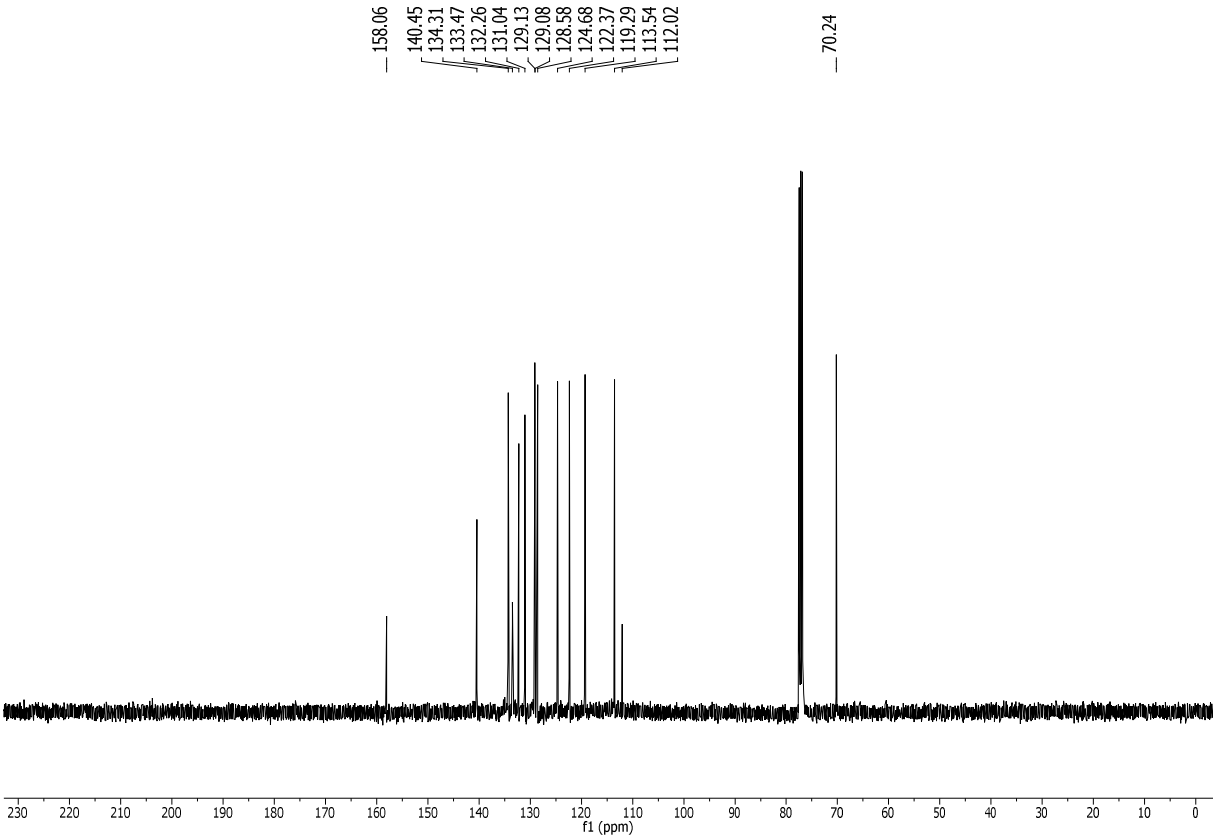

8.24
8.19
7.77
7.72
7.08
7.07
7.05
6.08
6.06
6.03
5.40
5.39
4.62
4.61
4.59
3.89
NO2
O
OMe
2h
1.00
1.00
3.02
1.01
1.01
1.00
2.01
3.02
f1 (ppm)

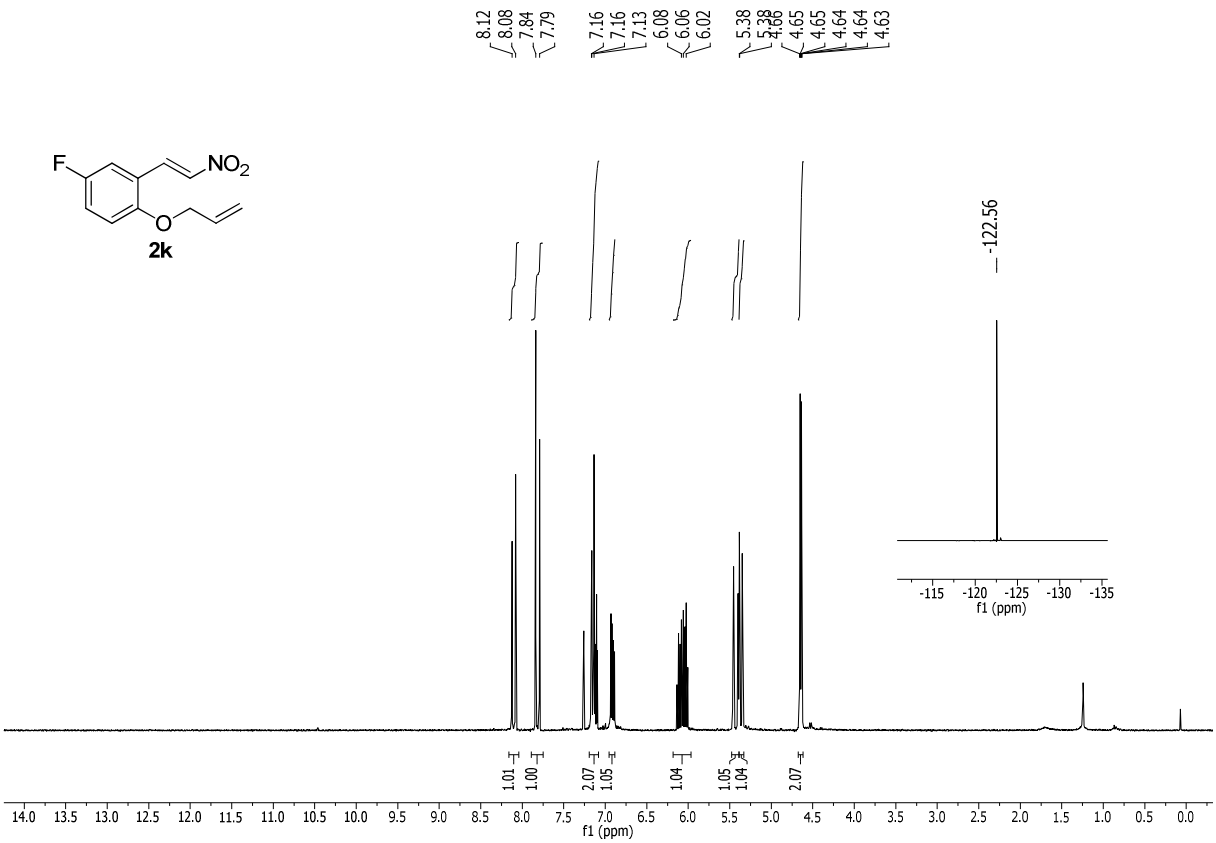

153.26
148.09
138.50
135.03
133.34
124.63
124.61
121.29
119.05
115.83
74.54
56.04
f1 (ppm)

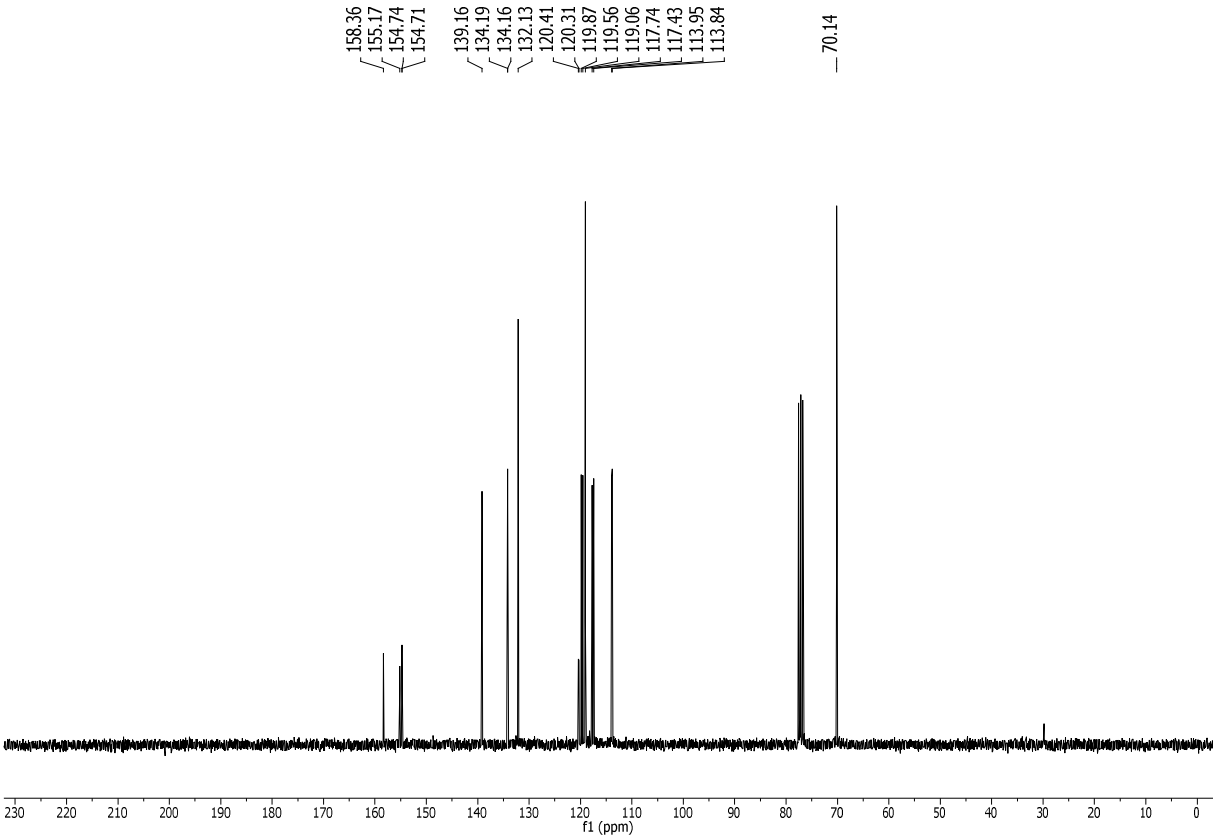

8.14
8.09
7.79
7.75
7.26
7.23
6.11
6.10
6.10
6.09
5.37
5.37
4.66
4.65
4.64
4.64
3.44
3.42
3.39
3.37
1.23
1.21
1.19
NO2
Et
N
Et
O
2i
1.00
1.00
1.24
0.98
1.99
1.01
1.00
2.03
4.00
6.00
f1 (ppm)

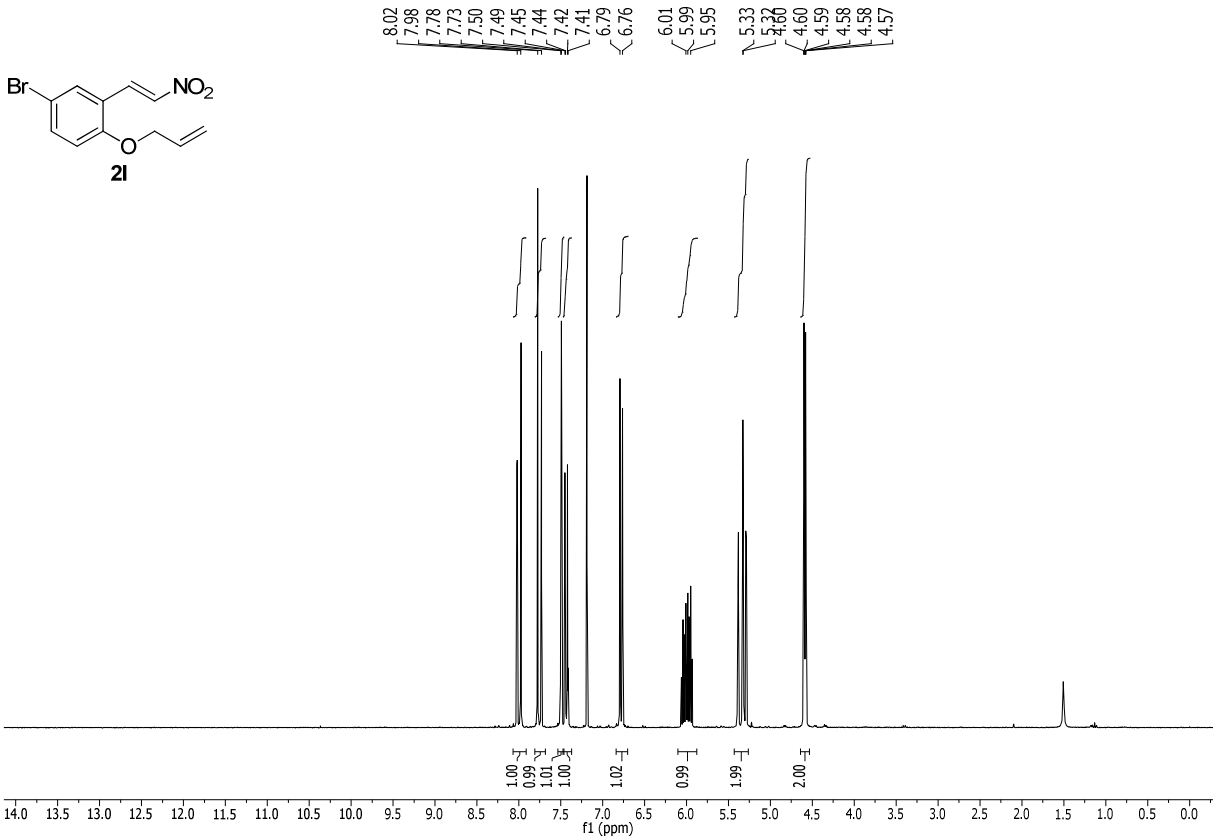

161.1
152.3
137.0
134.8
132.8
132.7
118.6
107.3
105.1
94.9
69.3
45.0
12.7
f1 (ppm)

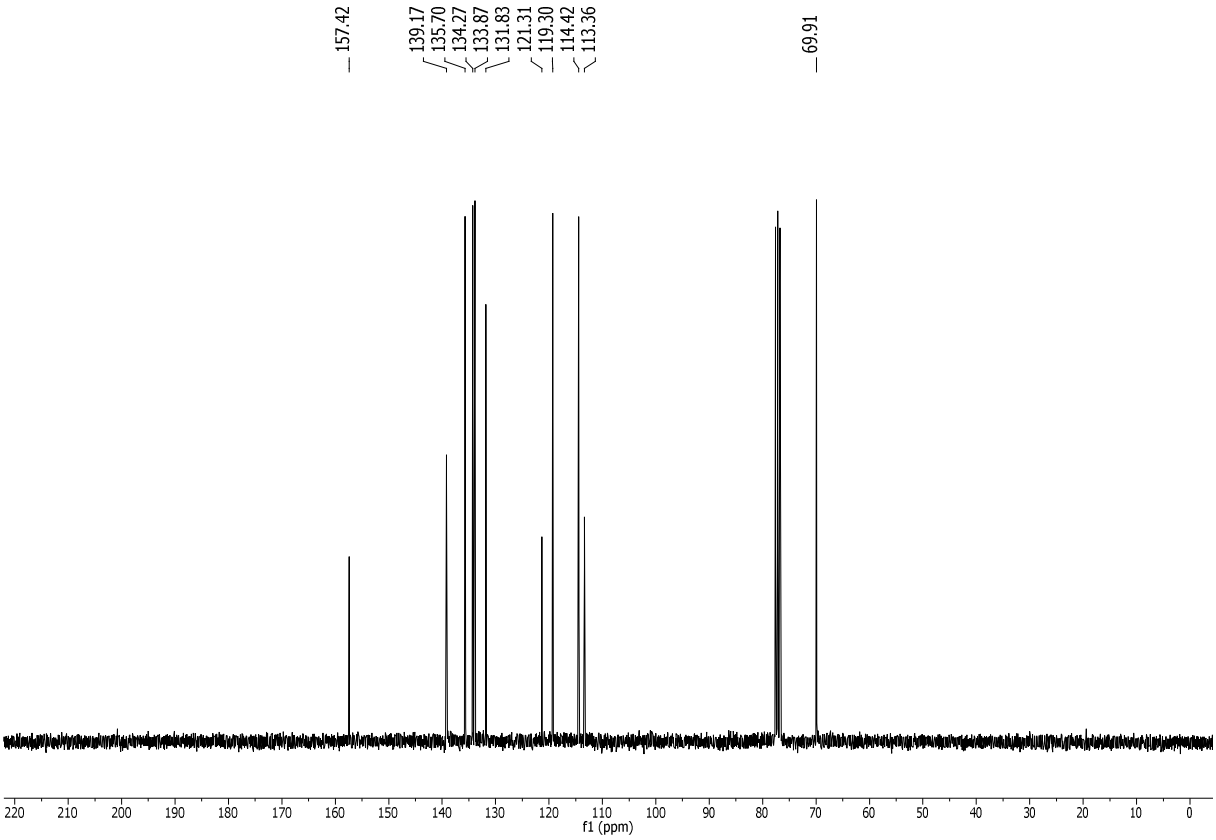

8.85 8.82 8.18 8.18 8.17 8.15 7.95 7.93 7.83 7.83 7.83 7.81 7.81 7.81 7.63 7.63 7.62 7.61 7.61 7.59 7.59 7.46 7.46 7.45 7.44 7.44 7.43 7.42 7.30 7.27 6.17 6.16 6.15 6.13 6.12 6.10 5.49 5.49 5.49 5.48 5.45 5.44 5.44 5.42 5.41 5.41 5.41 5.39 5.39 5.38 4.85 4.85 4.84 4.84 4.83 4.83
NO2
O
2j
1.01 1.89 1.00 1.00 1.00 1.00 0.97 1.05 1.00 1.00 2.00
14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


158.06 140.45 134.31 133.47 132.26 131.04 129.13 129.08 128.58 124.68 122.37 119.29 113.54 112.02
70.24
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.12
8.08
7.84
7.79
7.16
7.16
7.13
6.08
6.06
6.02
5.38
5.38
4.66
4.65
4.65
4.64
4.64
4.63
F
NO2
O
2k
-122.56
-115 -120 -125 -130 -135
f1 (ppm)
1.01
1.00
2.07
1.05
1.04
1.05
1.04
2.07
14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


158.36
155.17
154.74
154.71
139.16
134.19
134.16
132.13
120.41
120.31
119.87
119.56
119.06
117.74
117.43
113.95
113.84
70.14
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.02
7.98
7.78
7.73
7.50
7.49
7.45
7.44
7.42
7.41
6.79
6.76
6.01
5.99
5.95
5.33
5.32
4.60
4.59
4.58
4.58
4.57
Br
NO2
O
2l
1.00
0.99
1.01
1.00
1.02
0.99
1.99
2.00
f1 (ppm)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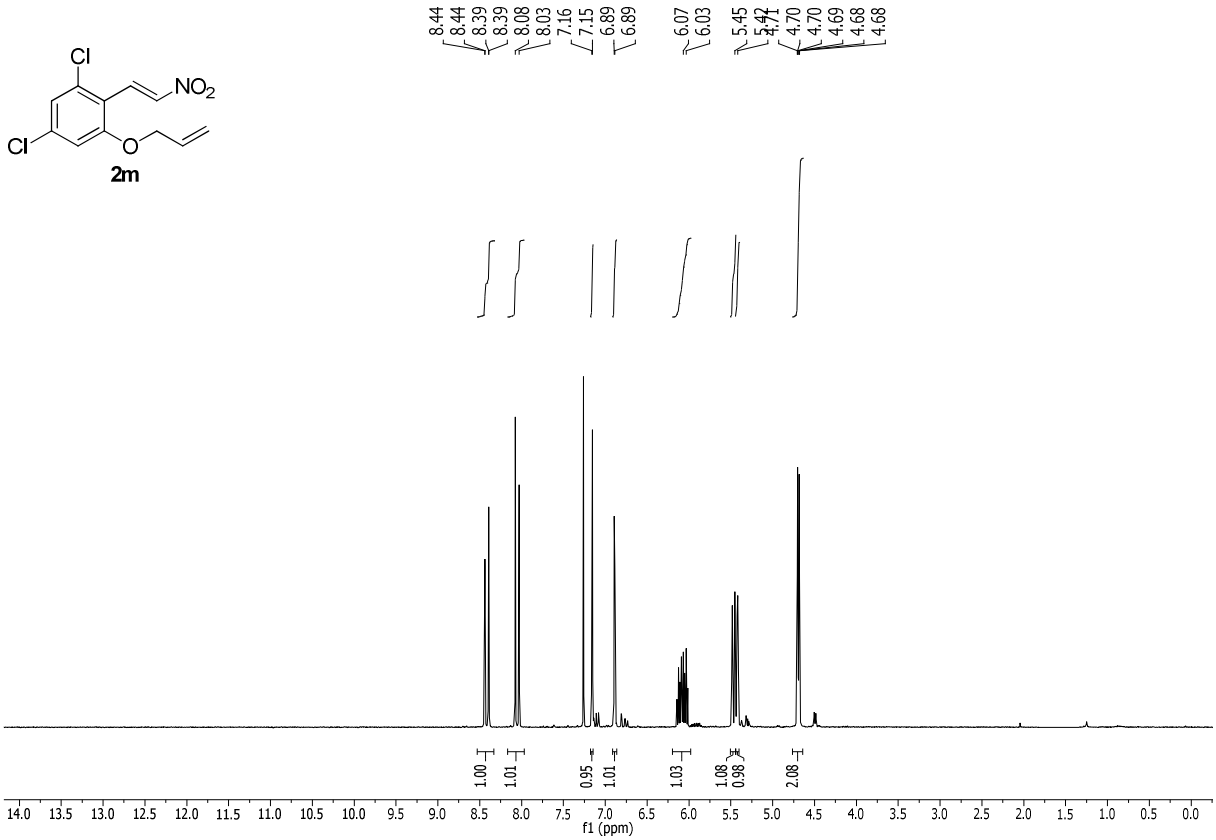
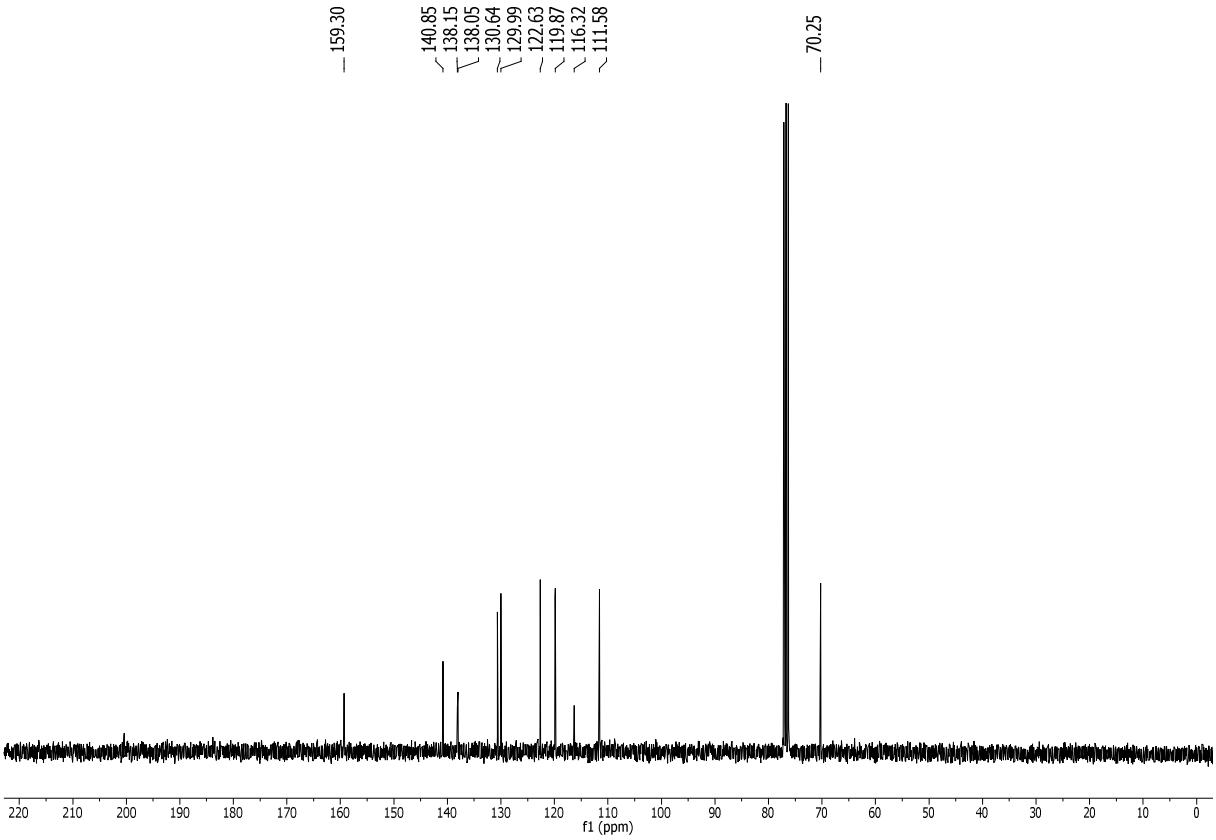
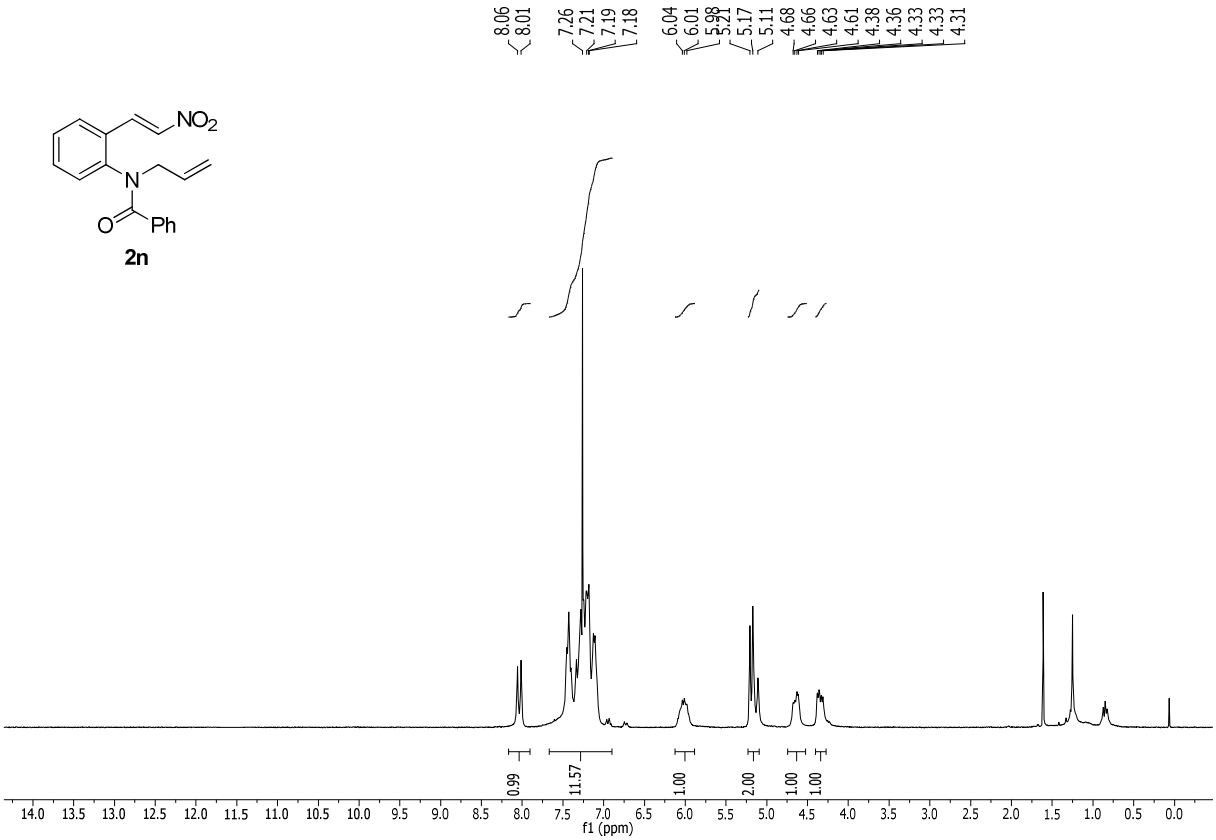
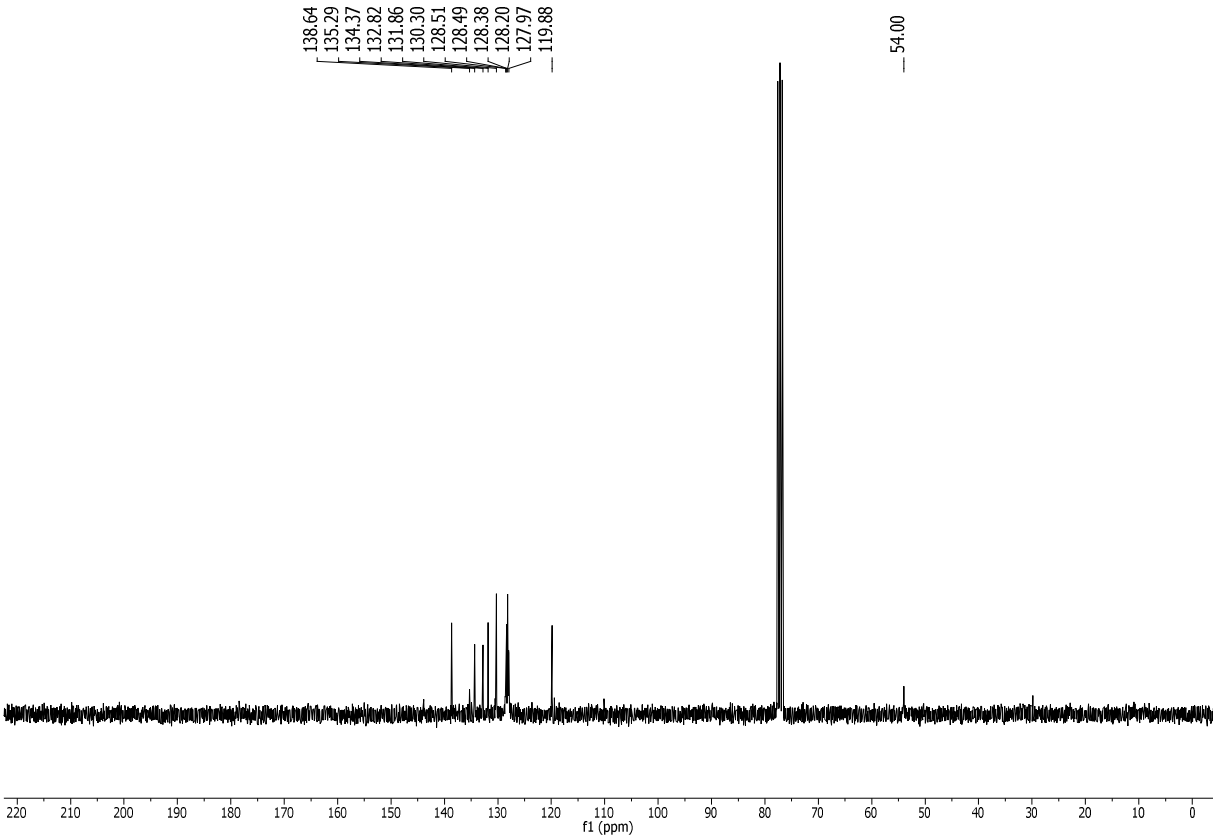
134.27
133.87
131.83
121.31
119.30
114.42
113.36
69.91
f1 (ppm)


8.44
8.44
8.39
8.39
8.08
8.03
7.16
7.15
6.89
6.89
6.07
6.03
5.45
5.42
4.71
4.70
4.70
4.69
4.68
4.68
Cl
NO2
Cl
O
2m
1.00
1.01
0.95
1.01
1.03
1.08
0.98
2.08
f1 (ppm)


159.30
140.85
138.15
138.05
130.64
129.99
122.63
119.87
116.32
111.58
70.25
f1 (ppm)


8.06
8.01
7.26
7.21
7.19
7.18
6.04
6.01
5.98
5.21
5.17
5.11
4.68
4.66
4.63
4.61
4.38
4.36
4.33
4.31
NO2
N
O
Ph
2n
0.99
11.57
1.00
2.00
1.00
1.00
f1 (ppm)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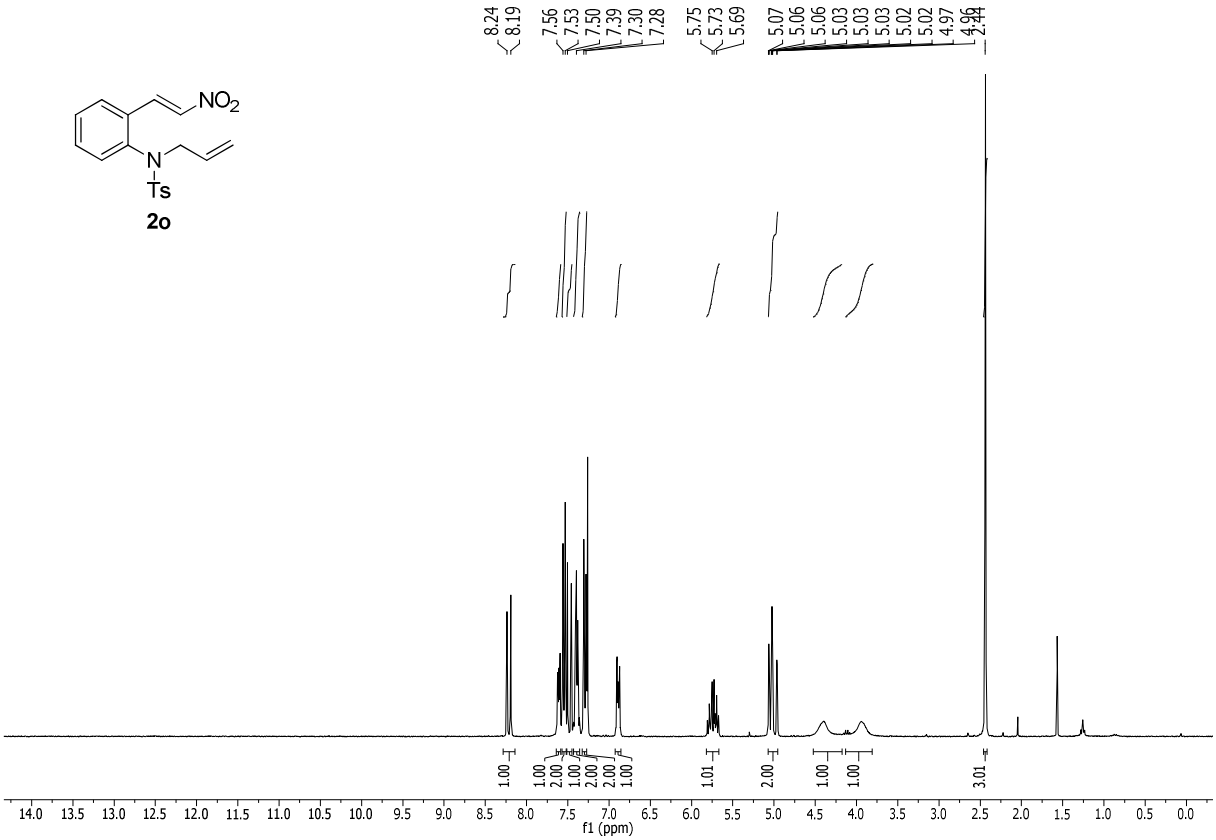
128.51
128.49
128.38
128.20
127.97
119.88
54.00
f1 (ppm)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7.30
7.28
5.75
5.73
5.69
5.07
5.06
5.06
5.03
5.03
5.02
5.02
4.97
4.96
2.44
NO2
N
Ts
2o
1.00
1.00
2.00
1.00
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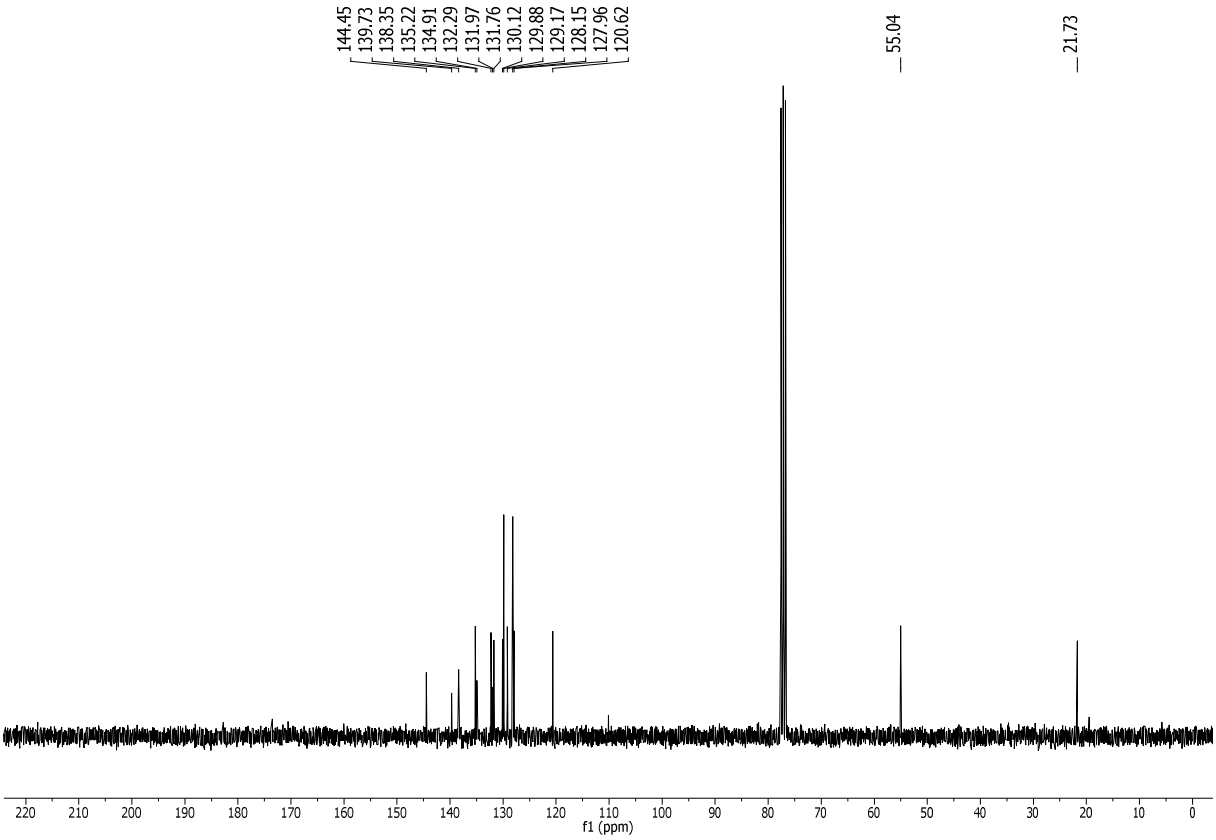
2.00
1.00
1.00
3.01
f1 (ppm)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138.35
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134.91
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131.97
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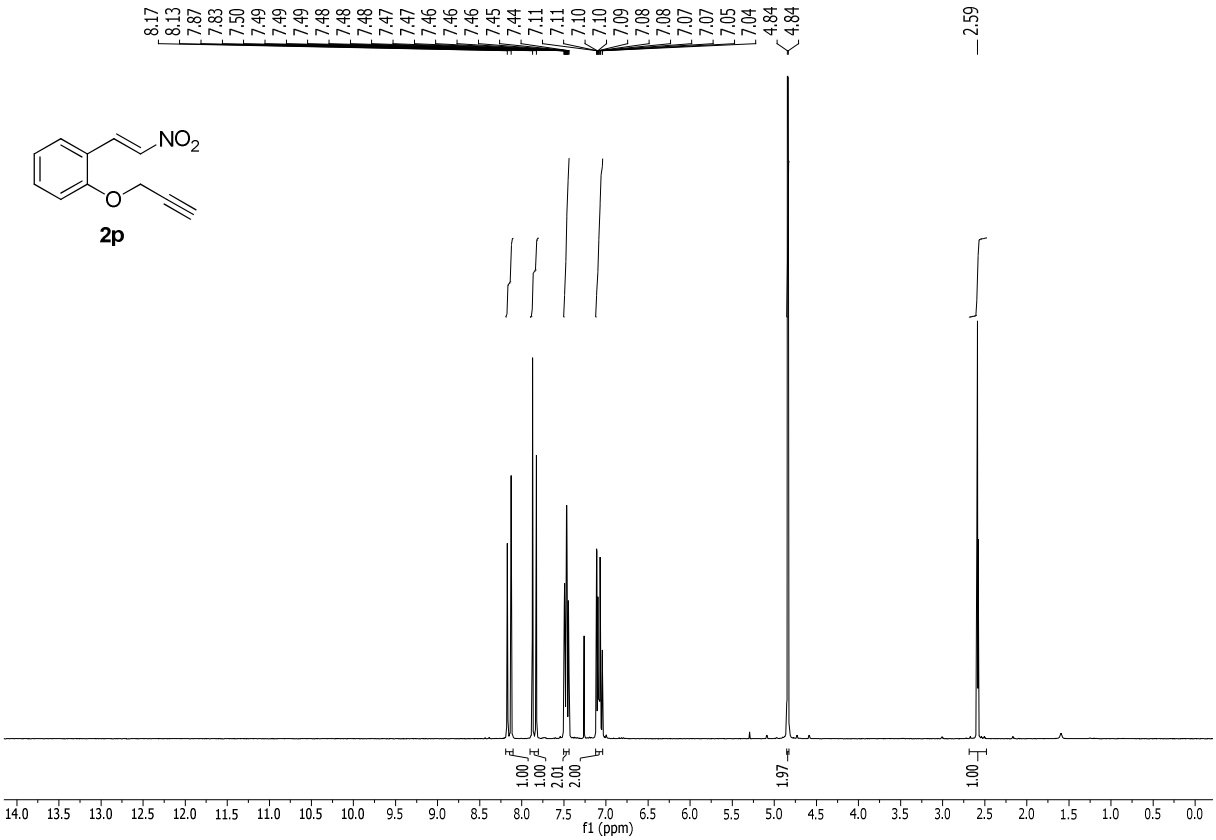
129.17
128.15
127.96
120.62
55.04
21.73
f1 (ppm)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7.87
7.83
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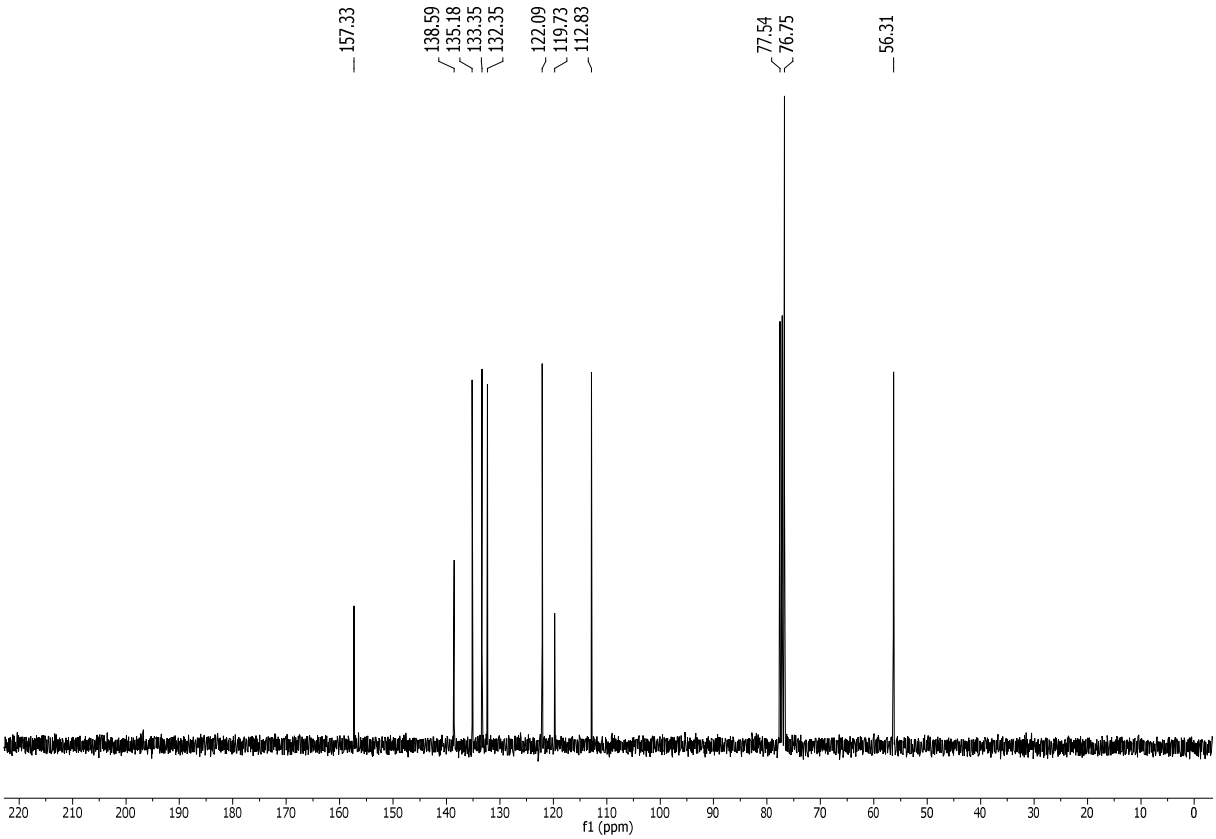
7.49
7.49
7.49
7.48
7.48
7.48
7.47
7.47
7.46
7.46
7.46
7.45
7.44
7.11
7.11
7.10
7.10
7.09
7.08
7.08
7.07
7.07
7.05
7.04
4.84
4.84
2.59
NO2
O
2p
1.00
1.00
2.01
2.00
1.97
1.00
f1 (ppm)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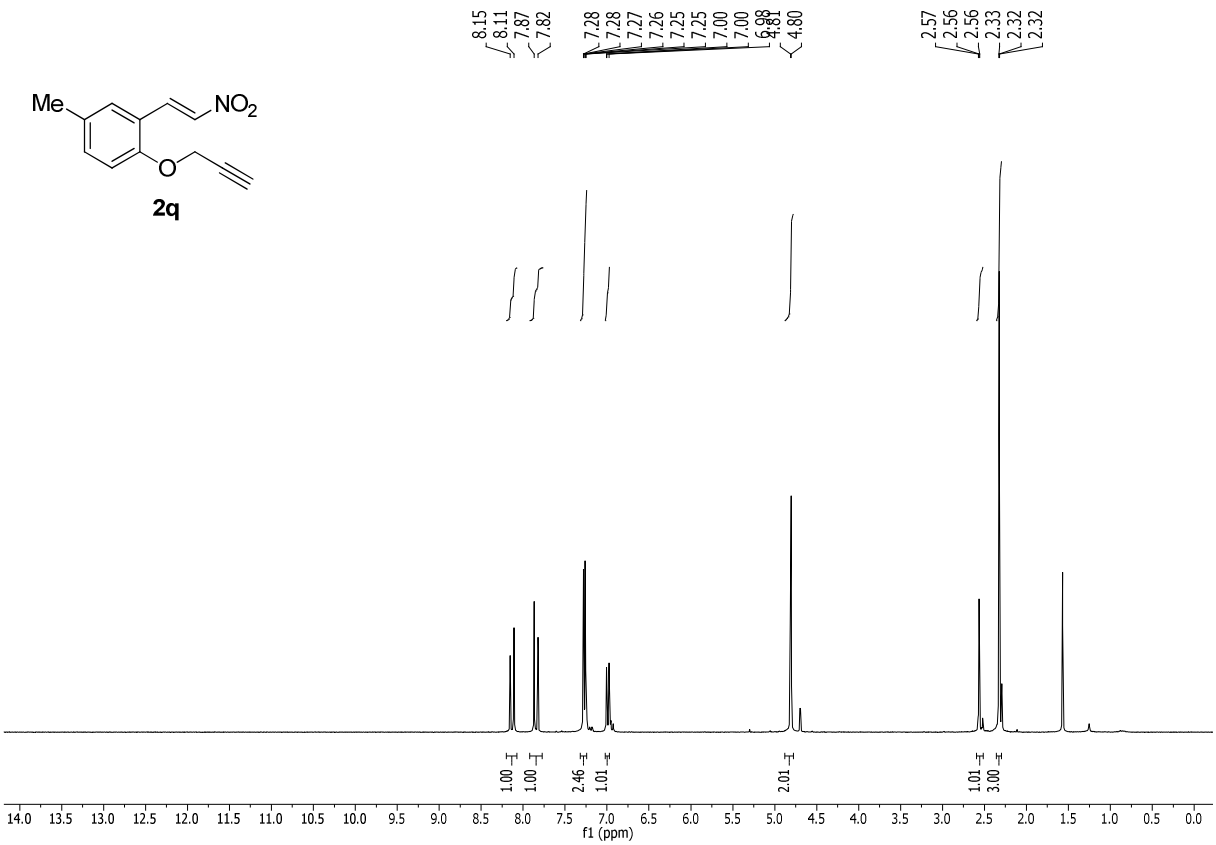
132.35
122.09
119.73
112.83
77.54
76.75
56.31
f1 (ppm)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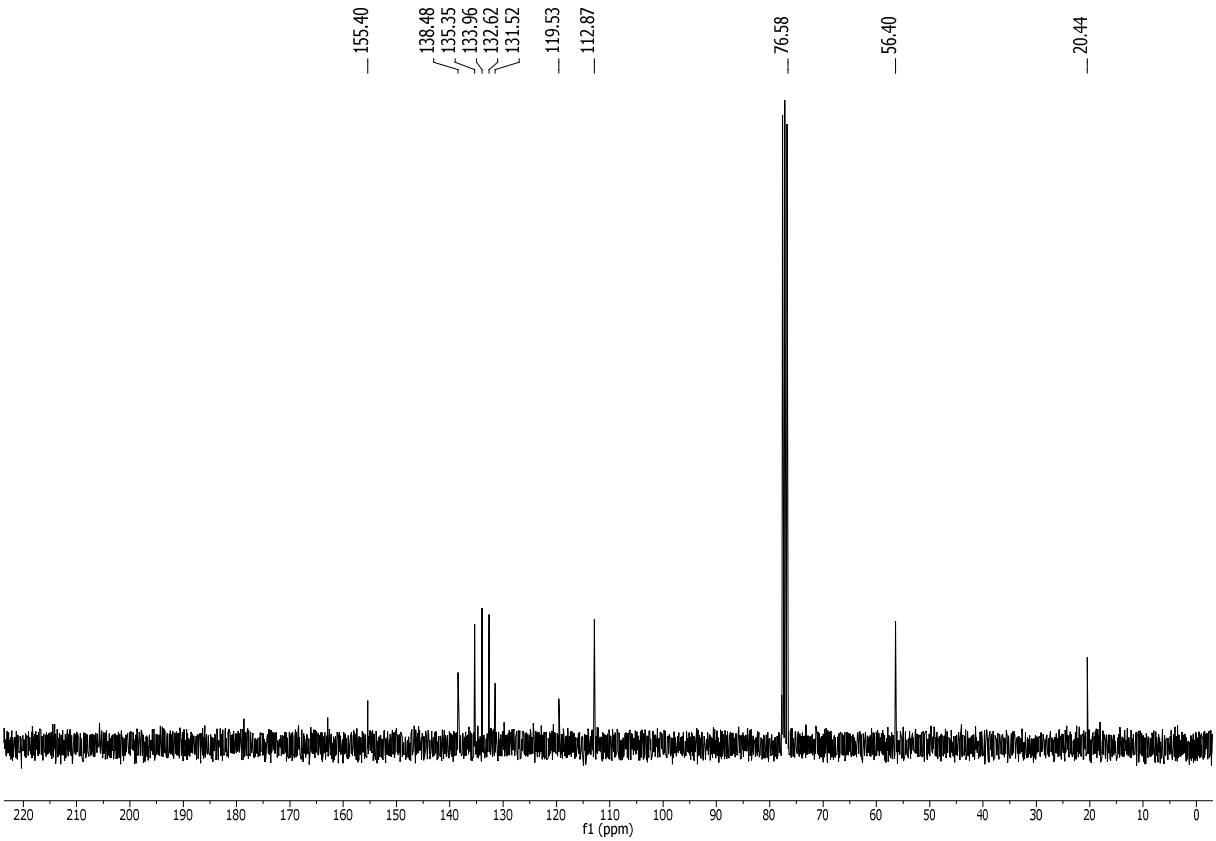
8.11
7.87
7.82
7.28
7.28
7.27
7.26
7.25
7.25
7.00
7.00
6.98
6.81
4.80
2.57
2.56
2.56
2.33
2.32
2.32
Me
NO2
O
2q
1.00
1.00
2.46
1.01
2.01
1.01
3.00
f1 (ppm)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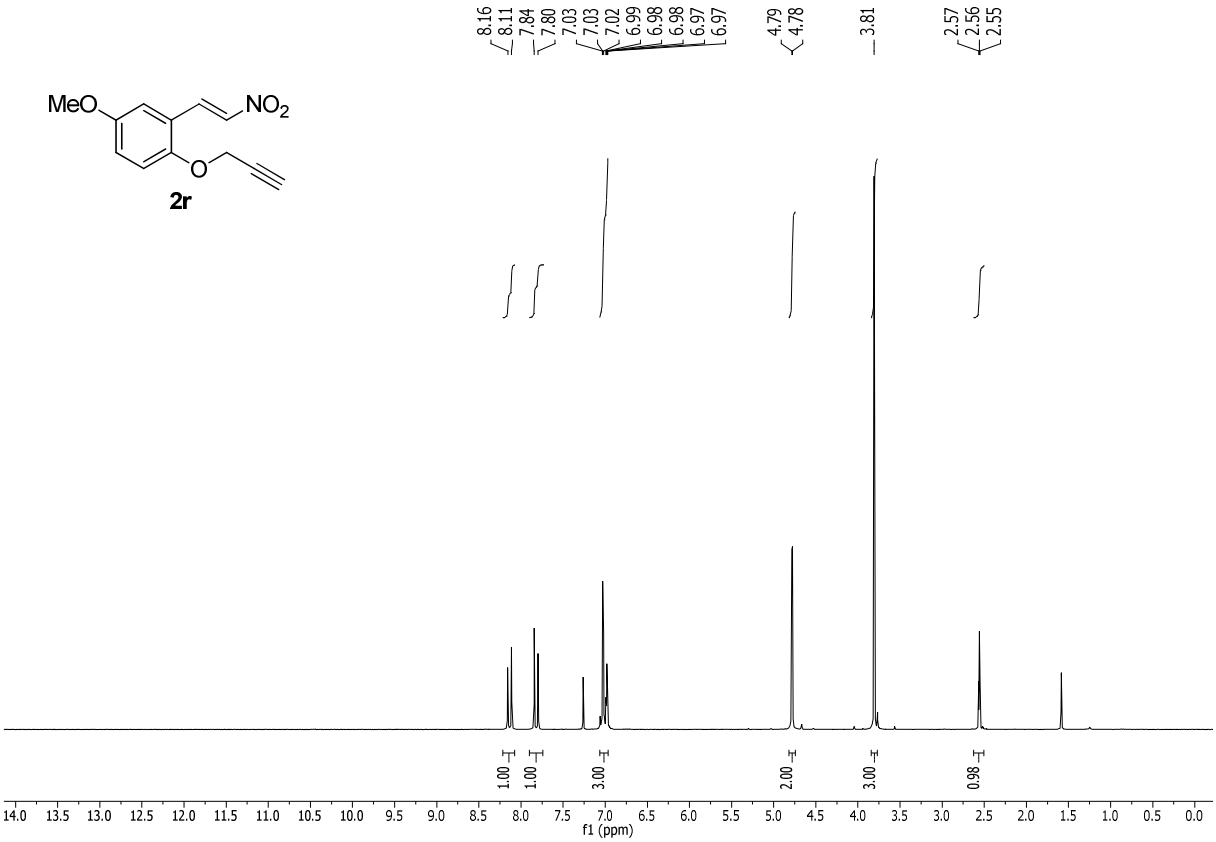
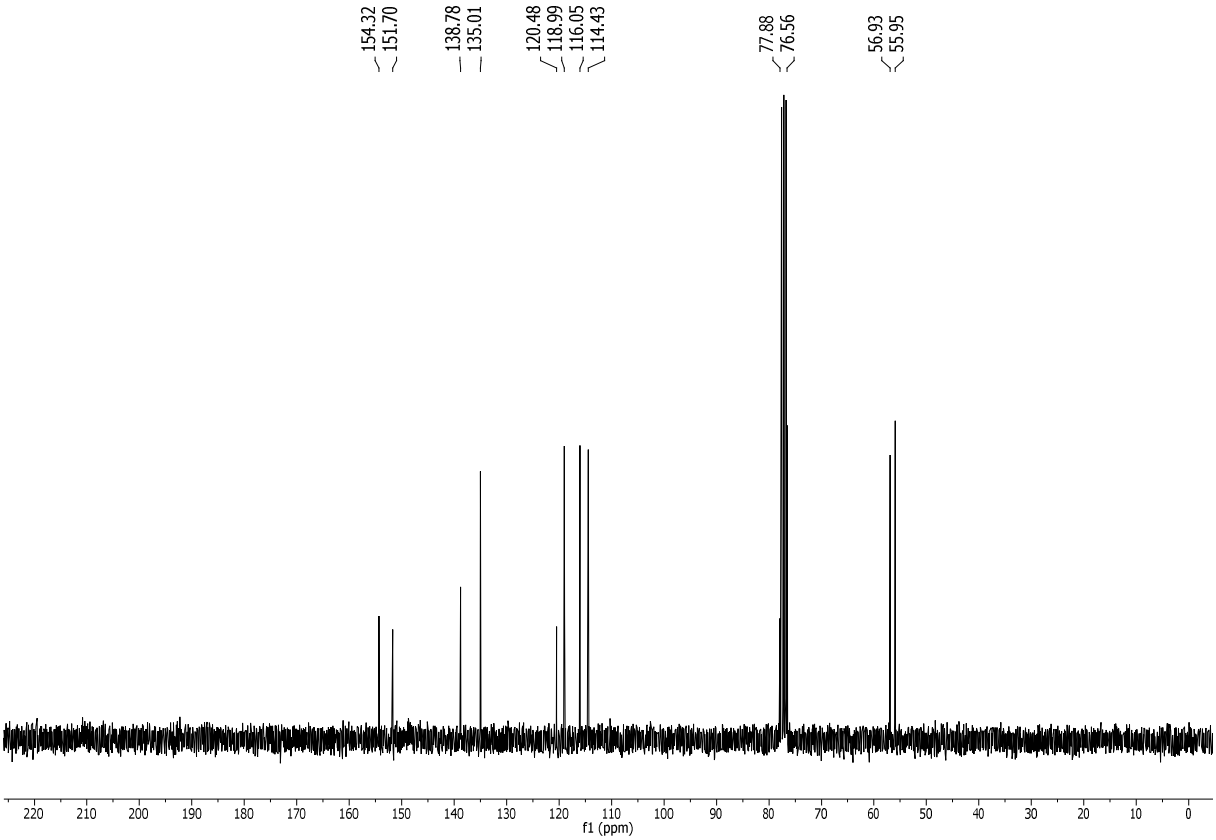
131.52
119.53
112.87
76.58
56.40
20.44
f1 (ppm)


8.16
8.11
7.84
7.80
7.03
7.03
7.02
6.99
6.98
6.98
6.97
6.97
4.79
4.78
3.81
2.57
2.56
2.55
MeO
NO2
O
2r
1.00
1.00
3.00
2.00
3.00
0.98
f1 (ppm)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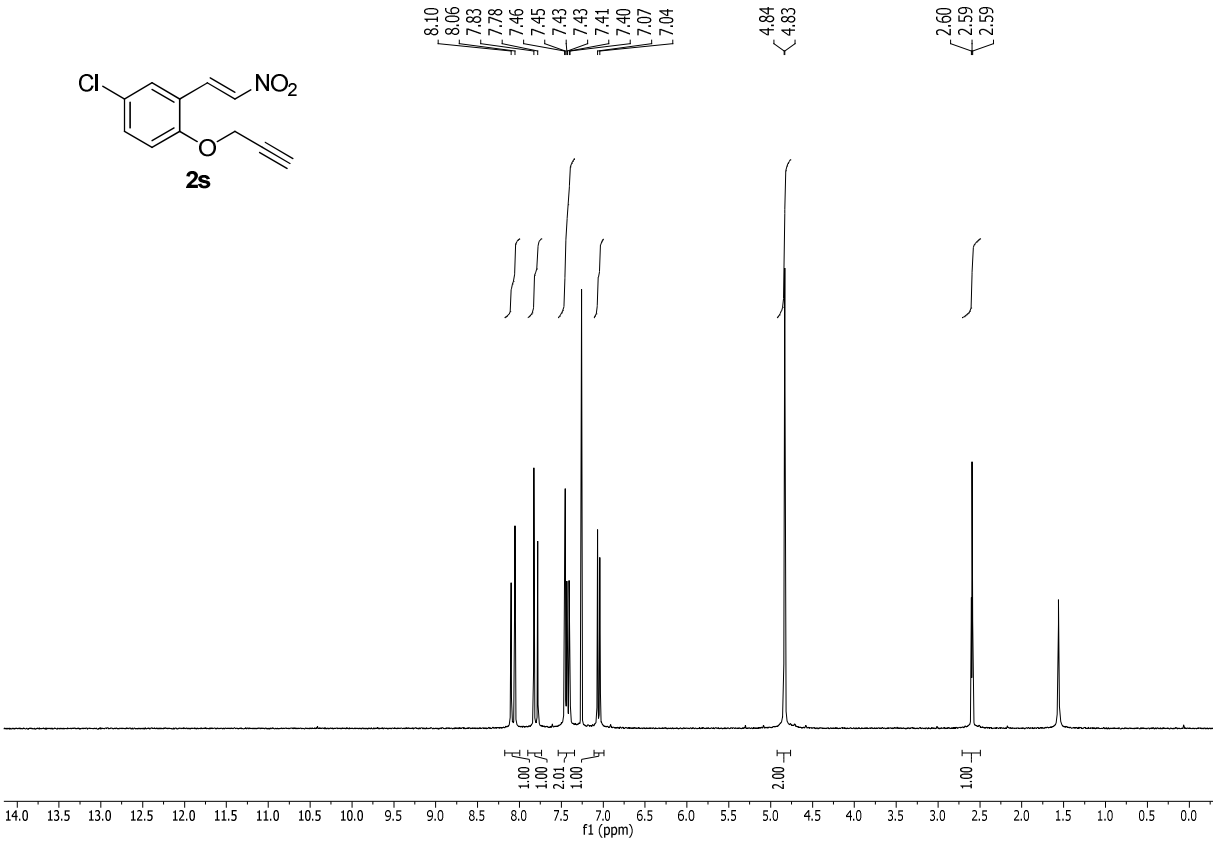
151.70
138.78
135.01
120.48
118.99
116.05
114.43
77.88
76.56
56.93
55.95
f1 (ppm)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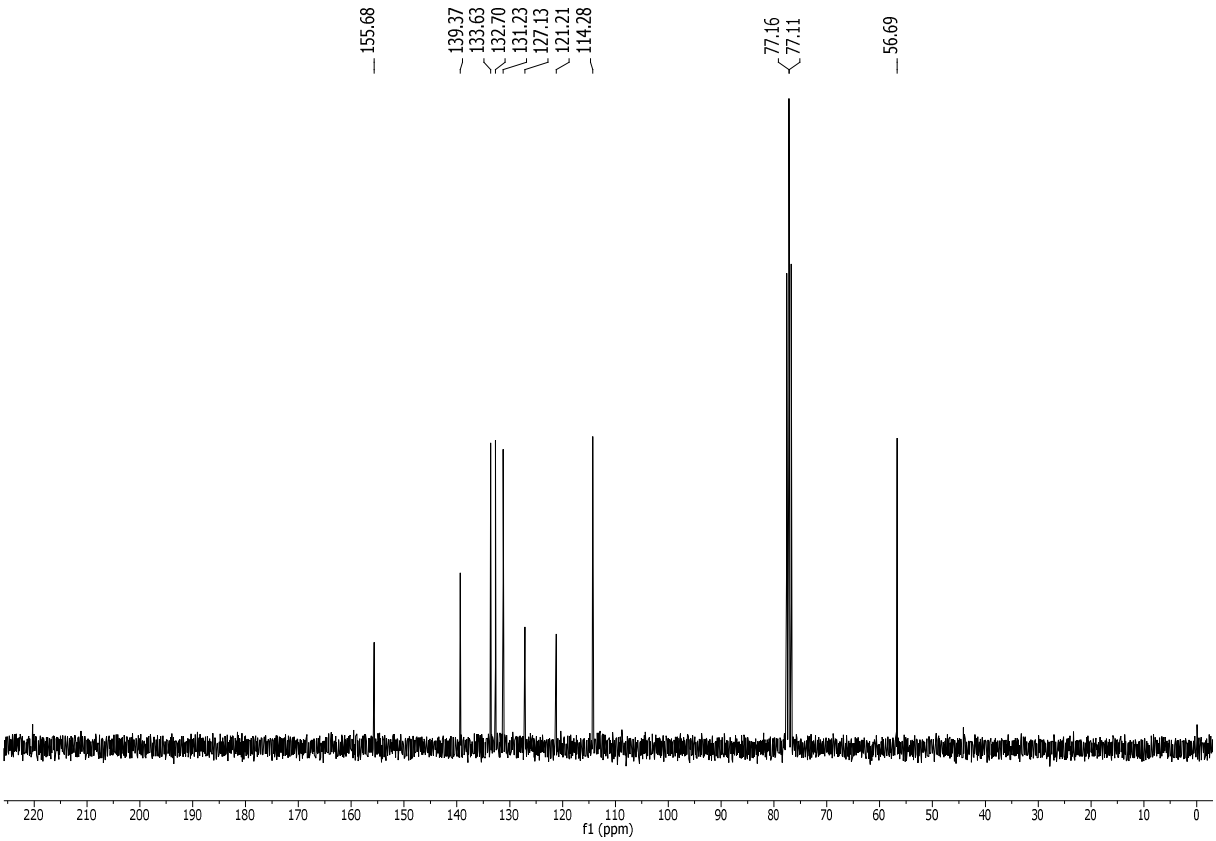
8.06
7.83
7.78
7.46
7.45
7.43
7.43
7.41
7.40
7.07
7.04
4.84
4.83
2.60
2.59
2.59
Cl
NO2
O
2s
1.00
1.00
2.01
1.00
2.00
1.00
f1 (ppm)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139.37
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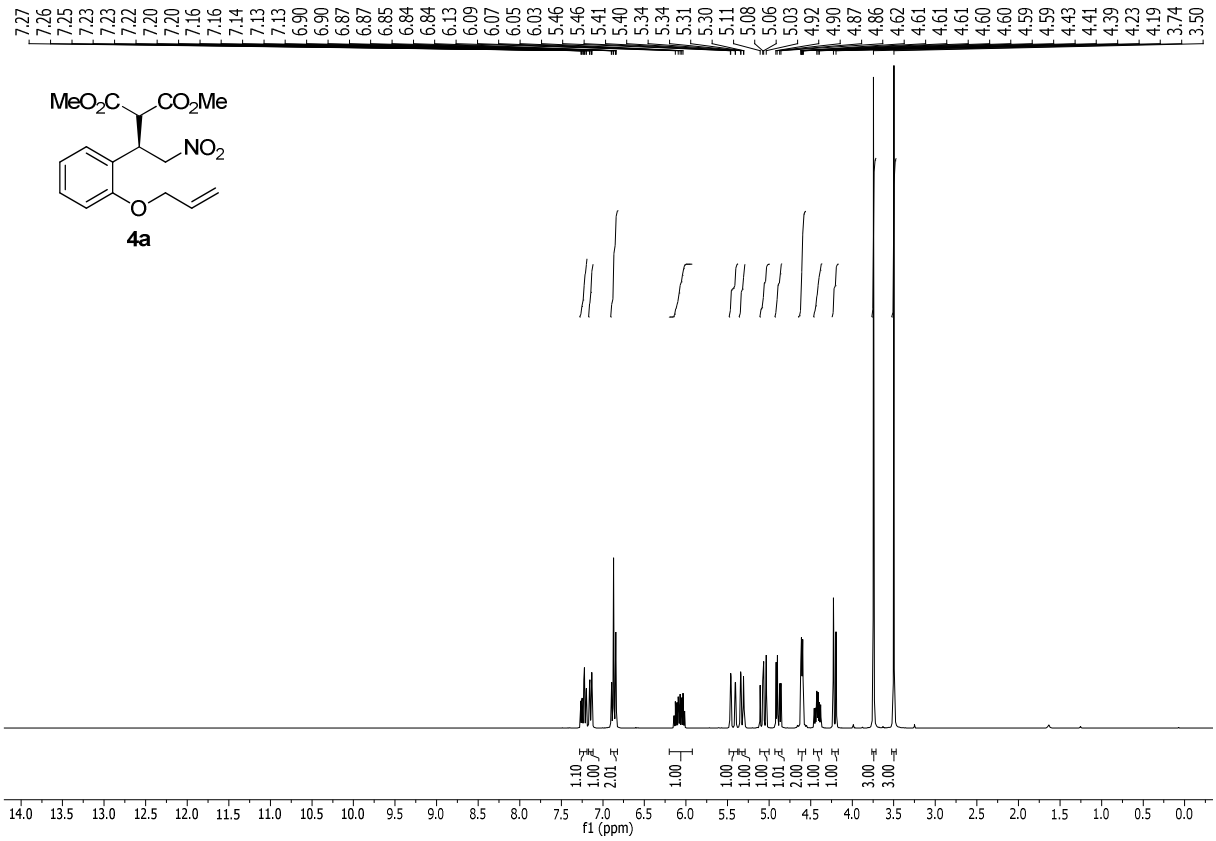
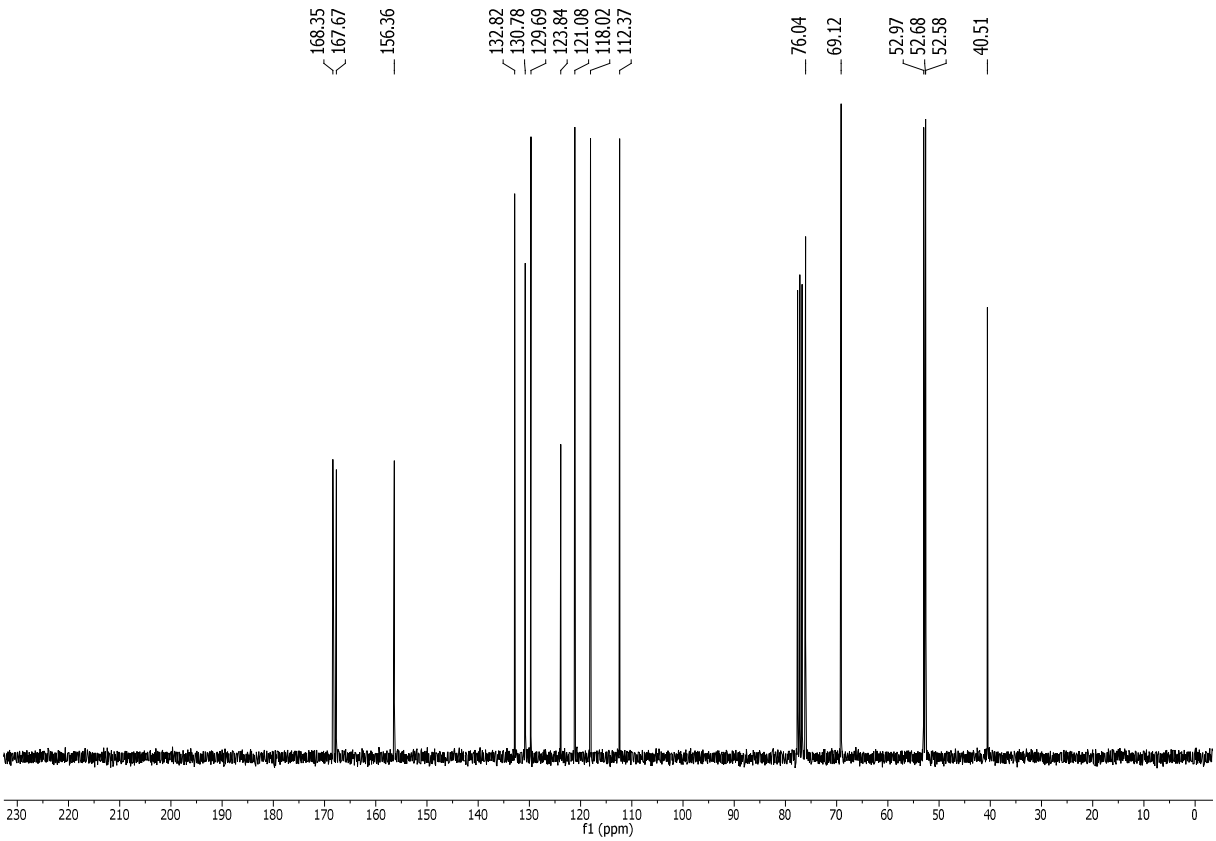
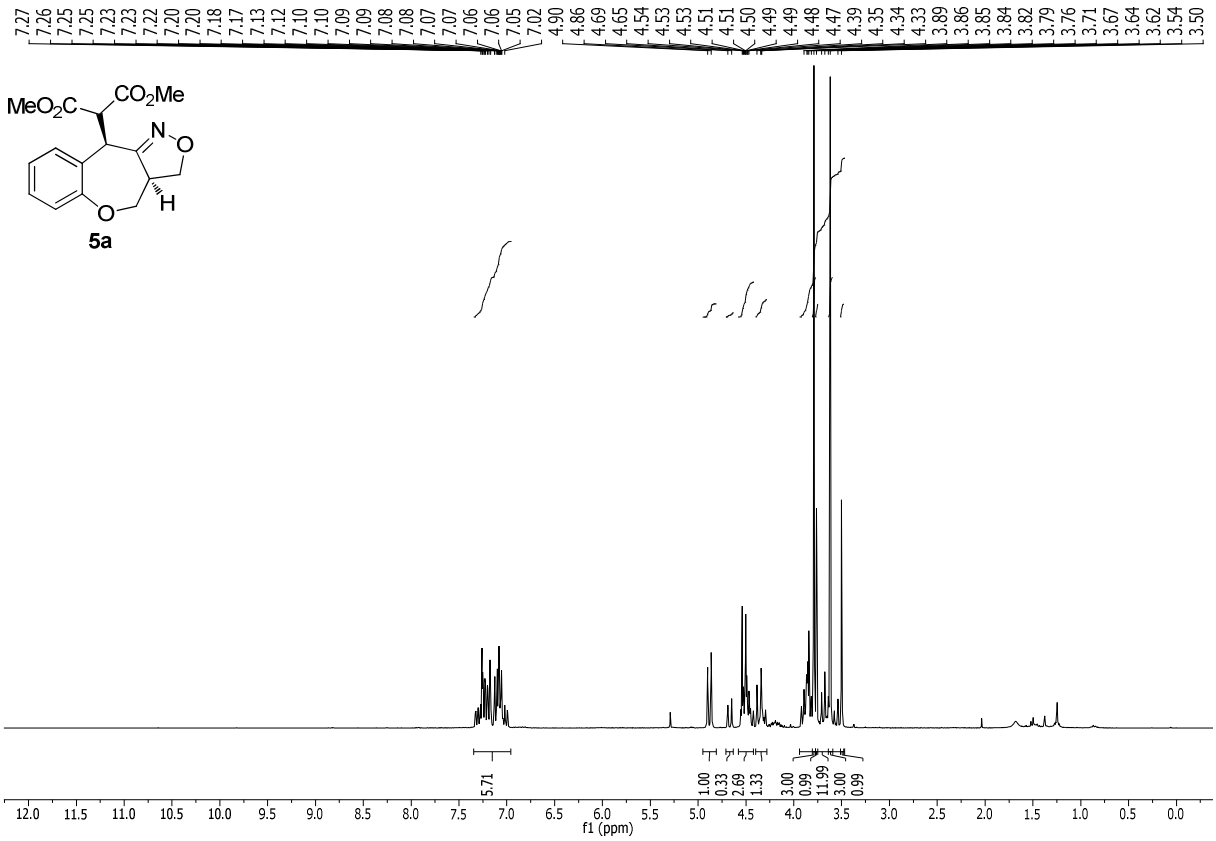
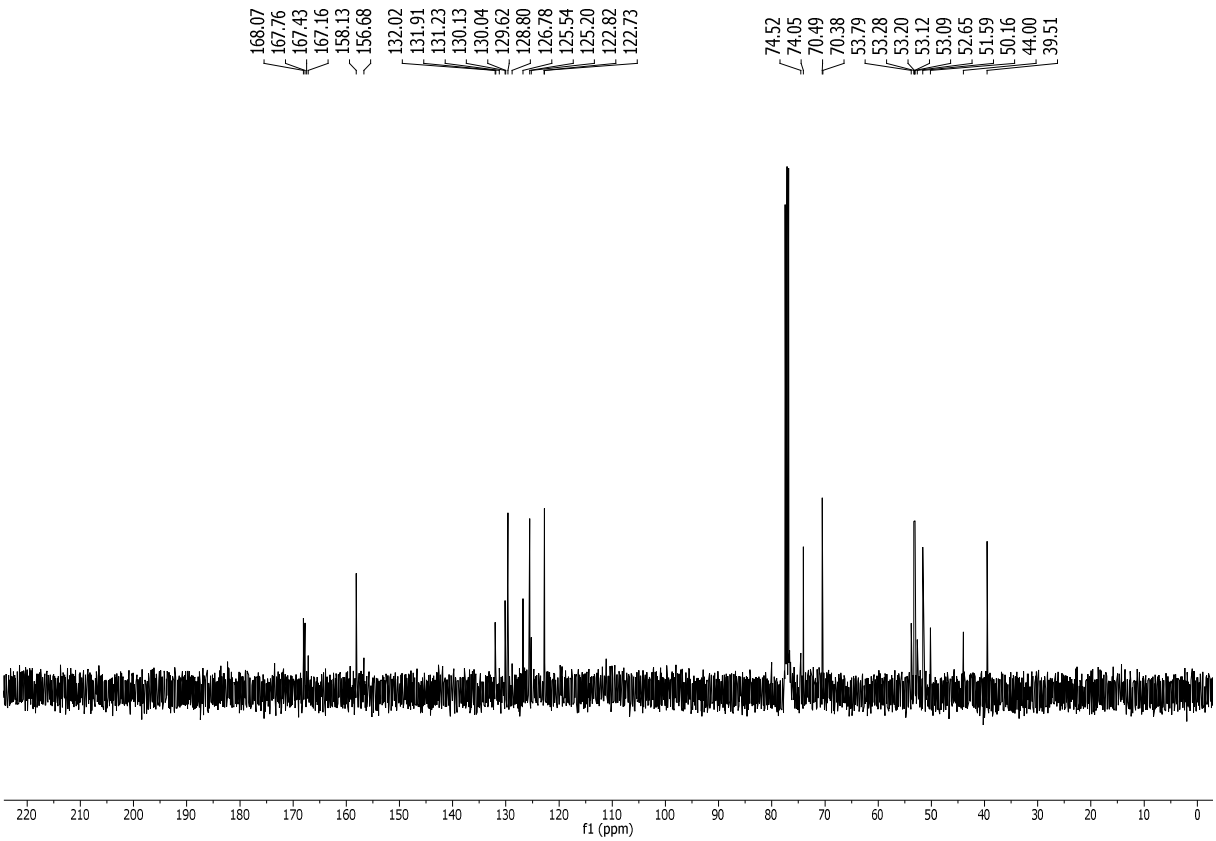
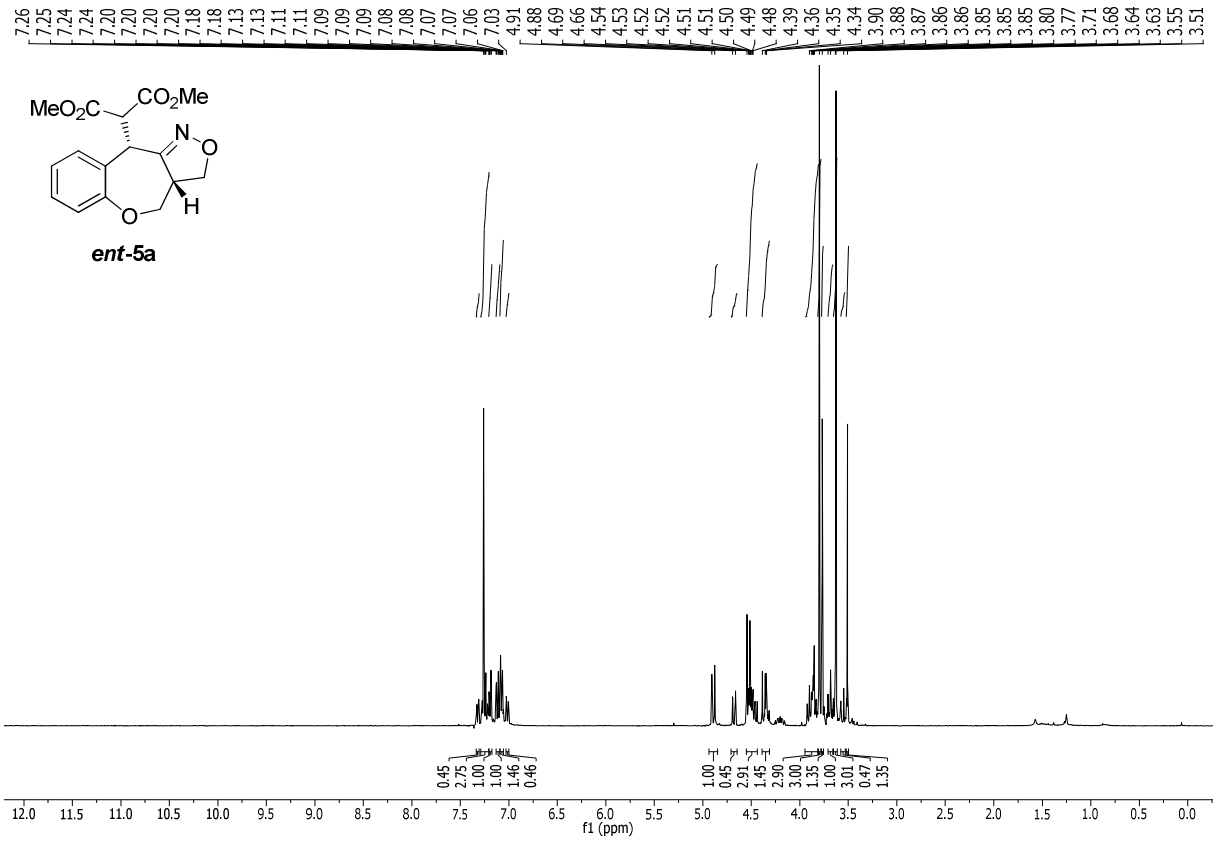
132.70
131.23
127.13
121.21
114.28
77.16
77.11
56.69
f1 (ppm)

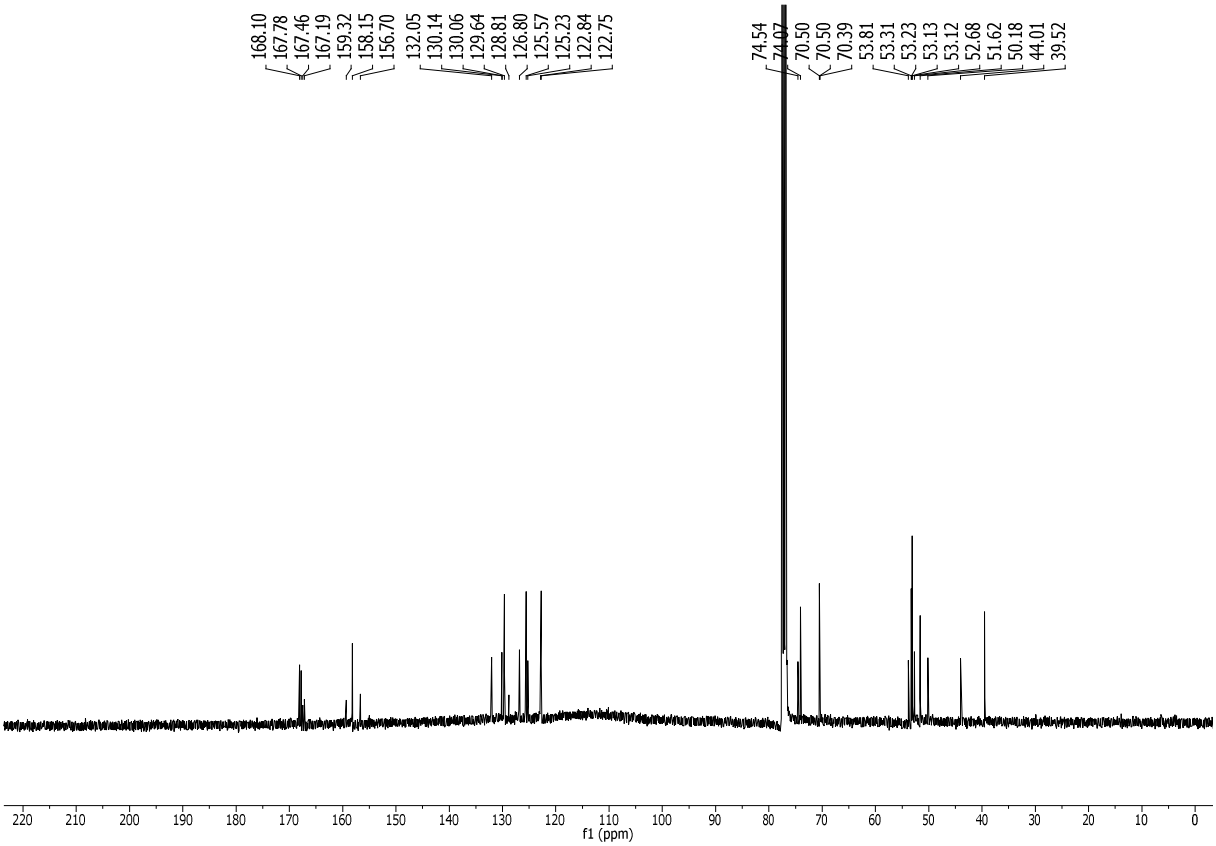

7.27 7.26 7.25 7.23 7.23 7.22 7.20 7.20 7.16 7.16 7.14 7.13 7.13 6.90 6.90 6.87 6.87 6.85 6.84 6.84 6.13 6.09 6.07 6.05 6.03 5.46 5.46 5.41 5.40 5.34 5.34 5.31 5.30 5.11 5.08 5.06 5.03 4.92 4.90 4.87 4.86 4.62 4.61 4.61 4.61 4.60 4.60 4.59 4.59 4.43 4.41 4.39 4.23 4.19 3.74 3.50
MeO2C
CO2Me
NO2
O
4a
1.10 1.00 2.01 1.00 1.00 1.00 1.00 1.01 2.00 1.00 1.00 3.00 3.00
14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

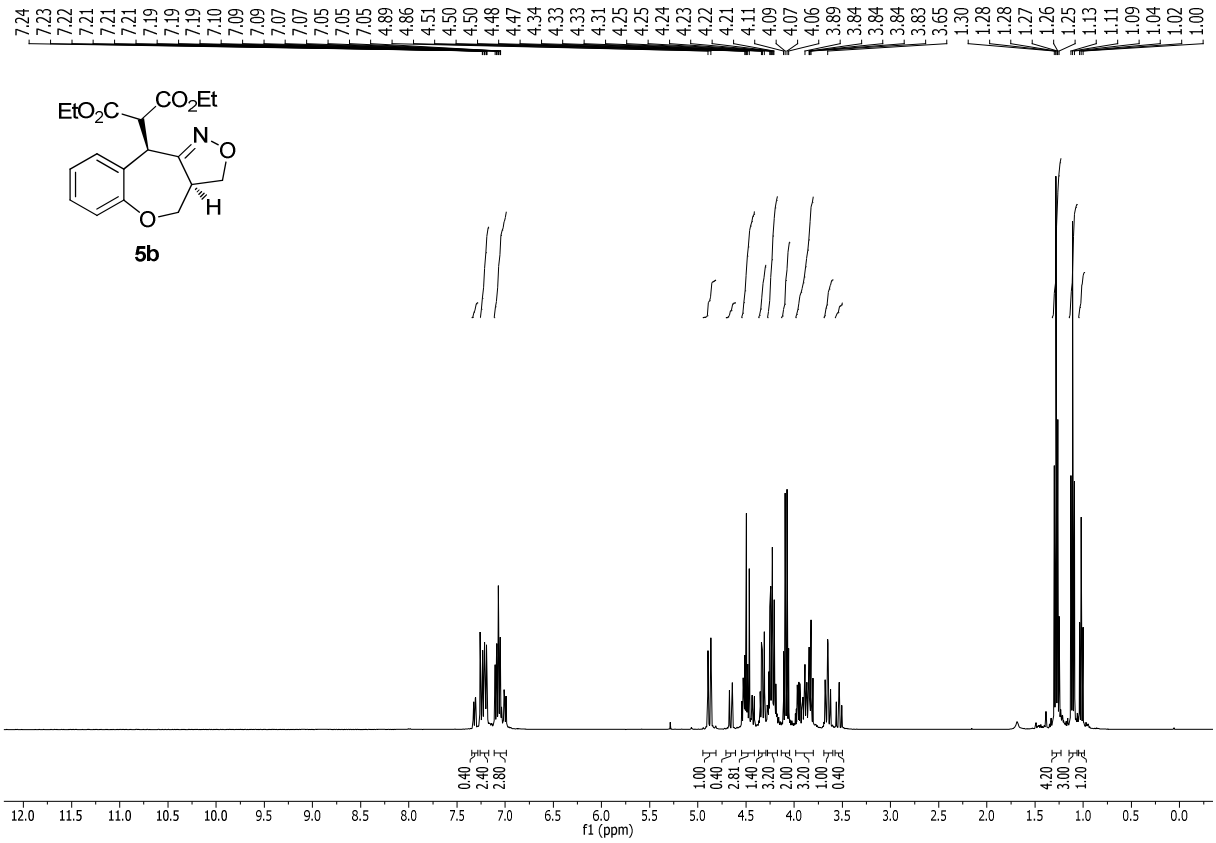

168.35 167.67 156.36 132.82 130.78 129.69 123.84 121.08 118.02 112.37 76.04 69.12 52.97 52.68 52.58 40.51
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

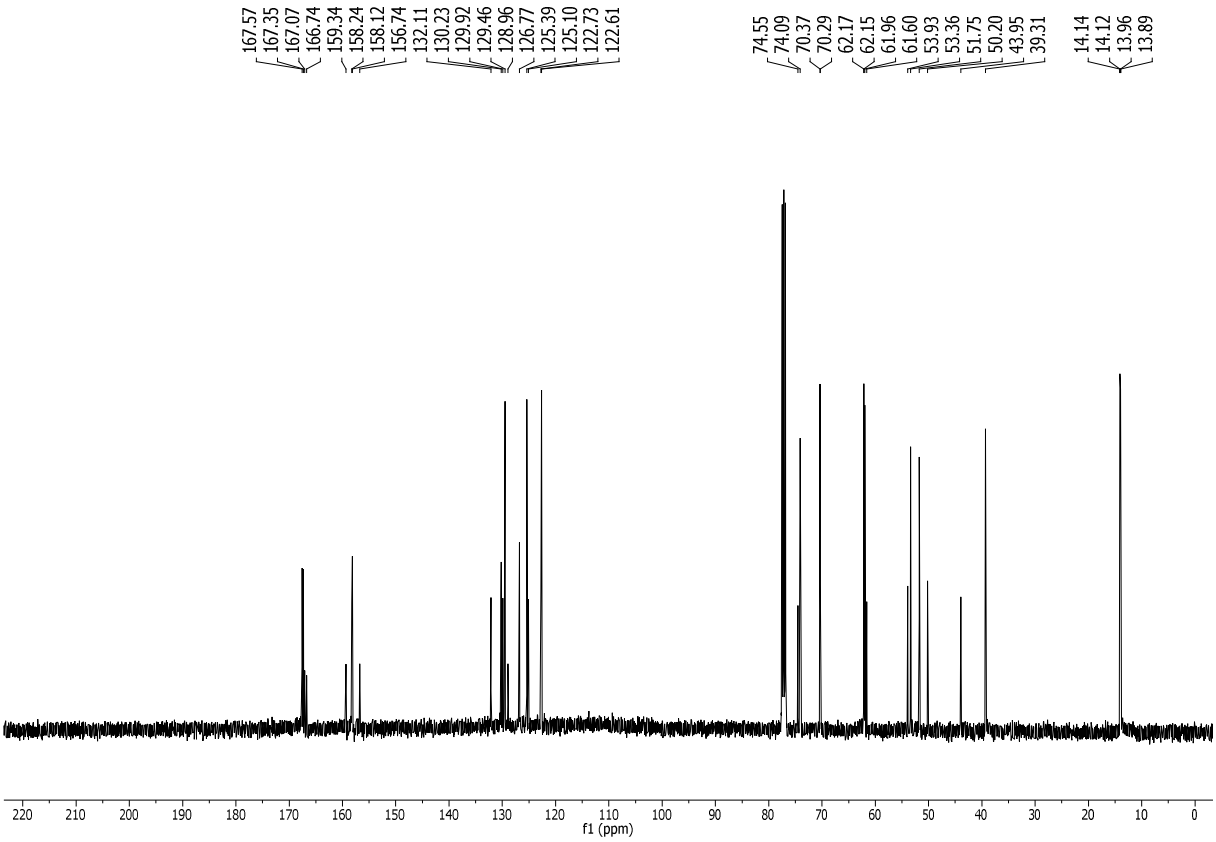

7.27 7.26 7.25 7.25 7.23 7.23 7.22 7.20 7.20 7.18 7.17 7.13 7.12 7.10 7.10 7.09 7.09 7.08 7.08 7.07 7.07 7.06 7.06 7.05 7.02 4.90 4.86 4.69 4.65 4.54 4.53 4.53 4.51 4.51 4.50 4.49 4.49 4.48 4.47 4.39 4.35 4.34 4.33 3.89 3.86 3.85 3.84 3.82 3.79 3.76 3.71 3.67 3.64 3.62 3.54 3.50
MeO2C
CO2Me
N
O
O
H
5a
5.71
1.00
0.33
2.69
1.33
3.00
0.99
11.99
3.00
0.99
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


168.07 167.76 167.43 167.16 158.13 156.68 132.02 131.91 131.23 130.13 130.04 129.62 128.80 126.78 125.54 125.20 122.82 122.73
74.52 74.05 70.49 70.38 53.79 53.28 53.20 53.12 53.09 52.65 51.59 50.16 44.00 39.51
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)






7.24 7.23 7.22 7.21 7.21 7.21 7.19 7.19 7.19 7.10 7.09 7.09 7.07 7.07 7.05 7.05 7.05 4.89 4.86 4.51 4.50 4.50 4.48 4.47 4.34 4.33 4.33 4.31 4.25 4.25 4.24 4.23 4.22 4.21 4.11 4.09 4.07 4.06 3.89 3.84 3.84 3.84 3.83 3.65 1.30 1.28 1.28 1.27 1.26 1.25 1.13 1.11 1.09 1.04 1.02 1.00
EtO2C
CO2Et
N
O
O
H
5b
0.40 2.40 2.80
1.00 0.40 2.81 1.40 3.20 2.00 3.20 1.00 0.40
4.20 3.00 1.20
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


167.57 167.35 167.07 166.74 159.34 158.24 158.12 156.74 132.11 130.23 129.92 129.46 128.96 126.77 125.39 125.10 122.73 122.61
74.55 74.09 70.37 70.29 62.17 62.15 61.96 61.60 53.93 53.36 51.75 50.20 43.95 39.31
14.14 14.12 13.96 13.89
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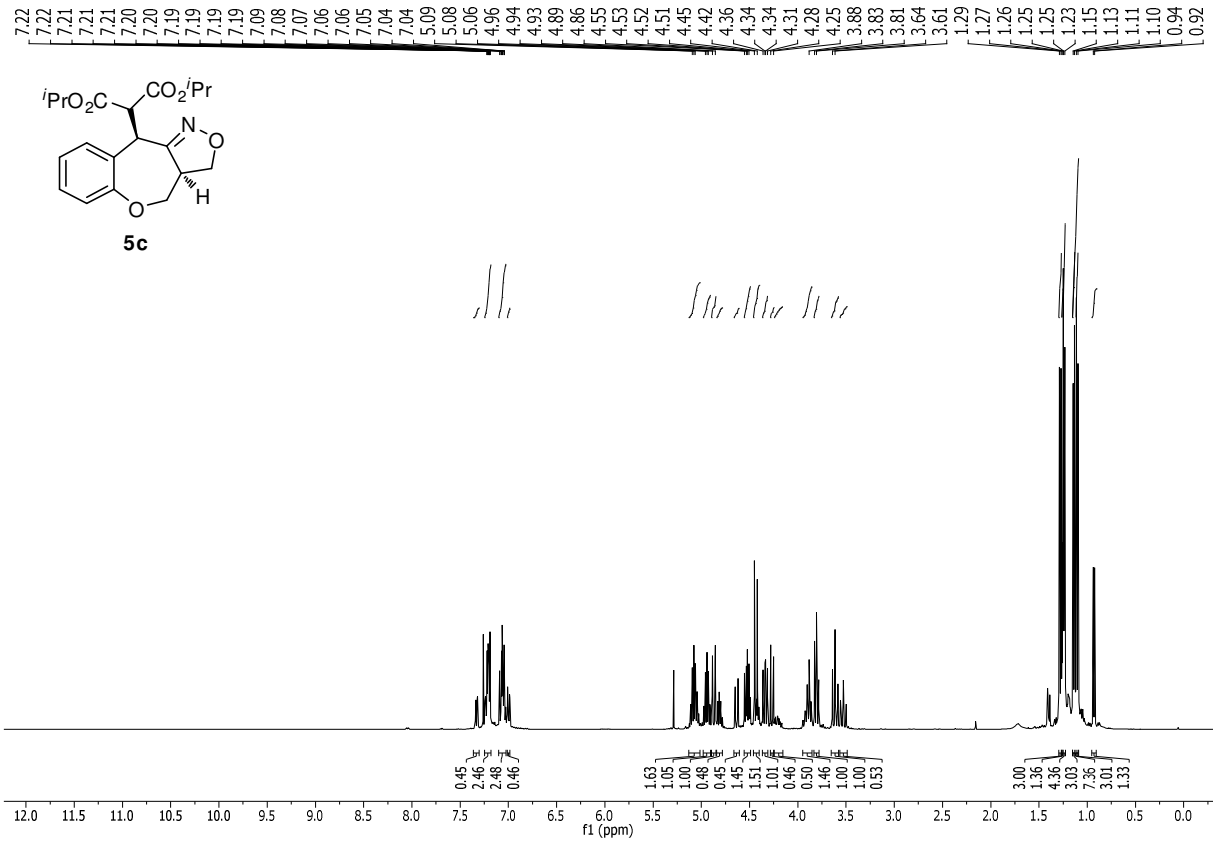
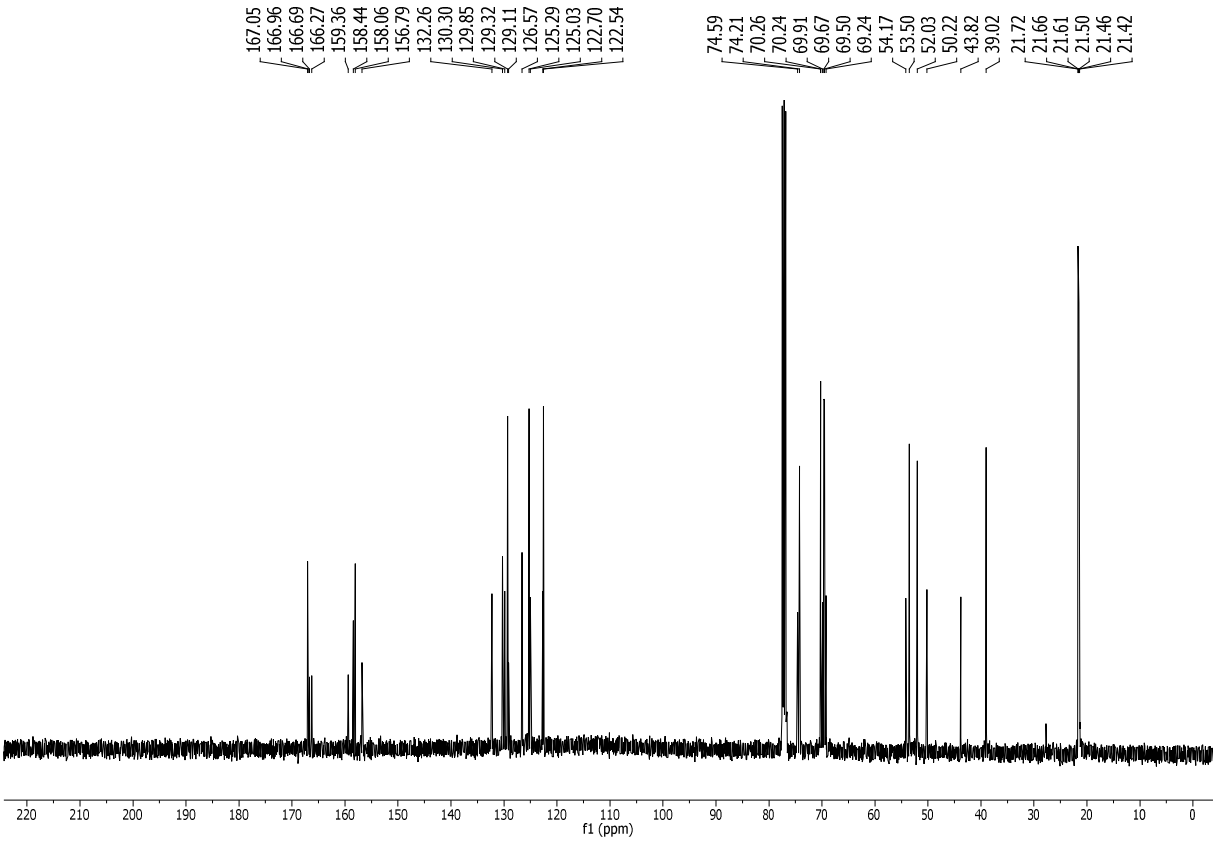
f1 (ppm)


7.22 7.22 7.21 7.21 7.21 7.20 7.20 7.19 7.19 7.19 7.19 7.09 7.08 7.07 7.06 7.06 7.05 7.04 7.04 5.09 5.08 5.06 4.96 4.94 4.93 4.89 4.86 4.55 4.53 4.52 4.51 4.45 4.42 4.36 4.34 4.34 4.31 4.28 4.25 3.88 3.83 3.81 3.64 3.61 1.29 1.27 1.26 1.25 1.25 1.23 1.15 1.13 1.11 1.10 0.94 0.92
iPrO2C
CO2iPr
N
O
H
O
5c
0.45 2.46 2.48 0.46 1.63 1.05 1.00 0.48 0.45 1.45 1.51 1.01 0.46 0.50 1.46 1.00 1.00 0.53 3.00 1.36 4.36 3.03 7.36 3.01 1.33
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


167.05 166.96 166.69 166.27 159.36 158.44 158.06 156.79 132.26 130.30 129.85 129.32 129.11 126.57 125.29 125.03 122.70 122.54
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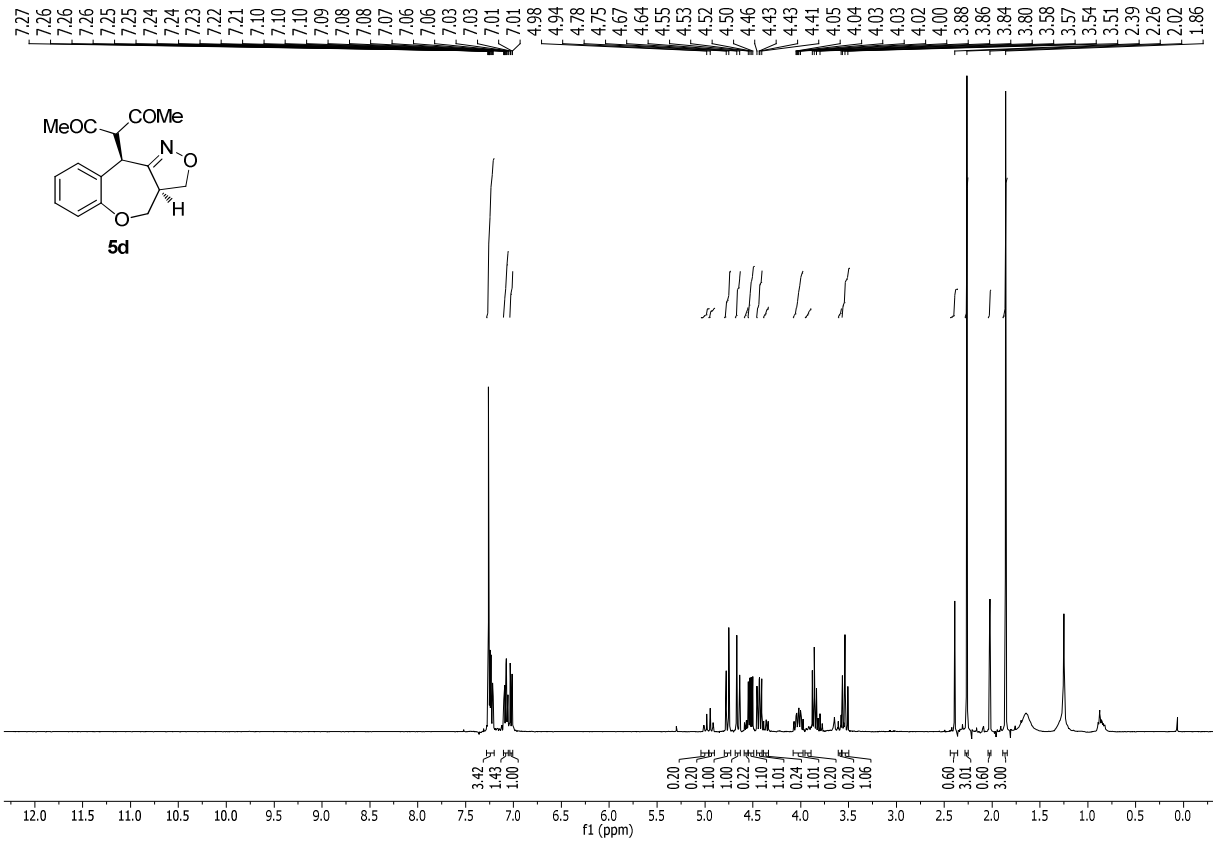
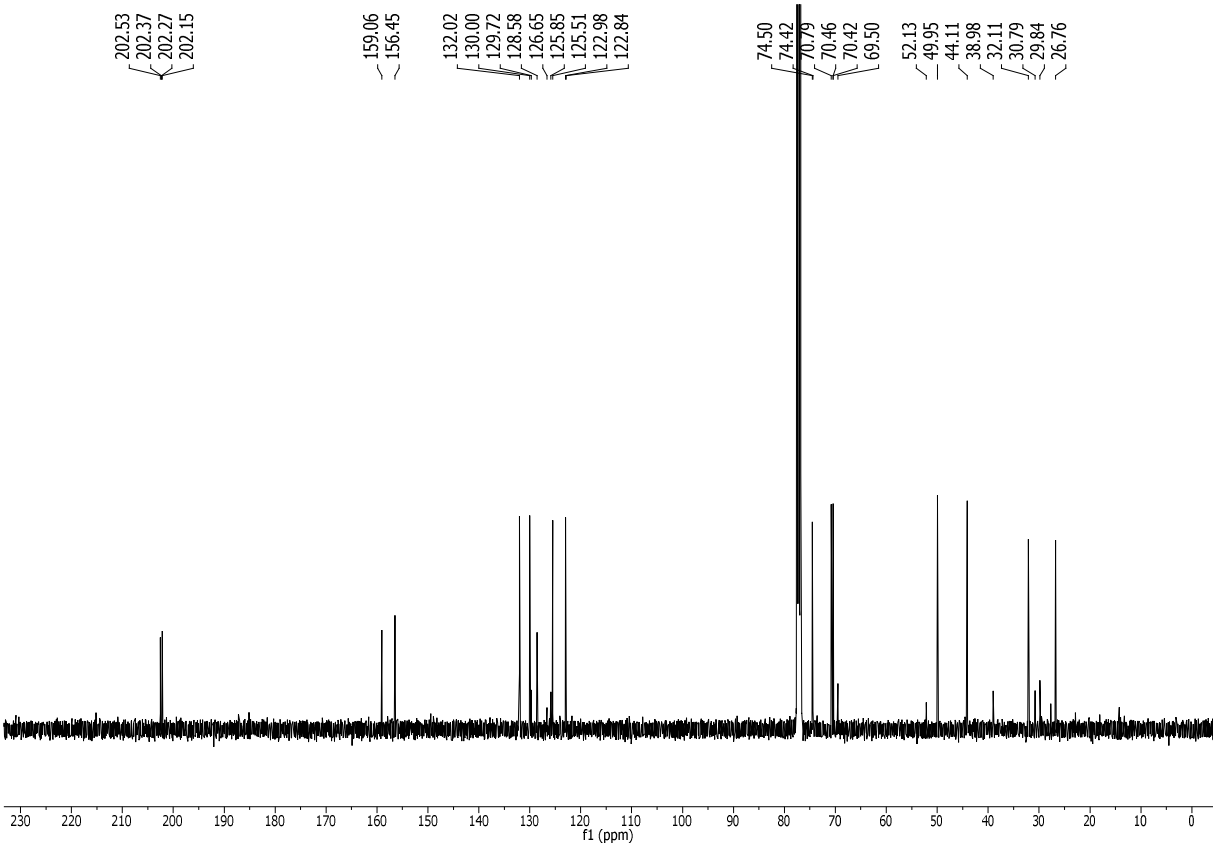
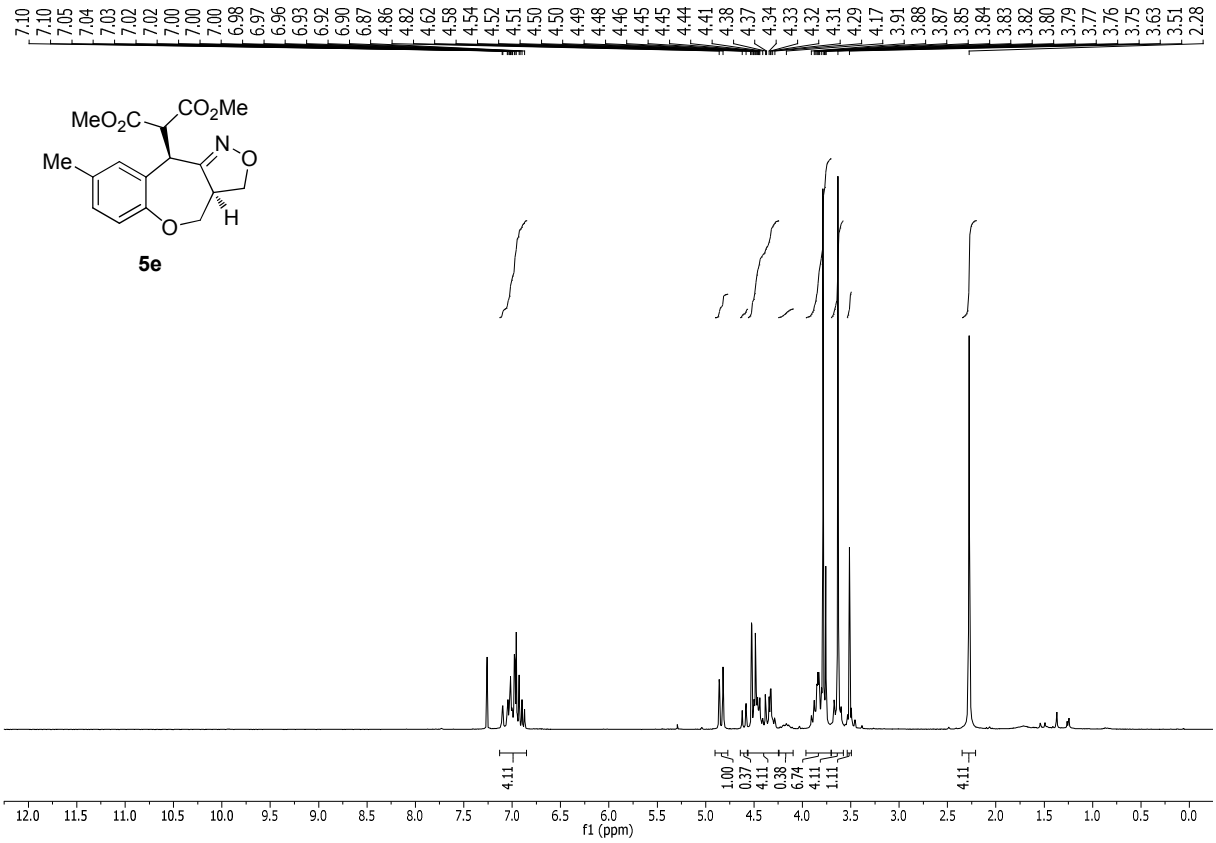
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


MeOC
COMe
N
O
O
H
5d
f1 (ppm)


f1 (ppm)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7.04
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7.02
7.02
7.00
7.00
7.00
6.98
6.97
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6.93
6.92
6.90
6.87
4.86
4.82
4.62
4.58
4.54
4.52
4.51
4.50
4.50
4.49
4.48
4.46
4.45
4.45
4.44
4.41
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4.34
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4.31
4.29
4.17
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3.87
3.85
3.84
3.83
3.82
3.80
3.79
3.77
3.76
3.75
3.63
3.51
2.28
MeO2C
CO2Me
N
O
Me
O
H
5e
4.11
1.00
0.37
4.11
0.38
6.74
4.11
1.11
4.11
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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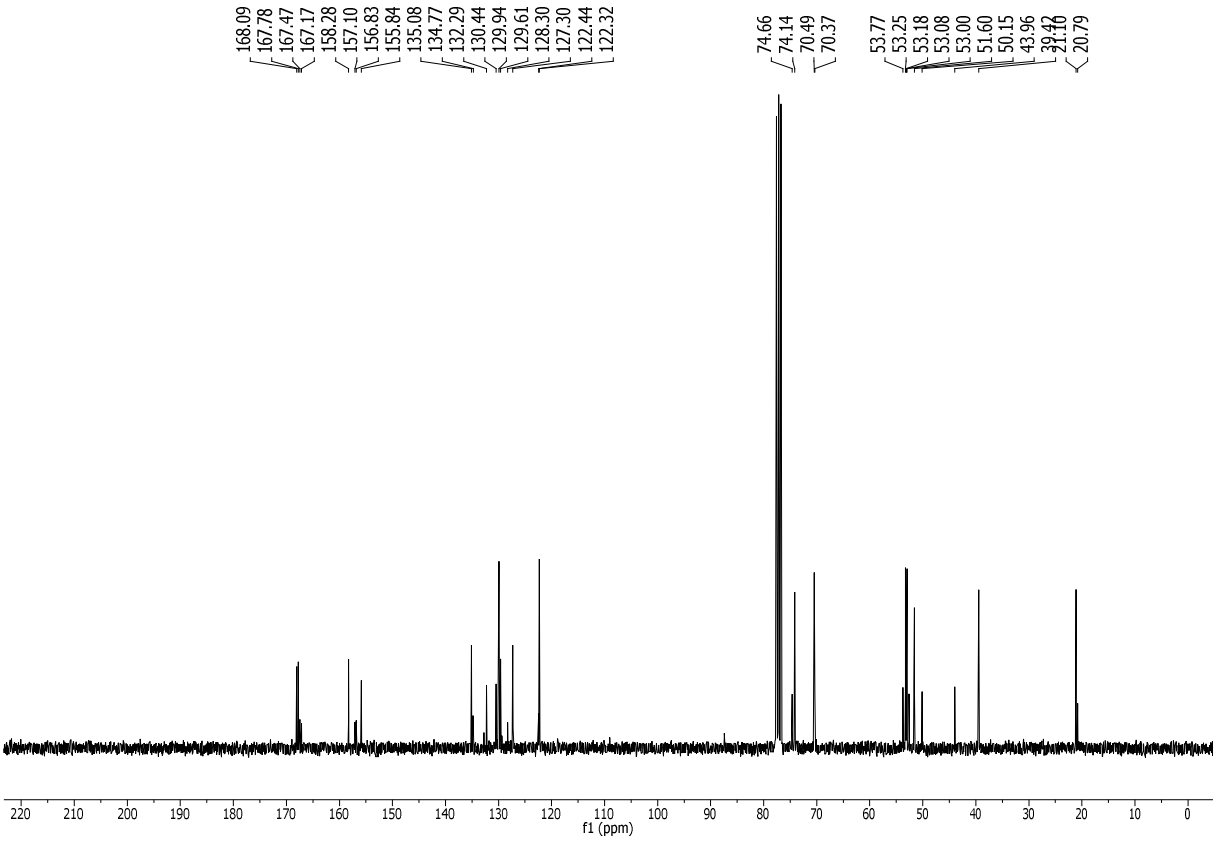
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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157.10
156.83
155.84
135.08
134.77
132.29
130.44
129.94
129.61
128.30
127.30
122.44
122.32
74.66
74.14
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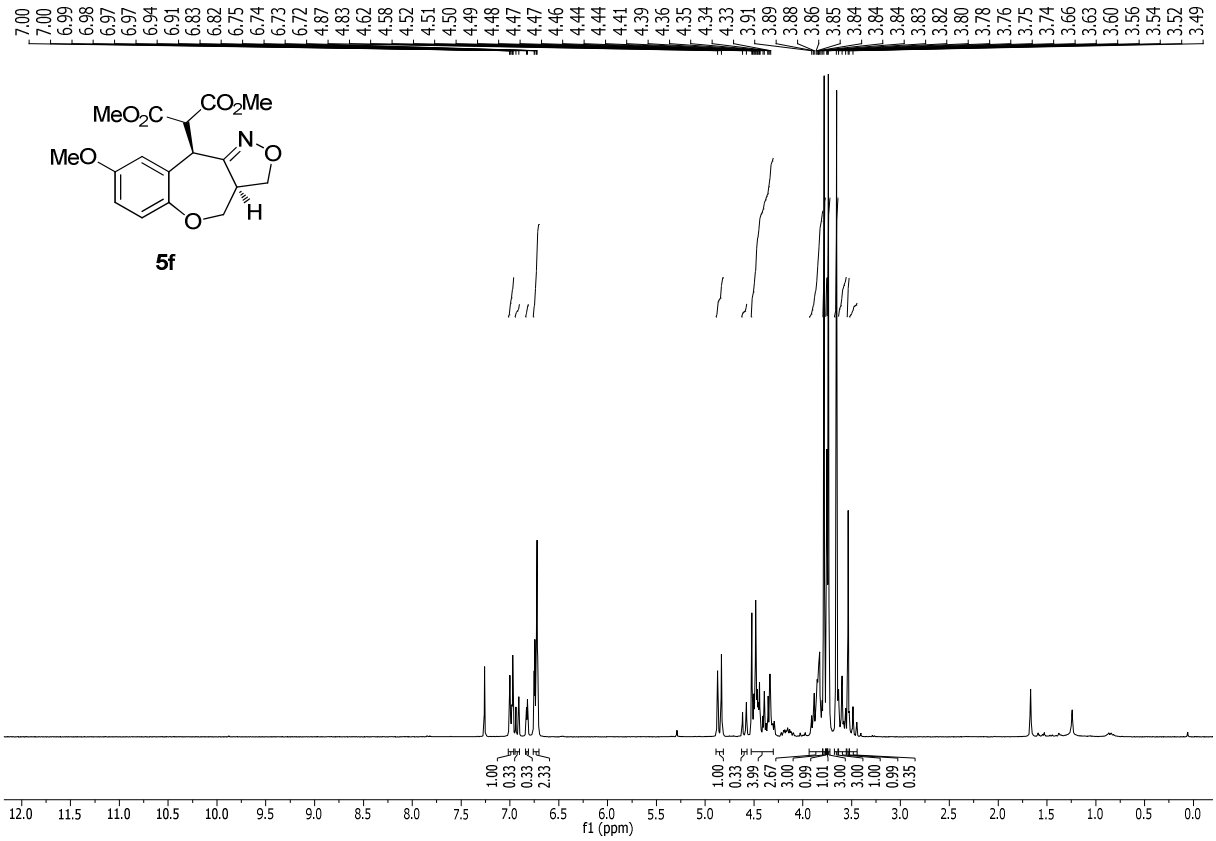
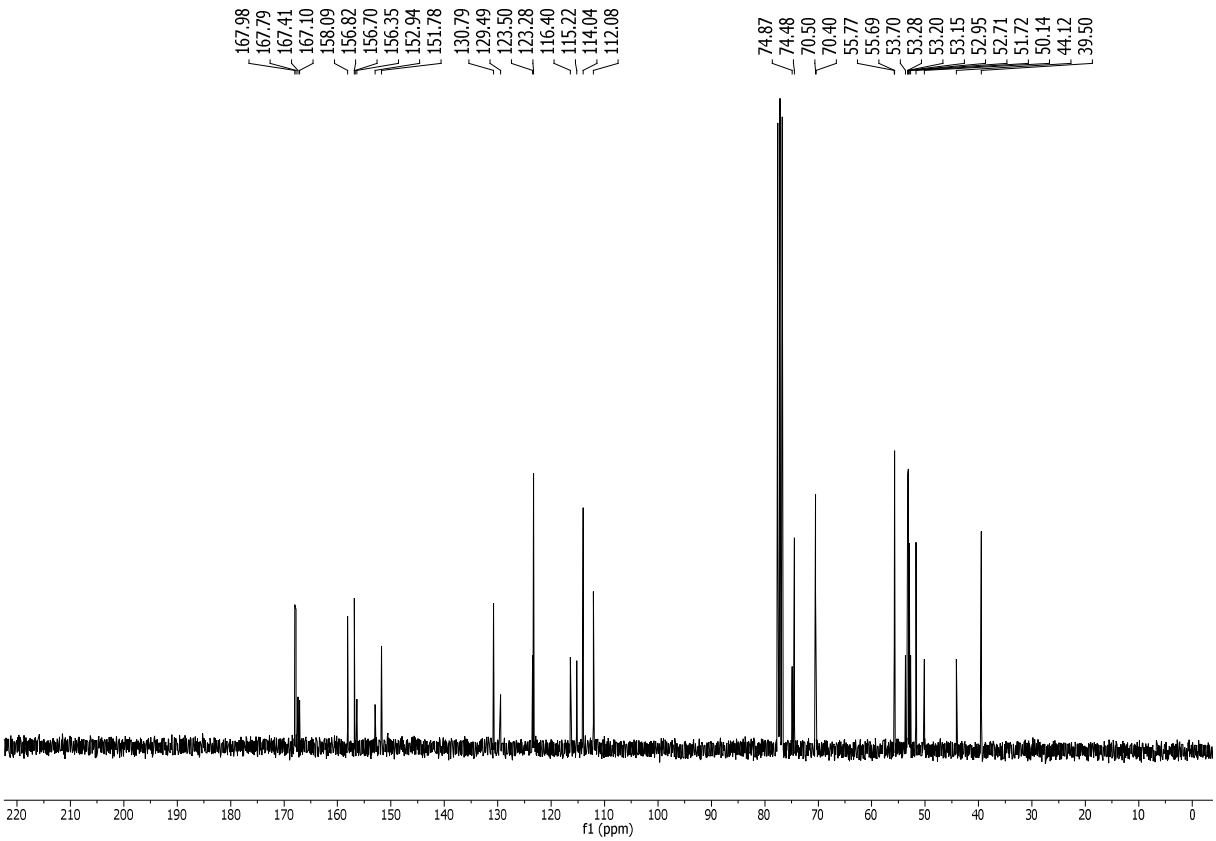
70.37
53.77
53.25
53.18
53.08
53.00
51.60
50.15
43.96
39.42
21.10
20.79
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


MeO2C
CO2Me
MeO
N
O
O
H
5f
f1 (ppm)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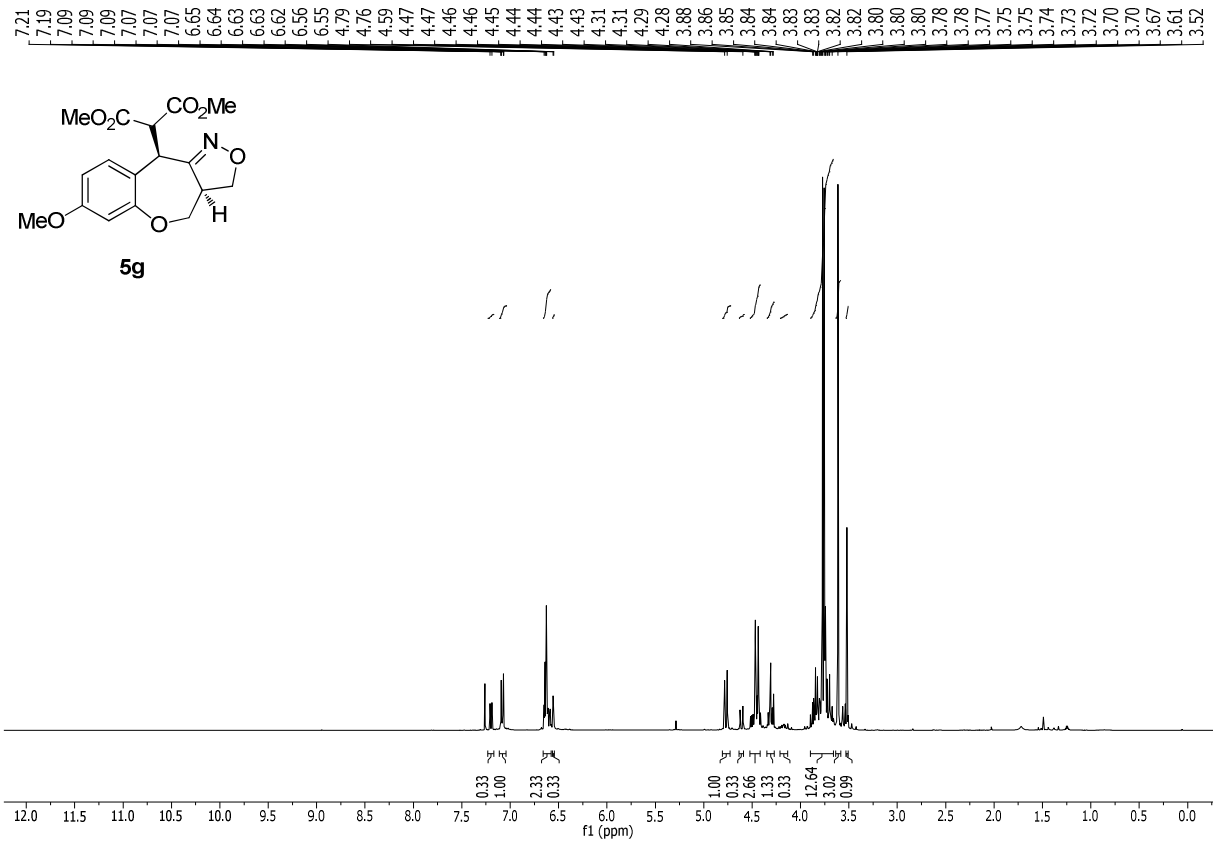
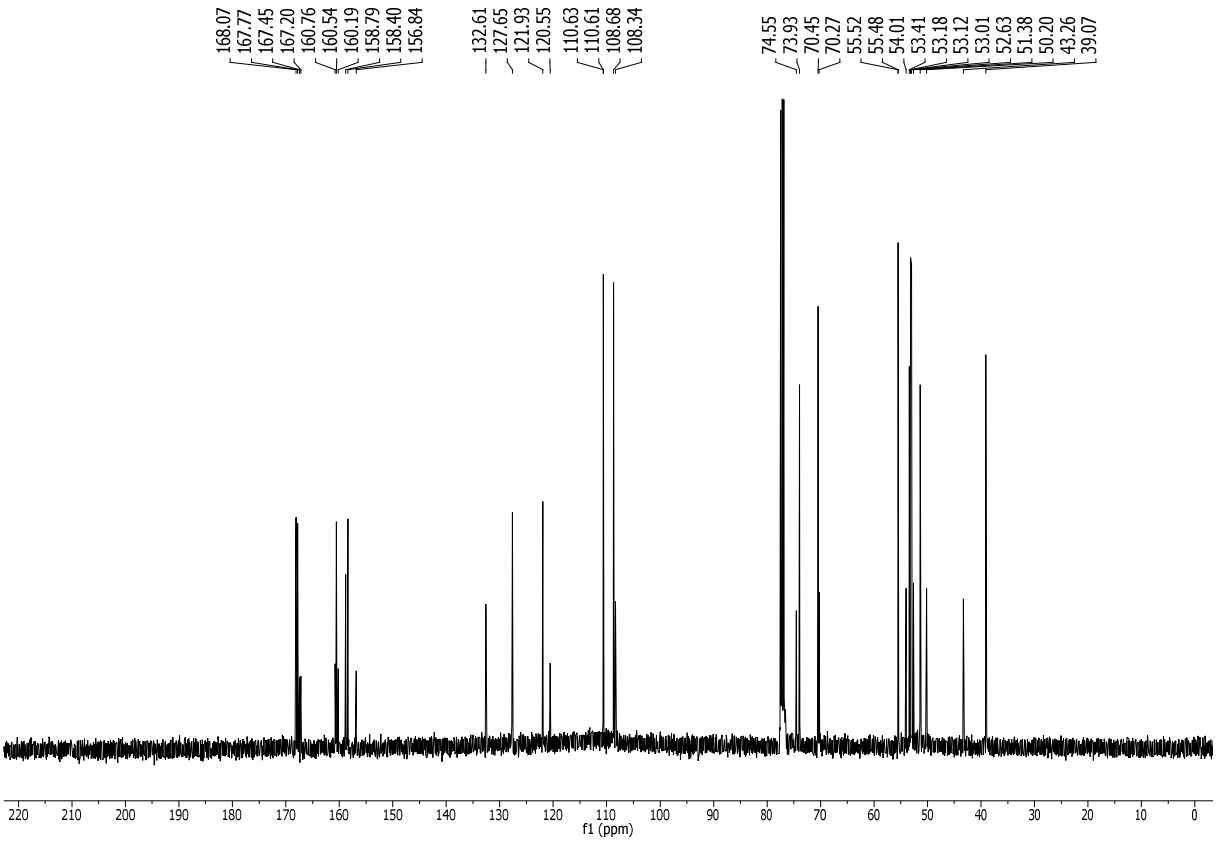
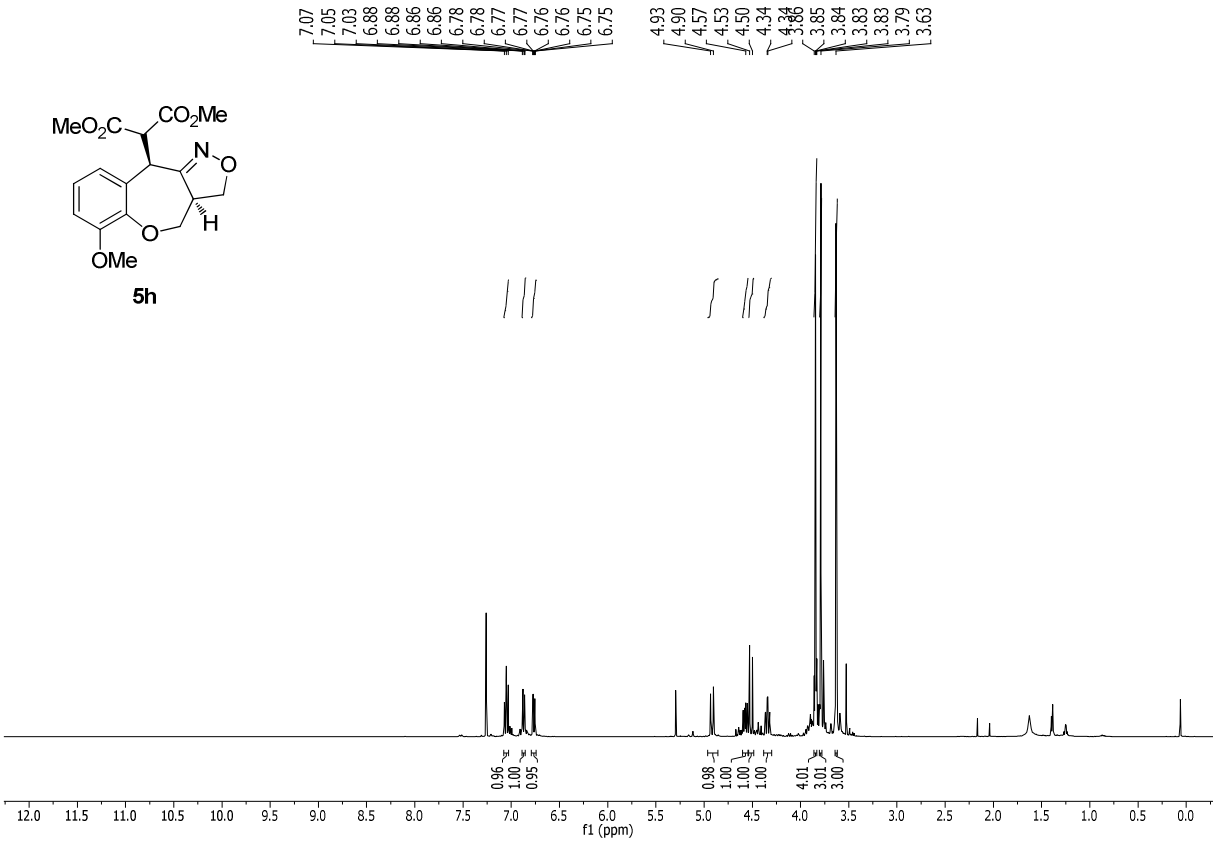
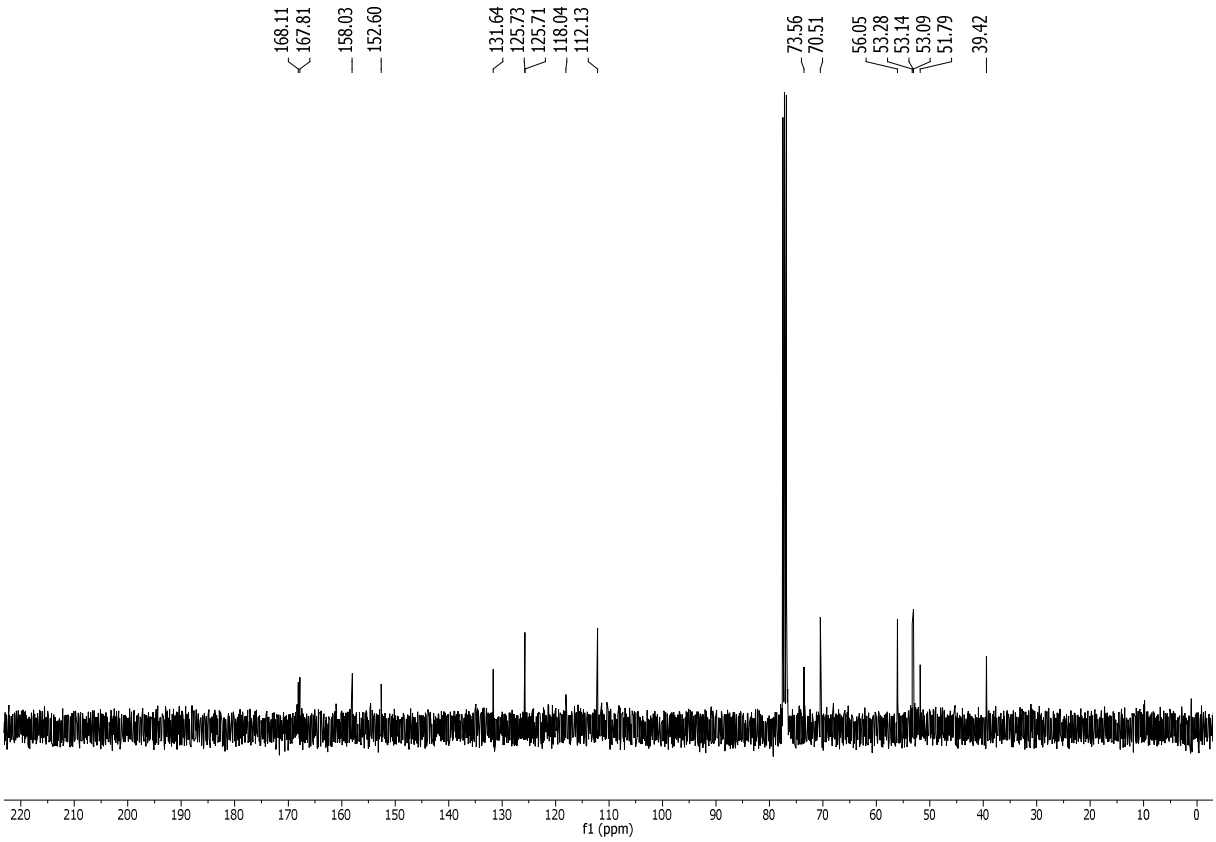
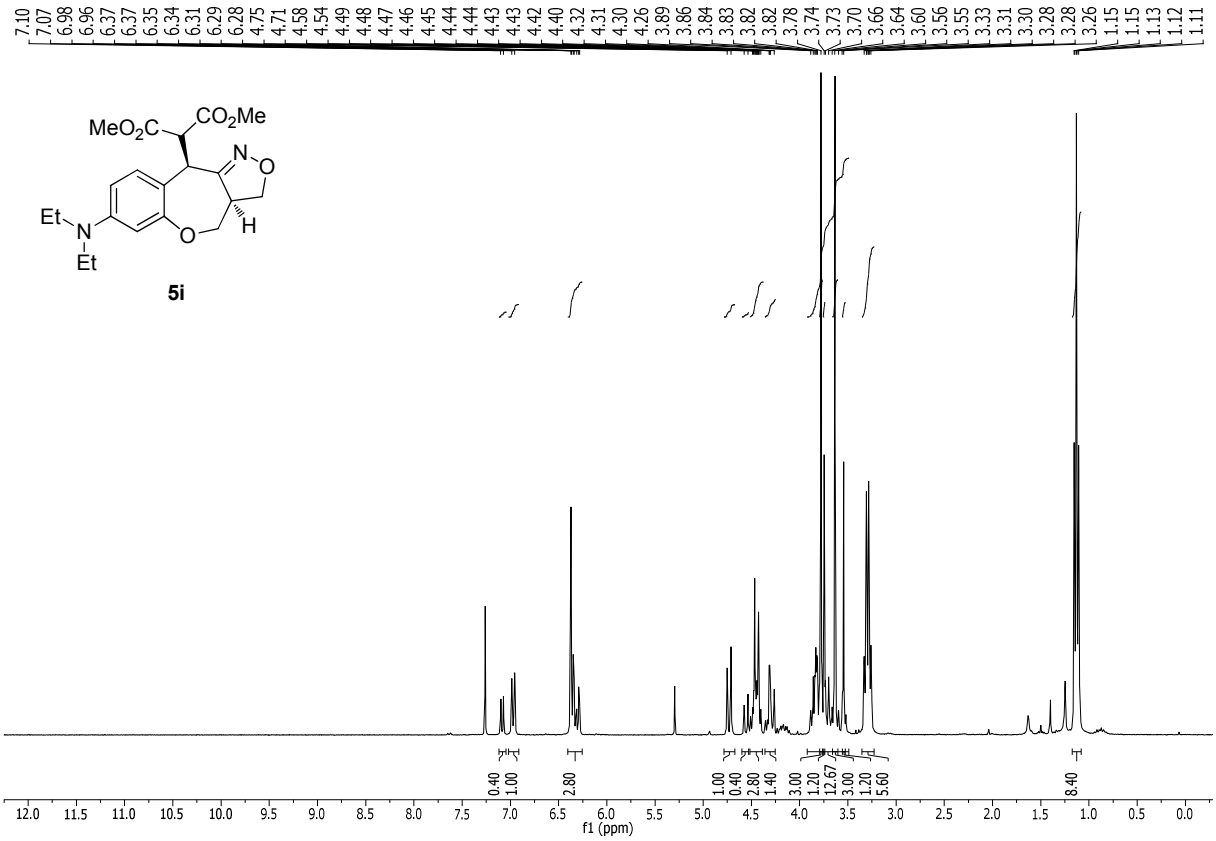
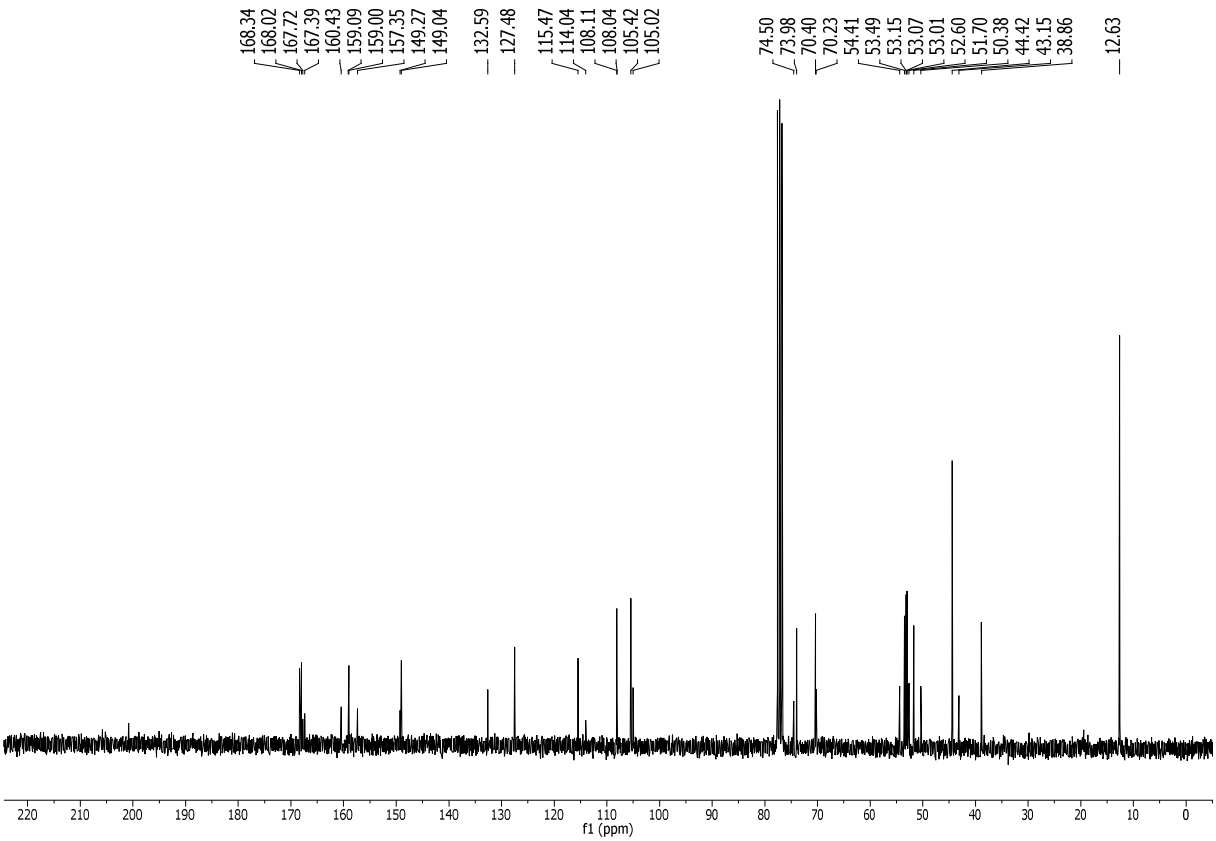

7.21 7.19 7.09 7.09 7.09 7.07 7.07 7.07 6.65 6.64 6.63 6.63 6.62 6.56 6.55 4.79 4.76 4.59 4.47 4.47 4.46 4.46 4.45 4.44 4.44 4.43 4.43 4.31 4.31 4.29 4.28 3.88 3.86 3.85 3.84 3.84 3.83 3.83 3.82 3.82 3.80 3.80 3.80 3.78 3.78 3.77 3.75 3.75 3.74 3.73 3.72 3.70 3.70 3.67 3.61 3.52
MeO2C
CO2Me
N
O
MeO
O
H
5g
0.33 1.00 2.33 0.33 1.00 0.33 2.66 1.33 0.33 12.64 3.02 0.99
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

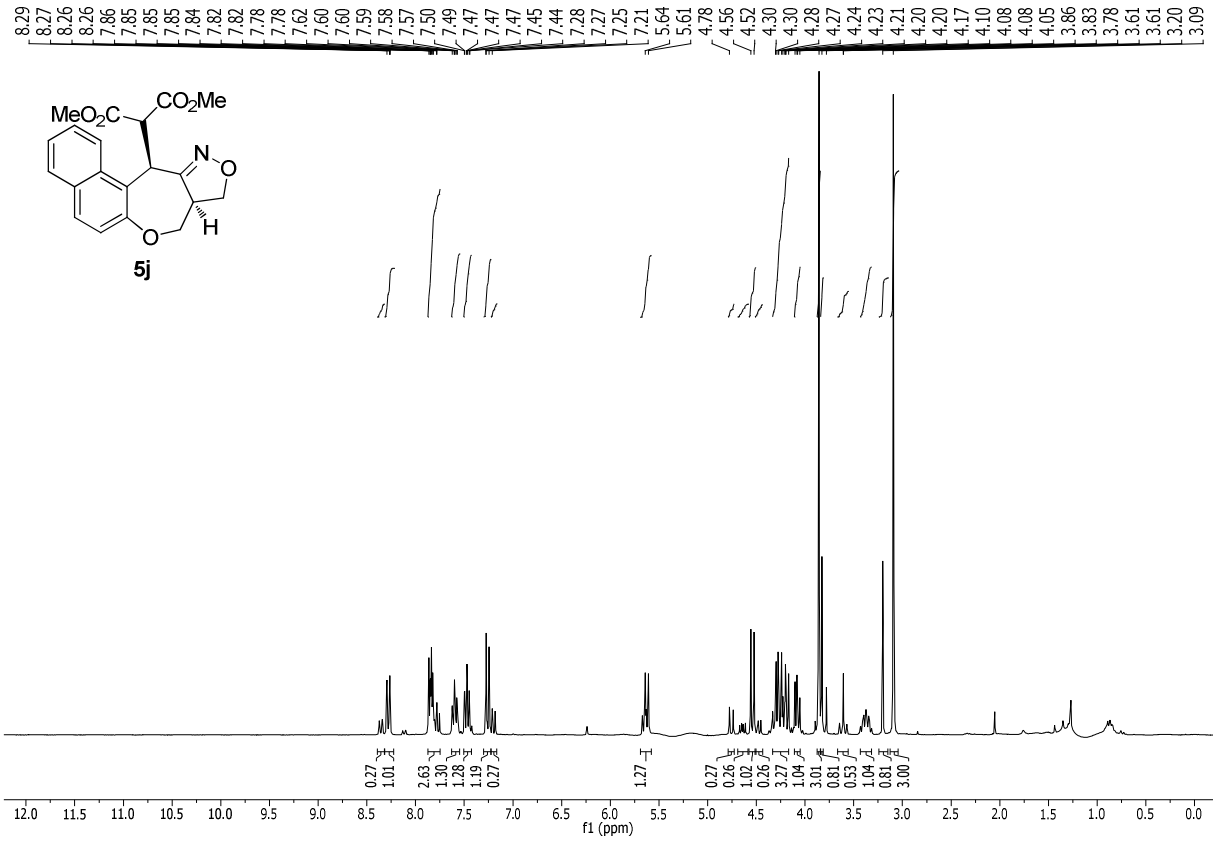

168.07 167.77 167.45 167.20 160.76 160.54 160.19 158.79 158.40 156.84
132.61 127.65 121.93 120.55 110.63 110.61 108.68 108.34
74.55 73.93 70.45 70.27 55.52 55.48 54.01 53.41 53.18 53.12 53.01 52.63 51.38 50.20 43.26 39.07
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

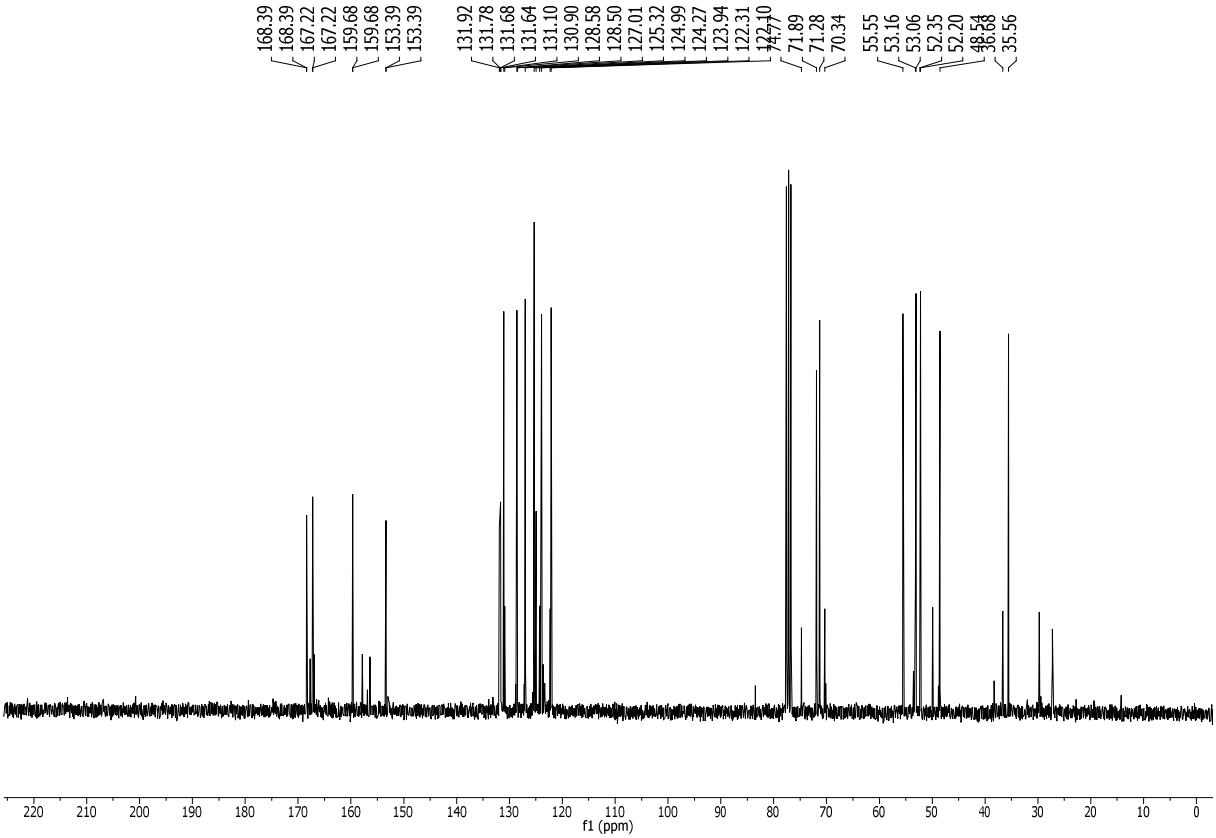

7.07
7.05
7.03
6.88
6.88
6.86
6.86
6.78
6.78
6.77
6.77
6.76
6.76
6.75
6.75
4.93
4.90
4.57
4.53
4.50
4.34
3.86
3.85
3.84
3.83
3.79
3.63
MeO2C
CO2Me
N
O
O
H
OMe
5h
0.96
1.00
0.95
0.98
1.00
1.00
1.00
4.01
3.01
3.00
f1 (ppm)

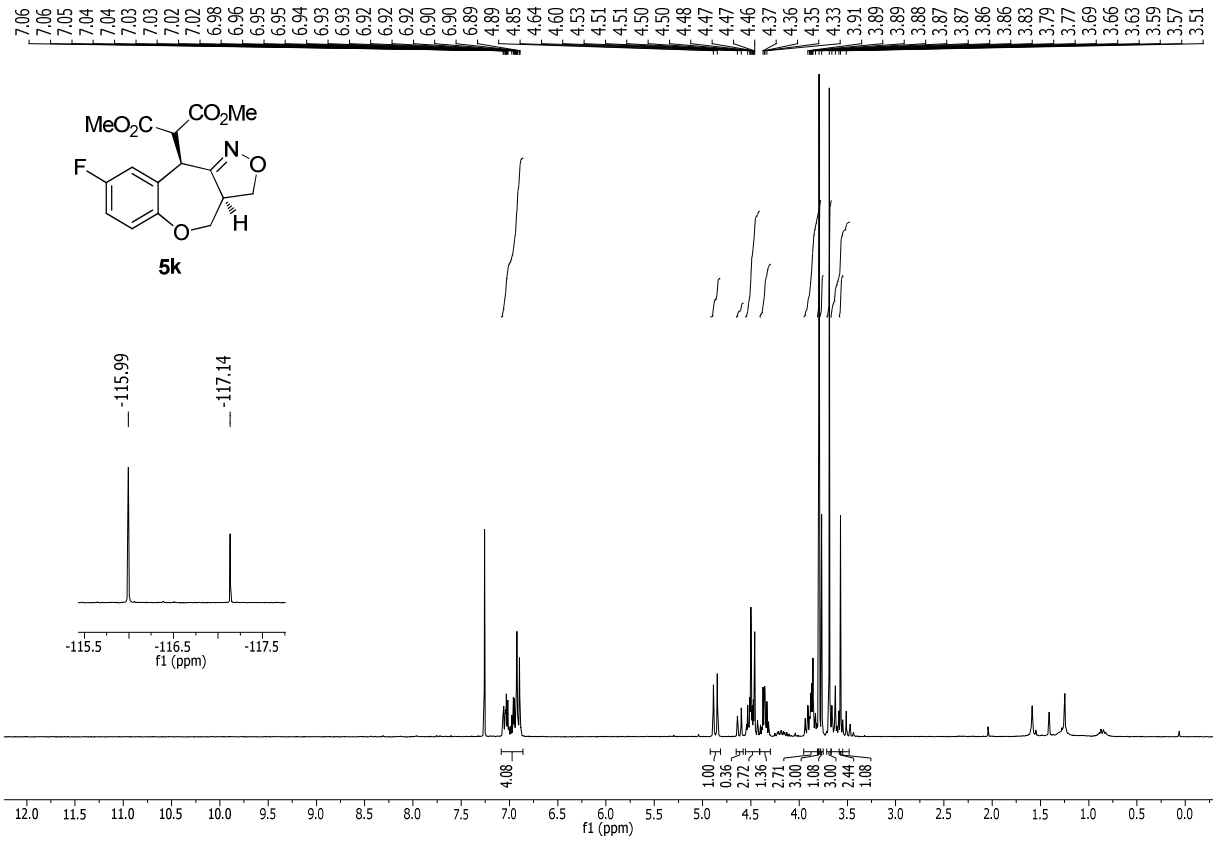

168.11
167.81
158.03
152.60
131.64
125.73
125.71
118.04
112.13
73.56
70.51
56.05
53.28
53.14
53.09
51.79
39.42
f1 (ppm)

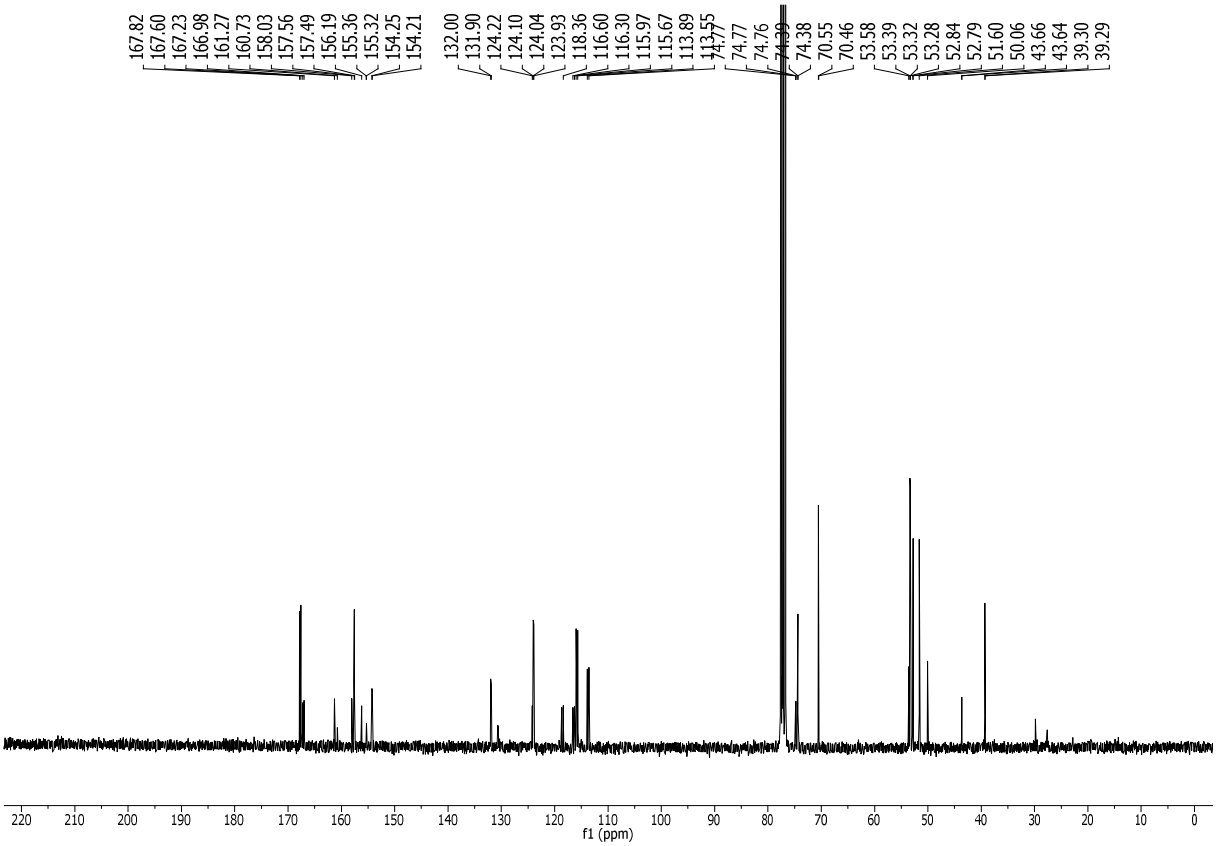

7.10 7.07 6.98 6.96 6.37 6.37 6.35 6.34 6.31 6.29 6.28 4.75 4.71 4.58 4.54 4.49 4.48 4.47 4.46 4.45 4.44 4.44 4.43 4.42 4.40 4.32 4.31 4.30 4.26 3.89 3.86 3.84 3.83 3.82 3.82 3.78 3.74 3.73 3.70 3.66 3.64 3.60 3.56 3.55 3.33 3.31 3.30 3.28 3.28 3.26 1.15 1.15 1.13 1.12 1.11
MeO2C
CO2Me
N
O
Et
N
Et
O
H
5i
0.40 1.00 2.80 1.00 0.40 2.80 1.40 3.00 1.20 12.67 3.00 1.20 5.60 8.40
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

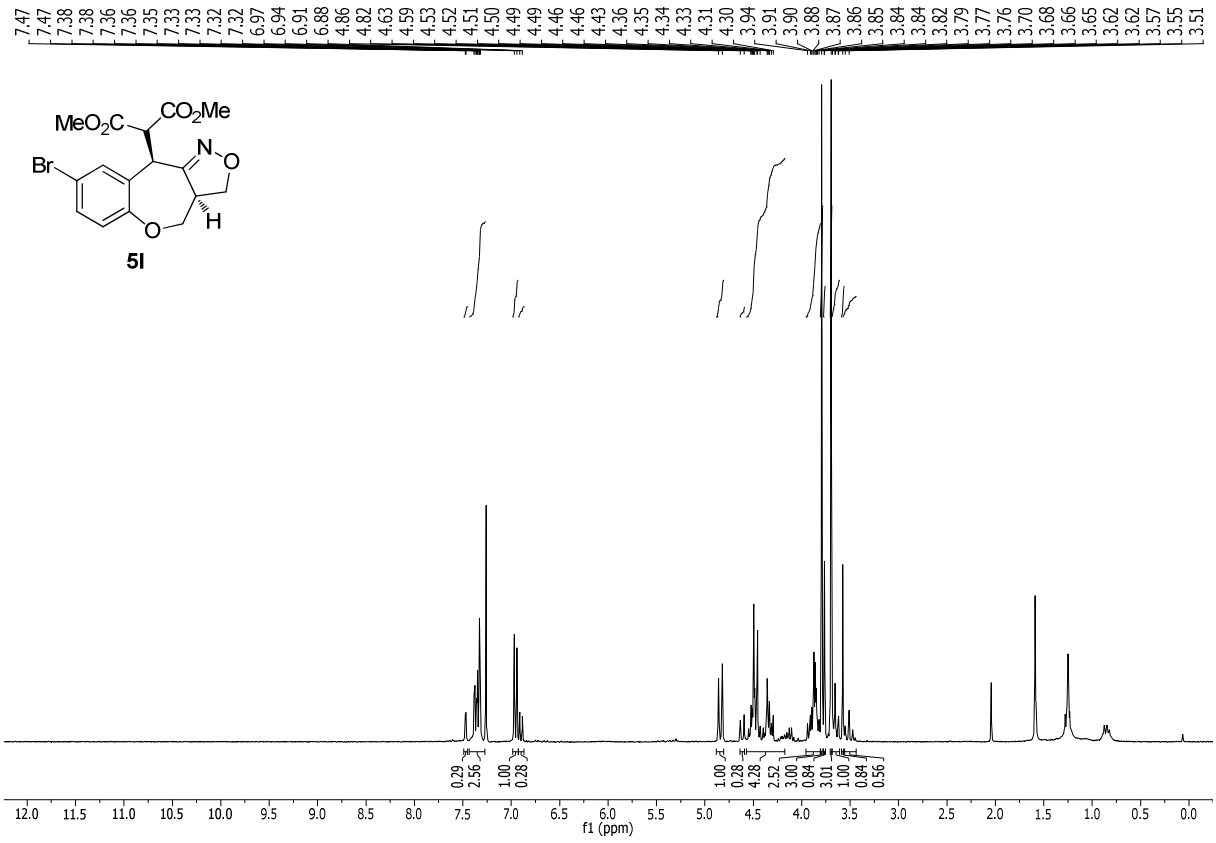

168.34 168.02 167.72 167.39 160.43 159.09 159.00 157.35 149.27 149.04 132.59 127.48 115.47 114.04 108.11 108.04 105.42 105.02 74.50 73.98 70.40 70.23 54.41 53.49 53.15 53.07 53.01 52.60 51.70 50.38 44.42 43.15 38.86 12.63
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

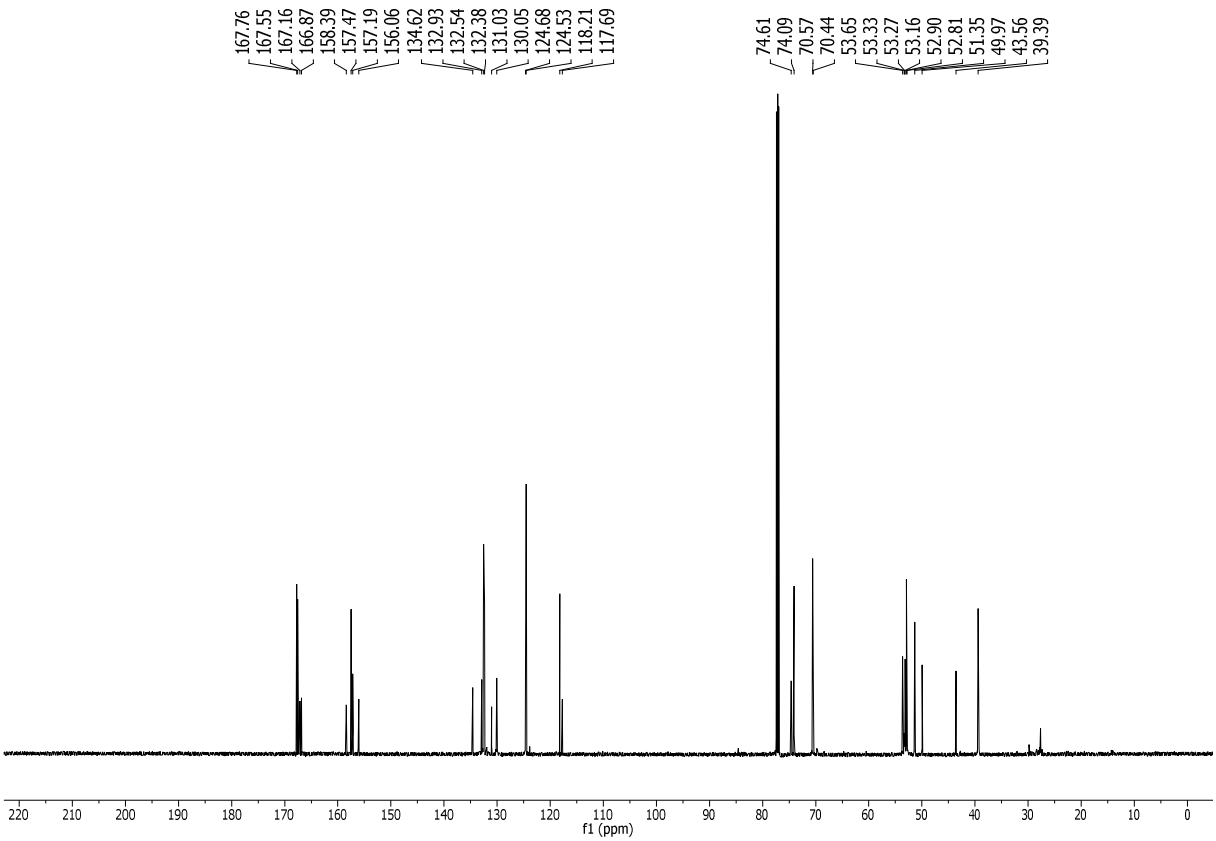

MeO2C
CO2Me
N
O
O
H
5j
f1 (ppm)

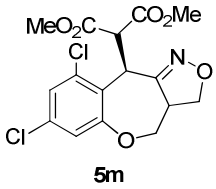

f1 (ppm)


MeO2C
CO2Me
N
O
F
O
H
5k
-115.99
-117.14
-115.5
-116.5
-117.5
f1 (ppm)
4.08
1.00
0.36
2.72
1.36
2.71
3.00
1.08
3.00
2.44
1.08
f1 (ppm)

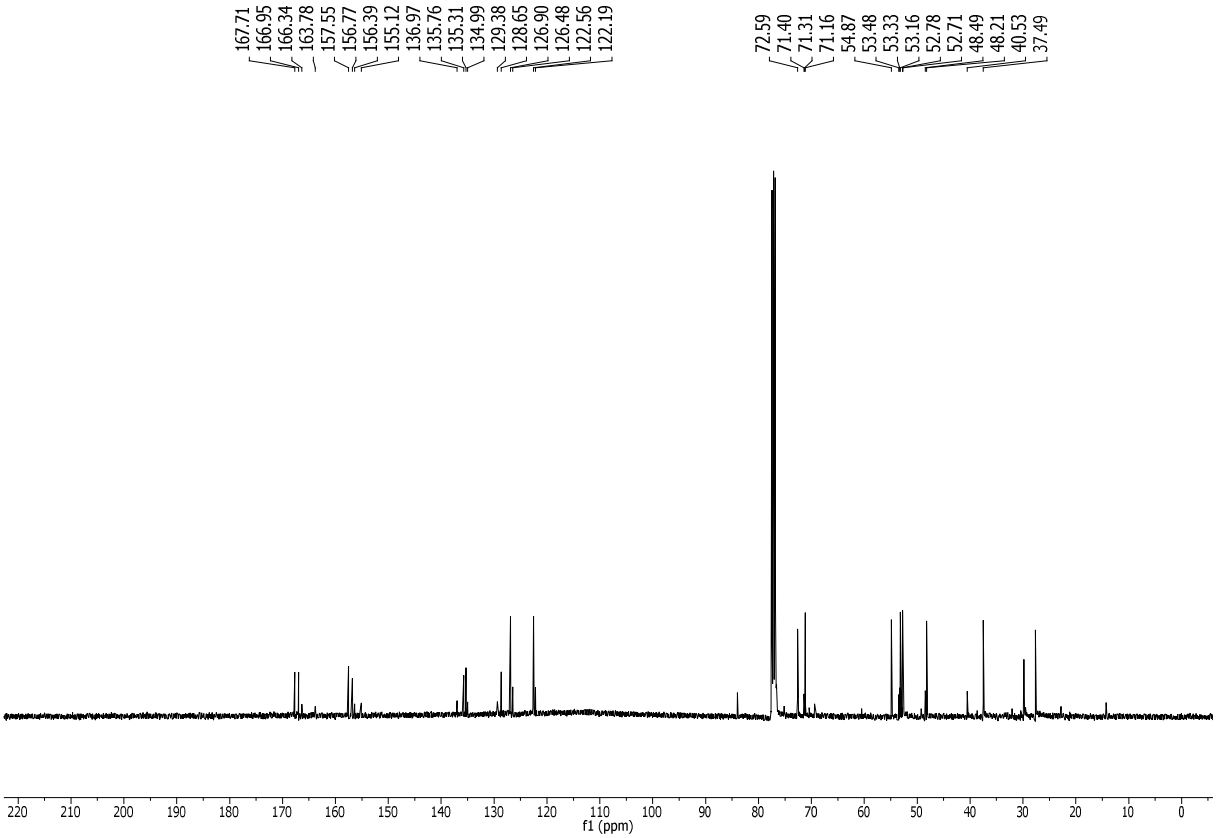

f1 (ppm)


7.47 7.47 7.38 7.38 7.36 7.36 7.35 7.33 7.33 7.32 7.32 6.97 6.94 6.91 6.88 4.86 4.82 4.63 4.59 4.53 4.52 4.51 4.50 4.49 4.49 4.46 4.46 4.43 4.36 4.35 4.34 4.33 4.31 4.30 3.94 3.91 3.90 3.88 3.87 3.86 3.85 3.84 3.84 3.82 3.79 3.77 3.76 3.70 3.68 3.66 3.65 3.62 3.62 3.57 3.55 3.51
MeO2C
CO2Me
N
O
Br
H
O
5l
0.29 2.56 1.00 0.28 1.00 0.28 4.28 2.52 3.00 0.84 3.01 1.00 0.84 0.56
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

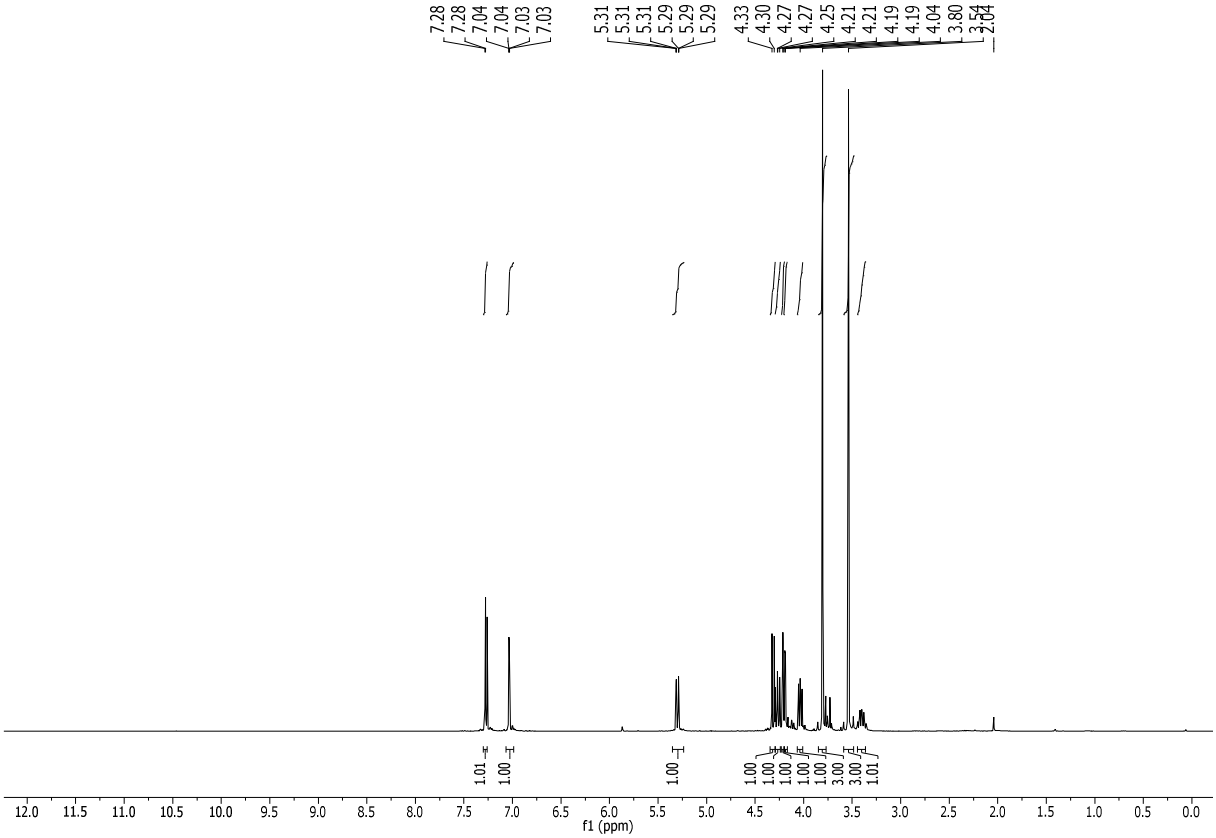

167.76 167.55 167.16 166.87 158.39 157.47 157.19 156.06 134.62 132.93 132.54 132.38 131.03 130.05 124.68 124.53 118.21 117.69
74.61 74.09 70.57 70.44 53.65 53.33 53.27 53.16 52.90 52.81 51.35 49.97 43.56 39.39
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

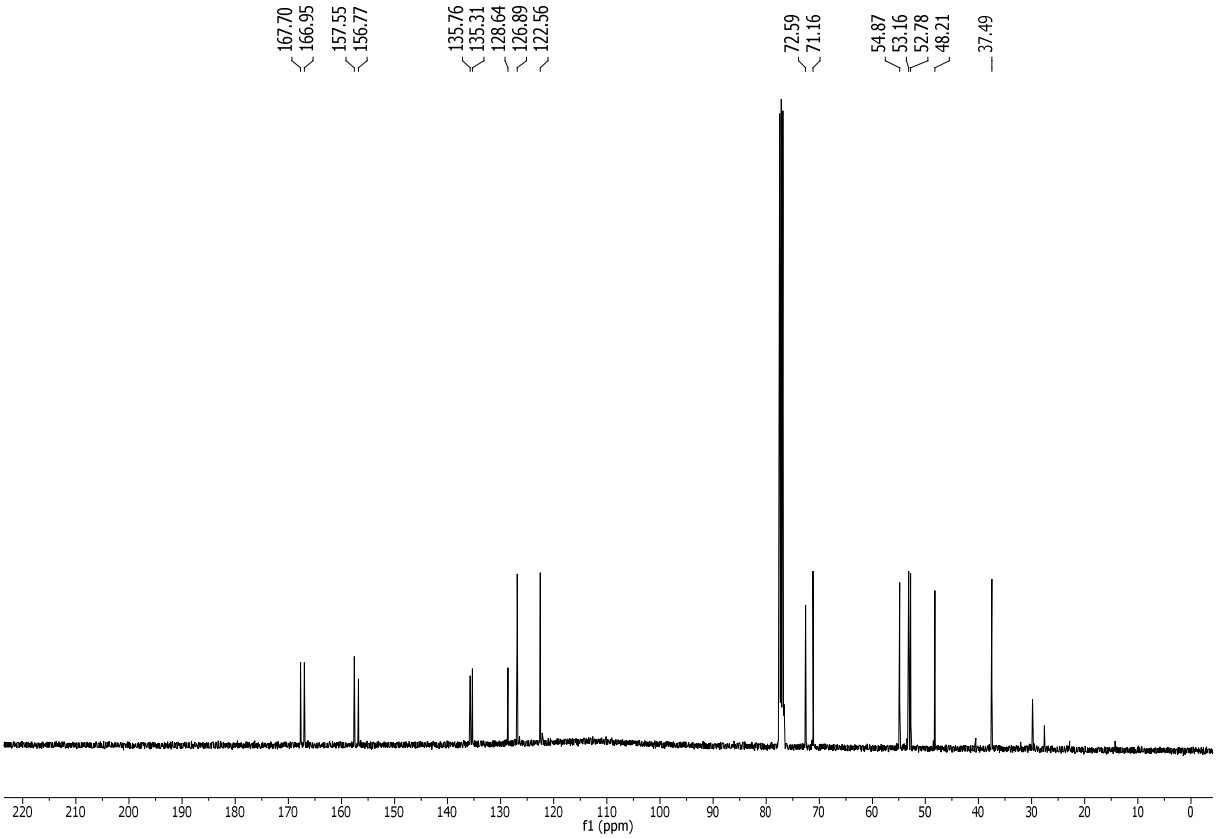


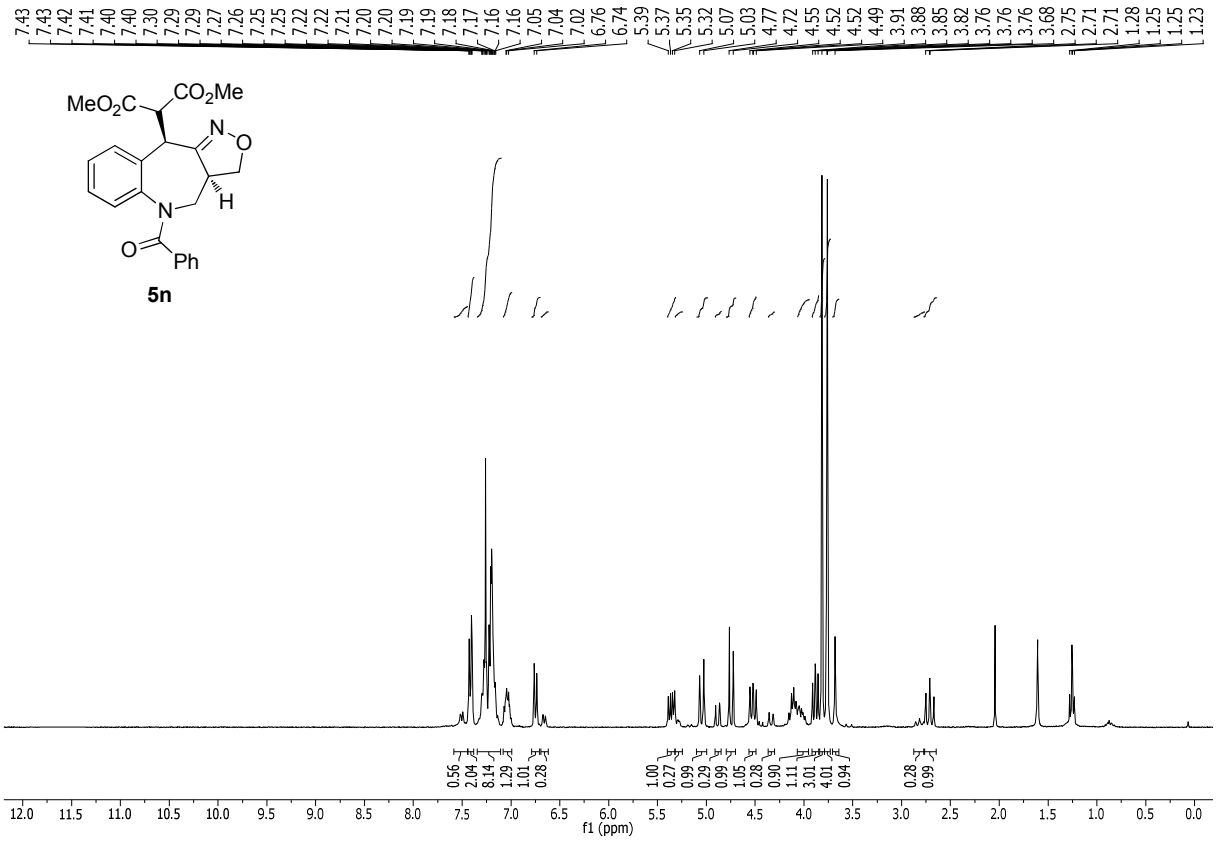
5m

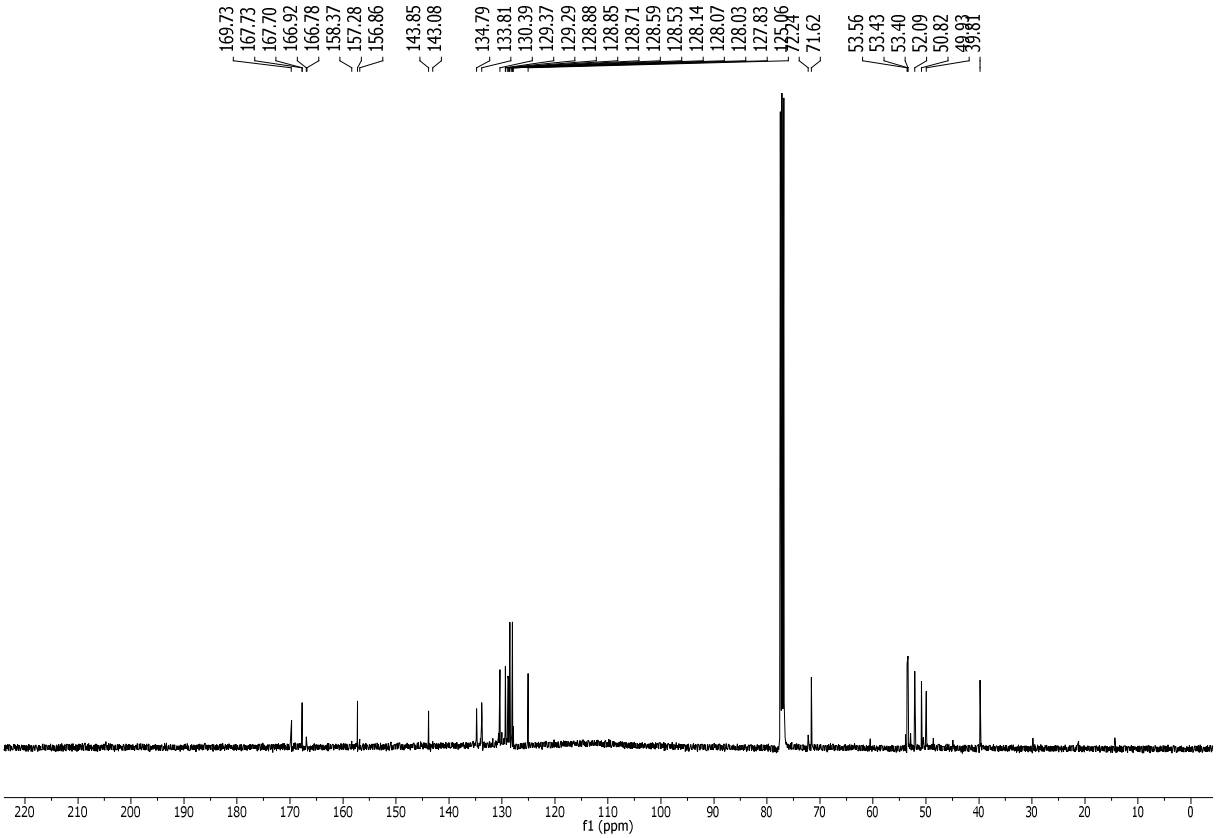


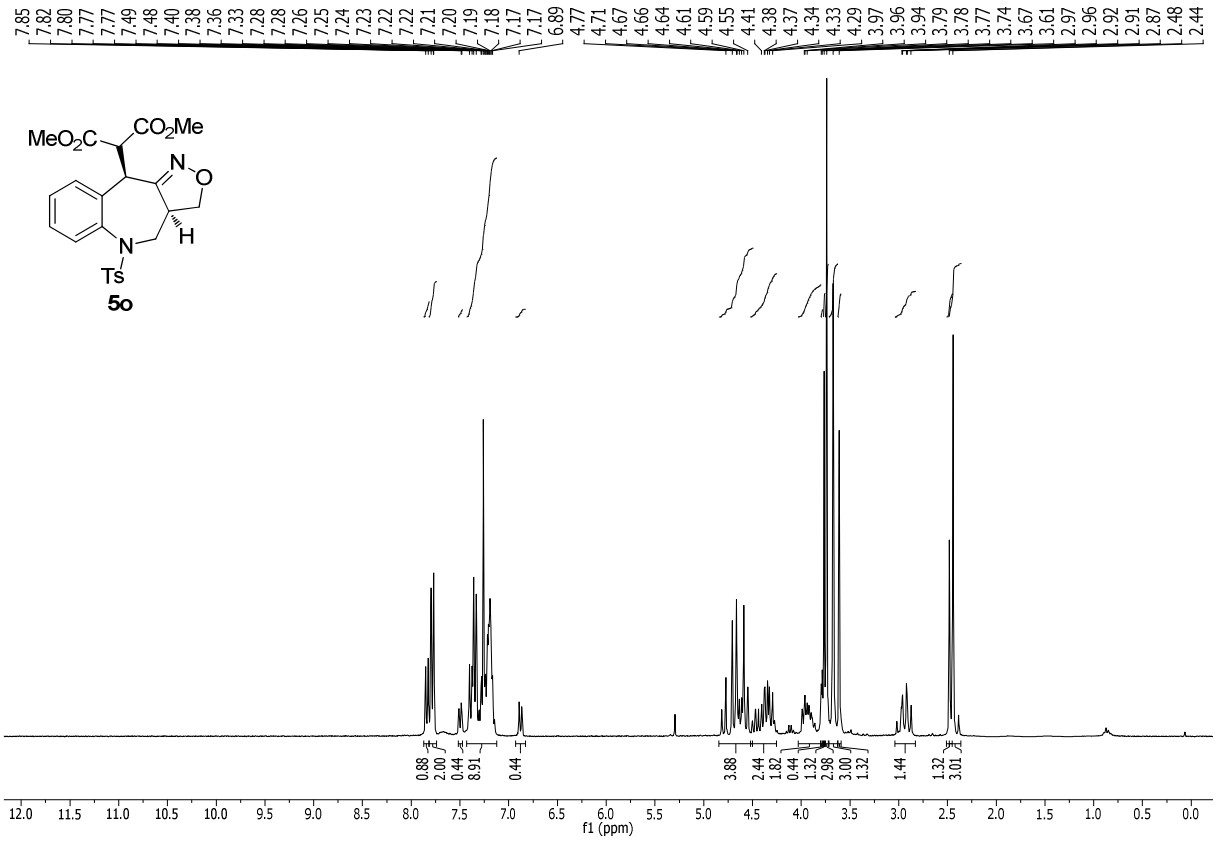
5m (major isomer):

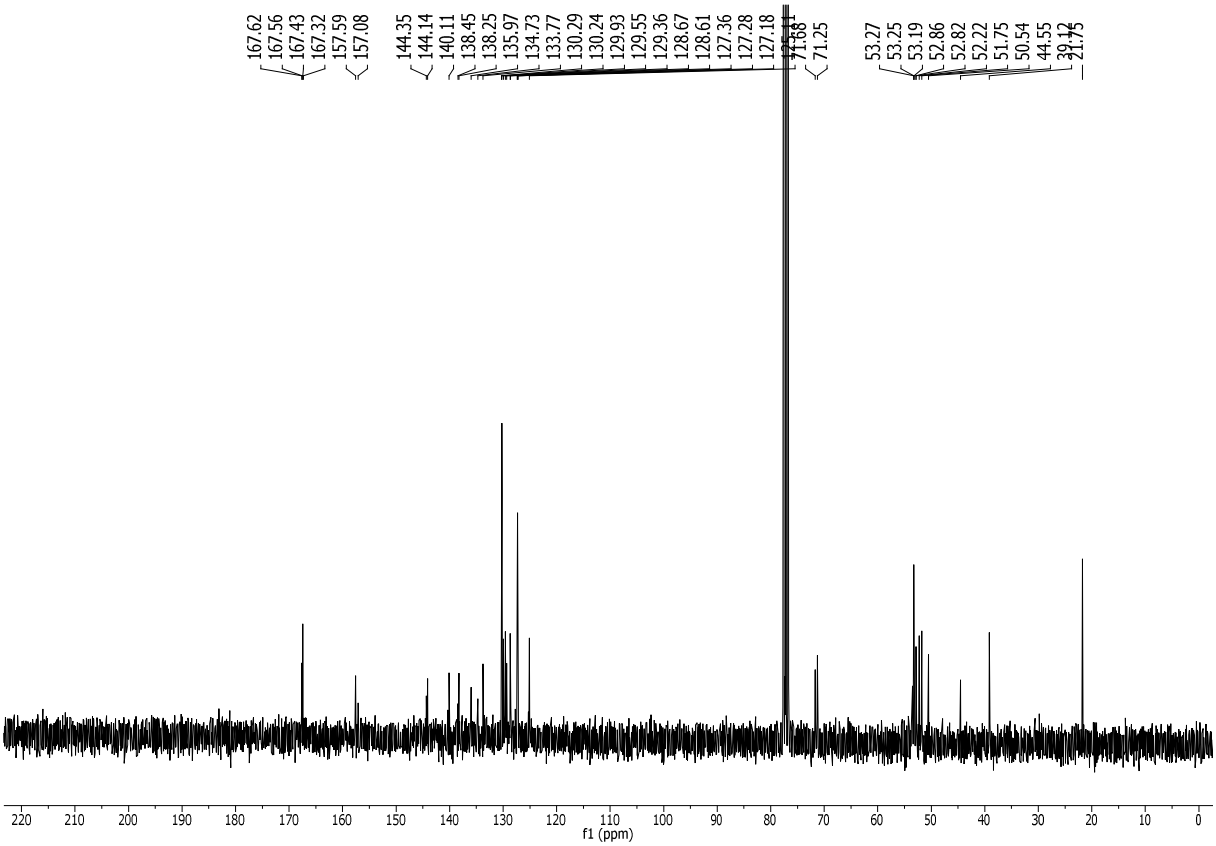


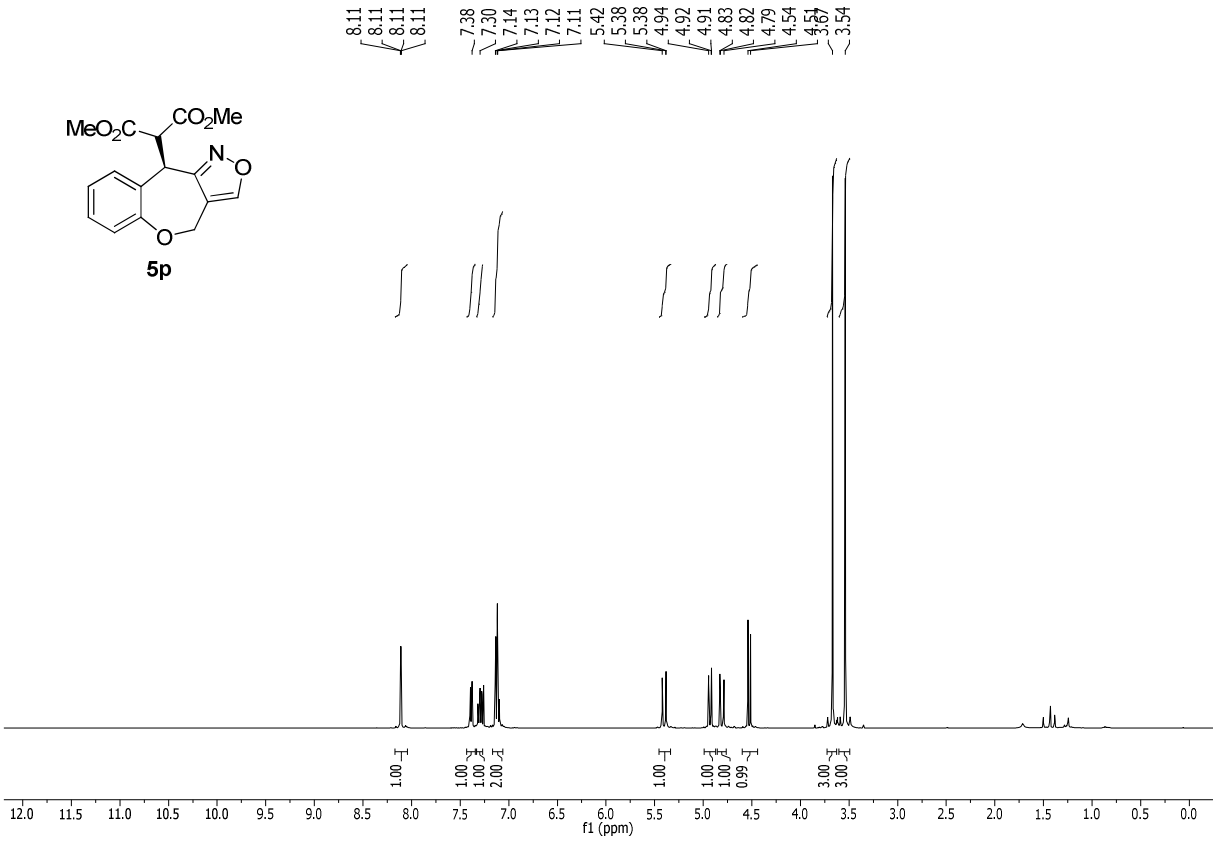


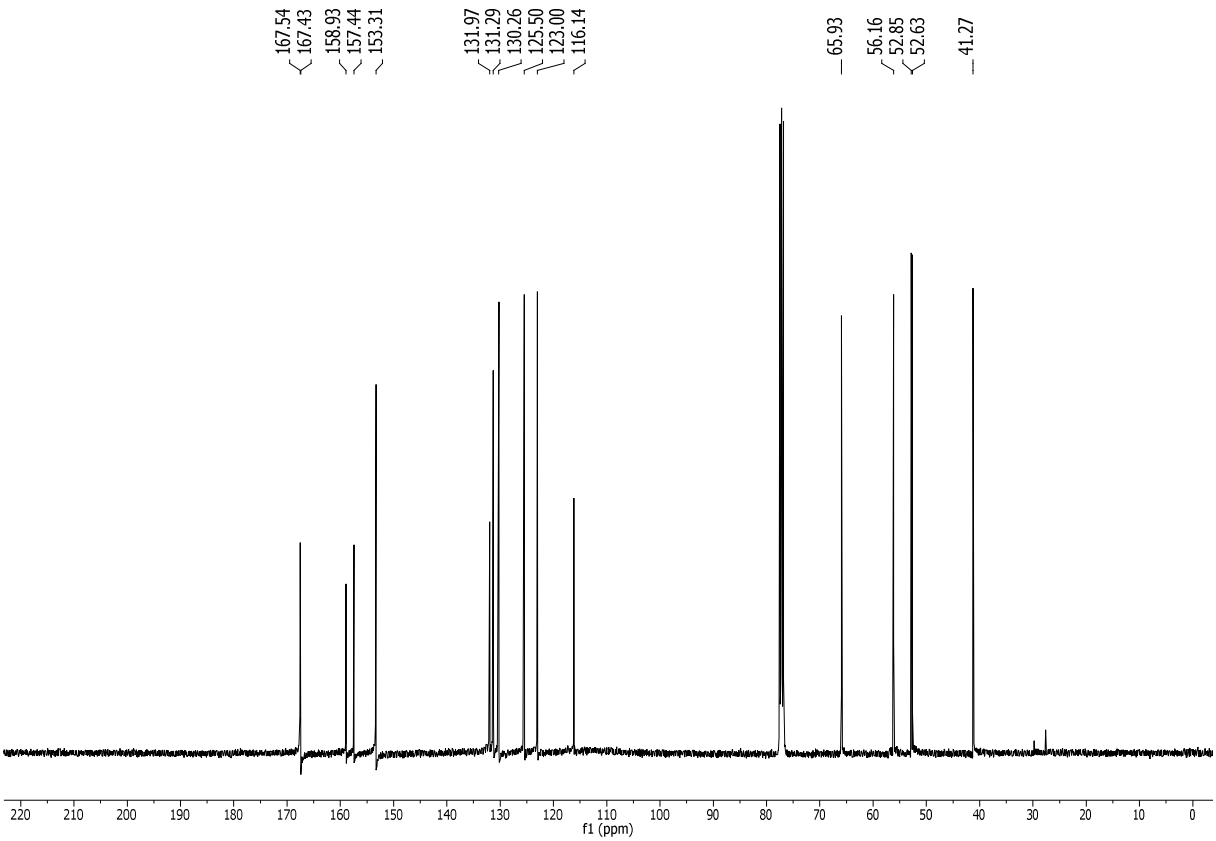

MeO2C
CO2Me
N
O
H
N
O
Ph
5n
f1 (ppm)

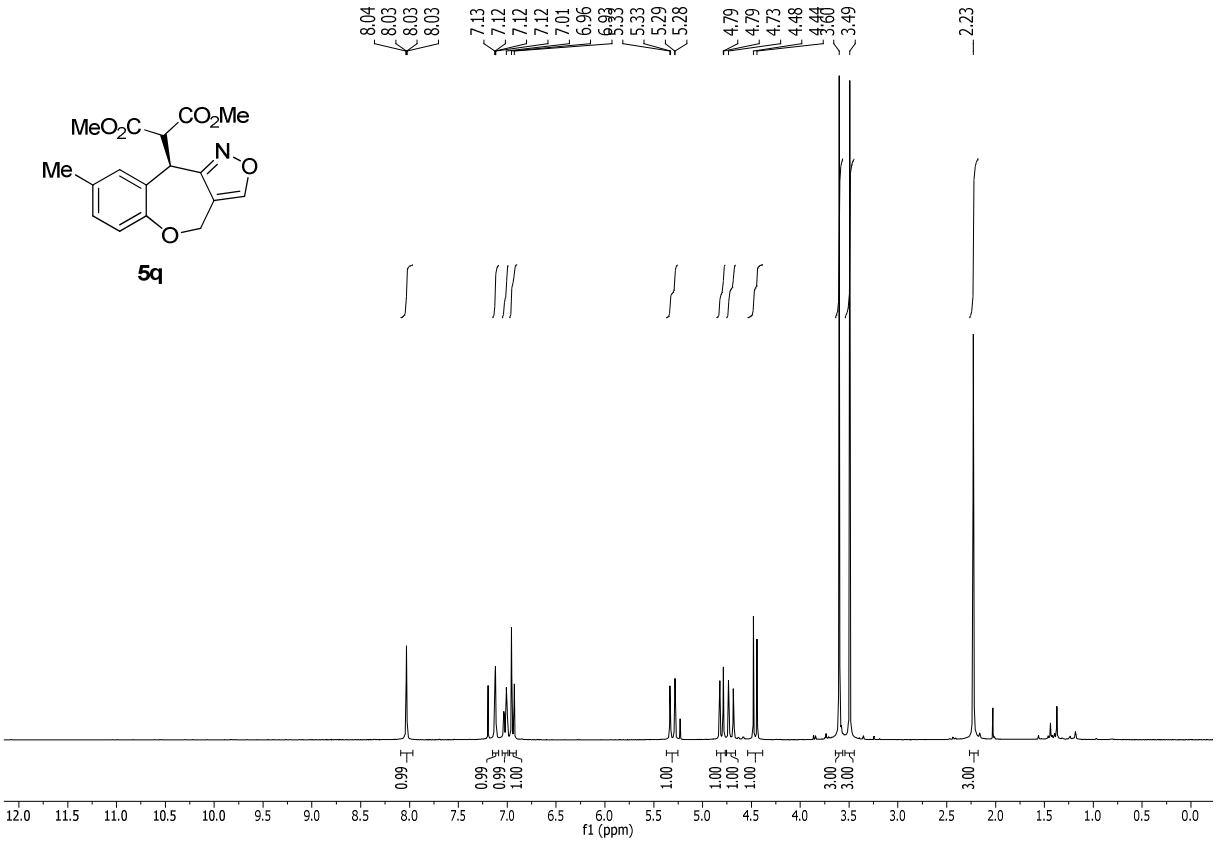

f1 (ppm)

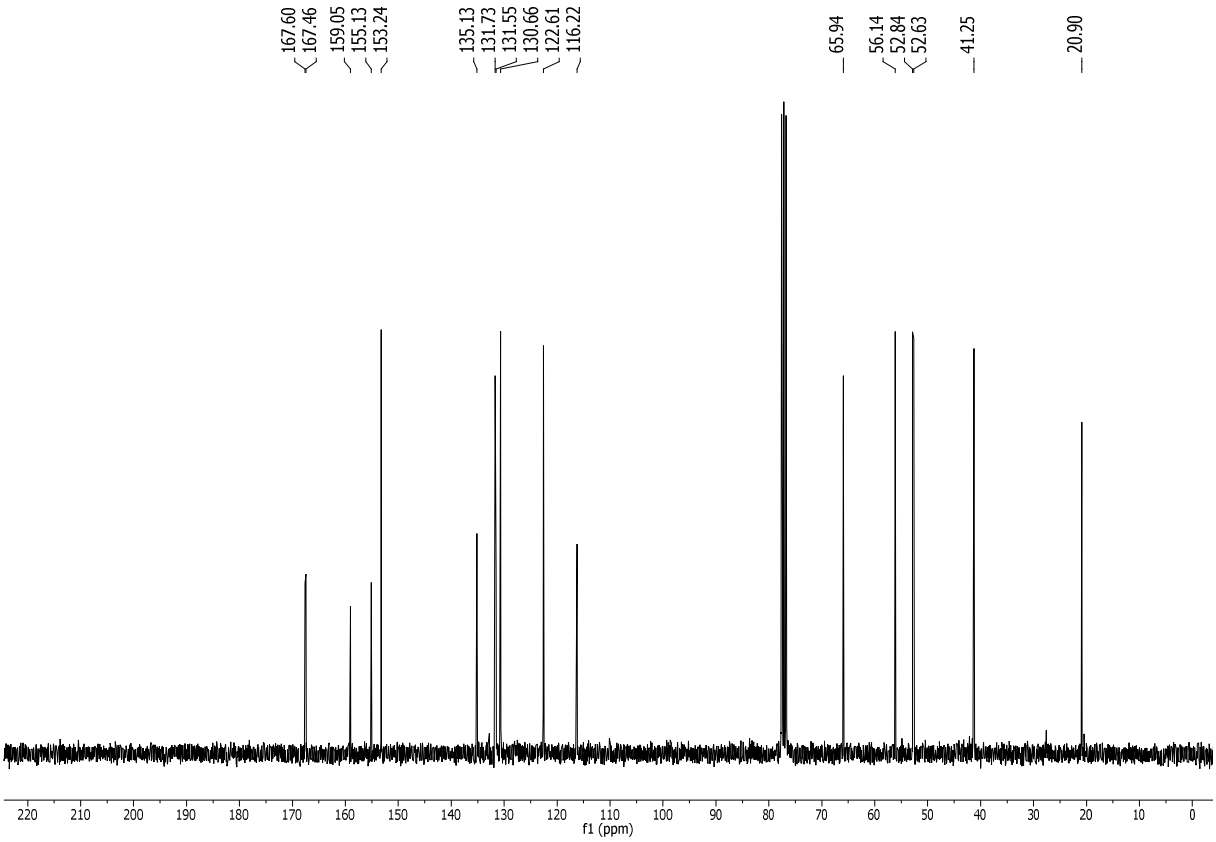

7.85 7.82 7.80 7.77 7.77 7.49 7.48 7.40 7.38 7.36 7.33 7.28 7.28 7.26 7.25 7.24 7.23 7.22 7.22 7.21 7.20 7.19 7.18 7.17 7.17 6.89
4.77 4.71 4.67 4.66 4.64 4.61 4.59 4.55 4.41 4.38 4.37 4.34 4.33 4.29 3.97 3.96 3.94 3.79 3.78 3.77 3.74 3.67 3.61 2.97 2.96 2.92 2.91 2.87 2.48 2.44
MeO2C
CO2Me
N
O
H
N
Ts
5o
0.88 2.00 0.44 8.91 0.44 3.88 2.44 1.82 0.44 1.32 2.98 3.00 1.32 1.44 1.32 3.01
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


167.62 167.56 167.43 167.32 157.59 157.08
144.35 144.14 140.11 138.45 138.25 135.97 134.73 133.77 130.29 130.24 129.93 129.55 129.36 128.67 128.61 127.36 127.28 127.18 71.68 71.25
53.27 53.25 53.19 52.86 52.82 52.22 51.75 50.54 44.55 31.42 21.75
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.11
8.11
8.11
8.11
7.38
7.30
7.14
7.13
7.12
7.11
5.42
5.38
5.38
4.94
4.92
4.91
4.83
4.82
4.79
4.54
4.51
3.67
3.54
MeO2C
CO2Me
N
O
O
5p
1.00
1.00
1.00
2.00
1.00
1.00
1.00
0.99
3.00
3.00
f1 (ppm)


167.54
167.43
158.93
157.44
153.31
131.97
131.29
130.26
125.50
123.00
116.14
65.93
56.16
52.85
52.63
41.27
f1 (ppm)


8.04
8.03
8.03
8.03
7.13
7.12
7.12
7.12
7.01
6.96
6.93
5.33
5.33
5.29
5.28
4.79
4.79
4.73
4.48
4.44
3.60
3.49
2.23
MeO2C
CO2Me
N
O
Me
O
5q
0.99
0.99
0.99
1.00
1.00
1.00
1.00
1.00
3.00
3.00
3.00
f1 (ppm)


167.60
167.46
159.05
155.13
153.24
135.13
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131.55
130.66
122.61
116.22
65.94
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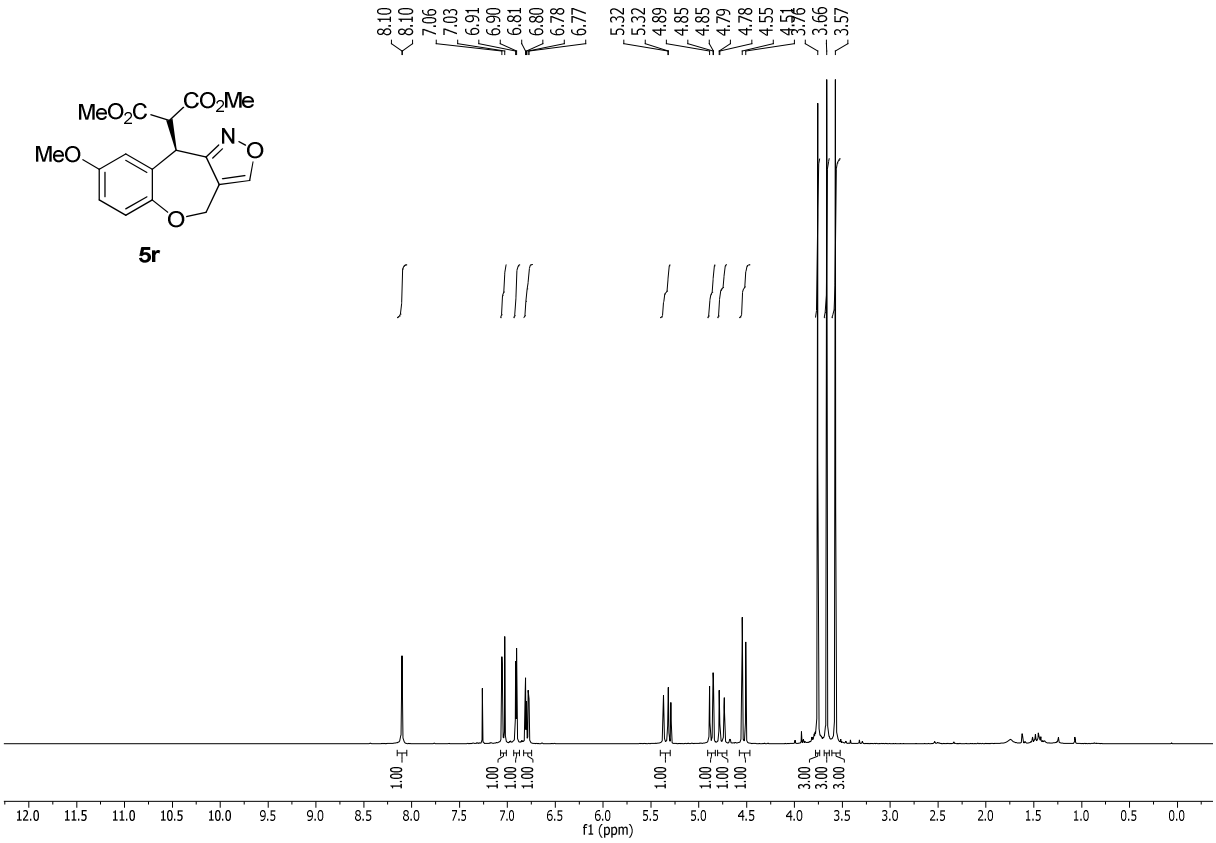
52.84
52.63
41.25
20.90
f1 (ppm)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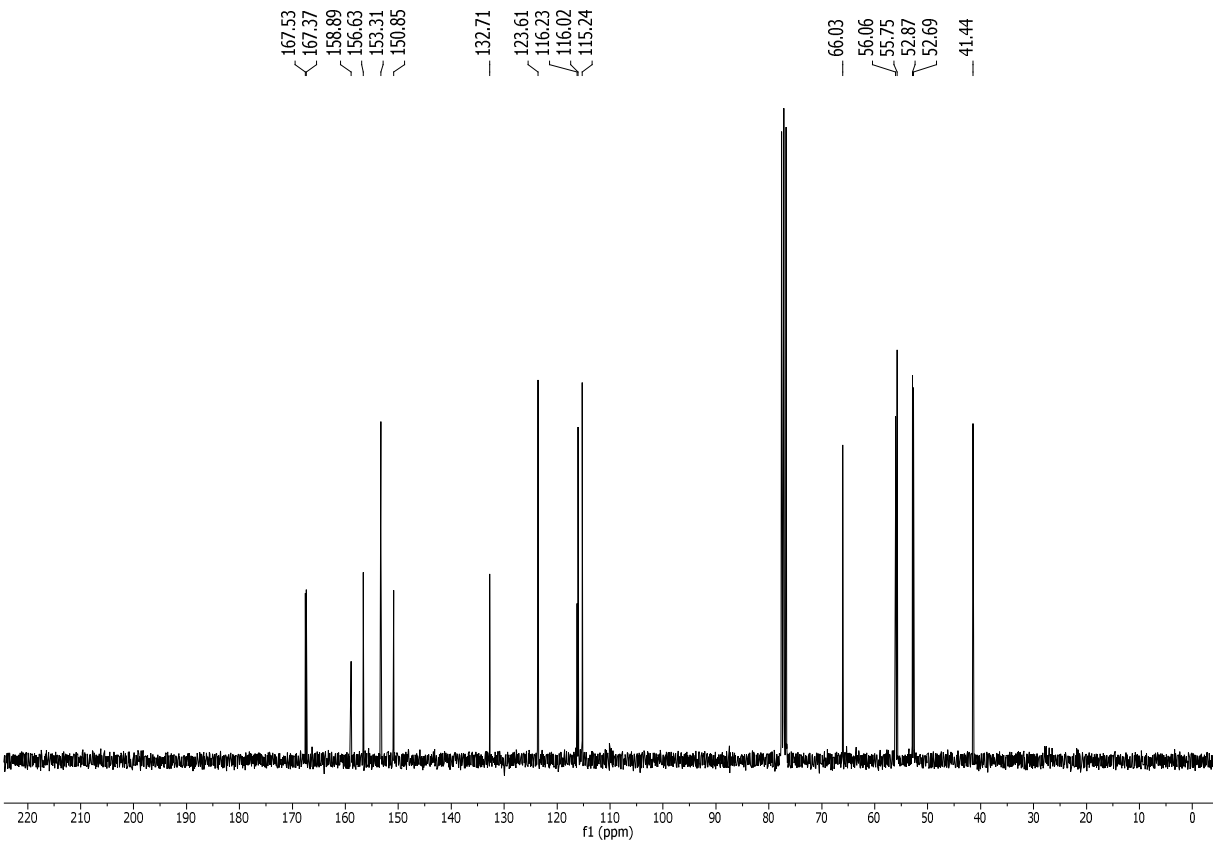
8.10
7.06
7.03
6.91
6.90
6.81
6.80
6.78
6.77
5.32
5.32
4.89
4.85
4.85
4.79
4.78
4.55
4.51
3.76
3.66
3.57
MeO2C
CO2Me
MeO
N
O
O
5r
1.00
1.00
1.00
1.00
1.00
1.00
1.00
1.00
3.00
3.00
3.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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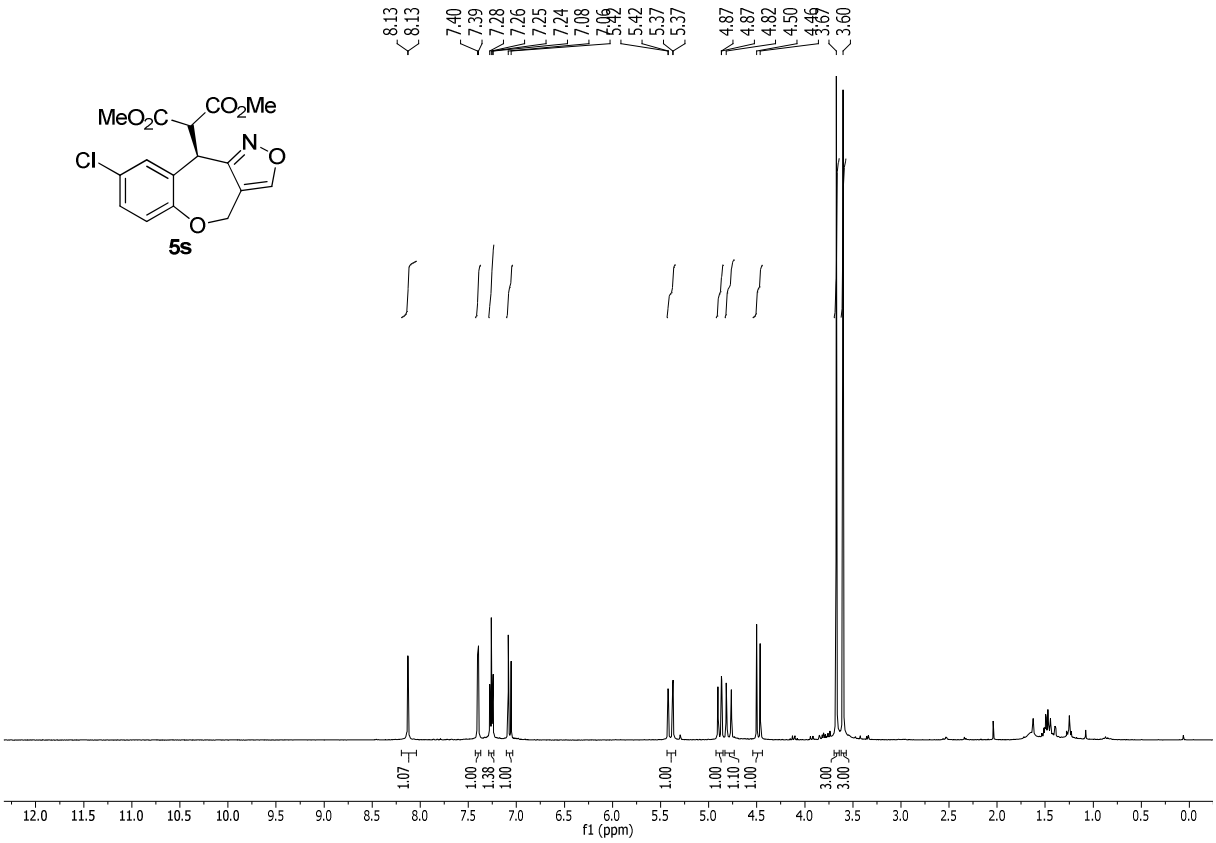
167.37
158.89
156.63
153.31
150.85
132.71
123.61
116.23
116.02
115.24
66.03
56.06
55.75
52.87
52.69
41.44
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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8.13
7.40
7.39
7.28
7.26
7.25
7.24
7.08
7.06
5.42
5.37
5.37
4.87
4.87
4.82
4.50
4.46
3.67
3.60
MeO2C
CO2Me
N
O
Cl
O
5s
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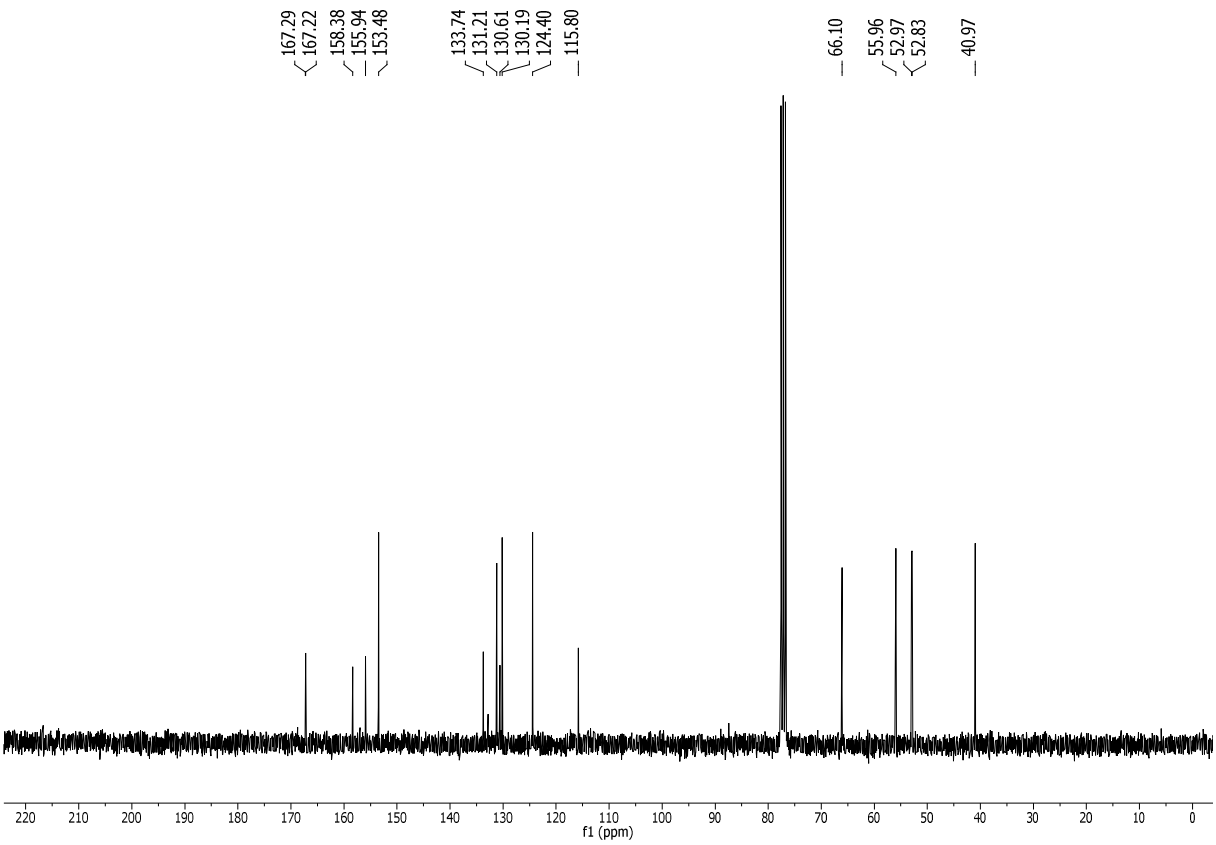
1.10
1.00
3.00
3.00
f1 (ppm)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153.48
133.74
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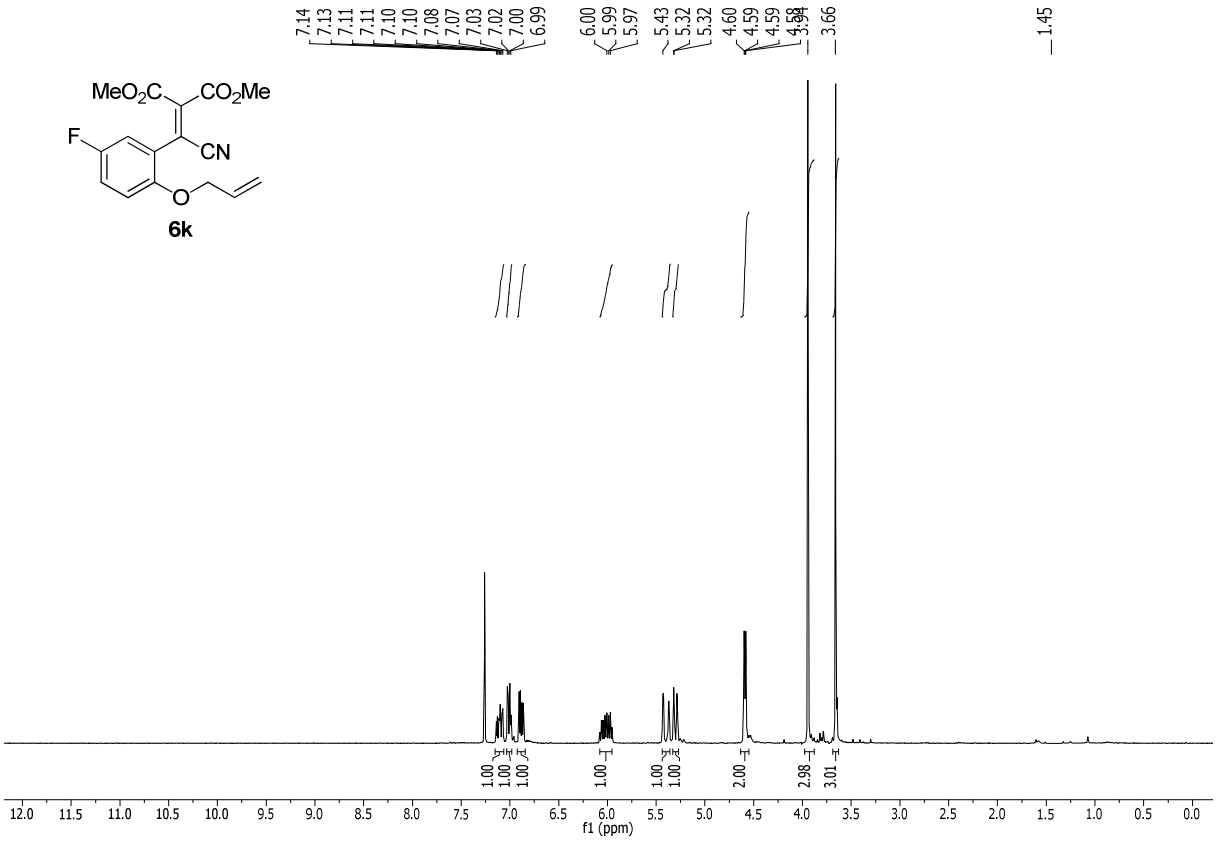
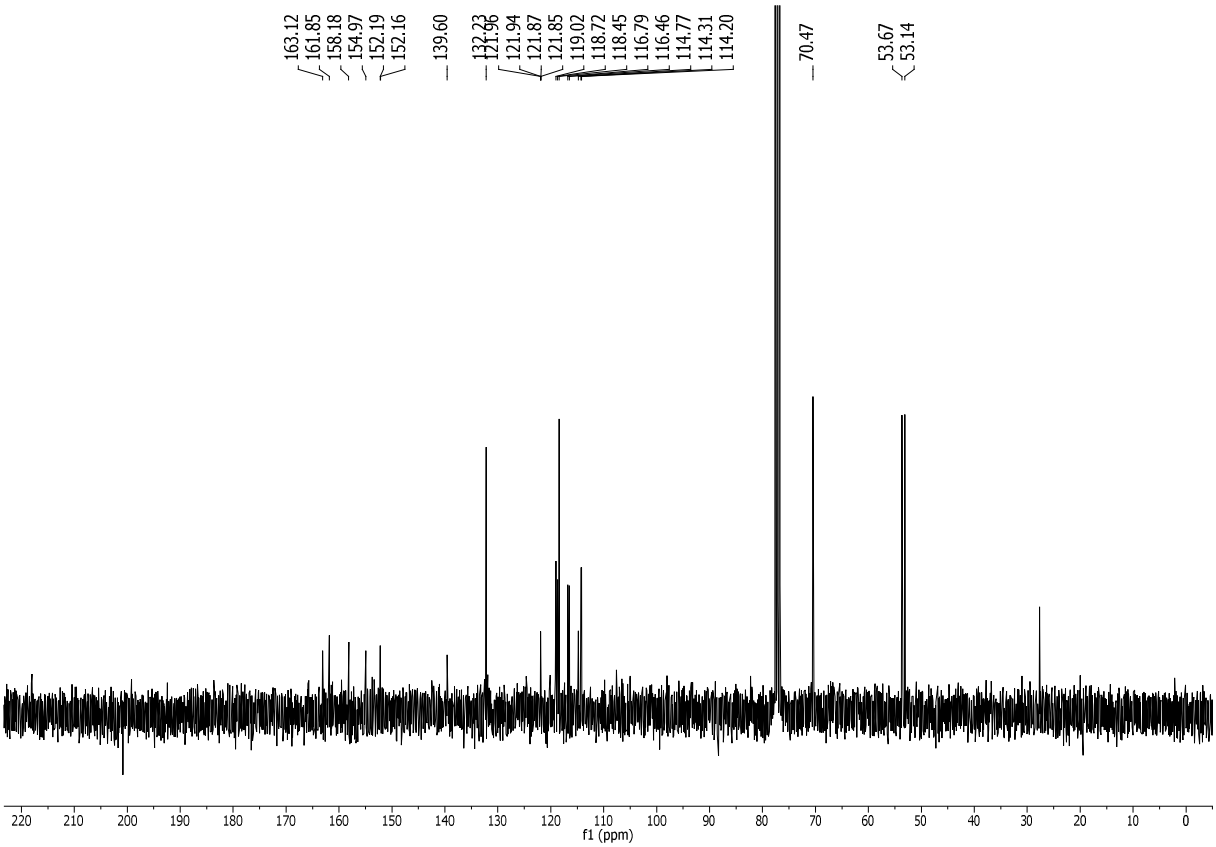
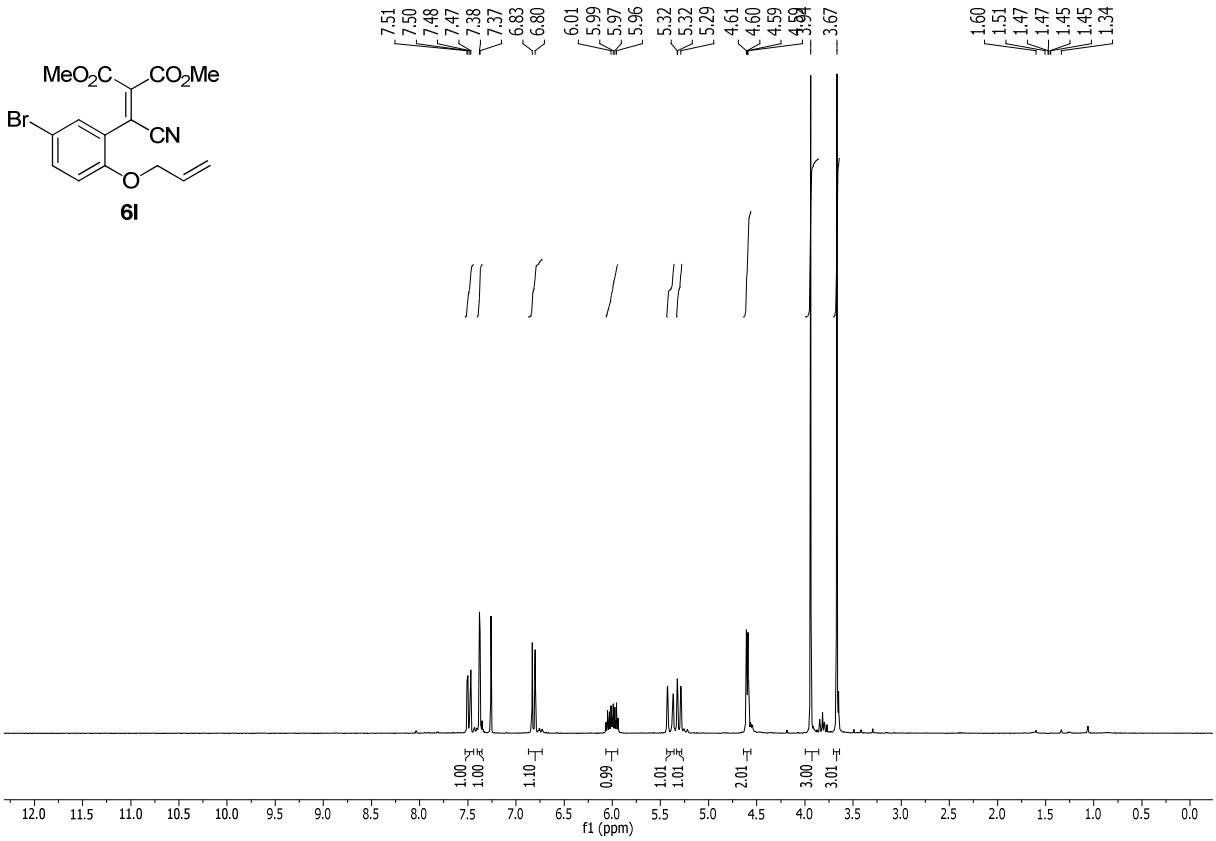
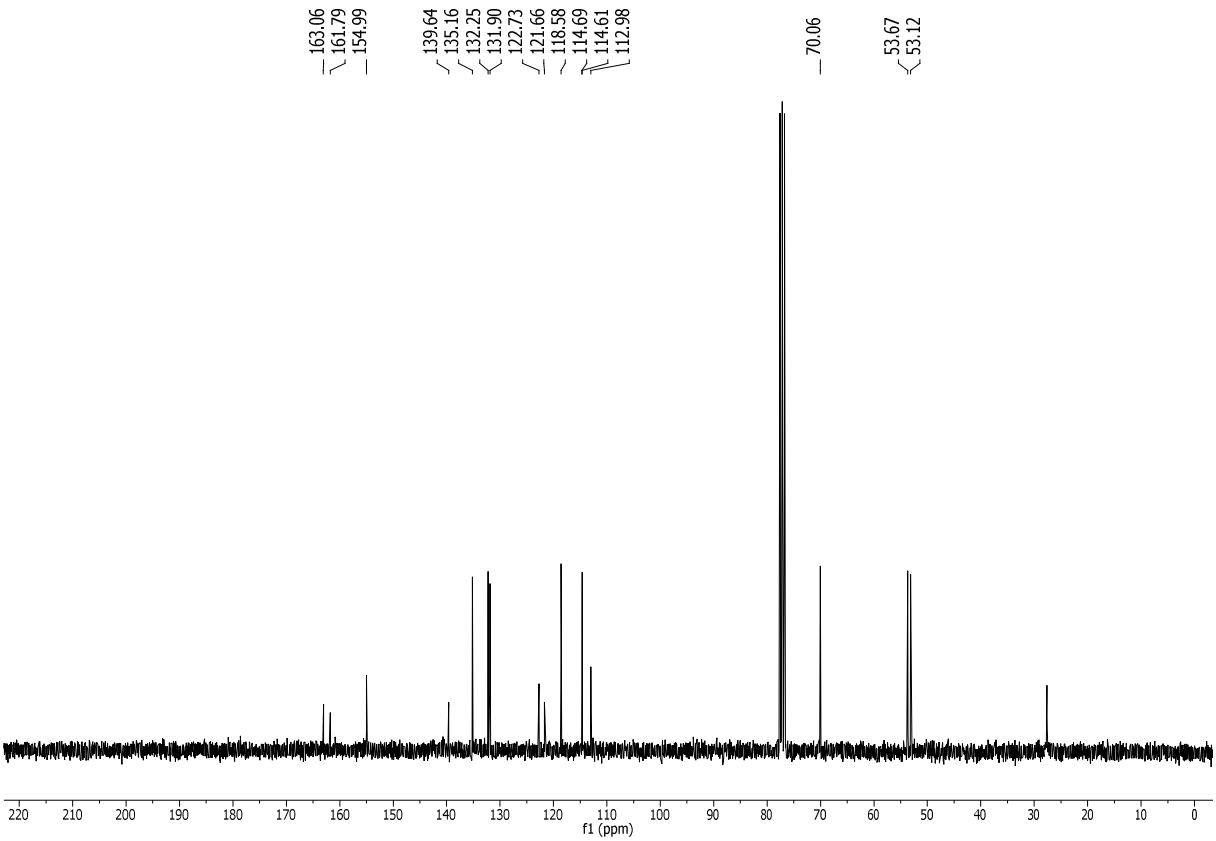
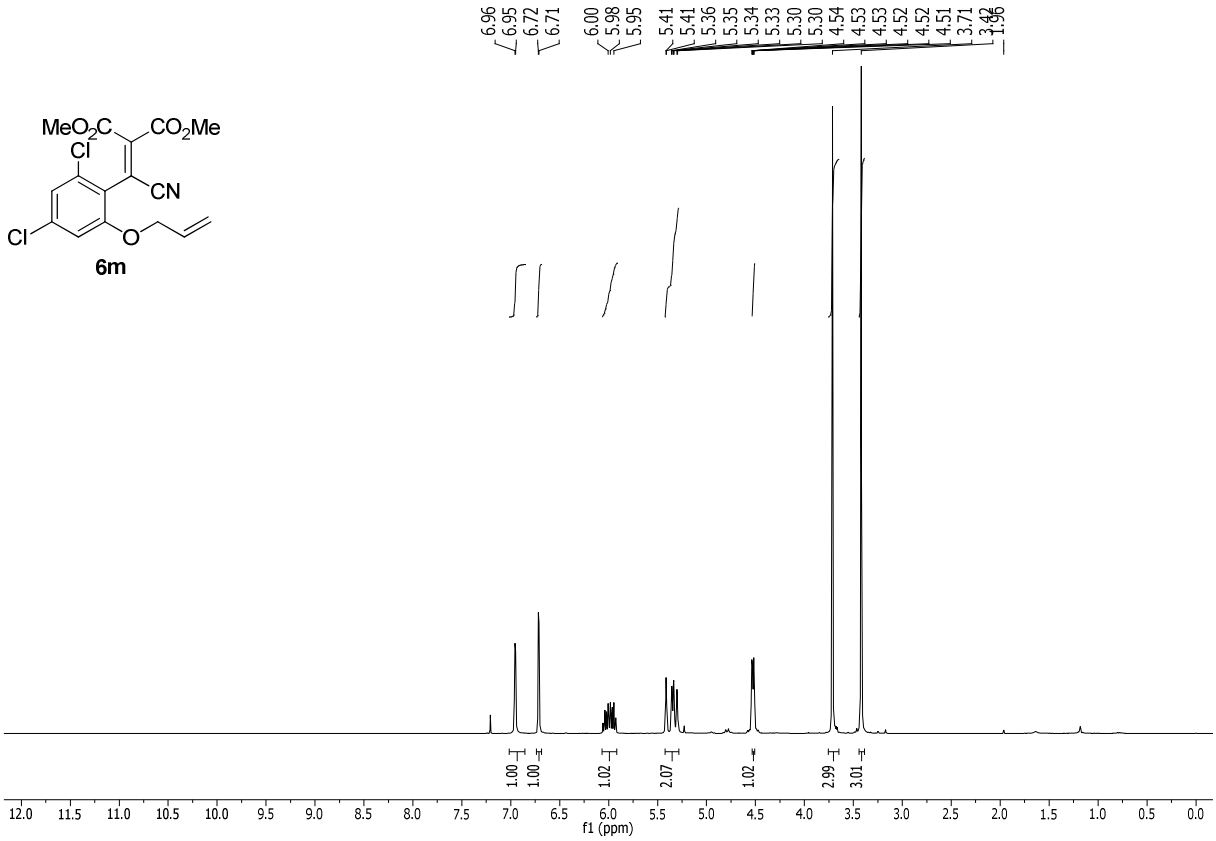
130.19
124.40
115.80
66.10
55.96
52.97
52.83
40.97
f1 (ppm)

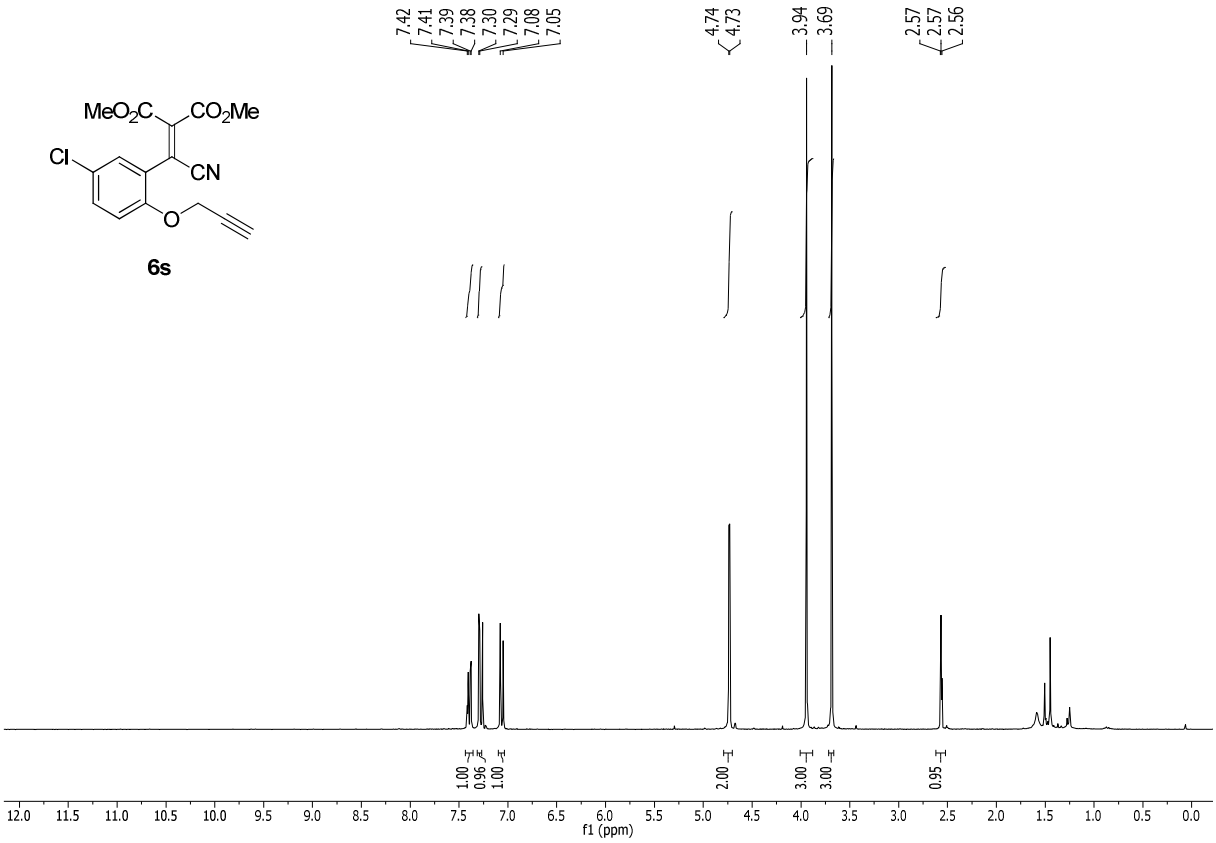


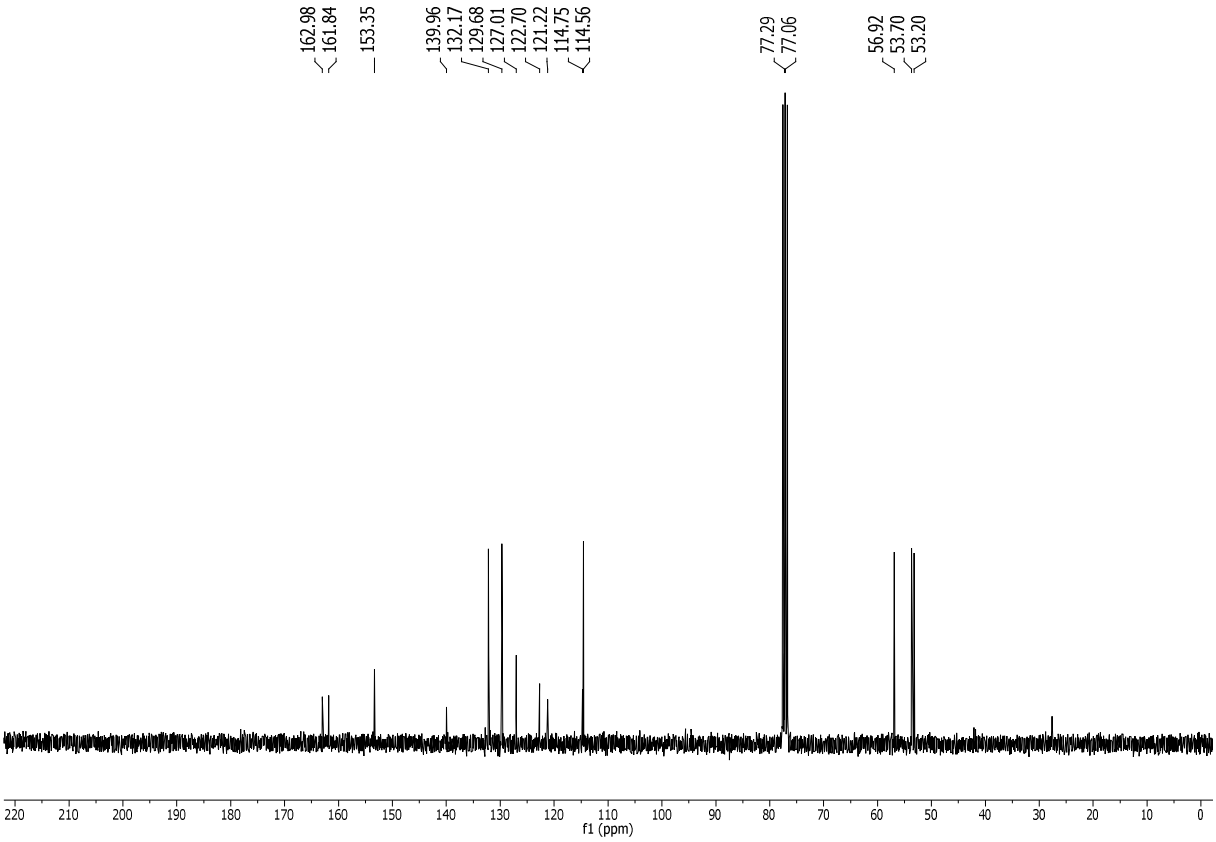









7.42
7.41
7.39
7.38
7.30
7.29
7.08
7.05
4.74
4.73
3.94
3.69
2.57
2.57
2.56
MeO2C
CO2Me
Cl
CN
O
6s
1.00
0.96
1.00
2.00
3.00
3.00
0.95
f1 (ppm)


162.98
161.84
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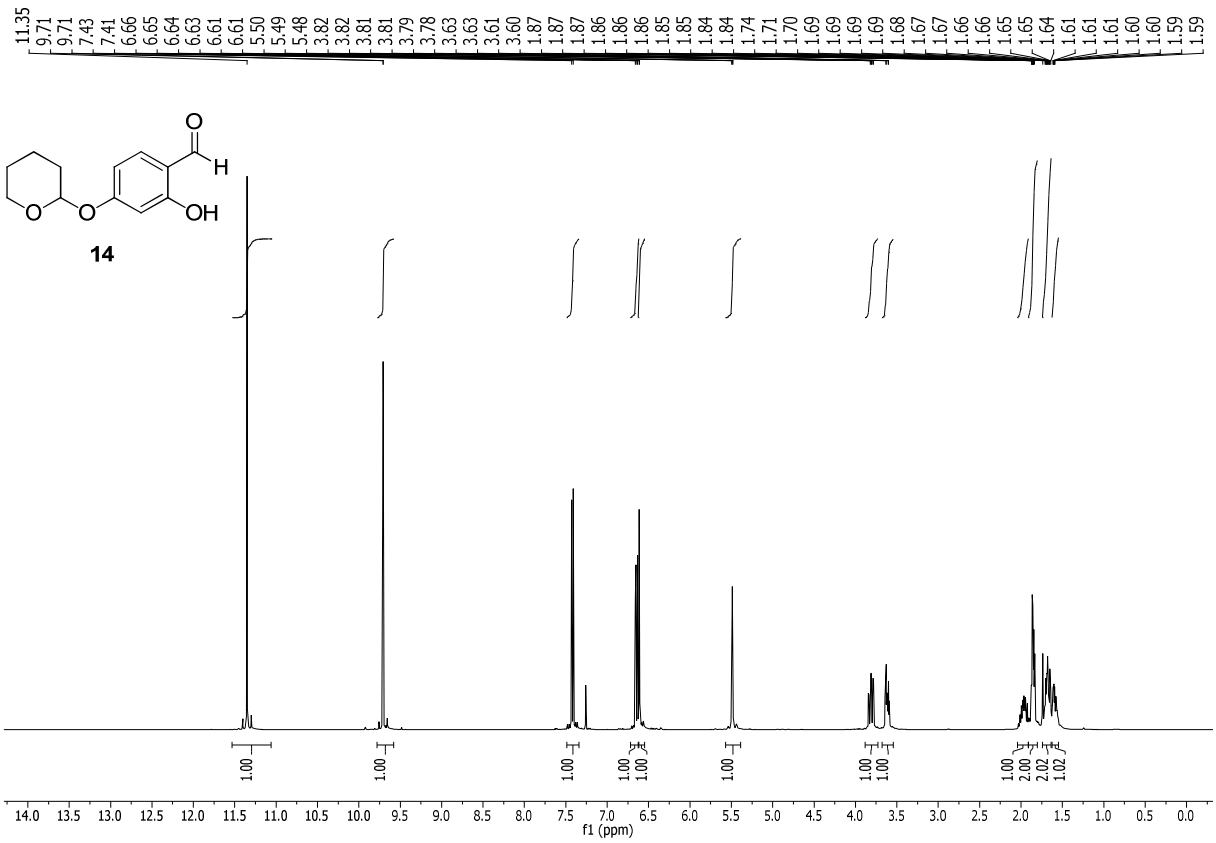
139.96
132.17
129.68
127.01
122.70
121.22
114.75
114.56
77.29
77.06
56.92
53.70
53.20
f1 (ppm)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9.71
9.71
7.43
7.41
6.66
6.65
6.64
6.63
6.61
6.61
5.50
5.49
5.48
3.82
3.82
3.81
3.81
3.79
3.78
3.63
3.63
3.61
3.60
1.87
1.87
1.86
1.86
1.86
1.85
1.85
1.84
1.84
1.74
1.71
1.70
1.69
1.69
1.69
1.68
1.67
1.67
1.66
1.66
1.65
1.65
1.64
1.61
1.61
1.61
1.60
1.60
1.59
1.59
O
H
O
O
OH
14
1.00
1.00
1.00
1.00
1.00
1.00
1.00
1.00
2.00
2.02
1.02
14.0
13.5
13.0
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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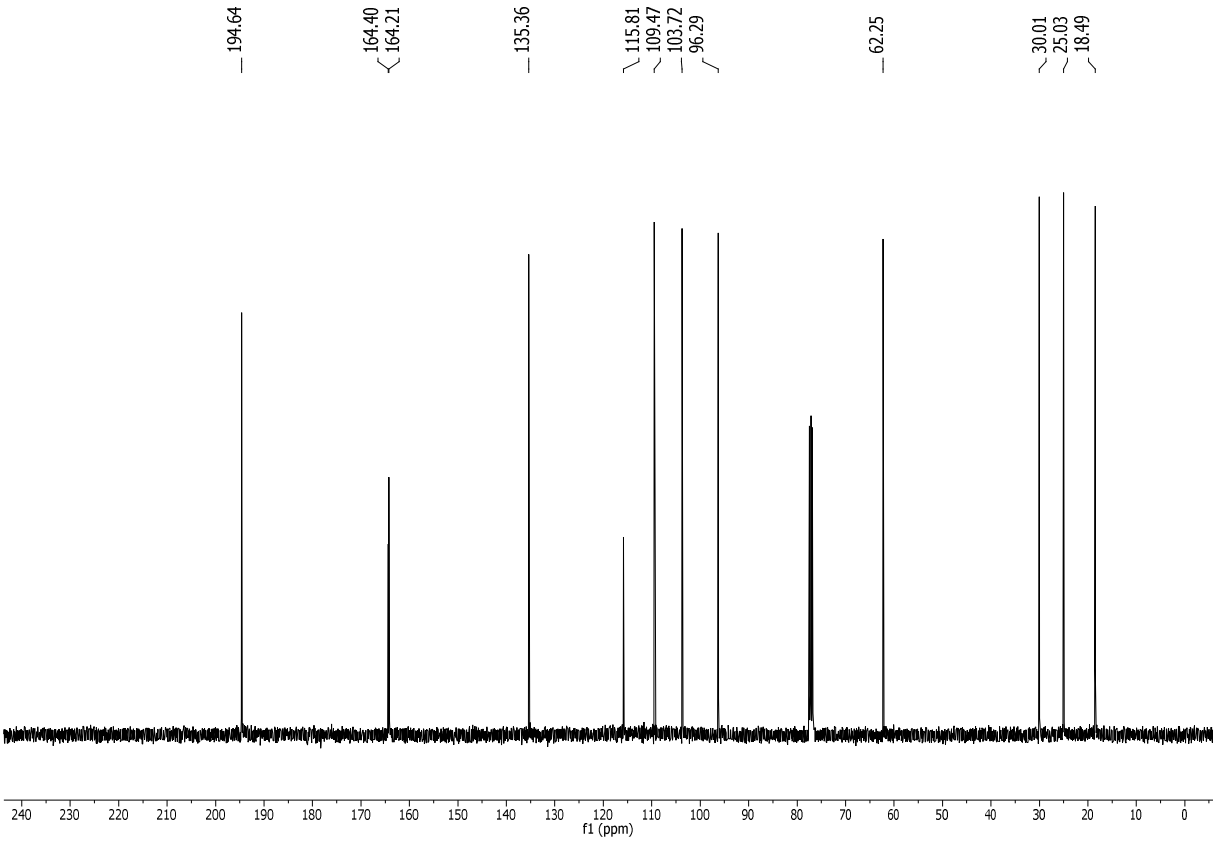
f1 (ppm)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164.40
164.21
135.36
115.81
109.47
103.72
96.29
62.25
30.01
25.03
18.49
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230
220
210
200
190
180
170
160
150
140
130
120
110
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90
80
70
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50
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30
20
10
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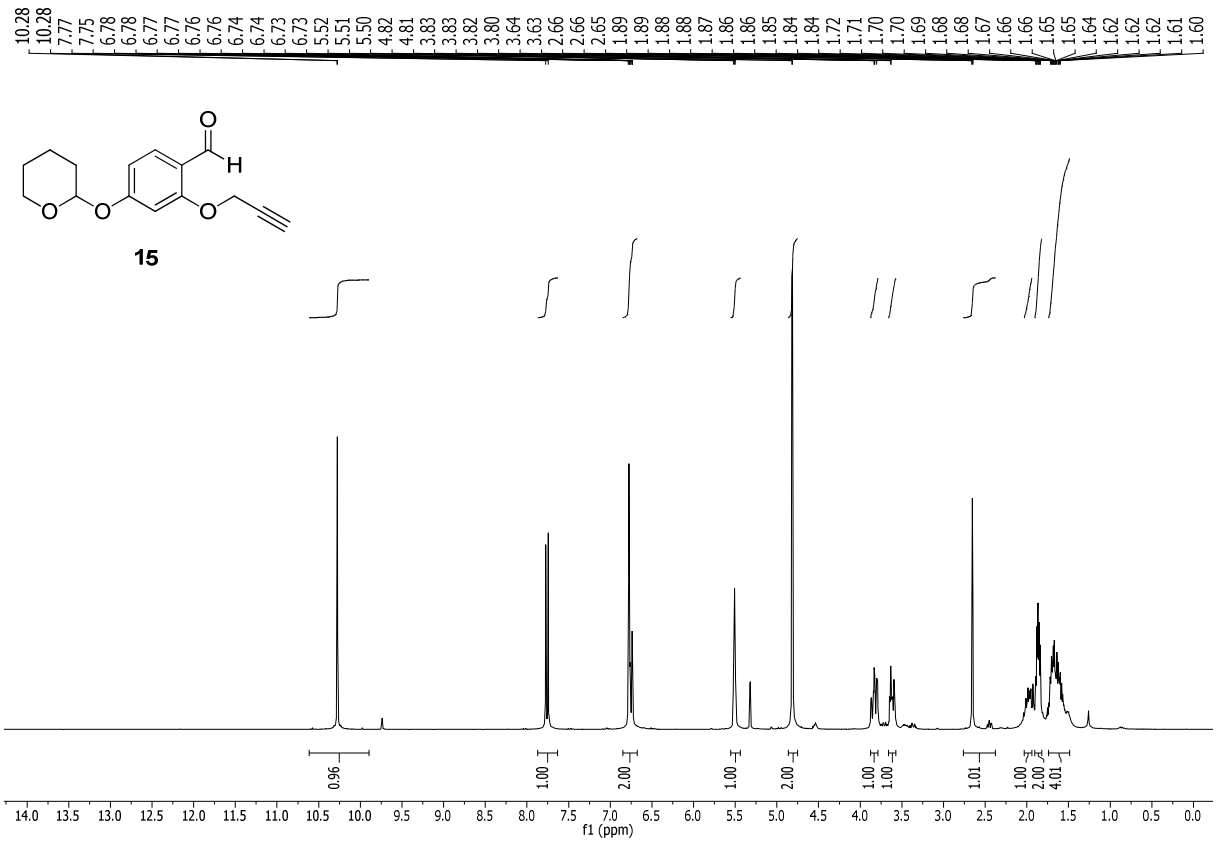
f1 (ppm)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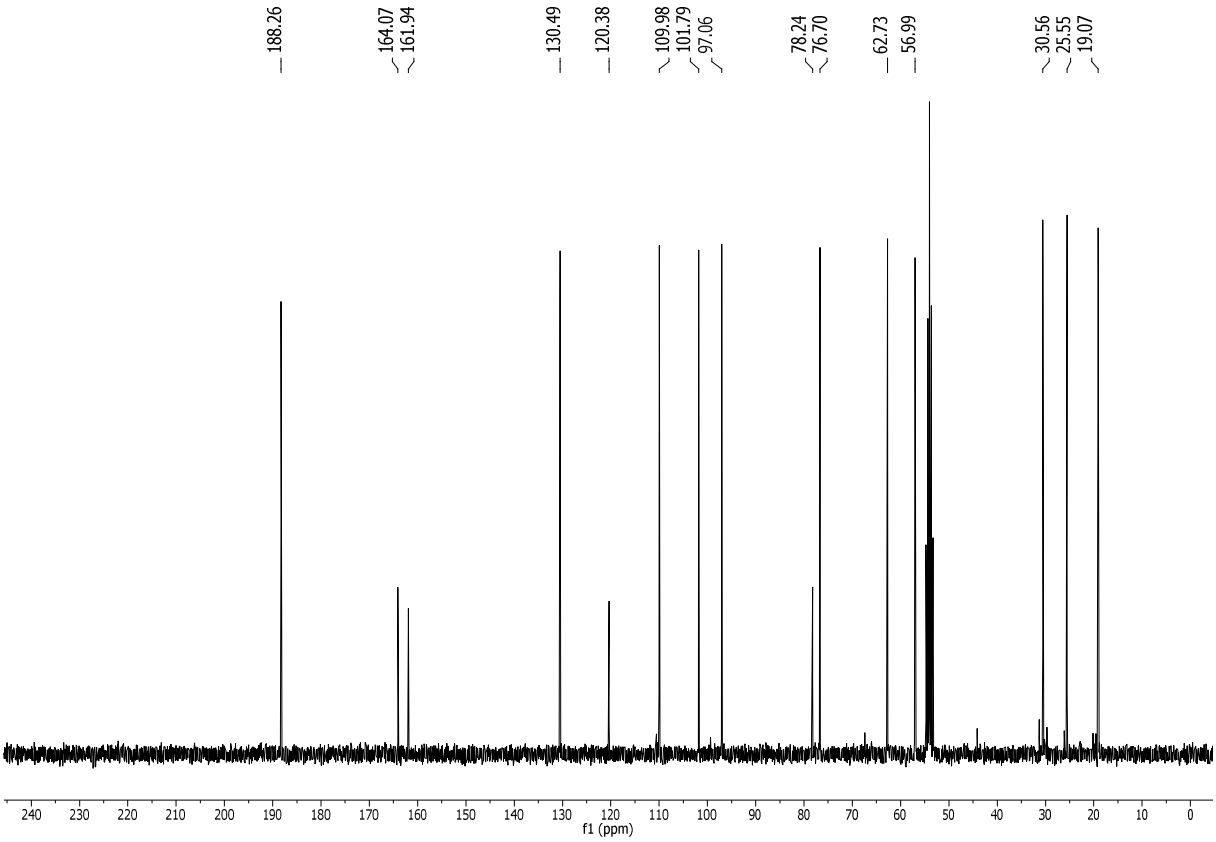
6.77
6.76
6.76
6.74
6.74
6.73
6.73
5.52
5.51
5.50
4.82
4.81
3.83
3.83
3.82
3.80
3.64
3.63
2.66
2.66
2.65
1.89
1.89
1.88
1.88
1.87
1.86
1.86
1.85
1.84
1.84
1.72
1.71
1.70
1.70
1.69
1.68
1.68
1.67
1.66
1.66
1.65
1.65
1.64
1.62
1.62
1.62
1.61
1.60
O
H
O
O
O
15
0.96
1.00
2.00
1.00
2.00
1.00
1.00
1.01
1.00
2.00
4.01
14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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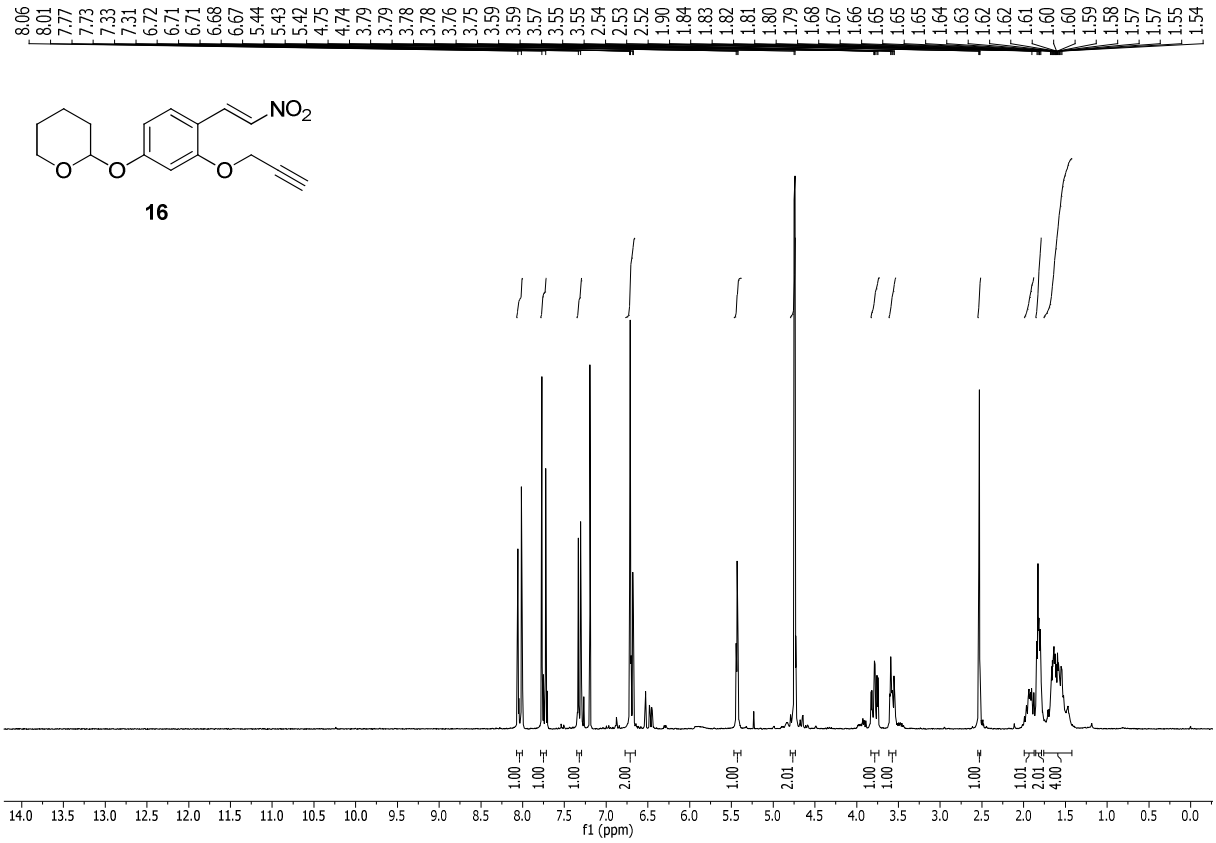
164.07
161.94
130.49
120.38
109.98
101.79
97.06
78.24
76.70
62.73
56.99
30.56
25.55
19.07
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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8.01
7.77
7.73
7.33
7.31
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6.71
6.71
6.68
6.67
5.44
5.43
5.42
4.75
4.74
3.79
3.79
3.78
3.78
3.76
3.75
3.59
3.59
3.57
3.55
3.55
2.54
2.53
2.52
1.90
1.84
1.83
1.82
1.81
1.80
1.79
1.68
1.67
1.66
1.65
1.65
1.65
1.64
1.63
1.62
1.62
1.61
1.60
1.60
1.59
1.58
1.57
1.57
1.55
1.54
NO2
O
O
O
16
1.00
1.00
1.00
2.00
1.00
2.01
1.00
1.00
1.00
1.01
2.01
4.00
14.0
13.5
13.0
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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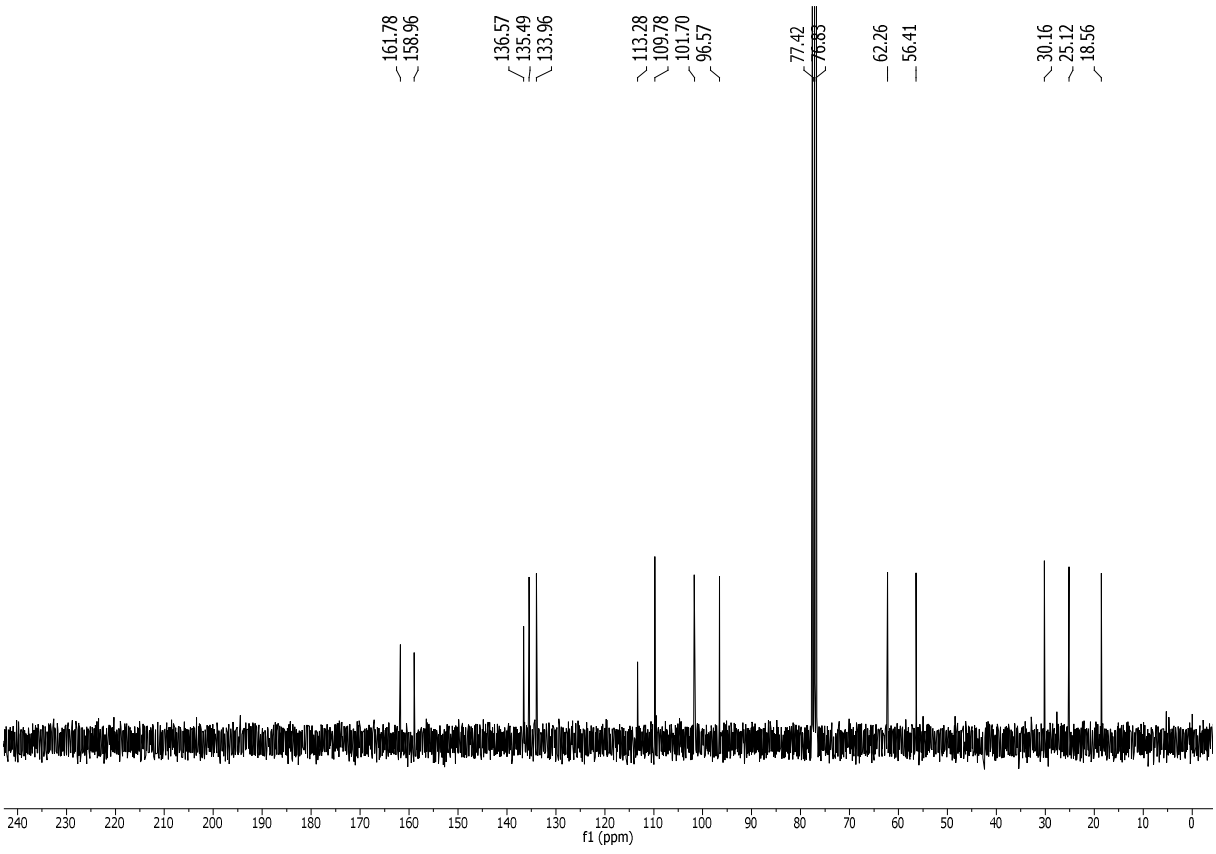
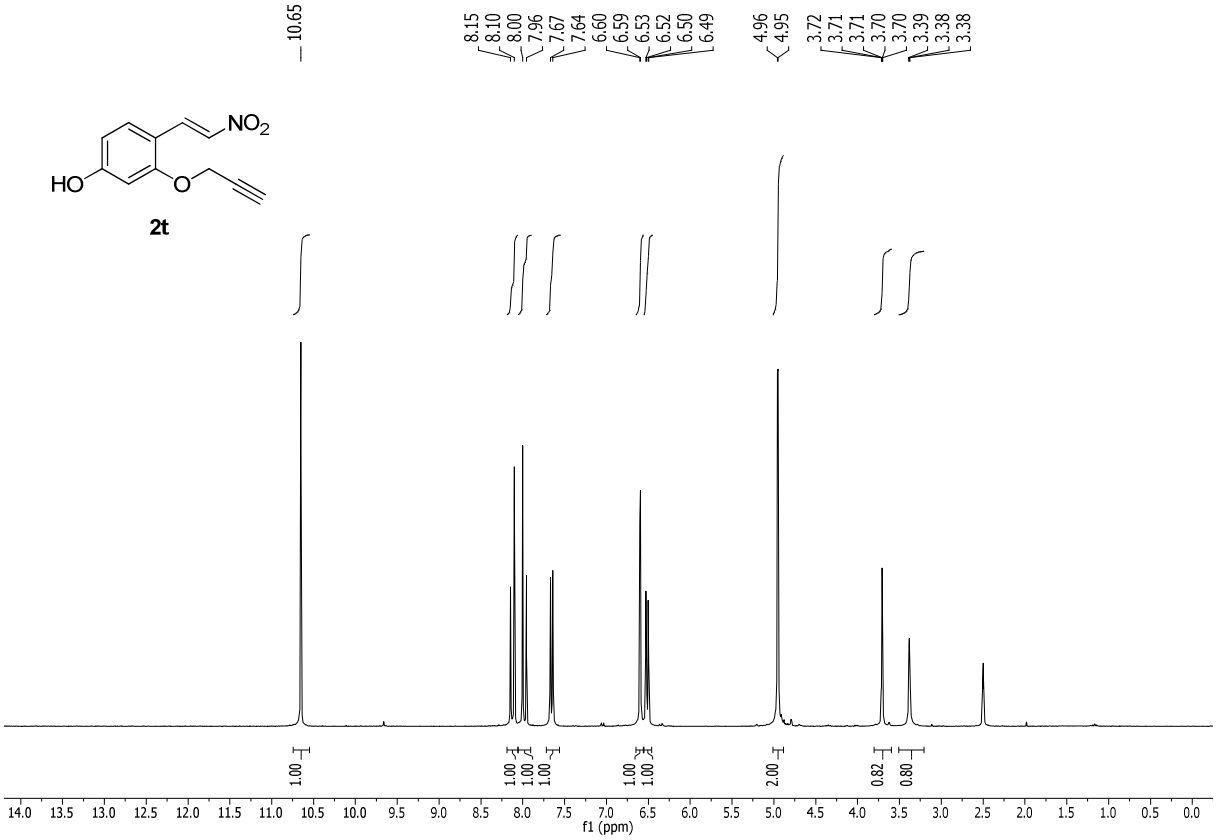
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


161.78
158.96
136.57
135.49
133.96
113.28
109.78
101.70
96.57
77.42
76.83
62.26
56.41
30.16
25.12
18.56
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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8.15
8.10
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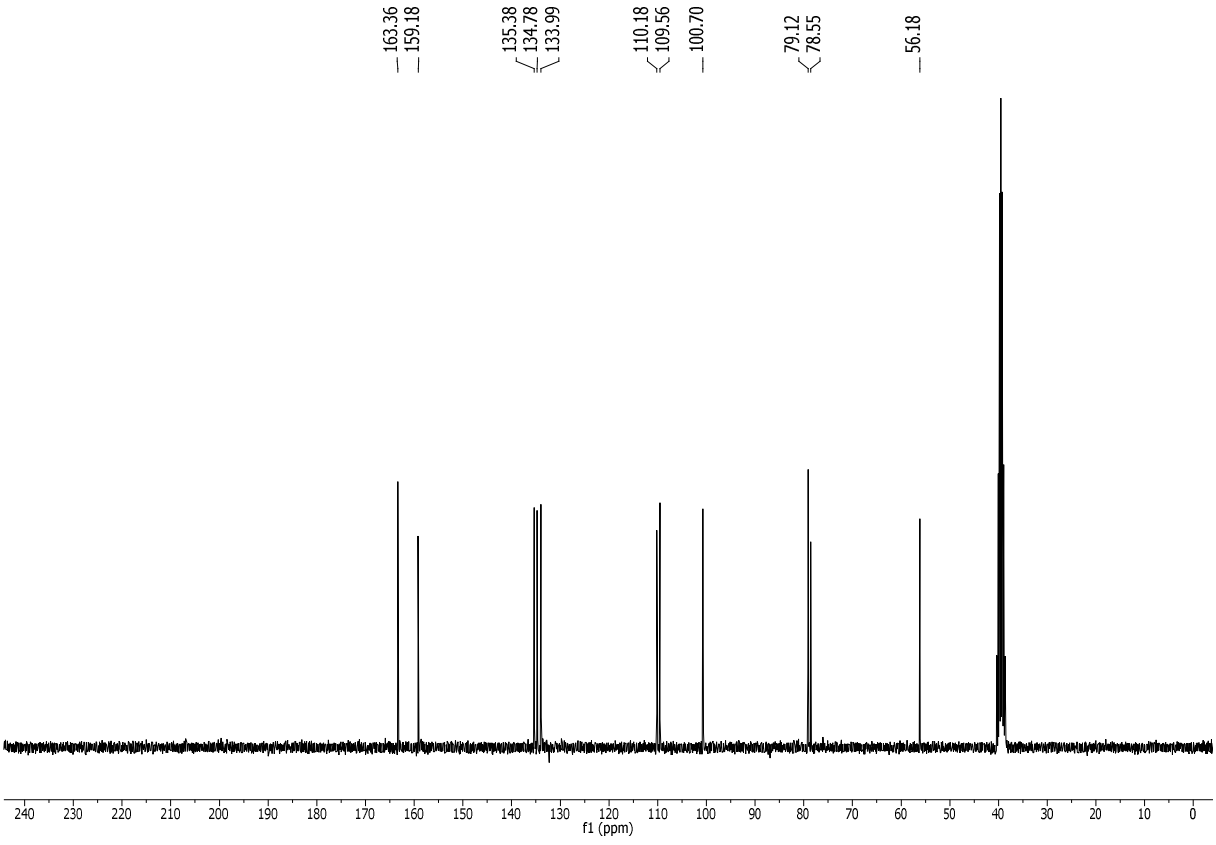
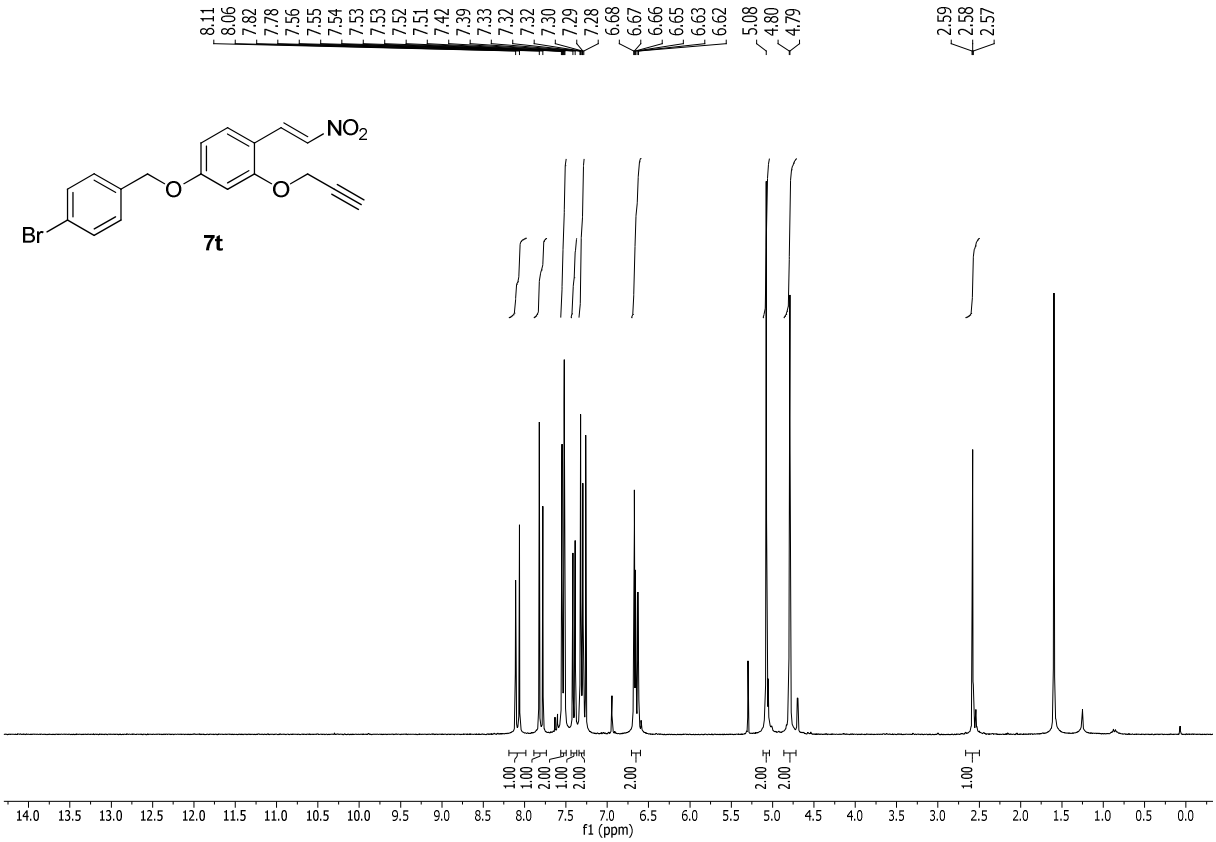
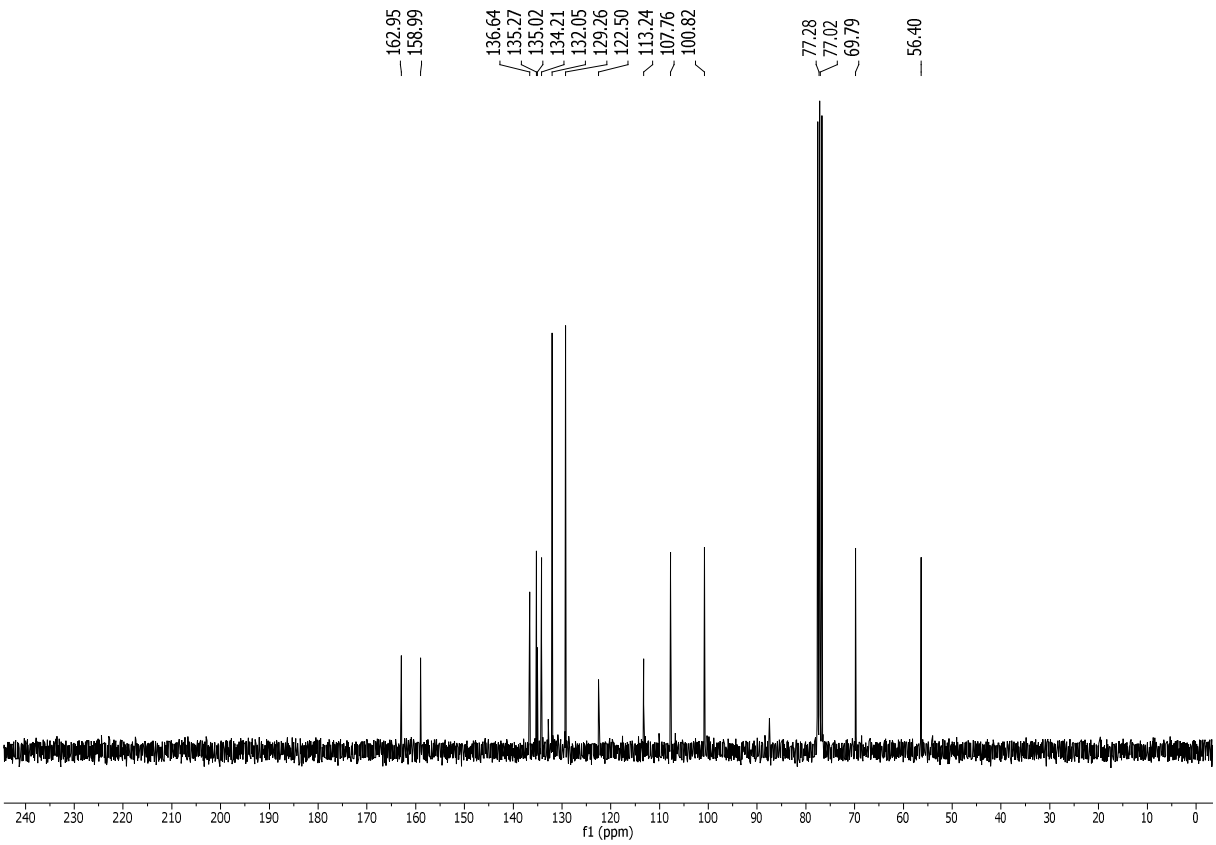
7.96
7.67
7.64
6.60
6.59
6.53
6.52
6.50
6.49
4.96
4.95
3.72
3.71
3.71
3.70
3.70
3.39
3.38
3.38
NO2
HO
O
2t
1.00
1.00
1.00
1.00
1.00
1.00
2.00
0.82
0.80
f1 (ppm)


163.36
159.18
135.38
134.78
133.99
110.18
109.56
100.70
79.12
78.55
56.18
f1 (ppm)


8.11
8.06
7.82
7.78
7.56
7.55
7.54
7.53
7.53
7.52
7.51
7.42
7.39
7.33
7.32
7.32
7.30
7.29
7.28
6.68
6.67
6.66
6.65
6.63
6.62
5.08
4.80
4.79
2.59
2.58
2.57
NO2
O
O
Br
7t
1.00
1.00
2.00
1.00
2.00
2.00
2.00
2.00
1.00
14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


162.95
158.99
136.64
135.27
135.02
134.21
132.05
129.26
122.50
113.24
107.76
100.82
77.28
77.02
69.79
56.40
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)