Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting information

Monofluorinated 5-membered rings via fluoromethylene transfer: synthesis of monofluorinated isoxazoline *N*-oxides

Arturs Sperga,[a] Armands Kazia,[a] and Janis Veliks*[a]

[a.] *Latvian Institute of Organic Synthesis, Aizkraukles 21, LV-1006, Riga, Latvia*
Email: janis.veliks@osi.lv

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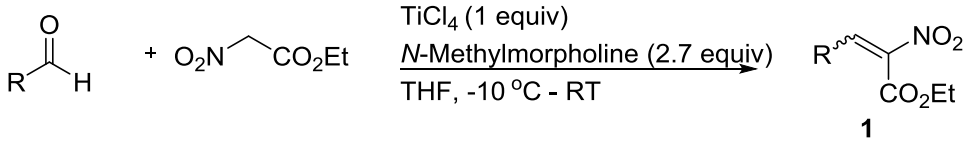
General Information

Reagents and starting materials were obtained from commercial sources and used as received. Starting materials and dry solvents (1,4-dioxane, MeCN, DMF, DMSO) were purchased form Fluorochem, SigmaAldrich, Acros or AlfaAeser and used as received. Dry THF, Et_2O and DCM were obtained from dry solvent still. Flash column chromatography was carried out using Kieselgel silica gel (35 -70 and 60 -200 μm). Thin layer chromatography (TLC) was performed on silica gel using Merck TLC Silca gel 60 F254 Aluminium sheets and was visualized by UV lamp, staining with $KMnO_4$. Preparative TLC was carrier out on 20x20 cm Merck TLC Silca gel 60 F254 Aluminium sheets. NMR spectra were recorded on 300 or 400 MHz Bruker spectrometers with chemical shift values (δ) in parts per million using the residual solvent signal as an internal standard. HRMS analyses were performed on a hybrid quadrupole time -of -flight mass spectrometer equipped with an electrospray ion source. Elemental analyses were performed by analytical service of LIOS. X-ray structures were investigated on a Rigaku, XtaLAB Synergy, Dualflex, HyPix diffractometer. The x-ray structures were deposited on the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures.

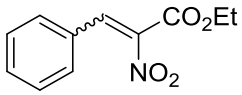
NOTE: Products **3** are prone to decomposition, in $CDCl_3$, C_6D_6, acetone-d_6, increased stability was observed in THF solution, *trans* diastereomer in pure form also decomposes, however *cis* diastereomer if crystalised showed superior stability. Product isolation should be conducted quickly after reaction.

General procedure A for synthesis of α-nitroacrylates



Scheme S1. Preperation of nitroacrylate substrates.

Ethyl 2-nitro-3-phenylacrylate (**1a**) [S1]

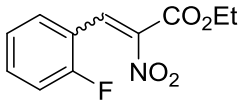


Nitroacrlyates **1a-t** were synthesised accoding to a slightly modified literature procedure [S2]. To a solution of benzaldehyde (500 mg, 4.71 mmol, 1 equiv) and ethyl nitroacetate (0.52 ml, 4.8 mmol, 1 equiv) in anhydrous THF (20 ml) under argon atmosphere at -10 °C was slowly added $TiCl_4$ (1M DCM solution, 4.71 ml, 4.71 mmol, 1 equiv). The reaction mixture was stirred at the same temperature for 40 minutes and then *N*-methylmorpholine (1.40 ml, 12.7 mmol, 2.7 equiv) was slowly added and further the stirring was continued at room temperature for 18 hours. The reaction mixture was quenched with H_2O (10 ml) and extracted with DCM (3 x 10 ml). The combined organic phases were dried over Na_2SO_4 and evaporated on silica gel under reduced pressure. The desired product was obtained by silica gel column chromatography using eluent PE:EtOAc 5:1. Ethyl 2-nitro-3-phenylacrylate (**1a**) (800 mg, 3.62 mmol, 77%) obtained as a yellow oil. A mixture of *E*, *Z* isomers (*E*:*Z*=1:1.3).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08 (s, 1 H), 7.57 – 7.36 (m, 11 H), 4.44 (q, *J* = 7.1 Hz, 2H), 4.38 (q, *J* = 7.1 Hz, 2H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.35 (t, *J* = 7.1 Hz, 3H).

Ethyl 3-(2-fluorophenyl)-2-nitroacrylate (**1b**) [S3]

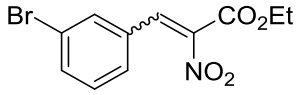
The product was obtained following general procedure A using 2-fluorobenzaldehyde



(0.17 ml, 1.6 mmol, 1 equiv), ethyl nitroacetate (0.18 ml, 1.6 mmol, 1 equiv), $TiCl_4$ (1M DCM solution, 1.61 ml, 1.61 mmol, 1 equiv), *N*-methylmorpholine (0.48 ml, 4.4 mmol, 2.7 equiv) and anhydrous THF (7 ml). Ethyl 3-(2-fluorophenyl)-2-nitroacrylate (**1b**) (109 mg, 0.456 mmol, 28%) obtained as a yellow oil. A mixture of *E*, *Z* isomers (*Z*:*E*=6.7:1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.53 – 7.44 (m, 1H), 7.45 – 7.33 (m, 1H), 7.23 – 7.11 (m, 2H), 4.40 (q, *J* = 7.0 Hz, 2H), 1.37 (t, *J* = 7.1 Hz, 3H). (main isomer peaks)

Ethyl 3-(3-bromophenyl)-2-nitroacrylate (**1c**)



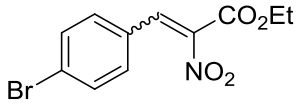
The product was obtained following general procedure A using 3-bromobenzaldehyde (0.19 ml, 1.6 mmol, 1 equiv), ethyl nitroacetate (0.18 ml, 1.6 mmol, 1 equiv), $TiCl_4$ (1M DCM solution, 1.61 ml, 1.61 mmol, 1 equiv), *N*-methylmorpholine (0.48 ml, 4.4 mmol, 2.7 equiv) and anhydrous THF (7 ml). Ethyl 3-(3-bromophenyl)-2-nitroacrylate (**1c**) (247.0 mg, 0.8230 mmol, 51%), (*E*:*Z*=1:1.4) obtained as a yellow oil, which upon standing slowly crystalises.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.69 – 7.56 (m, 3H), 7.55 (t, *J* = 1.5 Hz, 1H), 7.50 – 7.39 (m, 2H), 7.40 – 7.27 (m, 3H), 4.45 (q, *J* = 7.1 Hz, 2H), 4.39 (q, *J* = 7.1 Hz, 2H), 1.37 (t, *J* = 7.1 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.74, 158.95, 143.23, 141.29, 135.15, 135.06, 134.85, 132.94, 132.73, 131.33, 131.13, 131.06, 130.99, 130.86, 128.95, 127.75, 123.49, 123.42, 63.53, 63.48, 14.17, 13.92.

Elementanalyses, %: calculated $C_{11}H_{10}BrNO_4$: C, 44.02; H, 3.36; N, 4.67. Found: C, 44.10; H, 3.40; N 4.67.

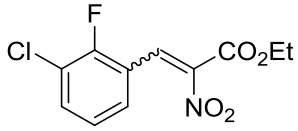
Ethyl 3-(4-bromophenyl)-2-nitroacrylate (**1d**) [S1]



The product was obtained following general procedure A using 4-bromobenzaldehyde (298.3 mg, 1.612 mmol, 1 equiv), ethyl nitroacetate (0.18 ml, 1.6 mmol, 1 equiv), $TiCl_4$ (1M DCM solution, 1.61 ml, 1.61 mmol, 1 equiv), *N*-methylmorpholine (0.48 ml, 4.4 mmol, 2.7 equiv) and anhydrous THF (7 ml). Ethyl 3-(4-bromophenyl)-2-nitroacrylate (**1d**) (354.4 mg, 1.1809 mmol, 73%), (*E*:*Z*=1:1.7) obtained as a yellow oil, which upon standing solidifies.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.00 (s, 1H), 7.64 – 7.51 (m, 4H), 7.47 (s, 1H), 7.43 – 7.32 (m, 2H), 7.33 – 7.22 (m, 2H), 4.43 (q, *J* = 7.2 Hz, 2H), 4.38 (q, *J* = 7.1 Hz, 2H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.36 (t, *J* = 7.1 Hz, 3H).

Ethyl 3-(3-chloro-2-fluorophenyl)-2-nitroacrylate (1e)



The product was obtained following general procedure A using 3-chloro-2-fluorobenzaldehyde (0.19 ml, 1.6 mmol, 1 equiv), ethyl nitroacetate (0.18 ml, 1.6 mmol, 1 equiv), $TiCl_4$ (1M DCM solution, 1.61 ml, 1.61 mmol, 1 equiv), *N*-methylmorpholine (0.48 ml, 4.4 mmol, 2.7 equiv) and anhydrous THF (7 ml). Ethyl 3-(3-chloro-2-fluorophenyl)-2-nitroacrylate (**1e**) (300.9 mg, 1.100 mmol, 68%), (*E*:*Z*=1:1.6) obtained as a yellow oil.

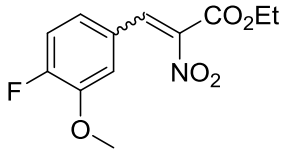
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.17 (s, 1H), 7.74 (s, 1H), 7.55 (ddd, *J* = 8.4, 7.1, 1.6 Hz, 1H), 7.52 (ddd, *J* = 8.5, 7.2, 1.6 Hz, 1H), 7.38 (dddd, *J* = 7.9, 6.3, 1.6, 0.7 Hz, 1H), 7.28 (dddd, *J* = 8.0, 6.3, 1.6, 0.6 Hz, 1H), 7.16 (ddd, *J* = 8.0, 1.2, 0.4 Hz, 1H), 7.13 (ddd, *J* = 8.1, 1.2, 0.4 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 4.40 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.36, 158.68, 156.82 (d, *J* = 257.1 Hz), 156.55 (d, *J* = 256.8 Hz), 144.41, 142.55, 134.40, 134.20, 128.66 (d, *J* = 4.6 Hz), 128.28, 126.89, 125.57 (d, *J* = 4.9 Hz), 125.27 (d, *J* = 4.9 Hz), 124.62 (d, *J* = 6.4 Hz), 122.69 (d, *J* = 17.4 Hz), 122.44 (d, *J* = 17.6 Hz), 119.37 (d, *J* = 12.6 Hz), 119.21 (d, *J* = 12.3 Hz), 63.63, 63.47, 14.14, 13.83.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -112.09 (t, *J* = 6.6 Hz), -113.33 (t, *J* = 6.7 Hz).

Elementanalyses, % calculated $C_{11}H_9ClFNO_4$ C, 48.28; H, 3.32; N, 5.12. Found: C, 48.31; H, 3.33; N 5.02.

Ethyl 3-(4-fluoro-3-methoxyphenyl)-2-nitroacrylate (1f)



The product was obtained following general procedure A using 4-fluoro-3-methoxybenzaldehyde (248.5 mg, 1.612 mmol, 1 equiv), ethyl nitroacetate (0.18 ml, 1.6 mmol, 1 equiv), $TiCl_4$ (1M DCM solution, 1.61 ml, 1.61 mmol, 1 equiv), *N*-methylmorpholine (0.48 ml, 4.4 mmol, 2.7 equiv) and anhydrous THF (7 ml). Ethyl 3-(4-fluoro-3-methoxyphenyl)-2-nitroacrylate (**1f**) (369.2 mg, 1.371 mmol, 85%), (*E*:*Z*=1:1.4) obtained as a yellow oil, which upon standing solidifies.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.01 (s, 1H), 7.46 (s, 1H), 7.18 – 7.07 (m, 4H), 7.04 – 6.98 (m, 2H), 4.43 (q, *J* = 7.2 Hz, 2H), 4.37 (q, *J* = 7.2 Hz, 2H), 3.89 (s, 3H), 3.87 (s, 3H), 1.36 (t, *J* = 7.2 Hz, 3H).

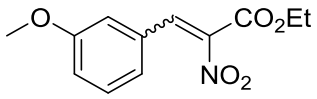
^{13}C NMR (101 MHz, Chloroform-*d*) δ 161.33, 159.23, 154.94 (d, *J* = 256.6 Hz), 154.74 (d, *J* = 256.0 Hz), 148.49 (d, *J* = 11.1 Hz), 148.45 (d, *J* = 11.1 Hz), 141.93 (d, *J* = 1.8 Hz), 140.10, 135.84 (d, *J* = 1.5 Hz), 132.05 (d, *J* = 1.5 Hz), 125.62 (d, *J* = 4.0 Hz), 125.60 (d, *J* = 4.1 Hz), 124.67 (d, *J* = 7.6 Hz), 123.98 (d, *J* = 7.6 Hz), 117.14 (d,

J = 19.1 Hz), 114.93 (d, *J* = 3.1 Hz), 113.96 (d, *J* = 3.1 Hz), 63.38, 63.29, 56.35, 14.16, 13.92.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -126.37 (ddd, *J* = 10.0, 8.1, 5.0 Hz), -126.77 – -126.86 (m).

HRMS (ESI) $[M+H]^+$: calculated $C_{12}H_{13}FNO_5$, 270.0778; found 270.0775.

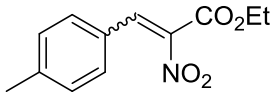
Ethyl 3-(3-methoxyphenyl)-2-nitroacrylate (**1g**) [S4]



The product was obtained following general procedure A using 3-methoxyphenylbenzaldehyde (0.20 ml, 1.6 mmol, 1 equiv), ethyl nitroacetate (0.18 ml, 1.6 mmol, 1 equiv), $TiCl_4$ (1M DCM, 1.61 ml, 1.61 mmol, 1 equiv), *N*-methylmorpholine (0.48 ml, 4.3 mmol, 2.7 equiv) and anhydrous THF (7 ml). Ethyl 3-(3-methoxyphenyl)-2-nitroacrylate (**1g**) (*E*:*Z*=1:1.7) (345.6 mg, 1.376 mmol, 85%) obtained as a yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.51 (s, 1H), 7.39 – 7.30 (m, 2H), 7.15 – 7.07 (m, 1H), 7.07 – 7.02 (m, 3H), 7.02 – 7.00 (m, 1H), 6.93 (t, *J* = 2.1 Hz, 1H), 4.44 (q, *J* = 7.2 Hz, 2H), 4.38 (q, *J* = 7.1 Hz, 2H), 3.82 (s, 3H), 3.80 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.36 (t, *J* = 7.1 Hz, 3H).

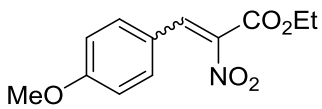
Ethyl 2-nitro-3-(*p*-tolyl)acrylate (1h) [S1]



The product was obtained following general procedure A using 4-methylbenzaldehyde (0.19 ml, 1.6 mmol, 1 equiv), ethyl nitroacetate (0.18 ml, 1.6 mmol, 1 equiv), $TiCl_4$ (1M DCM, 1.61 ml, 1.61 mmol, 1 equiv), *N*-methylmorpholine (0.48 ml, 4.3 mmol, 2.7 equiv) and anhydrous THF (7 ml). Ethyl 2-nitro-3-(*p*-tolyl)acrylate (**1h**) (*E*:*Z*=1:2) (148.2 mg, 0.6300 mmol, 39%) obtained as a yellow oil.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.05 (s, 1H), 7.49 (s, 1H), 7.44 – 7.18 (m, 8H), 4.44 (q, *J* = 7.2 Hz, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 2.41 (s, 3H), 2.38 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.36 (t, *J* = 7.1 Hz, 3H).

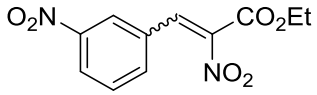
Ethyl 3-(4-methoxyphenyl)-2-nitroacrylate (**1i**) [S5]



The product was obtained following general procedure A using 4-metoxybenzaldehhyde (0.20 ml, 1.6 mmol, 1 equiv), ethyl nitroacetate (0.18 ml, 1.6 mmol, 1 equiv), $TiCl_4$ (1M DCM, 1.61 ml, 1.61 mmol, 1 equiv), *N*-methylmorpholine (0.48 ml, 4.4 mmol, 2.7 equiv) and anhydrous THF (7 ml). Ethyl 3-(4-methoxyphenyl)-2-nitroacrylate (**1i**) (*E*:*Z*=1:1.8) (349.0 mg, 1.389 mmol, 86%) obtained as a yellow oil.

^{1}H NMR (300 MHz, CDCl3) δ 8.04 (s, 1H), 7.52 – 7.45 (m, 3H), 7.43 – 7.36 (m, 3H), 6.98 – 6.89 (m, 4H), 4.46 (q, *J* = 7.1 Hz, 2H), 4.36 (q, *J* = 7.2 Hz, 2H), 3.87 (s, 3H), 3.85 (s, 3H), 1.37 (q, *J* = 7.2 Hz, 6H).

Ethyl 2-nitro-3-(3-nitrophenyl)acrylate (**1j**)



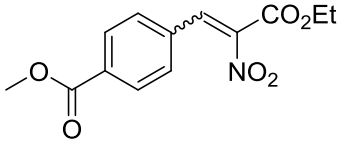
The product was obtained following general procedure A using 3-nitrobenzaldehyde (243.3 mg, 1.610 mmol, 1 equiv), ethyl nitroacetate (0.20 ml, 1.8 mmol, 1.1 equiv), $TiCl_4$ (1M DCM, 1.77 ml, 1.77 mmol, 1.1 equiv), *N*-methylmorpholine (0.48 ml, 4.3 mmol, 2.7 equiv) and anhydrous THF (7 ml). Ethyl 2-nitro-3-(3-nitrophenyl)acrylate (**1j**) (*E*:*Z*=2:1) (371.1 mg, 1.394 mmol, 87%), obtained as yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.40 (m, 1H), 8.36 (m, 1H), 8.33 (m, 1H), 8.31 (m, 1H), 8.31 – 8.24 (m, 1H), 8.09 (s, 1H), 7.88 – 7.79 (m, 1H), 7.77 – 7.67 (m, 1H), 7.70 – 7.60 (m, 1H), 7.61 (s, 1H), 4.47 (q, *J* = 7.1 Hz, 2H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.37 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.47, 148.64, 142.30, 134.16, 130.67, 130.66, 130.19, 126.17, 124.72, 63.66, 14.02. (*E*-isomer peaks)

Elementanalyses, %: calculated $C_{11}H_{10}N_2O_6$: C, 49.63; H, 3.79; N, 10.52. Found: C, 49.75; H, 3.80; N 10.23.

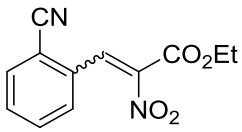
Methyl 4-(3-ethoxy-2-nitro-3-oxoprop-1-en-1-yl)benzoate (**1k**) [S1]



The product was obtained following general procedure A using methyl 4-formylbenzoate (264.8mg, 1.613 mmol, 1 equiv), ethyl nitroacetate (0.18 ml, 1.6 mmol, 1 equiv), $TiCl_4$ (1M DCM, 1.61 ml, 1.61 mmol, 1 equiv), *N*-methylmorpholine (0.48 ml, 4.4 mmol, 2.7 equiv) and anhydrous THF (7 ml). Methyl 4-(3-ethoxy-2-nitro-3-oxoprop-1-en-1-yl)benzoate (**1k**) (*E*:*Z*=1:1.9) (296.7 mg, 1.063 mmol, 66%), obtained as white solid after washing with PE.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.12 – 8.03 (m, 5H), 7.60 – 7.55 (m, 3H), 7.48 (m, 2H), 4.43 (q, *J* = 7.1 Hz, 2H), 4.40 (q, *J* = 7.1 Hz, 2H), 3.95 (s, 3H), 3.94 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.34 (t, *J* = 7.1 Hz, 3H).

Ethyl 3-(2-cyanophenyl)-2-nitroacrylate (**1l**)



The product was obtained following general procedure A using methyl 2-formylbenzonitrile (211.6 mg, 1.613 mmol, 1 equiv), ethyl nitroacetate (0.18 ml, 1.6 mmol, 1 equiv), $TiCl_4$ (1M DCM, 1.61 ml, 1.61 mmol, 1 equiv), *N*-methylmorpholine (0.48 ml, 4.4 mmol, 2.7 equiv) and

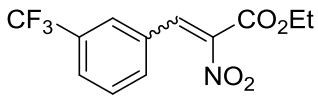
anhydrous THF (7 ml). Ethyl 3-(2-cyanophenyl)-2-nitroacrylate (**1l**) (*E*:*Z*=1:1.3) (296.7 mg, 1.063 mmol, 66%), obtained as yellow solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.31 (s, 1H), 7.86 (s, 1H), 7.82 – 7.77 (m, 2H), 7.70 – 7.55 (m, 5H), 7.52 (ddd, *J* = 7.9, 1.4, 0.7 Hz, 1H), 4.47 – 4.35 (m, 4H), 1.39 (t, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.04, 158.34, 145.24, 143.56, 133.89, 133.83, 133.72, 133.26, 132.54, 132.32, 132.10, 131.87, 131.74, 129.15, 128.30, 128.25, 116.38, 116.35, 114.32, 113.77, 63.86, 63.65, 14.12, 13.81.

Elementanalyses, %: calculated $C_{12}H_{10}N_2O_4$: C, 58.54; H, 4.09; N, 11.38. Found: C, 57.42; H, 3.92; N 11.13.

Ethyl 2-nitro-3-(3-(trifluoromethyl)phenyl)acrylate (**1m**)



The product was obtained following general procedure A using 3-(trifluoromethyl)benzaldehyde (0.22 ml, 1.6 mmol, 1 equiv), ethyl nitroacetate (0.20 ml, 1.8 mmol, 1.1 equiv), $TiCl_4$ (1M, DCM) (1.77 ml, 1.77 mmol, 1.1 equiv), *N*-methylmorpholine (0.48 ml, 4.3 mmol, 2.7 equiv) and anhydrous THF (7 ml). Ethyl 2-nitro-3-(3-(trifluoromethyl)phenyl)acrylate (**1m**) (*Z*:*E*=2.3:1) (409.7 mg, 1.417 mmol, 88%), obtained as a yellow oil.

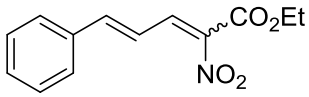
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.80 – 7.75 (m, 1H), 7.75 – 7.73 (m, 1H), 7.73 – 7.70 (m, 1H), 7.69 – 7.68 (m, 1H), 7.68 – 7.64 (m, 2H), 7.63 – 7.54 (m, 4H), 4.42 (m, 4H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.35 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.53, 158.73, 143.52, 141.59, 134.63, 133.33 (q, *J* = 1.2 Hz), 132.13 (q, *J* = 32.9 Hz), 131.90 (q, *J* = 33.1 Hz), 131.81 (q, *J* = 1.1 Hz), 131.13, 130.08, 129.94, 129.91, 129.83, 128.56 (q, *J* = 3.4 Hz), 128.43 (q, *J* = 3.7 Hz), 126.85 (q, *J* = 3.8 Hz), 126.69 (q, *J* = 3.8 Hz), 123.38 (q, *J* = 271.7 Hz), 123.35 (q, *J* = 272.7 Hz), 63.49, 63.45, 14.02, 13.67.

Elementanalyses, %: calculated $C_{12}H_{10}F_3NO_4$: C, 49.84; H, 3.49; N, 4.84. Found: C, 50.30; H, 3.65; N 4.54

Ethyl (4E)-2-nitro-5-phenylpenta-2,4-dienoate (**1n**) [S6]

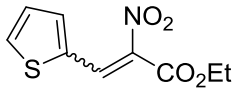
The product was obtained following general procedure A using cinnamaldehyde (0.20



ml, 1.612 mmol, 1 equiv), ethyl nitroacetate (0.18 ml, 1.6 mmol, 1 equiv), $TiCl_4$ (1M DCM, 1.61 ml, 1.61 mmol, 1 equiv), *N*-methylmorpholine (0.48 ml, 4.4 mmol, 2.7 equiv) and anhydrous THF (7 ml). Ethyl 3-(2-cyanophenyl)-2-nitroacrylate (**1l**) (*E*:*Z*=1:1.8) (203.9 mg, 0.8247 mmol, 51%), obtained as a yellow oil which solidified upon standing.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.78 (d, *J* = 11.2 Hz, 1H), 7.58 – 7.49 (m, 4H), 7.47 – 7.37 (m, 7H), 7.34 (dd, *J* = 15.4, 11.2 Hz, 1H), 7.24 (d, *J* = 15.4 Hz, 1H), 7.21 (d, *J* = 15.4 Hz, 1H), 6.99 (dd, *J* = 15.4, 11.5 Hz, 1H), 4.44 (q, *J* = 7.1 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H), 1.36 (t, *J* = 7.2 Hz, 3H).

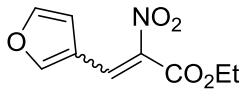
Ethyl 2-nitro-3-(thiophen-2-yl)acrylate (**1o**) [S5]



The product was obtained following general procedure A using thiophene-2-carbaldehyde (0.15 ml, 1.6 mmol, 1 equiv), ethyl nitroacetate (0.18 ml, 1.6 mmol, 1 equiv), $TiCl_4$ (1M DCM solution, 1.61 ml, 1.61 mmol, 1 equiv), *N*-methylmorpholine (0.48 ml, 4.4 mmol, 2.7 equiv) and anhydrous THF (7 ml). Ethyl 2-nitro-3-(thiophen-2-yl)acrylate (**1o**) (*E*:*Z*=1:1.1), (169.0 mg, 0.7437 mmol, 46%) obtained as a yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.25 (s, 1H), 7.75 – 7.66 (m, 3H), 7.57 (ddd, *J* = 3.8, 1.2, 0.6 Hz, 1H), 7.47 (ddd, *J* = 3.9, 1.2, 0.6 Hz, 1H), 7.17 (m, 2H), 4.49 (q, *J* = 7.2 Hz,2), 4.37 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H), 1.36 (t, *J* = 7.1 Hz, 3H).

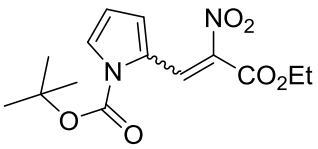
Ethyl 3-(furan-3-yl)-2-nitroacrylate (**1p**) [S5]



The product was obtained following general procedure A using furan-3-carbaldehyde (0.14 ml, 1.6 mmol, 1 equiv), ethyl nitroacetate (0.20 ml, 1.8 mmol, 1.1 equiv), $TiCl_4$ (1M DCM solution, 1.77 ml, 1.77 mmol, 1.10 equiv), *N*-methylmorpholine (0.48 ml, 4.3 mmol, 2.7 equiv) and anhydrous THF (7 ml). Ethyl 3-(furan-3-yl)-2-nitroacrylate (**1p**) (*Z*:*E*=2.3:1) (203.6 mg, 0.9641 mmol, 60%) obtained as a yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.95 – 7.93 (m, 1H), 7.83 – 7.82 (m, 1H), 7.52 – 7.50 (m, 1H), 7.49 – 7.47 (m, 1H), 7.46 (s, 1H), 6.56 (d, *J* = 1.8 Hz, 1H), 6.47 (d, *J* = 1.7 Hz, 1H), 4.45 (q, *J* = 7.1 Hz, 2H), 4.36 (q, *J* = 7.2 Hz, 2H), 1.38 (m, 6H).

***tert*-Butyl 2-(3-ethoxy-2-nitro-3-oxoprop-1-en-1-yl)-1H-pyrrole-1-carboxylate (1q)**



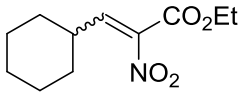
The product was obtained following general procedure A using tert-butyl 2-formyl-1*H*-pyrrole-1-carboxylate (314.9 mg, 1.613 mmol, 1 equiv), ethyl nitroacetate (0.18 ml, 1.6 mmol, 1.0 equiv), $TiCl_4$ (1M DCM solution, 1.61 ml, 1.61 mmol, 1 equiv), *N*-methylmorpholine (0.48 ml, 4.3 mmol, 2.7 equiv) and anhydrous THF (7 ml). *tert*-Butyl 2-(3-ethoxy-2-nitro-3-oxoprop-1-en-1-yl)-1*H*-pyrrole-1-carboxylate (**1q**) (*Z*:*E*=1.4:1) (491.3 mg, 1.5833 mmol, 98%) obtained as a brown oil.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.90 (s, 1H), 8.39 (s, 1H), 7.58 (dd, *J* = 3.2, 1.6 Hz, 1H), 7.51 (dd, *J* = 3.3, 1.5 Hz, 1H), 6.84 (ddd, *J* = 3.9, 1.6, 0.8 Hz, 1H), 6.75 (ddd, *J* = 3.8, 1.6, 0.8 Hz, 1H), 6.31 (ddd, *J* = 3.8, 3.2, 0.6 Hz, 1H), 6.27 (ddd, *J* = 3.9, 3.2, 0.6 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 4.34 (q, *J* = 7.1 Hz, 2H), 1.64 (s, 9H), 1.63 (s, 9H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.34 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 161.78, 159.66, 148.56, 148.46, 138.98, 137.31, 128.49, 127.46, 127.06, 124.42, 124.02, 122.74, 121.42, 120.38, 112.74, 86.41, 86.07, 63.03, 62.80, 28.04, 14.22, 13.90.

HRMS (ESI) $[M-H]^-$: calculated $C_{14}H_{17}N_2O_6$, 309.1087; found 309.1084

Ethyl 3-cyclohexyl-2-nitroacrylate (**1r**)



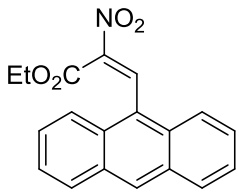
The product was obtained following general procedure A using cyclohexanecarbaldehyde (0.20 ml, 1.6 mmol, 1 equiv), ethyl nitroacetate (0.18 ml, 1.6 mmol, 1.0 equiv), $TiCl_4$ (1M DCM solution, 1.61 ml, 1.61 mmol, 1 equiv), *N*-methylmorpholine (0.48 ml, 4.3 mmol, 2.7 equiv) and anhydrous THF (7 ml). Ethyl 3-cyclohexyl-2-nitroacrylate (**1r**) (*Z*:*E*=2.4:1) (217.7 mg, 0.9579 mmol, 59%) obtained as a yellow oil.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.06 (d, *J* = 10.8 Hz, 1H), 6.68 (d, *J* = 10.8 Hz, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 2.55 (m, 1H), 2.32 (m, 1H), 1.82 – 1.65 (m, 10H), 1.36 (d, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.28 – 1.21 (m, 10H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.16, 159.06, 147.28, 144.11, 143.43, 142.95, 62.85, 62.69, 37.81, 37.40, 31.61, 25.51, 25.05, 24.95, 14.12, 14.06.

Elementanalyses, %: calculated $C_{11}H_{17}NO_4$: C, 58.14; H, 7.54; N, 6.16. Found: C, 58.99; H, 7.82; N 5.54

Ethyl (E)-3-(anthracen-9-yl)-2-nitroacrylate (**1s**)



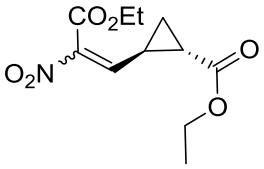
The product was obtained following general procedure A using anthracene-9-carbaldehyde (332.4 mg, 1.612 mmol, 1 equiv), ethyl nitroacetate (0.18 ml, 1.6 mmol, 1.0 equiv), $TiCl_4$ (1M DCM solution, 1.61 ml, 1.61 mmol, 1 equiv), *N*-methylmorpholine (0.48 ml, 4.3 mmol, 2.7 equiv) and anhydrous THF (7 ml). Ethyl (*E*)-3-(anthracen-9-yl)-2-nitroacrylate (**1s**) (134 mg, 0.417 mmol, 26%) obtained as orange solid after washing with PE.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.90 (s, 1H), 8.53 (s, 1H), 8.06 – 8.02 (m, 2H), 7.99 – 7.92 (m, 2H), 7.59 – 7.50 (m, 4H), 3.80 (q, *J* = 7.1 Hz, 2H), 0.51 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 159.54, 146.82, 137.04, 131.04, 129.95, 129.18, 129.15, 127.29, 125.85, 124.70, 123.28, 62.47, 13.02.

Elementanalyses, %: calculated $C_{19}H_{15}NO_4$: C, 71.02; H, 4.71; N, 4.36. Found: C, 71.10; H, 4.65; N 4.32.

Ethyl (1S*,2R*)-2-(3-ethoxy-2-nitro-3-oxoprop-1-en-1-yl)cyclopropane-1-carboxylate (**1t**)



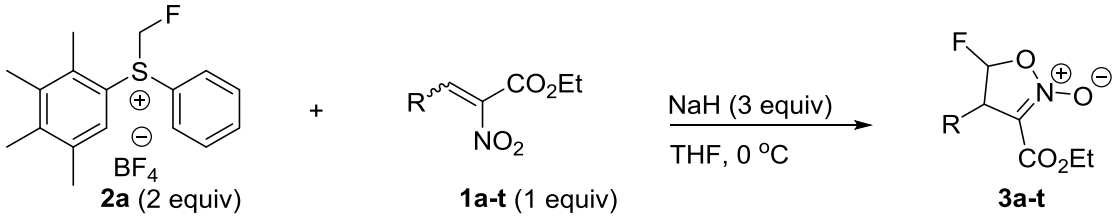
The product was obtained following general procedure A using ethyl 2-formylcyclopropane-1-carboxylate (0.23 ml, 1.6 mmol, 1 equiv, predominantly *trans* isomer), ethyl nitroacetate (0.18 ml, 1.6 mmol, 1.0 equiv), $TiCl_4$ (1M DCM solution, 1.61 ml, 1.61 mmol, 1 equiv), *N*-methylmorpholine (0.48 ml, 4.3 mmol, 2.7 equiv) and anhydrous THF (7 ml). Ethyl 3-cyclohexyl-2-nitroacrylate (**1r**) (*Z*:*E*=1.5:1) (75.1 mg, 0.309 mmol, 19%) obtained as a yellow oil. After column chromatography product was repurified with preperative TLC (eluent: PE:Et_2O 2:1)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.61 (d, *J* = 11.4 Hz, 1H), 6.24 (d, *J* = 11.2 Hz, 2H), 4.43 – 4.35 (m, 2H), 4.34 – 4.27 (m, 2H), 4.21 – 4.12 (m, 4H), 2.67 – 2.58 (m, 1H), 2.34 – 2.23 (m, 1H), 2.09 – 1.98 (m, 3H), 1.81 – 1.69 (m, 3H), 1.40 – 1.18 (m, 18H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.15, 170.91, 159.74, 158.66, 145.41, 144.35, 144.31, 62.97, 62.94, 61.58, 24.47, 24.18, 20.82, 20.57, 17.54, 17.02, 14.27, 14.25, 14.12, 14.05.

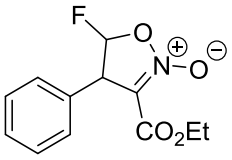
HRMS (ESI) $[M-H]^-$: calculated $C_{11}H_{14}NO_6$, 256.0821; found 256.0819

General procedure B for the synthesis of monofluorinated isoxazoline *N*-oxides 3



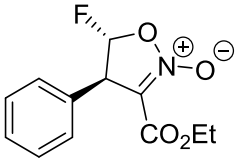
Scheme S2. Nitroacrylate fluorocyclization.

3-(Ethoxycarbonyl)-5-fluoro-4-phenyl-4,5-dihydroisoxazole 2-oxide (**3a**)



To a suspension of ethyl 2-nitro-3-phenylacrylate (**1a**) (24.0 mg, 0.109 mmol, 1 equiv) and (fluoromethyl)(phenyl)(2,3,4,5-tetramethylphenyl)sulfonium tetrafluoroborate (**2a**) (78.6 mg, 0.217 mmol, 2 equiv) in anhydrous THF (4.3 ml) under Ar atmosphere at 0 °C was added NaH (60% dispersion in mineral oil, 13.0 mg, 0.326 mmol, 3 equiv). The reaction mixture was further stirred at 0 °C until full nitroacrylate **1a** consumption (determined by TLC eluent: PE:EtOAc 5:1, ~1 hour). The reaction mixture was diluted with Et_2O (5 ml) and it was allowed to warm up to room temperature. The resulting suspenison was filtered through a cotton plug. The filtrate was evaporated under reduced pressure at room temperature to obtain crude product **3a** (84%, *d.r.* = 1.6:1, determined by ^{1}H NMR, internal standard EtOAc). The crude product was dry loaded on silica gel and purified by column chromatography using eluent gradient PE 100% to PE:EtOAc 5:1. Two separate diastereomers were obtained:

(4R*,5S*)-3-(Ethoxycarbonyl)-5-fluoro-4-phenyl-4,5-dihydroisoxazole 2-oxide (*trans*-**3a**)



1st fraction: *trans* isomer (13.0 mg, 0.0513 mmol, 47%) a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.35 (m, 3H), 7.30 – 7.22 (m, 2H), 5.98 (d, *J* = 63.4 Hz, 1H), 4.75 (d, *J* = 19.7 Hz, 1H), 4.25 (dq, *J* = 10.8, 7.2 Hz, 1H), 4.23 (dq, *J* = 10.8, 7.1 Hz, 1H), 1.22 (t, *J* = 7.1 Hz, 3H).

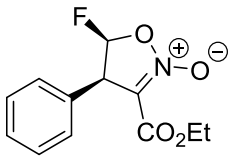
^{13}C NMR (101 MHz, $CDCl_3$) δ 157.91, 133.49 (d, *J* = 11.4 Hz), 129.65, 129.30, 127.46, 108.61, 108.23, 106.19, 62.53, 57.22 (d, *J* = 26.4 Hz), 14.07.

^{19}F NMR (376 MHz, $CDCl_3$) δ -108.36 (dd, *J* = 63.5, 19.8 Hz).

HRMS : Calculated $[M\text{-}COF]^+$: $C_{11}H_{12}NO_3$, 206.0812, Found 206.0818.

LC/MS: Calculated $[M+H]^+$: $C_{12}H_{13}FNO_4$, 254.08, found 254.35.

(4R*,5R*)-3-(Ethoxycarbonyl)-5-fluoro-4-phenyl-4,5-dihydroisoxazole 2-oxide (*cis*-**3a**)



2nd fraction: *cis* isomer, obtained as a yellow oil, trituration with PE afforded an off-white solid (8.5 mg, 0.034 mmol, 31%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.29 (m, 3H), 7.23 – 7.16 (m, 2H), 6.13 (dd, *J* = 64.6, 5.5 Hz, 1H), 5.03 (dd, *J* = 29.7, 5.4 Hz, 1H), 4.12 (dq, *J* = 10.8, 7.1 Hz, 1H), 4.01 (dq, *J* = 10.8, 7.1 Hz, 1H), 0.94 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.99, 130.45 (d, *J* = 4.2 Hz), 129.32 (d, *J* = 1.4 Hz), 128.95, 128.81, 107.33, 102.85 (d, *J* = 244.7 Hz), 62.28, 55.85 (d, *J* = 22.0 Hz), 13.79.

^{19}F NMR (376 MHz, $CDCl_3$) δ -123.64 (dd, *J* = 64.6, 29.7 Hz).

HRMS : Calculated $[M\text{-}CO\text{-}F]^+$: $C_{11}H_{12}NO_3$ 206.0812, found 206.0825.

LC/MS: Calculated $[M+H]^+$: $C_{12}H_{13}FNO_4$ 254.08, found 254.36.

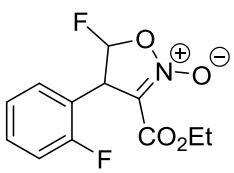
Upscale reactions 3-(Ethoxycarbonyl)-5-fluoro-4-phenyl-4,5-dihydroisoxazole 2-oxide (**3a**)

The upscale was performed following the modified general procedure B using ethyl 2-nitro-3-phenylacrylate (**1a**) (221.2 mg, 1.000 mmol, 1 equiv) or (856 mg, 3.87 mmol, 1 equiv) and (2,4-dimethylphenyl)(fluoromethyl)(phenyl)sulfonium tetrafluoroborate (**2b**) (668.3 mg, 2.000 mmol, 2 equiv) or (2.59 g, 7.74 mmol, 2 equiv) correspondingly. The product **3a** yields for 1 mmol scale reaction: NMR yield (80% d.r.=1.4:1), isolated (83% d.r.=1.9:1).

The product **3a** yield for 3.87 mmol scale reaction: isolated (80%, d.r. = 1.9:1).

(80% d.r.=1.4:1).

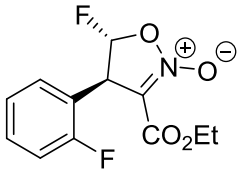
3-(Ethoxycarbonyl)-5-fluoro-4-(2-fluorophenyl)-4,5-dihydroisoxazole 2-oxide (**3b**)



The product was obtained following general procedure B using ethyl 3-(2-fluorophenyl)-2-nitroacrylate (**1b**) (51.9 mg, 0.217 mmol, 1 equiv), (fluoromethyl)(phenyl)(2,3,4,5-tetramethylphenyl)sulfonium tetrafluoroborate ***(2a)*** (157.2 mg, 0.4340 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 26.0 mg, 0.651 mmol, 3 equiv) and anhydrous THF (8.7 ml) to obtain the crude product **3b** (50%, *d.r.* = 2.3:1,

determined by ^{1}H NMR, internal standard EtOAc). After purification two separate diastereomers were obtained:

(4R*,5S*)-3-(Ethoxycarbonyl)-5-fluoro-4-(2-fluorophenyl)-4,5-dihydroisoxazole 2-oxide (*trans*-**3b**)



1st fraction: *trans* isomer (20.0 mg, 0.0737 mmol, 34%), a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.34 (m, 1H), 7.21 – 7.13 (m, 3H), 5.99 (d, *J* = 63.0 Hz, 1H), 5.11 (d, *J* = 19.8 Hz, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 1.21 (t, *J* = 7.1 Hz, 3H).

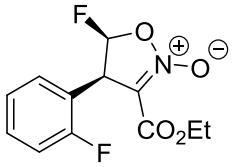
^{13}C NMR (101 MHz, $CDCl_3$) δ 160.28 (d, *J* = 249.0 Hz), 157.75, 131.19 (d, *J* = 8.3 Hz), 128.39 (d, *J* = 3.0 Hz), 125.20 (d, *J* = 3.8 Hz), 120.70 (dd, *J* = 14.1, 11.5 Hz), 116.41 (d, *J* = 21.3 Hz), 106.92, 106.71 (dd, *J* = 244.1, 1.6 Hz), 62.59, 50.69 (dd, *J* = 28.9, 4.1 Hz), 14.01.

^{19}F NMR (376 MHz, $CDCl_3$) δ -108.37 (dd, *J* = 63.1, 19.7 Hz), -117.34 (dt, *J* = 11.0, 6.1 Hz).

Compound is unstable under HRMS conditions.

LC/MS: Calculated $[M+H]^+$: $C_{12}H_{12}F_2NO_4$ 272.07, Found 272.36.

(4*R,5*R**) 3-(ethoxycarbonyl)-5-fluoro-4-(2-fluorophenyl)-4,5-dihydroisoxazole 2-oxide** (*cis*-**3b**)



2nd fraction: *cis* isomer, a yellow crystalline solid after trituration with PE (12.0 mg, 0.0442 mmol, 20%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.33 (m, 1H), 7.25 – 7.20 (m, 1H), 7.19 – 7.09 (m, 2H), 6.25 (dd, *J* = 64.9, 5.4 Hz, 1H), 5.44 (dd, *J* = 29.4, 5.5 Hz, 1H), 4.23 (dq, *J* = 10.8, 7.1 Hz, 1H), 4.13 (dq, *J* = 10.8, 7.1 Hz, 1H), 1.06 (t, *J* = 7.1 Hz, 3H).

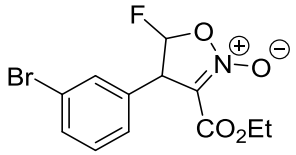
^{13}C NMR (101 MHz, $CDCl_3$) δ 160.87 (d, *J* = 247.8 Hz), 157.88, 130.84 (t, *J* = 2.7 Hz), 130.71 (d, *J* = 8.5 Hz), 124.41 (d, *J* = 3.7 Hz), 118.02 (dd, *J* = 12.9, 4.6 Hz), 115.77 (d, *J* = 21.7 Hz), 106.32, 102.26 (d, *J* = 244.2 Hz), 62.39, 48.90 (d, *J* = 22.1 Hz), 13.83.

^{19}F NMR (376 MHz, $CDCl_3$) δ -117.52, -122.97 (dd, *J* = 64.9, 29.3 Hz).

Compund is unstable under HRMS conditions.

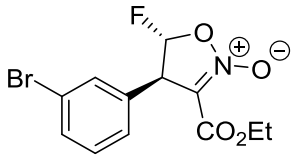
LC/MS: Calculated $[M+H]^+$ $C_{12}H_{12}F_2NO_4$ 272.07, found 272.35.

4-(3-Bromophenyl)-3-(ethoxycarbonyl)-5-fluoro-4,5-dihydroisoxazole 2-oxide (**3c**)



The product was obtained following general procedure B using ethyl 3-(3-bromophenyl)-2-nitroacrylate (**1c**) (65.1 mg, 0.217 mmol, 1 equiv), (fluoromethyl)(phenyl)(2,3,4,5-tetramethylphenyl)sulfonium tetrafluoroborate (**2a**) (157.2 mg, 0.4340 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 26.0 mg, 0.6511 mmol, 3 equiv) and anhydrous THF (8.7 ml) to obtain the crude product **3c** (74%, *d.r.* = 2.5:1, determined by ^{1}H NMR, internal standard EtOAc). After purification two separate diastereomers were obtained:

(4R*,5S*)-4-(3-Bromophenyl)-3-(ethoxycarbonyl)-5-fluoro-4,5-dihydroisoxazole 2-oxide (*trans*-**3c**)



1st fraction: *trans* isomer (36.3 mg, 0.109 mmol, 50%), yellow oil

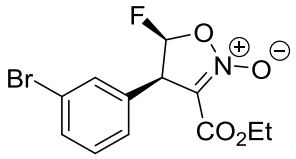
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (ddd, *J* = 7.9, 2.0, 1.1 Hz, 1H), 7.42 (t, *J* = 1.9 Hz, 1H), 7.29 (t, *J* = 7.9 Hz, 1H), 7.20 (ddd, *J* = 7.7, 1.8, 1.1 Hz, 1H), 5.98 (d, *J* = 62.9 Hz, 1H), 4.71 (d, *J* = 19.2 Hz, 1H), 4.28 (dq, *J* = 10.9, 7.1 Hz, 1H), 4.24 (dq, *J* = 10.7, 7.1 Hz, 1H), 1.24 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.72, 135.62 (d, *J* = 11.7 Hz), 132.56, 131.19, 130.67, 126.07, 123.63, 107.68, 106.91 (d, *J* = 244.2 Hz), 62.73, 56.79 (d, *J* = 27.2 Hz), 14.09.

^{19}F NMR (376 MHz, $CDCl_3$) δ -108.39 (dd, *J* = 62.8, 19.3 Hz).

Compound is unstable in HRMS and LC/MS conditions.

(4R*,5R*)-4-(3-Bromophenyl)-3-(ethoxycarbonyl)-5-fluoro-4,5-dihydroisoxazole 2-oxide (*cis*-**3c**)



2nd fraction: *cis* isomer (15.5 mg, 0.0467 mmol, 22%), a yellow crystalline solid after PE trituration.

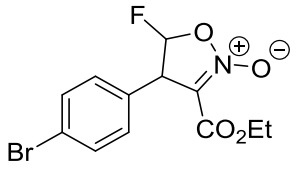
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (ddd, *J* = 7.8, 2.0, 1.3 Hz, 1H), 7.43 (q, *J* = 1.7 Hz, 1H), 7.26 (t, *J* = 7.7 Hz, 1H), 7.21 (dq, *J* = 7.8, 1.5 Hz, 1H), 6.20 (dd, *J* = 64.6, 5.4 Hz, 1H), 5.06 (dd, *J* = 29.2, 5.4 Hz, 1H), 4.23 (dq, *J* = 10.8, 7.1 Hz, 1H), 4.10 (dq, *J* = 10.8, 7.1 Hz, 1H), 1.05 (t, *J* = 7.1 Hz, 3H)

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.77, 132.73 (d, *J* = 4.4 Hz), 132.36 (d, *J* = 1.5 Hz), 132.11, 130.29, 128.00, 122.74, 106.71, 102.52 (d, *J* = 244.9 Hz), 62.44, 55.26 (d, *J* = 21.9 Hz), 13.86.

^{19}F NMR (376 MHz, $CDCl_3$) δ -123.42 (dd, *J* = 64.6, 29.4 Hz).

Compound is unstable in HRMS and LC/MS conditions**.**

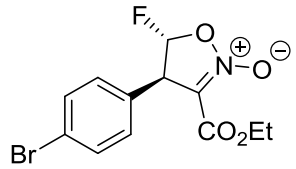
4-(4-Bromophenyl)-3-(ethoxycarbonyl)-5-fluoro-4,5-dihydroisoxazole 2-oxide (**3d**)



The product was obtained following general procedure B using ethyl 3-(4-bromophenyl)-2-nitroacrylate (**1d**) (63.3 mg, 0.211 mmol, 1 equiv), (fluoromethyl)(phenyl)(2,3,4,5-tetramethylphenyl)sulfonium tetrafluoroborate (**2a**) (152.9 mg, 0.4220 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 25.3 mg, 0.6331 mmol, 3 equiv) and anhydrous THF (8.4 ml) to obtain the crude product **3d** (78%, *d.r.* = 1.8:1, determined by ^{1}H NMR, internal standard EtOAc). After purification two separate diastereomers were obtained:

(4R*,5S*)-4-(4-Bromophenyl)-3-(ethoxycarbonyl)-5-fluoro-4,5-dihydroisoxazole 2-oxide (*trans*-**3d**)

1st fraction: *trans* isomer (34.6 mg, 0.1042 mmol, 49%) a yellow oil.



^{1}H NMR (400 MHz, THF-d_8) δ 7.59 – 7.52 (m, 2H), 7.29 – 7.24 (m, 2H), 6.20 (d, *J* = 62.7 Hz, 1H), 4.87 (d, *J* = 19.3 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 1.18 (t, *J* = 7.1 Hz, 3H).

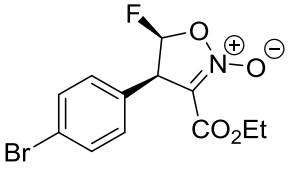
^{13}C NMR (101 MHz, THF-d_8) δ 158.36, 134.82 (d, *J* = 12.0 Hz), 133.32, 130.59, 123.60, 108.28 (d, *J* = 241.4 Hz), 108.27, 62.78, 57.44 (d, *J* = 27.5 Hz), 14.39.

^{19}F NMR (376 MHz, THF-d_8) δ -110.17 (dd, *J* = 62.7, 18.4 Hz).

HRMS: Calculated $[M+Na]^+$: $C_{12}H_{11}NO_4FNaBr$, 353.9753, Found 353.9738.

(4R*,5R*)-4-(4-bromophenyl)-3-(ethoxycarbonyl)-5-fluoro-4,5-dihydroisoxazole 2-oxide (*cis*-**3d**)

2nd fraction: *cis* isomer (12.2 mg, 0.0367 mmol, 17%) a brown-yellow oil



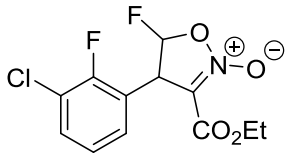
^{1}H NMR (400 MHz, THF-d_8) δ 7.54 – 7.47 (m, 2H), 7.27 – 7.22 (m, 2H), 6.35 (dd, *J* = 65.5, 5.4 Hz, 1H), 5.26 (dd, *J* = 30.2, 5.4 Hz, 1H), 4.08 (dq, *J* = 10.9, 7.1 Hz, 2H), 1.02 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, THF-d_8) δ 158.50, 132.40, 132.33 (d, *J* = 1.5 Hz), 132.23 (d, *J* = 4.7 Hz), 123.03, 107.51, 104.11 (d, *J* = 241.3 Hz), 62.39, 55.91 (d, *J* = 21.4 Hz), 14.25.

^{19}F NMR (376 MHz, THF-d_8) δ -124.76 (dd, *J* = 65.4, 30.0 Hz).

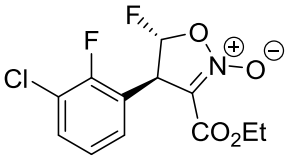
HRMS: Calculated $[M+Na]^+$: $C_{12}H_{11}NO_4FNaBr$, 353.9753, Found 353.9744.

4-(3-Chloro-2-fluorophenyl)-3-(ethoxycarbonyl)-5-fluoro-4,5-dihydroisoxazole 2-oxide (**3e**)



The product was obtained following general procedure B using ethyl 3-(3-chloro-2-fluorophenyl)-2-nitroacrylate (**1e**) (57.7 mg, 0.211 mmol, 1 equiv), (fluoromethyl)(phenyl)(2,3,4,5-tetramethylphenyl)sulfonium tetrafluoroborate (**2a**) (152.8 mg, 0.4219 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 25.3 mg, 0.633 mmol, 3 equiv) and anhydrous THF (8.4 ml) to obtain the crude product **3d** (62%, *d.r.* = 1.8:1, determined by ^{1}H NMR, internal standard EtOAc). After purification two separate diastereomers were obtained:

(4R*,5S*)-4-(3-Chloro-2-fluorophenyl)-3-(ethoxycarbonyl)-5-fluoro-4,5-dihydroisoxazole 2-oxide (*trans*-**3e**)



1st fraction: *trans* isomer (30.1 mg, 0.0985 mmol, 47%) a yellow oil.

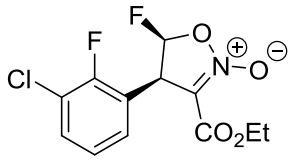
^{1}H NMR (400 MHz, THF-d_8) δ 7.52 (td, *J* = 7.2, 2.6 Hz, 1H), 7.27 – 7.16 (m, 2H), 6.31 (d, *J* = 62.7 Hz, 1H), 5.17 (d, *J* = 19.9 Hz, 1H), 4.19 (dq, *J* = 10.8, 7.1 Hz, 2H), 1.18 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, THF-d_8) δ 158.17, 156.99 (d, *J* = 250.2 Hz), 132.22, 128.48 (d, *J* = 2.6 Hz), 126.58 (d, *J* = 4.8 Hz), 124.55 (dd, *J* = 14.0, 12.1 Hz), 122.42 (d, *J* = 17.8 Hz), 107.56 (dd, *J* = 241.5, 1.7 Hz), 107.02, 62.82, 52.08 (dd, *J* = 29.8, 3.9 Hz), 14.33.

^{19}F NMR (376 MHz, THF-d_8) δ -109.96 (dd, *J* = 62.9, 19.9 Hz), -120.34 – -120.38 (m).

HRMS: Calculated [M +Na]$^+$: $C_{12}H_{10}NO_4F_2NaCl$, 328.0164, Found 328.0172

(4R*,5R*)-4-(3-chloro-2-fluorophenyl)-3-(ethoxycarbonyl)-5-fluoro-4,5-dihydroisoxazole 2-oxide (*cis*-**3e**)



2nd fraction: *cis* isomer (17.7 mg, 0.0579 mmol, 27%) a yellow oil.

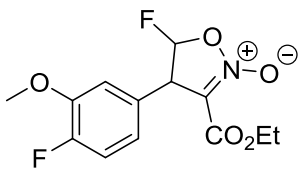
^{1}H NMR (400 MHz, THF-d_8) δ 7.30 (ddt, *J* = 8.0, 6.5, 1.6 Hz, 1H), 7.15 (td, *J* = 7.9, 1.2 Hz, 1H), 6.45 (dd, *J* = 65.8, 5.4 Hz, 1H), 5.57 (dd, *J* = 30.1, 5.4 Hz, 1H), 4.12 (dq, *J* = 10.8, 7.1 Hz, 3H), 1.04 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, THF-d_8) δ 158.42, 157.60 (d, *J* = 249.5 Hz), 131.66, 131.03 (t, *J* = 2.6 Hz), 125.69 (d, *J* = 4.7 Hz), 122.28 (dd, *J* = 12.7, 4.8 Hz), 121.83 (d, *J* = 18.1 Hz), 106.64, 103.64 (d, *J* = 241.3 Hz), 62.48, 50.23 (d, *J* = 21.5 Hz), 14.23.

^{19}F NMR (376 MHz, THF-d_8) δ -120.18, -124.07 (dd, *J* = 66.5, 30.2 Hz).

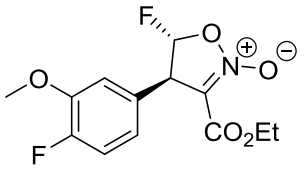
HRMS: Calculated [M +Na]$^+$: $C_{12}H_{10}NO_4F_2NaCl$, 328.0164, Found 328.0163.

3-(Ethoxycarbonyl)-5-fluoro-4-(4-fluoro-3-methoxyphenyl)-4,5-dihydroisoxazole 2-oxide (**3f**)



The product was obtained following general procedure B using ethyl 3-(4-fluoro-3-methoxyphenyl)-2-nitroacrylate (**1f**) (56.8 mg, 0.211 mmol, 1 equiv), (fluoromethyl)(phenyl)(2,3,4,5-tetramethylphenyl)sulfonium tetrafluoroborate (**2a**) (152.9 mg, 0.4220 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 25.3 mg, 0.6331 mmol, 3 equiv) and anhydrous THF (8.4 ml) to obtain the crude product **3f** (76%, *d.r.* = 1.9:1, determined by ^{1}H NMR, internal standard EtOAc). After purification two separate diastereomers were obtained:

(4R*,5S*)-3-(ethoxycarbonyl)-5-fluoro-4-(4-fluoro-3-methoxyphenyl)-4,5-dihydroisoxazole 2-oxide (*trans*-**3f**)



1st fraction: *trans* isomer (29.5 mg 0.0979 mmol, 46%) a yellow oil.

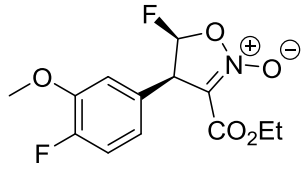
^{1}H NMR (400 MHz, THF-d_8) δ 7.11 (dd, *J* = 11.1, 8.3 Hz, 1H), 7.05 (dd, *J* = 8.0, 2.2 Hz, 1H), 6.83 (ddd, *J* = 8.4, 4.1, 2.3 Hz, 1H), 6.19 (d, *J* = 62.9 Hz, 1H), 4.85 (d, *J* = 19.4 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.87 (s, 3H), 1.19 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, THF-d_8) δ 158.44, 153.59 (d, *J* = 247.4 Hz), 149.54 (d, *J* = 10.9 Hz), 131.86 (dd, *J* = 12.2, 3.9 Hz), 120.52 (d, *J* = 7.1 Hz), 117.38 (d, *J* = 18.8 Hz), 114.21 (d, *J* = 2.3 Hz), 108.56 (d, *J* = 240.4 Hz), 108.43, 62.74, 57.64 (d, *J* = 27.1 Hz), 56.67, 14.42.

^{19}F NMR (376 MHz, THF-d_8) δ -110.05 (dd, *J* = 63.1, 19.8 Hz), -135.81 (ddd, *J* = 11.1, 8.0, 4.0 Hz).

HRMS: Calculated $[M+Na]^+$: $C_{13}H_{13}NO_5F_2Na$, 324.0659, Found 324.0656.

(4R*,5R*)-3-(Ethoxycarbonyl)-5-fluoro-4-(4-fluoro-3-methoxyphenyl)-4,5-dihydroisoxazole 2-oxide (*cis*-**3f**)



2nd fraction: *cis* isomer (17.7 mg, 0.0588 mmol, 28%) a yellow oil.

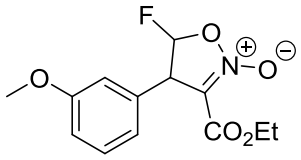
^{1}H NMR (400 MHz, THF-d_8) δ 7.05 (dd, *J* = 11.1, 8.3 Hz, 1H), 7.02 (dt, *J* = 8.0, 1.8 Hz, 1H), 6.89 – 6.81 (m, 1H), 6.34 (dd, *J* = 65.6, 5.4 Hz, 1H), 5.24 (dd, *J* = 30.3, 5.4 Hz, 1H), 4.09 (dq, *J* = 10.8, 7.2 Hz, 2H), 3.83 (s, 3H), 1.02 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, THF-d_8) δ 158.59, 153.43 (d, *J* = 246.7 Hz), 148.90 (d, *J* = 11.0 Hz), 129.14 (t, *J* = 4.3 Hz), 122.83 (d, *J* = 7.0 Hz), 116.47 (d, *J* = 18.7 Hz), 115.89 (t, *J* = 2.1 Hz), 107.76, 104.31 (d, *J* = 242.0 Hz), 62.32, 56.66, 56.07 (d, *J* = 21.5 Hz), 14.31.

^{19}F NMR (376 MHz, THF-d_8) δ -110.05 (dd, *J* = 63.0, 19.8 Hz), -135.81 (ddd, *J* = 11.6, 8.0, 4.0 Hz).

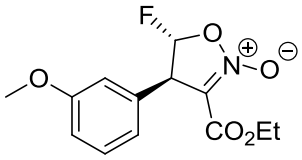
HRMS: Calculated $[M+Na]^+$: $C_{13}H_{13}NO_5F_2Na$, 324.0659, Found 324.0659.

3-(Ethoxycarbonyl)-5-fluoro-4-(3-methoxyphenyl)-4,5-dihydroisoxazole 2-oxide (3g)



The product was obtained following general procedure B using 3-methoxyphenylbenzaldehyde (**1g**) (54.5 mg, 0.217 mmol, 1 equiv), (fluoromethyl)(phenyl)(2,3,4,5-tetramethylphenyl)sulfonium tetrafluoroborate (**2a**) (157.2 mg, 0.4340 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 26.0 mg, 0.651 mmol, 3 equiv) and anhydrous THF (8.7 ml) to obtain the crude product **3g** (47%, *d.r.* = 4.2:1, determined by ^{1}H NMR, internal standard EtOAc). After purification two separate diastereomers were obtained:

(4*R,5*S**) 3-(Ethoxycarbonyl)-5-fluoro-4-(3-methoxyphenyl)-4,5-dihydroisoxazole 2-oxide** (*trans*-**3g**)



1st fraction: *trans* isomer (20.3 mg, 0.0717 mmol, 33%), a yellow oil.

^{1}H NMR (400 MHz, THF-d_8) δ 7.28 (t, *J* = 7.9 Hz, 1H), 6.90 (ddd, *J* = 8.3, 2.6, 0.9 Hz, 1H), 6.87 (t, *J* = 2.1 Hz, 1H), 6.84 (dt, *J* = 7.6, 1.4 Hz, 1H), 6.17 (d, *J* = 63.2 Hz, 1H), 4.82 (d, *J* = 19.6 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.78 (s, 3H), 1.18 (t, *J* = 7.1 Hz, 3H).

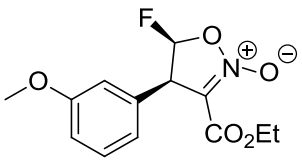
^{13}C NMR (101 MHz, THF-d_8) δ 161.64, 158.45, 136.87 (d, *J* = 11.9 Hz), 131.19, 120.21, 114.95, 114.41, 108.65 (d, *J* = 241.1 Hz), 108.48, 62.65, 57.98 (d, *J* = 26.9 Hz), 55.66, 14.40.

^{19}F NMR (376 MHz, THF-d_8) δ -109.99 (dd, *J* = 63.0, 19.6 Hz).

HRMS: Calculated $[M+H]^+$: $C_{13}H_{15}FNO_5$ 284.0934, Found 284.0934.

LC/MS: Calculated $[M+H]^+$: $C_{13}H_{15}FNO_5$ 284.09, Found 284.36.

(4*R,5*R**) 3-(Ethoxycarbonyl)-5-fluoro-4-(3-methoxyphenyl)-4,5-dihydroisoxazole 2-oxide** (*cis*-**3g**)



2nd fraction: *cis* isomer (6.2 mg, 0.022 mmol, 10%), a yellow oil.

^{1}H NMR (300 MHz, THF-d_8) δ 7.21 (m, 1H), 6.92 – 6.84 (m, 1H), 6.86 – 6.82 (m, 2H), 6.33 (dd, *J* = 65.5, 5.4 Hz, 1H), 5.22 (dd, *J* = 30.3, 5.4 Hz, 1H), 4.13 (dq, *J* = 10.8, 7.1 Hz, 1H), 4.02 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.75 (s, 3H), 0.99 (t, *J* = 7.1 Hz, 3H).

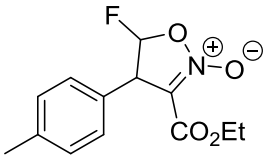
^{13}C NMR (101 MHz, THF-d_8) δ 161.04, 158.63, 134.10 (d, *J* = 4.5 Hz), 130.08, 122.48, 116.12, 114.47, 107.89, 104.35 (d, *J* = 241.8 Hz), 62.22, 56.47 (d, *J* = 21.6 Hz), 55.58, 14.24.

^{19}F NMR (376 MHz, THF-d_8) δ -124.86 (dd, *J* = 65.5, 30.3 Hz).

HRMS: Calculated $[M+H]^+$: $C_{13}H_{15}FNO_5$ 284.0934, Found 284.0939.

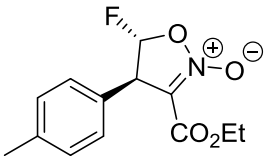
LC/MS: Calculated $[M+H]^+$: $C_{13}H_{15}FNO_5$ 284.09, Found 284.37.

3-(Ethoxycarbonyl)-5-fluoro-4-(p-tolyl)-4,5-dihydroisoxazole 2-oxide (**3h**) **(AS-771)**



The product was obtained following general procedure B using ethyl 2-nitro-3-(*p*-tolyl)acrylate (**1h**) (49.6 mg, 0.211 mmol, 1 equiv), (fluoromethyl)(phenyl)(2,3,4,5-tetramethylphenyl)sulfonium tetrafluoroborate (**2a**) (152.8 mg, 0.4219 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 25.3 mg, 0.633 mmol, 3 equiv) and anhydrous THF (8.4 ml) to obtain the crude product **3h** (84%, *d.r.* = 1.5:1, determined by ^{1}H NMR, internal standard EtOAc). After purification two separate diastereomers were obtained:

(4R*,5S*)-3-(Ethoxycarbonyl)-5-fluoro-4-(p-tolyl)-4,5-dihydroisoxazole 2-oxide (*trans*-**3h**)



1st fraction: *trans* isomer (27.8 mg, 0.104 mmol, 49%), a yellow oil.

^{1}H NMR (400 MHz, THF-d_8) δ 7.22 – 7.16 (m, 4H), 6.13 (d, *J* = 63.2 Hz, 1H), 4.80 (d, *J* = 19.4 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 2.32 (s, 3H), 1.17 (t, *J* = 7.1 Hz, 3H).

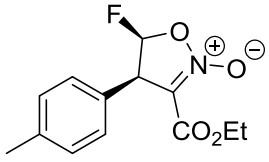
^{13}C NMR (101 MHz, THF-d_8) δ 158.46, 139.52, 132.49 (d, *J* = 11.9 Hz), 130.78, 128.37, 108.78 (d, *J* = 241.2 Hz), 108.61, 62.62, 57.68 (d, *J* = 26.6 Hz), 21.28, 14.39.

^{19}F NMR (376 MHz, THF-d_8) δ -109.99 (dd, *J* = 63.4, 19.8 Hz).

HRMS: Calculated $[M+Na]^+$: $C_{13}H_{14}NO_4FNa$, 290.0805, Found 290.0802.

(4R*,5R*)-3-(Ethoxycarbonyl)-5-fluoro-4-(p-tolyl)-4,5-dihydroisoxazole 2-oxide (*cis*-**3h**)

2nd fraction: *cis* isomer (14.3 mg, 0.0535 mmol, 25%), a yellow oil.



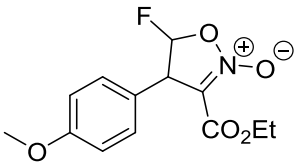
^{1}H NMR (400 MHz, THF-d_8) δ 7.18 – 7.11 (m, 4H), 6.30 (dd, *J* = 65.6, 5.4 Hz, 1H), 5.20 (dd, *J* = 30.4, 5.4 Hz, 1H), 4.06 (dq, *J* = 10.8, 7.0 Hz, 2H), 2.31 (s, 3H), 0.98 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, THF-d_8) δ 158.64, 138.80, 130.21 (d, *J* = 1.2 Hz), 129.85, 129.73 (d, *J* = 4.4 Hz), 107.96, 104.43 (d, *J* = 241.2 Hz), 62.20, 56.19 (d, *J* = 21.7 Hz), 21.32, 14.21.

^{19}F NMR (376 MHz, THF-d_8) δ -124.94 (dd, *J* = 65.4, 30.3 Hz).

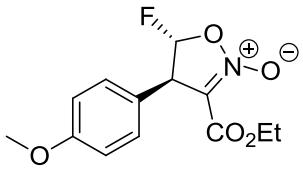
HRMS: Calculated $[M+Na]^+$: $C_{13}H_{14}NO_4FNa$, 290.0805, Found 290.0807.

3-(Ethoxycarbonyl)-5-fluoro-4-(4-methoxyphenyl)-4,5-dihydroisoxazole 2-oxide (**3i**)



The product was obtained following general procedure B using ethyl 3-(4-methoxyphenyl)-2-nitroacrylate (**1i**) (54.5 mg, 0.217 mmol, 1equiv), (fluoromethyl)(phenyl)(2,3,4,5-tetramethylphenyl)sulfonium tetrafluoroborate (**2a**) (157.2 mg, 0.4340 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 26.0 mg, 0.651 mmol, 3 equiv) and anhydrous THF (8.7 ml) to obtain the crude product **3i** (80%, *d.r.* = 1.7:1, determined by ^{1}H NMR, internal standard EtOAc). After purification two separate diastereomers were obtained:

(4*R,5*S**) 3-(Ethoxycarbonyl)-5-fluoro-4-(4-methoxyphenyl)-4,5-dihydroisoxazole 2-oxide** (*trans*-**3i**)



1st fraction: *trans* isomer (28.9 mg, 0.102 mmol, 47%), a yellow oil.

^{1}H NMR (400 MHz, THF-d_8) δ 7.24 – 7.18 (m, 2H), 6.95 – 6.90 (m, 2H), 6.13 (d, *J* = 63.3 Hz, 1H), 4.78 (d, *J* = 19.3 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.76 (s, 1H), 1.17 (t, *J* = 7.1 Hz, 3H).

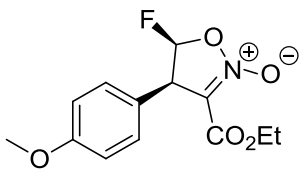
^{19}F NMR (376 MHz, CDCl3) δ -106.47 (dd, *J* = 63.3, 19.2 Hz).

^{13}C NMR (101 MHz, CDCl3) δ 161.32, 158.48, 129.61, 127.12 (d, *J* = 12.1 Hz), 115.50, 108.87 (d, *J* = 241.3 Hz), 108.66, 62.60, 57.35 (d, *J* = 26.7 Hz), 55.66, 14.40.

HRMS : Calculated $[M-COF]^+$: $C_{12}H_{14}NO_4$ 236.0917, Found 236.0925.

LC/MS: Calculated $[M+H]^+$: $C_{13}H_{15}FNO_5$ 284.09, Found 284.32.

(4*R,5*R**) 3-(Ethoxycarbonyl)-5-fluoro-4-(4-methoxyphenyl)-4,5-dihydroisoxazole 2-oxide** (*cis*-**3i**)



2nd fraction: *cis* isomer (20.0 mg, 0.0219 mmol, 33%), a yellow crystalline solid after PE trituration.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 – 7.17 (m, 2H), 6.93 – 6.88 (m, 2H), 6.15 (dd, *J* = 64.8, 5.4 Hz, 1H), 5.05 (dd, *J* =

29.8, 5.4 Hz, 1H), 4.19 (dq, *J* = 10.8, 7.1 Hz, 1H), 4.10 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.81 (s, 3H), 1.05 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.05, 158.08, 130.49 (d, *J* = 1.6 Hz), 122.22 (d, *J* = 4.3 Hz), 114.23, 107.40, 103.00 (d, *J* = 244.2 Hz), 62.28, 55.44, 55.17 (d, *J* = 21.9 Hz), 13.90.

^{19}F NMR (376 MHz, $CDCl_3$) δ -123.99 (dd, *J* = 64.7, 29.6 Hz).

HRMS : Calculated $[M\text{-}CO\text{-}F]^+$: $C_{12}H_{14}NO_4$ 236.0917, Found 236.0925.

LC/MS: Calculated $[M+H]^+$: $C_{13}H_{15}FNO_5$ 284.09, Found 284.38.

Slow diffusion of PE vapour into THF solution of *cis*-**3i** resulted in formation of moncrystals suitable for a single crystal X-ray analysis.

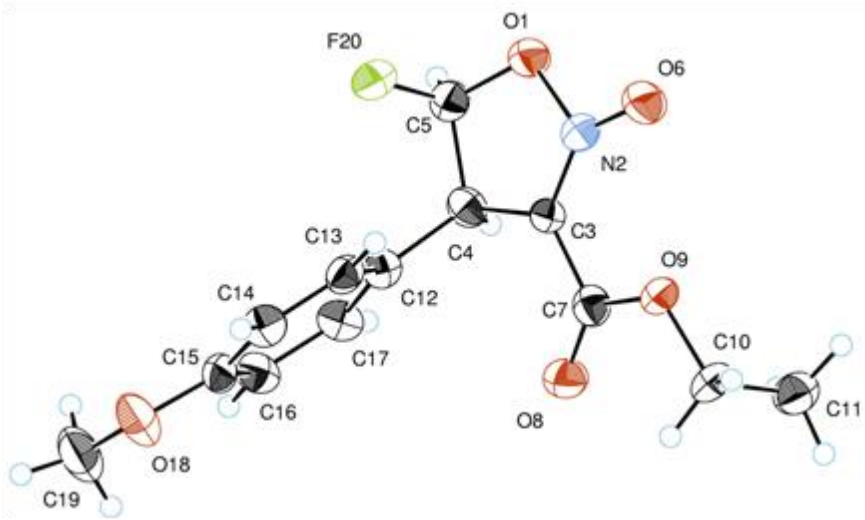
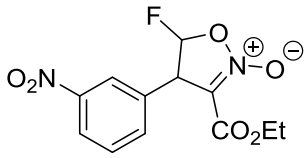


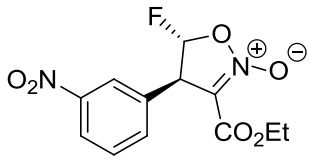
Figure S1. Crystal structure of (*cis*-**3i**). [CCDC 2057602]

3-(Ethoxycarbonyl)-5-fluoro-4-(3-nitrophenyl)-4,5-dihydroisoxazole 2-oxide (**3j**)



The product was obtained following general procedure B using ethyl 2-nitro-3-(3-nitrophenyl)acrylate (**1j**) (56.2 mg, 0.211 mmol, 1 equiv), (fluoromethyl)(phenyl)(2,3,4,5-tetramethylphenyl)sulfonium tetrafluoroborate (**2a**) (152.9 mg, 0.4222 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 25.3 mg, 0.633 mmol, 3 equiv) and anhydrous THF (8.4 ml) to obtain the crude product **3j** (78%, *d.r.* = 1.2:1, determined by ^{1}H NMR, internal standard EtOAc). After purification two separate diastereomers were obtained:

(4*R,5*S**) 3-(Ethoxycarbonyl)-5-fluoro-4-(3-nitrophenyl)-4,5-dihydroisoxazole 2-oxide** (*trans*-**3j**)



1st fraction: *trans* isomer (24.2 mg, 0.0811 mmol, 38%), white crystalline solid, after PE trituration.

^{1}H NMR (400 MHz, THF-d_8) δ 8.29 (t, *J* = 2.0 Hz, 1H), 8.24 (ddd, *J* = 8.0, 2.3, 1.2 Hz, 1H), 7.73 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.67 (t, *J* = 7.9 Hz, 1H), 6.33 (d, *J* = 62.1 Hz, 1H), 5.12 (d, *J* = 19.1 Hz, 1H), 4.18 (q, *J* = 7.2 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 1H), 1.18 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, THF-d_8) δ 158.30, 149.89, 137.72 (d, *J* = 12.5 Hz), 134.44, 131.44, 124.51, 124.21, 108.13, 108.01 (d, *J* = 241.4 Hz), 62.89, 57.42 (d, *J* = 28.3 Hz), 14.36.

^{19}F NMR (376 MHz, THF-d_8) δ -110.53 (dd, *J* = 62.2, 19.1 Hz).

Compound is unstable in HRMS and LC/MS conditions.

Slow diffusion of PE vapour into THF solution of *trans*-**3j** resulted in formation of moncrystals suitable for a single crystal X-ray analysis.

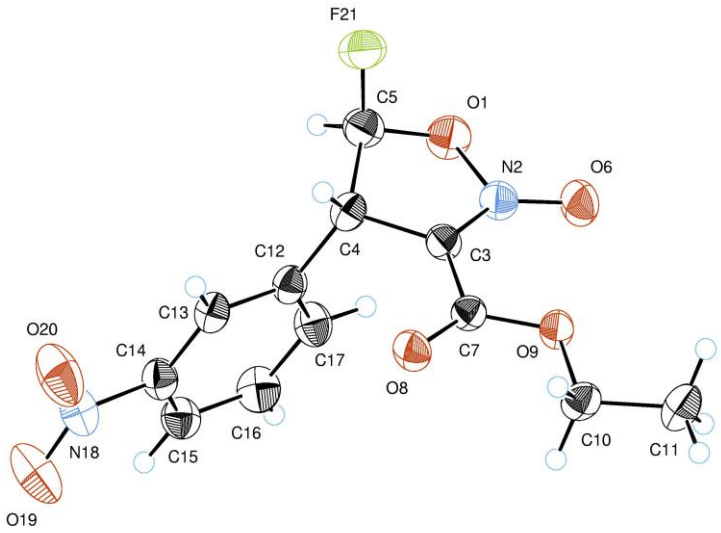
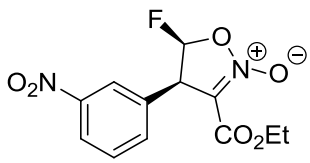


Figure S2. Crystal structure of (*trans*-**3j**). [CDD 2057603]

(4*R,5*R**) 3-(Ethoxycarbonyl)-5-fluoro-4-(3-nitrophenyl)-4,5-dihydroisoxazole 2-oxide** (*cis*-**3j**)



2nd fraction: *cis* isomer: (20.5 mg, 0.0687 mmol, 33%), a yellow oil.

^{1}H NMR (400 MHz, THF-d_8) δ 8.27 (t, *J* = 2.1 Hz, 1H), 8.22 (ddd, *J* = 8.2, 2.3, 1.1 Hz, 1H), 7.74 (dq, *J* = 7.7, 1.5

Hz, 1H), 7.60 (t, *J* = 8.0 Hz, 1H), 6.45 (dd, *J* = 65.5, 5.4 Hz, 1H), 5.49 (dd, *J* = 30.2, 5.4 Hz, 1H), 4.14 (dq, *J* = 10.8, 7.1 Hz, 1H), 4.04 (dq, *J* = 10.8, 7.1 Hz, 1H), 1.01 (t, *J* = 7.1 Hz, 3H).

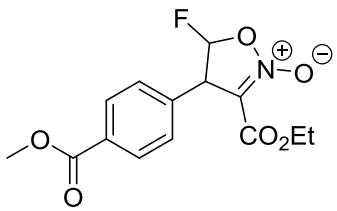
^{13}C NMR (101 MHz, THF-d_8) δ 158.45, 149.52, 136.68 (d, *J* = 2.0 Hz), 135.24 (d, *J* = 4.6 Hz), 130.36, 125.35, 124.11, 107.15, 104.05 (d, *J* = 241.1 Hz), 62.51, 55.90 (d, *J* = 21.2 Hz), 14.25.

^{19}F NMR (376 MHz, THF-d_8) δ -124.59 (dd, *J* = 65.6, 30.0 Hz).

Compund is unstable under HRMS conditions.

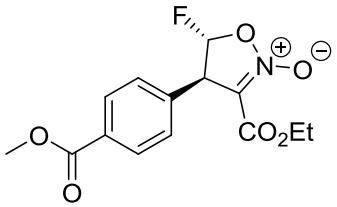
LC/MS: Calculated $[M+H]^+$: $C_{12}H_{12}FN_2O_6$ 299.07, Found 299.29.

3-(Ethoxycarbonyl)-5-fluoro-4-(4-(methoxycarbonyl)phenyl)-4,5-dihydroisoxazole 2-oxide (**3k**)



The product was obtained following general procedure B using methyl 4-(3-ethoxy-2-nitro-3-oxoprop-1-en-1-yl)benzoate (**1k**) (58.9 mg, 0.211 mmol, 1 equiv), (fluoromethyl)(phenyl)(2,3,4,5-tetramethylphenyl)sulfonium tetrafluoroborate (**2a**) (152.8 mg, 0.4219 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 25.3 mg, 0.633 mmol, 3 equiv) and anhydrous THF (8.4 ml) to obtain the crude product **3k** (86%, *d.r.* = 1.5:1, determined by ^{1}H NMR, internal standard EtOAc). After purification two separate diastereomers were obtained:

(4R*,5S*)-3-(Ethoxycarbonyl)-5-fluoro-4-(4-(methoxycarbonyl)phenyl)-4,5-dihydroisoxazole 2-oxide (*trans*-**3k**).



1st fraction: *trans* isomer (30.1 mg, 0.0967 mmol, 46%), a yellow oil.

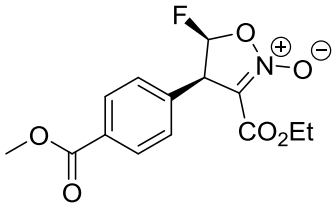
^{1}H NMR (400 MHz, THF-d_8) δ 8.07 – 8.00 (m, 2H), 7.47 – 7.42 (m, 2H), 6.25 (d, *J* = 62.6 Hz, 1H), 4.97 (d, *J* = 19.5 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 3H), 1.16 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, THF-d_8) δ 166.63, 158.33, 140.42 (d, *J* = 11.9 Hz), 131.87, 131.19, 128.84, 108.29, 108.22 (d, *J* = 241.4 Hz), 62.77, 57.85 (d, *J* = 27.5 Hz), 52.45, 14.37.

^{19}F NMR (376 MHz, THF-d_8) δ -110.07 (dd, *J* = 62.4, 19.1 Hz).

HRMS: Calculated $[M+Na]^+$: $C_{14}H_{14}NO_6FN$, 334.0703, Found 334.0714.

(4R*,5R*)-3-(Ethoxycarbonyl)-5-fluoro-4-(4-(methoxycarbonyl)phenyl)-4,5-dihydroisoxazole 2-oxide (*cis*-**3k**).



2nd fraction: *cis* isomer (18.2 mg, 0.0585 mmol, 28%), a yellow oil.

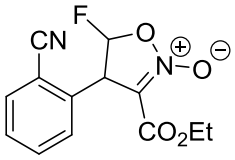
^{1}H NMR (400 MHz, THF-d_8) δ 8.03 – 7.95 (m, 2H), 7.46 – 7.39 (m, 2H), 6.40 (dd, *J* = 65.4, 5.4 Hz, 1H), 5.36 (dd, *J* = 30.2, 5.4 Hz, 1H), 4.06 (dq, *J* = 10.7, 7.0 Hz, 2H), 3.86 (s, 3H), 0.98 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, THF-d_8) δ 166.80, 158.48, 137.99 (d, *J* = 4.6 Hz), 131.35, 130.54 (d, *J* = 1.5 Hz), 130.30, 107.58, 104.13 (d, *J* = 241.3 Hz), 62.39, 56.29 (d, *J* = 21.4 Hz), 52.33, 14.22.

^{19}F NMR (376 MHz, THF-d_8) δ -124.39 (dd, *J* = 65.3, 30.1 Hz).

HRMS: Calculated $[M+Na]^+$: $C_{14}H_{14}NO_6FN$, 334.0703, Found 334.0707.

4-(2-Cyanophenyl)-3-(ethoxycarbonyl)-5-fluoro-4,5-dihydroisoxazole 2-oxide (**3l**).



The product was obtained following general procedure B using ethyl 3-(2-cyanophenyl)-2-nitroacrylate (**1l**) (51.9 mg, 0.211 mmol, 1 equiv), (fluoromethyl)(phenyl)(2,3,4,5-tetramethylphenyl)sulfonium tetrafluoroborate (**2a**) (152.8 mg, 0.4219 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 25.3 mg, 0.633 mmol, 3 equiv) and anhydrous THF (8.4 ml) to obtain the crude product **3l** (58%, *d.r.* = 1.2:1, determined by ^{1}H NMR, internal standard EtOAc). After purification **3l** was obtained as mixture of diastereomers (40.2 mg, 0.1445 mmol, 69%, *d.r.*= 1.4^{trans}:1^{cis})

Due to a hindered rotation of aryl group in *cis* isomer broadened signals in ^{1}H NMR and complicated ^{13}C NMR can be observed:

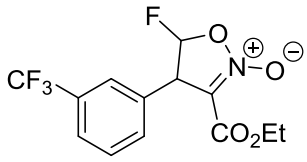
^{1}H NMR (400 MHz, THF-d_8) δ 7.84 (ddd, *J* = 7.8, 1.5, 0.6 Hz, 1H), 7.79 – 7.77 (m, 1H), 7.70 (td, *J* = 7.7, 1.4 Hz, 1H), 7.66 – 7.60 (m, 1H), 7.57 – 7.48 (m, 3H), 7.42 (dd, *J* = 7.9, 0.7 Hz, 1H), 6.54 (dd, *J* = 66.0, 5.5 Hz, 1H)^{cis}, 6.31 (d, *J* = 62.1 Hz, 1H)^{trans}, 5.70 (dm, *J* = 31.7 Hz, 1H)cis, 5.24 (d, *J* = 19.3 Hz, 1H)^{trans}, 4.17 (dq, *J* = 10.9, 7.1 Hz, 2H), 4.04 (q, *J* = 7.1 Hz, 2H), 1.19 (t, *J* = 7.2 Hz, 3H), 1.17 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, THF-d_8) δ 158.35, 158.02, 138.61 (d, *J* = 11.9 Hz), 136.47 (d, *J* = 4.3 Hz), 134.74, 134.52, 133.59, 131.96, 130.46, 129.94, 128.49, 126.10, 124.03, 117.90, 117.52, 114.30, 107.87, 107.55 (d, *J* = 242.6 Hz), 107.13, 103.30 (d, *J* = 241.7 Hz), 62.89, 62.49, 56.49 (d, *J* = 28.9 Hz), 54.60 (br s), 14.34, 14.19.

^{19}F NMR (376 MHz, THF-d_8) δ -109.12 (dd, J = 62.2, 19.4 Hz), -123.04 (br.d, J = 40.2 Hz).

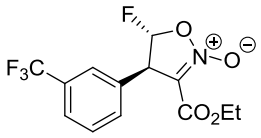
HRMS: Calculated [M +Na]$^+$: $C_{13}H_{11}N_2O_4FNa$, 301.0601, Found 301.0608.

3-(Ethoxycarbonyl)-5-fluoro-4-(3-(trifluoromethyl)phenyl)-4,5-dihydroisoxazole 2-oxide (**3m**)



The product was obtained following general procedure B using ethyl 2-nitro-3-(3-(trifluoromethyl)phenyl)acrylate (**1m**) (100 mg, 0.346 mmol, 1 equiv), (fluoromethyl)(phenyl)(2,3,4,5-tetramethylphenyl)sulfonium tetrafluoroborate (**2a**) (250.5 mg, 0.6915 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 41.5 mg, 1.04 mmol, 3 equiv) and anhydrous THF (14 ml) to obtain the crude product **3m** (62%, *d.r.* = 1.7:1, determined by ^{1}H NMR, internal standard EtOAc). The crude product was purified by silica gel column chromatography followed by preparative TLC. Two separate diastereomers were obtained:

(4R*,5S*)-3-(Ethoxycarbonyl)-5-fluoro-4-(3-(trifluoromethyl)phenyl)-4,5-dihydroisoxazole 2-oxide (*trans*-**3m**)



1st fraction: *trans* isomer (30.8 mg, 0.0959 mmol, 31%), a yellow oil.

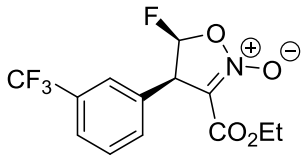
^{1}H NMR (400 MHz, THF-d_8) δ 7.75 – 7.70 (m, 1H), 7.74 – 7.66 (m, 1H), 7.66 – 7.59 (m, 1H), 7.58 (dt, J = 7.9, 1.6 Hz, 1H), 6.30 (d, J = 62.3 Hz, 1H), 5.03 (d, J = 19.3 Hz, 1H), 4.20 (dq, J = 10.8, 7.1 Hz, 1H), 4.15 (dq, J = 10.8, 7.0 Hz, 1H), 1.17 (t, J = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, THF-d_8) δ 158.31, 137.02 (d, J = 12.2 Hz), 132.15 (q, J = 32.3 Hz), 132.06, 131.11, 126.50 (q, J = 3.8 Hz), 126.11 (q, J = 3.9 Hz), 125.23 (q, J = 272.1 Hz), 108.26, 108.19 (d, J = 241.2 Hz), 62.81, 57.63 (d, J = 27.9 Hz), 14.32.

^{19}F NMR (376 MHz, THF-d_8) δ -63.44, -110.34 (dd, J = 62.4, 19.6 Hz).

HRMS: Calculated [M +Na]$^+$: $C_{13}H_{11}NO_4F_4Na$, 344.0522, Found 344.0524.

((4R*,5R*)-3-(Ethoxycarbonyl)-5-fluoro-4-(3-(trifluoromethyl)phenyl)-4,5-dihydroisoxazole 2-oxide (*cis*-**3m**)



2nd fraction: *cis* isomer (5.1 mg, 0.016 mmol, 5%), a yellow oil.

^{1}H NMR (400 MHz, THF-d_8) δ 7.69 (s, 1H), 7.70 – 7.62 (m, 1H), 7.59 (dd, J = 7.9, 1.7 Hz, 1H), 7.59 – 7.50 (m, 1H), 6.42

(dd, *J* = 65.4, 5.4 Hz, 1H), 5.40 (dd, *J* = 30.3, 5.4 Hz, 1H), 4.13 (dq, *J* = 10.8, 7.1 Hz, 1H), 4.01 (dq, *J* = 10.8, 7.1 Hz, 1H), 0.97 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, THF-d_8) δ 158.43, 134.44 (d, *J* = 4.5 Hz), 134.30, 131.46 (q, *J* = 32.1 Hz), 130.02, 127.32 (q, *J* = 3.7 Hz), 126.75 (q, *J* = 272.0, 271.6 Hz), 125.96 (q, *J* = 3.9 Hz), 107.34, 104.13 (d, *J* = 241.2 Hz), 62.36, 56.11 (d, *J* = 21.3 Hz), 14.15.

^{19}F NMR (376 MHz, THF-d_8) δ -63.35, -124.73 (dd, *J* = 65.3, 30.3 Hz).

HRMS: Calculated $[M+Na]^+$: $C_{13}H_{11}NO_4F_4Na$, 344.0522, Found 344.0517.

(*E*)-3-(Ethoxycarbonyl)-5-fluoro-4-styryl-4,5-dihydroisoxazole 2-oxide (**3n**)

The product was obtained following general procedure B using ethyl (4*E*)-2-nitro-5-phenylpenta-2,4-dienoate (**1n**) (52.2 mg, 0.211 mmol, 1 equiv), (fluoromethyl)(phenyl)(2,3,4,5-tetramethylphenyl)sulfonium tetrafluoroborate (**2a**) (152.9 mg, 0.4222 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 25.3 mg, 0.633 mmol, 3 equiv) and anhydrous THF (8.4 ml) to obtain the crude product **3n** (44%, *d.r.* = 2.1:1, determined by ^{1}H NMR, internal standard EtOAc). After purification two separate diastereomers were obtained:

(4R*,5S*)-3-(Ethoxycarbonyl)-5-fluoro-4-((E)-styryl)-4,5-dihydroisoxazole 2-oxide (*trans*-**3n**)

1st fraction: *trans* isomer (21.6 mg, 0.0773 mmol, 37%), a yellow oil.

^{1}H NMR (400 MHz, THF-d_8) δ 7.47 – 7.39 (m, 2H), 7.34 – 7.25 (m, 2H), 7.27 – 7.20 (m, 1H), 6.73 (d, *J* = 15.9 Hz, 1H), 6.26 (dd, *J* = 15.9, 8.3 Hz, 1H), 6.19 (d, *J* = 62.9 Hz, 1H), 4.44 (ddd, *J* = 18.4, 8.3, 1.0 Hz, 1H), 4.26 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, THF-d_8) δ 158.61, 137.27, 136.43, 129.55, 129.23, 127.65, 121.25 (d, *J* = 12.3 Hz), 107.83 (d, *J* = 241.0 Hz), 107.31, 62.64, 55.59 (d, *J* = 27.3 Hz), 14.54.

^{19}F NMR (376 MHz, THF-d_8) δ -113.97 (dd, *J* = 62.9, 18.4 Hz).

HRMS: Calculated $[M-CO-F]^+$: $C_{13}H_{14}NO_3$, 232,0968, Found 232.0991.

(4R*,5R*)-3-(Ethoxycarbonyl)-5-fluoro-4-((*E*)-styryl)-4,5-dihydroisoxazole 2-oxide (*cis*-**3n**)

2nd fraction: *cis* isomer (8.5 mg 0.0304 mmol, 14%), a yellow oil.

^{1}H NMR (400 MHz, THF-d_8) δ 7.46 – 7.38 (m, 2H), 7.34 – 7.25 (m, 2H), 7.27 – 7.18 (m, 1H), 6.75 (d, *J* = 15.7 Hz, 1H), 6.29 (dd, *J* = 64.5, 5.2 Hz, 1H), 6.22 (dd, *J* = 9.4, 1.4

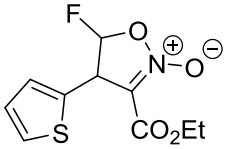
Hz, 1H), 4.78 (dddd, *J* = 29.6, 9.4, 5.2, 0.8 Hz, 1H), 4.20 (dq, *J* = 10.8, 7.1 Hz, 2H), 1.18 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, THF-d_8) δ 158.75, 137.66, 137.15, 129.52, 128.97, 127.58, 120.39 (d, *J* = 10.1 Hz), 106.94, 105.41 (d, *J* = 238.0 Hz), 62.37, 54.44 (d, *J* = 21.4 Hz), 14.50.

^{19}F NMR (376 MHz, THF-d_8) δ -128.34 (dd, *J* = 64.6, 29.6 Hz).

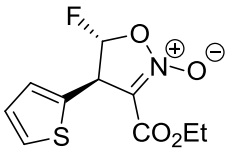
HRMS: Calculated $[M\text{-}CO\text{-}F]^+$: $C_{13}H_{14}NO_3$, 232,0968, Found 232.0986.

3-(Ethoxycarbonyl)-5-fluoro-4-(thiophen-2-yl)-4,5-dihydroisoxazole 2-oxide (**3o**)



The product was obtained following general procedure B using ethyl 2-nitro-3-(thiophen-2-yl)acrylate (**1o**) (49.3 mg, 0.217 mmol, 1 equiv), (fluoromethyl)(phenyl)(2,3,4,5-tetramethylphenyl)sulfonium tetrafluoroborate (**2a**) (157.2 mg, 0.4340 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 26.0 mg, 0.651 mmol, 3 equiv) and anhydrous THF (8.7 ml) to obtain the crude product **3o** (69%, *d.r.* = 2.0:1, determined by ^{1}H NMR, internal standard EtOAc). After purification two separate diastereomers were obtained:

(4*R,5*S**) 3-(Ethoxycarbonyl)-5-fluoro-4-(thiophen-2-yl)-4,5-dihydroisoxazole 2-oxide** (*trans*-**3o**)



1st fraction: *trans* isomer: (26.1 mg, 0.101 mmol, 46%), a yellow oil.

^{1}H NMR (400 MHz, THF-d_8) δ 7.43 (dd, *J* = 5.1, 1.3 Hz, 1H), 7.10 (ddd, *J* = 3.6, 1.2, 0.6 Hz, 1H), 7.02 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.27 (d, *J* = 62.2 Hz, 1H), 5.20 (d, *J* = 17.2 Hz, 1H), 4.23 (dq, *J* = 10.7, 7.1 Hz, 1H), 4.20 (dq, *J* = 10.9, 7.1 Hz, 1H), 1.20 (t, *J* = 7.1 Hz, 3H).

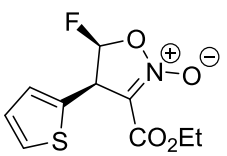
^{13}C NMR (101 MHz, THF-d_8) δ 158.24, 136.69 (d, *J* = 13.7 Hz), 128.41, 127.65, 127.26, 108.41 (d, *J* = 242.2 Hz), 108.09, 62.79, 53.14 (d, *J* = 29.9 Hz), 14.41.

^{19}F NMR (376 MHz, THF-d_8) δ -112.30 (dd, *J* = 62.2, 17.3 Hz).

HRMS : Calculated $[M\text{-}COF]^+$: $C_9H_{10}NO_3S$, 212.0376, Found 212.0383.

LC/MS: Calculated $[M+H]^+$: $C_{10}H_{11}FNO_4S$, 260.04, Found 260.29.

(4*R,5*R**) -(Ethoxycarbonyl)-5-fluoro-4-(thiophen-2-yl)-4,5-dihydroisoxazole 2-oxide** (*cis*-**3o**)



2nd fraction: *cis* isomer (12.8 mg, 0.0494 mmol, 23%), brown solid after PE trituration.

^{1}H NMR (400 MHz, THF-d_8) δ 7.40 (ddd, *J* = 5.1, 1.2, 1.2, 0.4, 0.4 Hz, 2H), 7.12 – 7.07 (m, 1H), 6.98 (dd, *J* = 5.2, 3.5 Hz, 1H), 6.35 (dd, *J* = 65.2, 5.1 Hz,

1H), 5.63 (dd, *J* = 30.2, 5.2 Hz, 1H), 4.13 (dq, *J* = 10.8, 7.1 Hz, 1H), 4.03 (dq, *J* = 10.8, 7.1 Hz, 1H), 1.02 (t, *J* = 7.1 Hz, 3H).

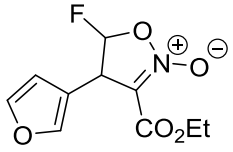
^{13}C NMR (101 MHz, THF-d_8) δ 158.36, 133.70 (d, *J* = 4.3 Hz), 129.83 (d, *J* = 0.9 Hz), 127.41, 127.32, 107.46, 103.98 (d, *J* = 241.9 Hz), 62.31, 51.42 (d, *J* = 21.9 Hz), 14.20.

^{19}F NMR (376 MHz, THF-d_8) δ -125.37 (dd, *J* = 65.3, 30.1 Hz).

HRMS : Calculated $[M\text{-}COF]^+$: $C_9H_{10}NO_3S$, 212.0376, Found 212.0390.

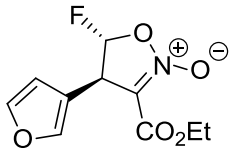
LC/MS: Calculated $[M+H]^+$: $C_{10}H_{11}FNO_4S$ 260.04, Found 260.30.

3-(Ethoxycarbonyl)-5-fluoro-4-(furan-3-yl)-4,5-dihydroisoxazole 2-oxide (**3p**)



The product was obtained following general procedure B using ethyl 3-(furan-3-yl)-2-nitroacrylate (**1p**) (45.8 mg, 0.217 mmol, 1 equiv), (fluoromethyl)(phenyl)(2,3,4,5-tetramethylphenyl)sulfonium tetrafluoroborate (**2a**) (157.2 mg, 0.4340 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 26.0 mg, 0.651 mmol, 3 equiv) and anhydrous THF (8.7 ml) to obtain the crude product **3p** (75%, *d.r.* = 2.0:1, determined by 1H NMR, internal standard EtOAc). After purification two separate diastereomers were obtained:

(4*R,5*S**) 3-(Ethoxycarbonyl)-5-fluoro-4-(furan-3-yl)-4,5-dihydroisoxazole 2-oxide** (*trans*-**3p**)



1st fraction: *trans* isomer (27.3 mg, 0.112 mmol, 53%), a yellow oil.

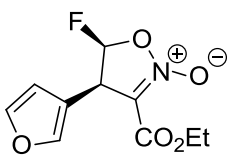
^{1}H NMR (400 MHz, THF-d_8) δ 7.62 (dt, *J* = 1.5, 0.8 Hz, 1H), 7.53 (dd, *J* = 1.6, 0.4 Hz, 1H), 6.46 (dd, *J* = 1.9, 0.9 Hz, 1H), 6.22 (d, *J* = 62.4 Hz, 1H), 4.82 (d, *J* = 17.7 Hz, 1H), 4.25 (dq, *J* = 10.9, 7.1 Hz, 1H), 4.22 (dq, *J* = 10.9, 7.1 Hz, 1H), 1.24 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, THF-d_8) δ 158.46, 145.32, 142.00 (d, *J* = 1.1 Hz), 119.63 (d, *J* = 13.5 Hz), 110.08, 108.27 (d, *J* = 240.2 Hz), 107.73, 62.72, 49.39 (d, *J* = 29.4 Hz), 14.44.

^{19}F NMR (376 MHz, THF-d_8) δ -112.81 (dd, *J* = 62.3, 17.3 Hz).

Compound is unstable under HRMS and LC/MS conditions.

(4*R,5*R**) 3-(Ethoxycarbonyl)-5-fluoro-4-(furan-3-yl)-4,5-dihydroisoxazole 2-oxide** (*cis*-**3p**)



2nd fraction: *cis* isomer (12.2 mg, 0.0502 mmol 23%), a yellow oil.

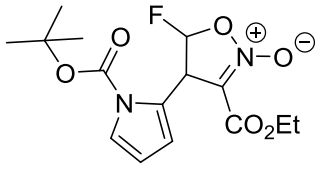
^{1}H NMR (400 MHz, THF-d_8) δ 7.57 (d, *J* = 1.1 Hz, 1H), 7.49 – 7.44 (m, 1H), 6.45 – 6.39 (m, 1H), 6.29 (dd, *J* = 65.0, 5.1 Hz, 1H), 5.22 (dd, *J* = 31.5, 5.1 Hz, 1H), 4.17 (dq, *J* = 10.8, 7.1 Hz, 1H), 4.08 (dq, *J* = 10.8, 7.1 Hz, 1H), 1.10 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, THF-d_8) δ 158.53, 144.21, 143.25, 116.93 (d, *J* = 5.3 Hz), 112.35 (d, *J* = 2.8 Hz), 107.11, 104.71 (d, *J* = 240.9 Hz), 62.30, 47.46 (d, *J* = 22.1 Hz), 14.27.

^{19}F NMR (376 MHz, THF-d_8) δ -126.25 (ddd, *J* = 65.2, 31.9, 2.8 Hz).

HRMS: Calculated $[M+Na]^+$: $C_{10}H_{10}NO_5FNa$, 266.0441, Found 266.0446.

4-(1-(tert-butoxycarbonyl)-1H-pyrrol-2-yl)-3-(ethoxycarbonyl)-5-fluoro-4,5-dihydroisoxazole 2-oxide (**3q**)



The product was obtained following general procedure B using ethyl tert-butyl 2-(3-ethoxy-2-nitro-3-oxoprop-1-en-1-yl)-1H-pyrrole-1-carboxylate (**1q**) (65.5 mg, 0.211 mmol, 1 equiv), (fluoromethyl)(phenyl)(2,3,4,5-tetramethylphenyl)sulfonium tetrafluoroborate (**2a**) (152.8 mg, 0.4219 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 25.3 mg, 0.633 mmol, 3 equiv) and anhydrous THF (8.4 ml) to obtain the crude product **3k** (77%, *d.r.* = 1:1, determined by ^{1}H NMR, internal standard EtOAc). After purification by column chromatography and preperative TLC a mixture of **3q** diastereomers was obtained (41.2 mg 0.1204 mmol, 57% *d.r.* = 1.1^{cis}:1^{trans}) as a brown oil.

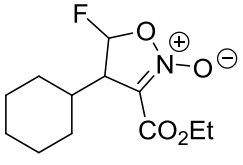
^{1}H NMR (400 MHz, THF-d_8) δ 7.34 (dd, *J* = 3.4, 1.8 Hz, 1H), 7.25 (t, *J* = 2.5 Hz, 1H), 6.45 (dd, *J* = 66.9, 5.6 Hz, 1H), 6.19 (d, *J* = 50.6 Hz, 1H), 6.16 – 6.08 (m, 3H), 6.07 (ddd, *J* = 3.5, 1.8, 1.0 Hz, 1H), 5.99 (dd, *J* = 26.3, 5.6 Hz, 1H), 5.44 (d, *J* = 15.0 Hz, 1H), 4.28 – 4.13 (m, 4H), 1.63 (s, 9H), 1.62 (s, 9H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.16 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, THF-d_8) δ 157.74, 157.51, 149.41, 149.13, 126.00 (d, *J* = 13.3 Hz), 124.31 (d, *J* = 7.0 Hz), 122.99, 121.63, 114.87 (d, *J* = 1.4 Hz), 112.90 (d, *J* = 1.5 Hz), 110.08, 110.06, 106.62, 106.04 (d, *J* = 243.8 Hz), 105.94, 102.58 (d, *J* = 239.7 Hz), 84.75, 84.25, 61.54, 61.32, 51.08 (d, *J* = 30.7 Hz), 48.74 (d, *J* = 22.3 Hz), 27.10, 27.06, 13.37, 13.32.

^{19}F NMR (376 MHz, THF-d_8) δ -116.49 (dd, *J* = 61.1, 14.9 Hz), -124.04 (dd, *J* = 67.1, 26.2 Hz).

HRMS: Calculated $[M+Na]^+$: $C_{15}H_{19}N_2O_6FNa$ 365.1125, Found 365.1127.

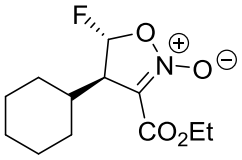
4-Cyclohexyl-3-(ethoxycarbonyl)-5-fluoro-4,5-dihydroisoxazole 2-oxide (**3r**)



The product was obtained following general procedure B using ethyl 3-cyclohexyl-2-nitroacrylate (**1r**) (48.0 mg, 0.211 mmol, 1 equiv), (fluoromethyl)(phenyl)(2,3,4,5-tetramethylphenyl)sulfonium tetrafluoroborate (**2a**) (152.9 mg, 0.4222 mmol, 2 equiv), NaH

(60% dispersion in mineral oil, 25.3 mg, 0.633 mmol, 3 equiv) and anhydrous THF (8.4 ml) to obtain the crude product **3r** (46%, *d.r.* = 1.6:1, determined by ^{1}H NMR, internal standard EtOAc). After purification by column chromatography two separate diastereomers were obtained:

(4R*,5S*)-4-Cyclohexyl-3-(ethoxycarbonyl)-5-fluoro-4,5-dihydroisoxazole 2-oxide (*trans*-**3r**)



1st fraction: *trans* isomer (18.2 mg, 0.0702 mmol, 33%) a slightly yellow oil.

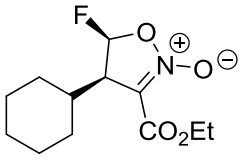
^{1}H NMR (400 MHz, THF-d_8) δ 6.20 (d, *J* = 63.1 Hz, 1H), 4.29 (dq, *J* = 10.7, 7.1 Hz, 2H), 3.53 (dd, *J* = 21.6, 4.6 Hz, 1H), 1.97 – 1.86 (m, 1H), 1.82 – 1.58 (m, 8H), 1.36 – 1.27 (m, 2H), 1.30 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, THF-d_8) δ 159.20, 107.58, 106.60 (d, *J* = 236.0 Hz), 62.65, 57.88 (d, *J* = 22.5 Hz), 39.13 (d, *J* = 10.2 Hz), 31.14, 29.58, 27.36, 27.27, 27.04, 14.52.

^{19}F NMR (376 MHz, THF-d_8) δ -113.37 (dd, *J* = 63.1, 21.7 Hz).

HRMS: Calculated $[M+H]^+$: $C_{12}H_{19}FNO_4$ 260.1293, Found 260.1300.

(4R*,5R*)-4-Cyclohexyl-3-(ethoxycarbonyl)-5-fluoro-4,5-dihydroisoxazole 2-oxide (*cis*-**3r**)



2nd fraction: *cis* isomer (14.4 mg, 0.0555 mmol, 26%) a slightly yellow oil.

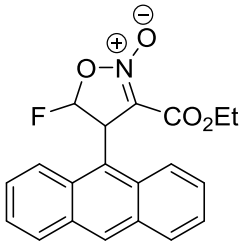
^{1}H NMR (400 MHz, THF-d_8) δ 6.33 (dd, *J* = 64.8, 5.0 Hz, 1H), 4.30 (dq, *J* = 10.9, 7.2 Hz, 2H), 3.94 (dt, *J* = 37.1, 5.2 Hz, 1H), 1.36 – 1.27 (m, 6H), 1.84 – 1.64 (m, 8H), 1.58 – 1.50 (m, 2H), 1.31 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, THF-d_8) δ 158.62, 105.92, 105.52 (d, *J* = 240.5 Hz), 61.43, 53.79 (d, *J* = 21.4 Hz), 36.46 (d, *J* = 1.8 Hz), 29.83 (d, *J* = 1.6 Hz), 29.34, 29.28, 26.79, 26.14, 13.40.

^{19}F NMR (376 MHz, THF-d_8) δ -128.70 (dd, *J* = 64.9, 37.1 Hz).

HRMS: Calculated $[M+H]^+$: C12H19FNO4 260,1293, Found 260.1298.

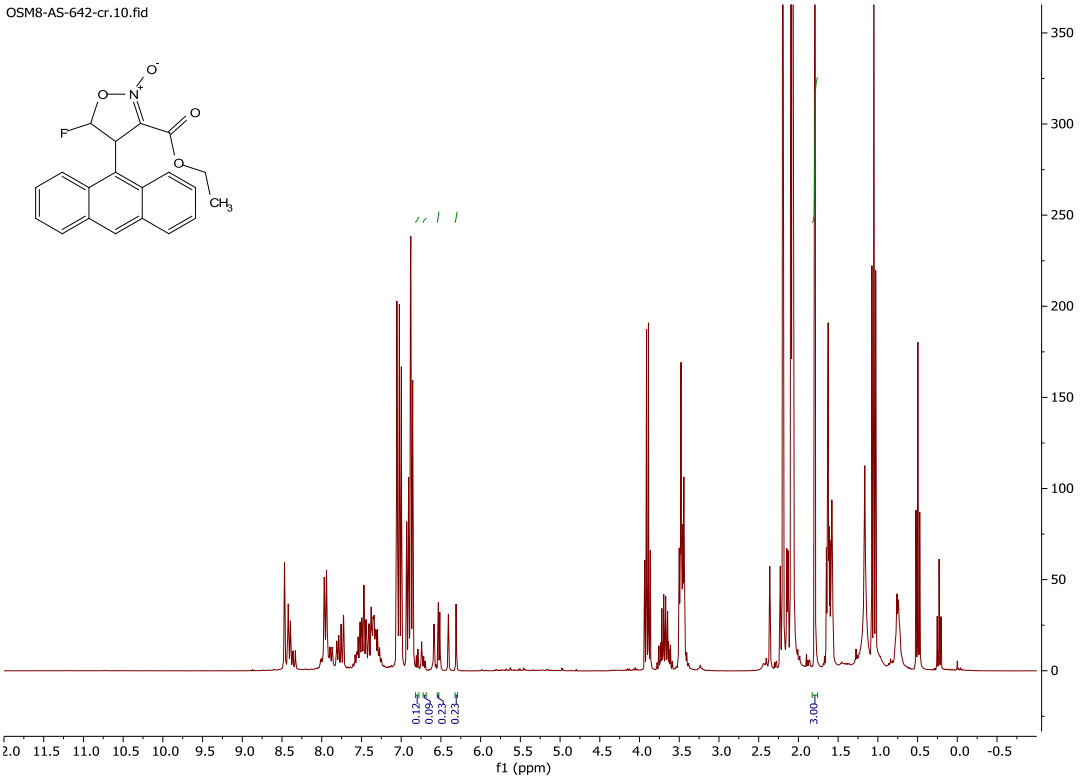
4-(anthracen-9-yl)-3-(ethoxycarbonyl)-5-fluoro-4,5-dihydroisoxazole 2-oxide (**3s**)



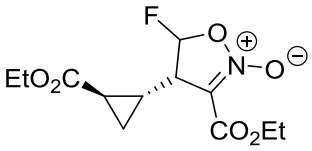
Prepared following general procedure using ethyl (E)-3-(anthracen-9-yl)-2-nitroacrylate (**1s**) (69.7 mg, 0.217 mmol, 1 equiv.), (fluoromethyl)(phenyl)(2,3,4,5-tetramethylphenyl)sulfonium tetrafluoroborate (**2a**) (157.2 mg, 0.4340 mmol, 2 equiv.), NaH (60% dispersion in mineral oil, 26.0

mg, 0.6511 mmol, 3 equiv.) and anhydrous THF (8.7 ml) to obtain crude reaction product **3s** (67%, *d.r.* = 2.2:1, determined by ^{1}H NMR, with internal standart EtOAc)

Crude compound (**3s**) ^{1}H-NMR spectra (300 MHz, THF-d8)

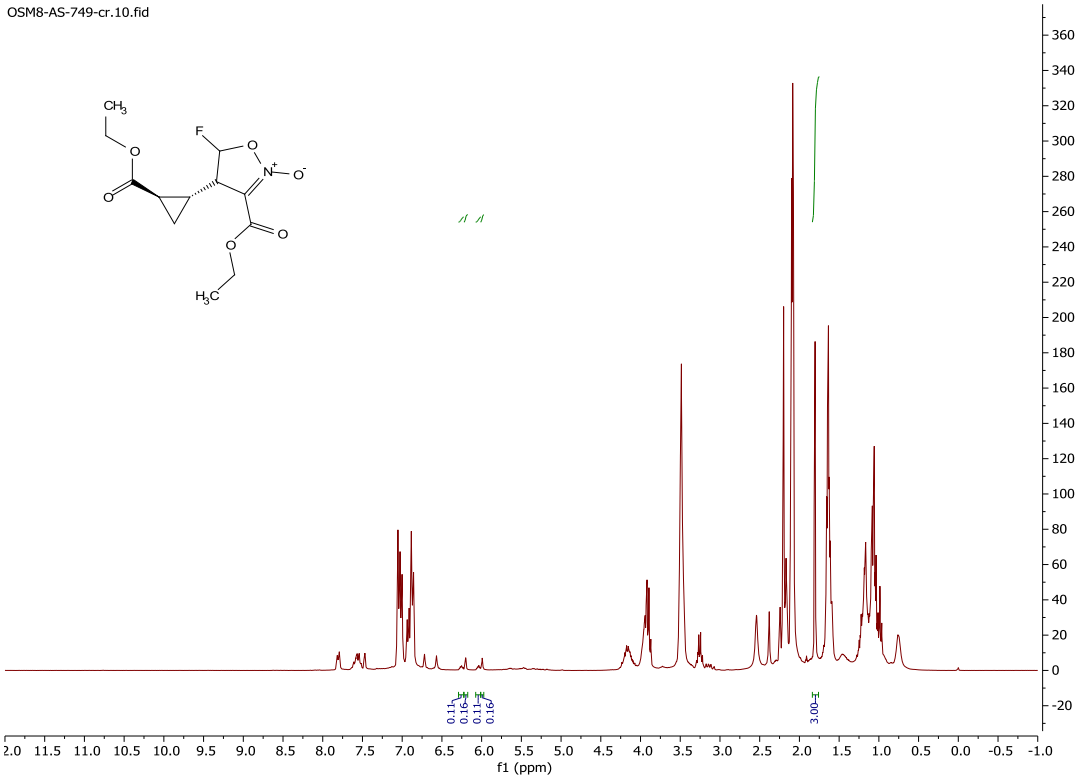


(4R)-3-(ethoxycarbonyl)-4-((1R,2R)-2-(ethoxycarbonyl)cyclopropyl)-5-fluoro-4,5-dihydroisoxazole 2-oxide (**3t**)



Prepared following general procedure using ethyl (1S*,2R*)-2-(3-ethoxy-2-nitro-3-oxoprop-1-en-1-yl)cyclopropane-1-carboxylate (**1t**) (40.5 mg, 0.1574 mmol, 1 equiv.), (fluoromethyl)(phenyl)(2,3,4,5-tetramethylphenyl)sulfonium tetrafluoroborate (**2a**) (114.1 mg, 0.3149 mmol, 2 equiv.), NaH (60% dispersion in mineral oil, 18.9 mg, 0.4723 mmol, 3 equiv.) and anhydrous THF (6.3 ml) to obtain crude reaction product **3t** (54%, *d.r.* = 1.5:1, determined by ^{1}H NMR, with internal standart EtOAc)

Crude compound (**3t**) ^{1}H-NMR spectra (300 MHz, THF-d8)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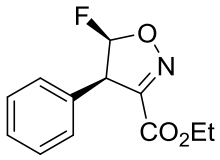
CH3
O
O
F
O
N+
O-
O
O
O
H3C
0.11
0.16
0.11
0.16
3.00
360
340
320
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
2.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

General procedure C for reduction of *N*-oxide *cis*-3a

Ethyl (4R*,5R*)-5-fluoro-4-phenyl-4,5-dihydroisoxazole-3-carboxylate (*cis*-**4a**)



To (4R*,5R*)-3-(ethoxycarbonyl)-5-fluoro-4-phenyl-4,5-dihydroisoxazole 2-oxide (*cis*-**3a**) (50 mg, 0.1975 mmol, 1 equiv) under Ar atmsophere was added $P(OMe)_3$ (1.16 ml, 9.87 mmol, 50 equiv). The reaction mixture was stirred at 40 ^oC for 7 h until full conversion of starting material (determined by TLC ($PE:Et_2O$ 2:1)). NMR yield for the crude (39% for *cis*-**4a** and 6% for *trans*-**4b**, determined by ^1H NMR, with internal standart EtOAc) The reaction mixutre was absorbed on celite by solvent evaporation under reduced pressure and dry loaded on silica gel chromatographic column and prufied by using eluent $PE:Et_2O$ 2:1. The obtained product was additionally washed with PE 0.5 ml x 2, to afford (*cis*-**4a**) as a white solid (12.1 mg, 0.051 mmol, 26%).

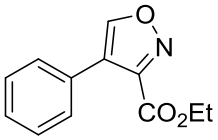
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.35 (m, 3H), 7.21 (m, 2H), 6.28 (dd, *J* = 65.3, 5.9 Hz, 1H), 4.80 (dd, *J* = 35.7, 6.0 Hz, 1H), 4.24 (dq, *J* = 10.8, 7.1 Hz, 2H), 1.20 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 159.01, 154.92, 129.62 (d, *J* = 1.4 Hz), 128.87, 128.83, 128.74 (d, *J* = 5.7 Hz), 109.58 (d, *J* = 245.1 Hz), 62.65, 58.97 (d, *J* = 20.6 Hz), 13.94.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -122.06 (dd, *J* = 65.3, 35.9 Hz).

HRMS: Calculated $[M-F]^+$: $C_{12}H_{12}NO_3$ 218,0812, Found 218.0821.

Ethyl 4-phenylisoxazole-3-carboxylate (**5**)



The title compound obtained as a side product from *N*-oxide *cis*-**3a** reduction reaction (general procedure C) as a slightly yellow oil (8.1 mg, 0.0373 mmol, 19 %).

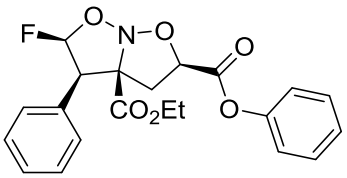
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.56 (s, 1H), 7.47 – 7.39 (m, 6H), 4.40 (q, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.29, 157.45, 153.29, 129.31, 128.73, 128.60, 127.49, 122.39, 62.41, 14.14.

HRMS: Calculated $[M+H]^+$: $C_{12}H_{12}NO_3$ 218.0812, Found 218.0823.

General procedure D for phenyl acrylate and *N*-oxide *cis*-3a [2+3] cycloaddition reaction

3a-ethyl 2-phenyl (2R*,3aR*,4R*,5R*)-5-fluoro-4-phenyltetrahydro-3aH-isoxazolo[2,3-b]isoxazole-2,3a-dicarboxylate (**7**).



(4R*,5R*)-3-(Ethoxycarbonyl)-5-fluoro-4-phenyl-4,5-dihydroisoxazole 2-oxide (*cis*-**3a**) (10 mg, 0.0395 mmol, 1 equiv) under Ar atmosphere was dissolved in anhydrous DMSO (0.4 ml) and phenyl acrylate (**6**) (109 µl, 0.790 mmol, 20 equiv) was added. The reaction mixture was stirred for 93 hours. After completion H_2O (1 ml) was added and the formed aqueous phase was extracted with Et_2O (2 ml x 5). The combined organic phases were washed with water (15 ml x 3), dried over Na_2SO_4, filterd and evaporated under reduced pressure. NMR yield for the crude (83% d.r. = 4.9:1, determined by ^{1}H NMR, with internal standart EtOAc). The crude product was dry loaded on silica gel and purified by silica gel column chromatography, using eluent gradient PE:EtOAc 10:1 - 4:1 - 2:1 to afford product **7** (11.5 mg, 0.0287 mmol, 73%, *d.r.*= 4.2:1) as a white solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 – 7.28 (m, 7H), 7.31 – 7.21 (m, 1H), 7.14 – 7.06 (m, 2H), 6.21 (dd, *J* = 65.2, 5.6 Hz, 1H), 5.37 (dd, *J* = 8.5, 6.5 Hz, 1H), 4.22 (dd, *J* = 18.5, 5.6 Hz, 1H), 3.81 (dq, *J* = 10.8, 7.1 Hz, 3H), 3.30 (dd, *J* = 13.2, 6.5 Hz, 1H), 2.88 (dd, *J* = 13.2, 8.4 Hz, 1H), 0.89 (t, *J* = 7.1 Hz, 3H) (major diastereomer).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.27, 166.75, 150.17, 131.51 (d, *J* = 2.5 Hz), 130.55 (d, *J* = 3.2 Hz), 129.74, 128.73, 128.43, 126.60, 121.20, 106.76 (d, *J* = 238.2 Hz), 86.29, 80.62, 62.36, 61.23 (d, *J* = 22.9 Hz), 41.66, 13.57 (major diastereomer).

^{19}F NMR (376 MHz, Chloroform-*d*) δ -116.59 (dd, *J* = 65.2, 18.2 Hz) (major diastereomer).

HRMS: Calculated $[M+Na]^+$: $C_{21}H_{20}NO_6FNa$ 424.1172, Found 424.1183.

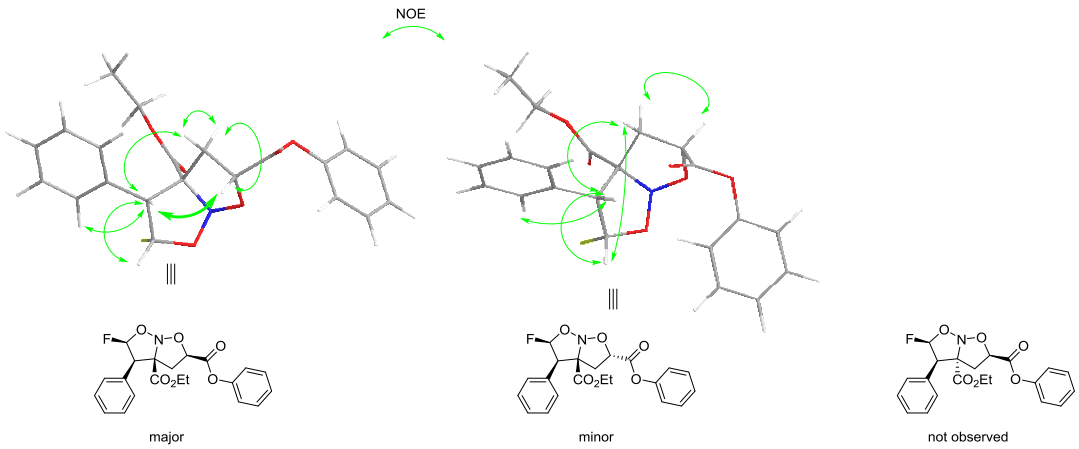
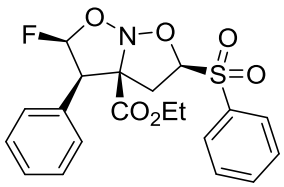


Figure S3. Determination of stereochemistry for **7** by 2D NOESY NMR.

General procedure E for vinyl sulphone and *N*-oxide *cis*-3a [2+3] cycloaddition reaction

Ethyl (2R,3R,3aR,5S)-2-fluoro-3-phenyl-5-(phenylsulfonyl)tetrahydro-3aH-isoxazolo[2,3-b]isoxazole-3a-carboxylate (**9**)



(4R*,5R*)-3-(Ethoxycarbonyl)-5-fluoro-4-phenyl-4,5-dihydroisoxazole 2-oxide (*cis*-**3a**) (15 mg, 0.059 mmol, 1 equiv) and phenyl vinyl sulphone (**8**) (199.3 mg, 1.185 mmol, 20 equiv) were dissolved in anhydrous DMSO (0.2 ml) under Ar atmosphere. The reaction mixture was stirred for 67 hours at 40 ºC. After completion H_2O (1 ml) was added and the formed aqueous phase was extracted with MTBE (2 ml x 5). The combined organic phases were washed with water (15 ml x 3), dried over Na_2SO_4, filtered and evaporated under reduced pressure. NMR yield for the crude (68% d.r. = 8.7:1, determined by ^{1}H NMR, with internal standart EtOAc). The crude product was dry loaded on silica gel and purified by silica gel column chromatography, using eluent gradient PE:EtOAc 4:1 - 2:1 to afford product **9** (16.7 mg, 0.0396 mmol, 67%, *d.r.*= 14.3:1) as a white solid.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.88 – 7.78 (m, 3H), 7.73 – 7.66 (m, 2H), 7.32 – 7.20 (m, 5H), 6.33 (dd, *J* = 68.1, 5.9 Hz, 1H), 5.96 (dd, *J* = 8.9, 4.9 Hz, 1H), 4.65 (dd, *J* = 17.5, 5.9 Hz, 1H), 3.21 (dd, *J* = 14.4, 9.0 Hz, 1H), 3.12 (dd, *J* = 14.2, 4.9 Hz, 1H), 0.75 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 165.91, 135.13, 135.07, 131.77 (d, *J* = 3.9 Hz), 130.67 (d, *J* = 2.3 Hz), 129.67, 129.27, 128.12, 127.85, 107.36 (d, *J* = 235.0 Hz), 94.27, 85.72, 61.37, 58.29 (d, *J* = 21.3 Hz), 36.74, 13.22.

^{19}F NMR (376 MHz, DMSO-d_6) δ -116.37 (dd, *J* = 68.1, 17.8 Hz).

HRMS: Calculated $[M+Na]^+$: $C_{20}H_{20}NO_6FNaS$ 444.0893, Found 444.0898.

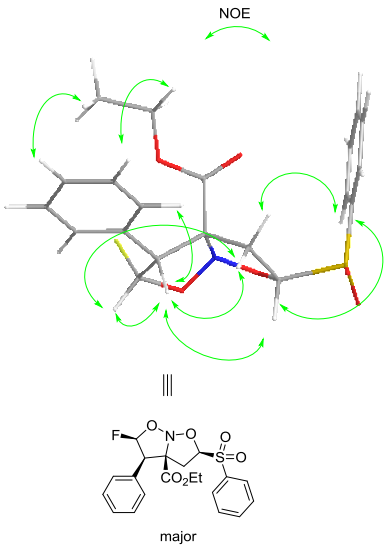


Figure S4. Determination of stereochemistry for **9** by 2D NOESY NMR.

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[S4] Gagnot, G.; Hervin, V.; Coutant, E. P.; Desmons, S.; Baatallah, R.; Monnot, V.; Janin, Y. L. *Beilstein J. Org. Chem.* **2018**, *14*, 2846–2852.

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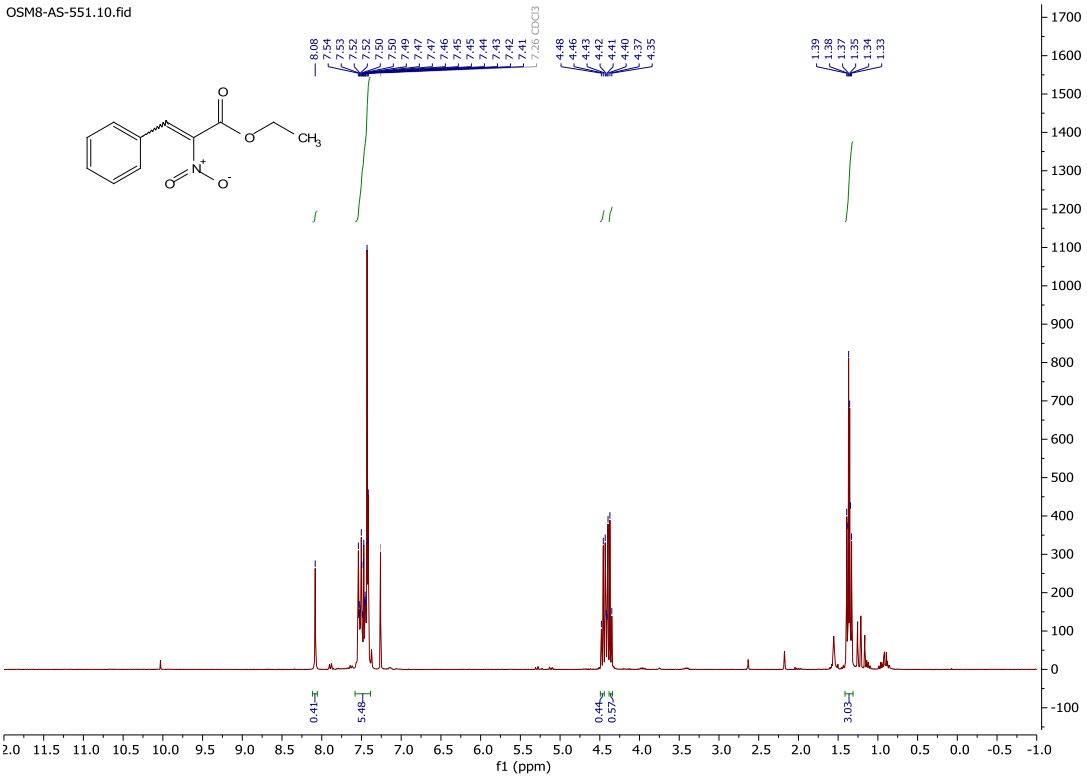
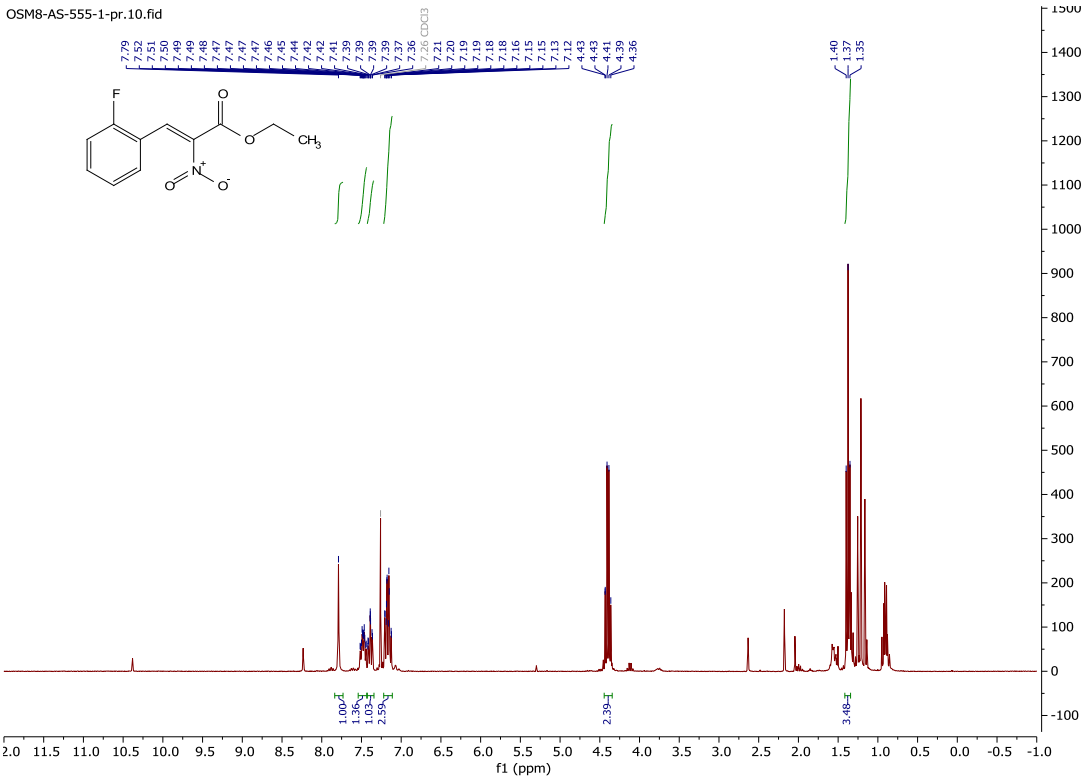
[S6] Baichurin, R. I.; Alizada, L. M.; Aboskalova, N. I.; Makarenko, S. V. *Russ. J. Gen. Chem*. **2018**, *88(1), 36–40.*

Copies of NMR spectra

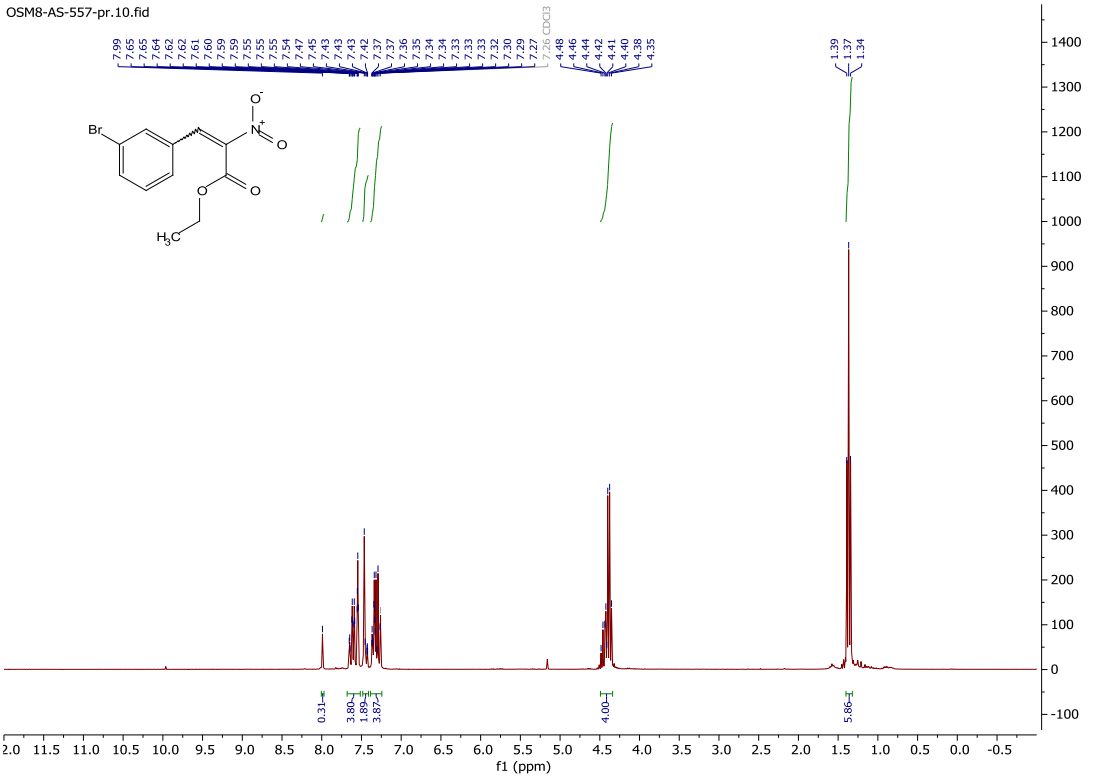
Compound (**1a**) ^{1}H-NMR spectra (300 MHz, $CDCl_3$)



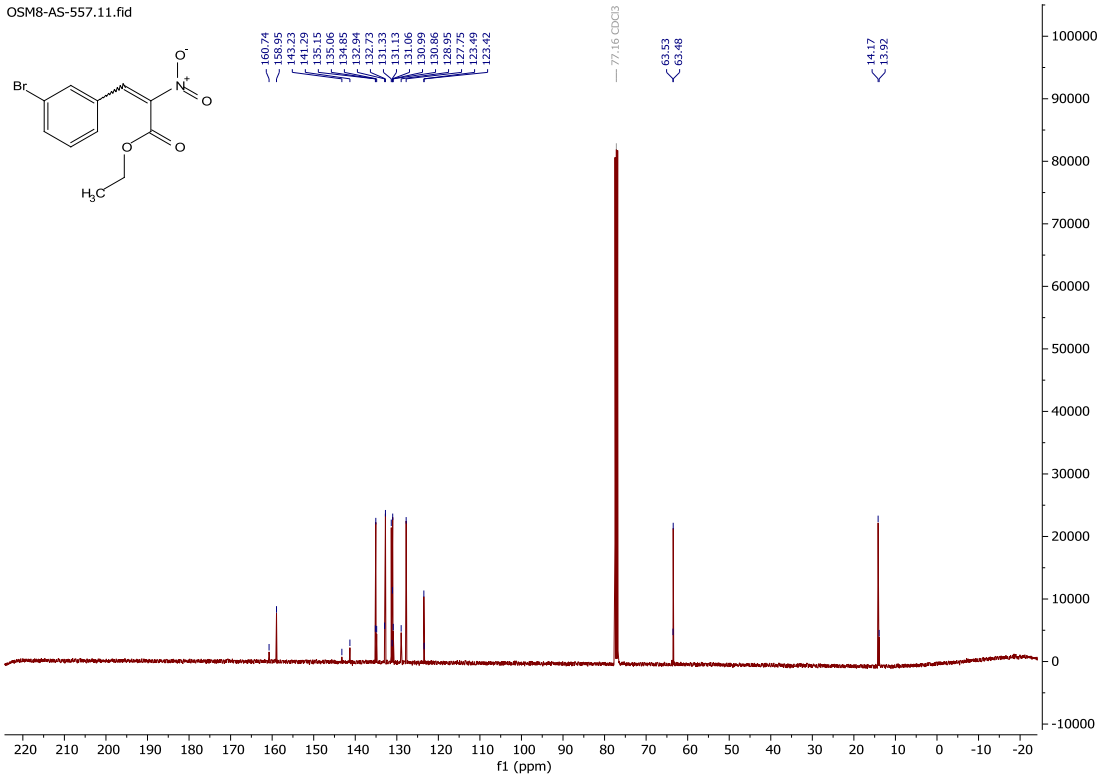
Compound (**1b**) ^{1}H-NMR spectra (300 MHz, $CDCl_3$)



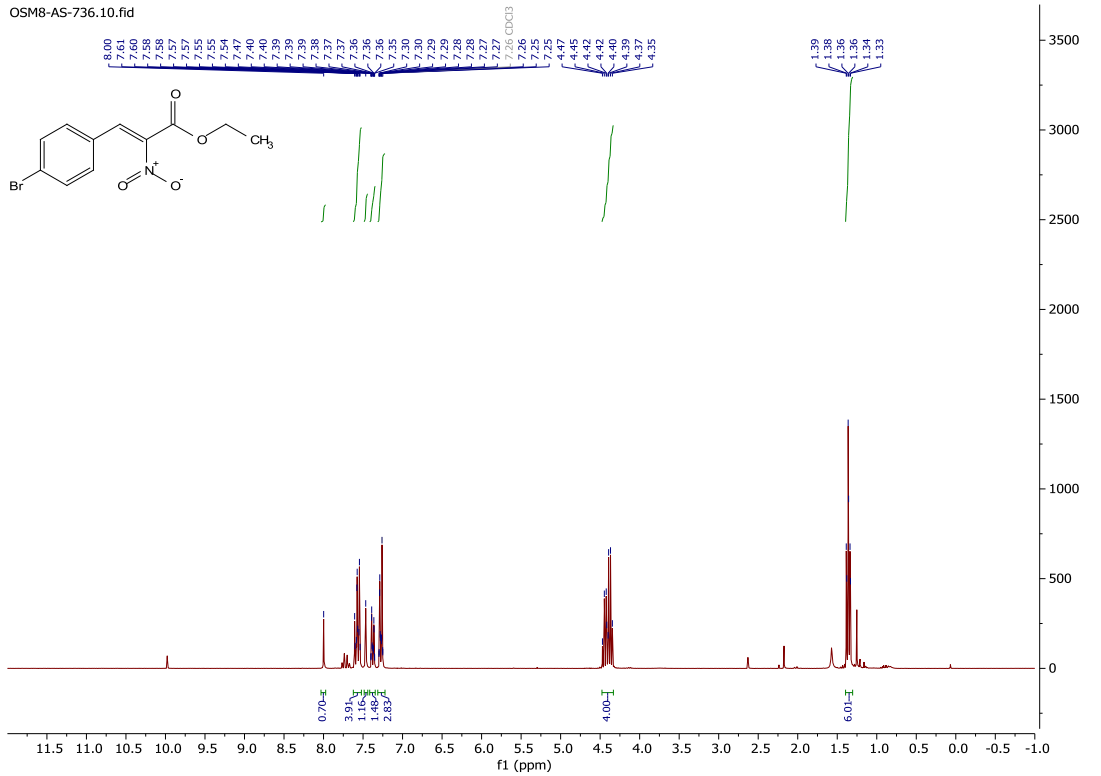
Compound (**1c**) ^{1}H-NMR spectra (400 MHz, $CDCl_3$)



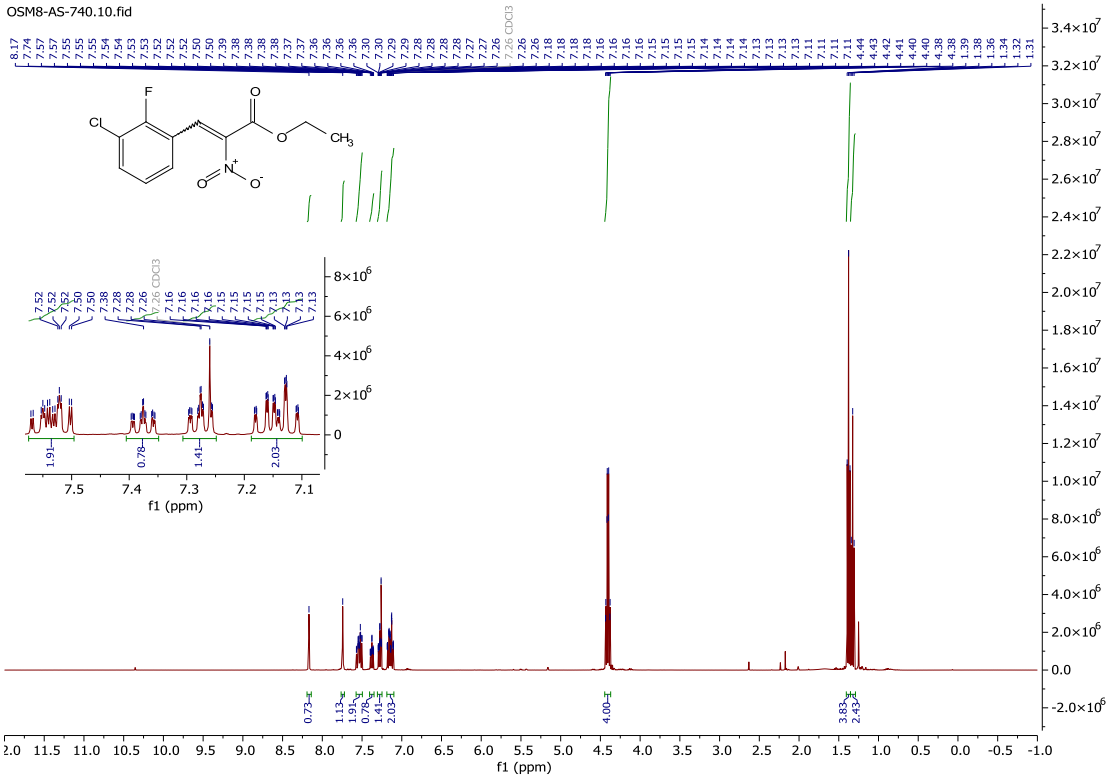
Compound (**1c**) ^{13}C-NMR spectra (101 MHz, $CDCl_3$)



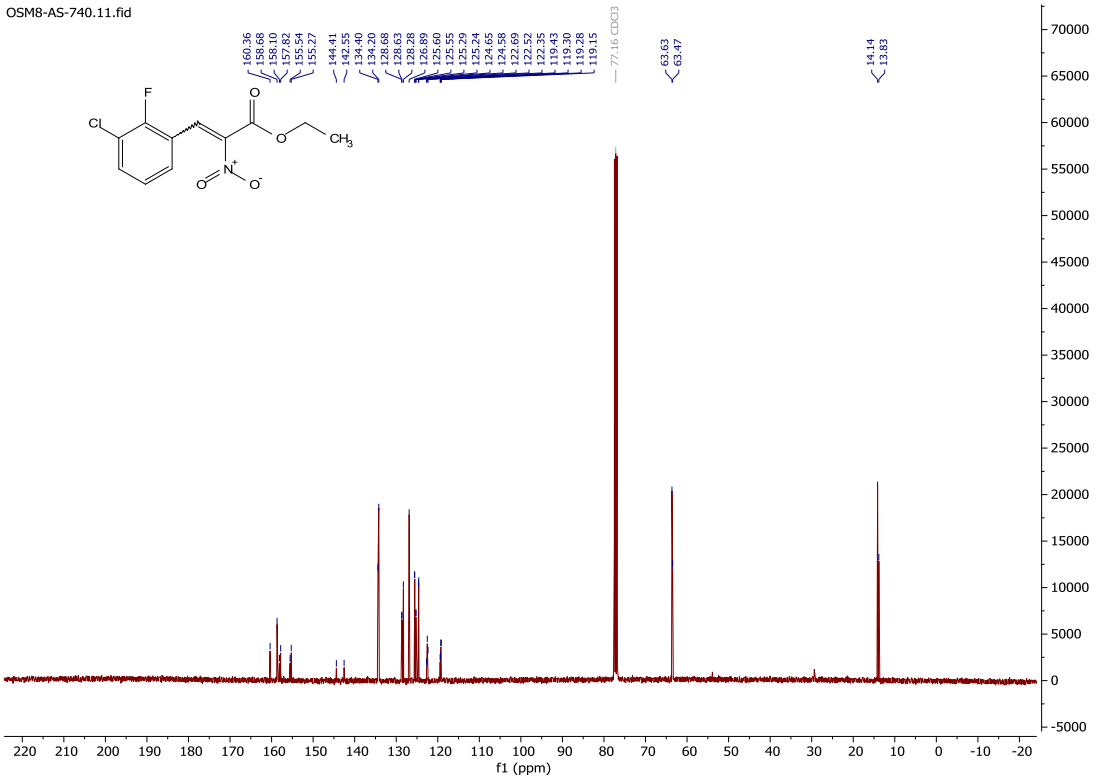
Compound (**1d**) ^{1}H-NMR spectra (400 MHz, $CDCl_3$)



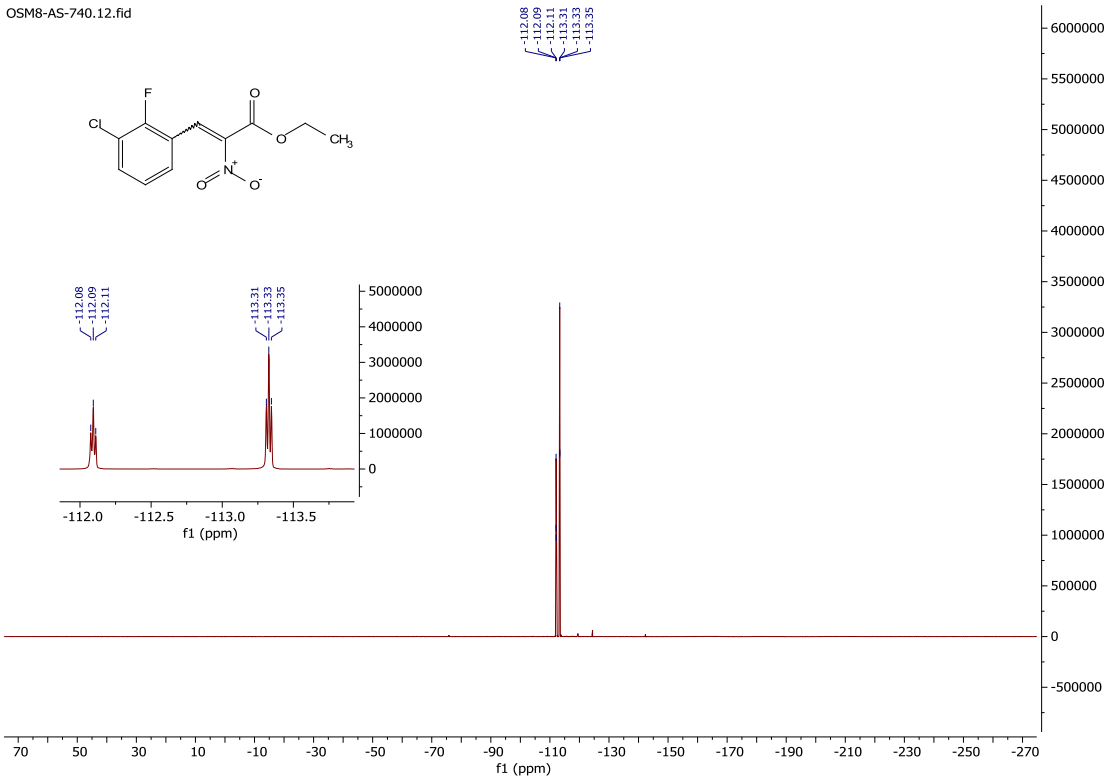
Compound (**1e**) ^{1}H-NMR spectra (400 MHz, $CDCl_3$)



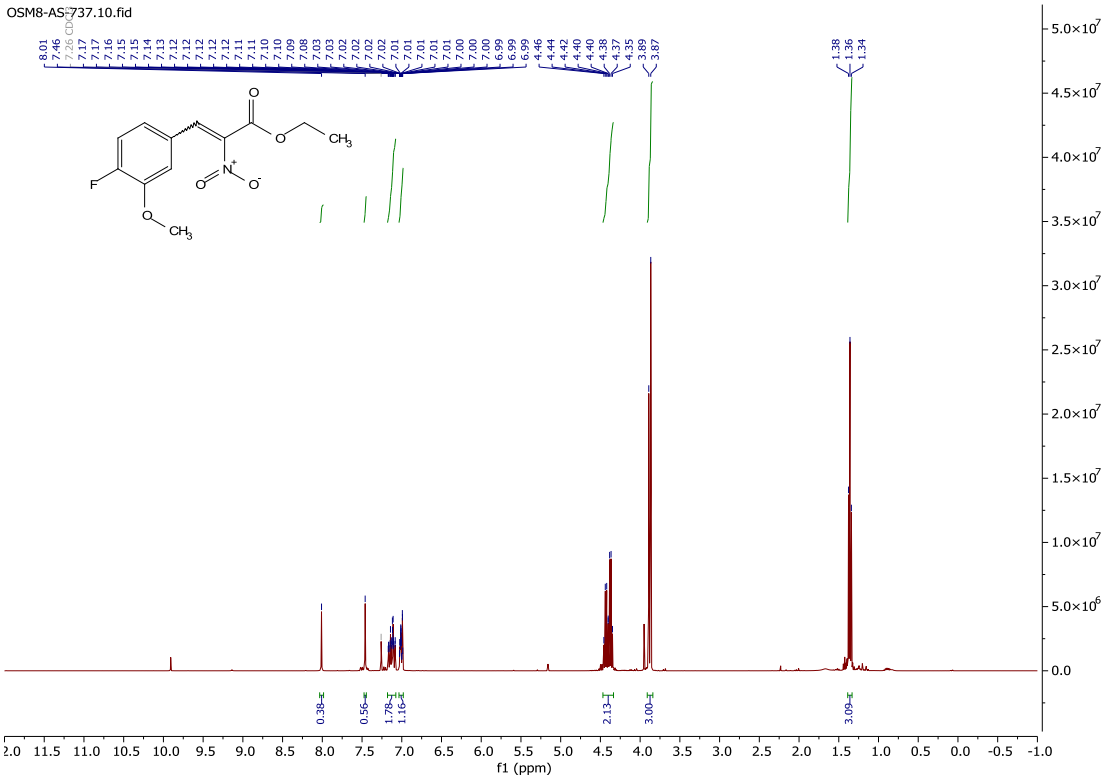
Compound (**1e**) ^{13}C-NMR spectra (101 MHz, $CDCl_3$)



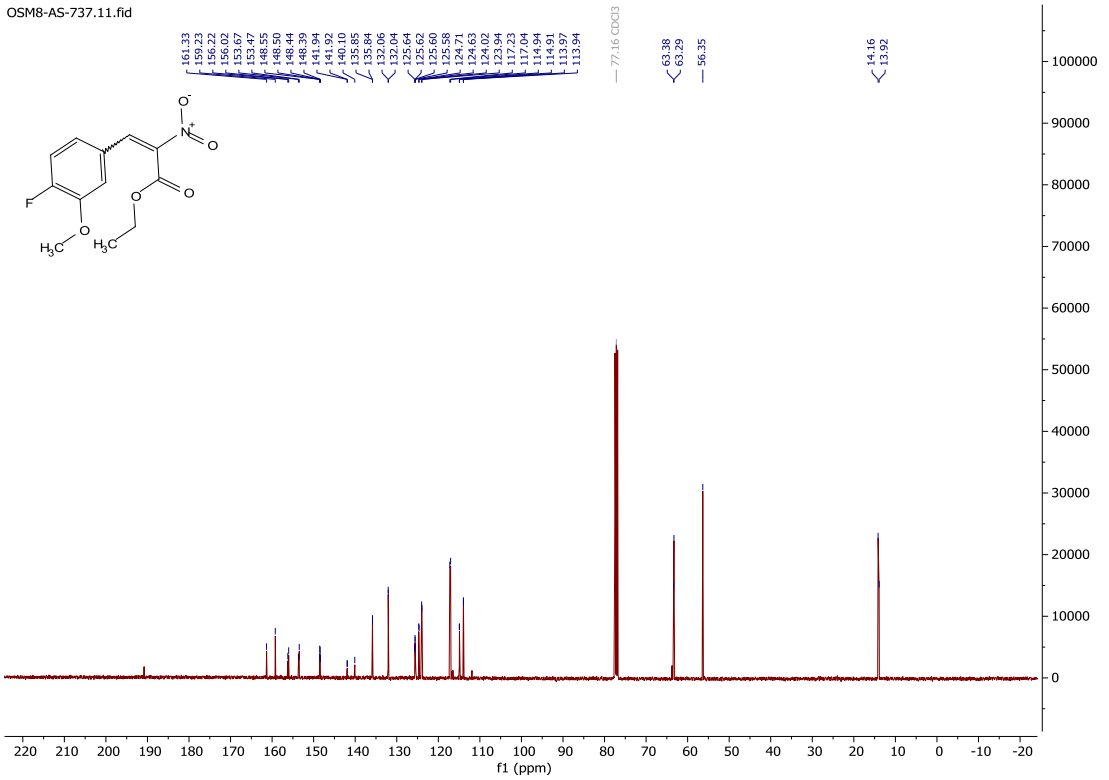
Compound (**1e**) ^{19}F-NMR spectra (376 MHz, $CDCl_3$)



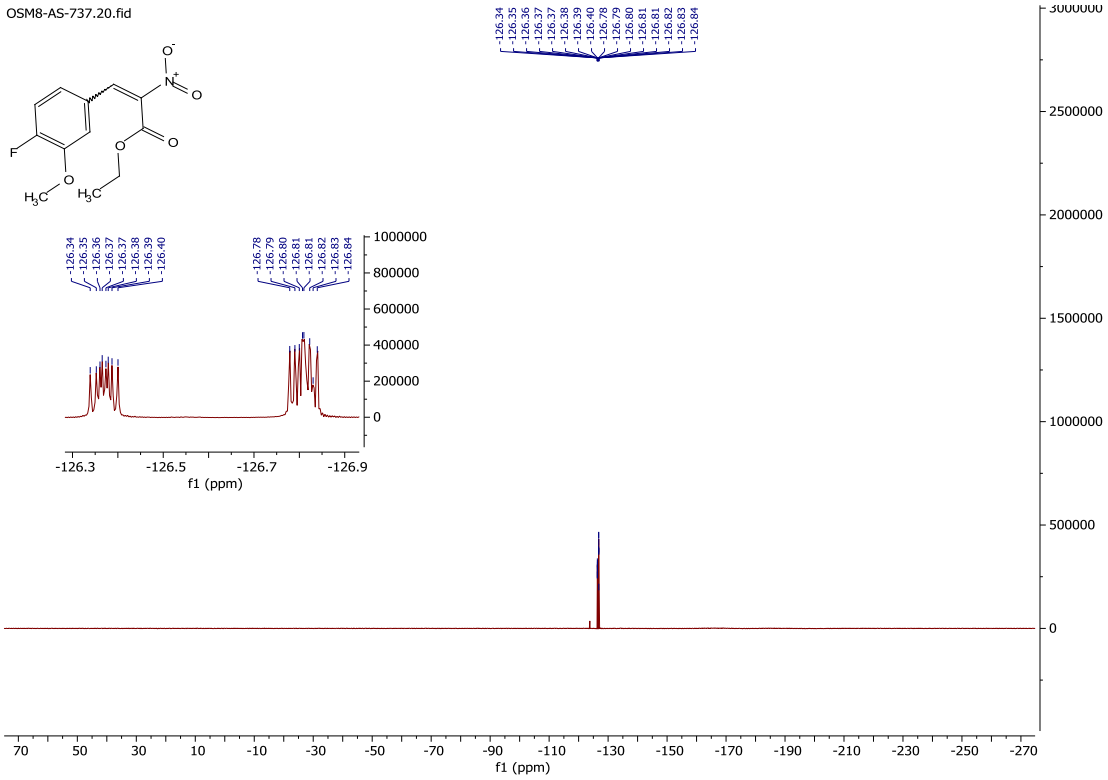
Compound (**1f**) ^{1}H-NMR spectra (400 MHz, $CDCl_3$)



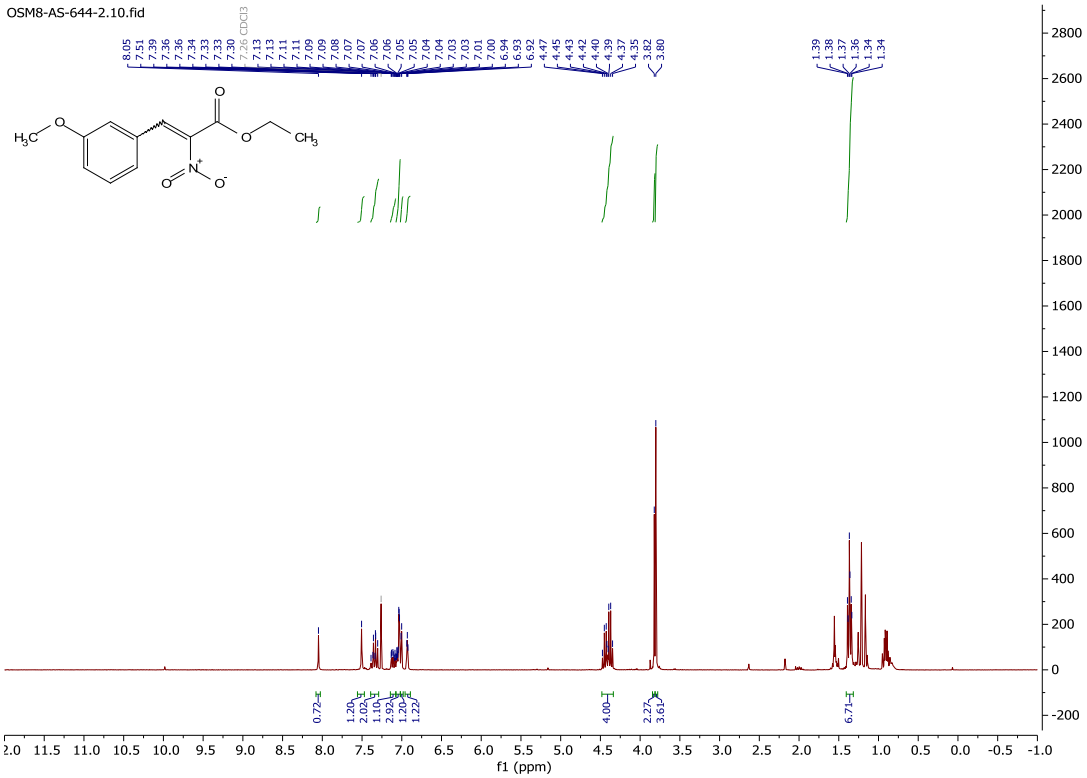
Compound (**1f**) ^{13}C-NMR spectra (101 MHz, $CDCl_3$)



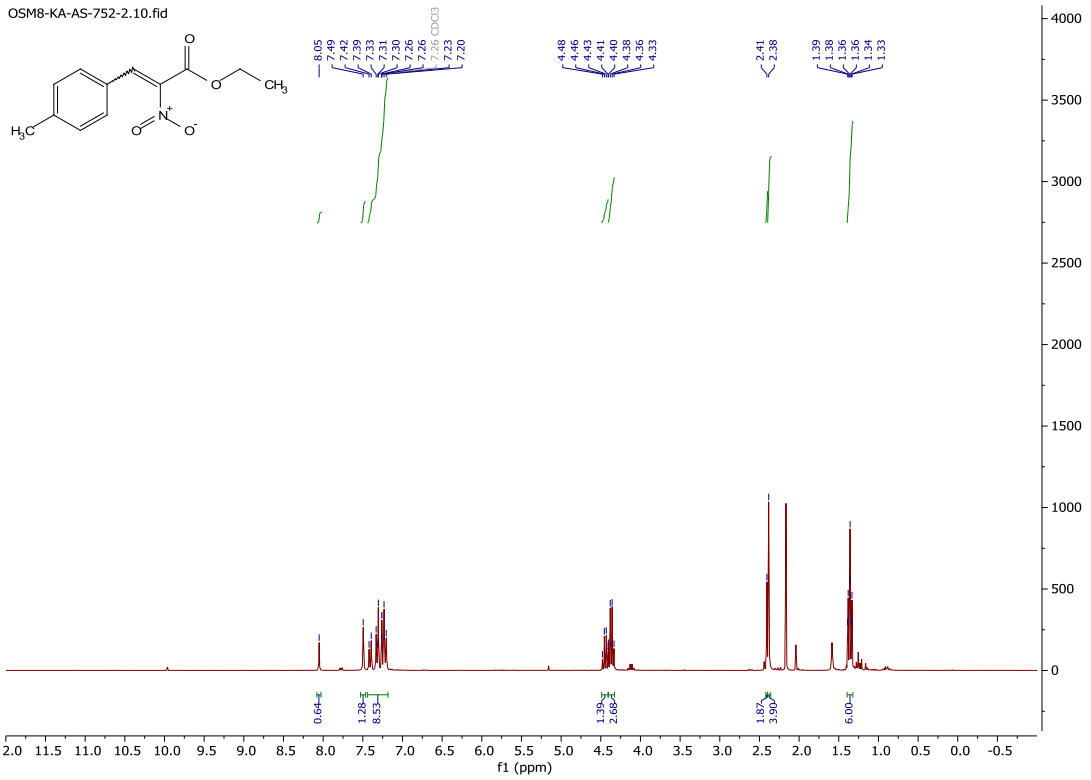
Compound (**1f**) ^{19}F-NMR spectra (376 MHz, $CDCl_3$)



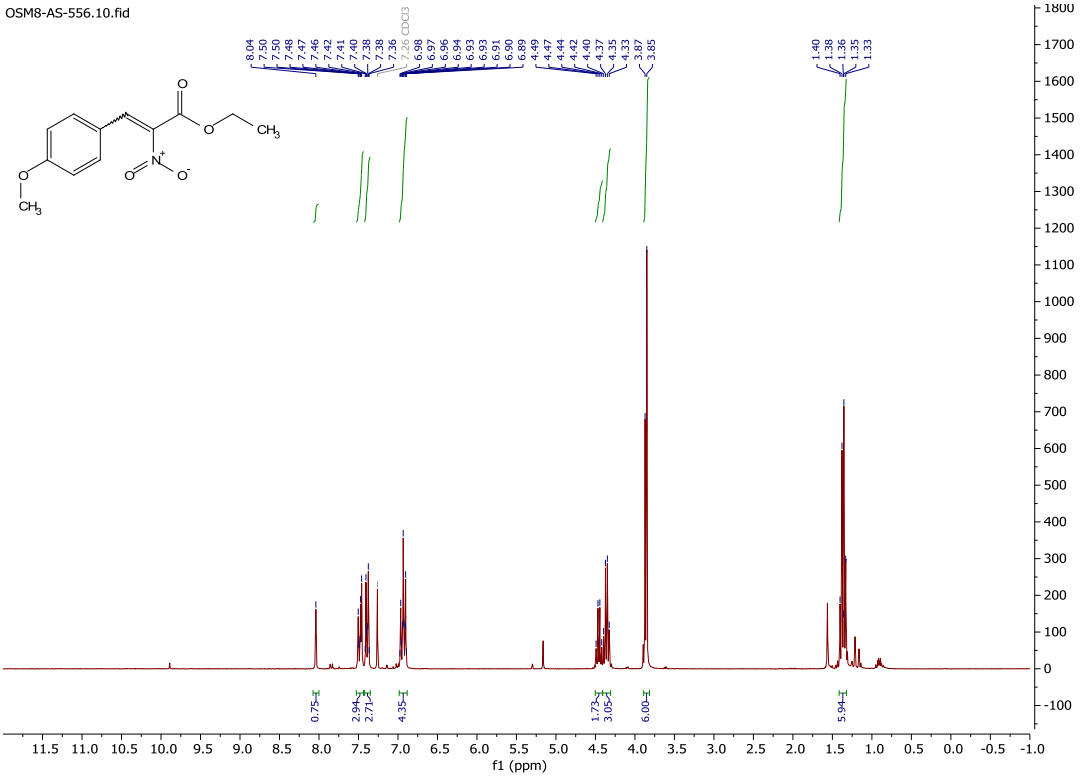
Compound (**1g**) ^{1}H-NMR spectra (300 MHz, $CDCl_3$)



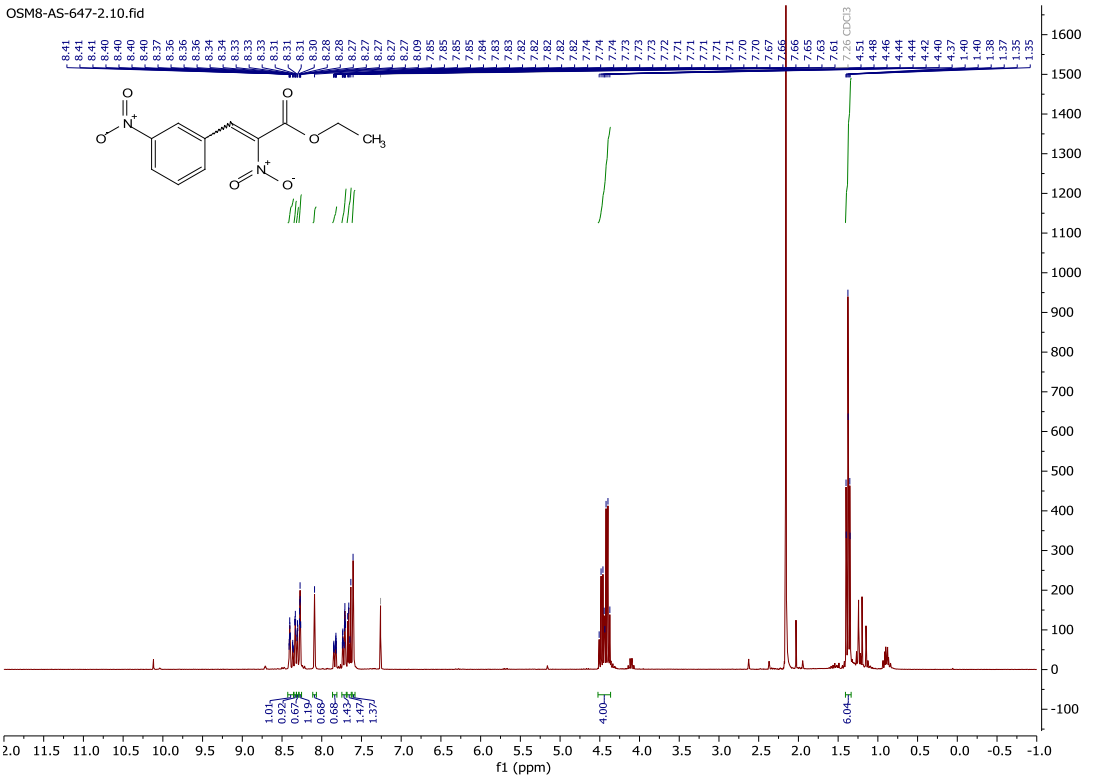
Compound (**1h**) ^{1}H-NMR spectra (300 MHz, $CDCl_3$)



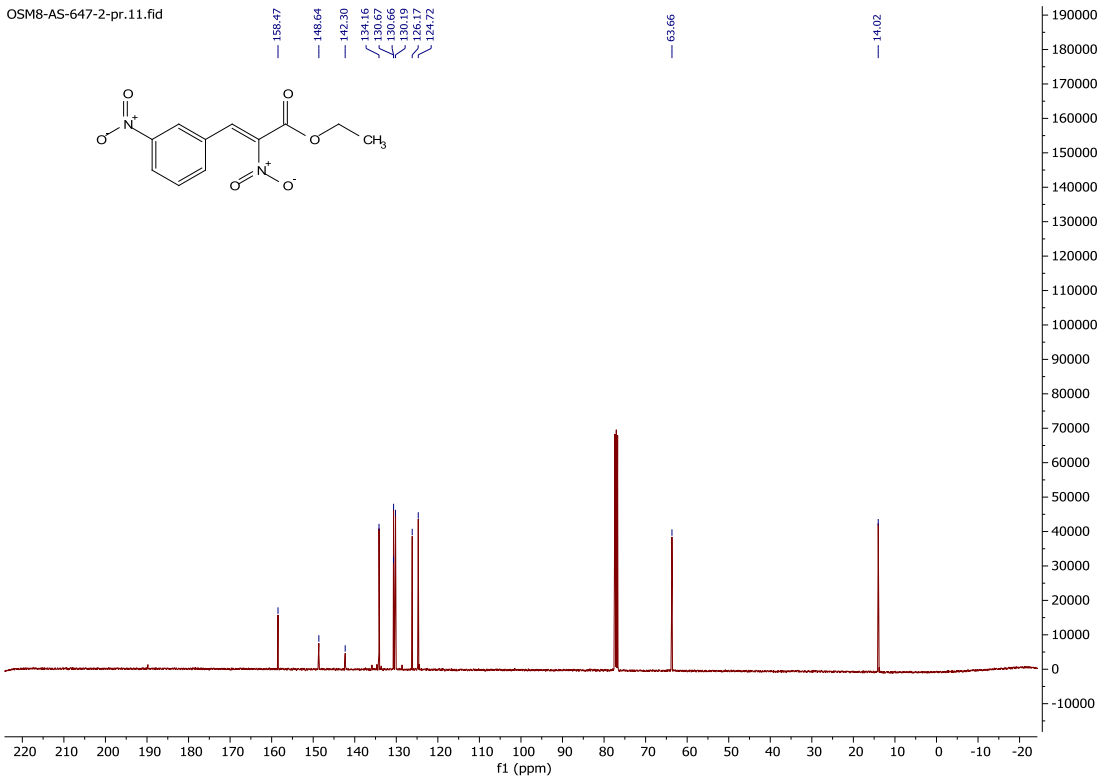
Compound (**1i**) ^{1}H-NMR spectra (300 MHz, $CDCl_3$)



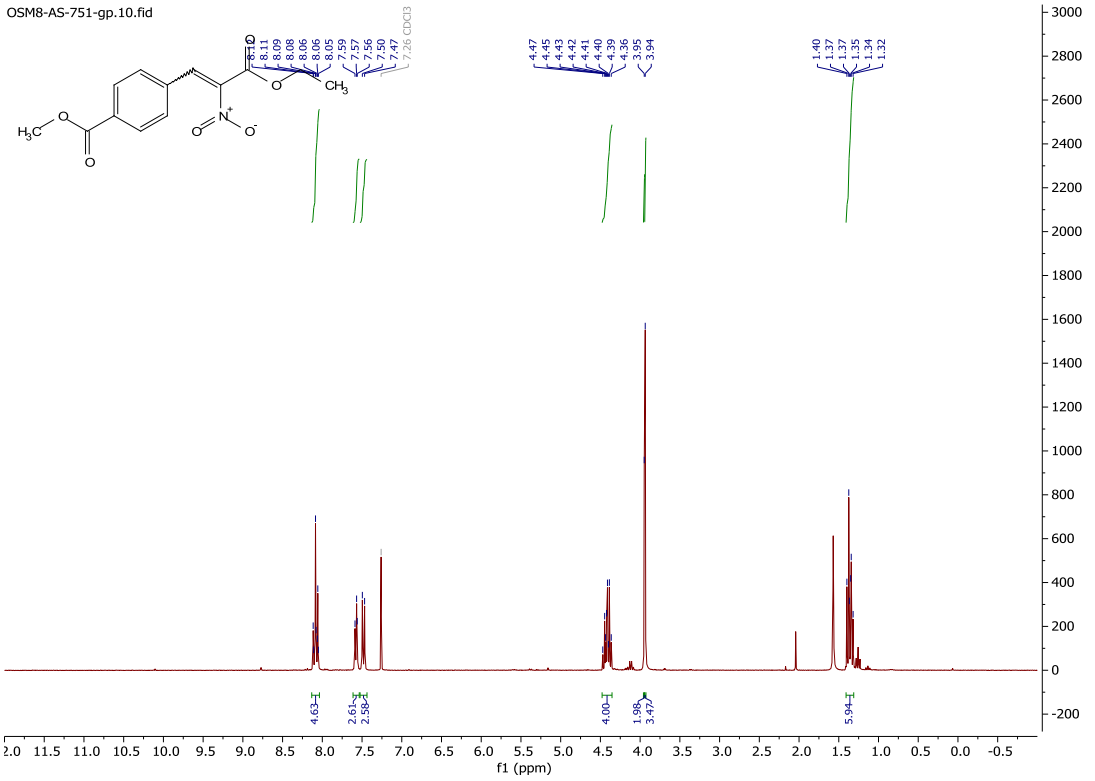
Compound (**1j**) ^{1}H-NMR spectra (300 MHz, $CDCl_3$)



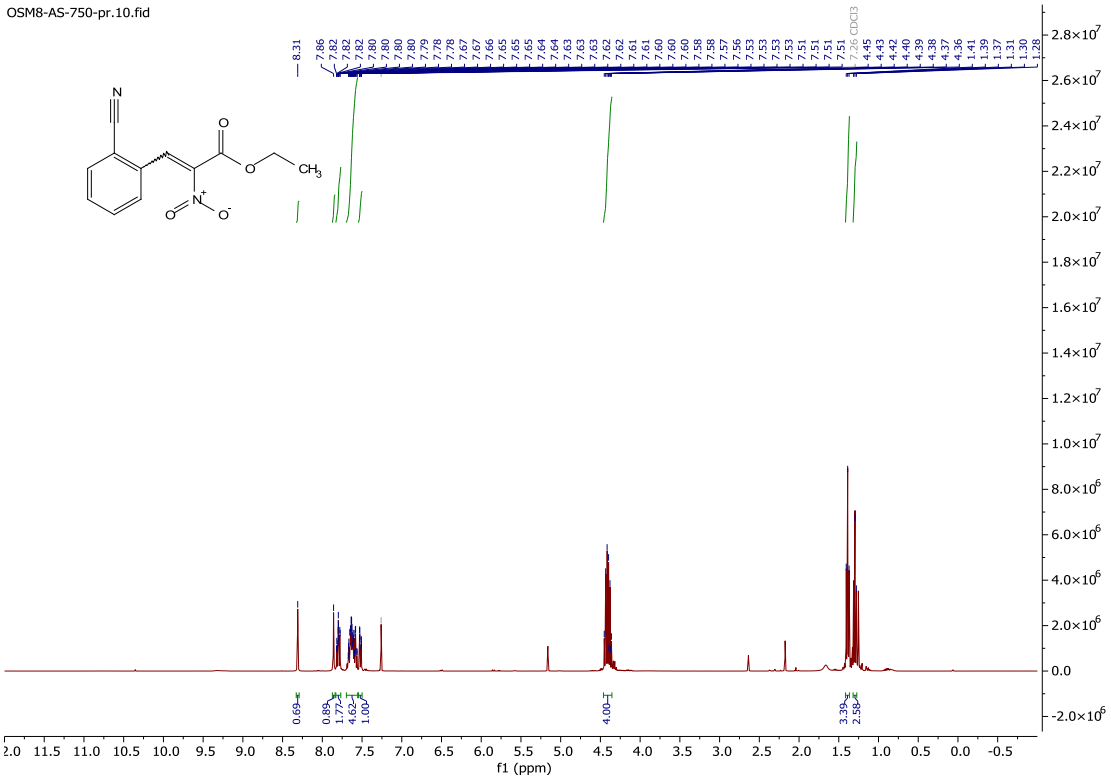
Compound (**1j**) ^{13}C-NMR spectra (101 MHz, $CDCl_3$)



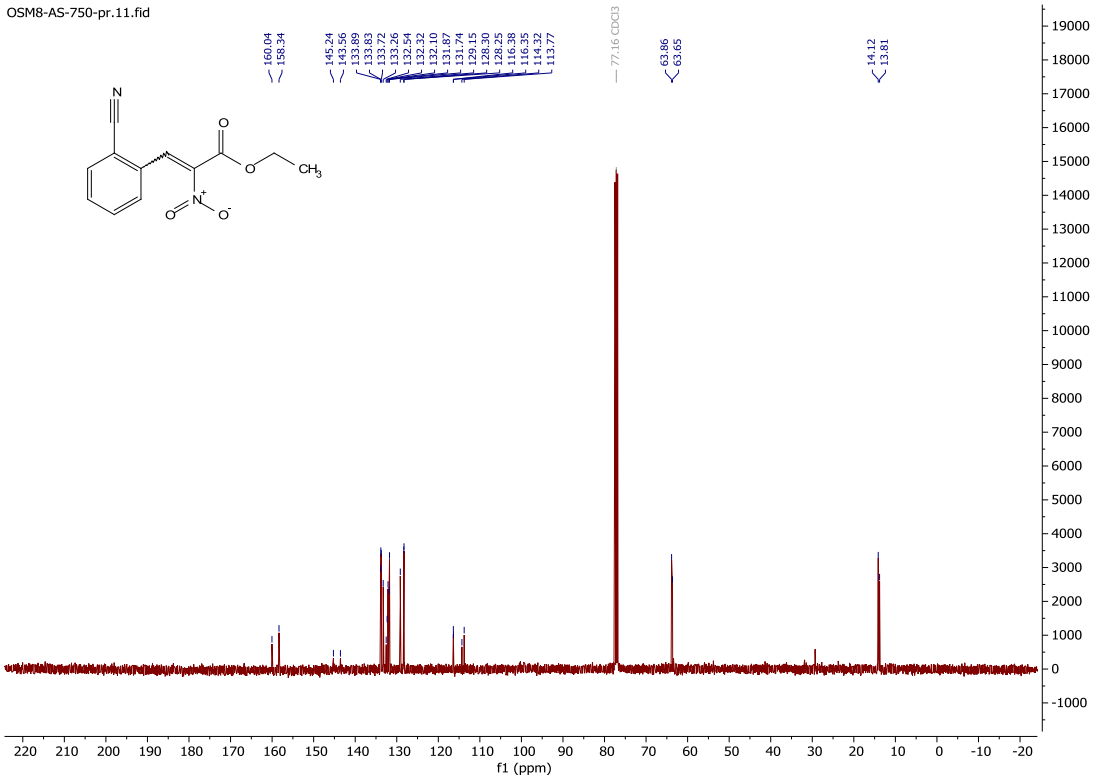
Compound (**1k**) ^{1}H-NMR spectra (300 MHz, $CDCl_3$)



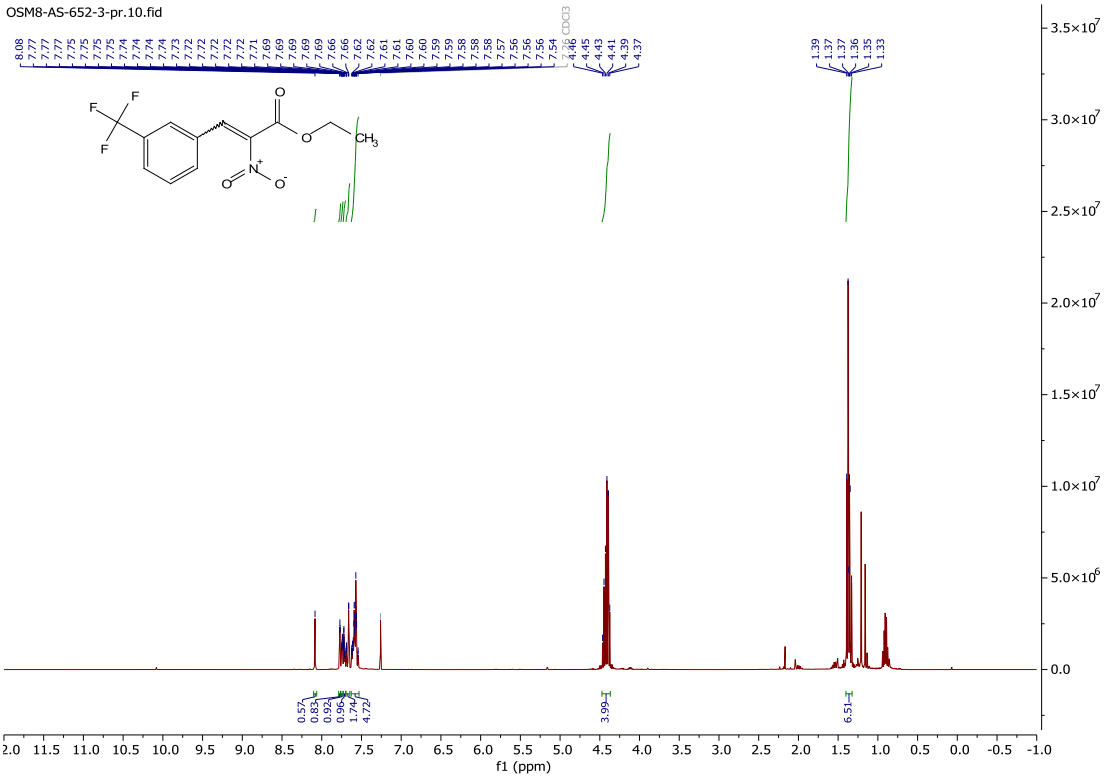
Compound (**1l**) ^{1}H-NMR spectra (400 MHz, $CDCl_3$)



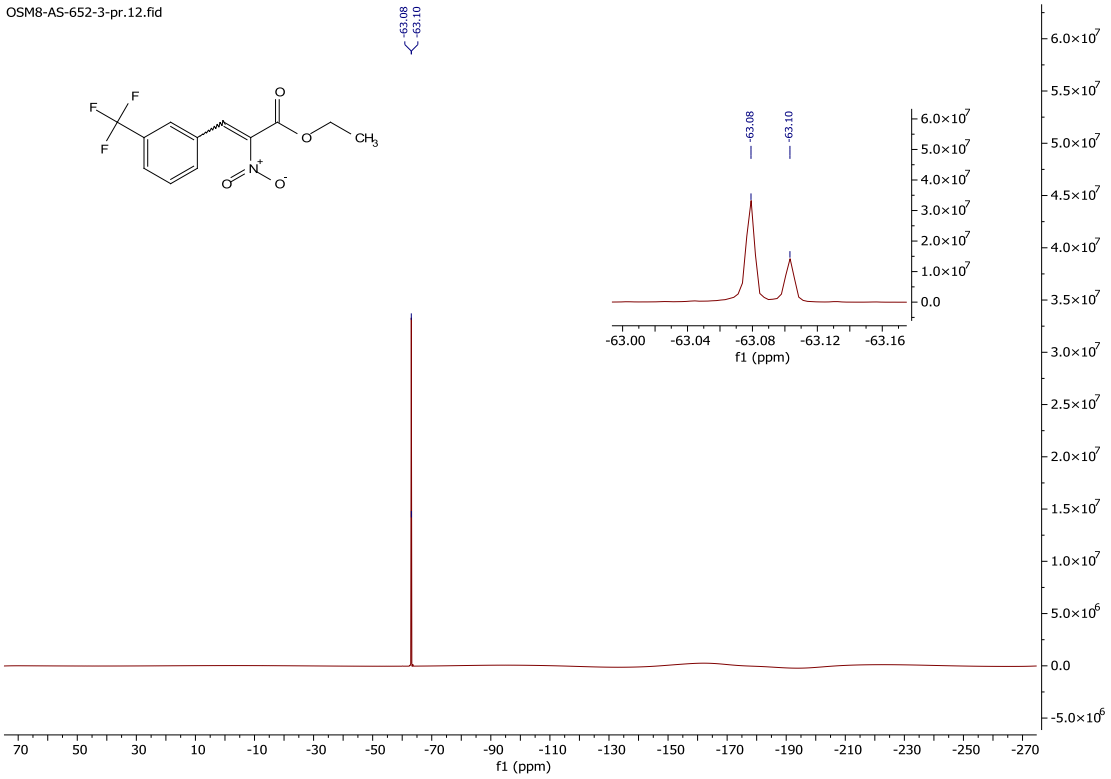
Compound (**1l**) ^{13}C-NMR spectra (101 MHz, $CDCl_3$)



Compound (**1m**) ^{1}H-NMR spectra (400 MHz, $CDCl_3$)



Compound (**1m**) ^{19}F-NMR spectra (376 MHz, $CDCl_3$)



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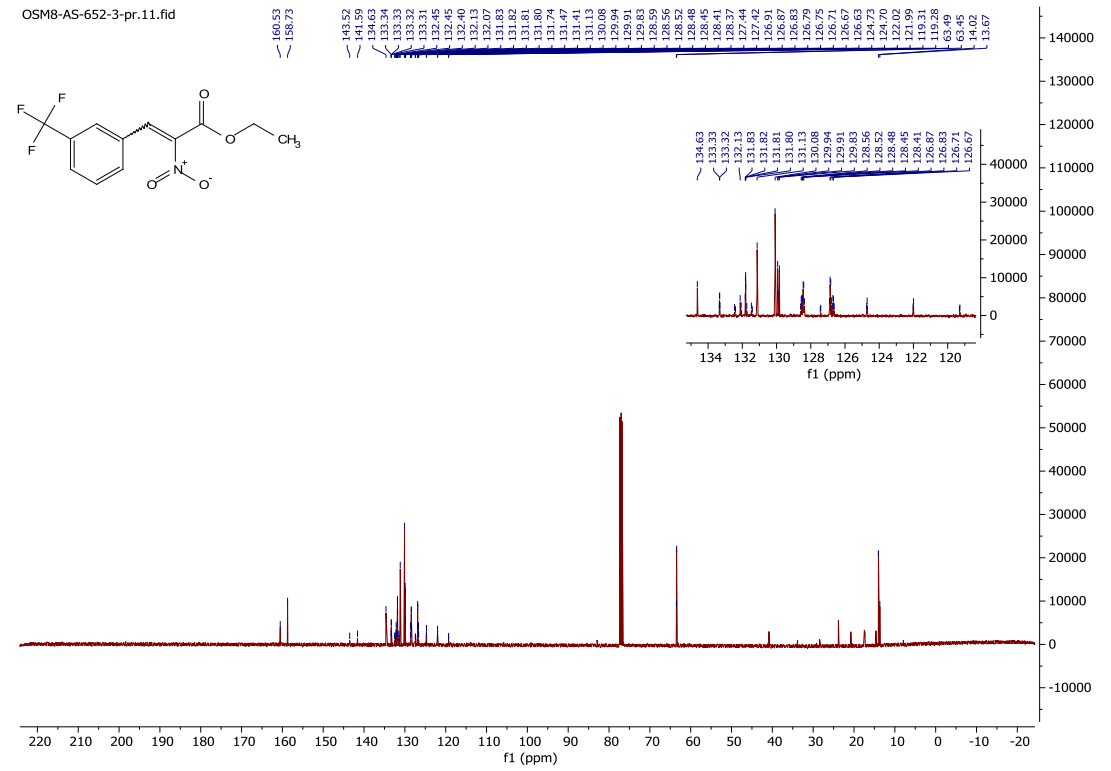
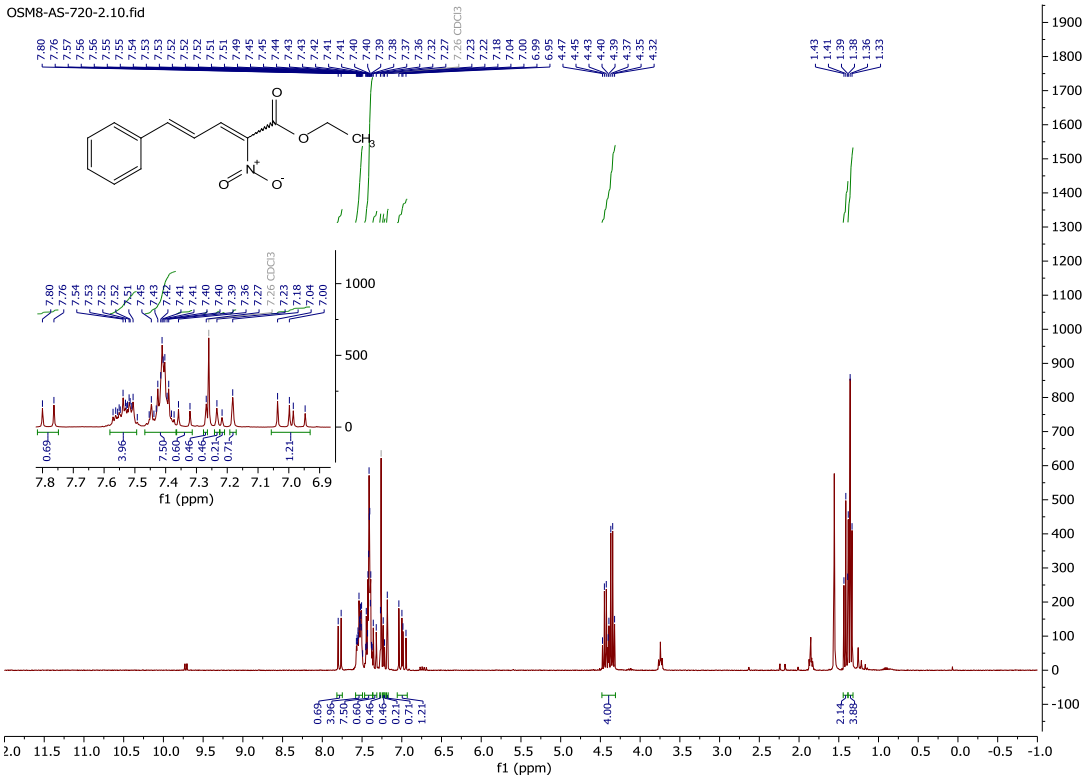
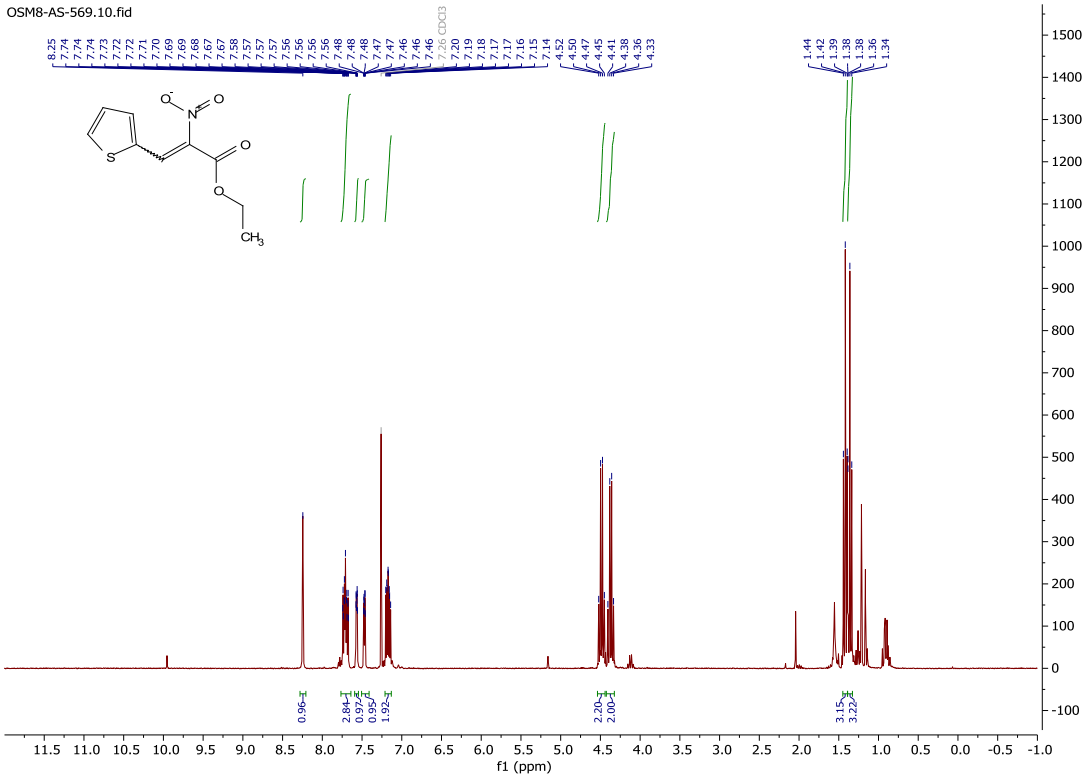


Compound (**1n**) ^{1}H-NMR spectra (300 MHz, $CDCl_3$)



Compound (**1o**) ^{1}H-NMR spectra (300 MHz, $CDCl_3$)



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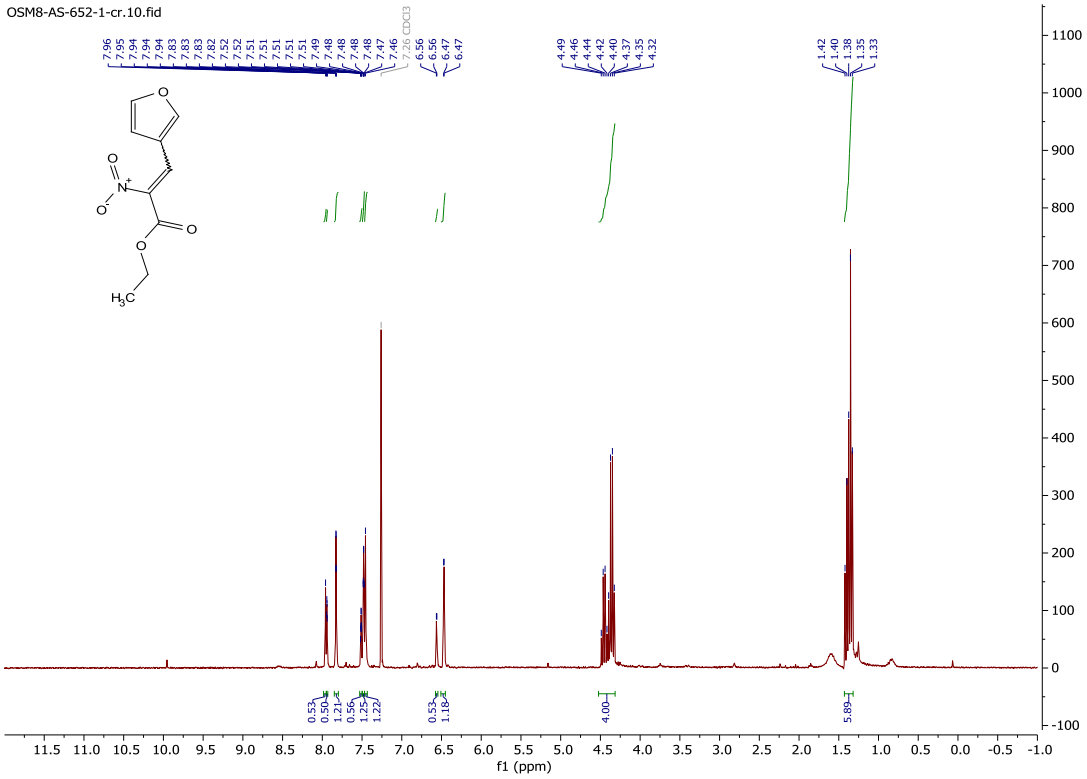
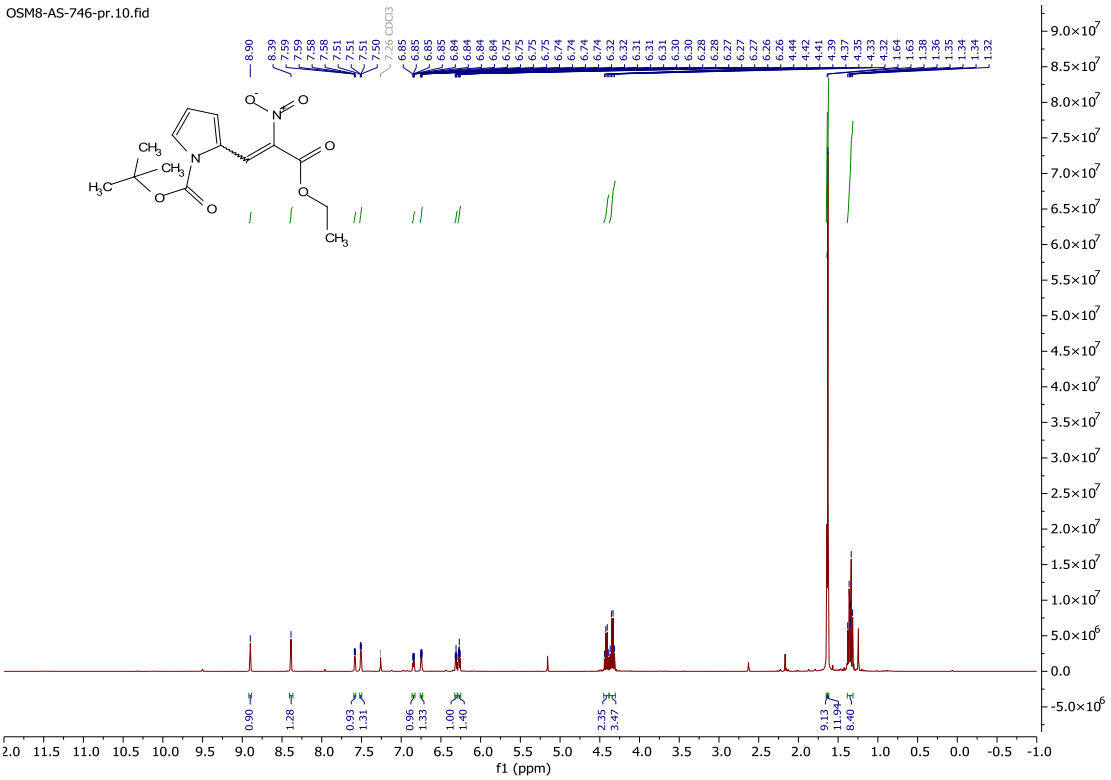
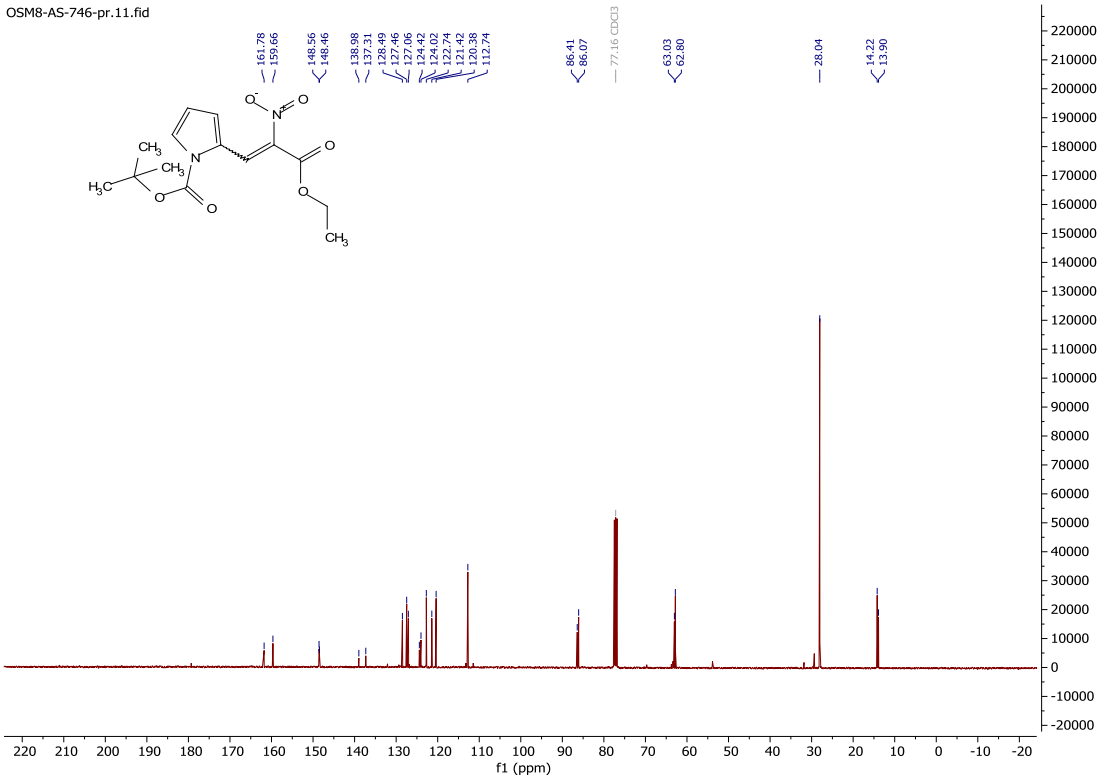


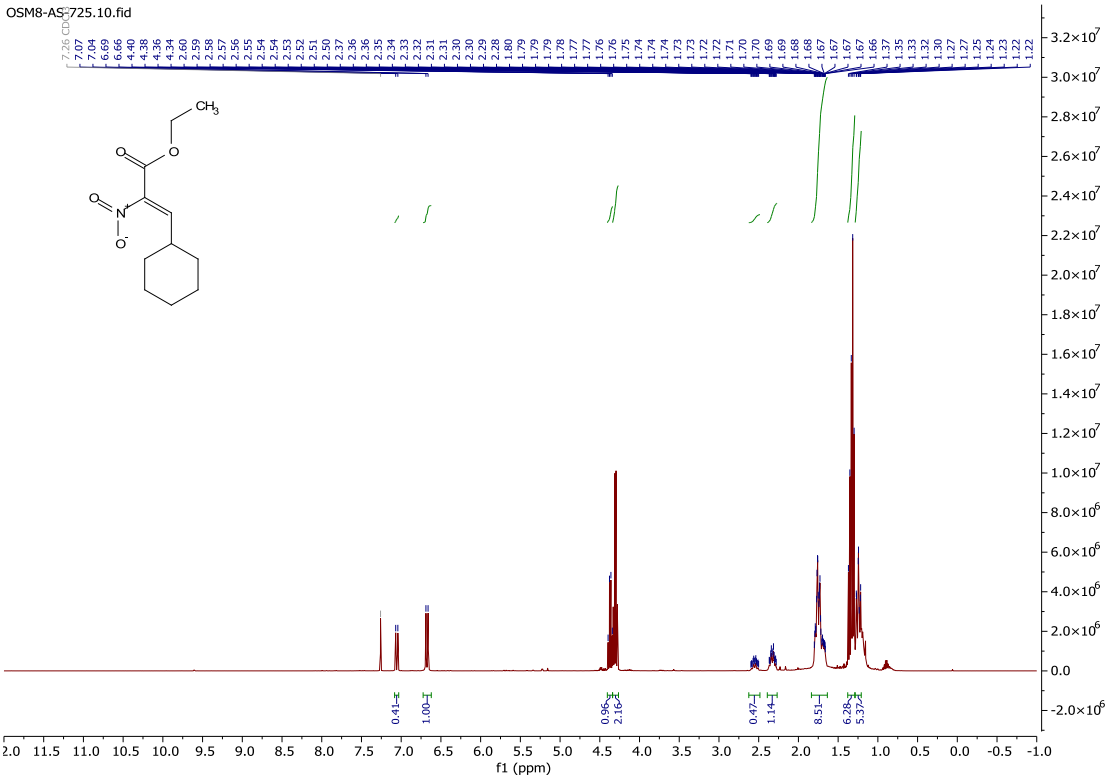
Compound (**1q**) ^{1}H-NMR spectra (400 MHz, $CDCl_3$)



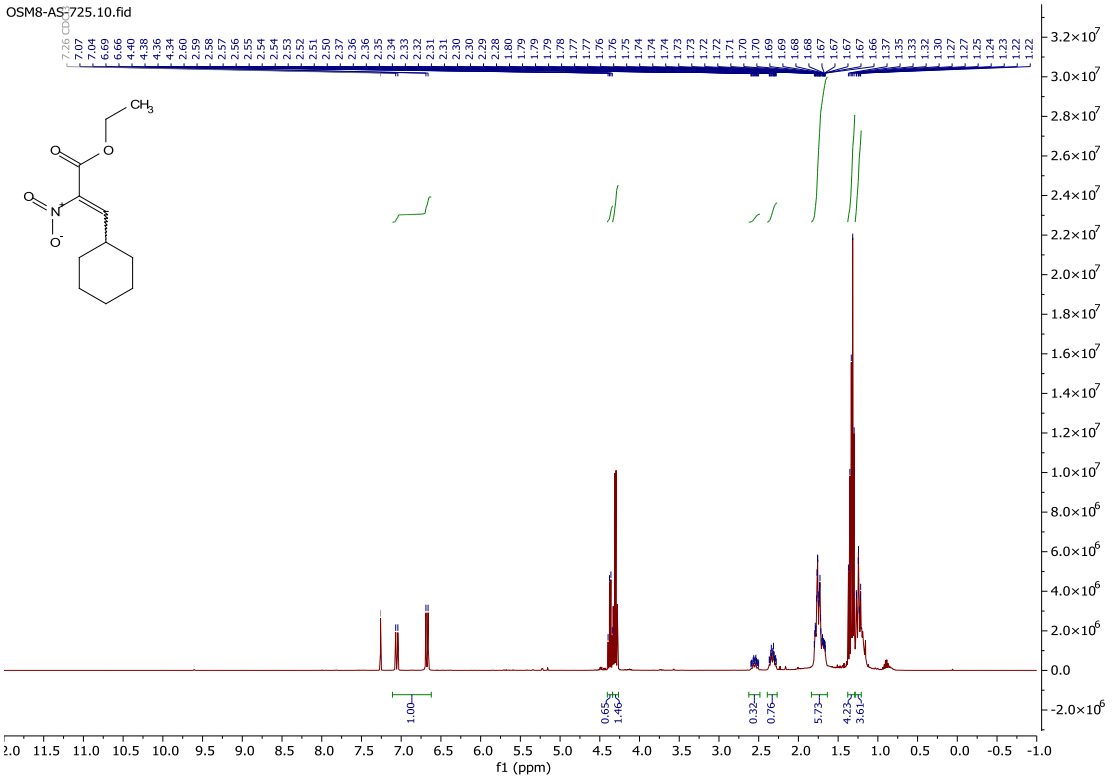
Compound (**1q**) ^{13}C-NMR spectra (101 MHz, $CDCl_3$)



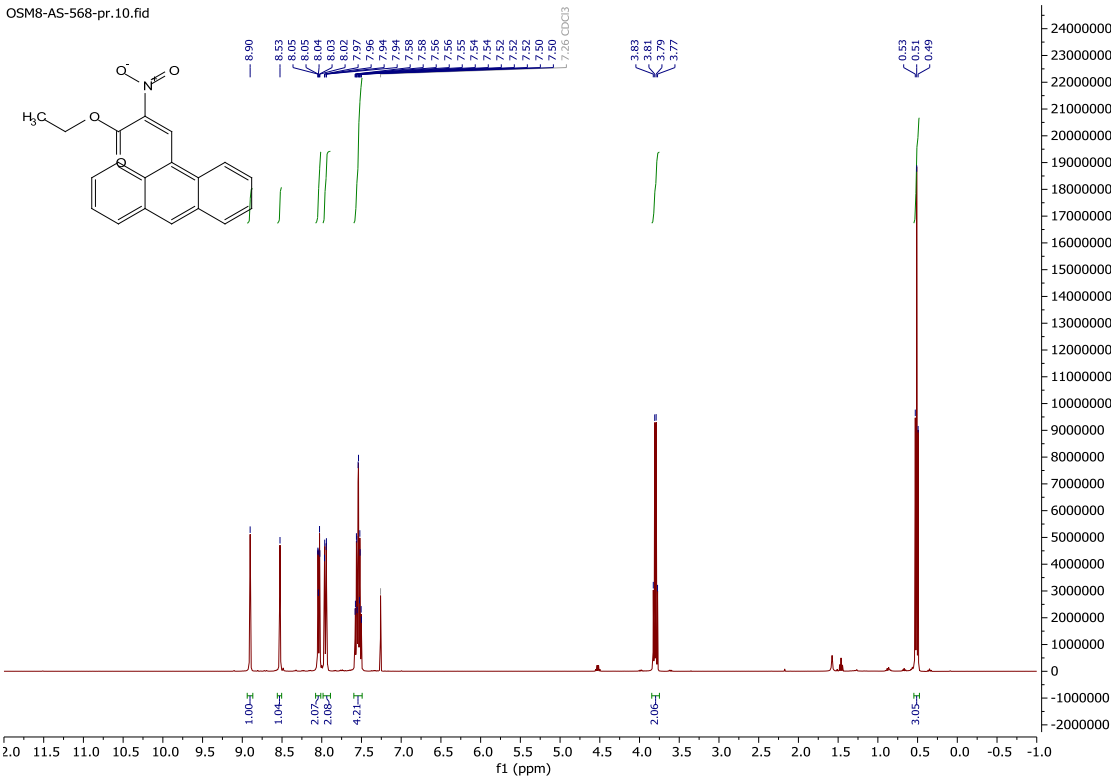
Compound (**1r**) ^{1}H-NMR spectra (400 MHz, $CDCl_3$)



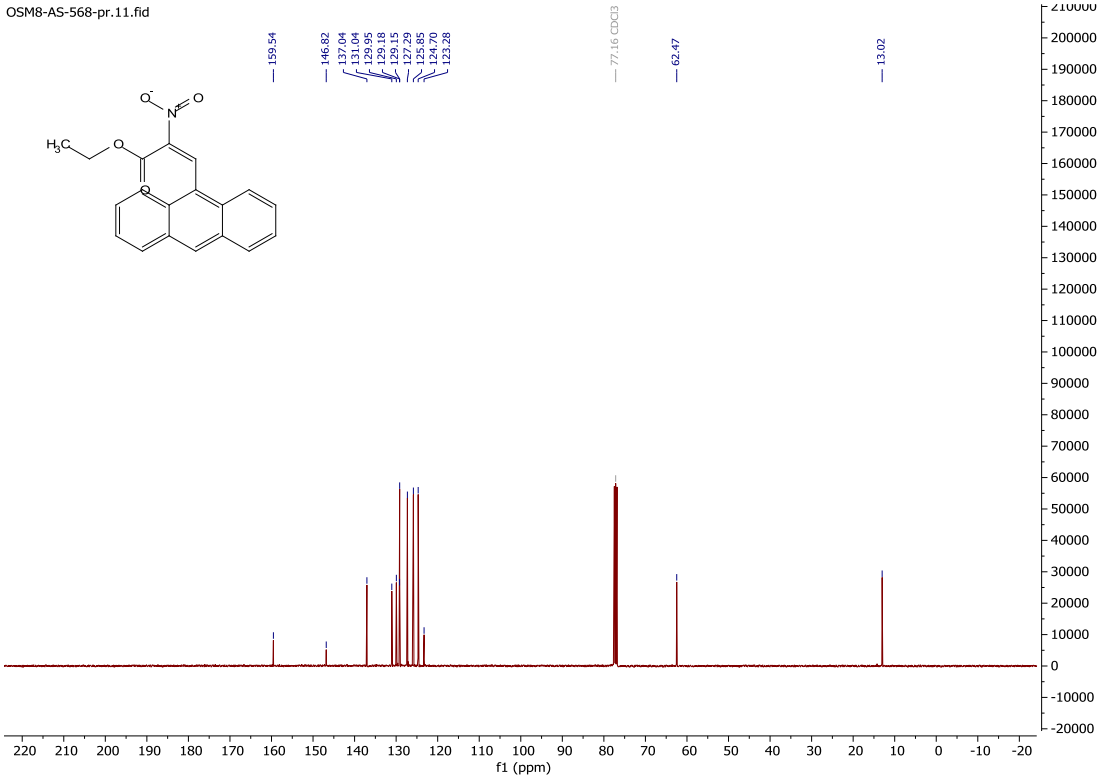
Compound (**1r**) ^{13}C-NMR spectra (101 MHz, $CDCl_3$)



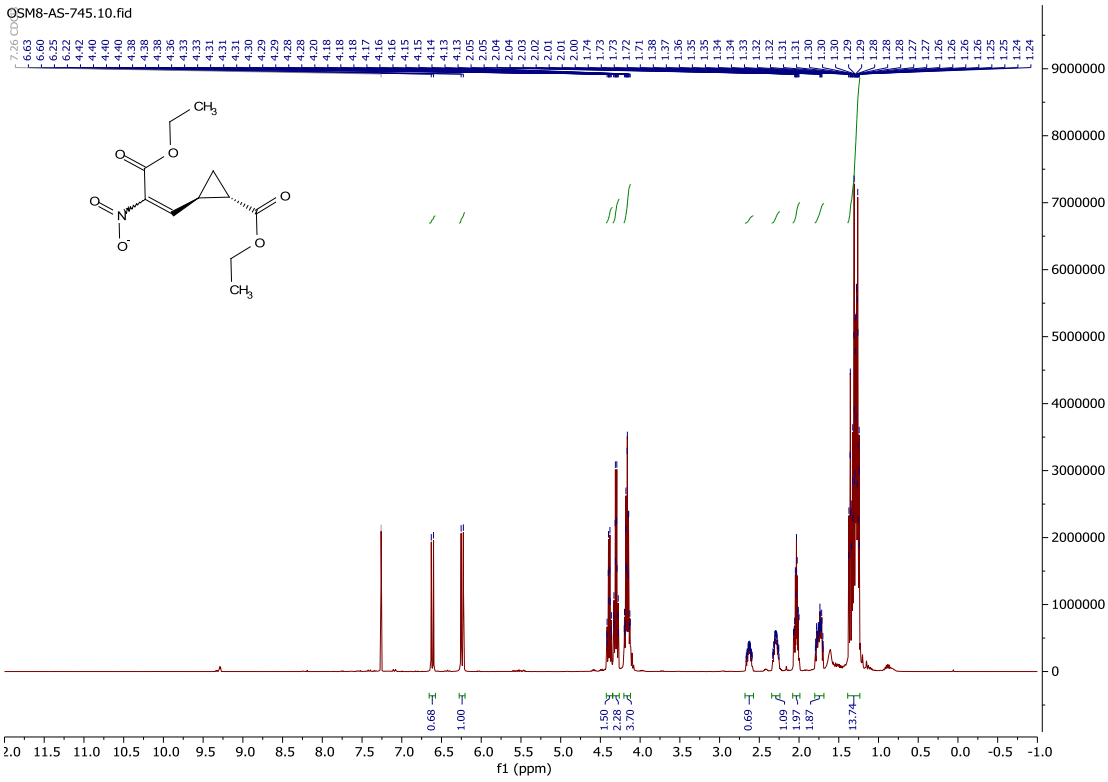
(**1s**) ^{1}H-NMR spectra (400 MHz, $CDCl_3$)



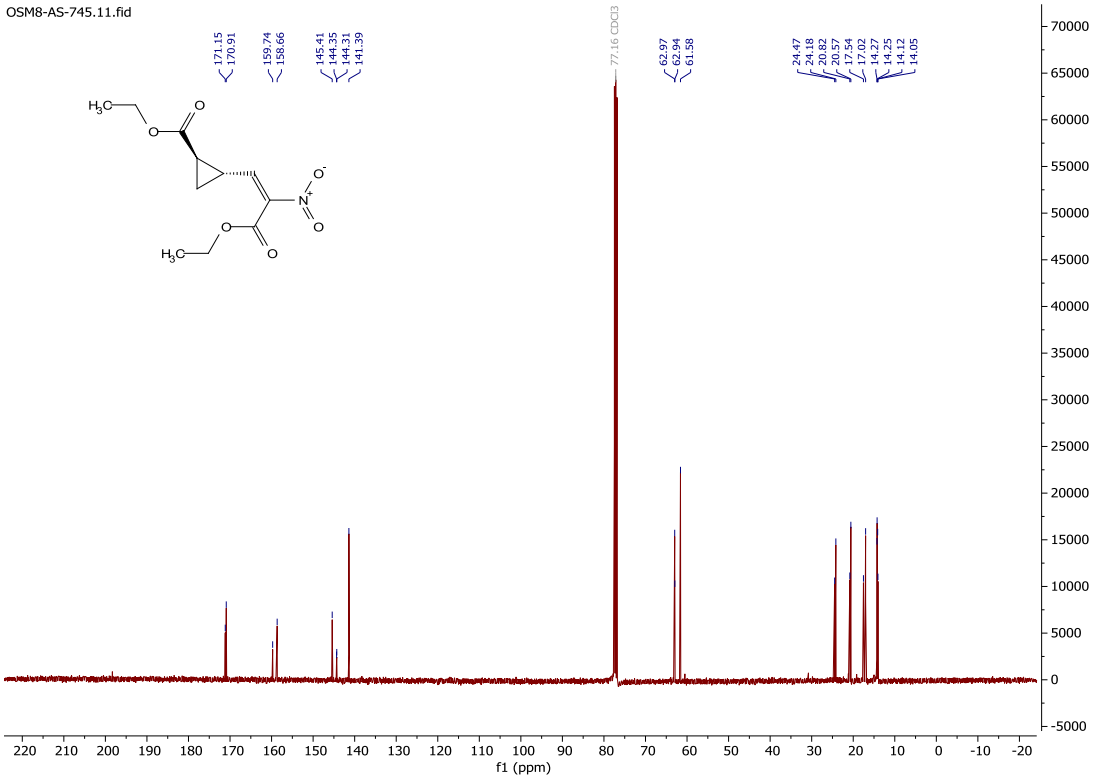
Compound (**1s**) ^{13}C-NMR spectra (101 MHz, $CDCl_3$)



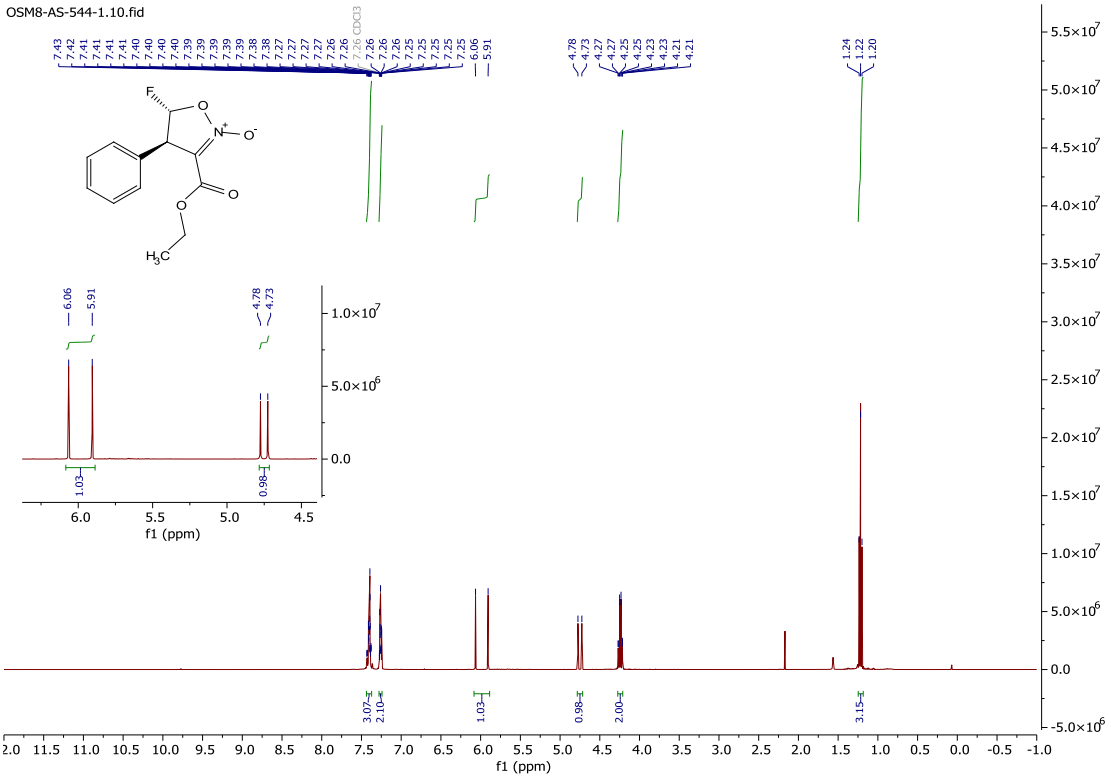
Compound (**1t**) ^{1}H-NMR spectra (400 MHz, $CDCl_3$)



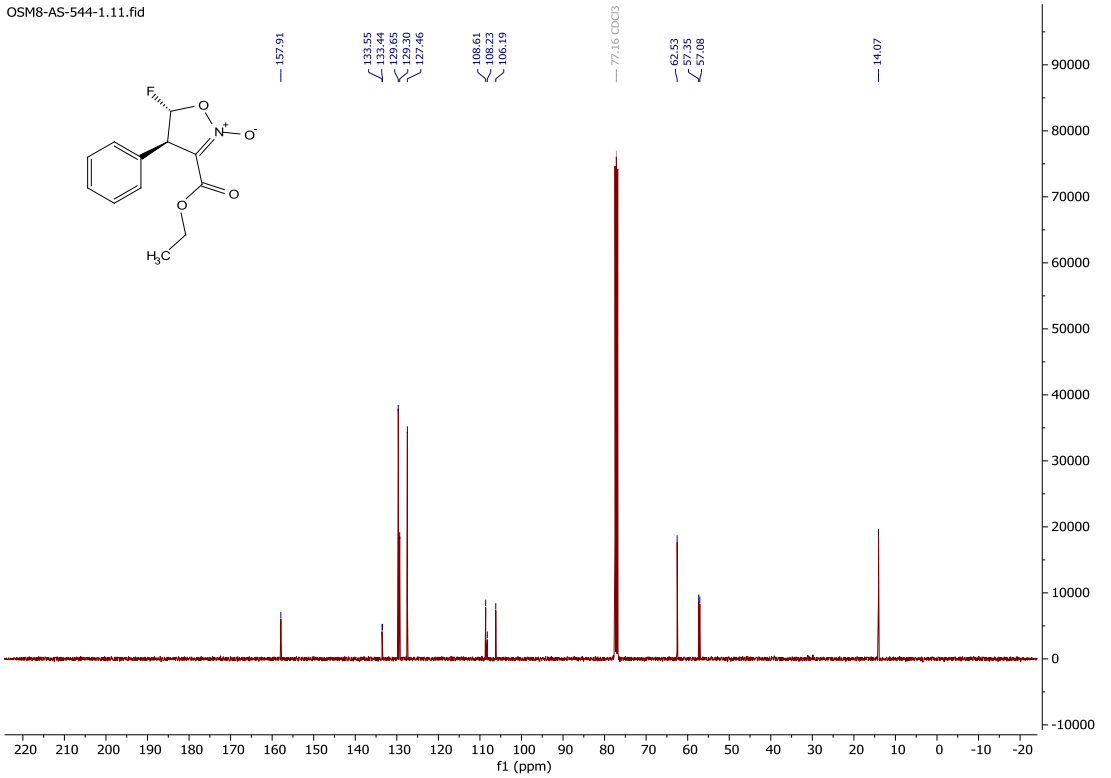
Compound (**1t**) ^{13}C-NMR spectra (101 MHz, $CDCl_3$)



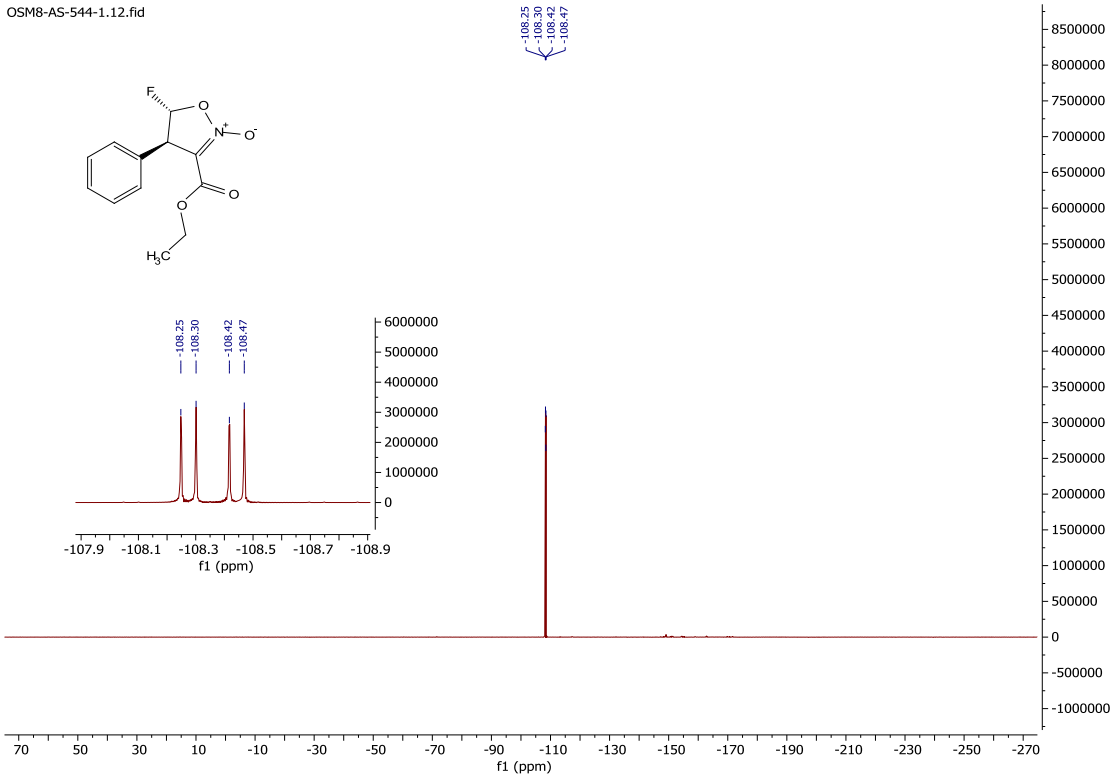
Compound (*trans*-**3a**) ^{1}H-NMR spectra (400 MHz, $CDCl_3$)



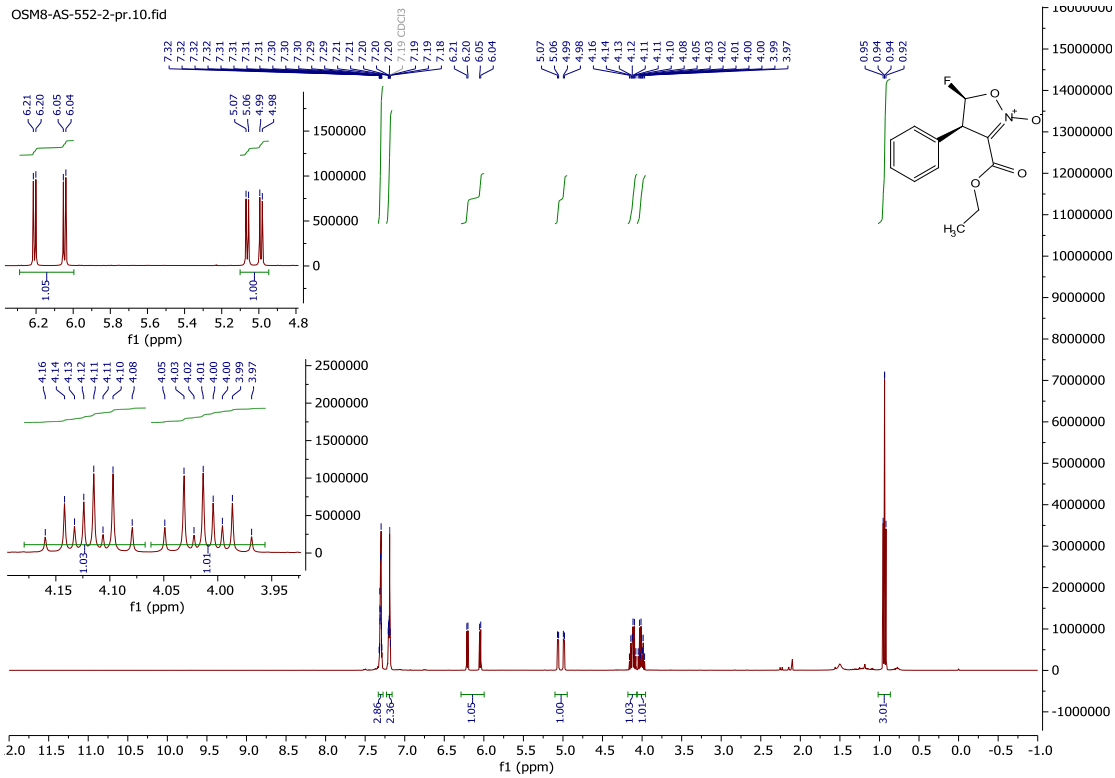
Compound (*trans*-**3a**) ^{13}C-NMR spectra (101 MHz, $CDCl_3$)



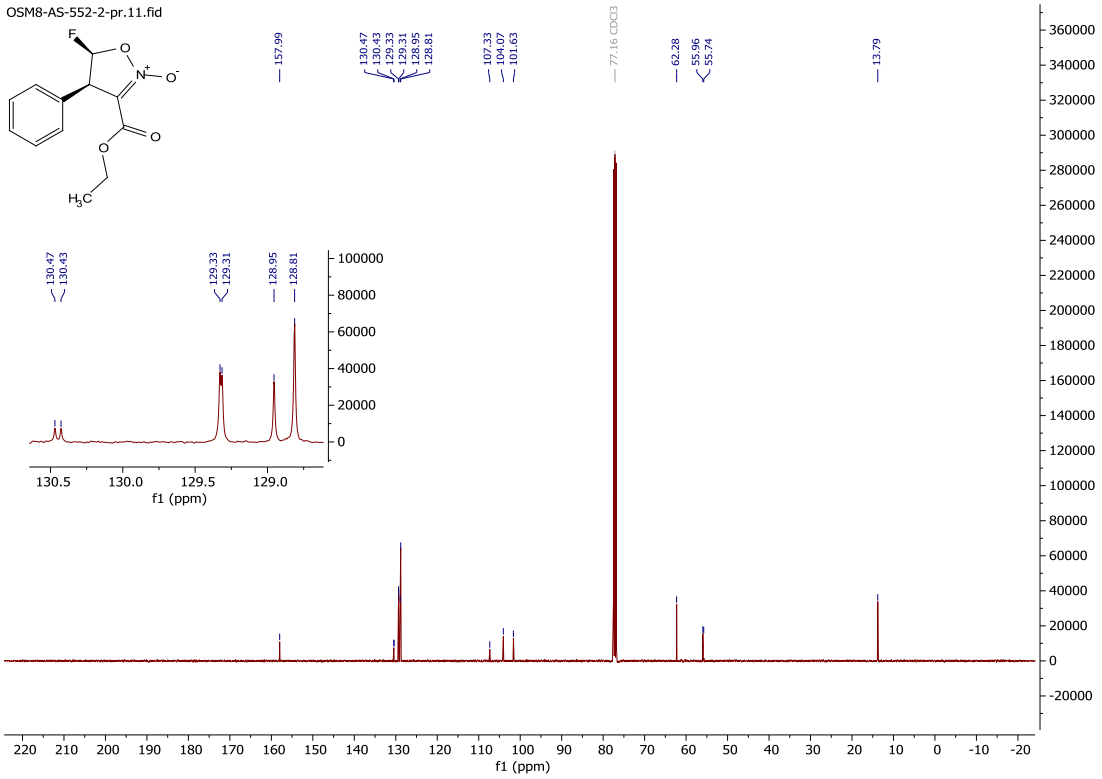
Compound (*trans*-**3a**)^{19}F-NMR spectra (376 MHz, $CDCl_3$)



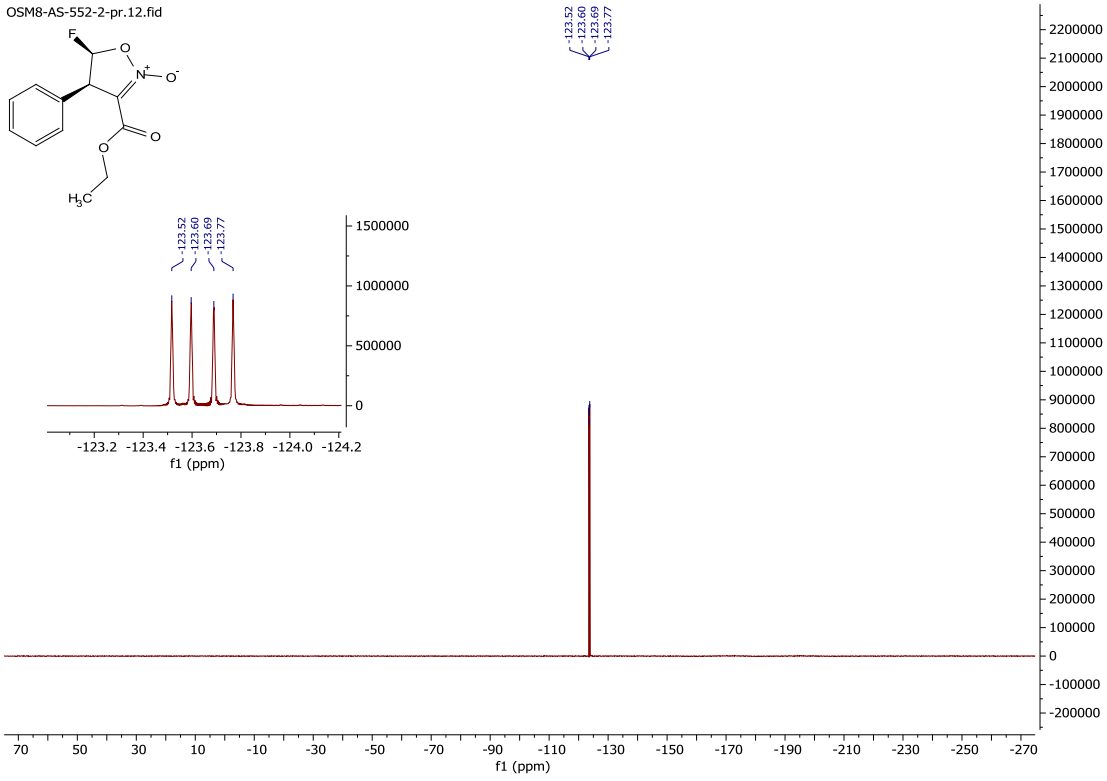
Compound (*cis*-**3a**) ^{1}H-NMR spectra (400 MHz, $CDCl_3$)



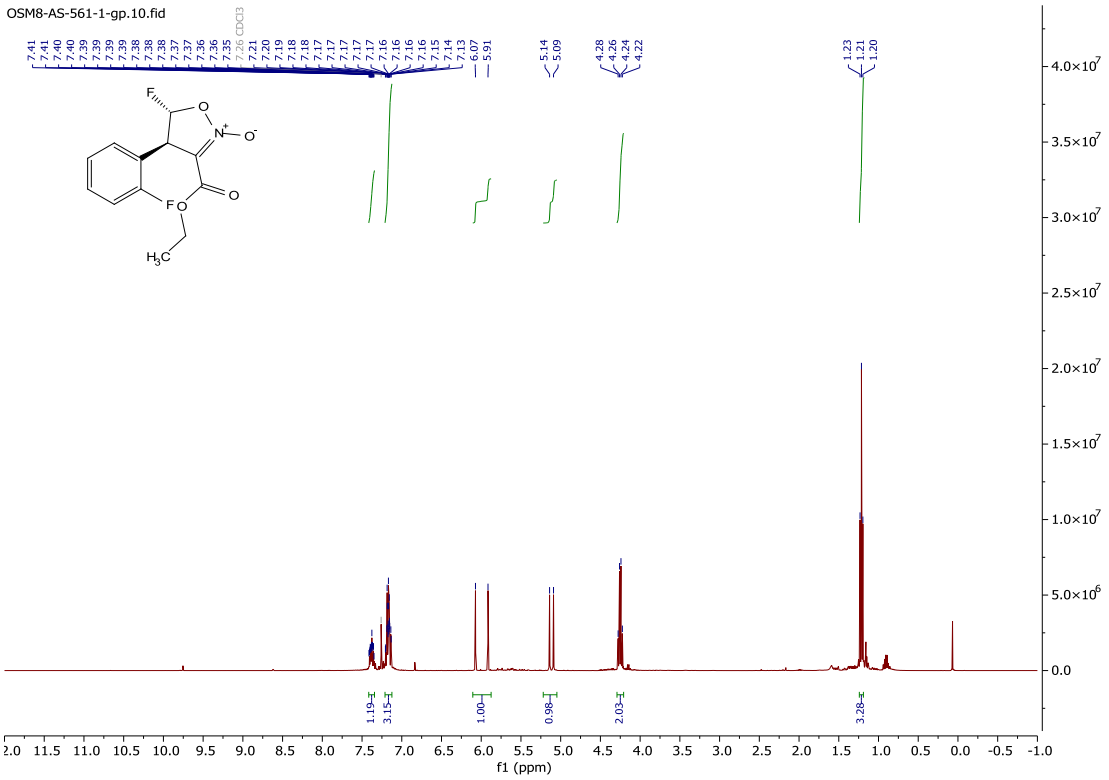
Compound (*cis*-**3a**) ^{13}C-NMR spectra (101 MHz, $CDCl_3$)



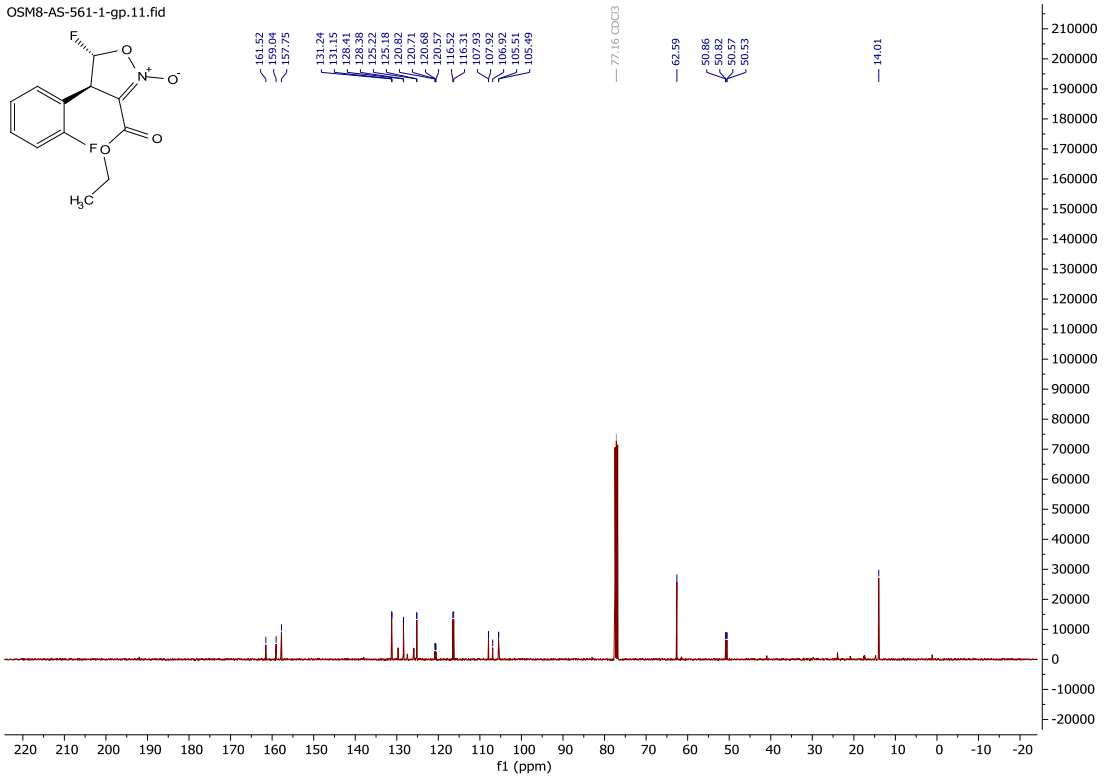
Compound (*cis*-**3a**)^{19}F-NMR spectra (376 MHz, $CDCl_3$)



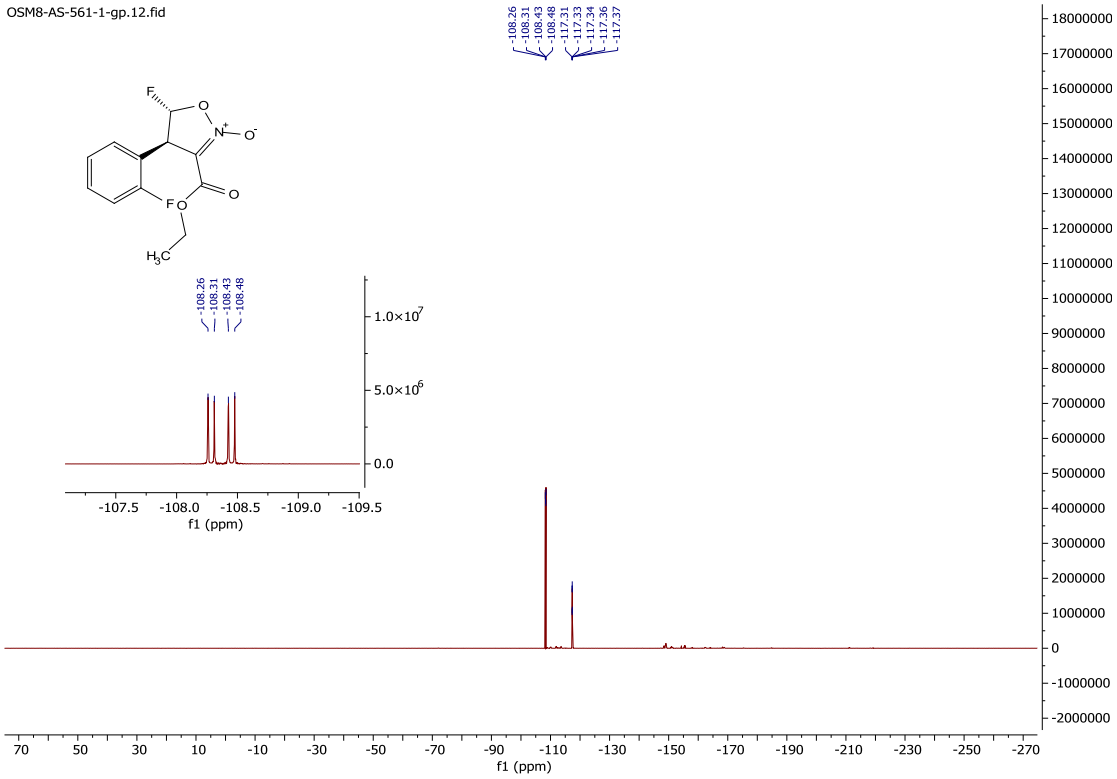
Compound (*trans*-**3b**) ^{1}H-NMR spectra (400 MHz, $CDCl_3$)



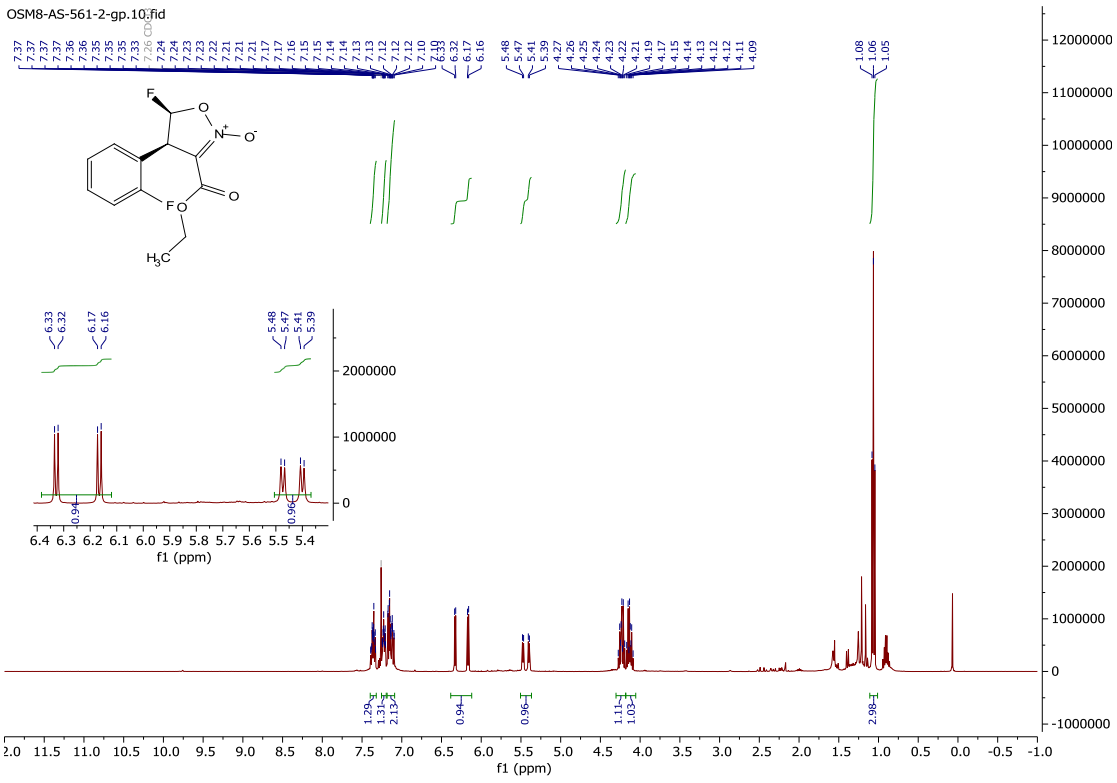
Compound (*trans*-**3b**) ^{13}C-NMR spectra (101 MHz, $CDCl_3$)



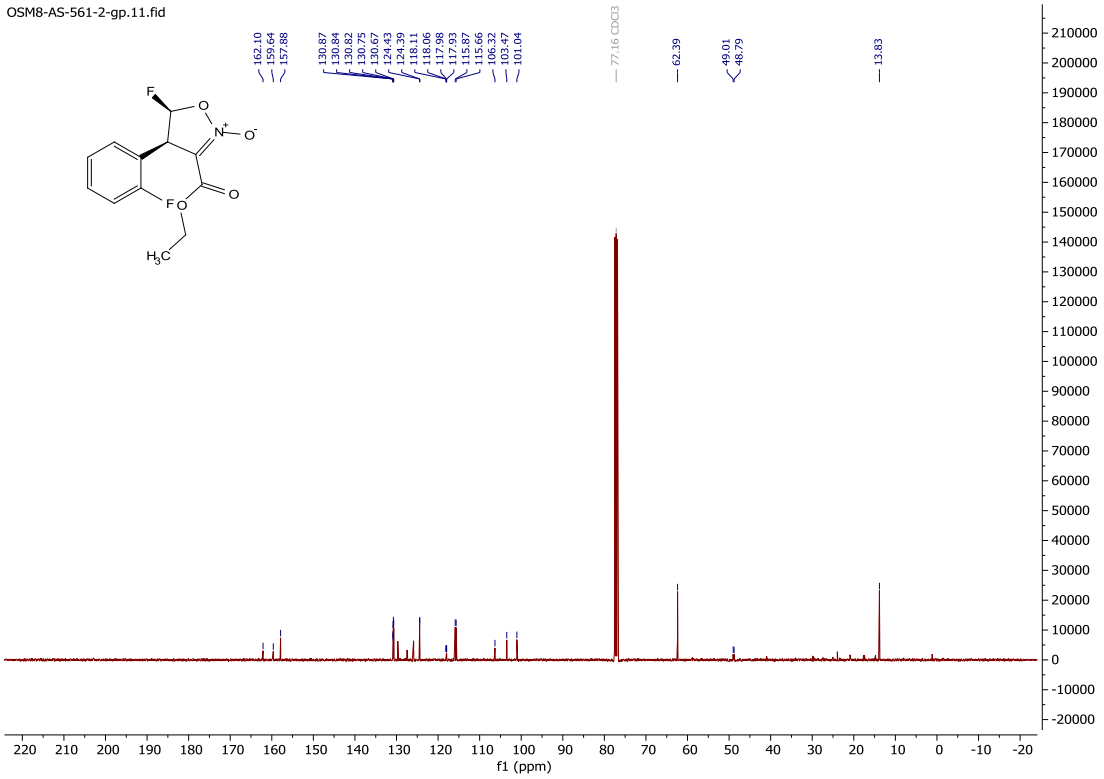
Compound (*trans*-**3b**)^{19}F-NMR spectra (376 MHz, $CDCl_3$)



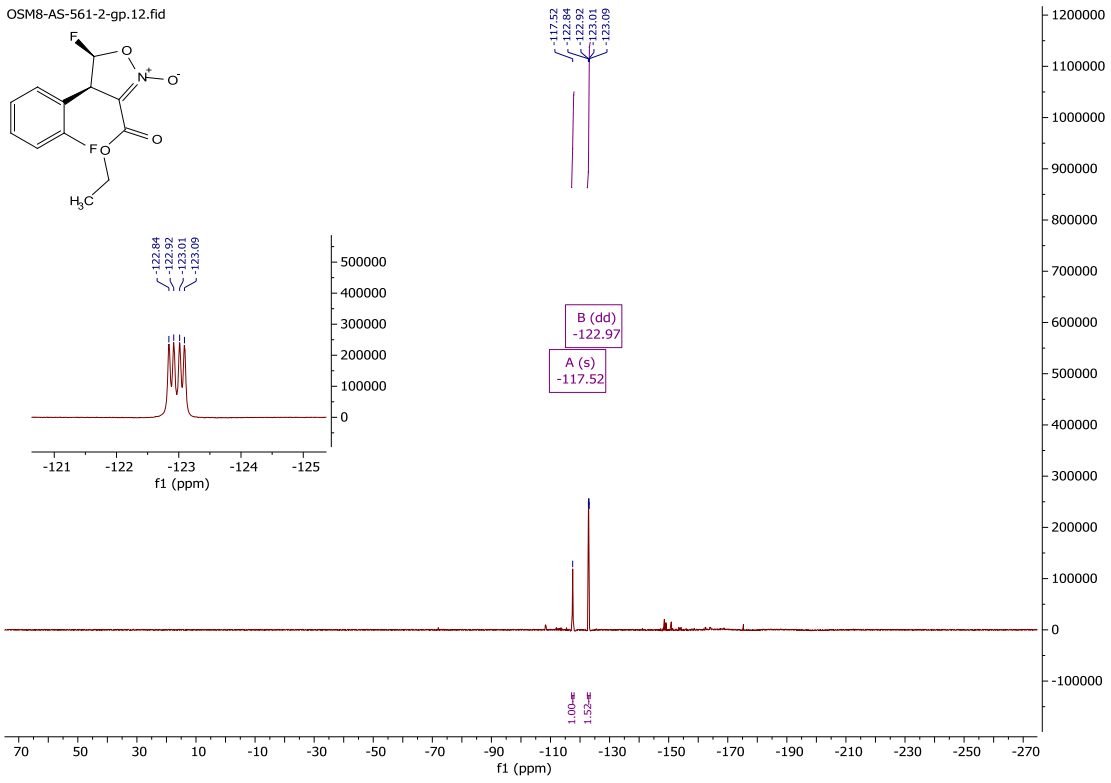
Compound (*cis*-**3b**) ^{1}H-NMR spectra (400 MHz, $CDCl_3$)



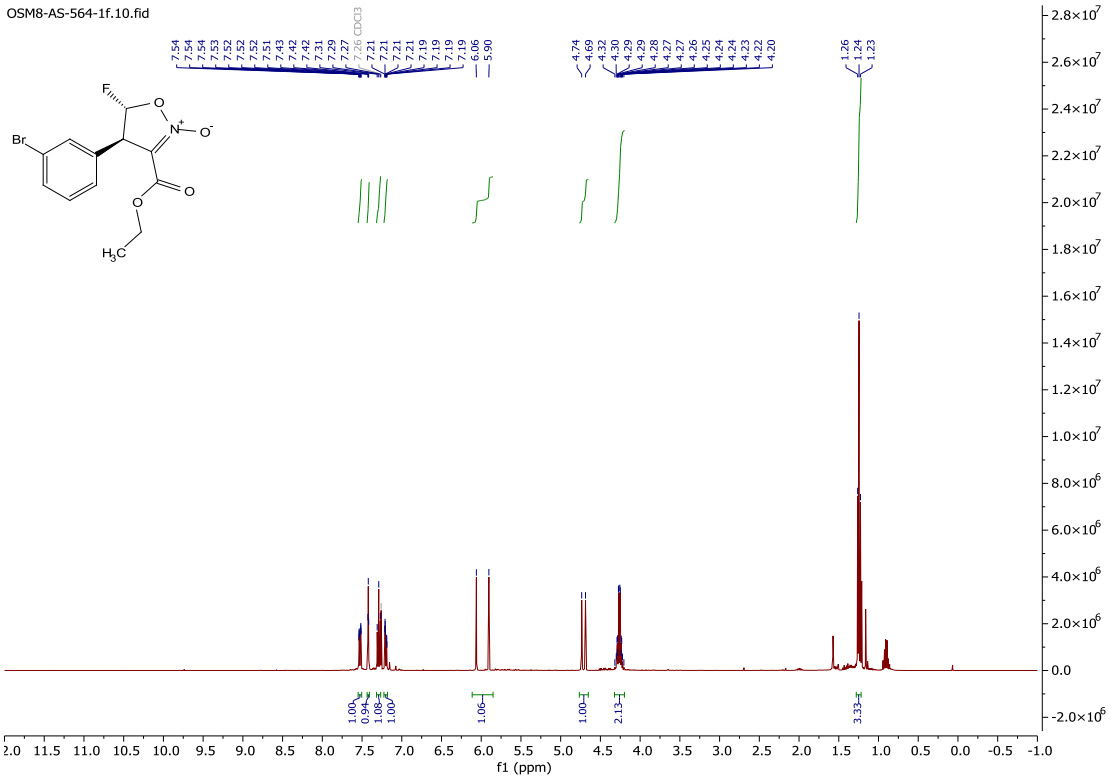
Compound (*cis*-**3b**) ^{13}C-NMR spectra (101 MHz, $CDCl_3$)



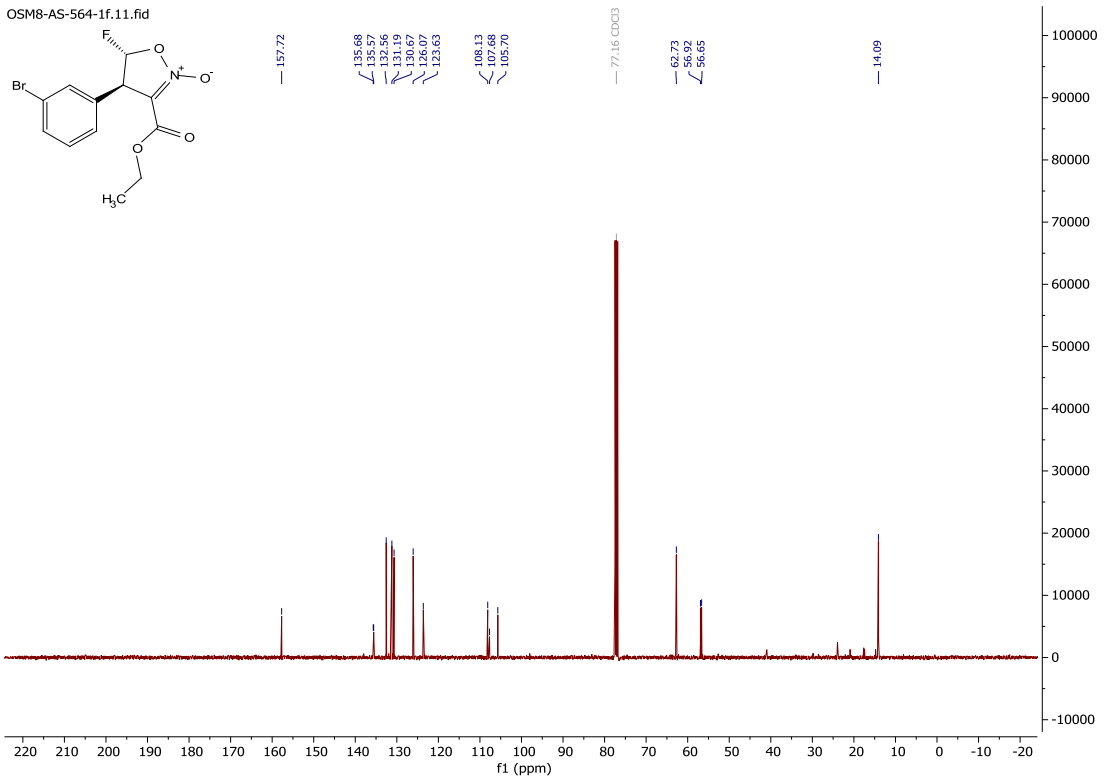
Compound (*cis*-**3b**)^{19}F-NMR spectra (376 MHz, $CDCl_3$)



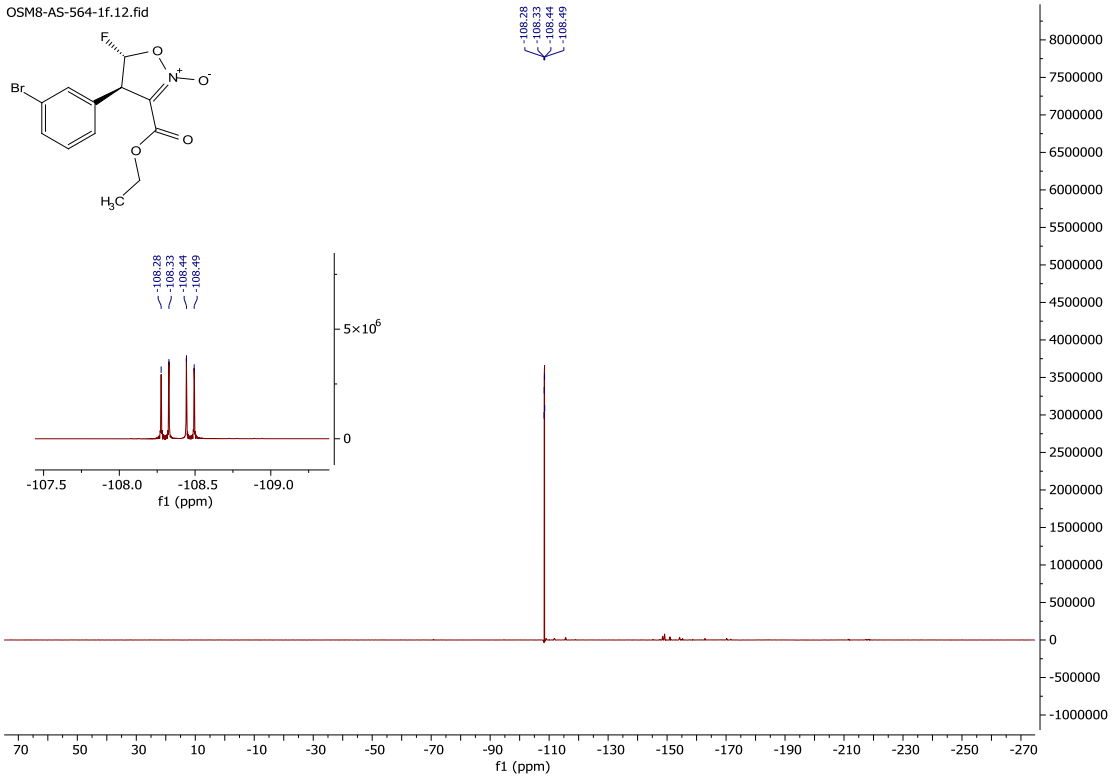
Compound (*trans*-**3c**) ^{1}H-NMR spectra (400 MHz, $CDCl_3$)



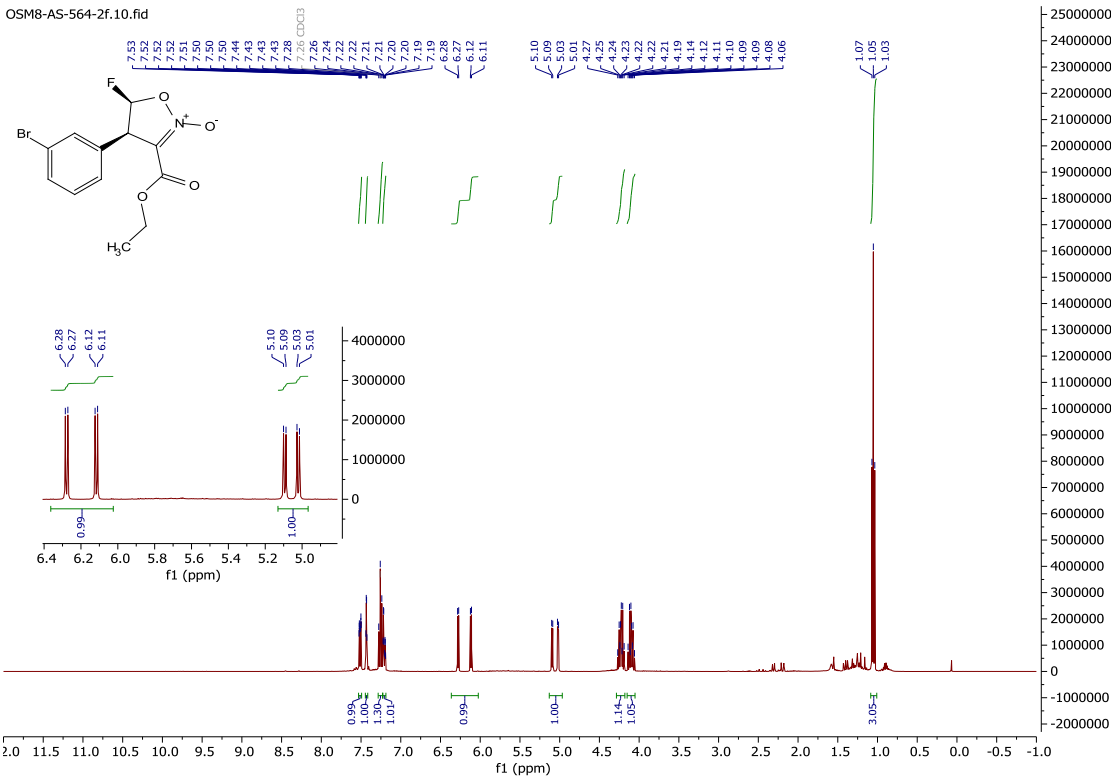
Compound (*trans*-**3c**) ^{13}C-NMR spectra (101 MHz, $CDCl_3$)



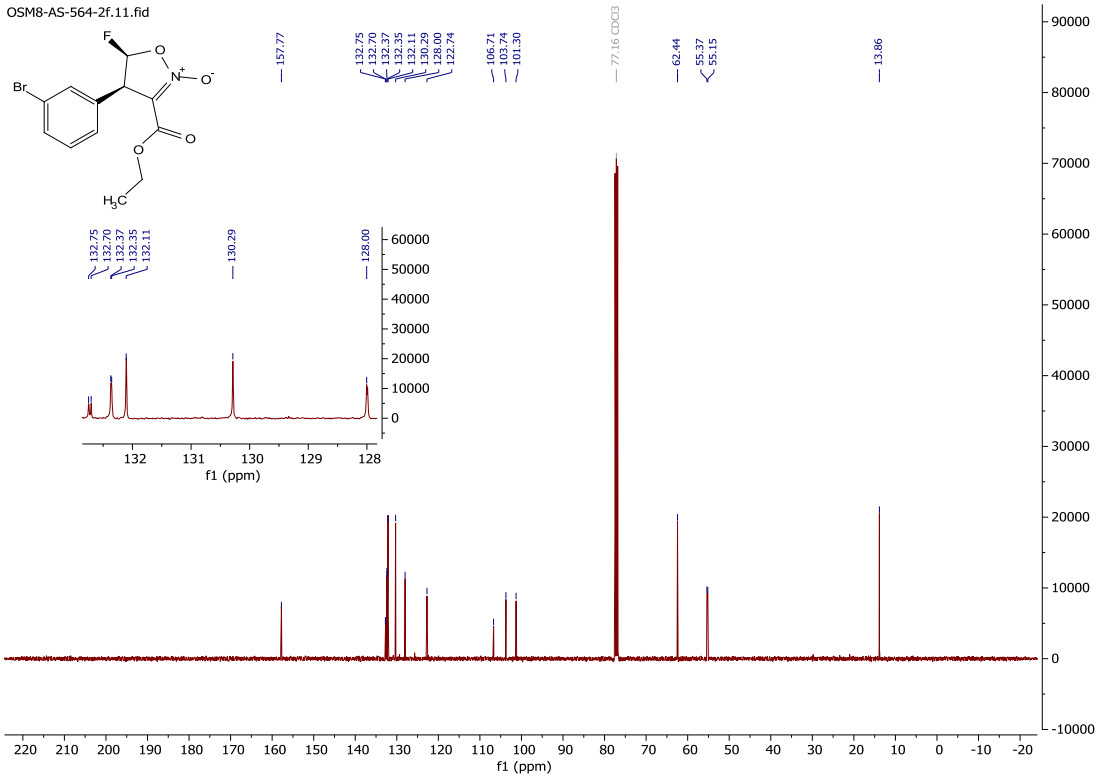
Compound (*trans*-**3c**) ^{19}F-NMR spectra (376 MHz, $CDCl_3$)



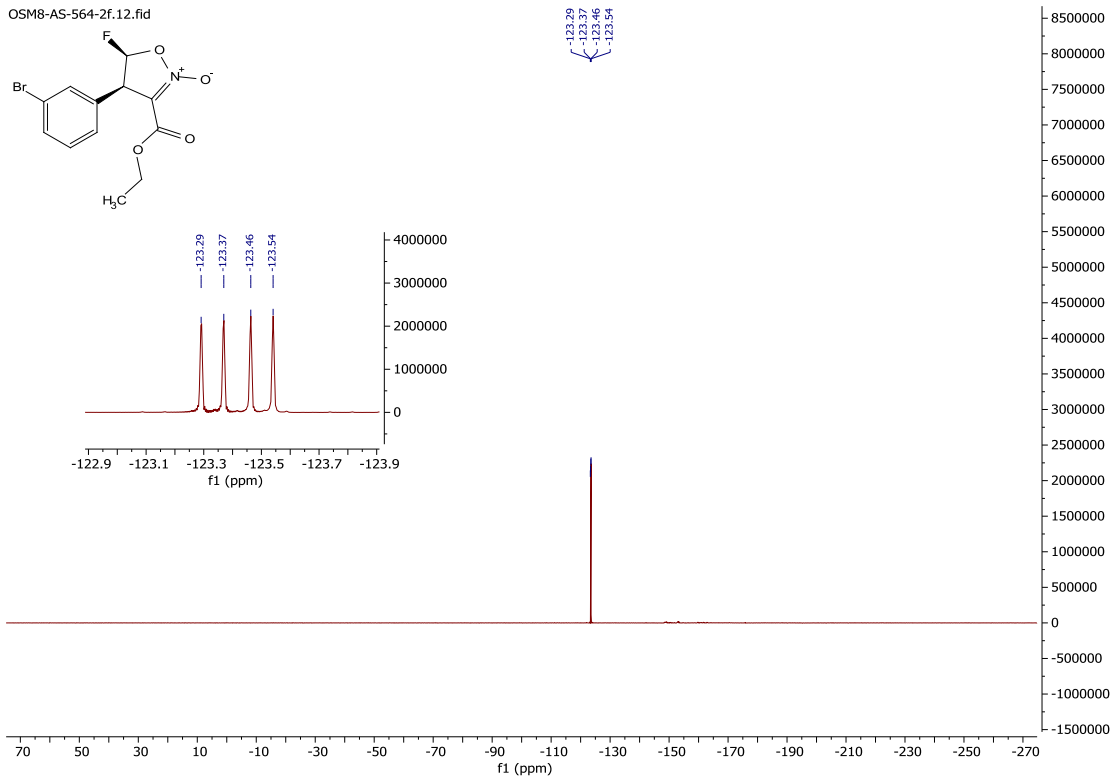
Compound (*cis*-**3c**) ^{1}H-NMR spectra (400 MHz, $CDCl_3$)



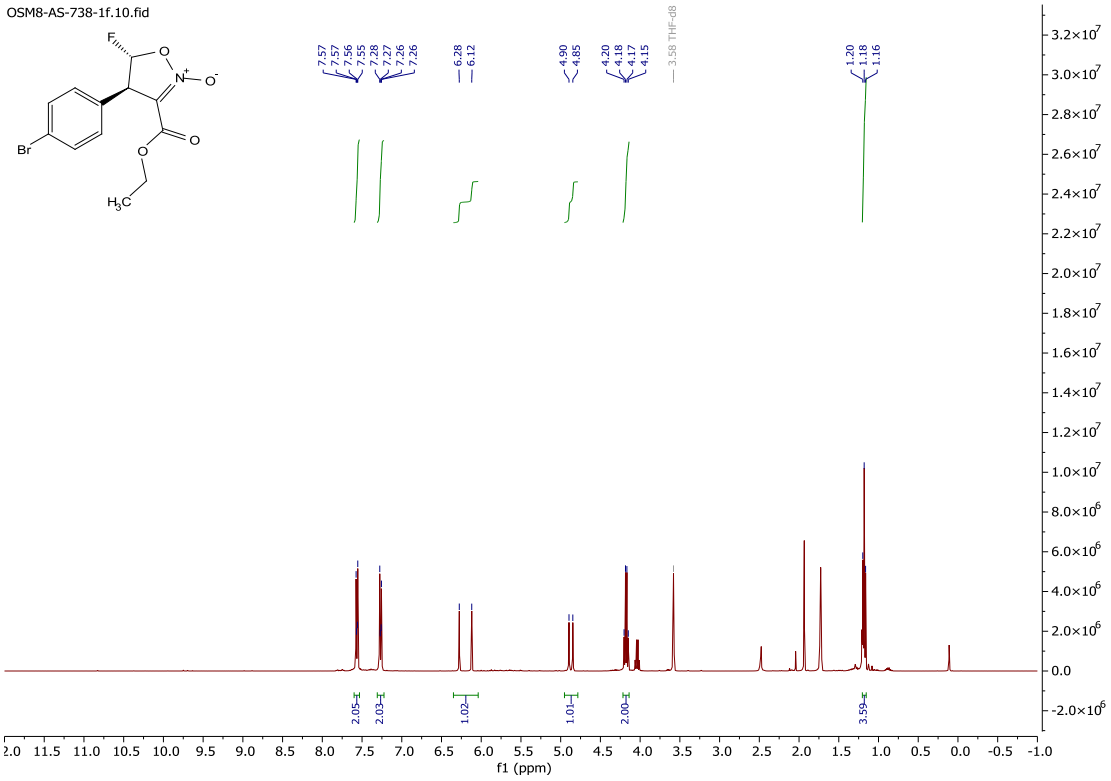
Compound (*cis*-**3c**) ^{13}C-NMR spectra (101 MHz, $CDCl_3$)



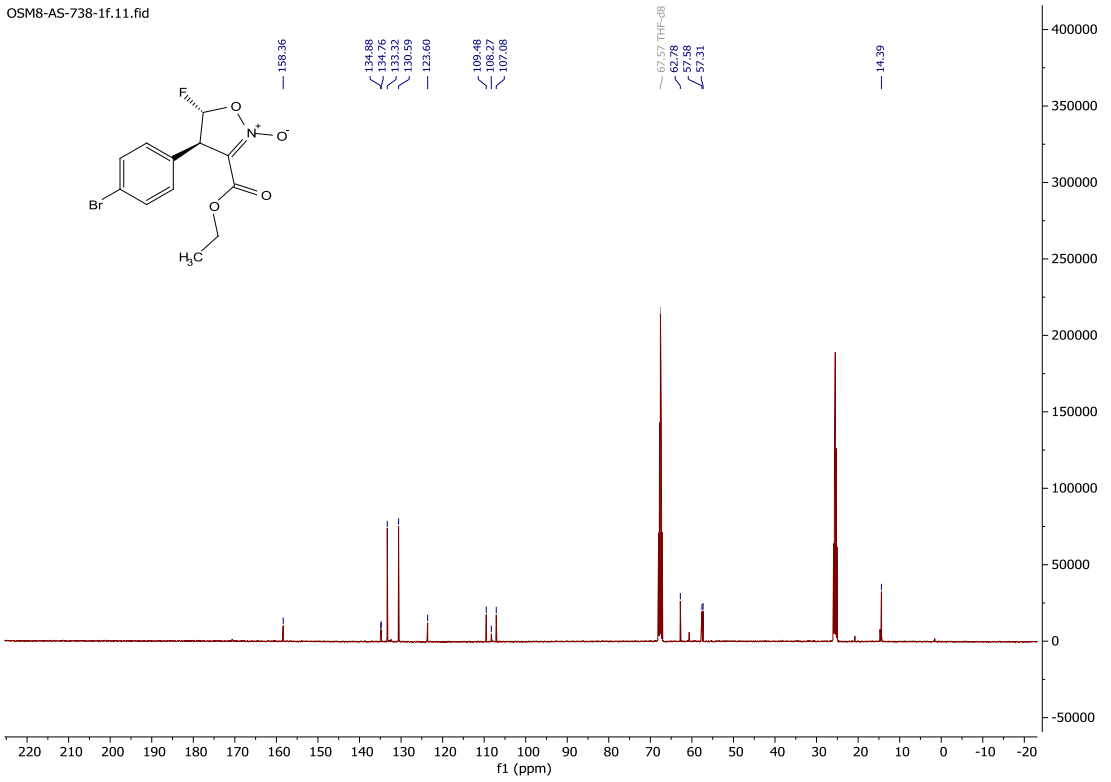
Compound (*cis*-**3c**)^{19}F-NMR spectra (376 MHz, $CDCl_3$)



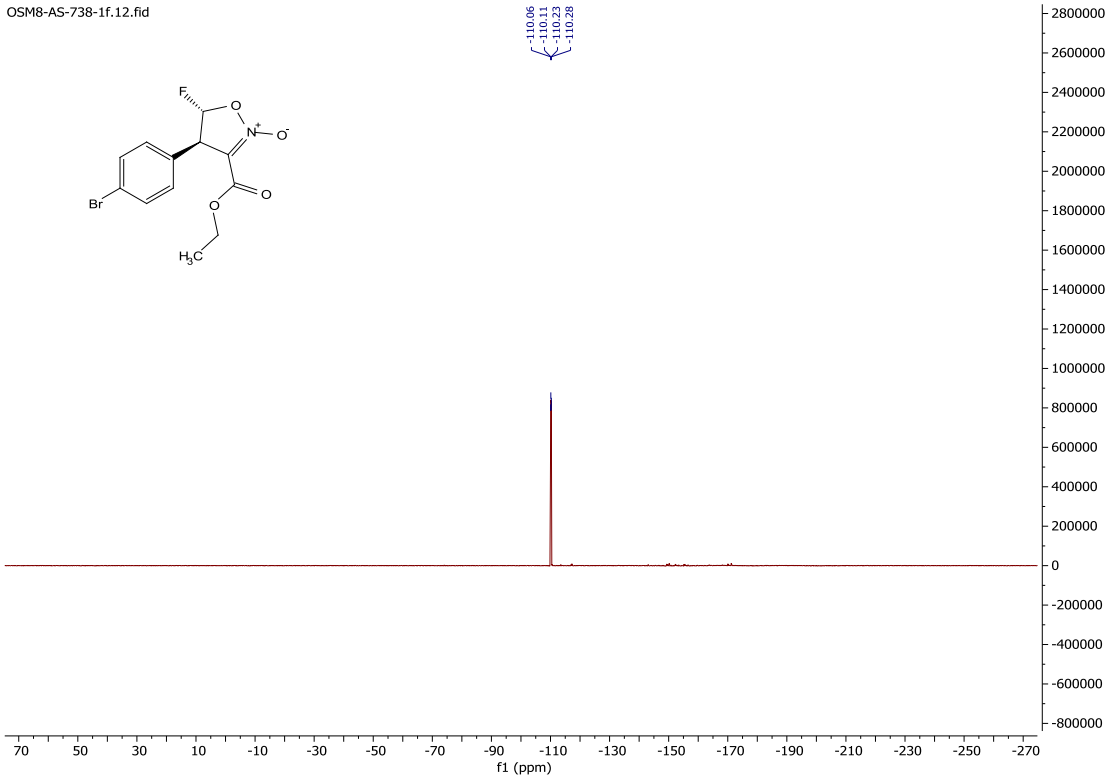
Compound (*trans*-**3d**) ^{1}H-NMR spectra (400 MHz, THF-d8)



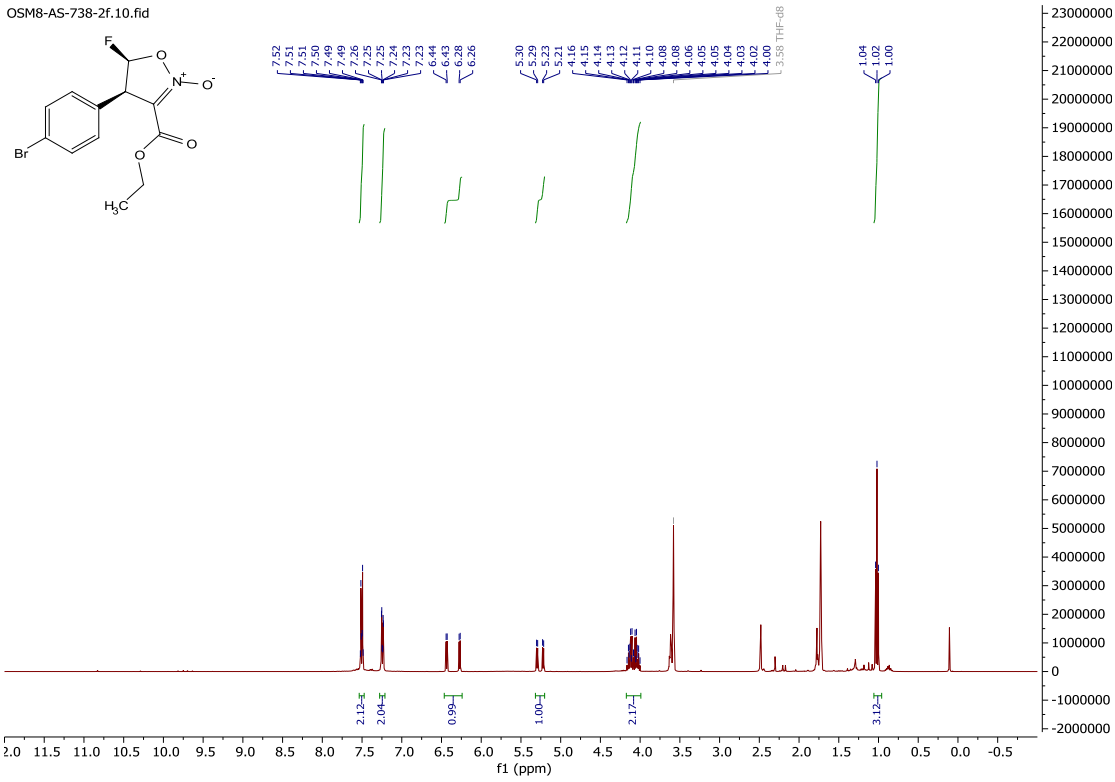
Compound (*trans*-**3d**) ^{13}C-NMR spectra (101 MHz, THF-d8)



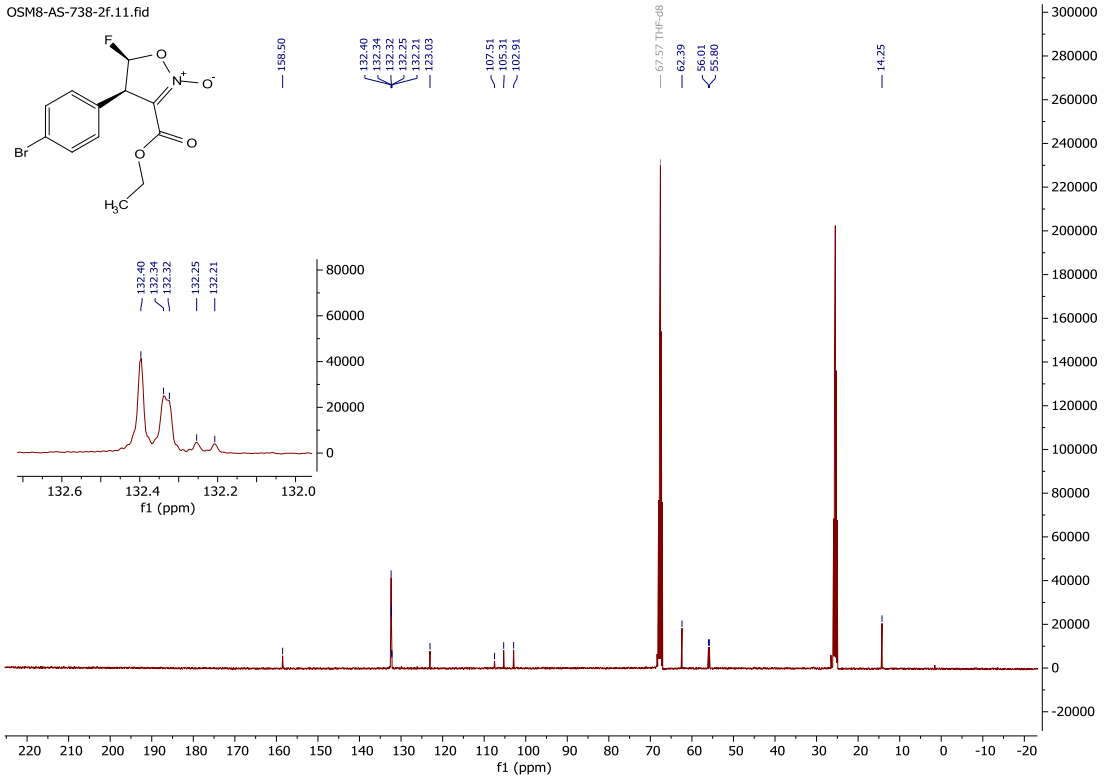
Compound (*trans*-**3d**)^{19}F-NMR spectra (376 MHz, THF-d8)



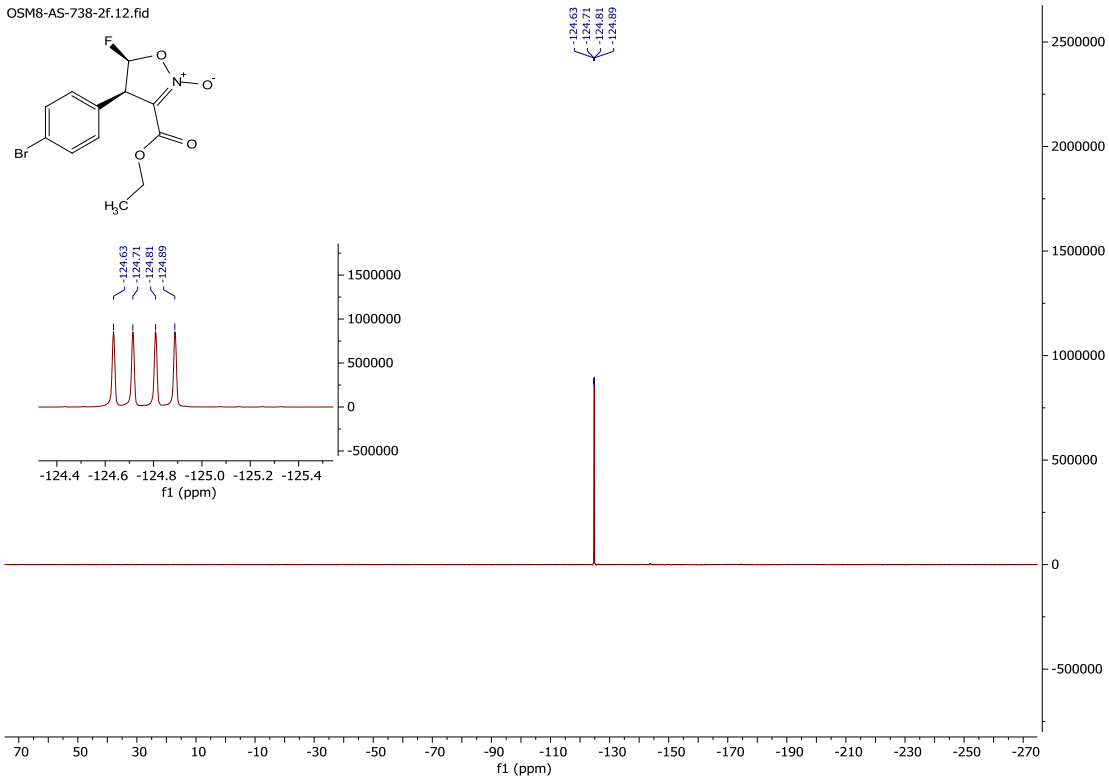
Compound (*cis*-**3d**) ^{1}H-NMR spectra (400 MHz, THF-d8)



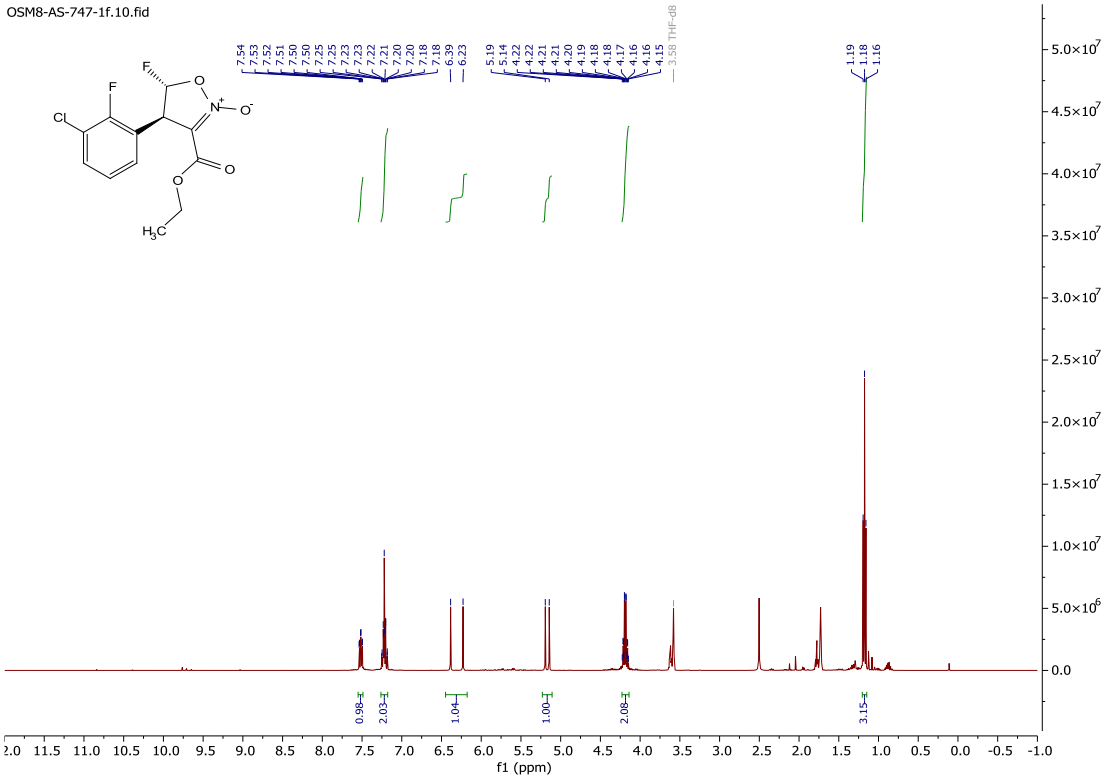
Compound (*cis*-**3d**) ^{13}C-NMR spectra (101 MHz, THF-d8)



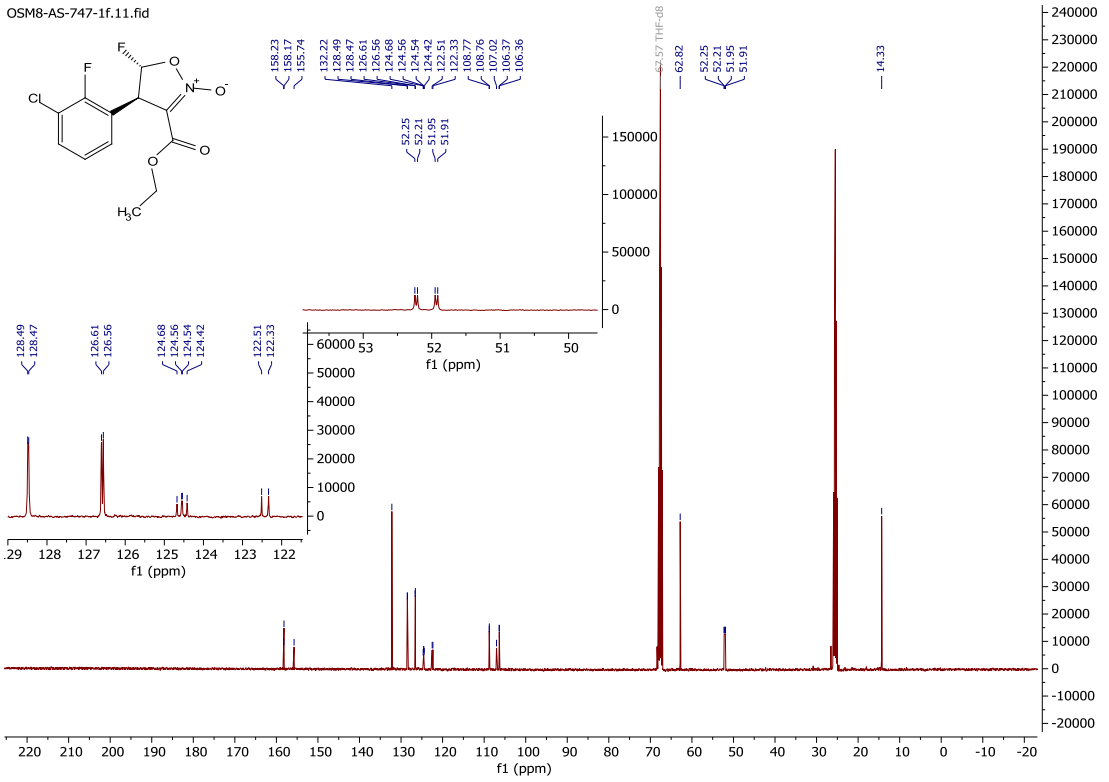
Compound (*cis*-**3d**)^{19}F-NMR spectra (376 MHz, THF-d8)



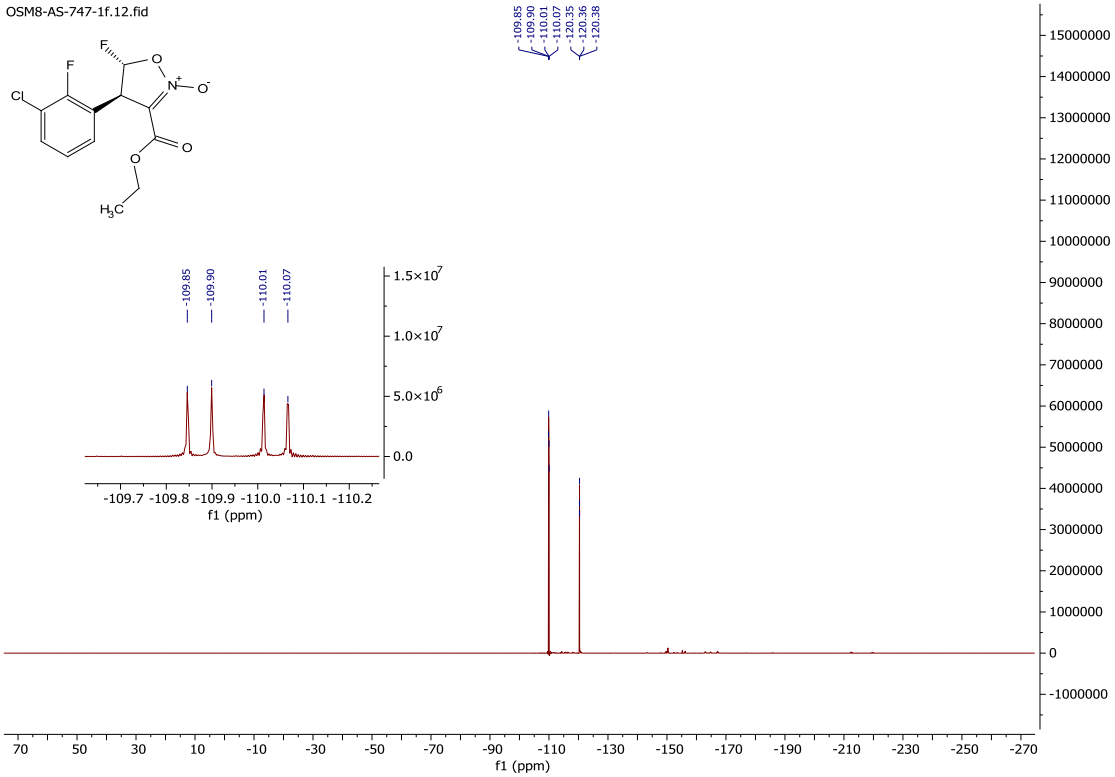
Compound (*trans*-**3e**) ^{1}H-NMR spectra (400 MHz, THF-d8)



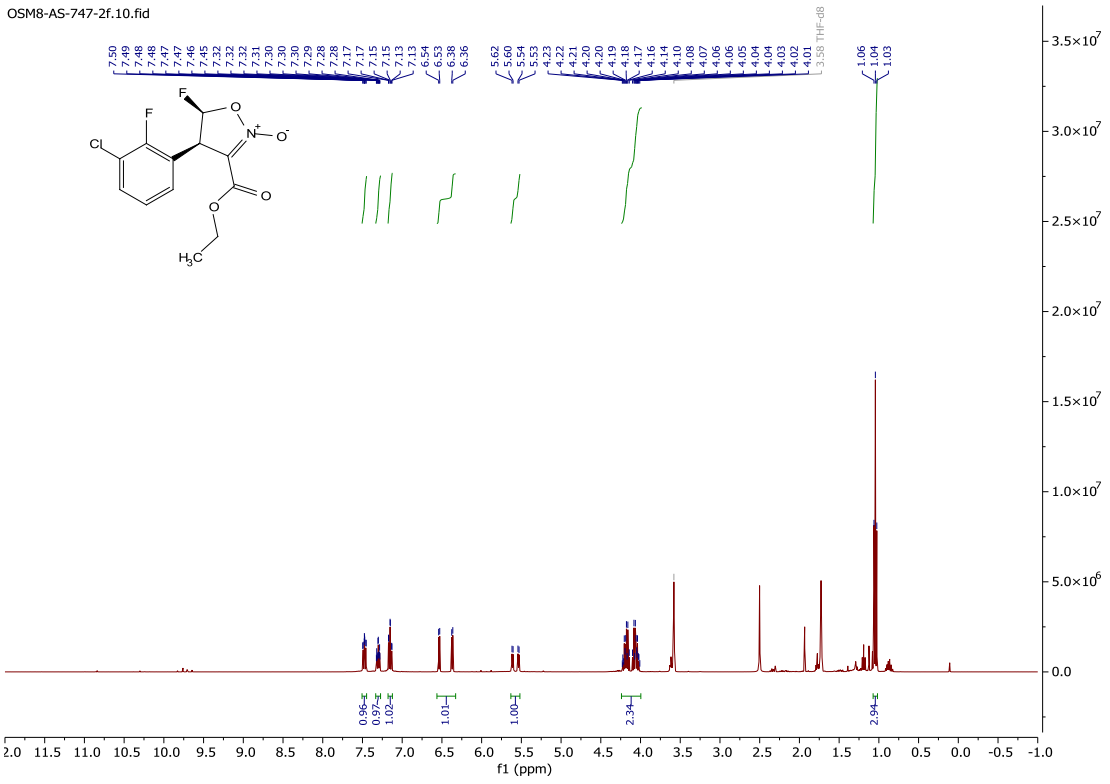
Compound (*trans*-**3e**) ^{13}C-NMR spectra (101 MHz, THF-d8)



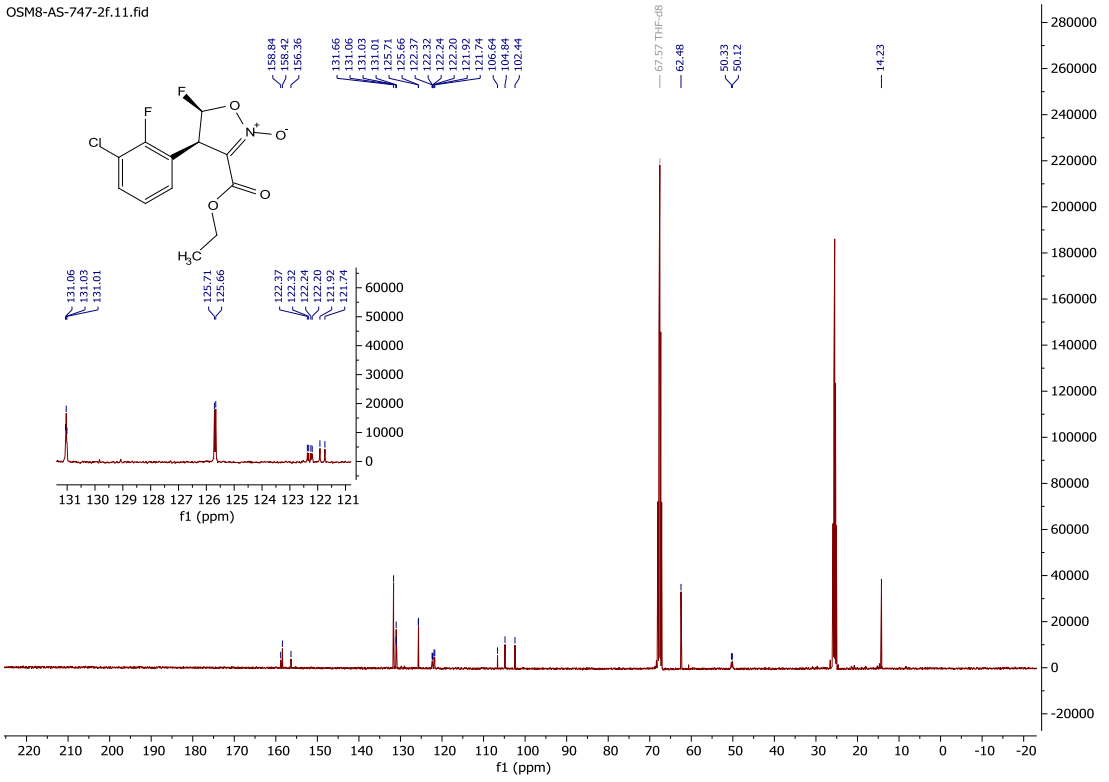
Compound (*trans*-**3e**)^{19}F-NMR spectra (376 MHz, THF-d8)



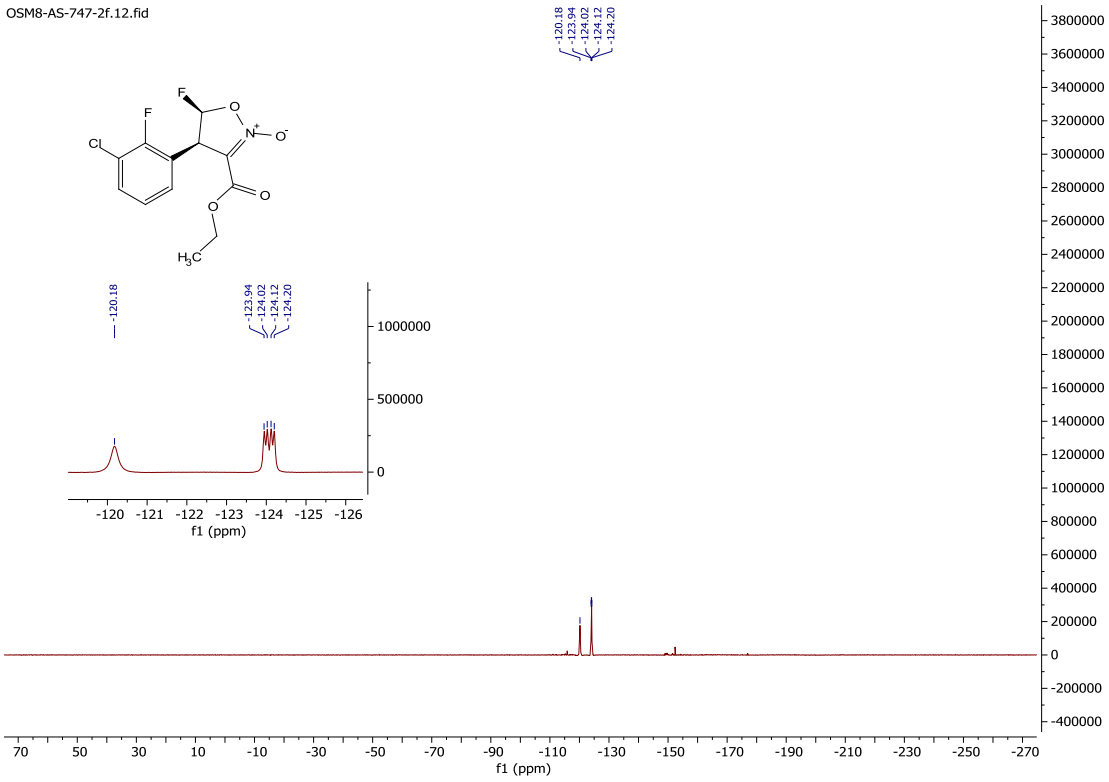
Compound (*cis*-**3e**) ^{1}H-NMR spectra (400 MHz, THF-d8)



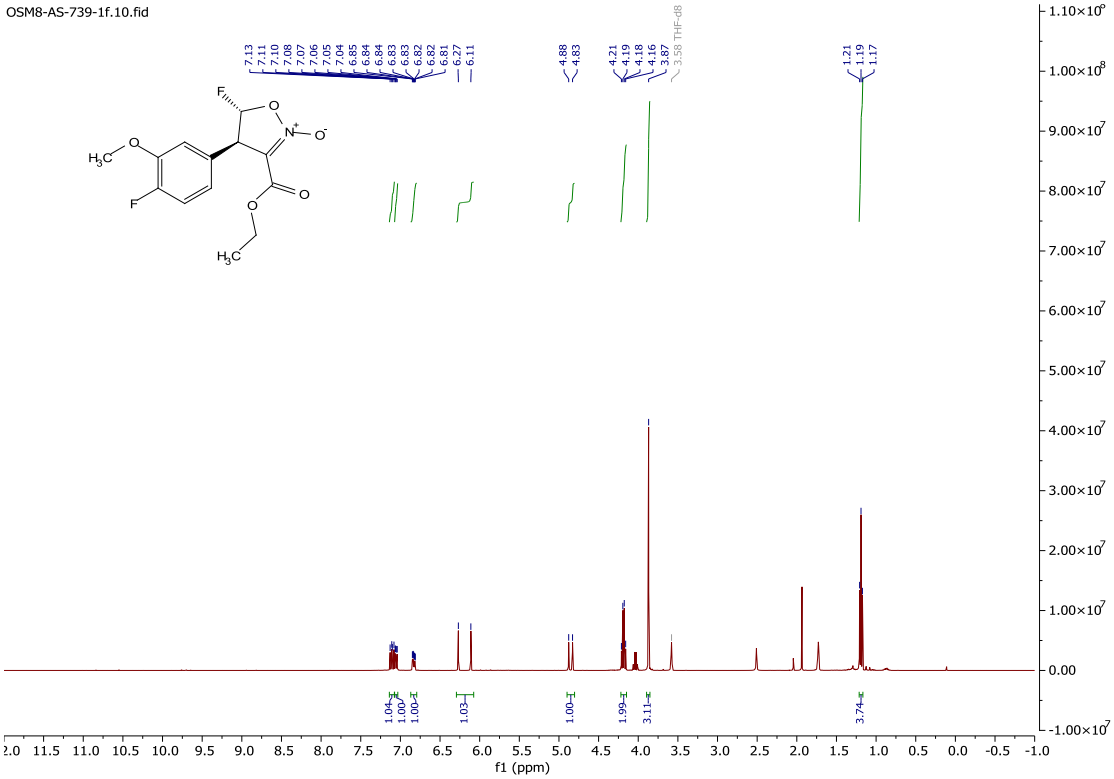
Compound (*cis*-**3e**) ^{13}C-NMR spectra (101 MHz, THF-d8)



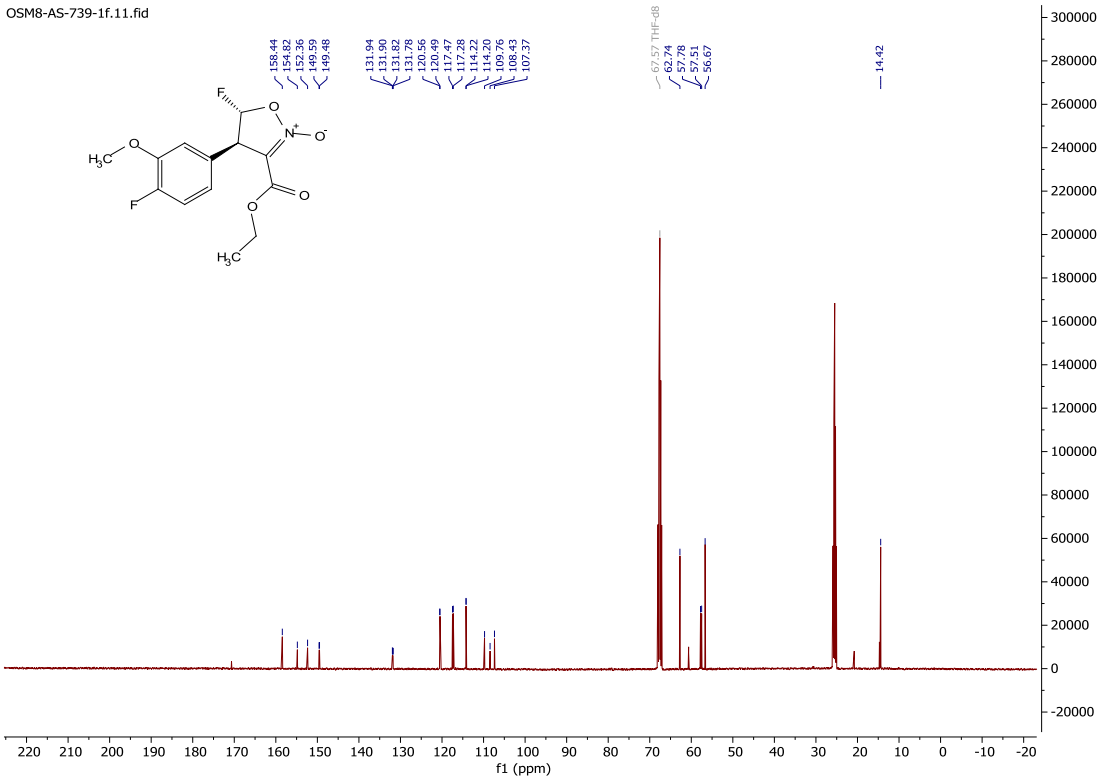
Compound (*cis*-**3e**)^{19}F-NMR spectra (376 MHz, THF-d8)



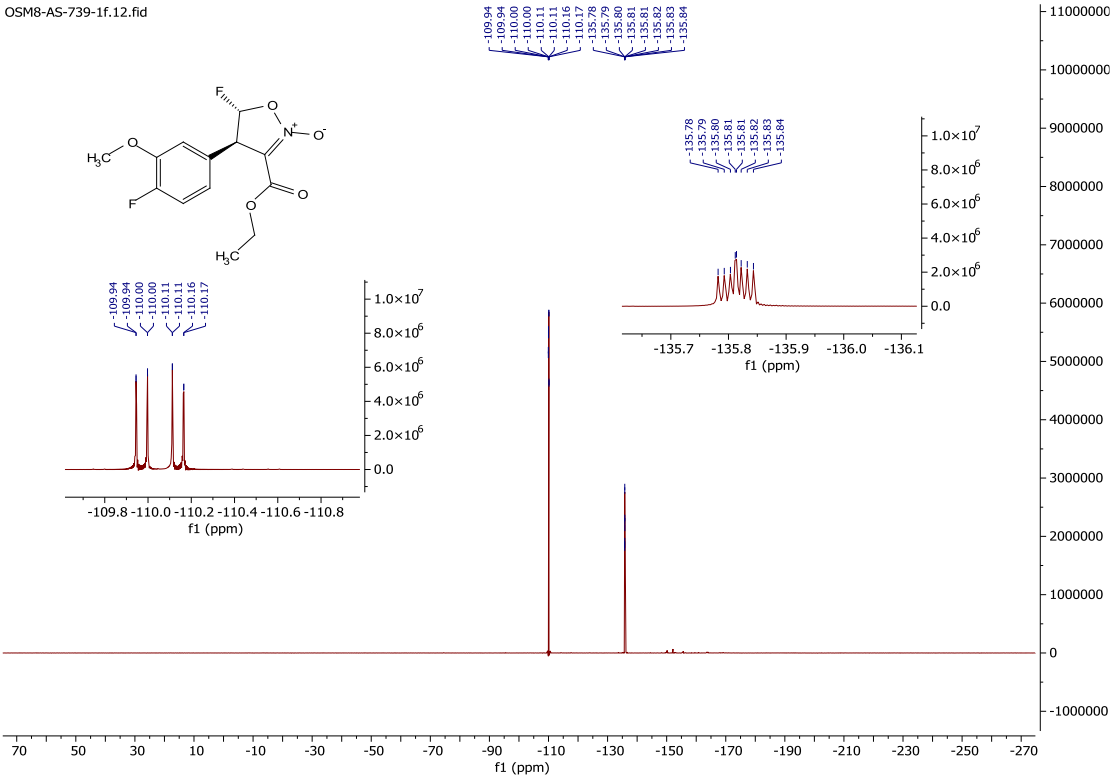
Compound (*trans*-**3f**) ^{1}H-NMR spectra (400 MHz, THF-d8)



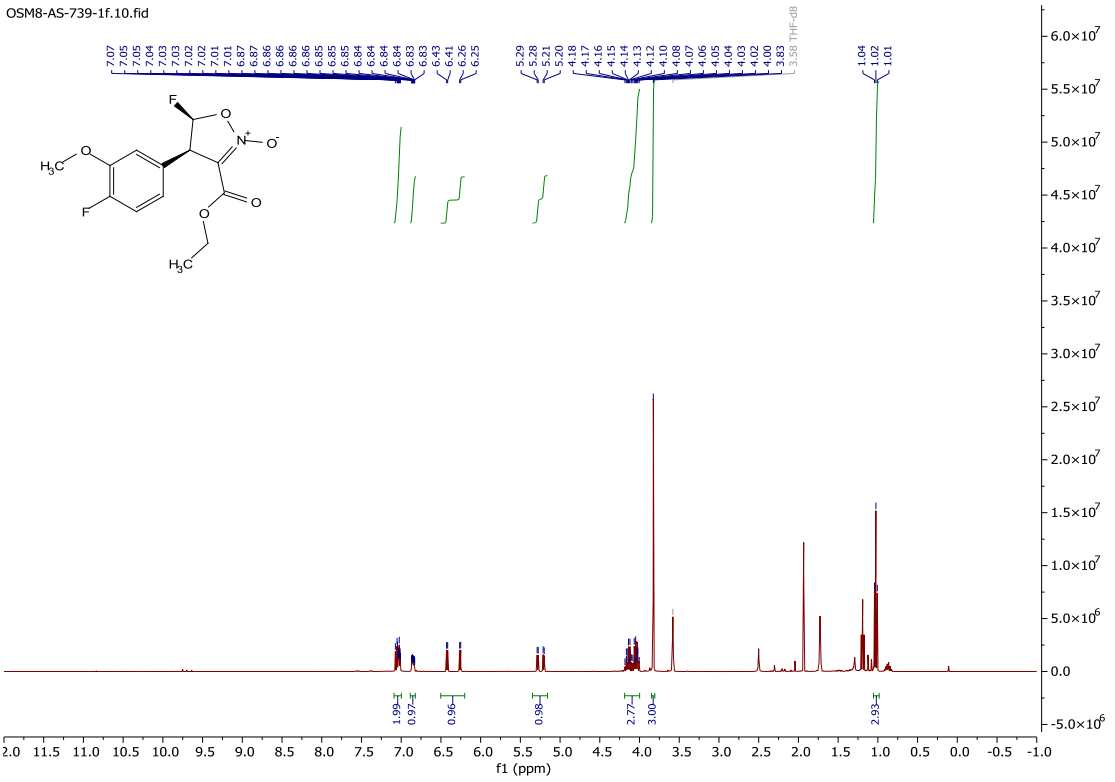
Compound (*trans*-**3f**) ^{13}C-NMR spectra (101 MHz, THF-d8)



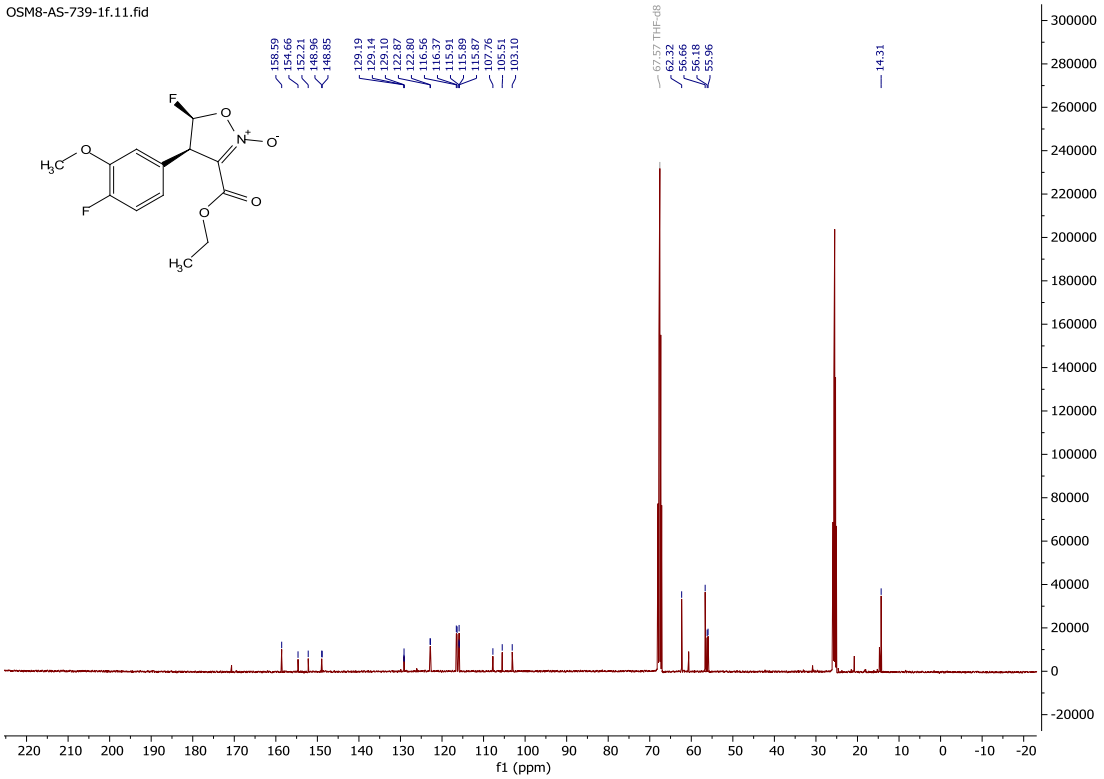
Compound (*trans*-**3f**)^{19}F-NMR spectra (376 MHz, THF-d8)



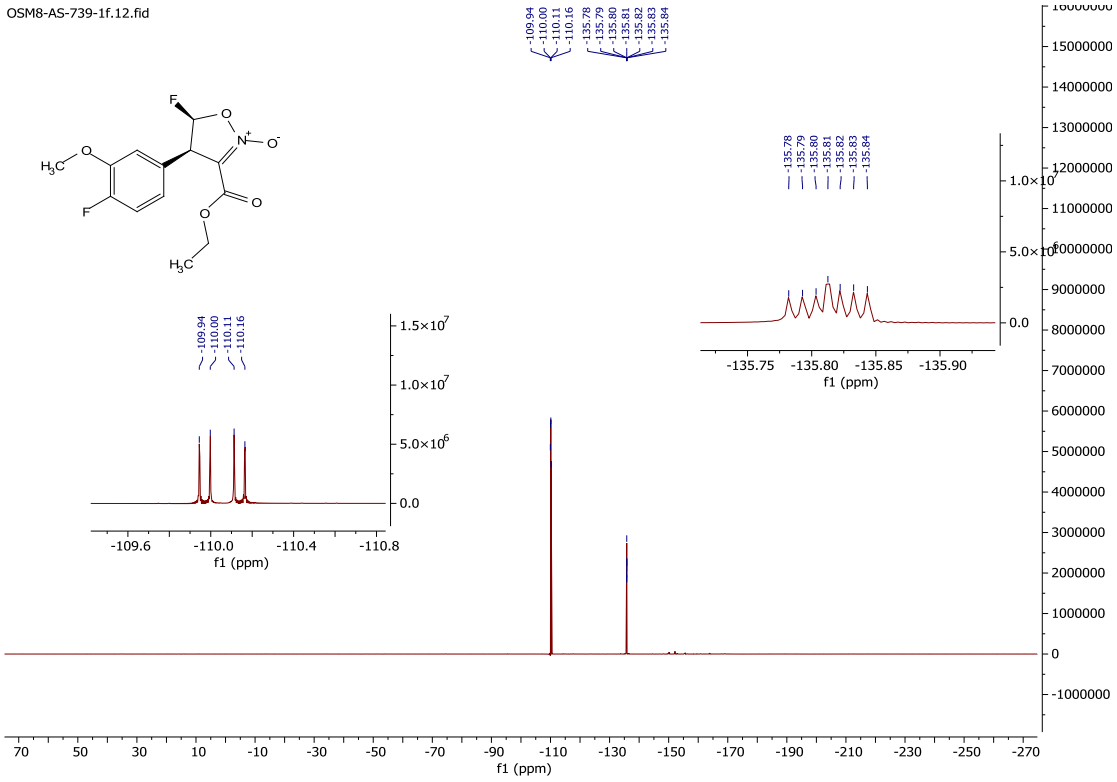
Compound (*cis*-**3f**) ^{1}H-NMR spectra (400 MHz, THF-d8)



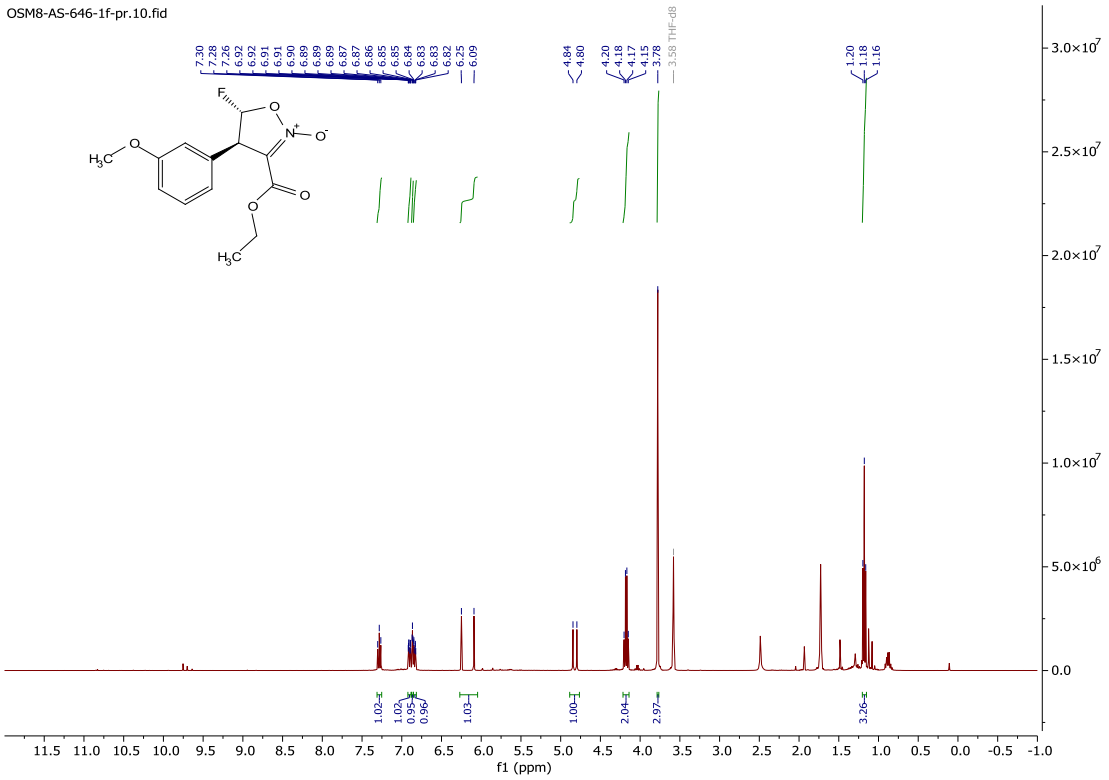
Compound (*cis*-**3f**) ^{13}C-NMR spectra (101 MHz, THF-d8)



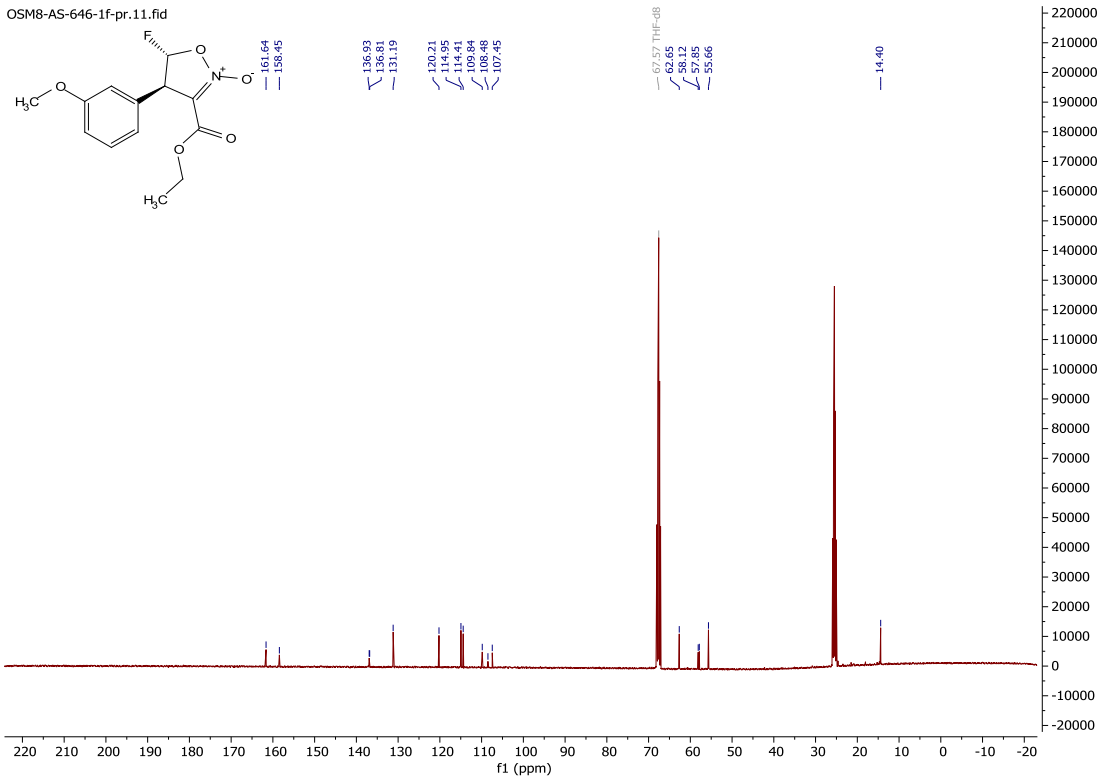
Compound (*cis*-**3f**)^{19}F-NMR spectra (376 MHz, THF-d8)



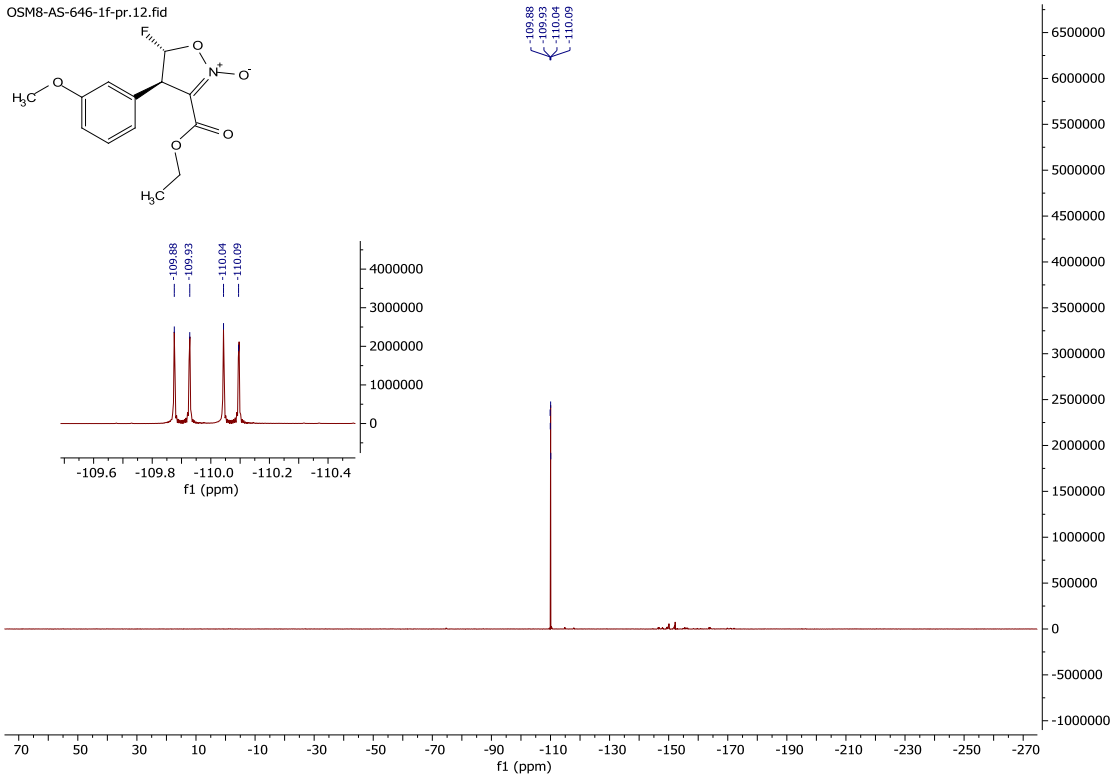
Compound (*trans*-**3g**) ^{1}H-NMR spectra (400 MHz, THF-d8)



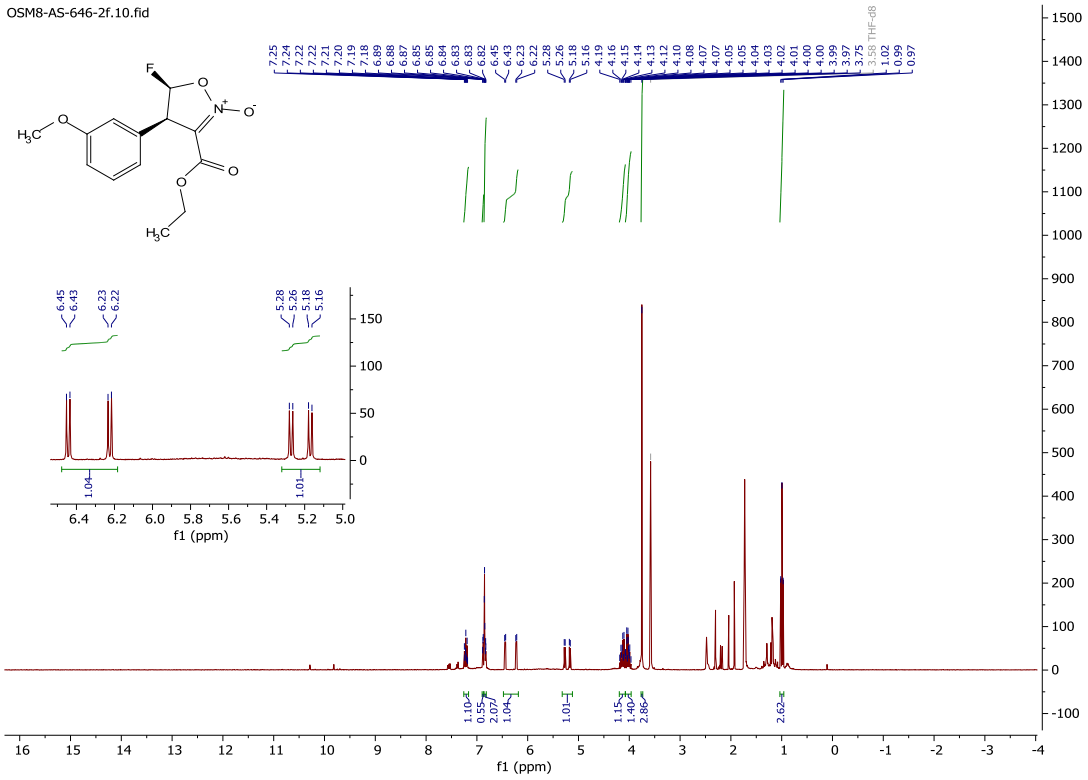
Compound (*trans*-**3g**) ^{13}C-NMR spectra (101 MHz, THF-d8)



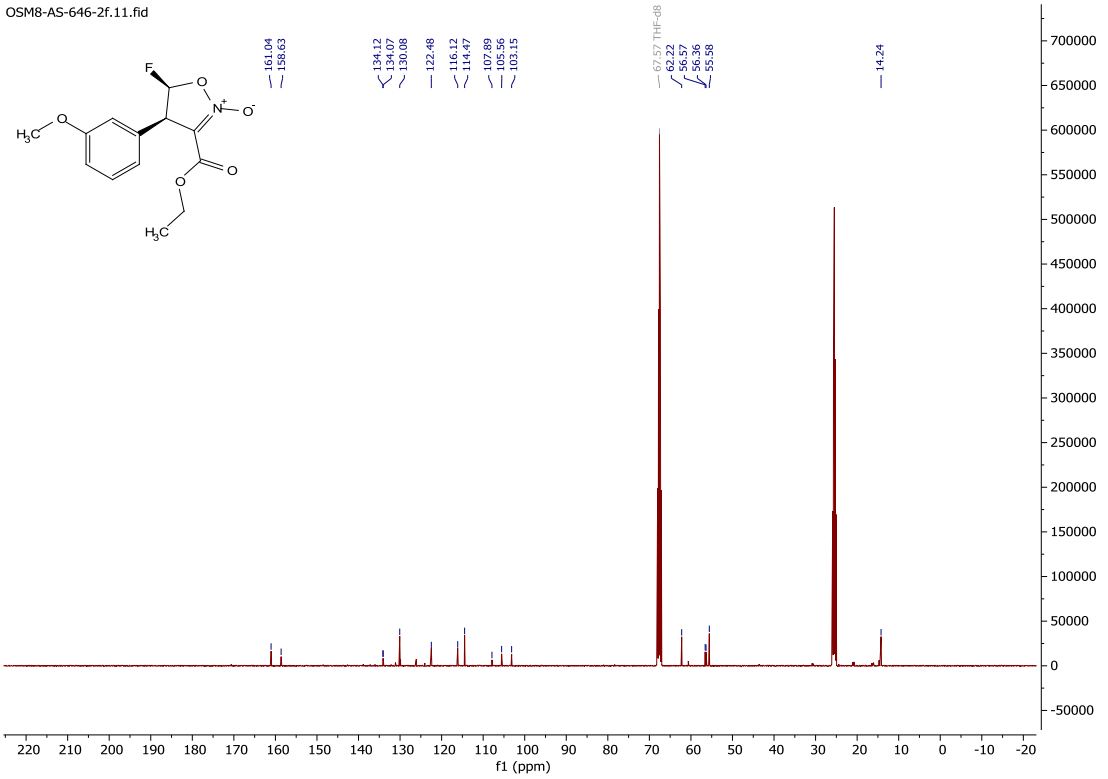
Compound (*trans*-**3g**)^{19}F-NMR spectra (376 MHz, THF-d8)



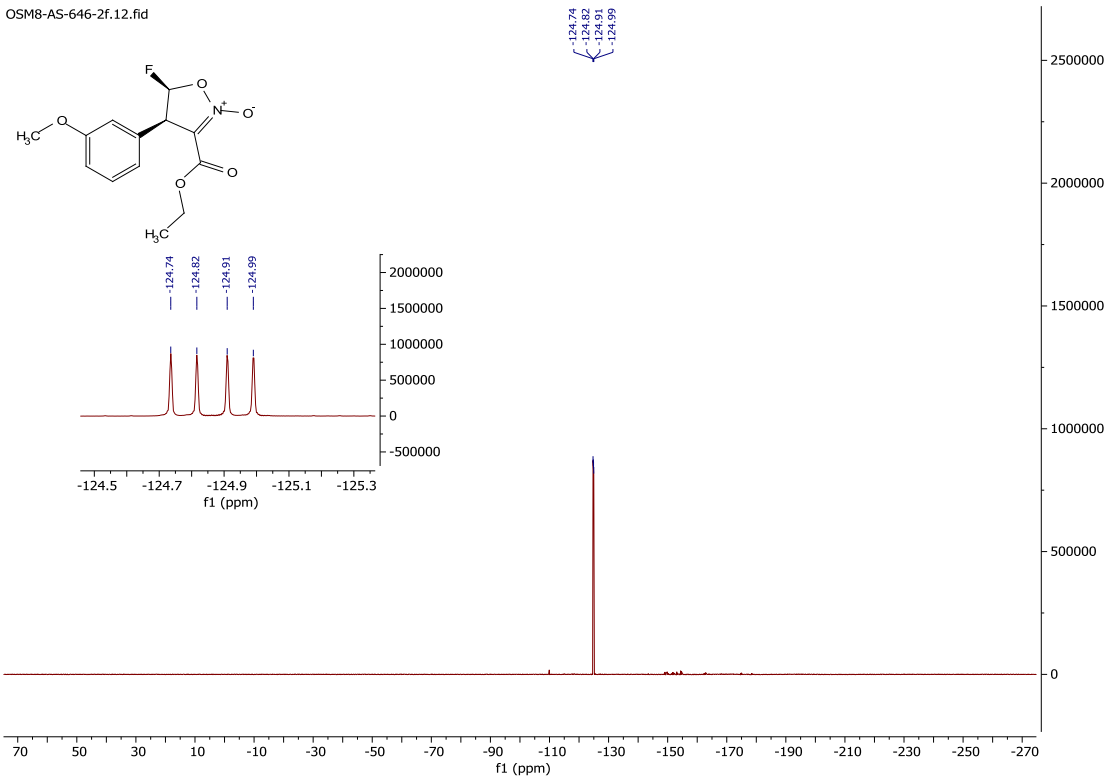
Compound (*cis*-**3g**) ^{1}H-NMR spectra (400 MHz, THF-d8)



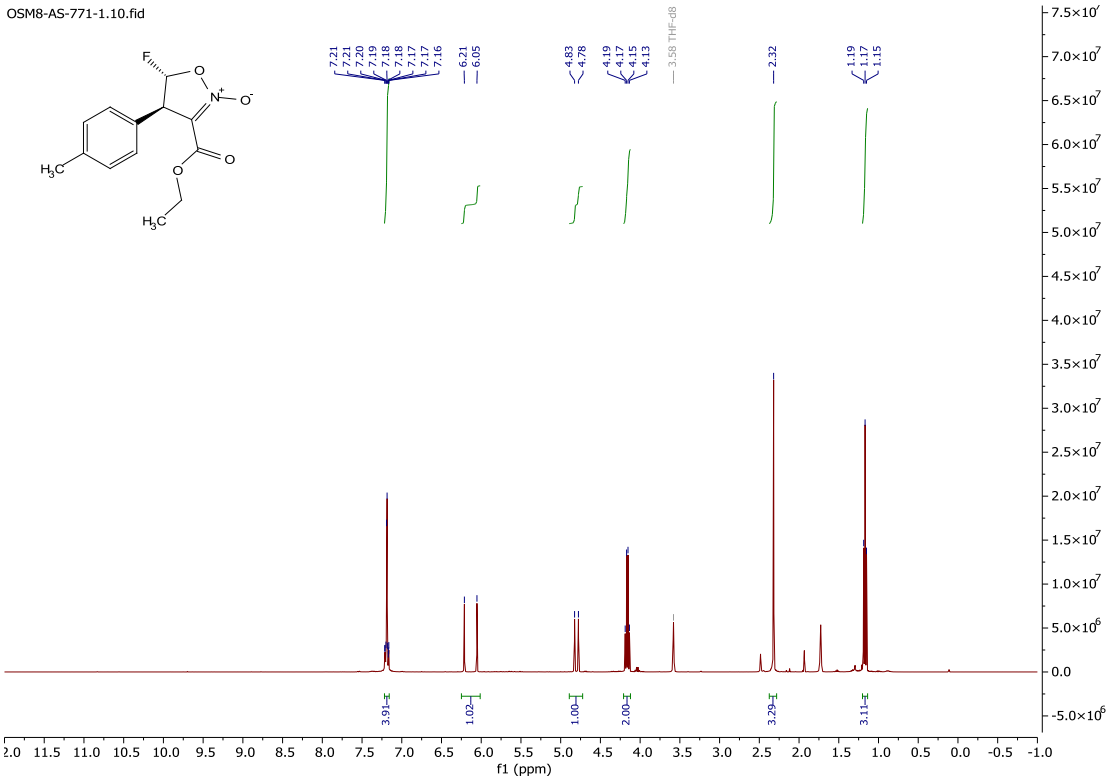
Compound (*cis*-**3g**) ^{13}C-NMR spectra (101 MHz, THF-d8)



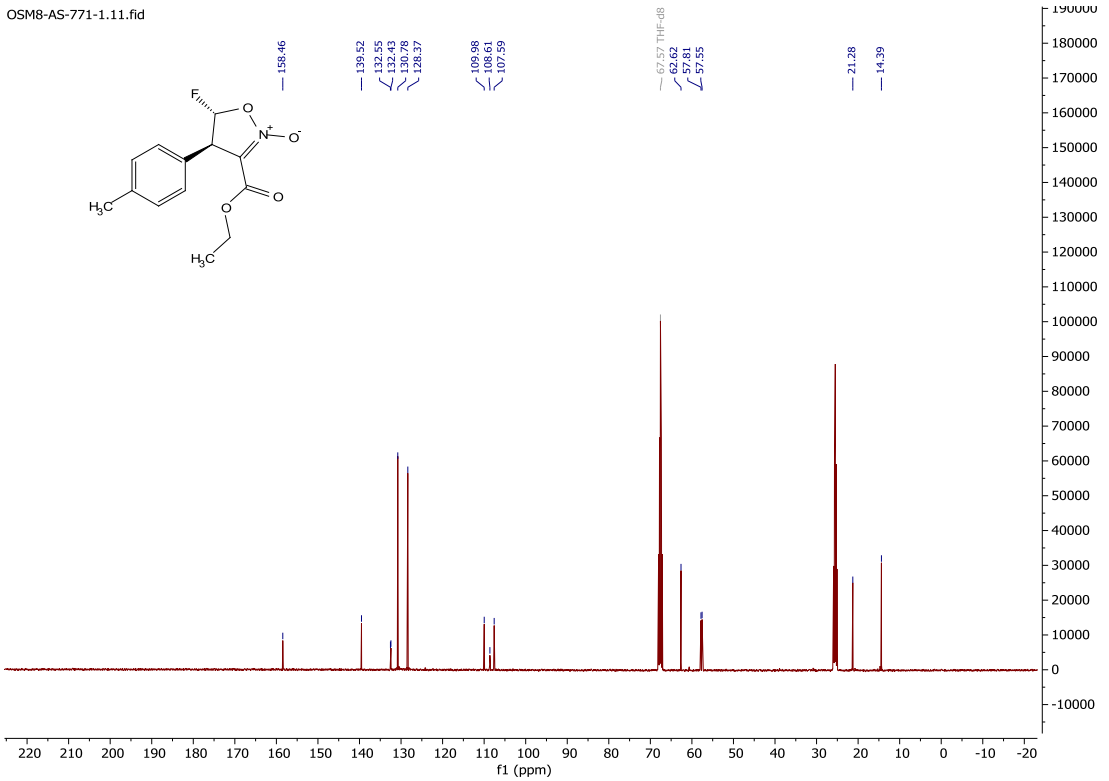
Compound (*cis*-**3g**)^{19}F-NMR spectra (376 MHz, THF-d8)



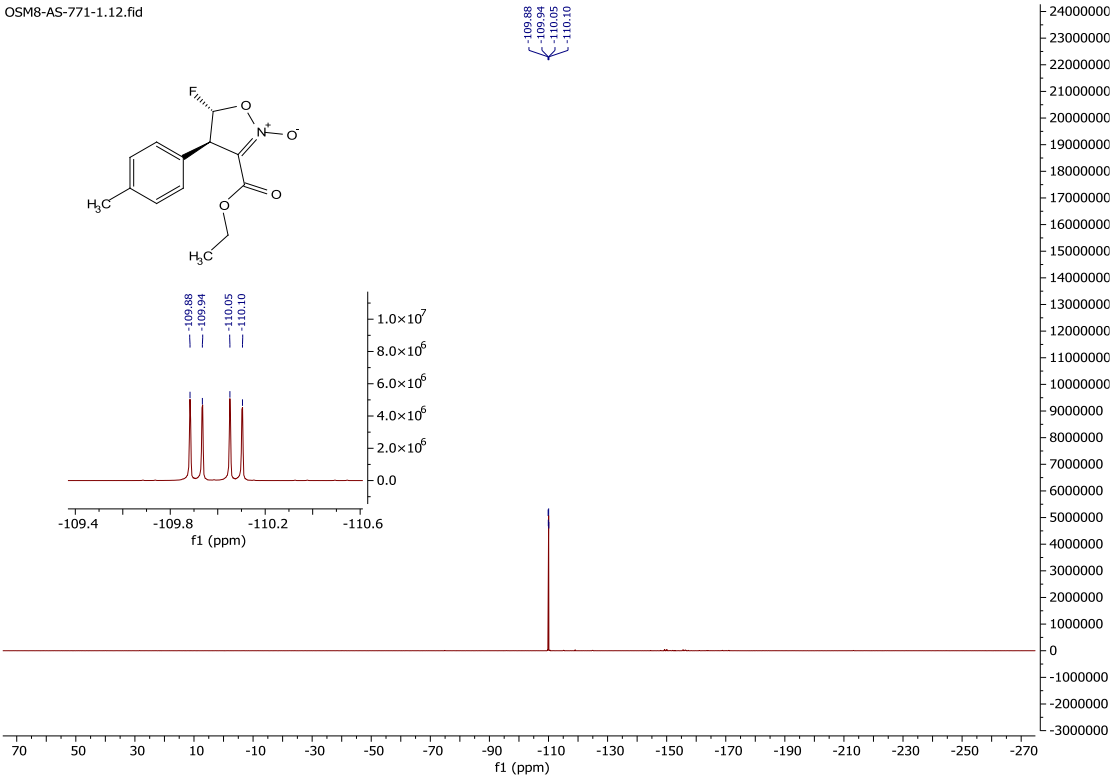
Compound (*trans*-**3h**) ^{1}H-NMR spectra (400 MHz, THF-d8)



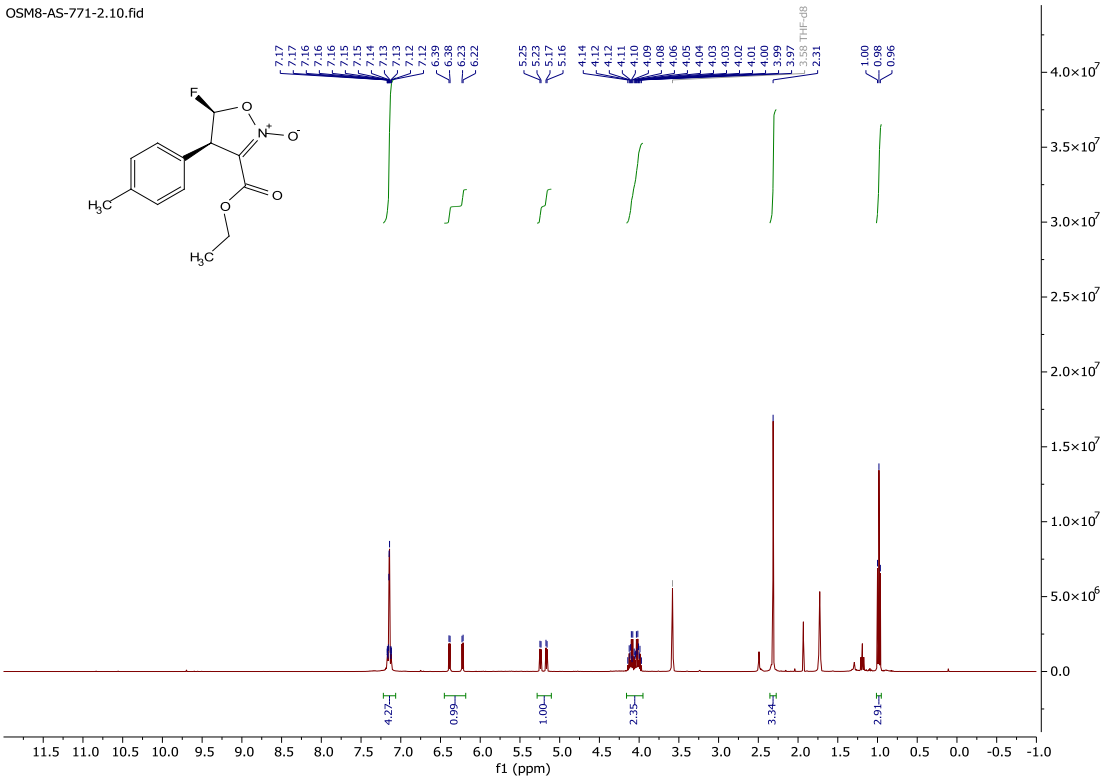
Compound (*trans*-**3h**) ^{13}C-NMR spectra (101 MHz, THF-d8)



Compound (*trans*-**3h**)^{19}F-NMR spectra (376 MHz, THF-d8)



Compound (*cis*-**3h**) ^{1}H-NMR spectra (400 MHz, THF-d8)



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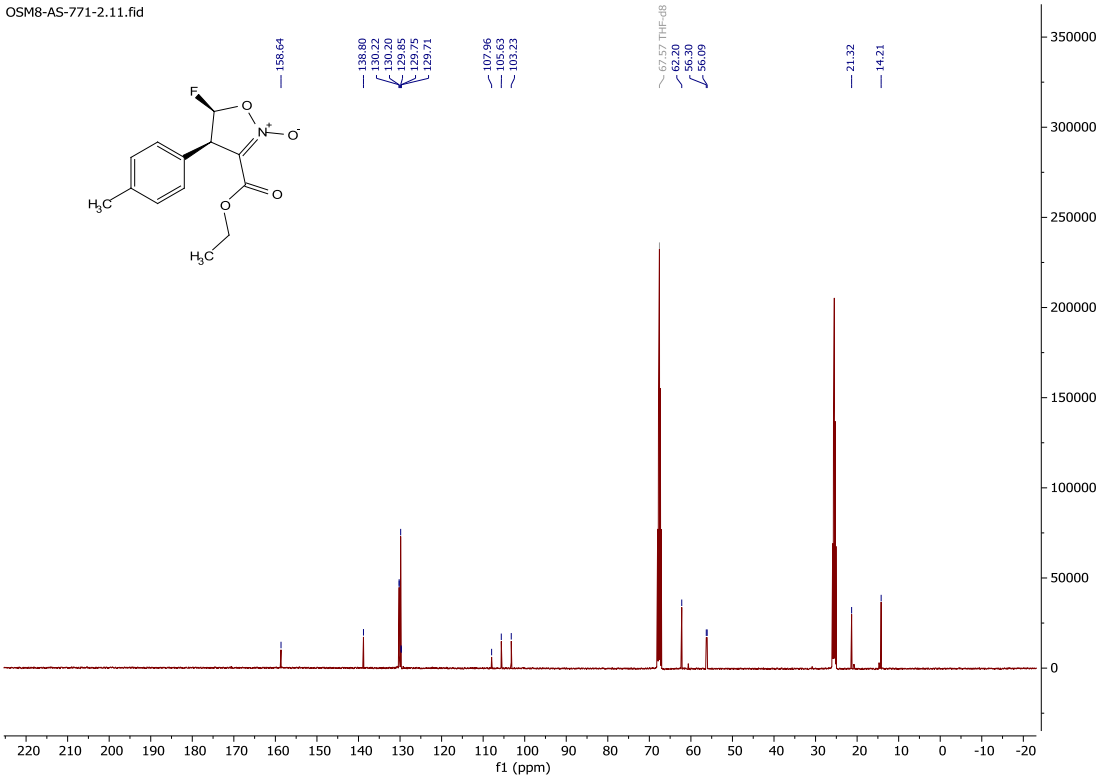
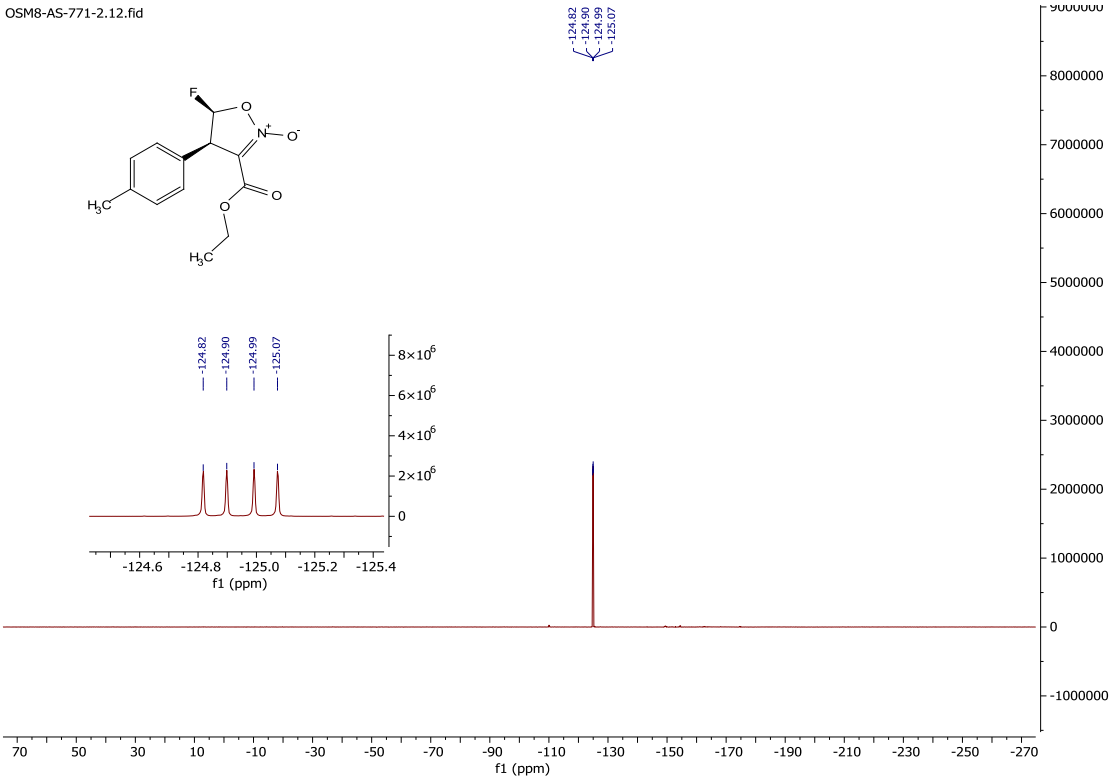
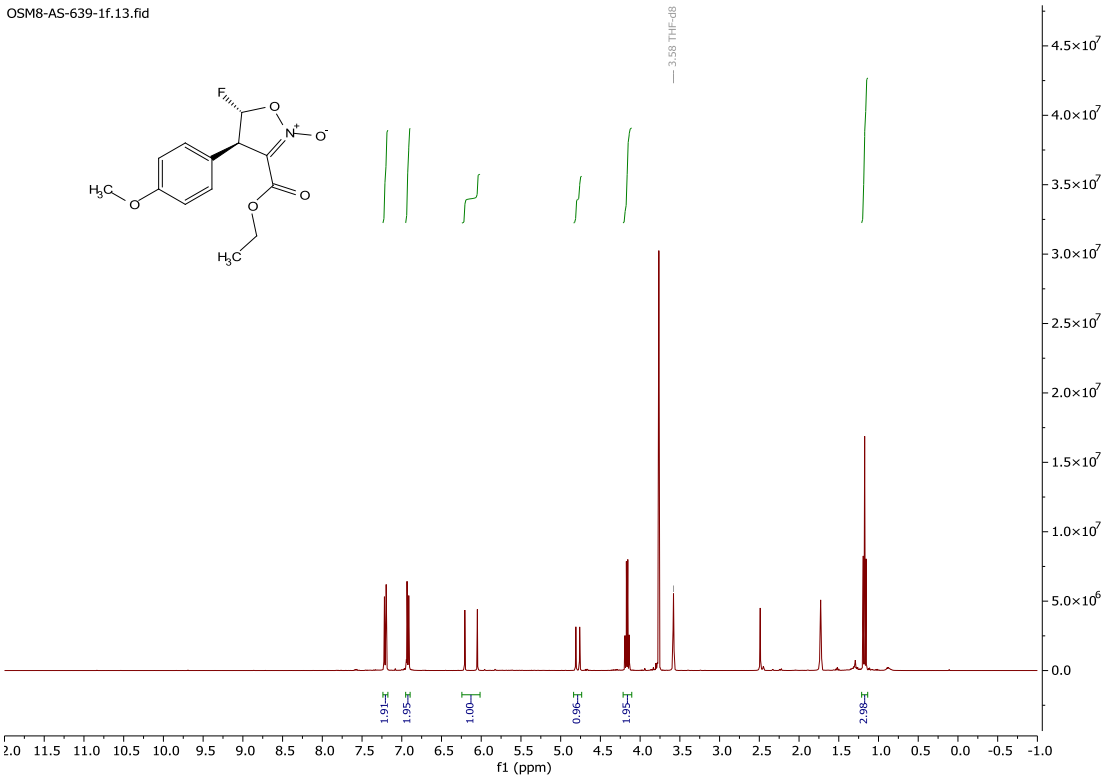


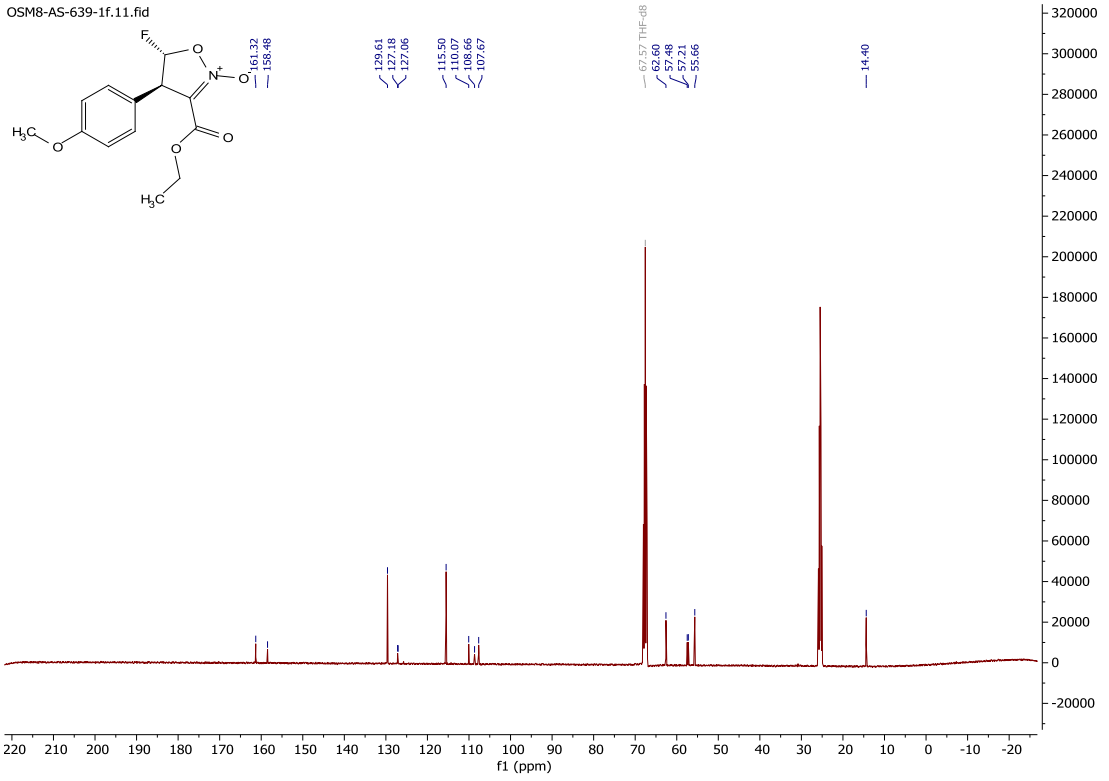
Compound (*cis*-**3h**)^{19}F-NMR spectra (376 MHz, THF-d8)



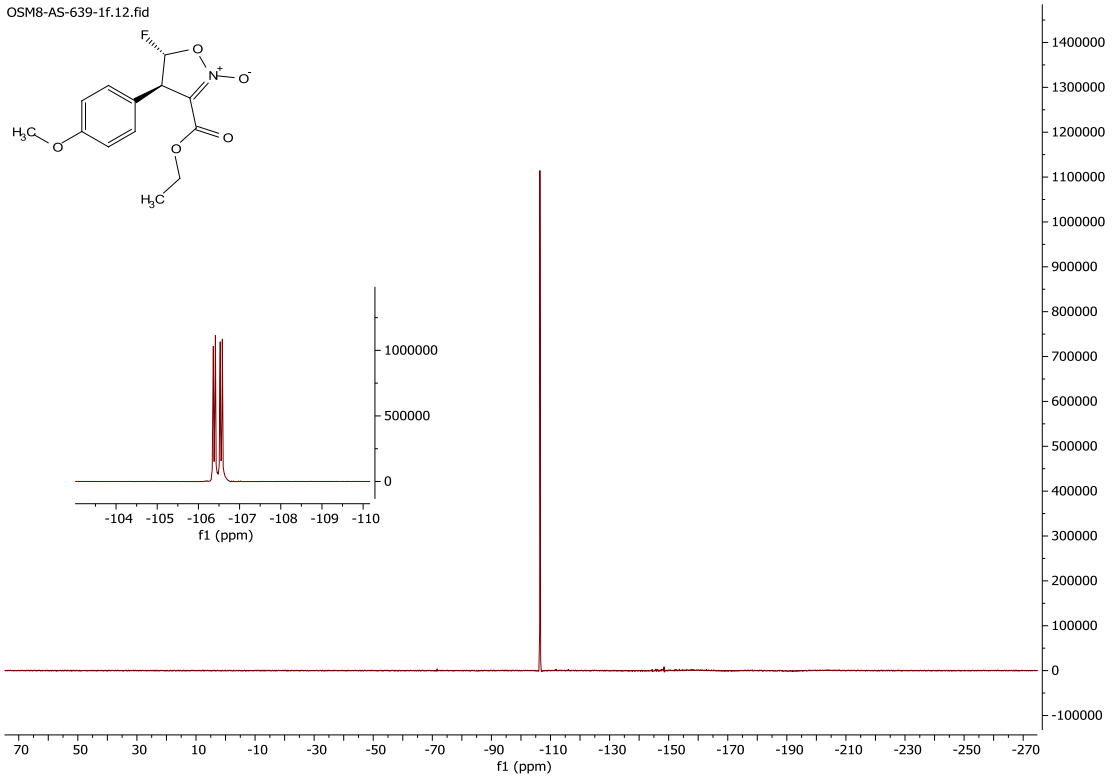
Compound (*trans*-**3i**) ^{1}H-NMR spectra (400 MHz, THF-d8)



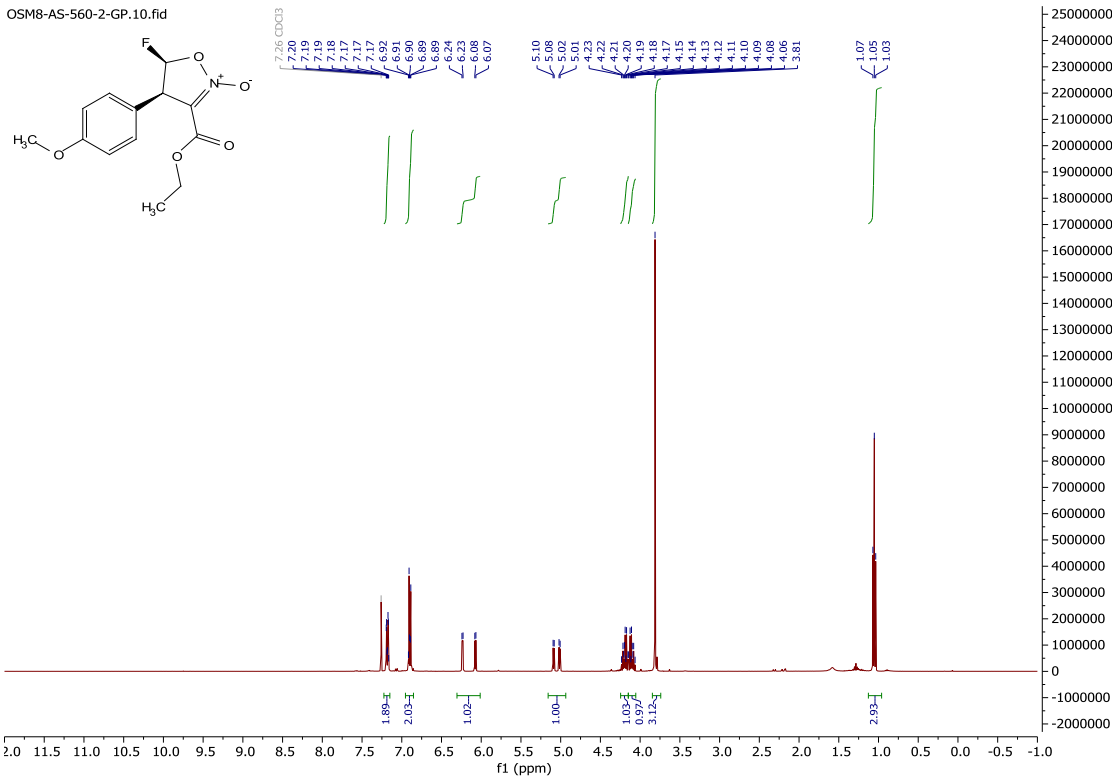
Compound (*trans*-**3i**) ^{13}C-NMR spectra (101 MHz, THF-d8)



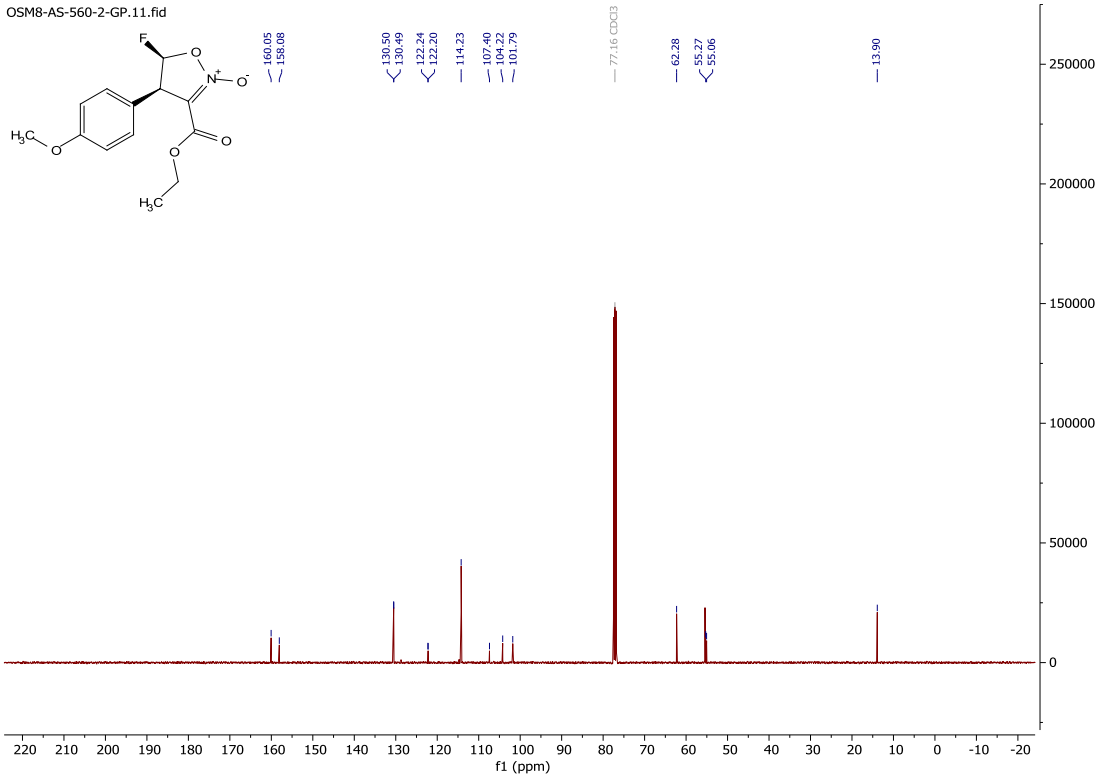
Compound (*trans*-**3i**)^{19}F-NMR spectra (376 MHz, THF-d8)



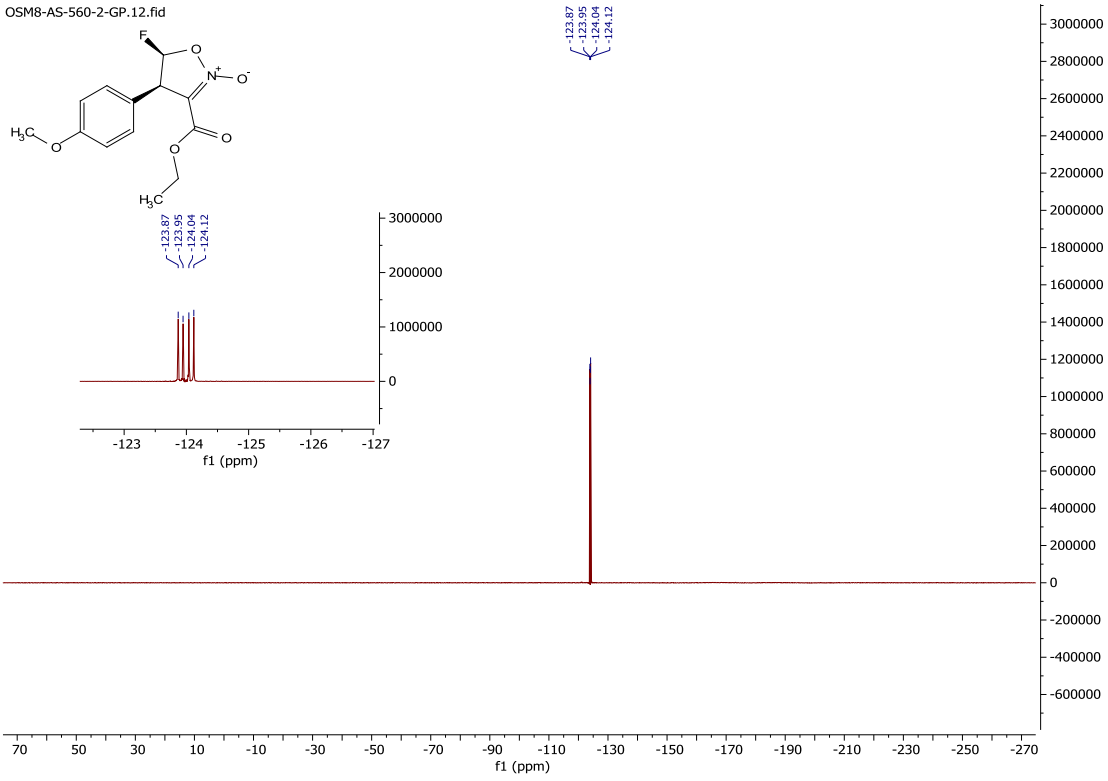
Compound (*cis*-**3i**) ^{1}H-NMR spectra (400 MHz, $CDCl_3$)



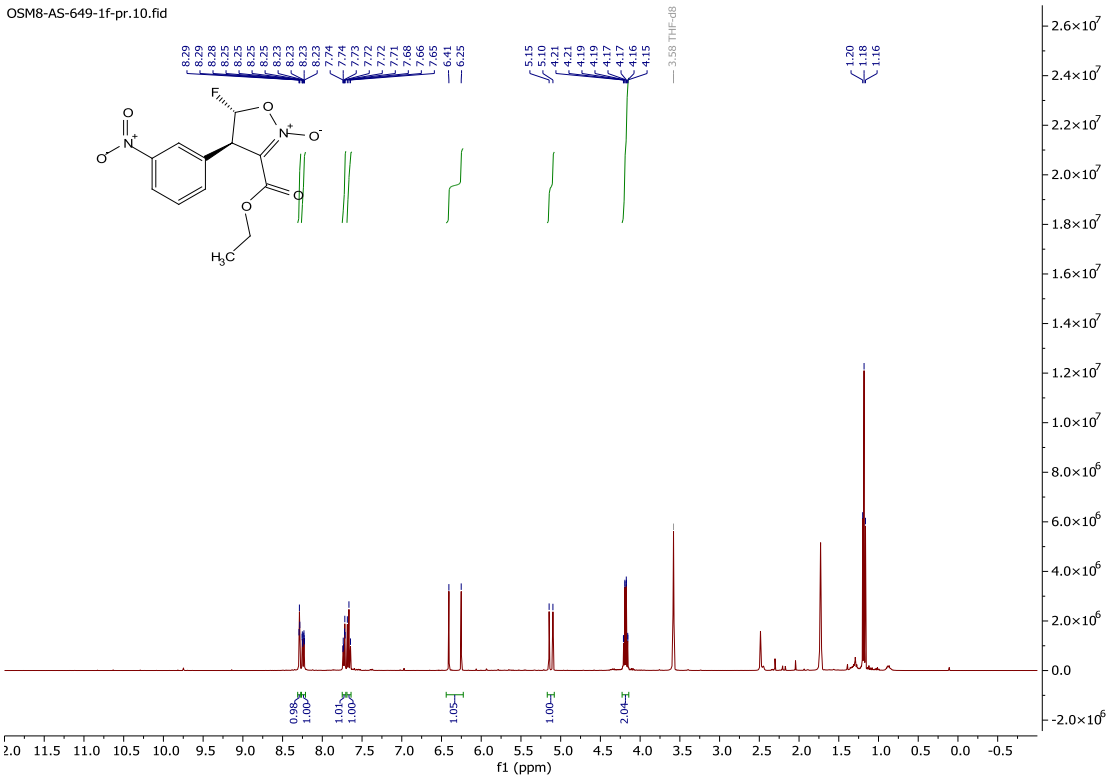
Compound (*cis*-**3i**) ^{13}C-NMR spectra (101 MHz, $CDCl_3$)



Compound (*cis*-**3i**)^{19}F-NMR spectra (376 MHz, $CDCl_3$)



Compound (*trans*-**3j**) ^{1}H-NMR spectra (400 MHz, THF-d8)



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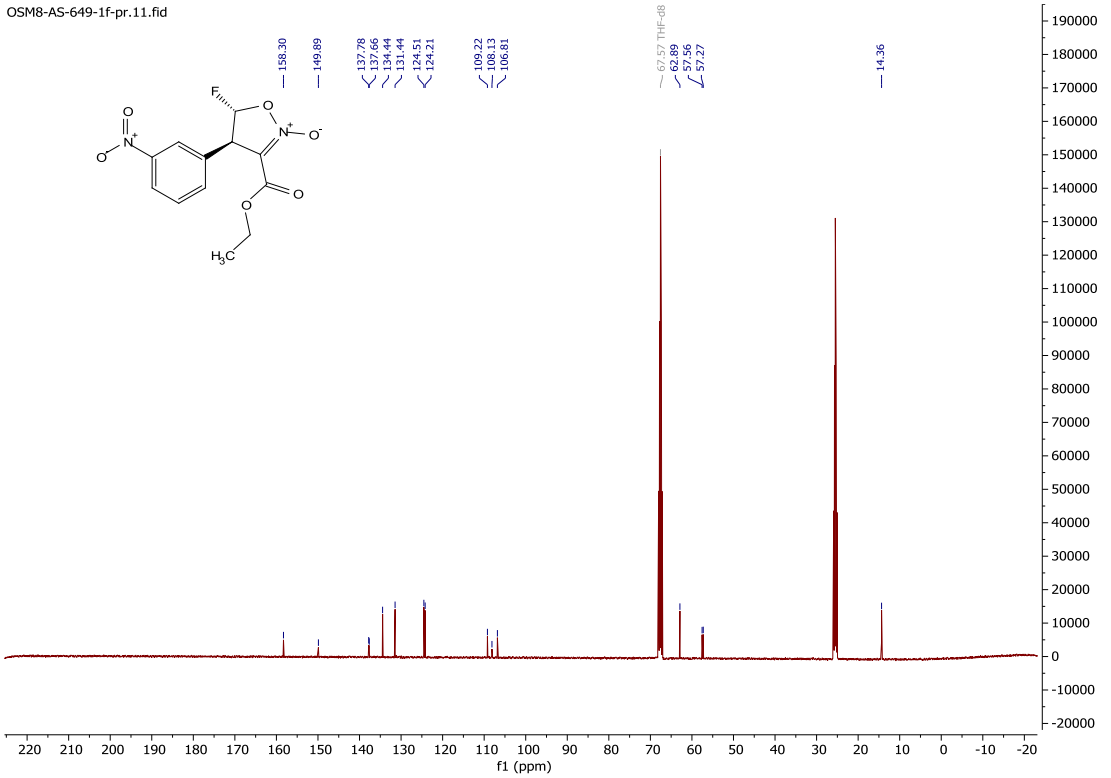
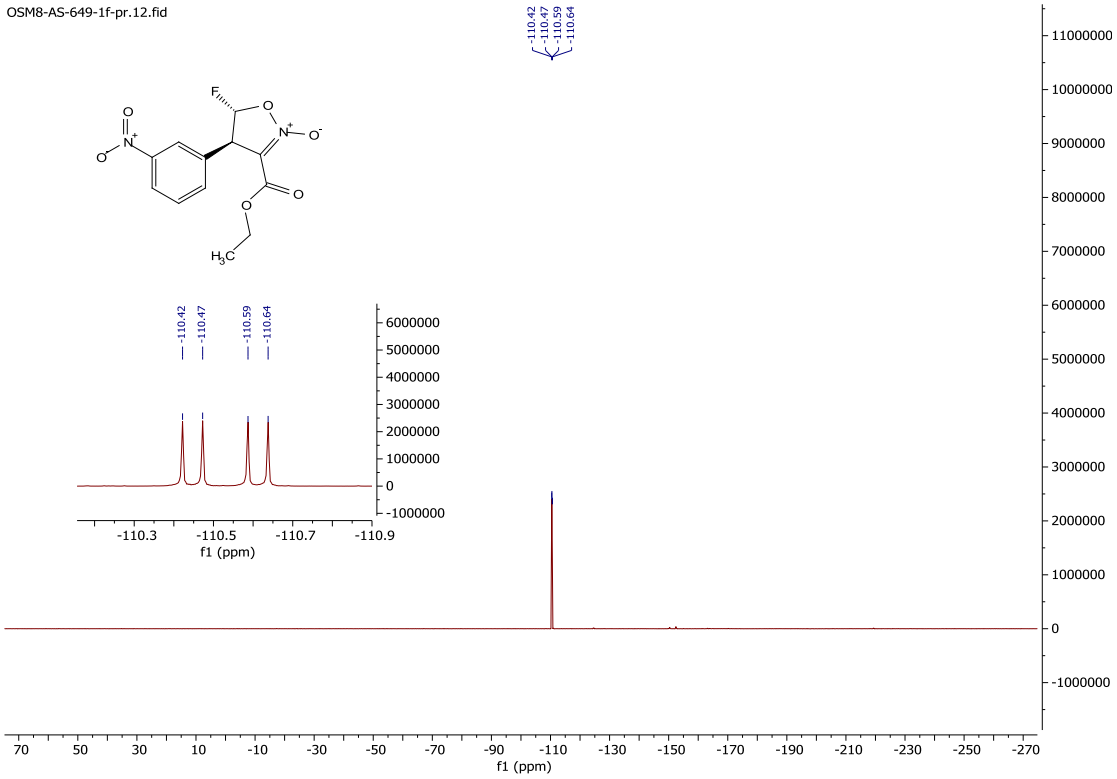
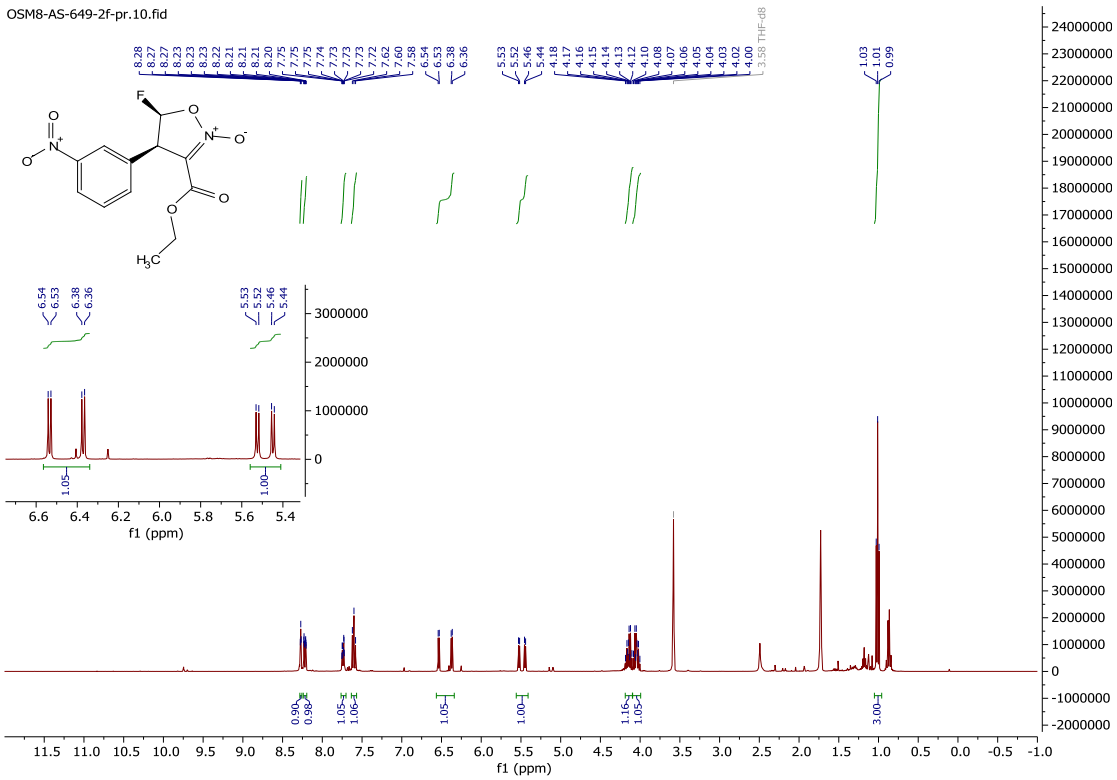


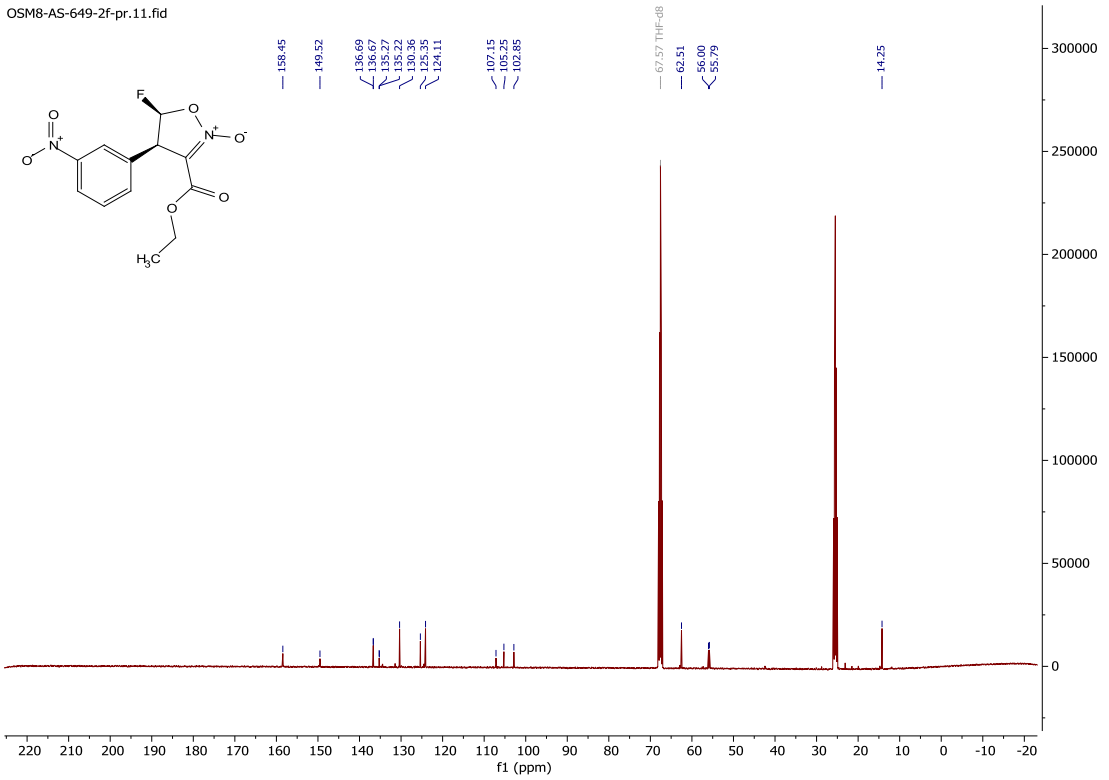
Compound (*trans*-**3j**)^{19}F-NMR spectra (376 MHz, THF-d8)



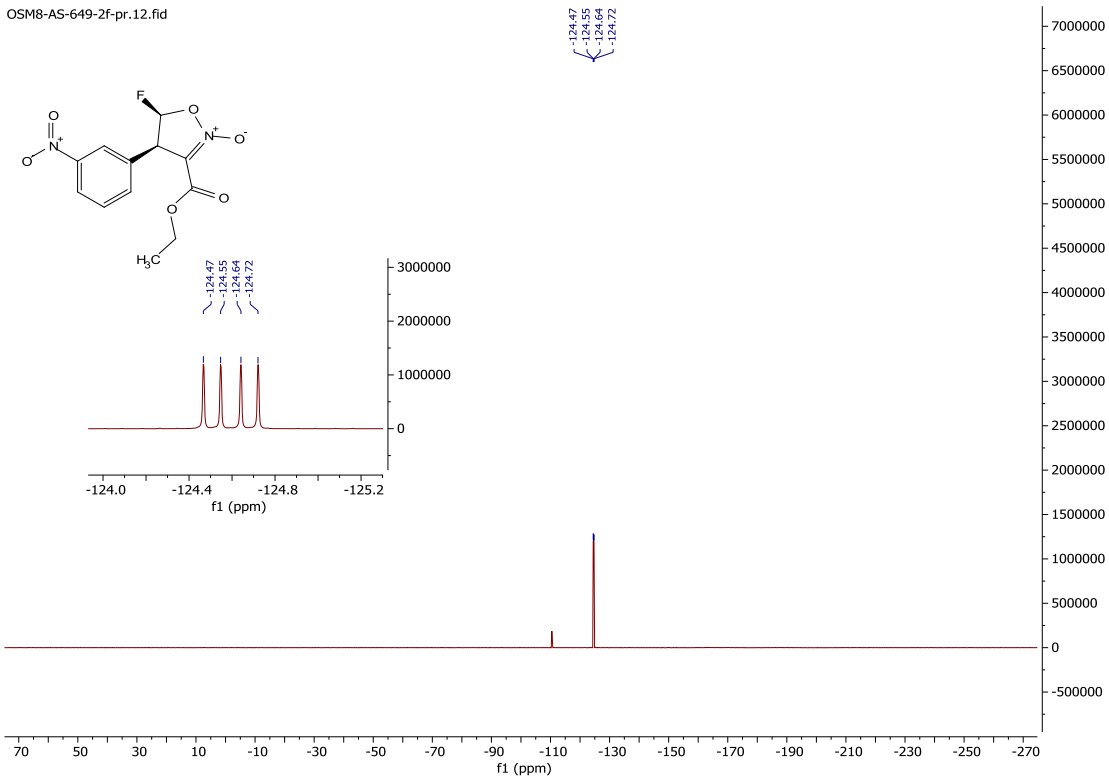
Compound (*cis*-**3j**) ^{1}H-NMR spectra (400 MHz, THF-d8)



Compound (*cis*-**3j**) ^{13}C-NMR spectra (101 MHz, THF-d8)



Compound (*cis*-**3j**)^{19}F-NMR spectra (376 MHz, THF-d8)



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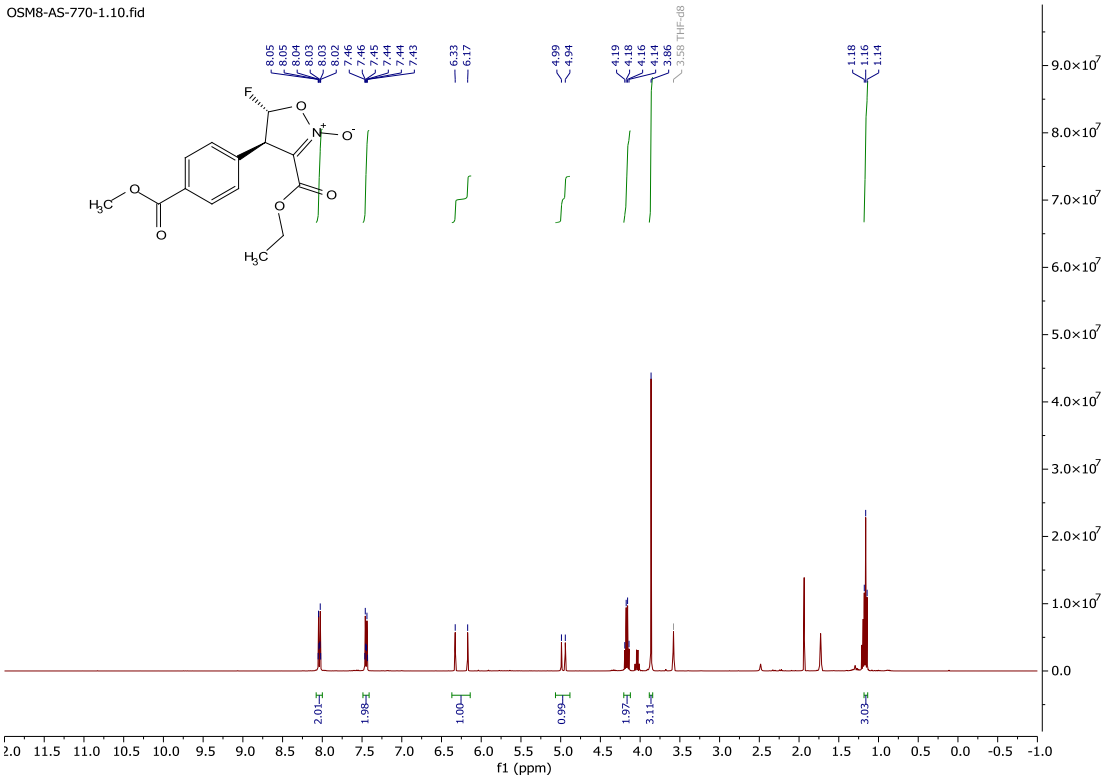
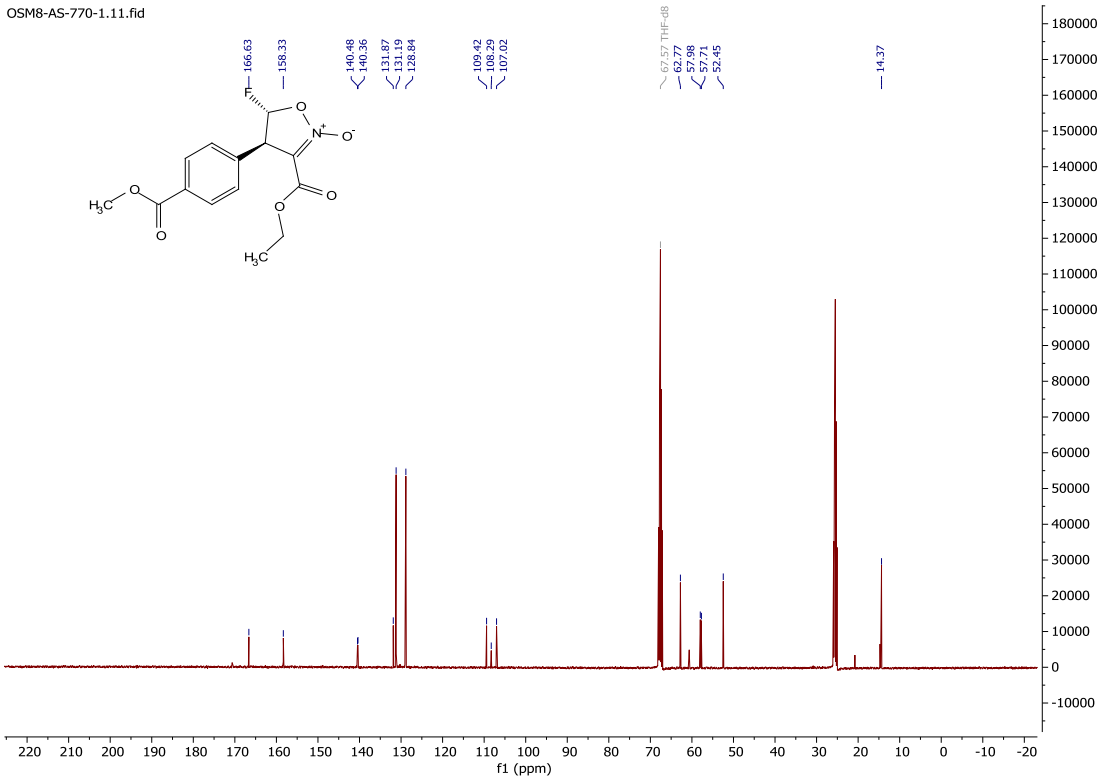
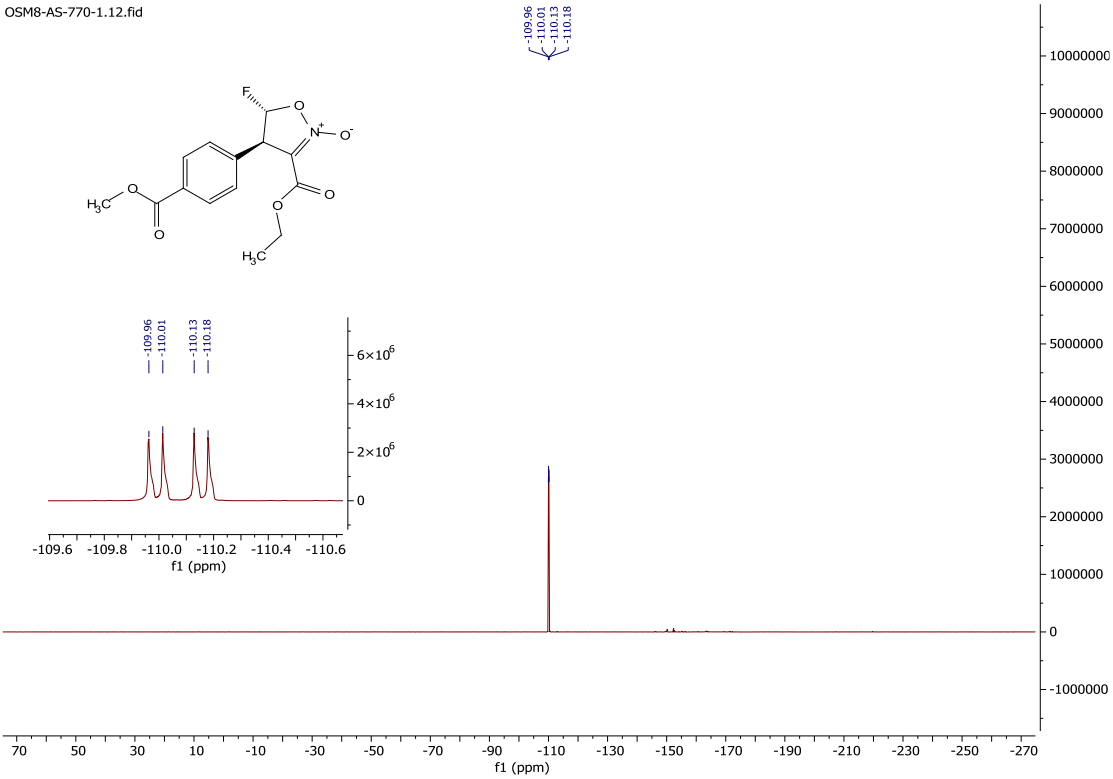


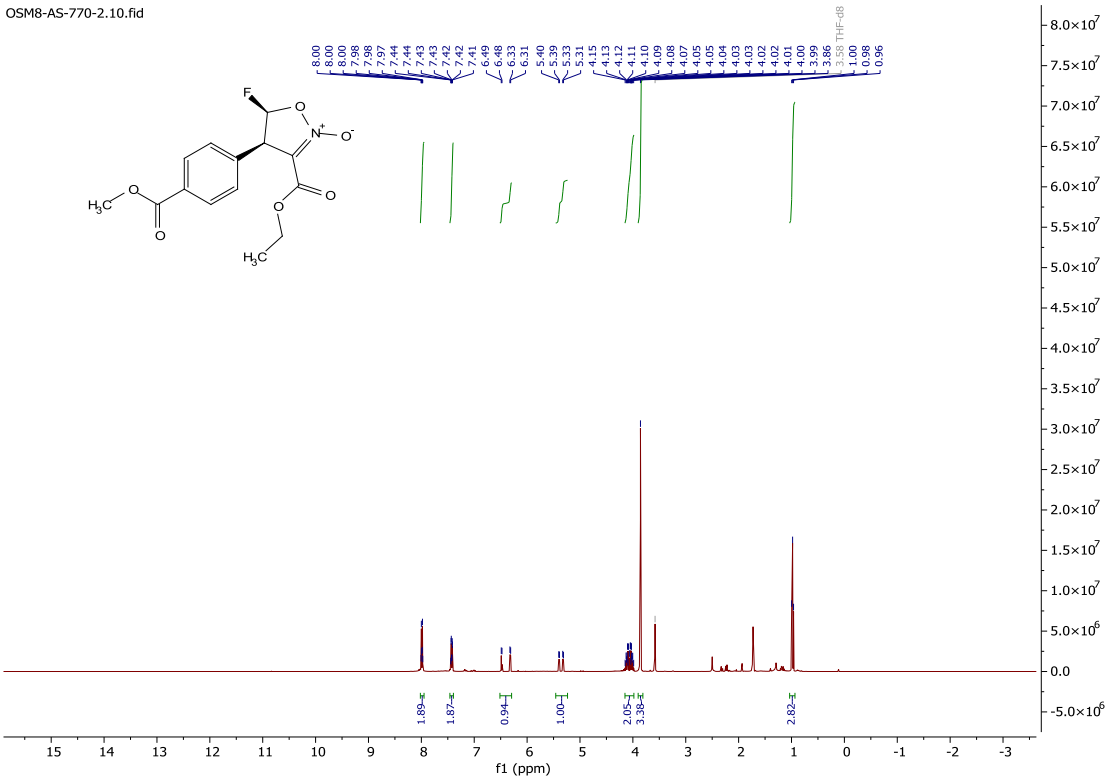
Compound (*trans*-**3k**) ^{13}C-NMR spectra (101 MHz, THF-d8)



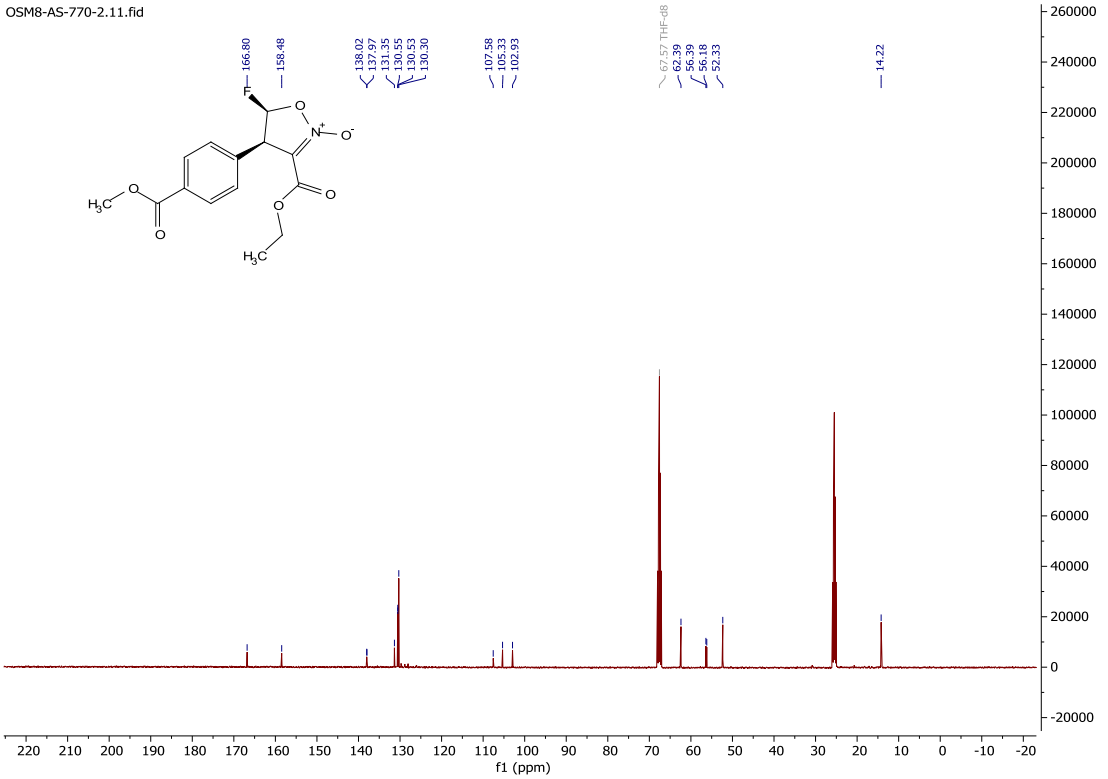
Compound (*trans*-**3k**)^{19}F-NMR spectra (376 MHz, THF-d8)



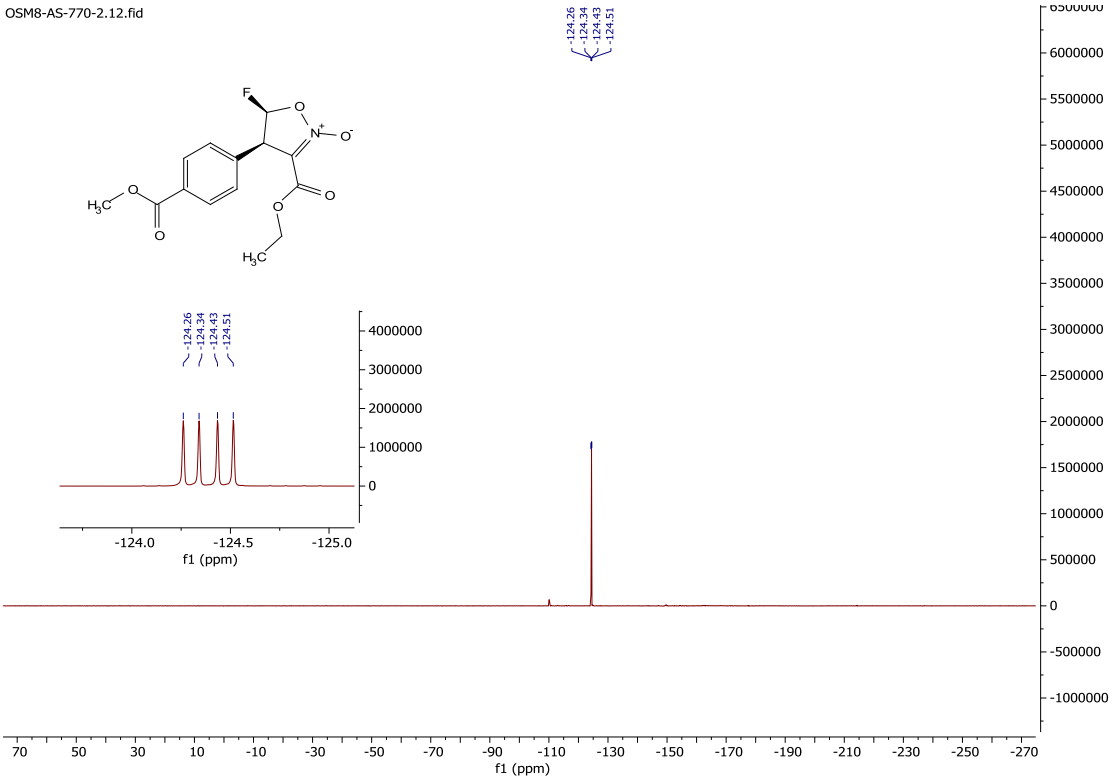
Compound (*cis*-**3k**) ^{1}H-NMR spectra (400 MHz, THF-d8)



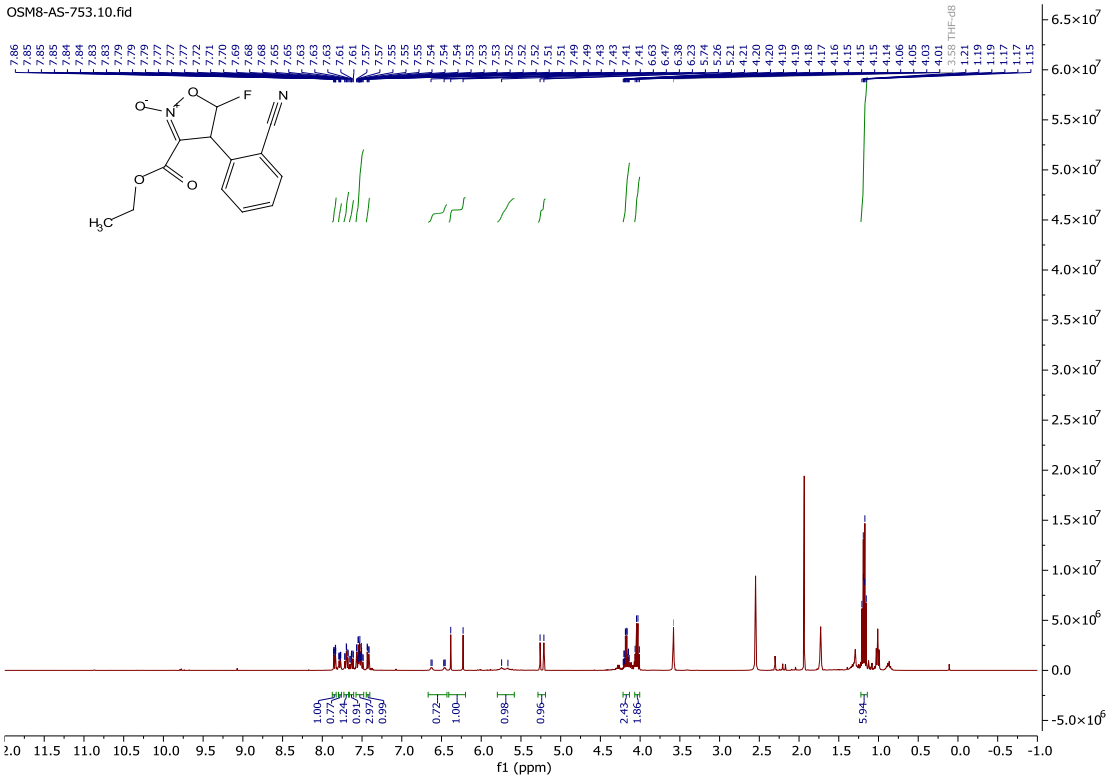
Compound (*cis*-**3k**) ^{13}C-NMR spectra (101 MHz, THF-d8)



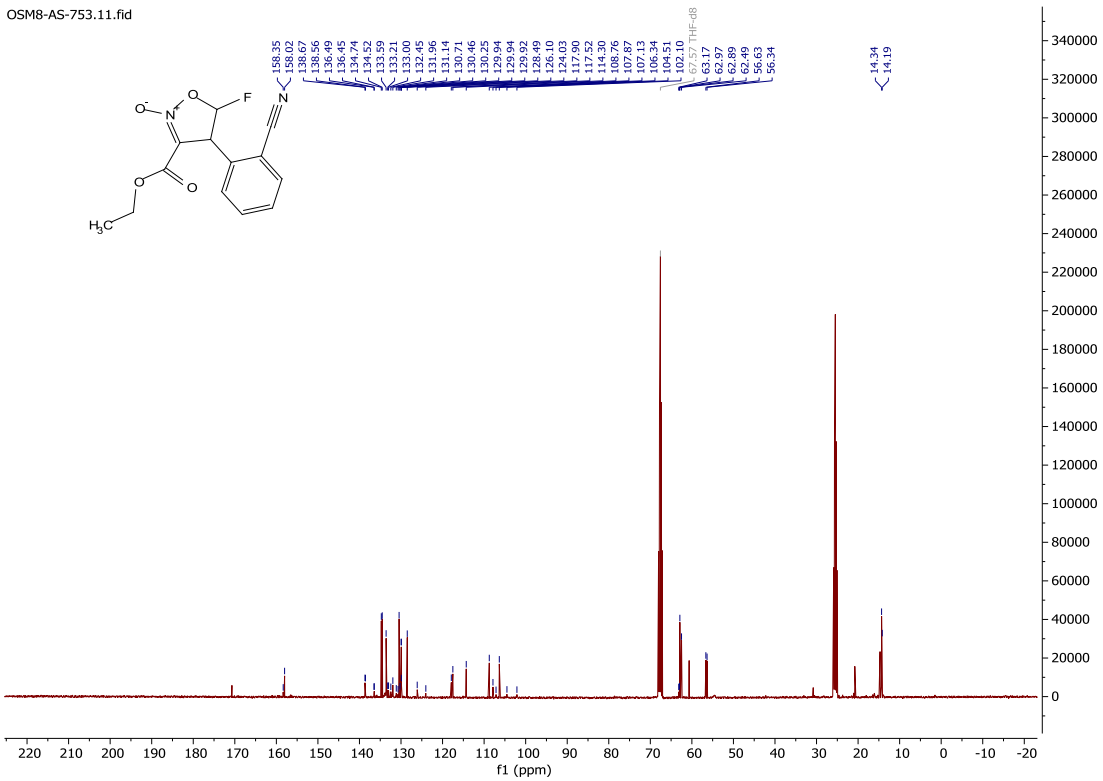
Compound (*cis*-**3k**)^{19}F-NMR spectra (376 MHz, THF-d8)



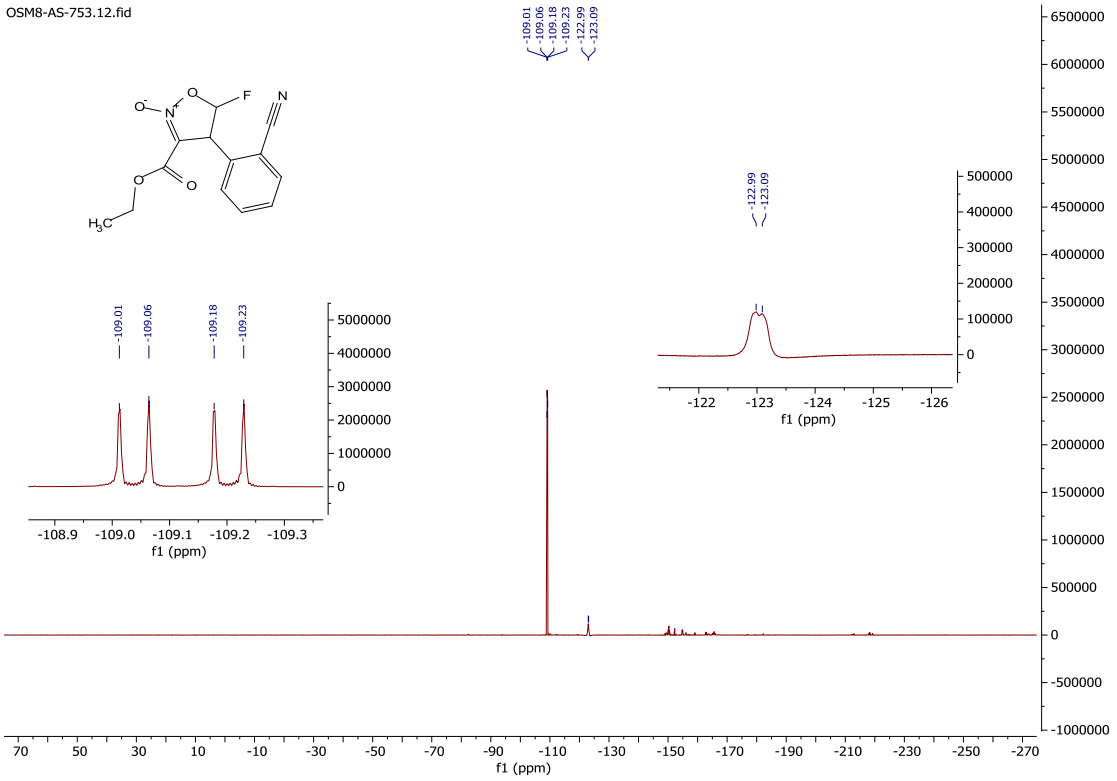
Compound (**3l**) ^{1}H-NMR spectra (400 MHz, $CDCl_3$)



Compound (**3l**) ^{13}C-NMR spectra (101 MHz, $CDCl_3$)



Compound (**3l**) ^{19}F-NMR spectra (376 MHz, $CDCl_3$)



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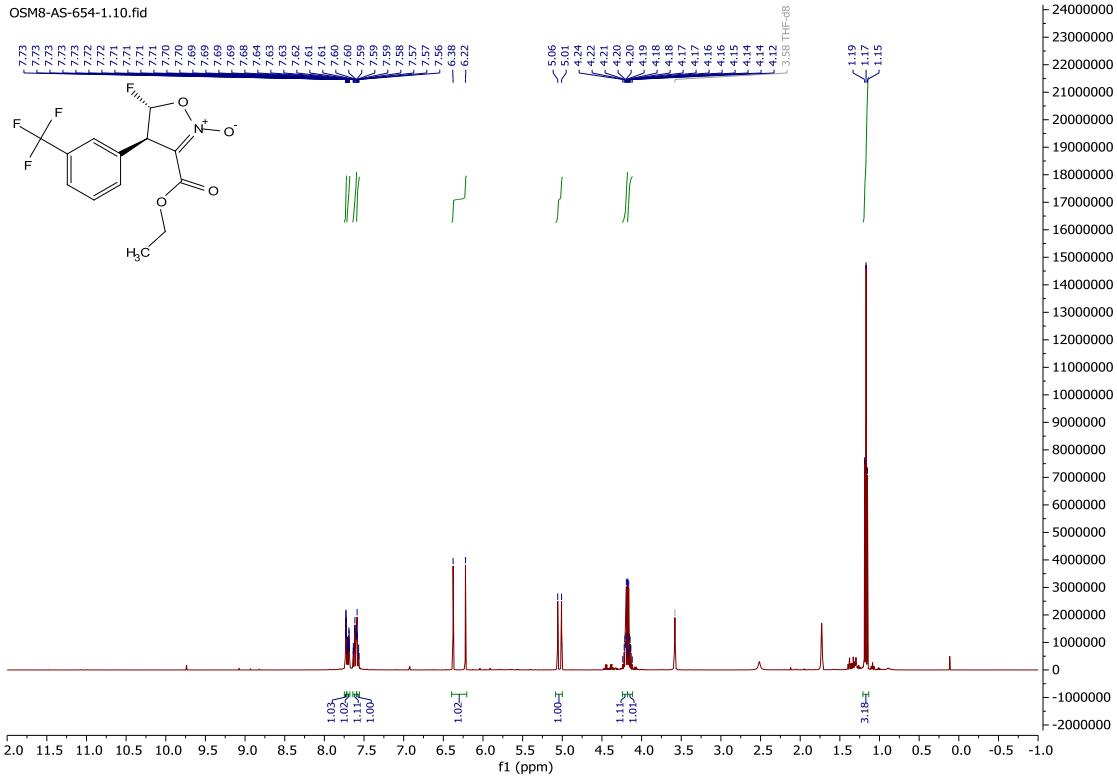

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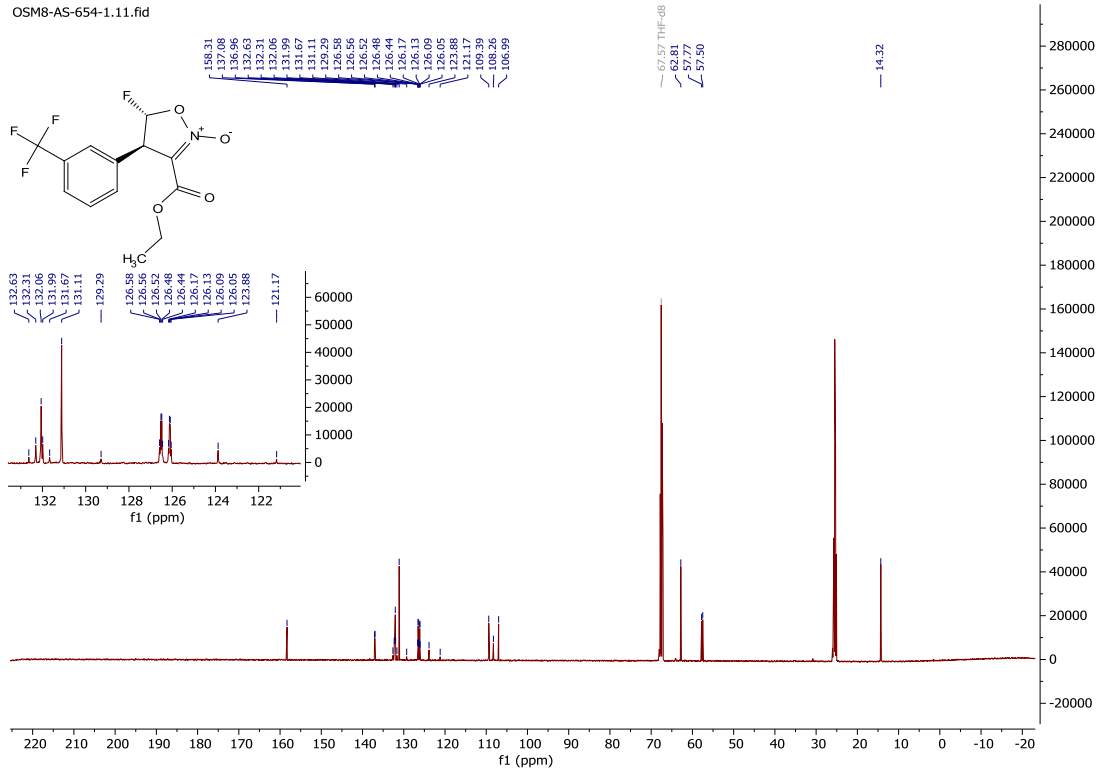

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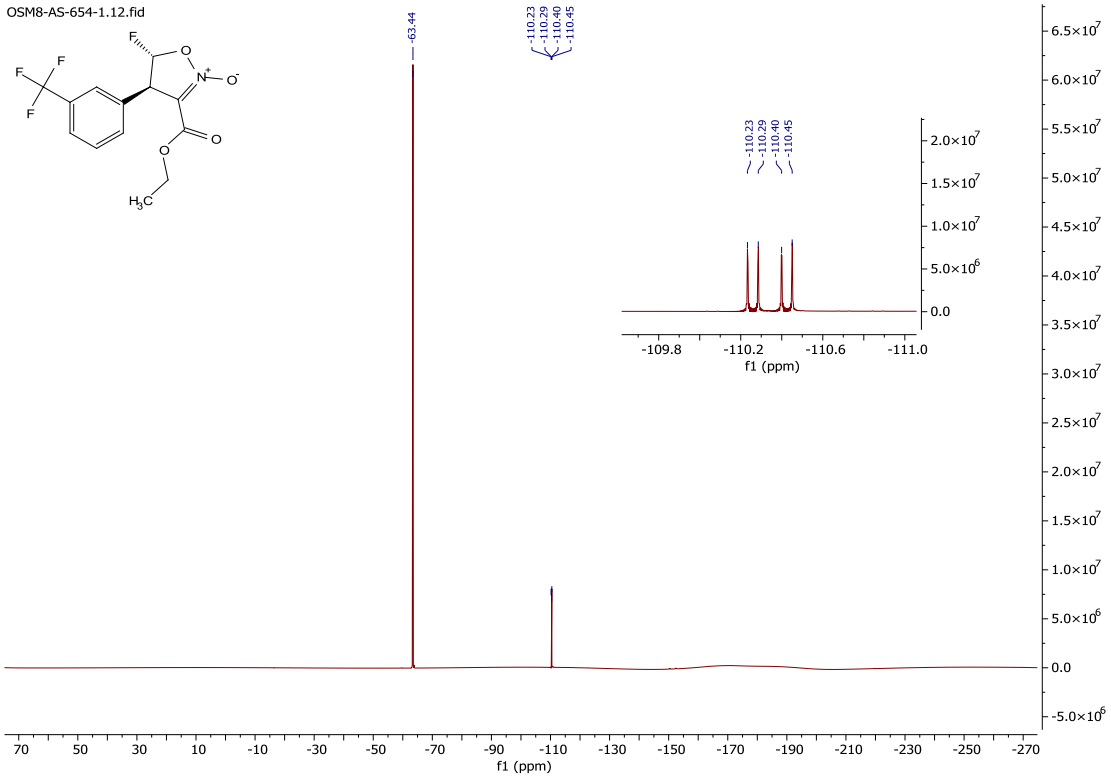
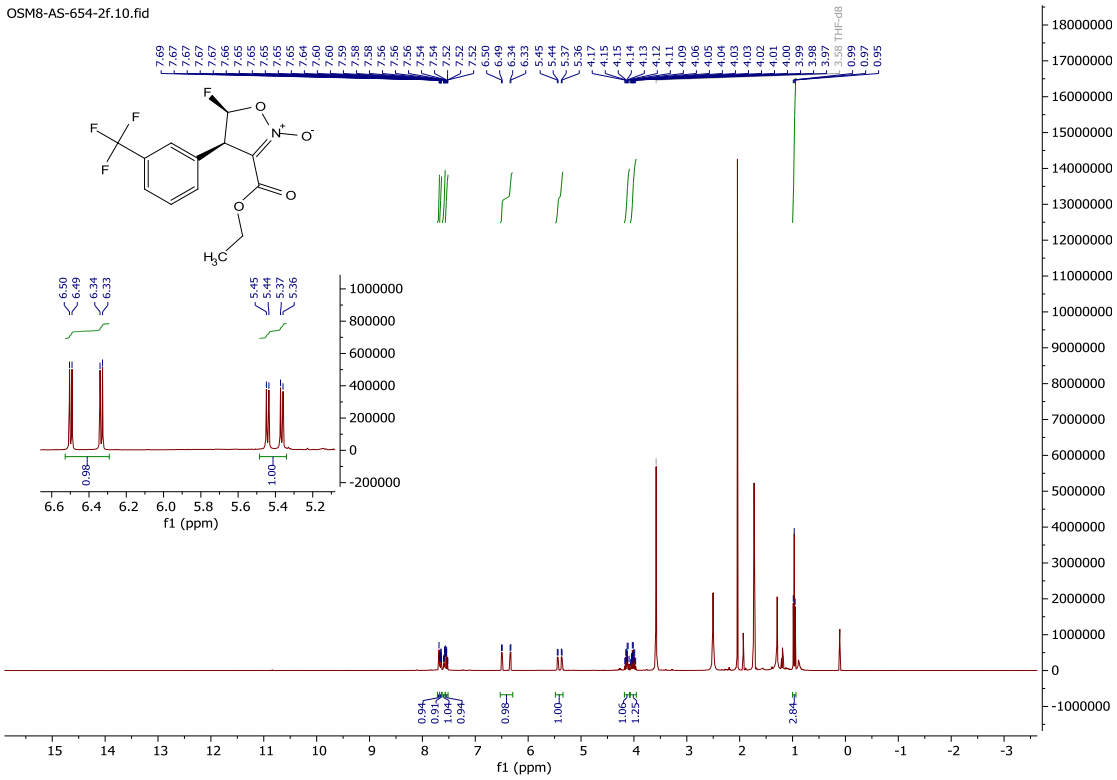


Compound (*cis*-**3m**) ^{1}H-NMR spectra (400 MHz, THF-d8)



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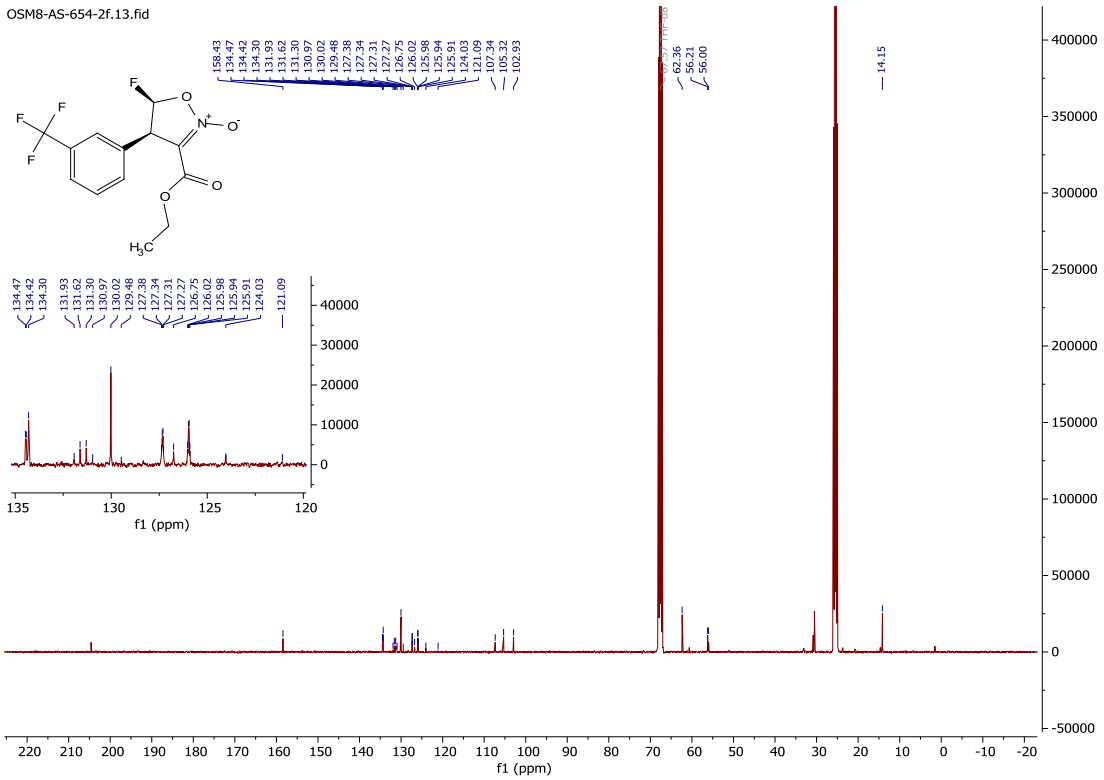

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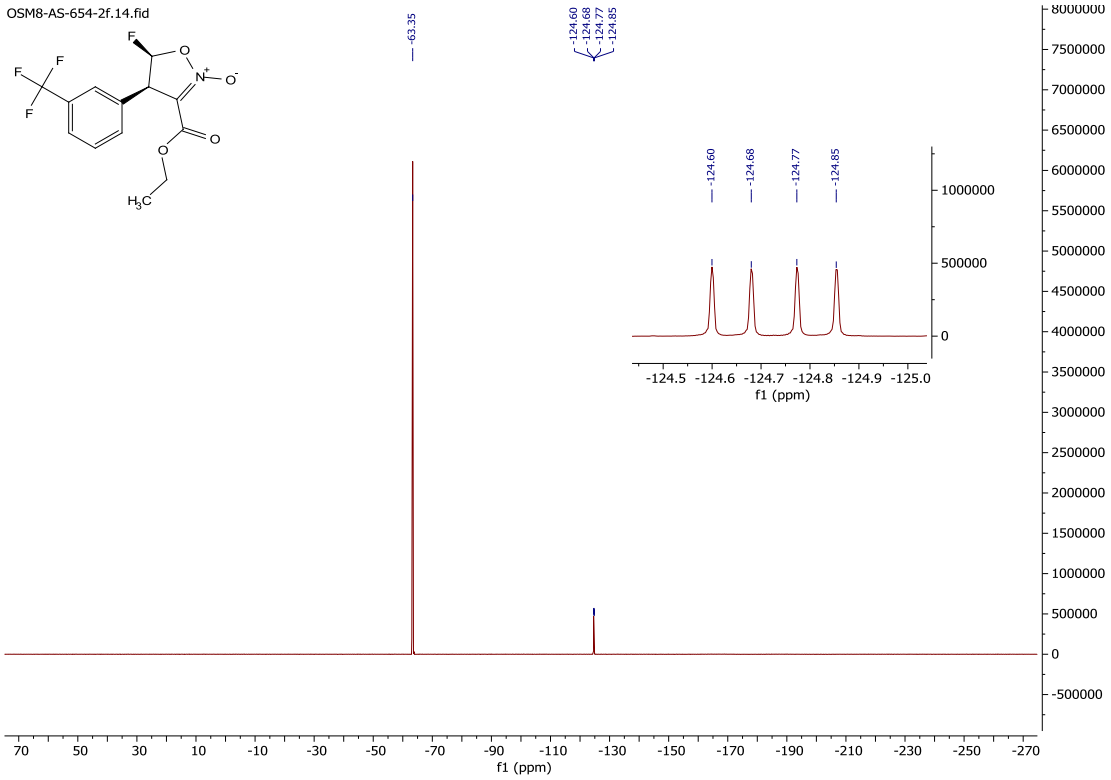
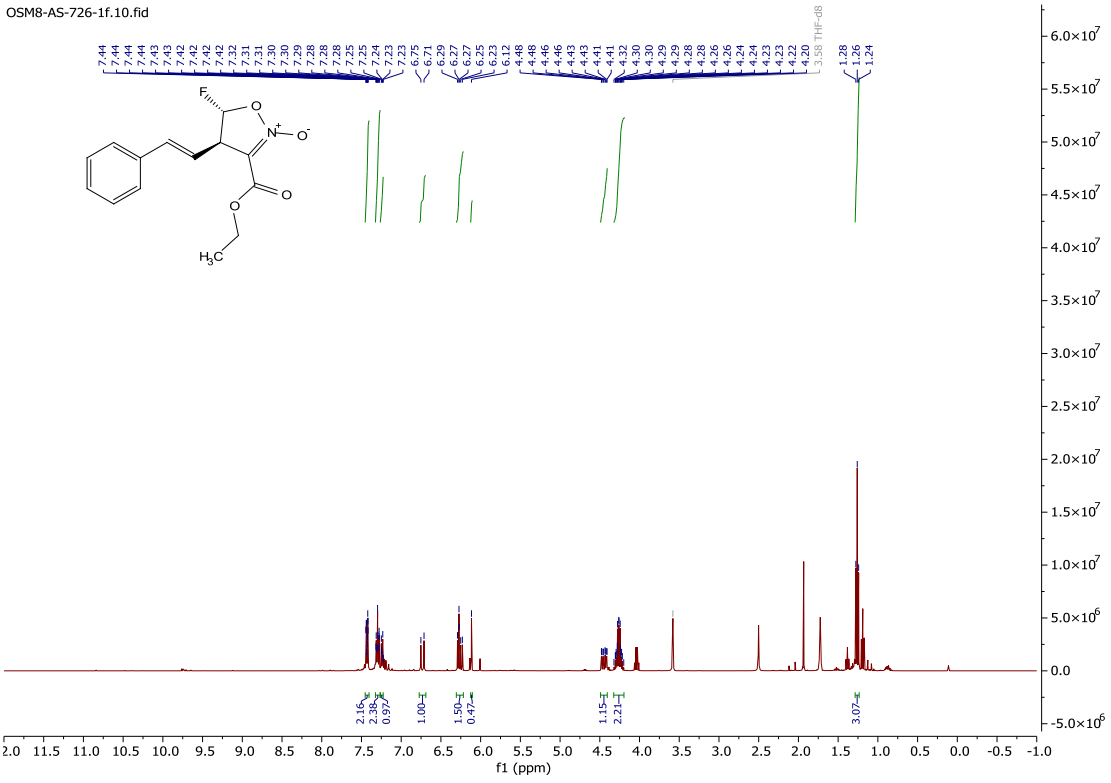
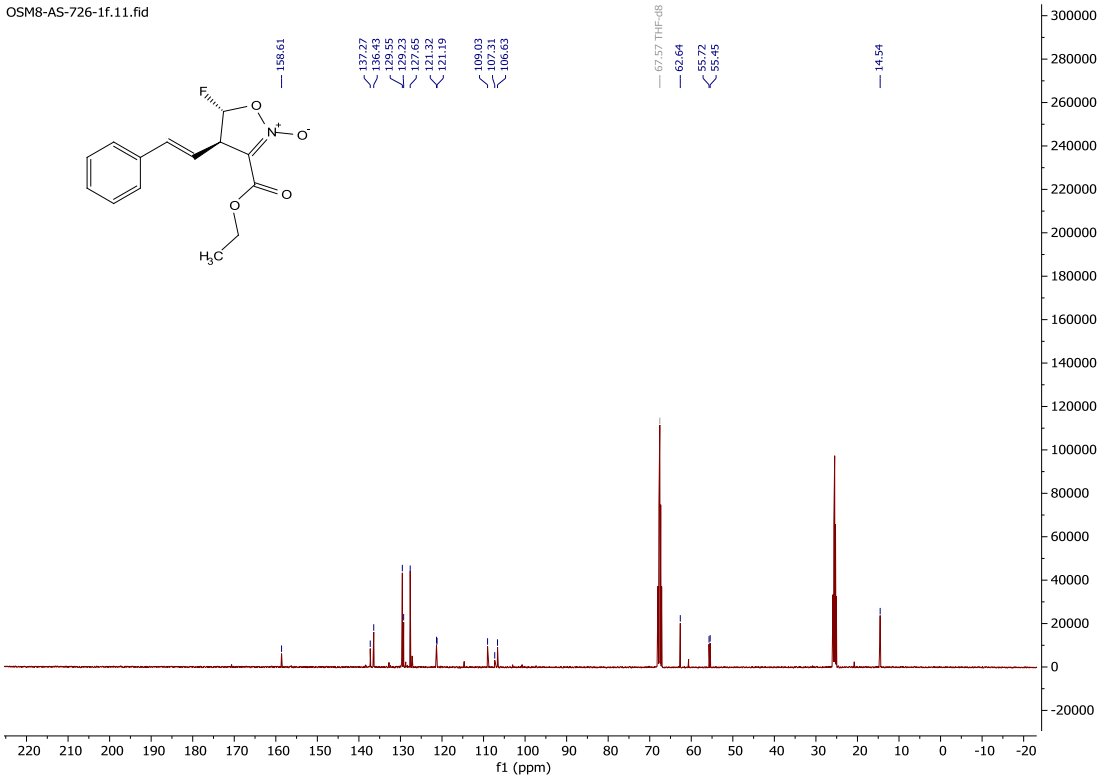


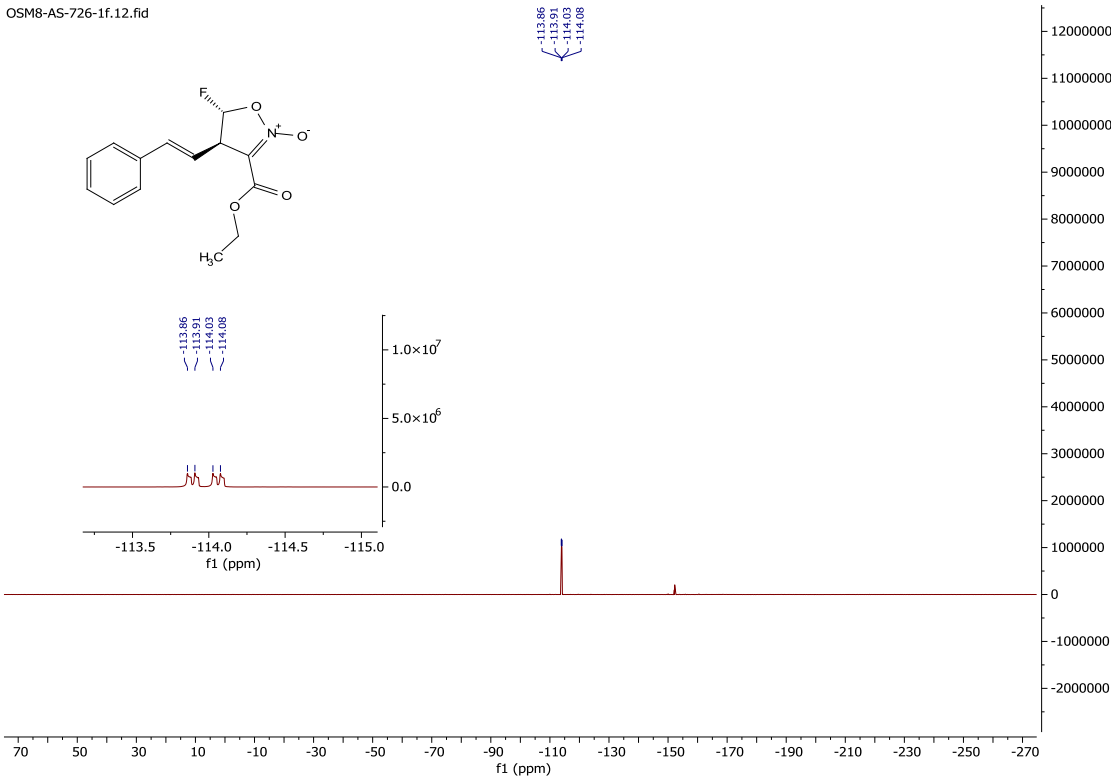
Compound (*trans*-**3n**) ^{1}H-NMR spectra (400 MHz, $CDCl_3$)



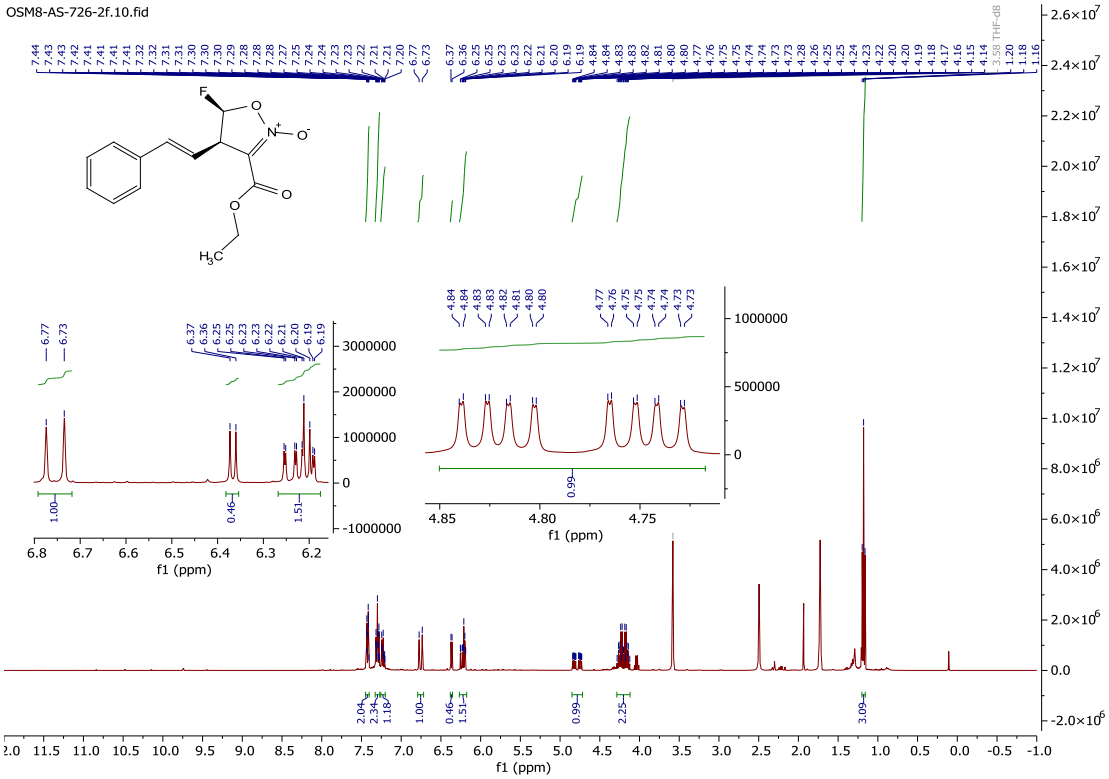
Compound (*trans*-**3n**) ^{13}C-NMR spectra (101 MHz, $CDCl_3$)



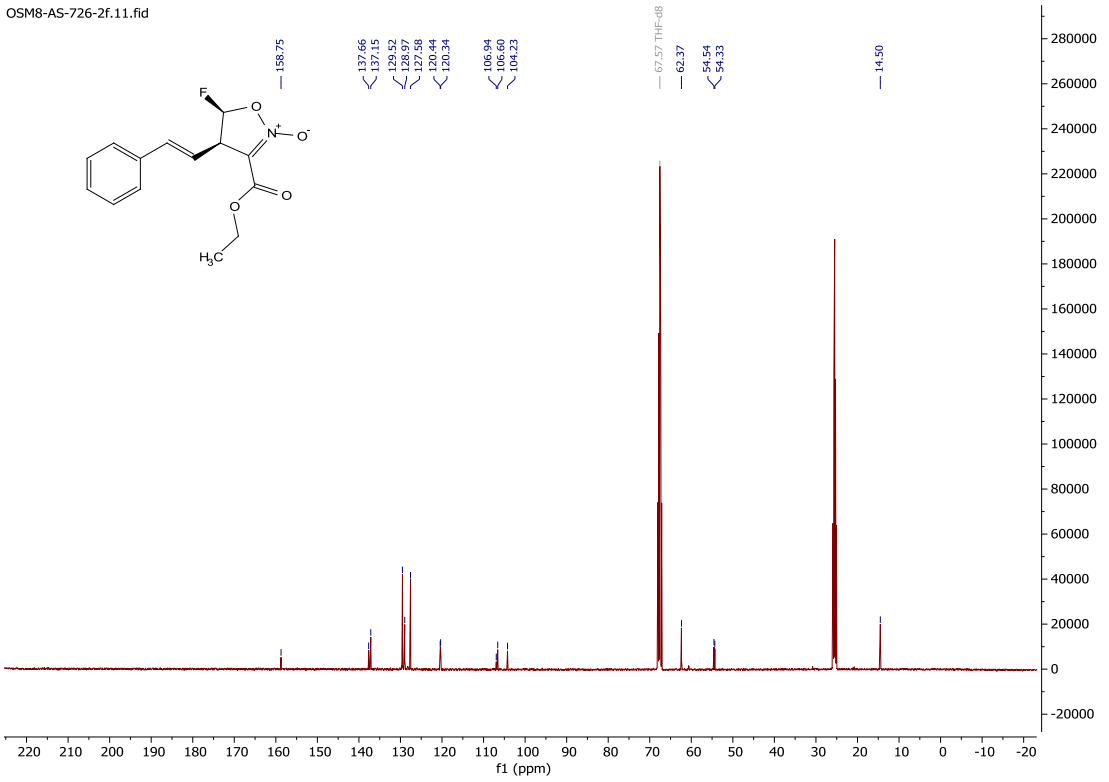
Compound (*trans*-**3n**) ^{19}F-NMR spectra (376 MHz, $CDCl_3$)



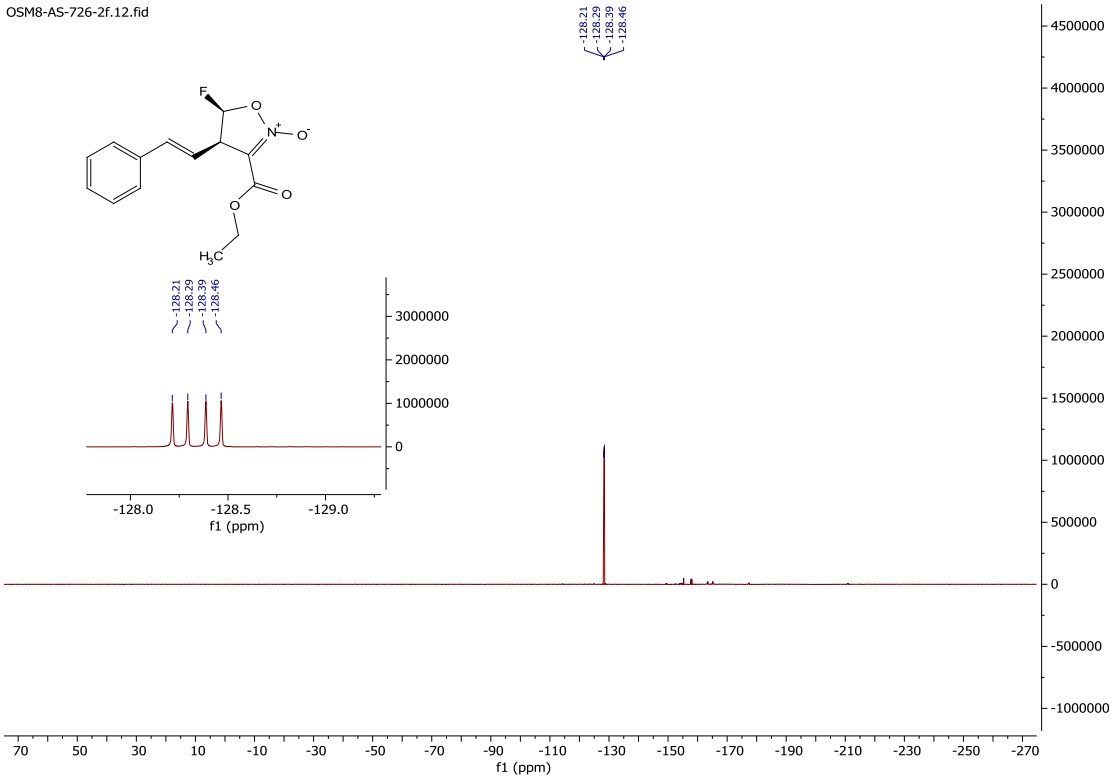
Compound (*cis*-**3n**) ^{1}H-NMR spectra (400 MHz, $CDCl_3$)



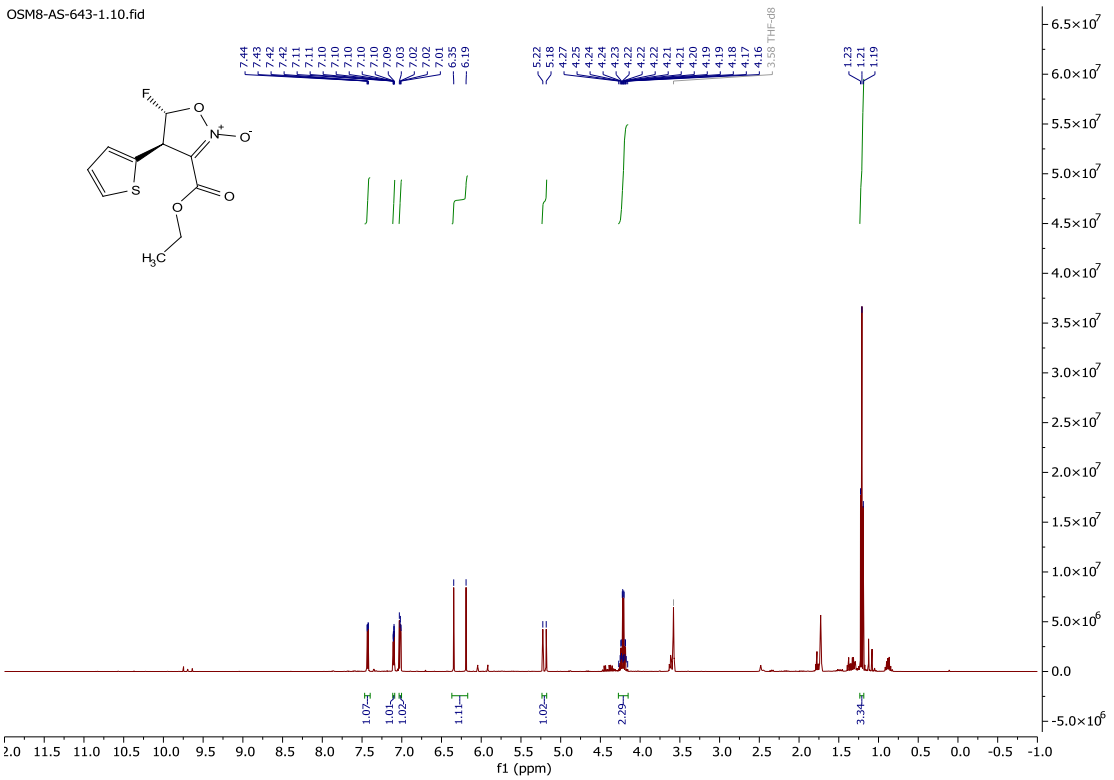
Compound (*cis*-**3n**) ^{13}C-NMR spectra (101 MHz, $CDCl_3$)



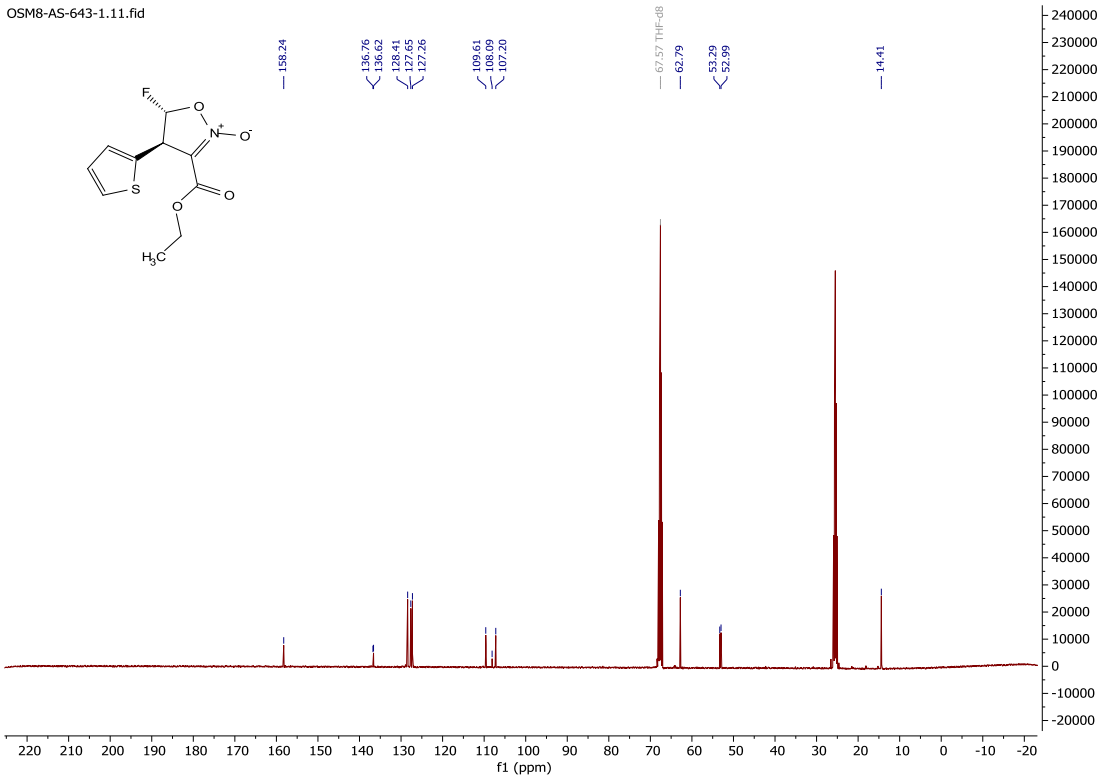
Compound (*cis*-**3n**) ^{19}F-NMR spectra (376 MHz, $CDCl_3$)



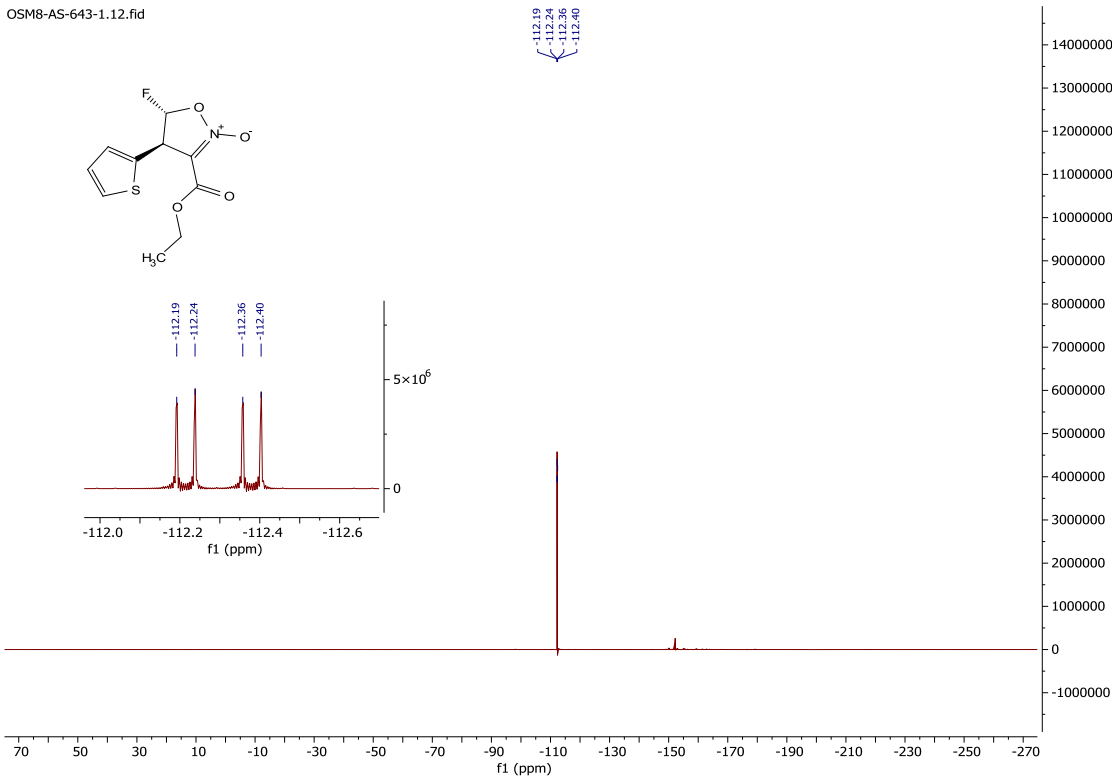
Compound (*trans*-**3o**) ^{1}H-NMR spectra (400 MHz, THF-d8)



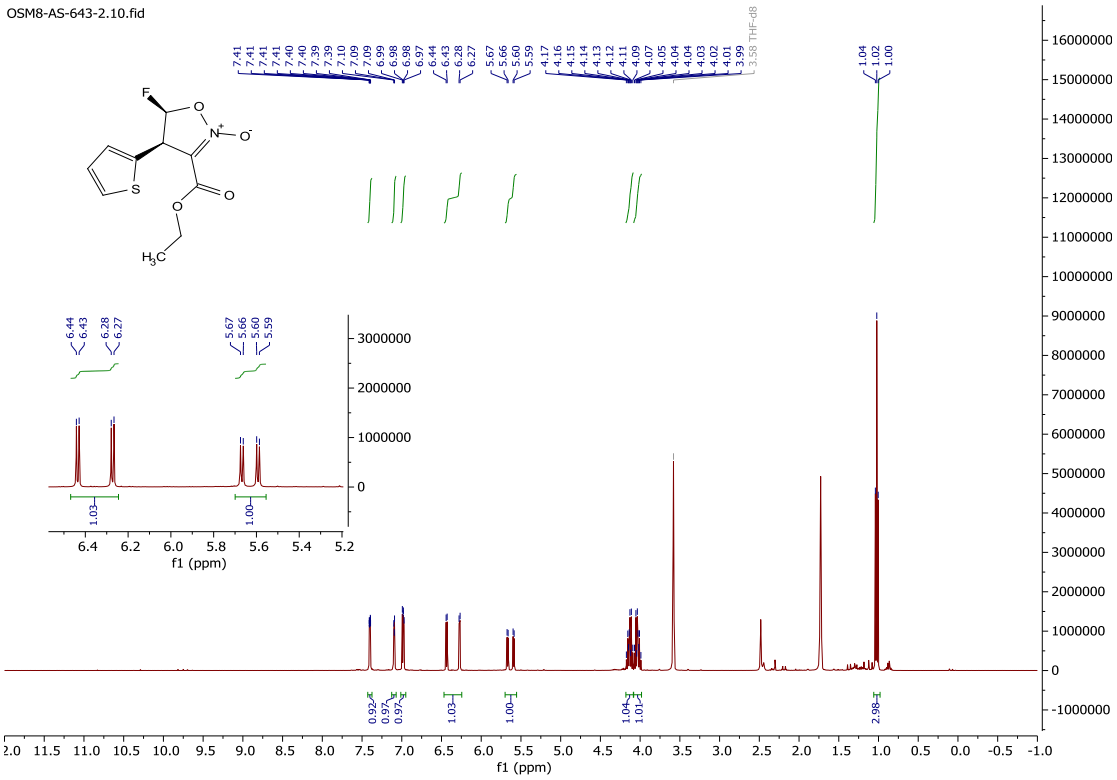
Compound (*trans*-**3o**) ^{13}C-NMR spectra (101 MHz, THF-d8)



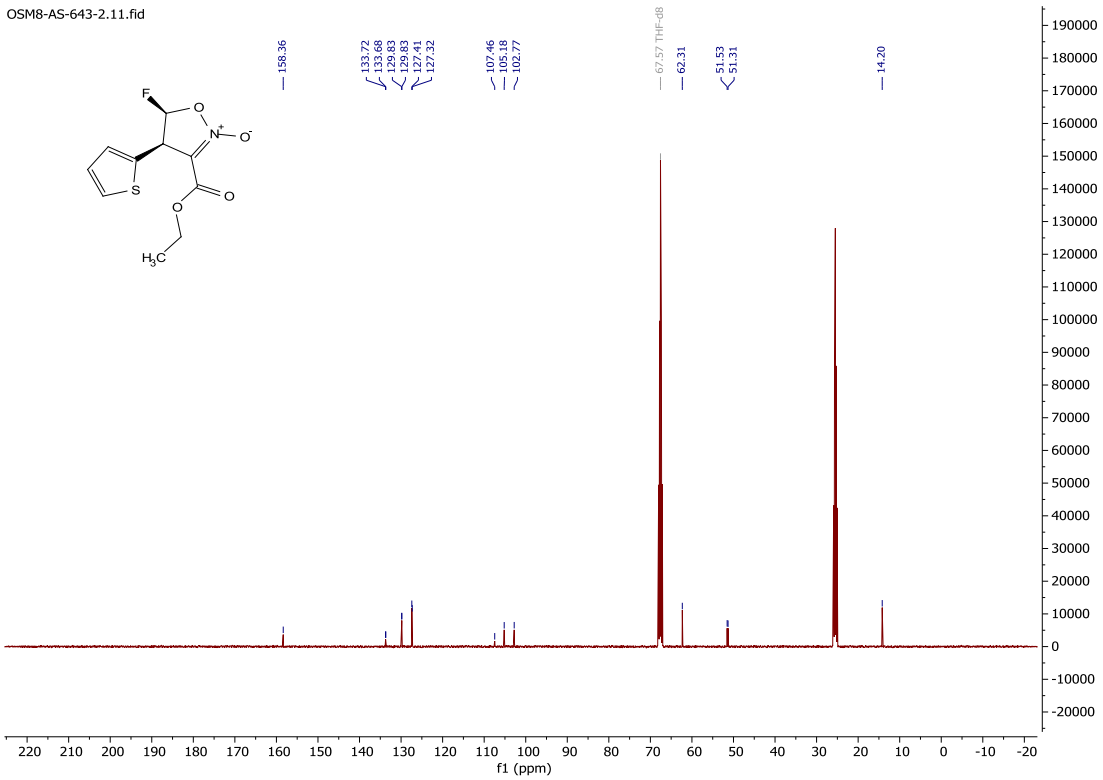
Compound (*trans*-**3o**)^{19}F-NMR spectra (376 MHz, THF-d8)



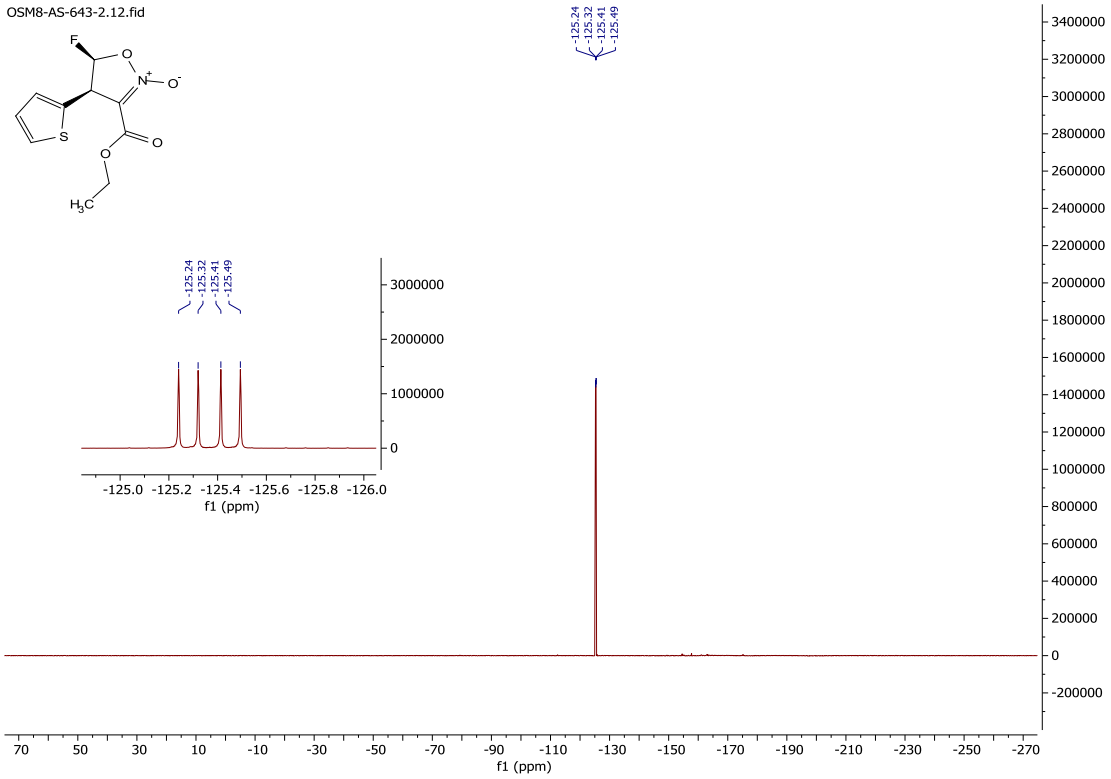
Compound (*cis*-**3o**) ^{1}H-NMR spectra (400 MHz, THF-d8)



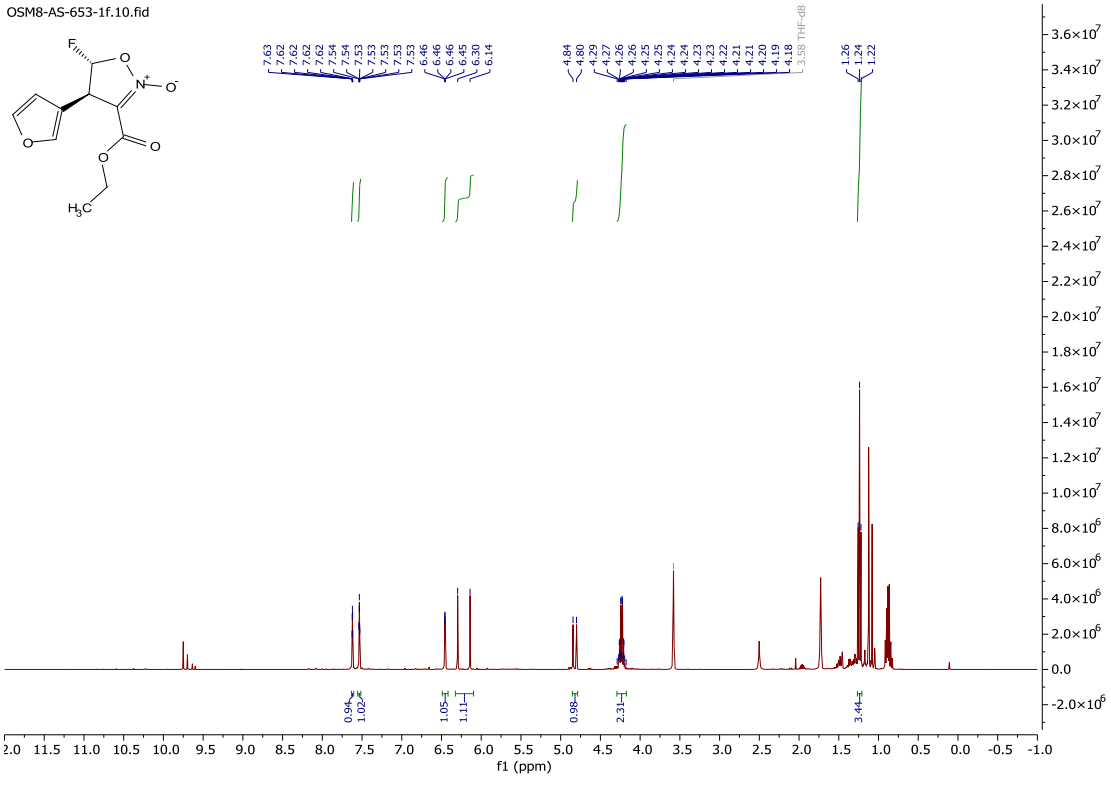
Compound (*cis*-**3o**) ^{13}C-NMR spectra (101 MHz, THF-d8)



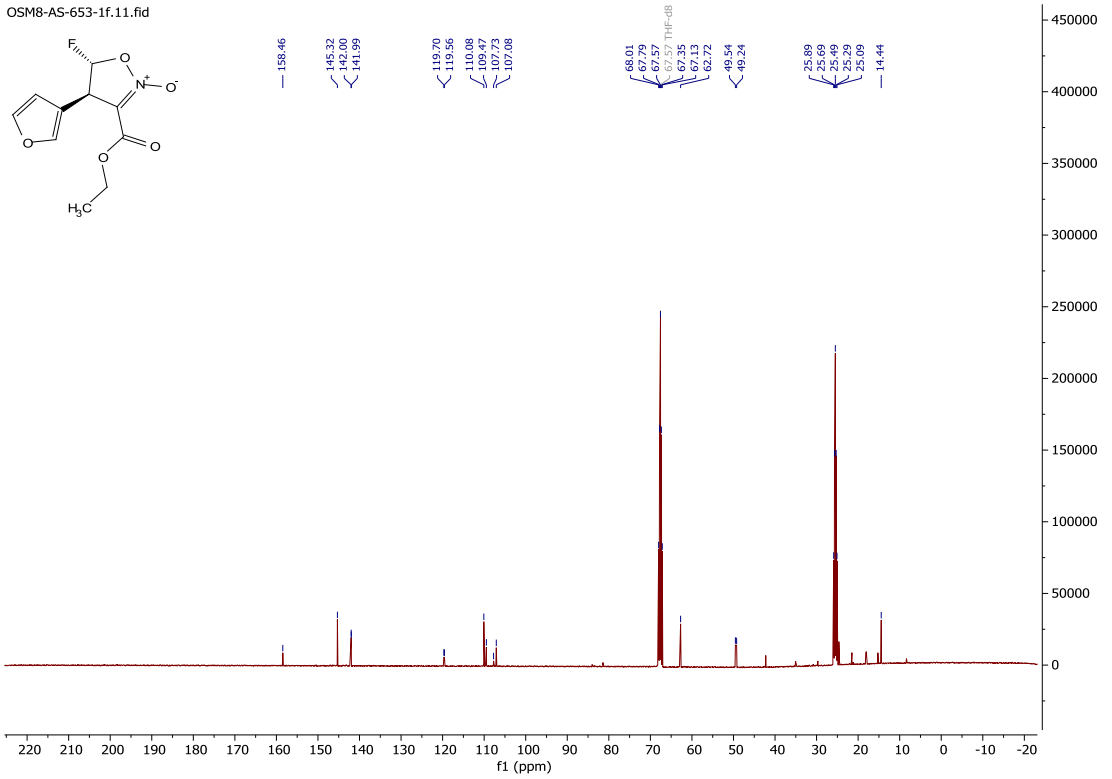
Compound (*cis*-**3o**)^{19}F-NMR spectra (376 MHz, THF-d8)



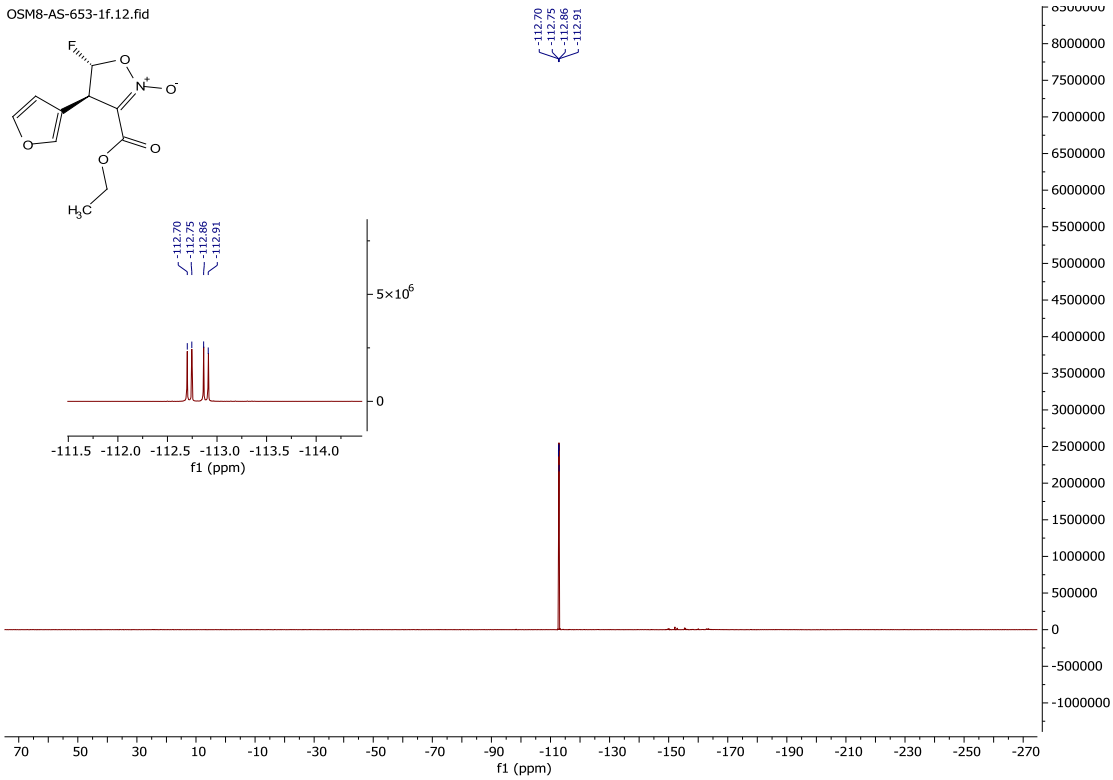
Compound (*trans*-**3p**) ^{1}H-NMR spectra (400 MHz, THF-d8)



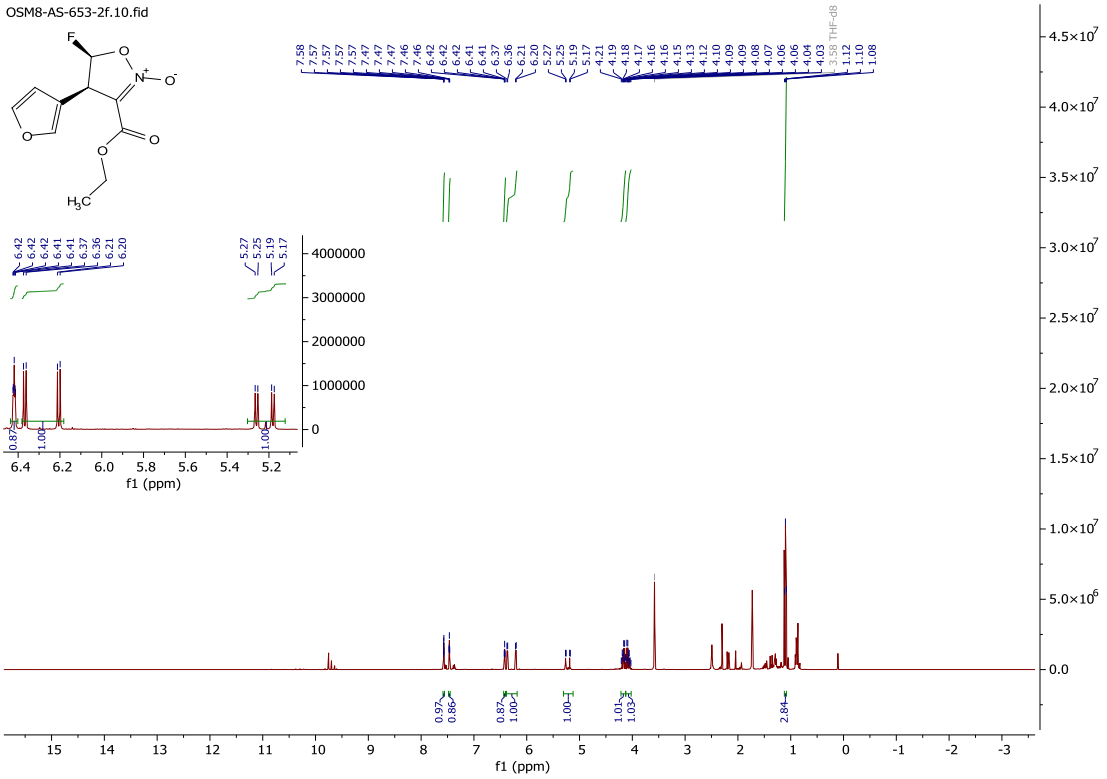
Compound (*trans*-**3p**) ^{13}C-NMR spectra (101 MHz, THF-d8)



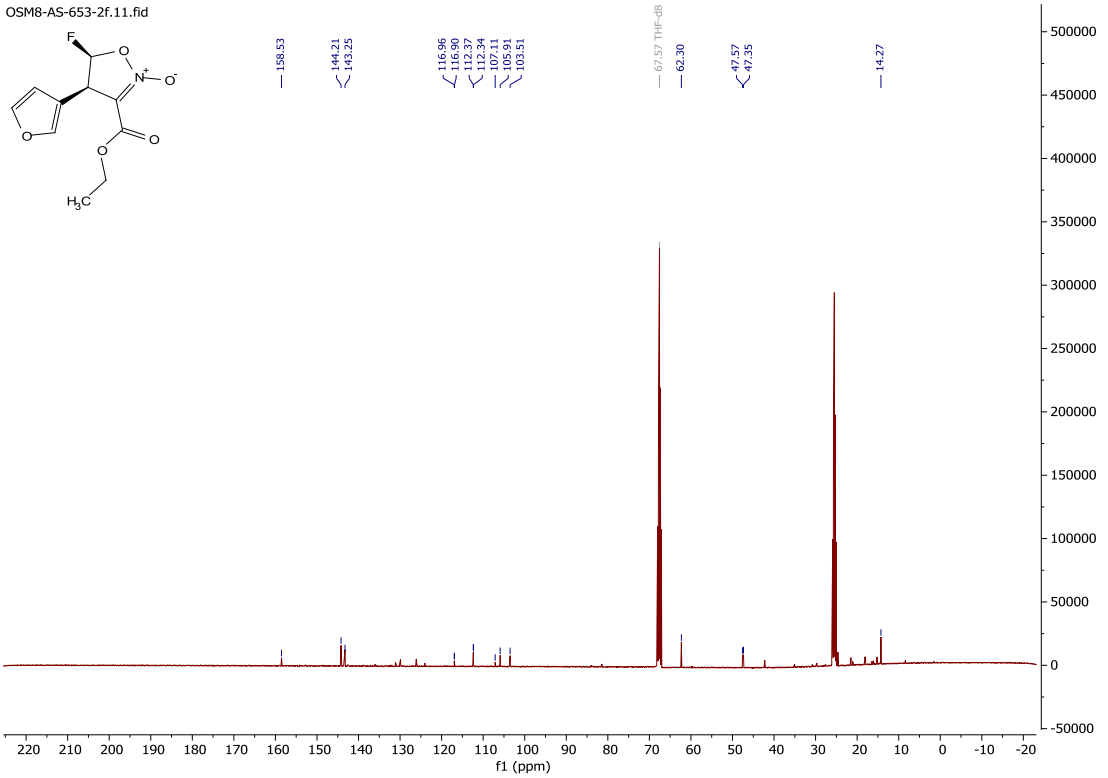
Compound (*trans*-**3p**)^{19}F-NMR spectra (376 MHz, THF-d8)



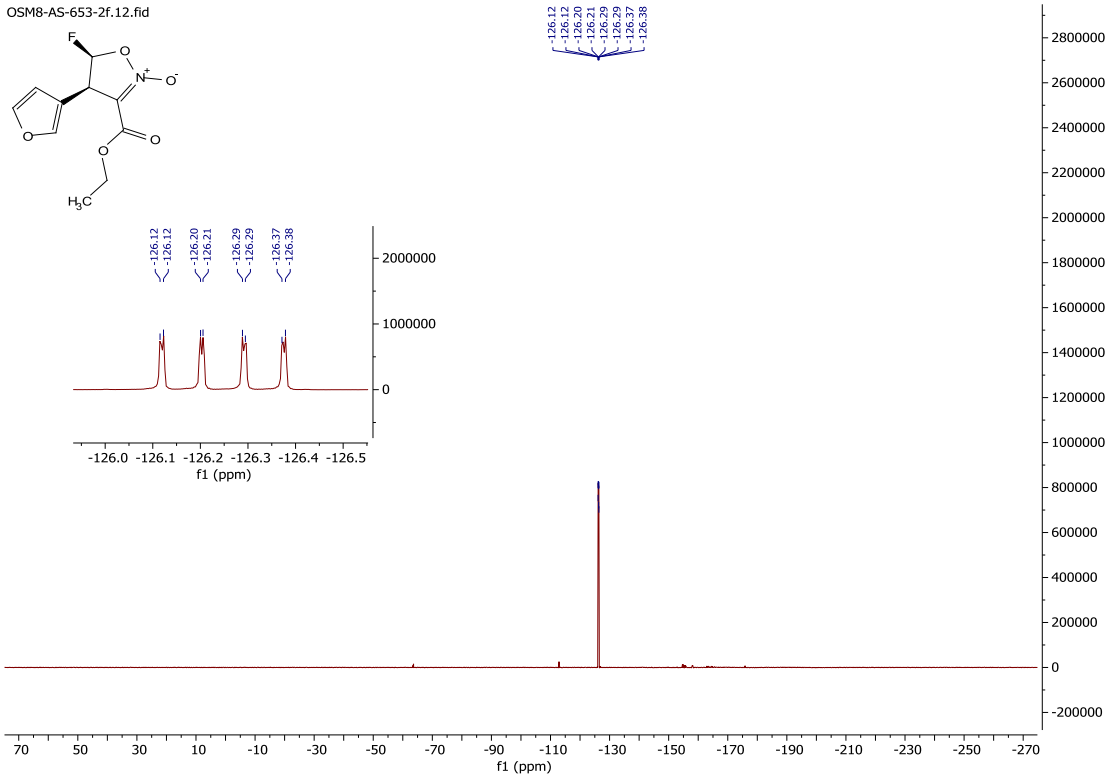
Compound (*cis*-**3p**) ^{1}H-NMR spectra (400 MHz, THF-d8)



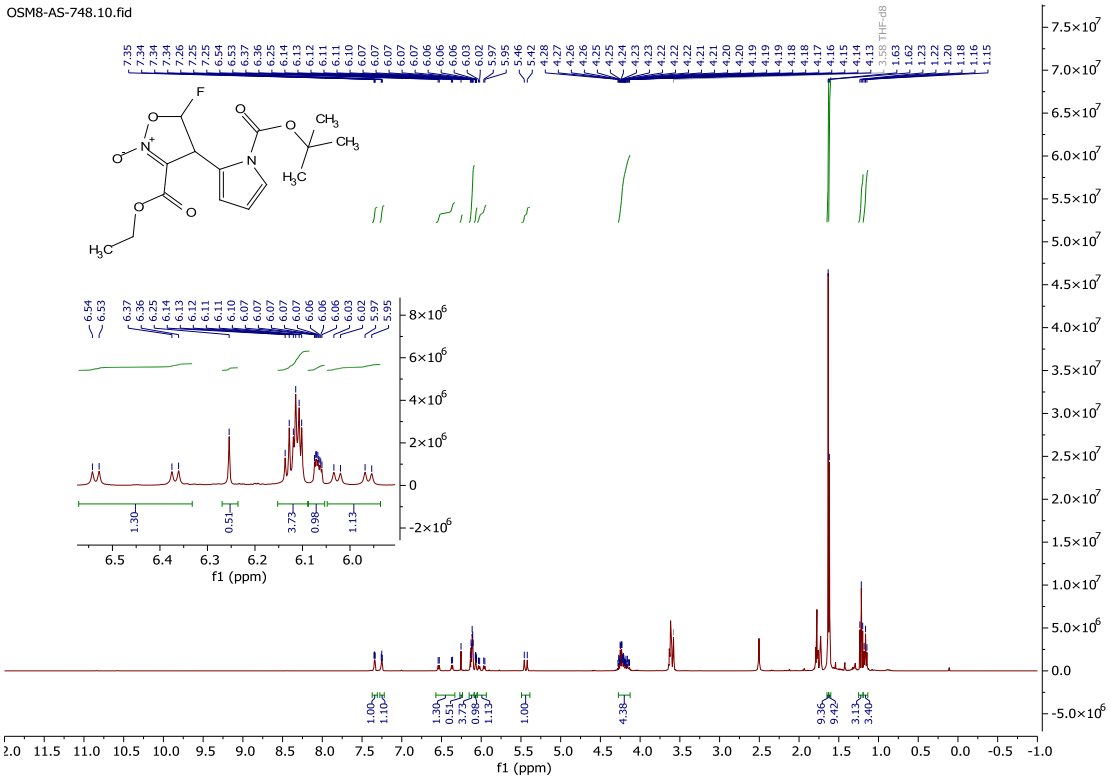
Compound (*cis*-**3p**) ^{13}C-NMR spectra (101 MHz, THF-d8)



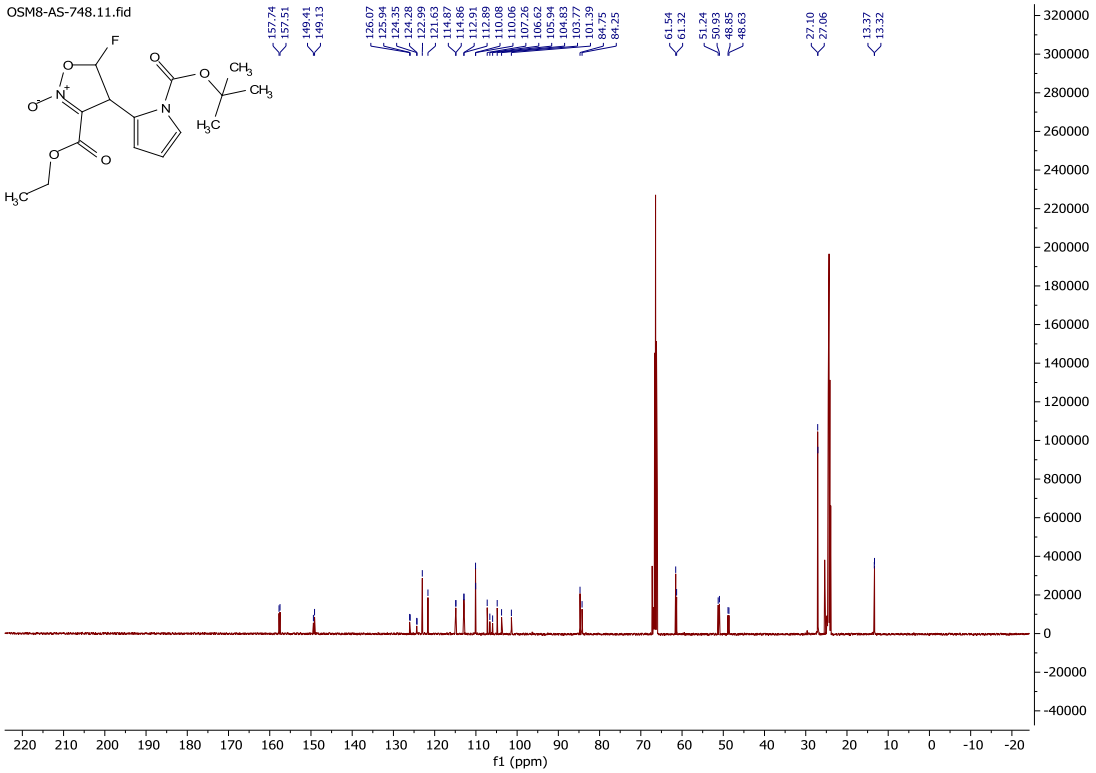
Compound (*cis*-**3p**)^{19}F-NMR spectra (376 MHz, THF-d8)



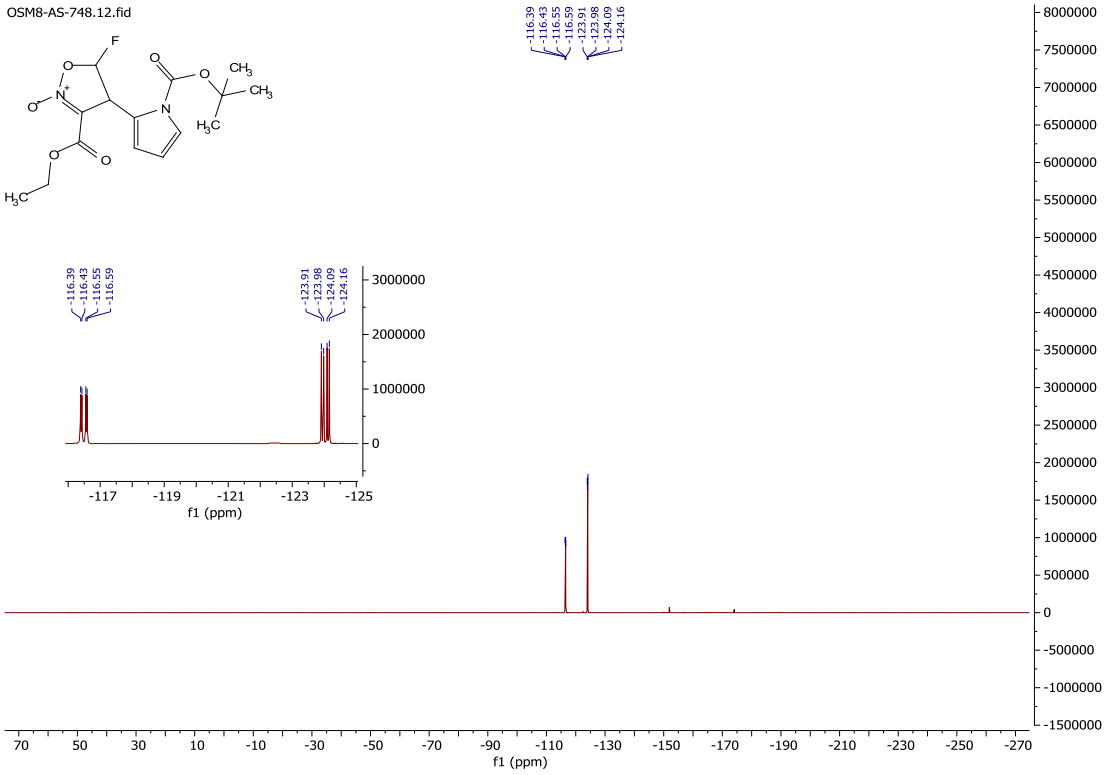
Compound (**3q**) ^{1}H-NMR spectra (400 MHz, THF-d8)



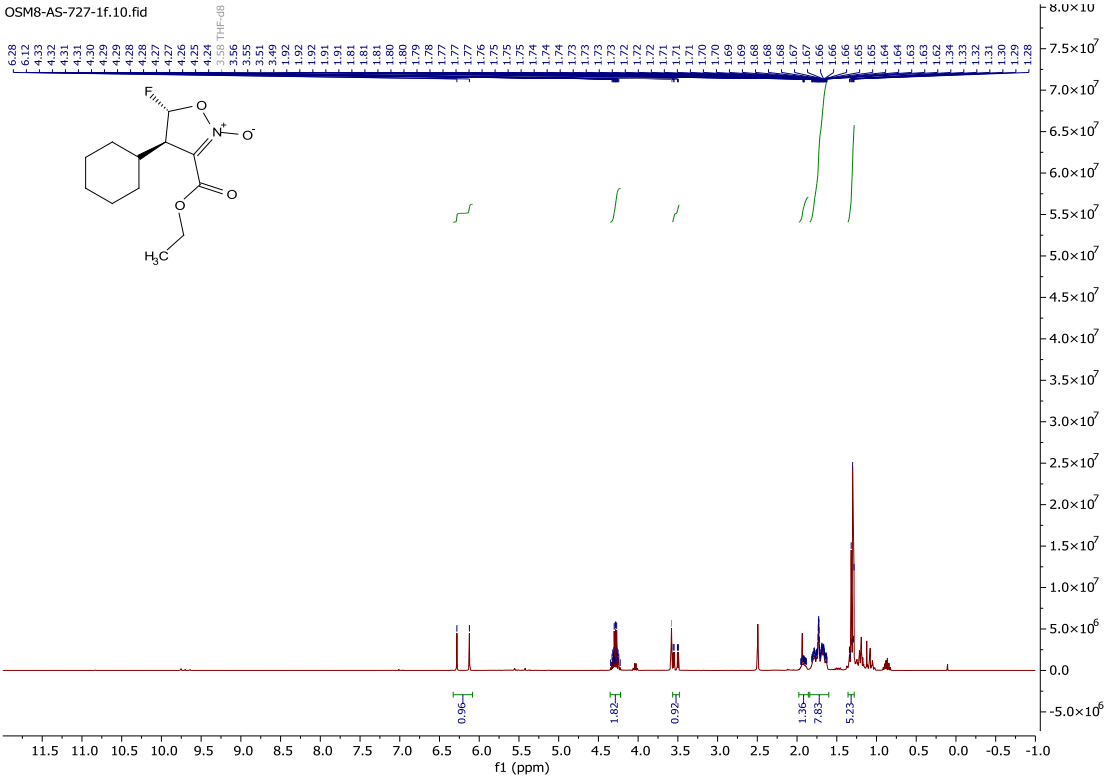
Compound (**3q**) ^{13}C-NMR spectra (101 MHz, THF-d8)



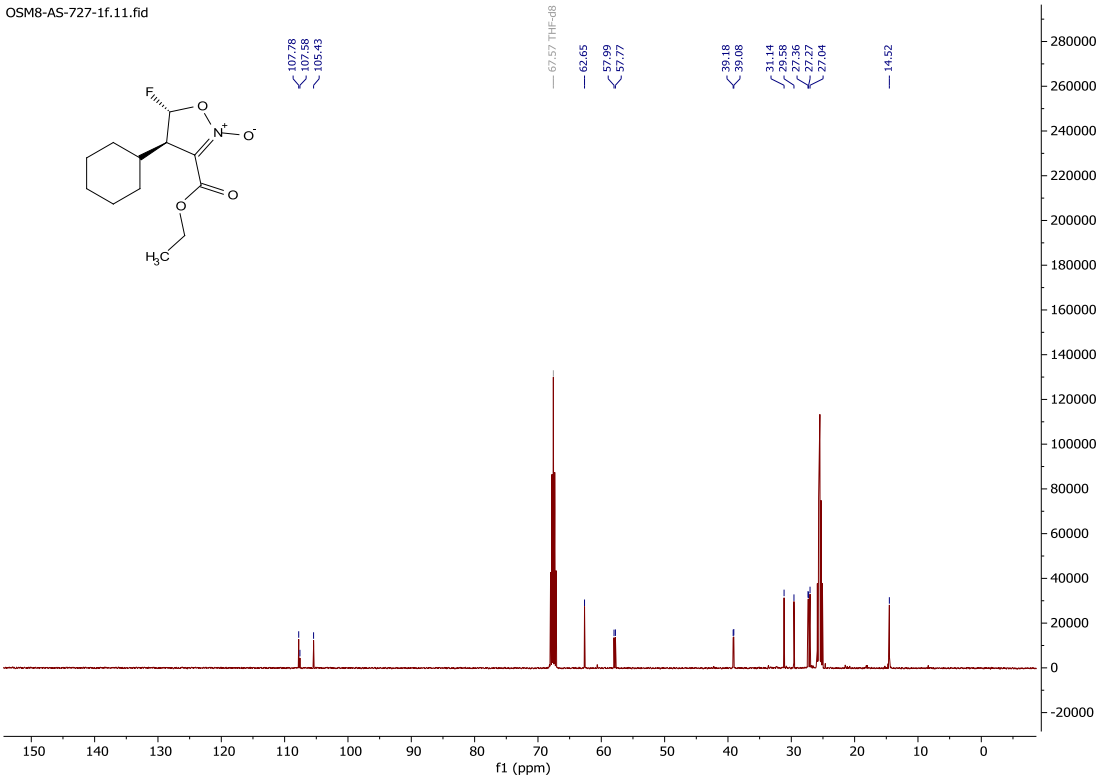
Compound (**3q**) ^{19}F-NMR spectra (376 MHz, THF-d8)



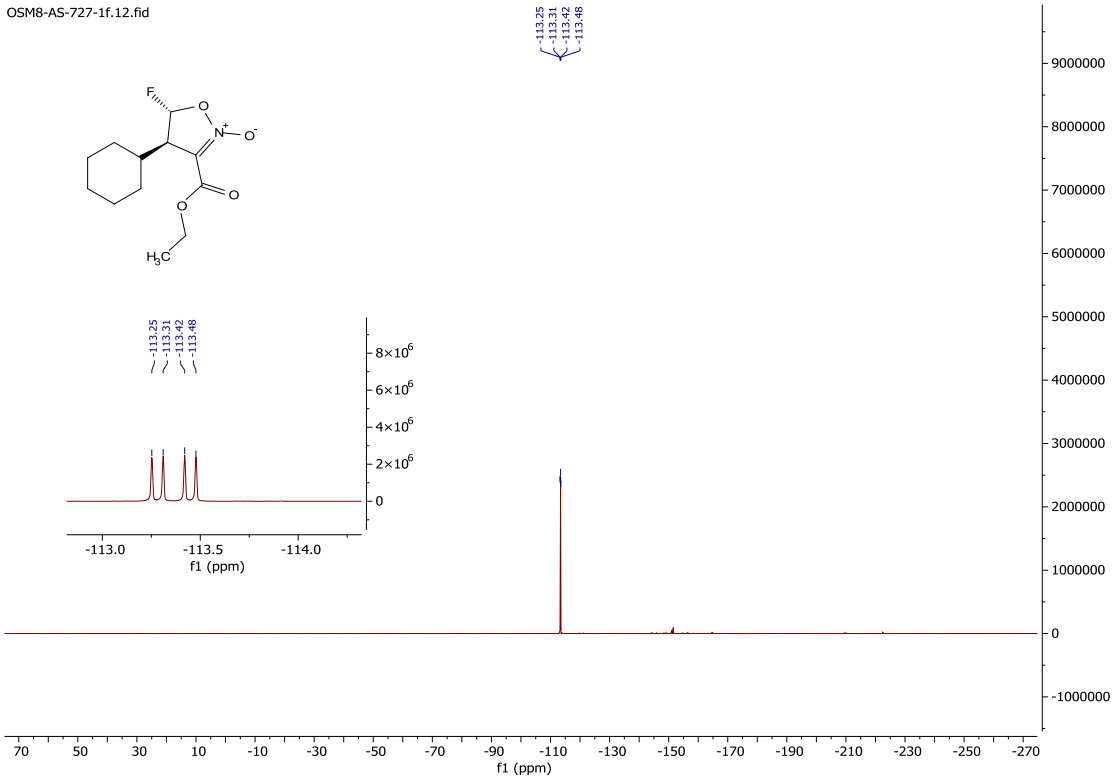
Compound (*trans*-**3r**) ^{1}H-NMR spectra (400 MHz, THF-d8)



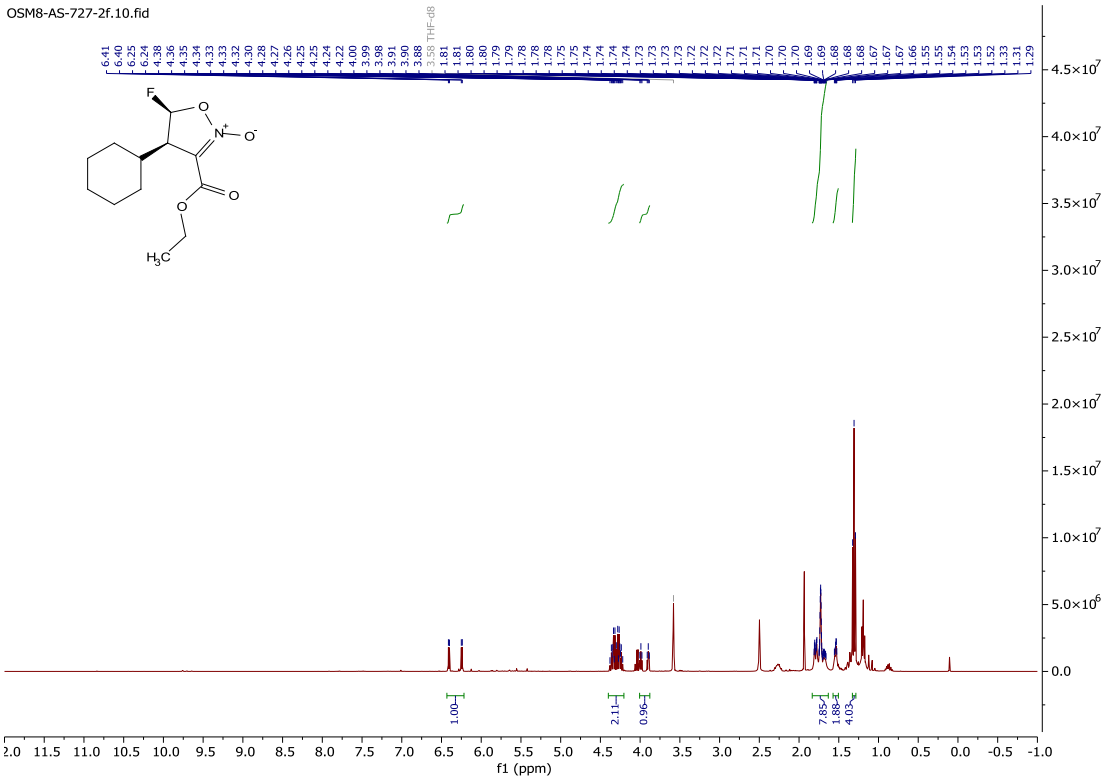
Compound (*trans*-**3r**) ^{13}C-NMR spectra (101 MHz, THF-d8)



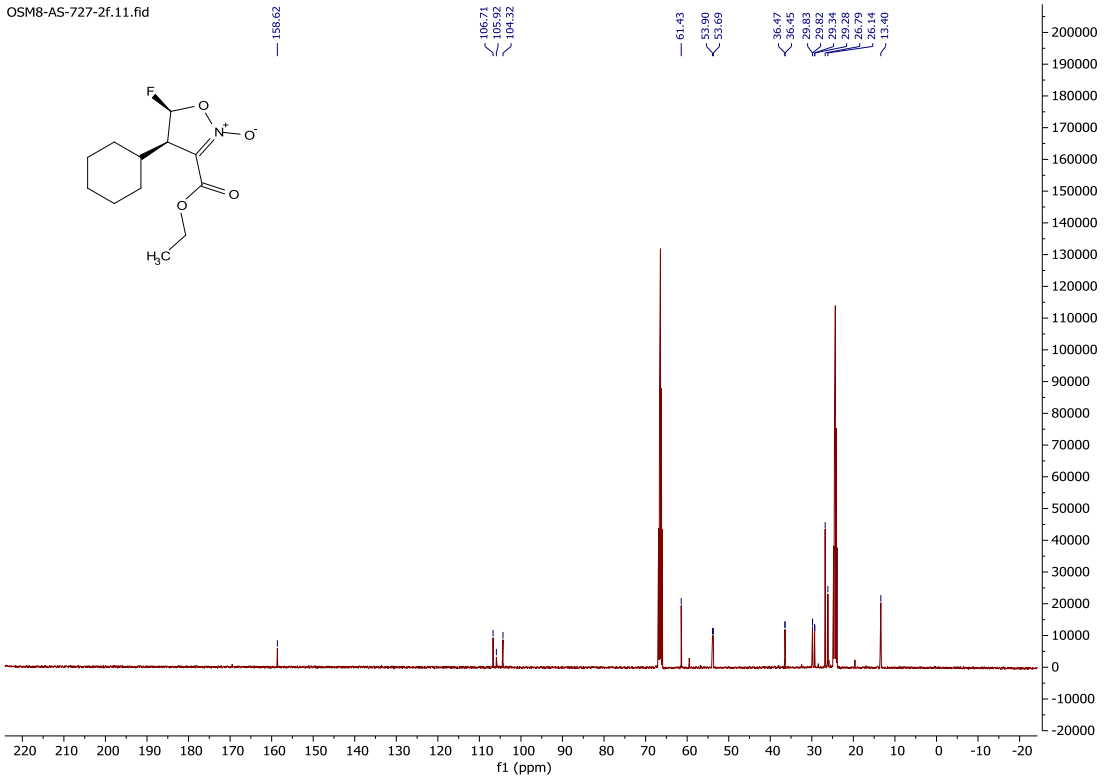
Compound (*trans*-**3r**) ^{19}F-NMR spectra (376 MHz, THF-d8)



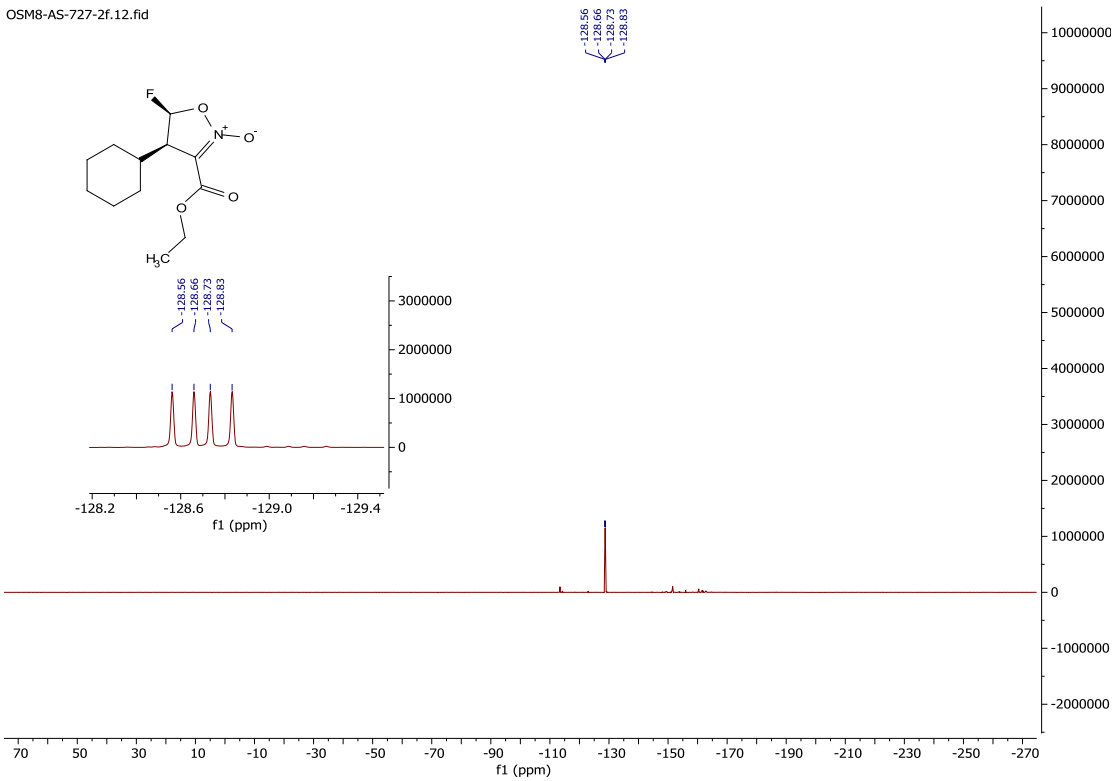
Compound (*cis*-**3r**) ^{1}H-NMR spectra (400 MHz, THF-d8)



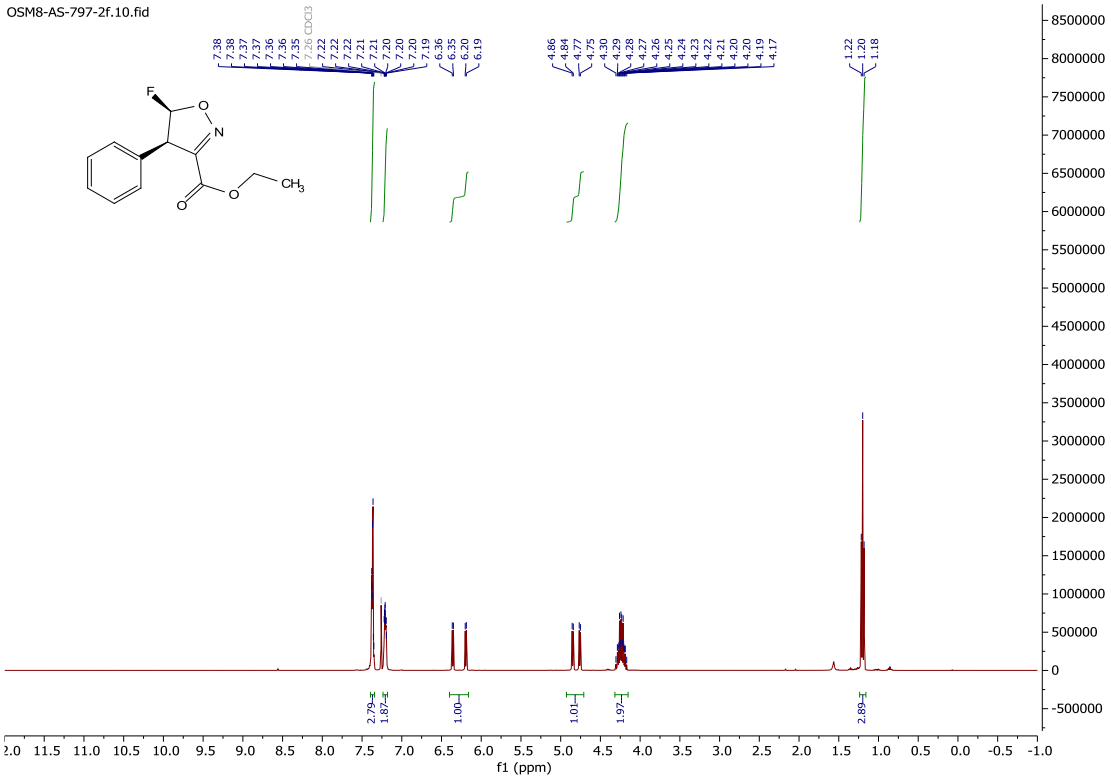
Compound (*cis*-**3r**) ^{13}C-NMR spectra (101 MHz, THF-d8)



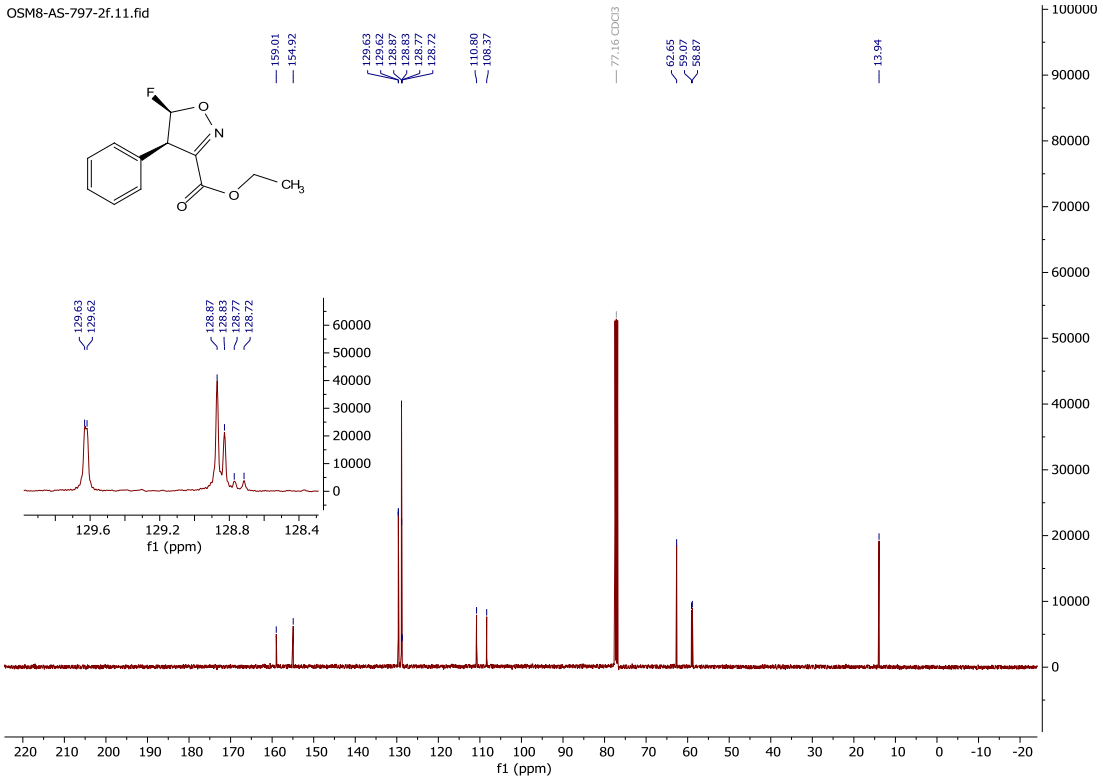
Compound (*cis*-**3r**) ^{19}F-NMR spectra (376 MHz, THF-d8)



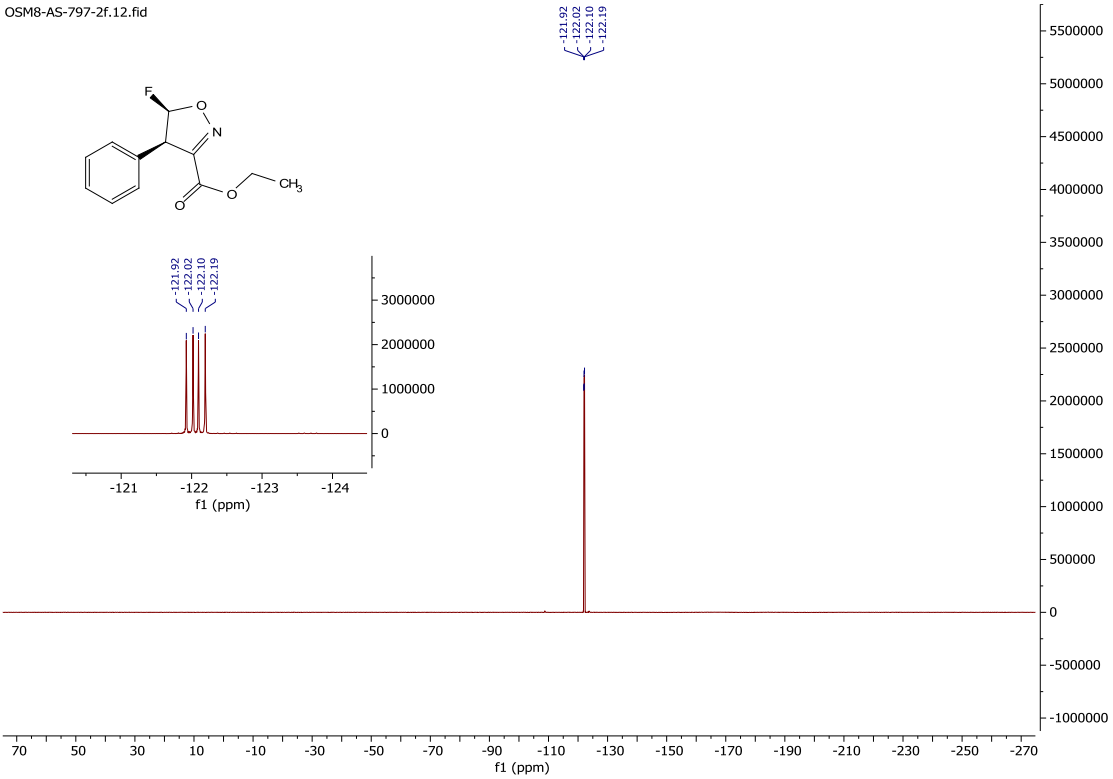
Compound (*cis*-**4a**) ^{1}H-NMR spectra (400 MHz, $CDCl_3$)



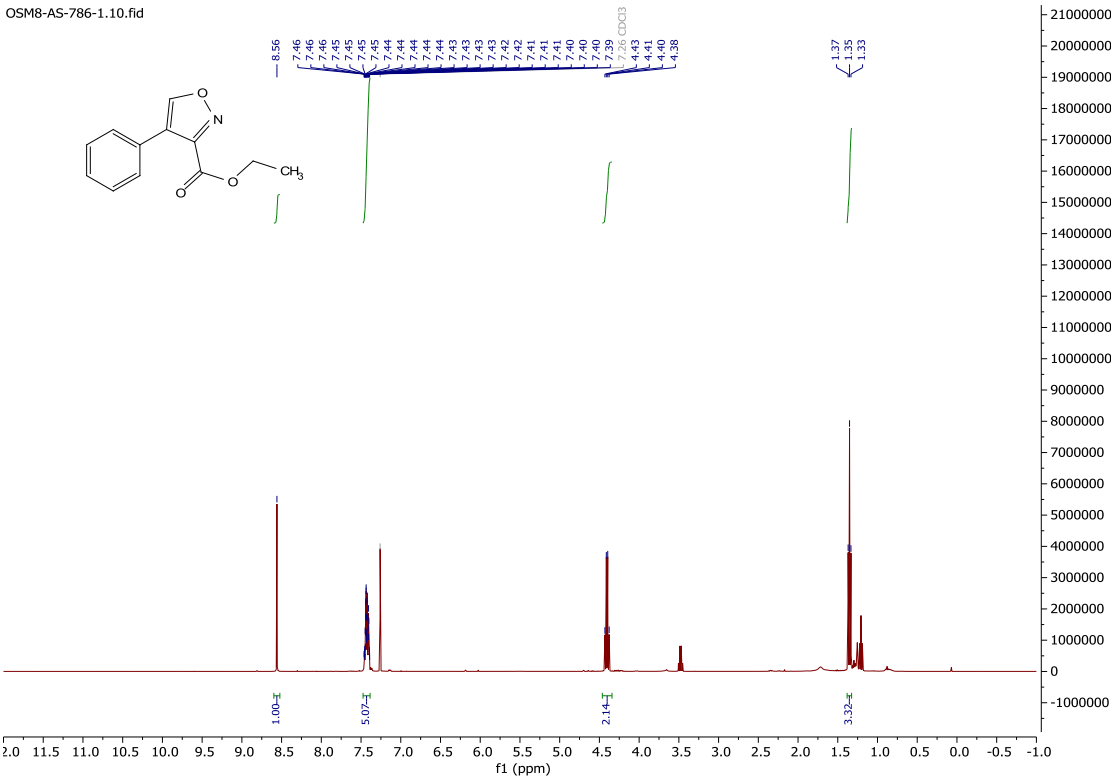
Compound (*cis*-**4a**) ^{13}C-NMR spectra (101 MHz, $CDCl_3$)



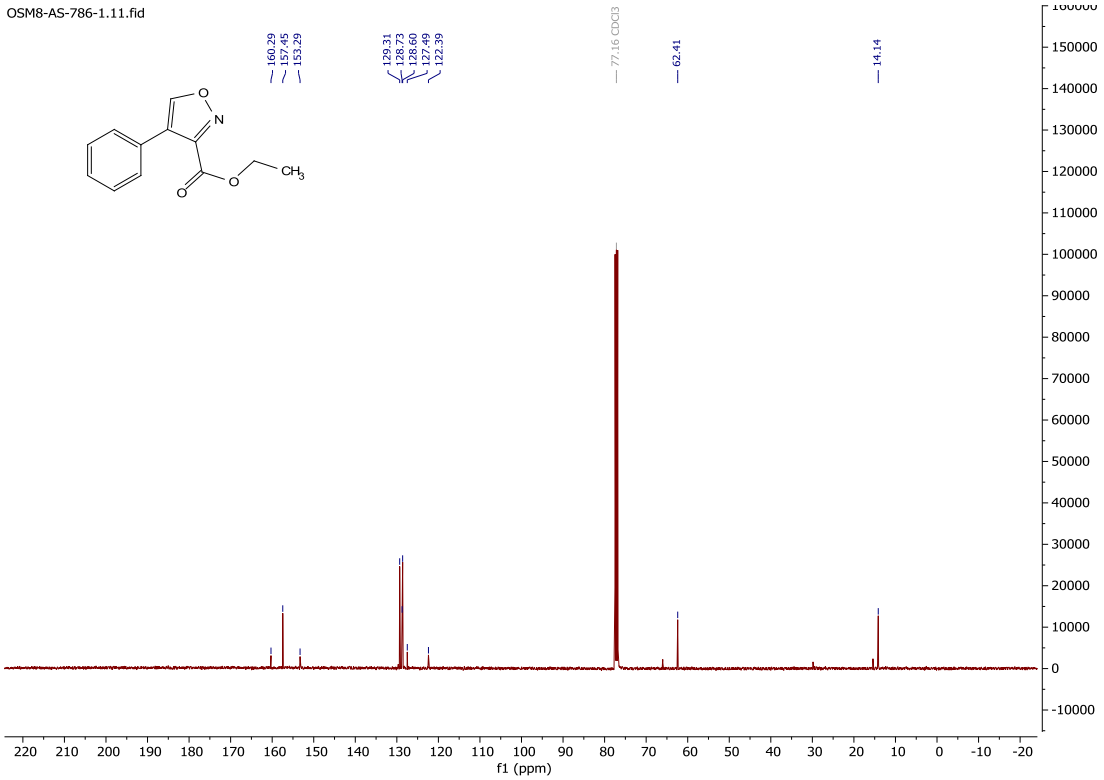
Compound (*cis*-**4a**) ^{19}F-NMR spectra (376 MHz, $CDCl_3$)



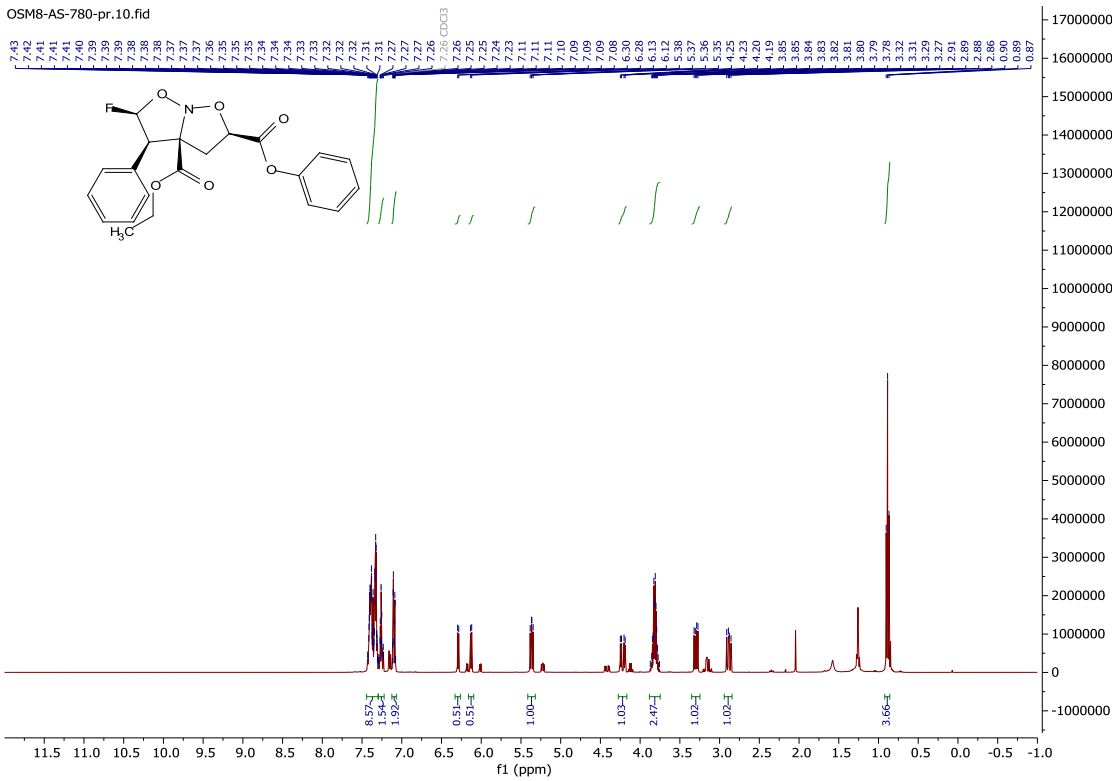
Compound (**5**) ^{1}H-NMR spectra (400 MHz, $CDCl_3$)



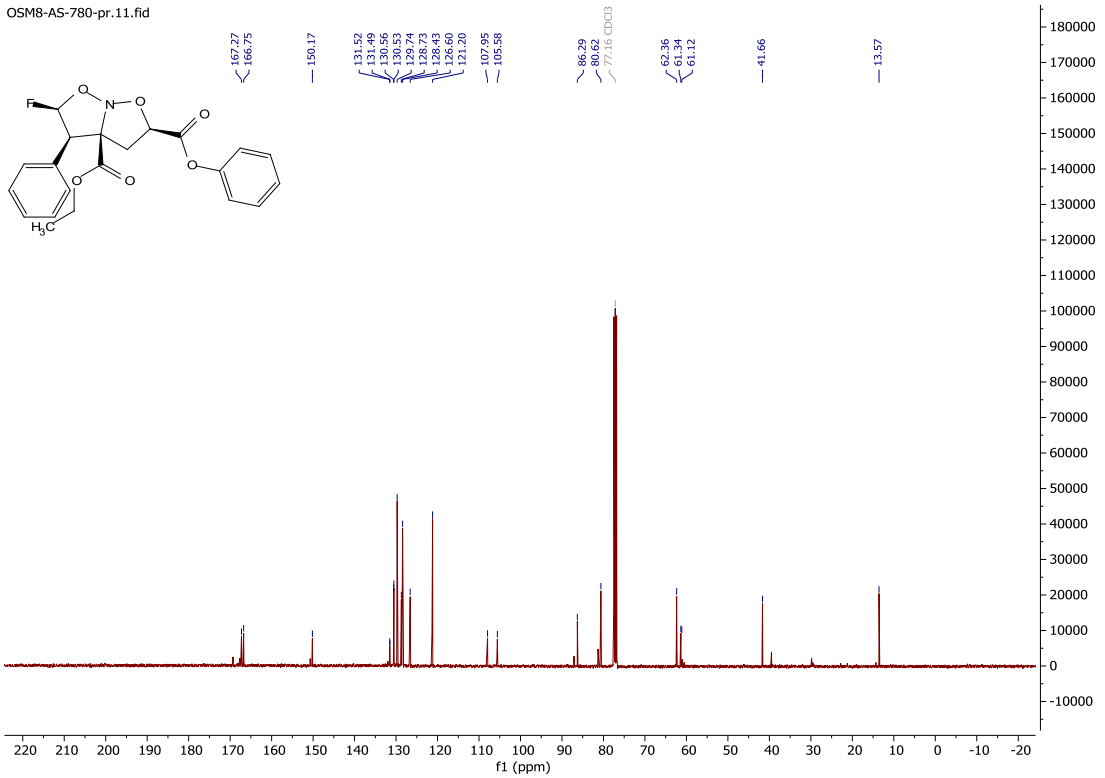
Compound (**5**) ^{13}C-NMR spectra (101 MHz, $CDCl_3$)



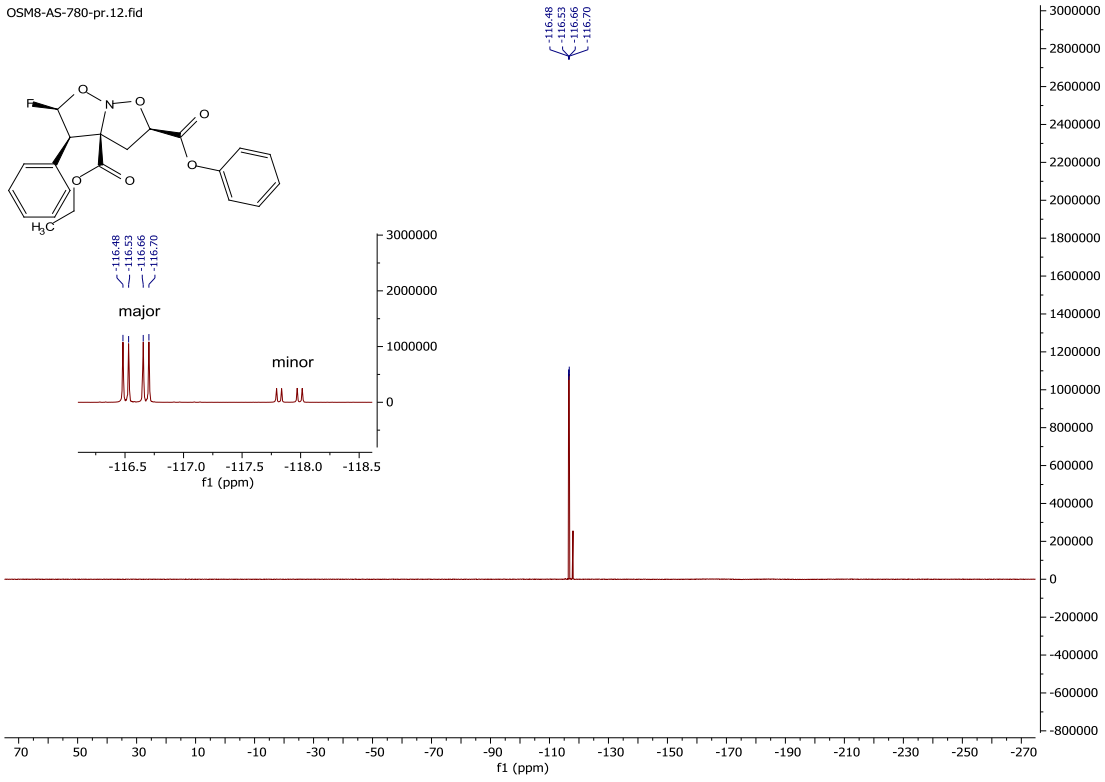
Compound (**7**) ^{1}H-NMR spectra (400 MHz, $CDCl_3$)



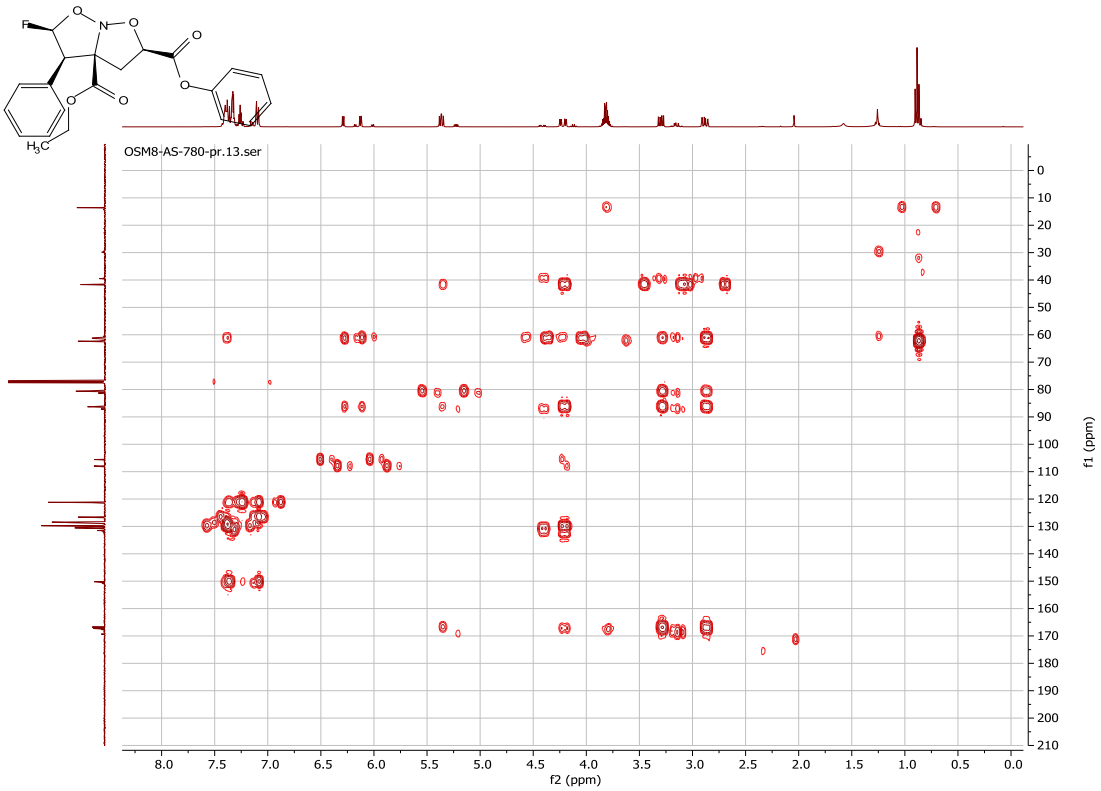
Compound (**7**) ^{13}C-NMR spectra (101 MHz, $CDCl_3$)



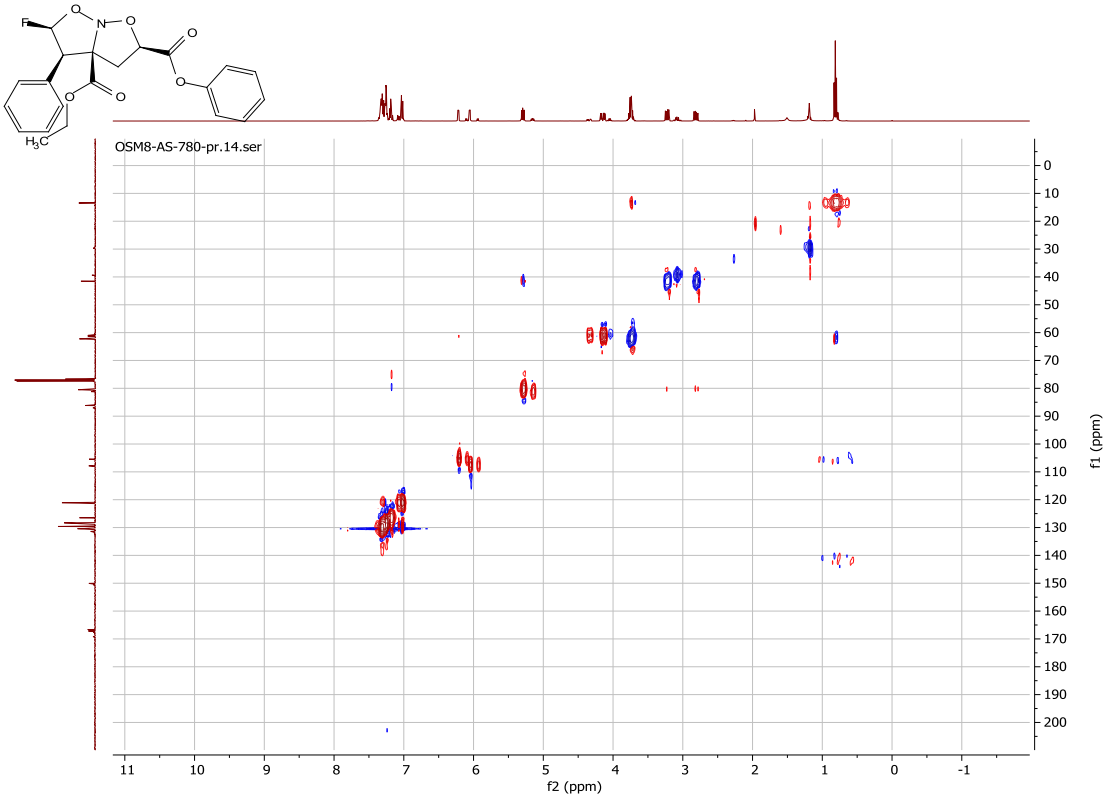
Compound (**7**) ^{19}F-NMR spectra (376 MHz, $CDCl_3$)



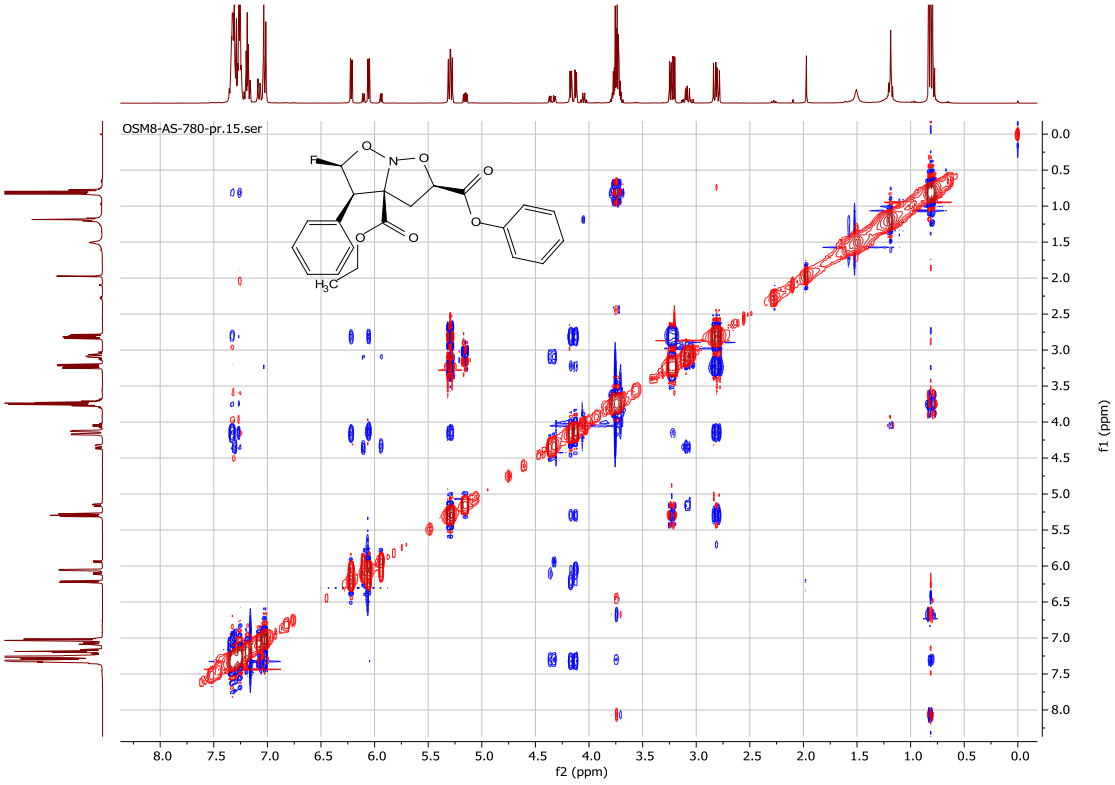
Compound (**7**) HMBC spectra



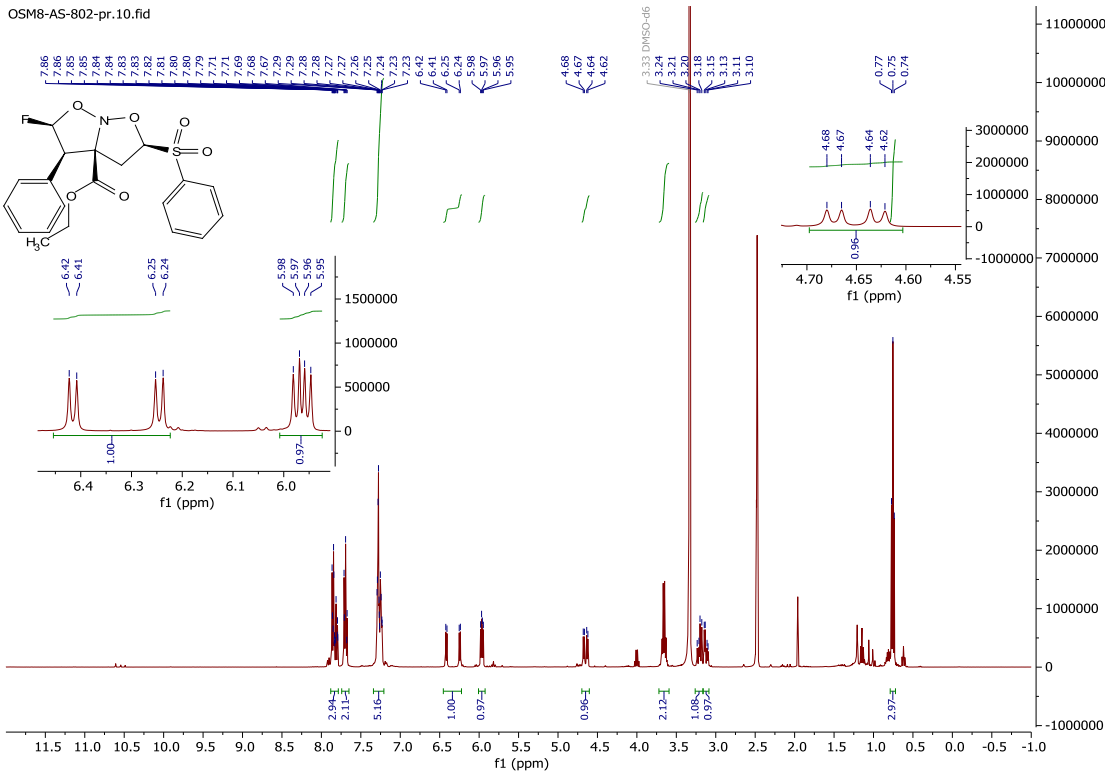
Compound (**7**) HSQC spectra



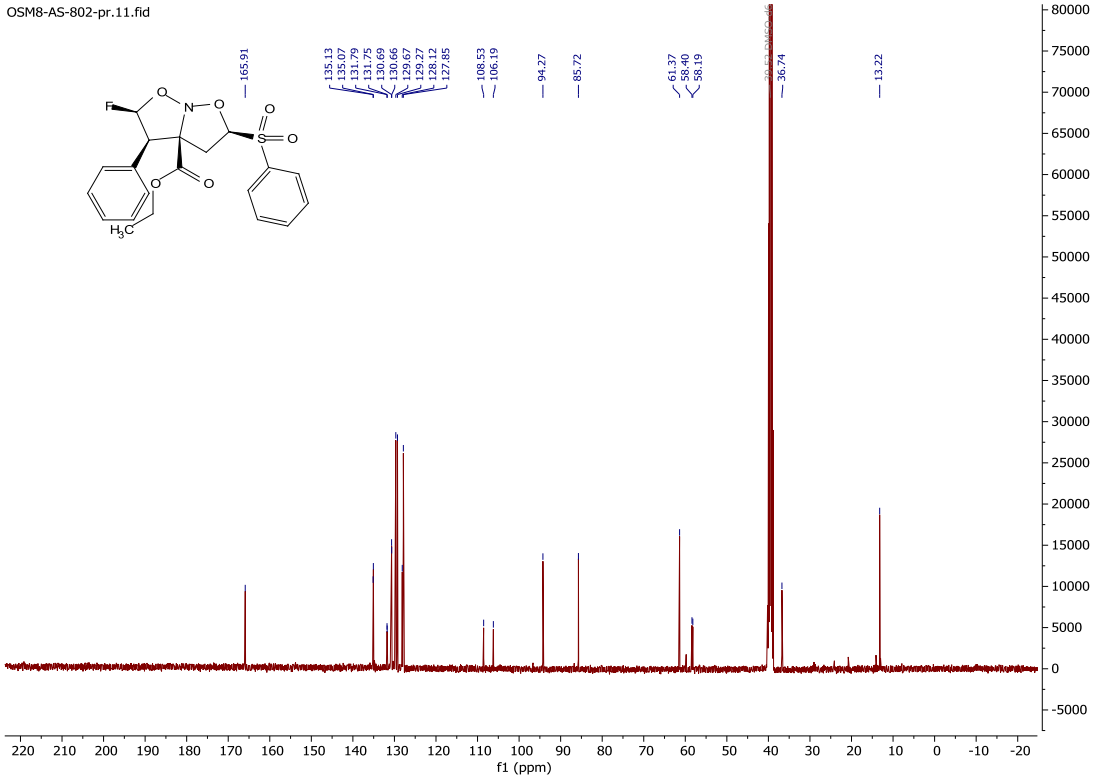
Compound (**7**) NOESY spectra



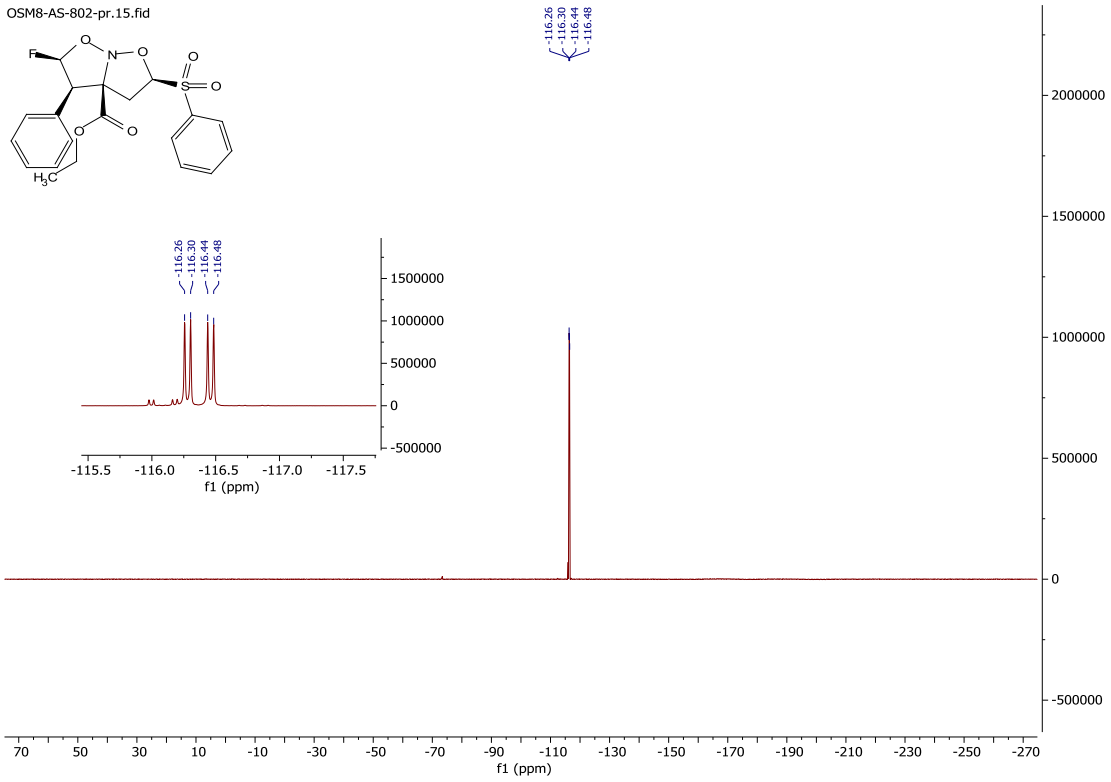
Compound (**9**) ^{1}H-NMR spectra (400 MHz, DMSO-*d6*)



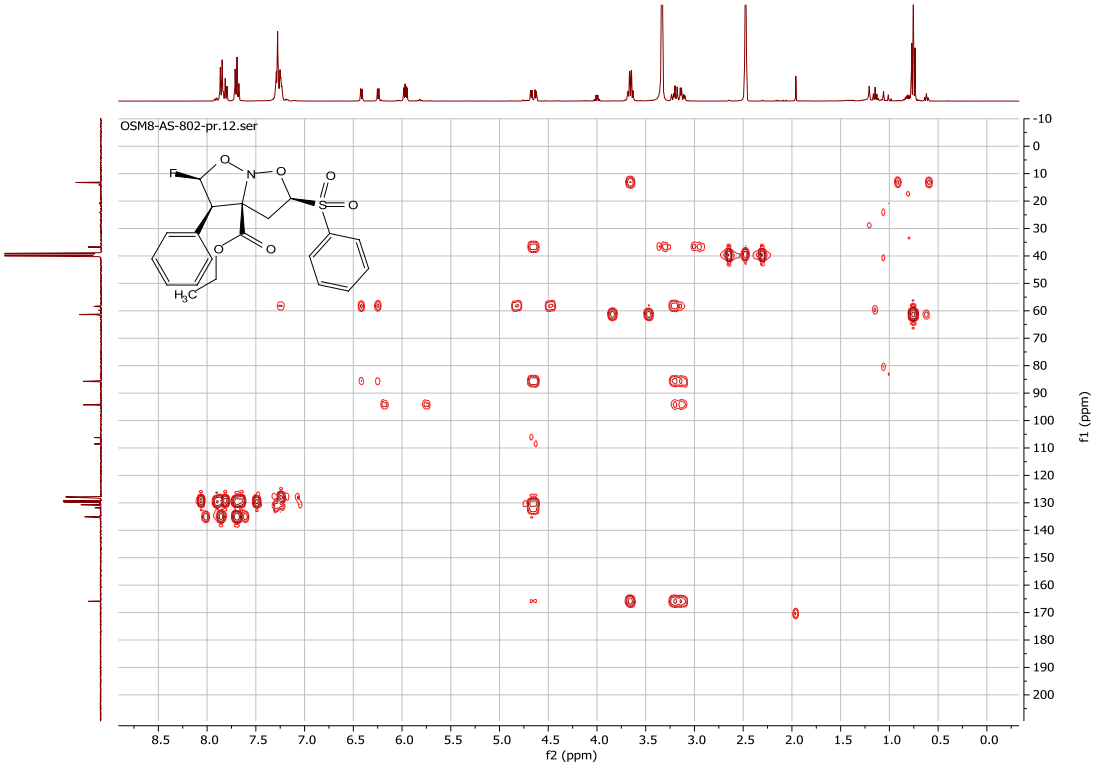
Compound (**9**) ^{13}C-NMR spectra (101 MHz, DMSO-*d6*)



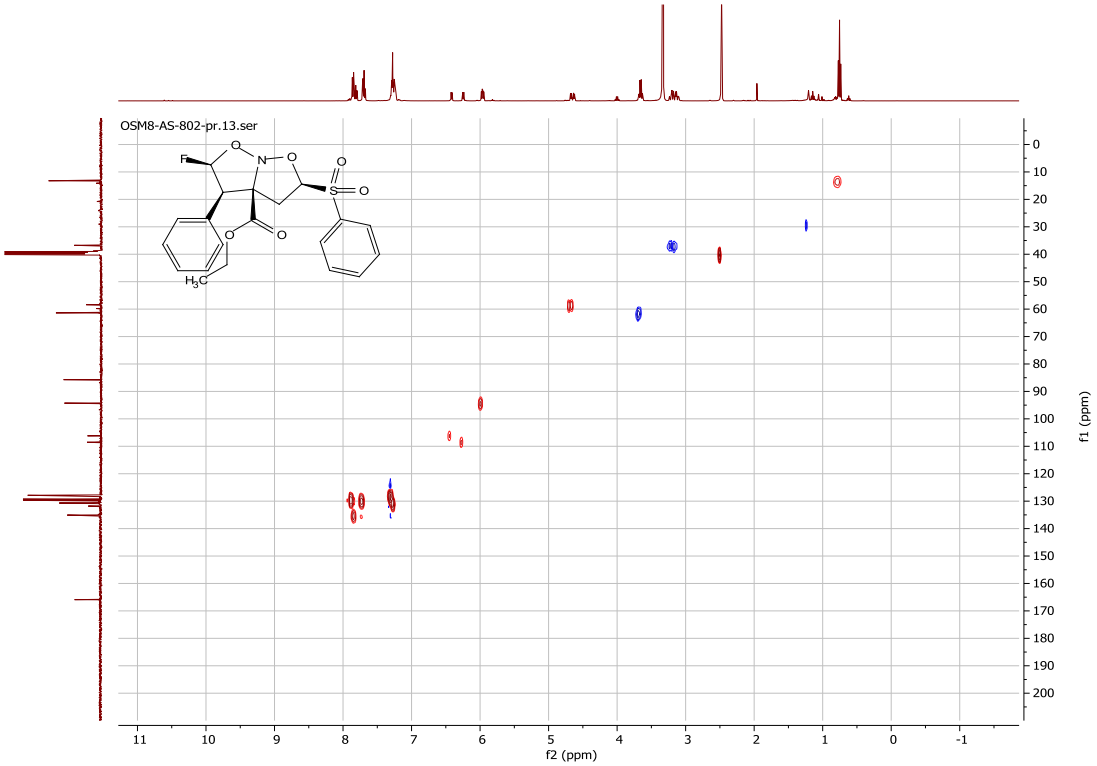
Compound (**9**) ^{19}F-NMR spectra (376 MHz, DMSO-*d6*)



Compound (**9**) HMBC spectra



Compound (**9**) HSQC spectra



Compound (**9**) NOESY spectra