

Supporting Information

Chemical Proteomics and Phenotypic Profiling Identifies the Aryl Hydrocarbon Receptor as a Molecular Target of the Utrophin Modulator Ezutromid

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Experimental section

Materials

The following materials were obtained from commercial sources: biotin azide (Sigma #762024), TAMRA-biotin-azide (DC Biosciences #CCR-1048), TBTA (Cayman Chemical #18816), TCEP (Sigma #C4706), CH-223191 (Selleckchem #S7711), GNF351 (Sigma #182707), ITE (R&D systems #1803/10) and heregulin (Recombinant Human NRG1-beta 1/HRG1-beta 1 EGF Domain Protein, R&D systems #396-HB-050). Ezutromid was provided by Summit Therapeutics PLC.

Analytical procedures and chemical synthesis of **2**, **3**, **4**, and SMT022332 are described in the supplementary information.

Cell culture

H2K-*mdx*¹¹ and H2K-*mdx* utrA-luc cells^{2,31} were maintained in DMEM (Life Technologies) supplemented with 20% Fetal Bovine Serum (Life Technologies), 2% CEE (SLI), 2 mM L-Glutamine (Life Technologies), 1% Penicillin Streptomycin (Life Technologies) and 2 µg/500 ml Mouse Interferon-γ (Roche). Cells were maintained at 10% CO₂ at 33 °C.

Immortalised DMD myoblasts isolated from the Fascia lata muscle of a 10 year old male, del 52 DMD (KM571DMD10FL) were acquired through collaboration with Professor Vincent Mouly (Insitut de Myologie, Paris). These were cultured in Skeletal Muscle Cell Growth Medium and Supplement (PromoCell C-23060), 20% Fetal Bovine Serum (Life Technologies) and 1% Penicillin Streptomycin (Life Technologies). Cells were maintained at 5% CO₂ at 37 °C.

Utrophin FLuc reporter gene assay

White flat bottomed 96 well plates (Corning) were seeded with 5000 H2K *mdx* utrA-luc cells. After 24 h, cells were dosed with compound in triplicate, in the following concentration series: 0.01, 0.03, 0.1, 0.3, 1.0, 3.0, 10.0 µM from 10 mM solution stocks in DMSO (final DMSO concentration was 0.3%). The cells were incubated for a further 24 h, (10% CO₂, 33 °C). Relative luminescence readout after using the Luciferase Assay System (Promega, E1500) reagents was measured using a FLUOstar Optima plate reader (BMG Labtech). The means from the biological triplicates were fitted with a four parameter logistic function with least squares regression (Levenberg-Marquardt algorithm) to calculate EC₅₀ values.

Utrophin Western blot assay

6 well plates were seeded with H2K *mdx* cells (1×10^5) per well. After 24 h (10% CO₂, 33 °C), the cells were dosed with query compounds in three concentrations from 10 mM solution stocks in DMSO (0.3% final DMSO concentration) in triplicate. Heregulin at 30 nM was used as a positive control. After 24 h, the cells were harvested (TrypLE Express, Gibco), washed (PBS) and lysed (RIPA buffer and protease inhibitors, Sigma #P8340). Protein content was quantified by a bicinchoninic acid protein assay (Thermo Scientific Pierce). For the Western blot, 30 µg lysate was separated by NuPAGE™ 3-8% Tris-Acetate protein gel electrophoresis

and transferred to a PVDF membrane (GE Healthcare). Utrophin protein was detected using Mancho-3 antibody (1: 50, kind gift from G.E. Morris, Oswestry, UK) and an AlexaFluor™ 680 anti-mouse antibody (1:10,000, Invitrogen). Blots were imaged with a Licor Odyssey system and relative protein quantitation was performed using Image Studio Lite. REVERT™ total protein stain (Licor) was used as a loading control, along with β -actin detected with anti- β -actin antibody (1: 20,000, Cell Signaling Technology #3700S) and an AlexaFluor™ 680 anti-mouse antibody (1:10,000, Invitrogen). Experiments were carried out at least three times.

DMD myoblast differentiation and fusion assay

Human DMD cells were seeded in black 384 well μ clear cell culture plates and cultured in a differentiation medium containing DMEM/F-12 (Life Technologies), 5% KnockOut™ Serum Replacement (Life Technologies), 1 μ M dexamethasone and 1% Penicillin Streptomycin (Life Technologies). The cells were dosed with compound ($n = 4$, 0.1 % final DMSO concentration) in differentiation medium on days 0 and 3. On day 5, the cells were fixed (4% paraformaldehyde in PBS, 15 min), permeabilised (0.5% Triton X-100 in PBS), blocked (5% FCS, 0.1% Tween-20 in PBS, 30 min) and stained with CellMask blue (Thermo Fisher). The cells were probed with anti-myosin heavy chain antibody (1:800, R&D #MAB4470), anti-mouse AlexaFluor™ 647 (1:500, Thermo Fisher #A21242) and DAPI. The cells were imaged using a Perkin Elmer Operetta high-content analysis system using a 10 \times objective. The % fusion index was calculated from nuclei detected in MHC positive area divided by all detected nuclei in four image fields per well.

Chemoproteomics workflow of intact cell labelling followed by LC-MS/MS analysis

H2K *mdx* cells were seeded in 12 \times 10 cm diameter dishes and grown to 80% confluency. Cells were treated with 3 μ M probe **3** (with and without 100 μ M competitor **7**), 3 μ M probe **4** and the DMSO vehicle, in triplicate for each condition, to a final DMSO concentration of 0.3% in serum-free media, for 2 h at 33 °C and 10% CO₂. The cells were then washed with 1 \times PBS and irradiated (3 min, 5 cm distance, 365 nm 100W lamp, VWR 36595-021) in serum-free media. The cells were washed with 1 \times PBS then lysed for 10 min at 4 °C with 300 μ L of a buffer containing 1% SDS, 1% triton X-100 and protease inhibitors (Sigma #P8340) in 1 \times PBS. The dishes were scraped to collect the lysate, which was sonicated (4 \times 2 s on, 3 s off, 20% amplitude) and the total protein concentration determined by a bicinchoninic acid protein assay (Thermo Scientific Pierce). 350 μ g of lysate at 0.8 mg/mL concentration per sample was then Clicked to biotin-azide (FAC of 0.1 mM from 10 mM in DMSO stock) with CuSO₄ (FAC of 1 mM, from 50 mM in H₂O stock), TCEP (FAC of 1 mM, from 50 mM in H₂O stock) and TBTA (FAC of 0.1 mM, from 10 mM in DMSO stock) for 1 h at rt, 1000 rpm shaking^[5]. Excess Click reagents were removed by protein precipitation (MeOH/CHCl₃) and washing of the protein pellet (MeOH \times 4). The proteins were then solubilized with 2% SDS in PBS before dilution to 0.5 mg/mL protein, 0.5% SDS using 1 \times PBS. Streptavidin beads (15 μ L per sample, Dynabeads™ MyOne™ T1, Invitrogen) were washed twice (1 \times PBS) then added to the labelled lysate samples. After 16 h rocking (65 rpm) at 4 °C, the beads were washed (3 \times

1% SDS, 1% triton X-100 in PBS, 3×4 M urea in 50 mM ammonium bicarbonate buffer (AB), 3×6 M urea in 50 mM AB).

On-bead digestion of pulled down proteins was achieved using a Filter Aided Sample Preparation (FASP) protocol^[6]. Briefly, Vivacon 500 filters (Sartorius, VN01H02 10 kDa/VNCT01) were washed with 0.1% trifluoroacetic acid in 50% acetonitrile. The beads were loaded on the filter in 8 M urea in 100 mM AB for 30 minutes at rt. On-bead proteins were reduced (10 mM TCEP, 30 minutes, rt), alkylated (50 mM chloroacetamide, 30 min, rt in the dark) and washed (2×1 M urea in 50 mM AB). The proteins were subjected to tryptic digestion (0.2 μ g enzyme, Promega, 1 M urea in 50 mM AB) overnight at 37°C. Trypsinised peptides collected from the filtrate were dried and resuspended in 50 μ L 5% formic acid and 5% DMSO.

LC-MS/MS analysis was carried out on an Ultimate 3000 ultra-HPLC system (Thermo Fisher) coupled to a QExactive mass spectrometer (Thermo Fisher). The peptides were trapped on a C18 PepMap100 pre-column (300 μ m i.d. \times 5 mm, 100 Å, Thermo Fisher) using solvent A (0.1% formic acid in water) at a pressure of 500 bar, then separated on an in-house packed analytical column (75 μ m i.d. packed with ReproSil-Pur 120 C18-AQ, 1.9 μ m, 120 Å, Dr. Maisch GmbH) using a linear gradient (length: 60 minutes, 15% to 35% solvent B (0.1% formic acid in acetonitrile), flow rate: 200 nl/min). Data were acquired in a data-dependent mode (DDA). Full scan MS spectra were acquired in the Orbitrap (scan range 350-1500 m/z , resolution 70000, AGC target 3×10^6 , maximum injection time 50 ms). The 10 most intense peaks were selected for HCD fragmentation at 30% of normalised collision energy (resolution 17500, AGC target 5×10^4 , maximum injection time 120 ms) with first fixed mass at 180 m/z .

Peptide identification and quantification were performed by MaxQuant (version 1.5.0.35i)^[7]. MS spectra were searched against the *Mus musculus* UniProt Reference proteome (retrieved 12/01/17) alongside a list of common contaminants. The search results were filtered to a 1% false discovery rate (FDR) for proteins, peptides and peptide-spectrum matches (PSM). Protein intensity distributions were log₂ transformed using Perseus (version 1.5.5.3) and missing values were imputed with an estimated background noise value. The three replicates for each condition were grouped and Student's *t*-test ($s_0 = 0$, FDR = 0.05) performed between the active probe samples and the two controls (inactive probe and competitor). Results of this analysis were plotted using Python plotting library Matplotlib.

Chemoproteomics followed by AhR immunoblotting

Human DMD cells were seeded in 10 cm diameter dishes and grown to 80% confluency. Cells were treated with 3 μ M probe **3** (with and without 100 μ M competitor **7**), 3 μ M probe **4** and the DMSO vehicle, in duplicate for each condition, to a final DMSO concentration of 1% in serum-free media, for 2 h at 37 °C and 5% CO₂. The cells were then irradiated and lysed as above. 500 μ g of lysate at 1 mg/mL concentration per sample was then Clicked to TAMRA-biotin-azide (FAC of 0.1 mM from 10 mM in DMSO stock) as above. Excess Click reagents were removed by protein precipitation (MeOH/CHCl₃) and washing of the protein pellet (MeOH \times 4). The proteins were then solubilized with 2% SDS in PBS before dilution to 1

mg/mL protein, 0.2% SDS using 1 × PBS. Streptavidin beads (30 µL per sample, Dynabeads™ MyOne™ T1, Invitrogen) were washed twice (1 × PBS) then added to the labelled lysate samples. After 16 h rocking (65 rpm) at 4 °C, the beads were washed as above. Proteins were eluted from the beads by heating at 95 °C for 5 min in 1 × Laemmli buffer, 50 mM DTT, 8 M urea in 50 mM AB. The eluted proteins were separated by NuPAGE™ 4-12% Bis-Tris protein gel electrophoresis and transferred to a PVDF membrane (Roche). AhR protein was detected with an anti-AhR antibody (1:5000 in 2% BLOT-QuickBlocker™ (#WB57) solution in PBST, Enzo BML-SA210) followed by an IRDye® 800CW anti-rabbit antibody (1: 5000, Licor). Blots were imaged with a Licor Odyssey system.

AhR:ARNT expression

The mAHR (residues 25-433) and mARNT (residues 82-464) proteins were co-expressed in *E. coli*, using an expression and purification strategy similar to the purification of related ARNT heterodimers (HIF-ARNT, NPAS1-ARNT, NPAS3-ARNT) described previously^[8,9]. For AHR-ARNT, the ARNT protein construct was expressed using a pMKH vector which did not provide any affinity tag while the AHR protein was expressed simultaneously in the same cells (BL21-CodonPlus DE3-RIL competent cells, from Agilent Technologies, Santa Clara, CA, #230245) using the PSJ2 vector which produced a C-terminal histidine tagged protein. Bacterial cultures were grown at 37°C, induced at 16°C overnight using 0.2 mM IPTG. Cells were then harvested, lysed using sonication, centrifuged to remove the pellet, and the supernatant applied to a Ni-NTA resin following the manufacturer's recommended procedure. After extensive washing with buffer, the protein complex was eluted using buffer containing 250 mM imidazole, and the heterodimer further purified using a 1-meter Superdex-200) gel filtration column, which eluted at the expected position of the heterodimer. SDS-PAGE gels stained with coomassie blue showed both subunits were co-purified in 1:1 stoichiometric amounts.

AhR:ARNT fluorescence quenching assay

Fluorescence quenching of ezutromid upon binding recombinant AhR:ARNT was monitored using a fluorescence microplate reader (Tecan Spark, 313 nm excitation/390 nm emission). 100 nM compound was incubated with AhR:ARNT (various concentrations ranging 0 – 10 µM) for 18 h (4 °C) in black 96 well plates, with a buffer containing 20 mM Tris pH 8, 200 mM NaCl and 1% DMSO. Fluorescence emission was measured and the K_D calculated by fitting the curve with a four parameter logistic function.

RT-qPCR

For assessment of mouse and human total utrophin, AhR, AhRR and Cyp1b1 transcript levels, two separate vials of H2K *mdx* and human DMD cells (KM571DMD10FL) were seeded in duplicate at a density of 350,000 per 150 mm dish. After 24 h, cells were dosed with 3 µM ezutromid (final concentration 0.3% DMSO) with non-treated controls supplemented with 0.3% DMSO. RNA was extracted using TRIzol™ Reagent (Invitrogen) according to the manufacturer's instructions. 500 ng of RNA from each sample was used to generate cDNA with the QuantiTect Reverse Transcription kit (Qiagen). All RT-qPCR reactions were

amplified using the StepOne™ Real-Time Polymerase chain reaction system (Applied Biosystems) with Fast SYBR™ Green Master Mix (Thermo Fisher). Amplification was performed in n=3 using cDNA synthesised from individual dishes (n = 2) and an RNA mix (n = 3 total) using the following primers: Utrophin exon 7-9 (mouse: forward 5'-GGACCGATGGACTCG CGTTC-3' reverse 5'- CTTGTCAGGGAGATGCACAGCAAC-3', human: forward 5'-GAAGGCC TCACAGGAACATCACTG-3' reverse 5'-TCCATCCACAATGTCAGTTCCCC3'), AhR (mouse: forward 5'-GCTACTCCACTTCAGCCACCCTCC-3' 5'-GAACTGGTACCCCGATCCTCTTG-3', human: forward primer 5'- GATAGCTACTCCACTTCAGCCACCATCC-3' reverse 5'-CTCTCGTGCACAGCTCTGCTTCAG-3'), AhRR (mouse: forward 5'-CATGTGGATGACCGGCA GGAC-3' reverse 5'-GCAAGCCCTTGCCCTCCTTCTTG-3', human: forward 5'-GGAGTGCACGTA CGCGGGCCGGAAG-3', human reverse 5'-CAGCTTGAGATGATGTCAGGCG-3'), Cyp1b1 (mouse forward 5'-GCCAGCCAGGACACCCTTTC-3', mouse reverse primer 5'-GGCAGGTTGGGCTGGTCACT-3', human forward primer 5'-GGAGAACGTACCGGCCACTAT CAC-3', human reverse 5'-CACGACCTGATCCAATTCTGCC-3') and S13 (mouse: forward 5'-CCCGAGGATCTCTACCATT-3' reverse 5'-GCCACTAGACAGAGGCTGT-3, human: forward 5'- CTGATCTTCCTGAAGATCTCTACC, reverse 5'-GGCAGAGGCTGTAGATGATTCA-3'). Values obtained according to the 2- $\Delta\Delta$ CT method^[4] were subject to tailed t-tests and P-values using Prism7 (GraphPad, La Jolla, USA).

AhR localisation immunofluorescence

Human DMD cells (3×10^4) were seeded on 18 mm coverslips. After 24 h (10% CO₂, 33 °C), the cells were dosed with ezutromid (3 μ M), ITE (1 μ M) or both (from 10 mM solution stocks in DMSO, 1% final DMSO concentration) in serum-free media alongside a vehicle control. After 2 h, the cells were fixed (4% paraformaldehyde in PBS, 15 min), permeabilised (0.1% Triton X-100 in PBS) and blocked (10% FBS, 0.1% Tween-20 in PBS, 1 h). The cells were probed with anti-AhR antibody (1:200, Invitrogen, #MA1-514), anti-mouse AlexaFluor™ 488 (1:2000, #A-11059, Invitrogen) and Hoescht 33342 (10 μ M, Sigma # 14533). The coverslips were mounted onto slides with FluorSave™ reagent. The cells were imaged using an Evos fluorescence microscope with a 40 \times objective. Immunofluorescence experiments were performed on different cell populations three times.

Statistics

Differences between group means were calculated by unpaired, two-tailed t-tests where *p* values ≤ 0.05 were considered statistically significant.

Chemistry Experimental

General Procedures:

Reactions were carried out under inert conditions using an atmosphere of nitrogen, anhydrous solvents and oven dried glassware, unless aqueous reagents were used or otherwise stated. Microwave reactions were carried out using a Biotage[®] Initiator Classic microwave synthesiser.

Anhydrous solvents were dried by passing over an activated alumina column, under an inert atmosphere, using a solvent purification system. Water was purified by an Elix[®] UV-10 system. All other solvents and reagents were used as supplied (analytical or HPLC grade) without prior purification. PE refers to the fraction of petroleum ether boiling in the range 30-40 °C. rt refers to room temperature. Aqueous solutions of ammonium chloride (NH₄Cl) and sodium bicarbonate (NaHCO₃) were saturated. Concentration of solvents *in vacuo* was achieved by rotary evaporation using a diaphragm pump. Purification by flash column chromatography was carried out using Kieselgel 60 and a positive solvent pressure.

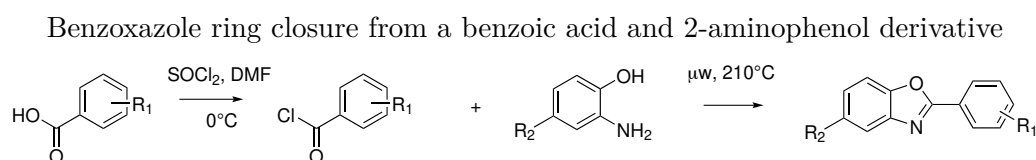
Analytical procedures:

TLC was carried out using Merck Kieselgel 60 F254 plates which were visualised using UV light (254 nm). Melting points were recorded on a EZ-Melt automated melting point apparatus. Fourier transform IR spectroscopy was carried out using a Bruker Tensor 27 FT-IR spectrometer as neat samples or thin films. Wavelengths of peak absorption are given in wavenumbers (cm⁻¹), with broad (br) signals indicated.

NMR spectra were recorded using Bruker Advance spectrometers (AVII 400 or AVII 500). ¹H NMR spectra were recorded at 298 K, locked to the relevant solvent standard. ¹H NMR and ¹³C NMR data were recorded at 298 K, locked to the relevant solvent standard. NMR data are presented as: chemical shift δ (in ppm, $\delta_{\text{TMS}} = 0$), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, obs = obscured), coupling constants (J in Hz) and integration. Proton peak assignments were based on 1D data and COSY analysis and carbon peak assignments were based on 1D data and HSQC and HMBC analysis. Low resolution mass spectroscopy was carried out on an Agilent 6120 mass spectrometer. Accurate mass measurements were run on either a Bruker MicroTOF internally calibrated with polyalanine, or a Micromass GCT instrument fitted with a Scientific Glass Instruments BPX5 column (15 m \times 0.25 mm) using amyl acetate as a lock mass. HR ESI and APCI were run on a Waters Acquity Ultraperformance LC system coupled to a Thermo Orbitrap Exactive MS. Optical rotations were recorded on a Perkin-Elmer PE241 polarimeter with a water-jacketed 1 cm cell. Specific rotations are reported in 10⁻¹ deg cm² g⁻¹ and concentrations in g/100 mL.

Chemical Experimental Procedures and Data:

General Procedure A:

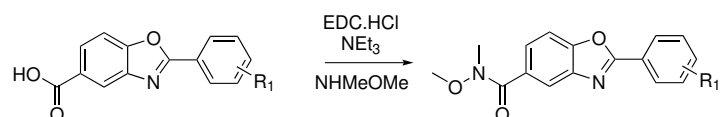


To a suspension of the benzoic acid derivative (1 eq.) in CH₂Cl₂ at 0 °C was added thionyl chloride (3 eq.) and dimethylformamide (cat.) The reaction mixture was warmed to rt and stirred for 16 h. When the reaction was complete, the reaction mixture was concentrated *in vacuo*, dissolved in Et₂O and filtered. The filtrate was concentrated *in vacuo* to yield the acid chloride, which was used immediately without further purification.

To a suspension of the 2-aminophenol derivative (1 eq.) in 1,4-dioxane was added a solution of the prepared acid chloride (1 eq.) in 1,4-dioxane at rt. The reaction vessel was heated under microwave activation at 210 °C for 15 min, then cooled to rt. The reaction mixture was poured into NaOH solution (1 M aq.), and extracted with EtOAc three times. The combined organic fractions were dried (Na₂SO₄) and concentrated *in vacuo* to yield the crude benzoxazole product.

General procedure B:

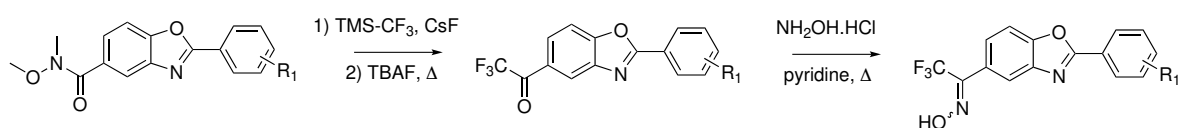
Formation of benzoxazole carboxamides



Acid benzoxazole derivatives were obtained by following General Procedure A, with no further purification. To a solution of the crude acid (1 eq.) in DMF was added EDC hydrochloride (2 eq.), *N,O*-dimethylhydroxylamine hydrochloride (2 eq.) and NEt₃ (2 eq.). The reaction mixture was stirred at rt for 16 h, then concentrated *in vacuo*. The residue was dissolved in EtOAc, then washed with citric acid solution (10% aq.), NaHCO₃ solution (10% aq.) and brine. The organic layer was concentrated *in vacuo* to yield the crude carboxamide product.

General procedure C:

Formation of trifluoromethylketone oximes from carboxamides

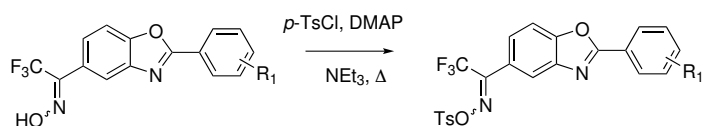


Adapting a known procedure,^[10] caesium fluoride (0.2 eq.) and trifluoromethyltrimethylsilane (2 eq.) were added to a solution of Weinreb amide derivative (1 eq.) in toluene. The reaction mixture was stirred at rt with further equivalents of caesium fluoride and trifluoromethyltrimethylsilane added every 24 h until the reaction was complete by TLC. At this point, the reaction was concentrated *in vacuo* and the residue dissolved in THF. TBAF (1.2 eq., 1 M in THF) was added dropwise and the reaction stirred at rt for 3 h at 50 °C. The reaction was cooled to rt, diluted with Et₂O and washed with water and brine. The organic layer was dried (Na₂SO₄) and concentrated *in vacuo* to yield the crude trifluoromethyl ketone product. The crude was filtered through a silica plug, eluting with PE : EtOAc (2:1), and concentrated *in vacuo*.

To a solution of the prepared crude trifluoromethylketone derivative (1 eq.) in pyridine (excess) and ethanol over molecular sieves (3 Å) was added hydroxylammonium chloride (3 eq.). The reaction mixture was heated under reflux for 16 h, then concentrated *in vacuo*. The residue was dissolved in EtOAc, washed with brine/water (1:1), dried (Na₂SO₄) and concentrated *in vacuo* to yield the crude oxime product.

General procedure D:

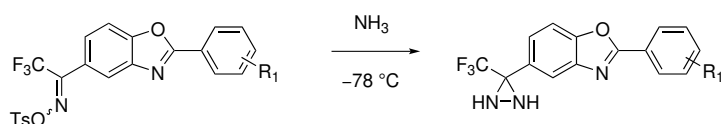
Formation of trifluoromethylketone tosyl oximes



To a solution of oxime (1 eq.), 4-dimethylaminopyridine (0.1 eq.) and triethylamine (3 eq.) in CH₂Cl₂ was added *p*-toluenesulfonyl chloride (2 eq., recrystallised from PE) portionwise. The reaction mixture was stirred at 40 °C for 16 h, then cooled to rt. The mixture was diluted with CH₂Cl₂, washed with water then brine, dried (Na₂SO₄) and concentrated *in vacuo* to yield the crude tosyl oxime products in a mixture of E/Z isomers.

General procedure E:

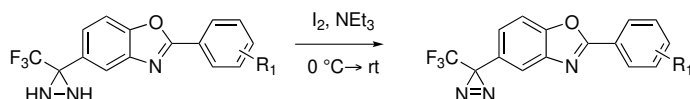
Formation of the diaziridine



NH₃ (excess) was condensed into a solution of tosyl oxime (1 eq.) in CH₂Cl₂ at -78 °C. The reaction mixture was stirred and warmed to rt over 6 h, then concentrated *in vacuo* to yield the crude diaziridine product.

General procedure F:

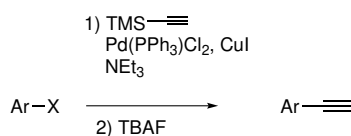
Formation of the diazirine



To a solution of diaziridine (1 eq.) and triethylamine (3 eq.) in CH₂Cl₂ was added iodine (1.2 eq.) portionwise. The reaction mixture was covered in foil to exclude light and stirred for 15 min at rt. The mixture was then concentrated *in vacuo* to yield the crude diazirine product.

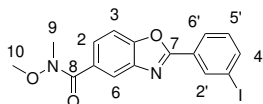
General procedure G:

Sonogashira coupling of aryl halide with TMS-acetylene



To a solution of aryl halide (1 eq.), bis(triphenylphosphine)palladium(II) dichloride (0.15 eq.) and copper (I) iodide (0.1 eq.) in THF was added NEt₃ (excess) and trimethylsilylacetylene (1 eq.) dropwise. The reaction mixture was degassed, put under a N₂ atmosphere, and stirred at 70 °C until the reaction was complete by TLC. The solvent was removed *in vacuo* and the residue purified by flash column chromatography. The isolated TMS-alkyne intermediate was dissolved in THF and TBAF (1.5 eq., 1 M in THF) was added dropwise. The reaction was stirred at rt until completion. The reaction mixture was diluted with EtOAc, washed with water and the phases separated. The organic layer was dried (Na₂SO₄) and concentrated *in vacuo* to yield the crude alkyne product.

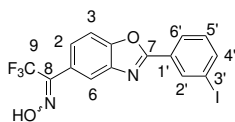
2-(3-Iodophenyl)-*N*-methoxy-*N*-methylbenzo[*d*]oxazole-5-carboxamide **9**



Carboxamide **9** was obtained according to General Procedure B, using 3-iodobenzoic acid (486 mg, 1.96 mmol), thionyl chloride (0.43 mL, 5.88 mmol) and DMF (0.10 mL) in CH₂Cl₂ (20 mL). The acid chloride intermediate formed was reacted with 3-amino-4-hydroxybenzoic acid (300 mg, 1.96 mmol) in 1,4-dioxane (5 mL). Amide coupling was performed on the crude product using EDC hydrochloride (752 mg, 3.92 mmol), *N,O*-dimethylhydroxylamine hydrochloride (382 mg, 3.92 mmol) and NEt₃ (0.60 mL, 4.31 mmol) in DMF (25 mL). The crude product was purified by flash column chromatography (PE : EtOAc, 7:3) to yield carboxamide **9** (392 mg, 0.960 mmol, 49%) as a white solid.

R_f 0.21 (PE : EtOAc, 7:3); **v_{max}** (cm⁻¹) 1635 ((C=O)NH), 1450, 1107 (C-N), 1085; **mp** 113-115 °C; **¹HNMR** (400 MHz, CDCl₃) δ_H 8.62 (1H, dd, *J* = 1.3, 1.3 Hz, H_{2'}), 8.22 (1H, ddd, *J* = 7.8, 1.3, 1.3 Hz, H_{6'}), 8.15 (1H, d, *J* = 1.7 Hz, H₆), 7.88 (1H, 1H, ddd, *J* = 7.8, 1.3, 1.3 Hz, H_{4'}), 7.77 (1H, dd, *J* = 8.5, 1.7 Hz, H₂), 7.61 (1H, d, *J* = 8.5 Hz, H₃), 7.27 (1H, dd, *J* = 7.8, 7.8 Hz, H_{5'}), 3.57 (3H, s, H₁₀), 3.41 (3H, s, H₉); **¹³CNMR** (125 MHz, CDCl₃) δ_C 169.2 (C₈), 162.5 (C₇), 152.1 (C₄), 141.6 (C_{4'}), 140.8 (C₅), 136.6 (C_{2'}), 131.0 (C₁), 130.7 (C_{5'}), 128.8 (C_{1'}), 126.9 (C_{6'}), 126.6 (C₂), 120.8 (C₆), 110.5 (C₃), 94.5 (C_{3'}), 61.3 (C₁₀), 33.9 (C₉); **HRMS** (APCI⁺) Calc. for C₁₆H₁₄IN₂O₃ [M+H]⁺ 409.0043, found 409.0035.

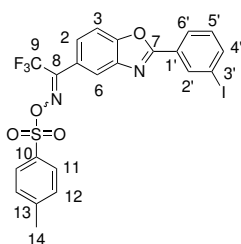
2,2,2-Trifluoro-1-(2-(3-iodophenyl)benzo[*d*]oxazol-5-yl)ethan-1-one oxime **10**



Oxime **10** was obtained according to General Procedure C, using carboxamide **9** (1.45 g, 3.55 mmol), trifluoromethyltrimethylsilane (1.05 mL, 7.10 mmol) and caesium fluoride (108 mg, 0.710 mmol) in toluene (40 mL). The reaction was stirred for three days, with further trifluoromethyltrimethylsilane (1.05 mL, 7.10 mmol) and caesium fluoride (108 mg, 0.710 mmol) added every 24 h. TBAF (4.26 mL, 1 M in THF) was used for desilylation of the intermediate formed. The crude trifluoromethylketone product was dissolved in pyridine (5 mL) and ethanol (25 mL) and refluxed with hydroxylammonium chloride (740 mg, 10.7 mmol). The crude product was purified by flash column chromatography (PE : EtOAc, 9:1) to yield oxime **10** (358 mg, 0.828 mmol, 23%) as a white solid.

R_f 0.28 (PE : EtOAc, 9:1); **v_{max}** (cm⁻¹) 1547, 1471, 1250 (C-F), 1151 (C-F), 973 (N-O); **mp** 182-184 °C; **¹HNMR** (500 MHz, CD₃OD) δ_H 8.60 (1H, dd, *J* = 1.6, 1.6 Hz, H_{2'}), 8.25 (1H, ddd, *J* = 7.8, 1.6, 1.0 Hz, H_{6'}), 7.97 (1H, ddd, *J* = 7.8, 1.6, 1.0 Hz, H_{4'}), 7.86 (1H, s, H₆), 7.80 (1H, d, *J* = 8.5 Hz, H₃), 7.53 (1H, dd, *J* = 8.5, 1.3 Hz, H₂), 7.36 (1H, dd, *J* = 7.8, 7.8 Hz, H_{5'}); **¹³CNMR** (125 MHz, CDCl₃) δ_C 163.8 (C₇), 152.7 (C₄), 146.5 (q, ²*J*_{C-F} = 32.6 Hz, C₈), 142.9 (C₅), 142.2 (C_{4'}), 137.5 (C_{2'}), 132.0 (C_{5'}), 129.7 (C_{1'}), 127.9 (C_{6'}), 127.8 (C₂), 125.5 (C₁), 122.5 (q, ¹*J*_{C-F} = 272.5 Hz, C₉), 121.8 (C₆), 112.1 (C₃), 95.1 (C_{3'}); **¹⁹FNMR** (376 MHz, CDCl₃) δ_F -66.5 (s); **HRMS** (ES⁺) Calc. for C₁₅H₇F₃IN₂O₂ [M-H]⁻ 430.9510, found 430.9513.

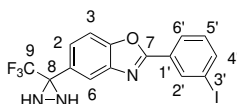
2,2,2-Trifluoro-1-(2-(3-iodophenyl)benzo[*d*]oxazol-5-yl)ethan-1-one *O*-tosyl oxime **11**



Tosyl oxime **11** was obtained according to General Procedure D, using oxime **10** (358 mg, 0.828 mmol), *p*-toluenesulfonyl chloride (316 mg, 1.66 mmol), 4-dimethylaminopyridine (10.1 mg, 82.8 μ mol) and NEt₃ (0.35 mL, 2.48 mmol) in CH₂Cl₂ (20 mL). The crude product was purified by flash column chromatography (PE : EtOAc, 37:3) to yield tosyl oxime **11** (402 mg, 0.685 mmol, 83%) as a pale yellow solid in a mixture of isomers (7:1).

R_f 0.24 (PE : EtOAc, 9:1); **v_{max}** (cm⁻¹) 2932 (C-H), 1622 (C=N-O), 1391 (S=O), 1250 (C-F), 1181 (S=O), 1149; **mp** 229-231 °C; **¹HNMR** (500 MHz, CDCl₃) δ _H 8.64 (1H, dd, *J* = 1.6, 1.6 Hz, H_{2'}), 8.25 (1H, ddd, *J* = 7.9, 1.6, 1.0 Hz, H_{6'}), 7.94 (1H, ddd, *J* = 7.9, 1.6, 1.0 Hz, H_{4'}), 7.93 (2H, d, *J* = 8.4 Hz, H₁₁), 7.82 (1H, d, *J* = 1.7 Hz, H₆), 7.72 (1H, d, *J* = 8.5 Hz, H₃), 7.46 (1H, dd, *J* = 8.5, 1.7 Hz, H₂), 7.43 (2H, d, *J* = 8.4 Hz, H₁₂), 7.32 (1H, dd, *J* = 7.9, 7.9 Hz, H_{5'}), 2.52 (3H, s, H₁₄); **¹³CNMR** (125 MHz, CDCl₃) δ _C 162.9 (C₇), 153.5 (q, ²J_{C-F} = 33.7 Hz, C₈), 152.3 (C₄), 146.3 (C₁₃), 142.2 (C₅), 141.0 (C_{4'}), 136.6 (C_{2'}), 131.1 (C₁₀), 130.7 (C_{5'}), 129.9 (C₁₂), 129.3 (C₁₁), 128.2 (C_{1'}), 127.0 (C_{6'}), 126.0 (C₂), 121.2 (C₁), 121.0 (C₆), 119.6 (q, ¹J_{C-F} = 277.6 Hz, C₉), 111.5 (C₃), 94.4 (C_{3'}), 21.8 (C₁₄); **¹⁹FNMR** (376 MHz, CDCl₃) δ _F -66.7 (s); **HRMS** (CI⁺) Calc. for C₂₂H₁₅F₃IN₂O₄ [M+H]⁺ 586.9744, found 586.9759.

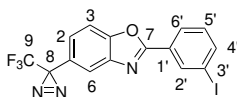
2-(3-Iodophenyl)-5-(3-(trifluoromethyl)diaziridin-3-yl)benzo[d]oxazole **12**



Diaziridine **12** was obtained according to General Procedure E, using tosyl oxime **11** (375 mg, 0.640 mmol) and NH₃ (5 mL) in CH₂Cl₂ (5 mL). The crude product was purified by flash column chromatography (PE : EtOAc, 4:1) to yield diaziridine **12** (270 mg, 0.626 mmol, 98%) as a white solid.

R_f 0.16 (PE : EtOAc, 9:1); **v_{max}** (cm⁻¹) 3243 (N-H), 1570 (N-H), 1216 (C-F), 1150; **mp** 128-130 °C; **¹HNMR** (500 MHz, CDCl₃) δ _H 8.62 (1H, dd, *J* = 1.7, 1.7 Hz, H_{2'}), 8.22 (1H, ddd, *J* = 7.9, 1.7, 1.1 Hz, H_{6'}), 8.06 (1H, d, *J* = 1.6 Hz, H₆), 7.90 (1H, ddd, *J* = 7.9, 1.7, 1.1 Hz, H_{4'}), 7.66 (1H, dd, *J* = 8.5, 1.6 Hz, H₂), 7.63 (1H, d, *J* = 8.5 Hz, H₃), 7.28 (1H, dd, *J* = 7.9, 7.9 Hz, H_{5'}), 2.89 (1H, d, *J* = 8.7 Hz, -NH), 2.32 (1H, d, *J* = 8.7 Hz, -NH); **¹³CNMR** (125 MHz, CDCl₃) δ _C 162.6 (C₇), 151.6 (C₄), 142.2 (C₅), 140.8 (C_{4'}), 136.5 (C_{2'}), 130.6 (C_{5'}), 128.7 (C₁), 128.5 (C_{1'}), 126.9 (C_{6'}), 125.5 (C₂), 123.5 (q, ¹J_{C-F} = 278.2 Hz, C₉), 120.6 (C₆), 111.1 (C₃), 94.4 (C_{3'}), 58.2 (q, ²J_{C-F} = 36.2 Hz, C₈); **¹⁹FNMR** (376 MHz, CDCl₃) δ _F -75.5 (s); **HRMS** (ES⁺) Calc. for C₁₅H₁₀F₃IN₃O [M+H]⁺ 431.9815, found 431.9815.

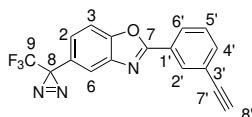
2-(3-Iodophenyl)-5-(3-(trifluoromethyl)-3H-diazirin-3-yl)benzo[d]oxazole **13**



Diazirine **13** was obtained according to General Procedure F, using diaziridine **12** (250 mg, 0.580 mmol), iodine (176 mg, 0.696 mmol) and NEt₃ (0.24 mL, 1.74 mmol) in CH₂Cl₂ (15 mL). The crude product was purified by flash column chromatography (PE : EtOAc, 19:1 → 9:1) to yield diazirene **13** (242 mg, 0.564 mmol, 97%) as a white solid.

R_f 0.81 (PE : EtOAc, 9:1); **v_{max}** (cm⁻¹) 1547, 1254 (C-F), 1194, 1154 (C-F), 723; **mp** 101-103 °C; **¹HNMR** (500 MHz, CDCl₃) δ _H 8.60 (1H, t, *J* = 1.7 Hz, H_{2'}), 8.21 (1H, ddd, *J* = 7.9, 1.7, 1.0 Hz, H_{6'}), 7.90 (1H, ddd, *J* = 7.9, 1.7, 1.0 Hz, H_{4'}), 7.72 (1H, d, *J* = 1.8 Hz, H₆), 7.61 (1H, d, *J* = 8.6 Hz, H₃), 7.28 (1H, t, *J* = 7.9 Hz, H_{5'}), 7.20 (1H, dd, *J* = 8.6, 1.8 Hz, H₂); **¹³CNMR** (125 MHz, CDCl₃) δ _C 162.9 (C₇), 151.5 (C₄), 142.6 (C₅), 141.0 (C_{4'}), 136.7 (C_{2'}), 130.8 (C_{5'}), 128.5 (C_{1'}), 127.0 (C_{6'}), 126.0 (C₁), 124.1 (C₂), 122.3 (q, ¹J_{C-F} = 274.7 Hz, C₉), 119.5 (C₆), 111.5 (C₃), 94.6 (C_{3'}), 28.7 (q, ²J_{C-F} = 40.6 Hz, C₈); **¹⁹FNMR** (376 MHz, CD₃OD) δ _F -67.4 (s); **HRMS** (ES⁺) Calc. for C₁₅H₈F₃IN₃O [M+H]⁺ 429.9659, found 429.9655.

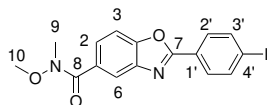
2-(3-Ethynylphenyl)-5-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)benzo[*d*]oxazole **2**



Diazirine **2** was obtained according to General Procedure G, using diazirine **13** (100 mg, 0.233 mmol), bis(triphenylphosphine)palladium(II) dichloride (24.5 mg, 35.0 μ mol), copper(I) iodide (4.44 mg, 23.3 μ mol), NEt_3 (0.70 mL) and trimethylsilylacetylene (40 μ L, 0.280 mmol) in THF (10 mL). The reaction was complete after 1 h. The TMS-protected alkyne intermediate formed was purified by flash column chromatography (PE : EtOAc, 1:0 \rightarrow 99:1), then deprotected with TBAF (0.70 mL, 1 M in THF) in THF (5 mL). The reaction was complete after 30 min. The crude product was purified by flash column chromatography (PE : EtOAc, 1:0 \rightarrow 49:1) to yield alkyne **2** (53.2 mg, 0.163 mmol, 70%) as a white solid.

R_f 0.62 (PE : EtOAc, 49:1); ν_{max} (cm^{-1}) 3310 (sharp, alkyne C-H), 1556, 1259 (C-F), 1197, 1154, 803; mp 105-107 $^{\circ}\text{C}$; $^1\text{HNMR}$ (500 MHz, CDCl_3) δ_{H} 8.40 (1H, dd, $J = 1.7, 1.7$ Hz, $\text{H}_{2'}$), 8.25 (1H, ddd, $J = 7.9, 1.4, 1.4$ Hz, $\text{H}_{6'}$), 7.75 (1H, d, $J = 1.3$ Hz, H_6), 7.70 (1H, ddd, $J = 7.9, 1.4, 1.4$ Hz, $\text{H}_{4'}$), 7.64 (1H, d, $J = 8.6$ Hz, H_3), 7.54 (1H, dd, $J = 7.9, 7.9$ Hz, $\text{H}_{5'}$), 7.24 (1H, dd, $J = 8.6, 1.3$ Hz, H_2), 3.20 (1H, s, $\text{H}_{8'}$); $^{13}\text{CNMR}$ (125 MHz, CDCl_3) δ_{C} 163.6 (C_7), 151.4 (C_4), 142.6 (C_5), 135.4 ($\text{C}_{4'}$), 131.4 ($\text{C}_{2'}$), 129.1 ($\text{C}_{5'}$), 127.9 ($\text{C}_{6'}$), 126.9 ($\text{C}_{1'}$), 125.8 (C_1), 123.9 (C_2), 123.3 ($\text{C}_{3'}$), 122.2 (q, $^1J_{\text{C-F}} = 274.7$ Hz, C_9), 119.3 (C_6), 111.3 (C_3), 82.4 ($\text{C}_{7'}$), 78.6 ($\text{C}_{8'}$), 28.7 (q, $^2J_{\text{C-F}} = 40.7$ Hz, C_8); $^{19}\text{FNMR}$ (376 MHz, CD_3OD) δ_{F} -67.4 (s); HRMS (ES^+) Calc. for $\text{C}_{17}\text{H}_9\text{F}_3\text{N}_3\text{O}$ $[\text{M}+\text{H}]^+$ 328.0692, found 328.0691.

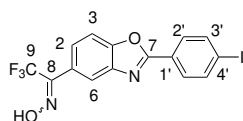
2-(4-Iodophenyl)-*N*-methoxy-*N*-methylbenzo[*d*]oxazole-5-carboxamide **14**



Carboxamide **14** was obtained according to General Procedure B, using 4-iodobenzoic acid (500 mg, 2.01 mmol), thionyl chloride (0.44 mL, 6.03 mmol) and DMF (0.10 mL) in CH_2Cl_2 (20 mL). The acid chloride intermediate formed was added to a solution of 3-amino-4-hydroxybenzoic acid (277 mg, 1.81 mmol, 0.9 eq.) in 1,4-dioxane (5 mL). Amide coupling was performed on the crude product using EDC hydrochloride (769 mg, 4.02 mmol), *N,O*-dimethylhydroxylamine hydrochloride (392 mg, 4.02 mmol) and NEt_3 (0.56 mL, 4.01 mmol) in DMF (25 mL). The crude product was purified by flash column chromatography (PE : EtOAc, 3:1) to yield carboxamide **14** (281 mg, 0.688 mmol, 38%) as a white solid.

R_f 0.11 (PE : EtOAc, 9:1); ν_{max} (cm^{-1}) 2980 (C-H), 1636 ((C=O)NH), 1396, 1261, 1060; mp 143-144 $^{\circ}\text{C}$; $^1\text{HNMR}$ (400 MHz, CDCl_3) δ_{H} 8.13 (1H, d, $J = 1.6$ Hz, H_6), 7.95 (2H, m, $\text{H}_{2'}$), 7.87 (2H, m, $\text{H}_{3'}$), 7.75 (1H, dd, $J = 1.6, 8.6$ Hz, H_2), 7.58 (1H, d, $J = 8.6$ Hz, H_3), 3.55 (3H, s, H_{10}), 3.39 (3H, s, H_9); $^{13}\text{CNMR}$ (125 MHz, CDCl_3) δ_{C} 169.2 (C_8), 163.4 (C_7), 152.1 (C_4), 141.7 (C_5), 138.4 ($\text{C}_{3'}$), 130.9 (C_1), 129.2 ($\text{C}_{2'}$), 126.5 (C_2), 126.3 ($\text{C}_{1'}$), 120.7 (C_6), 110.4 (C_3), 99.1 ($\text{C}_{4'}$), 61.2 (C_{10}), 33.9 (C_9); HRMS (ES^+) Calc. for $\text{C}_{16}\text{H}_{14}\text{IN}_2\text{O}_3$ $[\text{M}+\text{H}]^+$ 409.0043, found 409.0041.

2,2,2-Trifluoro-1-(2-(4-iodophenyl)benzo[*d*]oxazol-5-yl)ethan-1-one oxime **15**

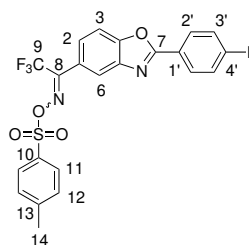


Oxime **15** was obtained according to General Procedure C, using carboxamide **14** (1.55 g, 3.81 mmol), trifluoromethyltrimethylsilane (1.13 mL, 7.62 mmol) and caesium fluoride (116 mg, 0.762

mmol) in toluene (50 mL). The reaction was stirred for three days, with further trifluoromethyltrimethylsilane (1.13 mL, 7.62 mmol) and caesium fluoride (116 mg, 0.762 mmol) added every 24 h. TBAF (4.57 mL, 1 M in THF) was used for desilylation of the intermediate formed. The crude trifluoromethylketone product was dissolved in pyridine (5 mL) and ethanol (25 mL) and refluxed after addition of hydroxylammonium chloride (794 mg, 11.4 mmol). The crude product was purified by flash column chromatography (PE : EtOAc, 9:1 → 4:1) to yield oxime **15** (527 mg, 1.22 mmol, 32%) as a pale green solid.

R_f 0.69 (PE : EtOAc, 4:1); **v_{max}** (cm⁻¹) 1476 (aromatic C=C), 1259 (C-F), 1151 (C-F), 970 (N-O); **mp** 197-199 °C; **¹HNMR** (400 MHz, CDCl₃) δ_H 7.97 (2H, m, H_{3'}), 7.95 (1H, d, *J* = 1.2 Hz, H₆), 7.91 (2H, m, H_{2'}), 7.68 (1H, d, *J* = 8.4 Hz, H₃), 7.51 (1H, dd, *J* = 8.4, 1.2 Hz, H₂); **¹³CNMR** (125 MHz, CDCl₃) δ_C 165.1 (C₇), 152.9 (C₄), 145.1 (q, ²*J*_{C-F} = 32.6 Hz, C₈), 143.3 (C₅), 139.9 (C_{3'}), 130.4 (C_{2'}), 128.0 (C₁), 127.5 (C₂), 125.8 (C_{1'}), 121.9 (C₆), 120.9 (q, ¹*J*_{C-F} = 271.9 Hz, C₉), 112.3 (C₃), 100.3 (C_{4'}); **¹⁹FNMR** (376 MHz, CDCl₃) δ_F -67.5 (s); **HRMS** (ES⁺) Calc. for C₁₅H₇F₃IN₂O₂ [M-H]⁻ 430.9510, found 430.9513.

2,2,2-Trifluoro-1-(2-(4-iodophenyl)benzo[d]oxazol-5-yl)ethan-1-one *O*-tosyl oxime **16**



Tosyl oxime **16** was obtained according to General Procedure D, using oxime **15** (1.80 g, 4.17 mmol), *p*-toluenesulfonyl chloride (1.59 g, 8.33 mmol), 4-dimethylaminopyridine (50.9 mg, 0.417 mmol) and NEt₃ (1.73 mL, 12.5 mmol) in CH₂Cl₂ (50 mL). The crude product was purified by flash column chromatography (PE : EtOAc, 19:1 → 4:1) to yield tosyl oxime **16** (1.35 g, 2.30 mmol, 55%) as a pale yellow solid in a mixture of isomers (2:1).

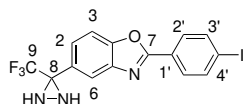
v_{max} (cm⁻¹) 2981 (C-H), 1622 (C=N-O), 1394 (S=O), 1245 (C-F), 1194 (S=O), 1159; **mp** 171-173 °C;

Major isomer: **R_f** 0.45 (PE : EtOAc, 17:3); **¹HNMR** (500 MHz, CDCl₃) δ_H 7.97 (2H, m, H_{3'}), 7.92 (2H, m, H_{2'}), 7.90 (2H, d, *J* = 8.1 Hz, H₁₁), 7.81 (1H, d, *J* = 1.6 Hz, H₆), 7.68 (1H, d, *J* = 8.5 Hz, H₃), 7.42 (1H, dd, *J* = 8.5, 1.6 Hz, H₂), 7.40 (2H, d, *J* = 8.1 Hz, H₁₂), 2.49 (3H, s, H₁₄). **¹³CNMR** (125 MHz, CDCl₃) δ_C 163.9 (C₇), 153.6 (q, ²*J*_{C-F} = 33.5 Hz, C₈), 152.3 (C₄), 146.3 (C₁₃), 142.3 (C₅), 138.4 (C_{3'}), 131.1 (C₁₀), 129.9 (C₁₂), 129.3 (C₁₁), 129.2 (C_{2'}), 125.9 (C₂), 125.8 (C₁₀), 121.1 (C₁), 120.9 (C₆), 119.6 (q, ¹*J*_{C-F} = 281.3 Hz, C₉), 111.4 (C₃), 99.4 (C_{4'}), 21.8 (C₁₄); **¹⁹FNMR** (376 MHz, CDCl₃) δ_F -66.7 (s).

Minor isomer: **R_f** 0.39 (PE : EtOAc, 17:3); **¹HNMR** (500 MHz, CDCl₃) δ_H 7.96 (2H, m, H_{3'}), 7.91 (2H, m, H_{2'}), 7.89 (2H, d, *J* = 8.1 Hz, H₁₁), 7.85 (1H, d, *J* = 1.6 Hz, H₆), 7.63 (1H, d, *J* = 8.5 Hz, H₃), 7.48 (1H, dd, *J* = 8.5, 1.6 Hz, H₂), 7.39 (2H, d, *J* = 8.1 Hz, H₁₂), 2.48 (3H, s, H₁₄). **¹³CNMR** (125 MHz, CDCl₃) δ_C 163.9 (C₇), 153.6 (q, ²*J*_{C-F} = 33.5 Hz, C₈), 152.7 (C₄), 146.1 (C₁₃), 142.3 (C₅), 138.4 (C_{3'}), 131.4 (C₁₀), 123.0 (C₁₂), 129.3 (C₁₁), 129.1 (C_{2'}), 125.9 (C₂), 125.8 (C₁₀), 121.2 (C₁), 120.9 (C₆), 119.6 (q, ¹*J*_{C-F} = 281.3 Hz, C₉), 111.1 (C₃), 99.5 (C_{4'}), 21.8 (C₁₄); **¹⁹FNMR** (376 MHz, CDCl₃) δ_F -66.7 (s);

HRMS (ES⁺) Calc. for C₂₂H₁₅F₃IN₂O₄S [M+H]⁺ 586.9744, found 586.9741.

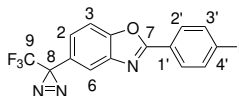
2-(4-Iodophenyl)-5-(3-(trifluoromethyl)diaziridin-3-yl)benzo[d]oxazole **17**



Diaziridine **17** was obtained according to General Procedure E, using tosyl oxime **16** (1.82 g, 3.11 mmol) and NH₃ (5 mL) in CH₂Cl₂ (25 mL). The crude product was purified by flash column chromatography (PE : EtOAc, 4:1) to yield diaziridine **17** (1.05 g, 2.43 mmol, 78%) as a pale yellow solid.

R_f 0.39 (PE : EtOAc, 4:1); **v_{max}** (cm⁻¹) 1593 (N-H), 1479, 1397, 1216 (C-F), 1150; **mp** 152-154 °C; **¹HNMR** (500 MHz, CDCl₃) δ_H 8.05 (1H, d, *J* = 1.5 Hz, H₆), 7.97 (2H, m, H_{3'}), 7.90 (2H, m, H_{2'}), 7.66 (1H, dd, *J* = 8.5, 1.5 Hz, H₂), 7.62 (1H, d, *J* = 8.5 Hz, H₃), 2.89 (1H, d, *J* = 8.9 Hz, -NH), 2.32 (1H, d, *J* = 8.9 Hz, -NH); **¹³CNMR** (125 MHz, CDCl₃) δ_C 164.0 (C₇), 152.0 (C₄), 142.7 (C₅), 138.7 (C_{2'}), 129.5 (C_{3'}), 129.0 (C₁), 126.5 (C_{1'}), 125.8 (C₂), 123.5 (q, ¹*J*_{C-F} = 277.6 Hz, C₉), 120.9 (C₆), 111.4 (C₃), 99.5 (C_{4'}), 58.2 (q, ²*J*_{C-F} = 36.2 Hz, C₈); **¹⁹FNMR** (376 MHz, CDCl₃) δ_F -75.5 (s); **HRMS** (ES⁺) Calc. for C₁₅H₁₀F₃IN₃O [M+H]⁺ 431.9815, found 431.9815.

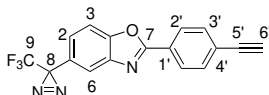
2-(4-Iodophenyl)-5-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)benzo[*d*]oxazole **18**



Diazirine **18** was obtained according to General Procedure F, using diaziridine **17** (580 mg, 1.35 mmol), iodine (409 mg, 1.61 mmol) and NEt₃ (0.56 mL, 4.04 mmol) in CH₂Cl₂ (25 mL). The crude product was purified by flash column chromatography (PE : EtOAc, 19:1 → 9:1) to yield diazirine **18** (564 mg, 1.31 mmol, 98%) as a white solid.

R_f 0.84 (PE : EtOAc, 9:1); **v_{max}** (cm⁻¹) 1478, 1397, 1252 (C-F), 1150, 810; **mp** 117-119 °C; **¹HNMR** (500 MHz, CDCl₃) δ_H 7.95 (2H, m, H_{3'}), 7.89 (2H, m, H_{2'}), 7.71 (1H, d, *J* = 1.8 Hz, H₆), 7.59 (1H, d, *J* = 8.5 Hz, H₃), 7.20 (1H, dd, *J* = 8.5, 1.8 Hz, H₂); **¹³CNMR** (125 MHz, CDCl₃) δ_C 164.0 (C₇), 151.5 (C₄), 142.7 (C₅), 138.5 (C_{2'}), 129.3 (C_{3'}), 126.1 (C_{1'}), 125.9 (C₁), 124.0 (C₂), 122.2 (q, ¹*J*_{C-F} = 274.7 Hz, C₉), 119.3 (C₆), 111.4 (C₃), 99.4 (C_{4'}). 28.7 (q, ²*J*_{C-F} = 40.7 Hz, C₈); **¹⁹FNMR** (376 MHz, CD₃OD) δ_F -67.4 (s); **HRMS** (ES⁺) Calc. for C₁₅H₈F₃IN₃O [M+H]⁺ 429.9659, found 429.9655.

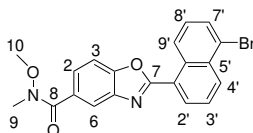
2-(4-Ethynylphenyl)-5-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)benzo[*d*]oxazole **3**



Diazirine **3** was obtained according to General Procedure G, using diazirine **18** (100 mg, 0.233 mmol), bis(triphenylphosphine)palladium(II) dichloride (24.5 mg, 35.0 μmol), copper(I) iodide (4.44 mg, 23.3 μmol), NEt₃ (0.70 mL) and trimethylsilylacetylene (39 μL, 0.280 mmol) in THF (10 mL). The reaction was complete after 1 h. The TMS-protected alkyne intermediate formed was purified by flash column chromatography (PE : EtOAc, 1:0 → 49:1), then deprotected with TBAF (0.70 mL, 1 M in THF) in THF (5 mL). The reaction was complete after 30 min. The crude product was purified by flash column chromatography (PE : EtOAc, 1:0 → 49:1) to yield alkyne **3** (38.2 mg, 0.117 mmol, 50%) as a white solid.

R_f 0.69 (PE : EtOAc, 49:1); **v_{max}** (cm⁻¹) 3311 (sharp, alkyne C-H), 1262 (C-F), 1149, 810, 740; **mp** 125-127 °C; **¹HNMR** (500 MHz, CDCl₃) δ_H 8.20 (2H, m, H_{2'}), 7.72 (1H, d, *J* = 1.8 Hz, H₆), 7.64 (2H, m, H_{3'}), 7.60 (1H, d, *J* = 8.6 Hz, H₃), 7.20 (1H, dd, *J* = 8.6, 1.8 Hz, H₂), 3.26 (1H, s, H_{6'}); **¹³CNMR** (125 MHz, CDCl₃) δ_C 163.9 (C₇), 151.5 (C₄), 142.8 (C₅), 132.9 (C_{3'}), 127.8 (C_{2'}), 126.7 (C_{4'}), 126.0 (C_{1'}), 125.9 (C₁), 124.0 (C₂), 122.3 (q, ¹*J*_{C-F} = 274.7 Hz, C₉), 119.4 (C₆), 111.4 (C₃), 82.9 (C_{5'}), 80.4 (C_{6'}), 28.8 (q, ²*J*_{C-F} = 40.6 Hz, C₈); **¹⁹FNMR** (376 MHz, CD₃OD) δ_F -67.4 (s); **HRMS** (ES⁺) Calc. for C₁₇H₉F₃N₃O [M+H]⁺ 328.0692, found 328.0691.

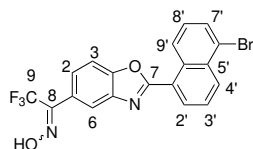
2-(5-Bromonaphthalen-1-yl)-*N*-methoxy-*N*-methylbenzo[*d*]oxazole-5-carboxamide **19**



Carboxamide **19** was obtained by a procedure based on General Procedure B except with the addition of 1-hydroxybenzotriazole in the amide coupling. 5-Bromonaphthoic acid (502 mg, 2.00 mmol), thionyl chloride (0.44 mL, 6.00 mmol) and DMF (0.10 mL) were used in CH₂Cl₂ (20 mL). The acid chloride intermediate formed was reacted with 3-amino-4-hydroxybenzoic acid (277 mg, 1.80 mmol, 0.9 eq.) in 1,4-dioxane (5 mL). Amide coupling was performed on the crude product using EDC hydrochloride (575 mg, 3.00 mmol, 1.5 eq.), *N,O*-dimethylhydroxylamine hydrochloride (293 mg, 3.00 mmol, 1.5 eq.), 1-hydroxybenzotriazole (135 mg, 1.00 mmol, 0.5 eq.) and NEt₃ (0.42 mL, 3.00 mmol, 1.5 eq.) in DMF (25 mL). The crude product was purified by flash column chromatography (PE : EtOAc, 1:1) to yield carboxamide **20** (459 mg, 1.12 mmol, 62%) as a white solid.

R_f 0.54 (PE : EtOAc, 1:1); **v_{max}** (cm⁻¹) 2930 (C-H), 1679 ((C=O)NH), 1460, 1251; **mp** 137-138 °C; **¹HNMR** (500 MHz, CDCl₃) δ_H 9.48 (1H, ddd, *J* = 8.7, 1.0, 1.0 Hz, H_{9'}), 8.48 (1H, ddd, *J* = 8.6, 1.1, 1.1 Hz, H_{4'}), 8.43 (1H, dd, *J* = 7.3, 1.1 Hz, H_{2'}), 8.24 (1H, d, *J* = 1.6 Hz, H₆), 7.87 (1H, dd, *J* = 7.4, 1.1 Hz, H_{7'}), 7.80 (1H, dd, *J* = 8.4, 1.6 Hz, H₂), 7.67 (1H, dd, *J* = 8.5, 7.3 Hz, H_{3'}), 7.64 (1H, d, *J* = 8.4 Hz, H₃), 7.50 (1H, dd, *J* = 8.7, 7.4 Hz, H_{8'}), 3.59 (3H, s, H₁₀), 3.42 (3H, s, H₉); **¹³CNMR** (125 MHz, CDCl₃) δ_C 169.2 (C₈), 163.2 (C₇), 151.4 (C₄), 141.8 (C₅), 132.4 (C_{5'}), 132.0 (C_{10'}), 131.6 (C_{4'}), 130.9 (C_{7'}), 130.7 (C₁), 130.2 (C_{2'}), 128.2 (C_{8'}), 126.5 (C₂), 126.3 (C_{3'}), 126.2 (C₉), 123.6 (C_{1'} or C_{6'}), 123.5 (C_{1'} or C_{6'}), 120.8 (C₆), 110.2 (C₃), 61.1 (C₁₀), 33.9 (C₉); **HRMS** (ES⁺) Calc. for C₂₀H₁₆⁷⁹BrN₂O₃ [M+H]⁺ 411.0339, found 411.0339.

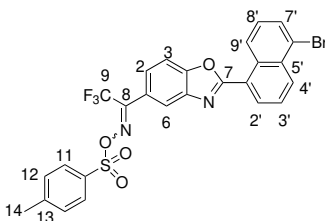
1-(2-(5-Bromonaphthalen-1-yl)benzo[*d*]oxazol-5-yl)-2,2,2-trifluoroethan-1-one oxime **21**



Oxime **21** was obtained according to General Procedure C, using carboxamide **22** (1.18 g, 2.87 mmol), trifluoromethyltrimethylsilane (0.85 mL, 5.74 mmol) and caesium fluoride (87.2 mg, 0.574 mmol) in toluene (40 mL). The reaction was stirred for three days, with further trifluoromethyltrimethylsilane (0.85 mL, 5.74 mmol) and caesium fluoride (87.2 mg, 0.574 mmol) added every 24 h. TBAF (3.44 mL, 1 M in THF) was used for desilylation of the intermediate formed. The crude trifluoromethylketone product was dissolved in pyridine (5 mL) and ethanol (25 mL) and refluxed with hydroxylammonium chloride (598 mg, 8.61 mmol). The crude product was purified by flash column chromatography (PE : EtOAc, 9:1) to yield oxime **21** (699 mg, 1.61 mmol, 56%) as a yellow solid.

R_f 0.31 (PE : EtOAc, 9:1); **v_{max}** (cm⁻¹) 3223 (-OH), 2981 (C-H), 1696 (C=N-OH), 1253 (C-F), 1154; **mp** 182-183 °C; **¹HNMR** (500 MHz, (CD₃)₂CO) δ_H 11.96 (1H, *br s*, -OH), 9.63 (1H, ddd, *J* = 8.7, 1.1, 1.1 Hz, H_{9'}), 8.61 (1H, dd, *J* = 7.4, 1.1 Hz, H_{2'}), 8.57 (1H, ddd, *J* = 8.6, 1.1, 1.1 Hz, H_{4'}), 8.06 (1H, s, H₆), 8.05 (1H, *obs m*, H_{7'}), 7.81 (1H, d, *J* = 8.4 Hz, H₃), 7.76 (1H, dd, *J* = 8.6, 7.4 Hz, H_{3'}), 7.67 (1H, dd, *J* = 8.7, 7.6 Hz, H_{8'}), 7.65 (1H, dd, *J* = 8.4, 1.6 Hz, H₂); **¹³CNMR** (125 MHz, CDCl₃) δ_C 163.8 (C₇), 151.9 (C₈), 151.7 (C₄), 143.1 (C₅), 133.1 (C₁), 132.8 (C_{5'}), 132.2 (C_{10'}), 132.0 (C_{4'}), 131.5 (C_{7'}), 131.4 (C_{2'}), 129.3 (C_{8'}), 127.8 (C_{3'}), 127.5 (C₂), 127.4 (C_{9'}), 124.6 (C_{1'}), 123.7 (C_{6'}), 122.2 (q, ¹*J*_{C-F} = 273.1 Hz, C₉), 121.9 (C₆), 111.8 (C₃); **¹⁹FNMR** (376 MHz, CDCl₃) δ_F -67.6 (s); **HRMS** (ES⁺) Calc. for C₁₉H₁₁F₃⁷⁹BrN₂O₂ [M+H]⁺ 434.9951, found 434.9951.

1-(2-(5-Bromonaphthalen-1-yl)benzo[*d*]oxazol-5-yl)-2,2,2-trifluoroethan-1-one *O*-tosyl oxime **23**



Tosyl oxime **23** was obtained according to General Procedure D, using oxime **24** (818 mg, 1.88 mmol), *p*-toluenesulfonyl chloride (717 mg, 3.76 mmol), 4-dimethylaminopyridine (23.0 mg, 0.188 mmol) and NEt₃ (0.78 mL, 5.64 mmol) in CH₂Cl₂ (30 mL). The crude product was purified by flash column chromatography (PE : EtOAc, 19:1) to yield tosyl oxime **23** (820 mg, 1.39 mmol, 74%) as a pale yellow solid in a mixture of isomers (50:50).

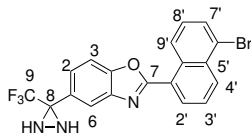
v_{max} (cm⁻¹) 2980 (C-H), 1334 (S=O), 1255 (C-F), 1196 (S=O), 1154; **mp** 148-150 °C;

Minor isomer: **R**_f (0.35, PE : EtOAc, 19:1); ¹HNMR (500 MHz, CDCl₃) δ_H 9.48 (1H, ddd, *J* = 8.8, 1.0, 1.0 Hz, H_{9'}), 8.54 (1H, ddd, *J* = 8.6, 1.1, 1.1 Hz, H_{4'}), 8.46 (1H, dd, *J* = 7.3, 1.2 Hz, H_{2'}), 7.94-7.89 (4H, m, H₆, H_{7'} and H₁₁), 7.73 (1H, d, *J* = 8.4 Hz, H₃), 7.71 (1H, dd, *J* = 8.6, 7.3 Hz, H_{3'}), 7.54 (1H, dd, *J* = 8.8, 7.4 Hz, H_{8'}), 7.47 (1H, dd, *J* = 8.5, 1.7 Hz, H₂), 7.41 (2H, m, H₁₂), 2.49 (3H, s, H₁₄); ¹³CNMR (125 MHz, CDCl₃) δ_C 163.8 (C₇), 153.7 (q, ²*J*_{C-F} = 34.1 Hz, C₈), 151.8 (C₄), 146.2 (C₁₄), 142.6 (C₅), 132.6 (C_{5'}), 132.2 (C_{10'}), 132.1 (C_{4'}), 131.3 (C_{1'}), 131.1 (C_{7'}), 130.6 (C_{2'}), 130.1 (C₁₂), 129.5 (C₁₀), 129.3 (C₁₁), 128.5 (C_{8'}), 126.4 (C_{3'}), 126.2 (C₂), 126.2 (C_{9'}), 123.7 (C_{6'}), 123.4 (C₁), 121.3 (C₆), 119.8 (q, ¹*J*_{C-F} = 277.5 Hz, C₉), 111.2 (C₃), 22.0 (C₁₄); ¹⁹FNMR (376 MHz, CDCl₃) δ_F -66.6 (s);

Major isomer: **R**_f (0.28, PE : EtOAc, 19:1); ¹HNMR (500 MHz, CDCl₃) δ_H 9.49 (1H, ddd, *J* = 8.8, 1.0, 1.0 Hz, H_{9'}), 8.54 (1H, ddd, *J* = 8.6, 1.1, 1.1 Hz, H_{4'}), 8.46 (1H, dd, *J* = 7.3, 1.2 Hz, H_{2'}), 7.96-7.91 (4H, m, H₆, H_{7'} and H₁₁), 7.71 (1H, dd, *J* = 8.6, 7.3 Hz, H_{3'}), 7.68 (1H, d, *J* = 8.4 Hz, H₃), 7.55 (1H, dd, *J* = 8.8, 7.4 Hz, H_{8'}), 7.52 (1H, dd, *J* = 8.5, 1.7 Hz, H₂), 7.40 (2H, m, H₁₂), 2.47 (3H, s, H₁₄); ¹³CNMR (125 MHz, CDCl₃) δ_C 163.9 (C₇), 153.9 (q, ²*J*_{C-F} = 32.9 Hz, C₈), 152.2 (C₄), 146.4 (C₁₃), 142.7 (C₅), 132.6 (C_{5'}), 132.2 (C_{10'}), 132.1 (C_{4'}), 131.3 (C_{1'}), 131.1 (C_{7'}), 130.6 (C_{2'}), 130.1 (C₁₂), 129.5 (C₁₀), 129.3 (C₁₁), 128.5 (C_{8'}), 126.4 (C_{3'}), 126.3 (C₂), 126.2 (C_{9'}), 123.7 (C_{6'}), 123.6 (C₁), 121.6 (C₆), 119.8 (q, ¹*J*_{C-F} = 277.5 Hz, C₉), 111.5 (C₃), 22.0 (C₁₄); ¹⁹FNMR (376 MHz, CDCl₃) δ_F -66.6 (s);

HRMS (ES⁺) Calc. for C₂₆H₁₇F₃⁷⁹BrN₂O₄S [M+H]⁺ 589.0039, found 589.0035.

2-(5-Bromonaphthalen-1-yl)-5-(3-(trifluoromethyl)diaziridin-3-yl)benzo[*d*]oxazole **25**

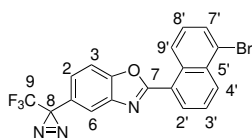


Diaziridine **25** was obtained according to General Procedure E, using tosyl oxime **23** (630 mg, 1.07 mmol) and NH₃ (5 mL) in CH₂Cl₂ (10 mL). The crude product was used without further purification, yielding diaziridine **25** (469 mg, 1.07 mmol, quant.) as a white solid.

R_f (0.67, PE : EtOAc, 4:1); **v**_{max} (cm⁻¹) 2981 (C-H), 1457, 1157, 1036; **mp** 149-150 °C; ¹HNMR (500 MHz, CDCl₃) δ_H 9.51 (1H, ddd, *J* = 8.5, 1.1, 1.1 Hz, H_{9'}), 8.55 (1H, ddd, *J* = 8.6, 1.1, 1.1 Hz, H_{4'}), 8.49 (1H, dd, *J* = 7.4, 1.1 Hz, H_{2'}), 8.17 (1H, s, H₆), 7.92 (1H, dd, *J* = 7.4, 1.1 Hz, H_{7'}), 7.73 (1H, dd, *J* = 8.6, 7.4 Hz, H_{3'}), 7.70 (2H, s, H₂ and H₃), 7.55 (1H, dd, *J* = 8.5, 7.4 Hz, H_{8'}), 2.91 (1H, d, *J* = 8.9 Hz, -NH), 2.34 (1H, d, *J* = 8.9 Hz, -NH); ¹³CNMR (125 MHz, CDCl₃) δ_C 163.5 (C₇), 151.0 (C₄), 142.5 (C₅), 132.5 (C_{5'}), 132.0 (C_{10'}), 131.9 (C_{4'}), 130.9 (C_{7'}), 130.3 (C_{2'}), 129.7 (C₁), 128.3 (C_{8'}), 127.2 (C_{1'}), 126.3 (C_{3'} or C_{9'}), 126.2 (C_{3'} or C_{9'}), 125.6 (C₂), 124.5 (q, ¹*J*_{C-F} = 276.6 Hz, C₉),

123.6 (C_{6'}), 120.8 (C₆), 110.9 (C₃), 58.3 (q, ²J_{C-F} = 36.1 Hz, C₈); ¹⁹FNMR (376 MHz, CDCl₃) δ_F -75.5 (s); HRMS (ES⁺) Calc. for C₁₉H₁₂⁷⁹BrF₃N₃O [M+H]⁺ 434.0105, found 434.0110.

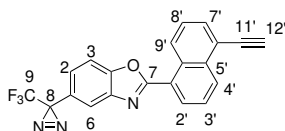
2-(5-Bromonaphthalen-1-yl)-5-(3-(trifluoromethyl)-3H-diazirin-3-yl)benzo[d]oxazole **26**



Diazirine **26** was obtained according to General Procedure F, using diaziridine **25** (439 mg, 1.01 mmol), iodine (308 mg, 1.21 mmol) and NEt₃ (0.42 mL, 3.03 mmol) in CH₂Cl₂ (20 mL). The crude product was purified by flash column chromatography (PE : EtOAc, 49:1 → 19:1) to yield diazirine **26** (407 mg, 0.945 mmol, 94%) as a white solid.

R_f (0.53, PE : EtOAc, 49:1); **v_{max}** (cm⁻¹) 2981 (C-H), 1258 (C-F), 1154, 773; **mp** 104-106 °C; ¹HNMR (500 MHz, CDCl₃) δ_H 9.50 (1H, ddd, *J* = 8.7, 1.1, 1.1 Hz, H_{9'}), 8.54 (1H, ddd, *J* = 8.6, 1.1, 1.1 Hz, H_{4'}), 8.47 (1H, dd, *J* = 7.3, 1.1 Hz, H_{2'}), 7.92 (1H, dd, *J* = 7.4, 1.0 Hz, H_{7'}), 7.83 (1H, dd, *J* = 1.8, 0.6 Hz, H₆), 7.72 (1H, dd, *J* = 8.6, 7.3 Hz, H_{3'}), 7.66 (1H, d, *J* = 8.6, 0.6 Hz, H₃), 7.54 (1H, dd, *J* = 8.7, 7.4 Hz, H_{8'}), 7.24 (1H, dd, *J* = 8.6, 1.8 Hz, H₂); ¹³CNMR (125 MHz, CDCl₃) δ_C 163.6 (C₇), 150.7 (C₄), 142.8 (C₅), 132.4 (C_{5'}), 132.1 (C_{10'}), 132.0 (C_{4'}), 131.0 (C_{7'}), 130.4 (C_{2'}), 128.3 (C_{8'}), 126.3 (C_{3'}), 126.1 (C_{9'}), 125.6 (C₁), 124.0 (C₂), 123.6 (C_{1'} or C_{6'}), 123.4 (C_{1'} or C_{6'}), 122.3 (q, ¹J_{C-F} = 274.7 Hz, C₉), 119.5 (C₆), 111.2 (C₃), 28.8 (q, ²J_{C-F} = 40.6 Hz, C₈); ¹⁹FNMR (376 MHz, CDCl₃) δ_F -65.4 (s); HRMS (ES⁺) Calc. for C₁₉H₁₀⁷⁹BrF₃N₃O [M+H]⁺ 431.9954, found 431.9950.

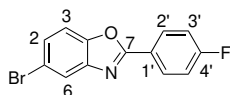
2-(5-Ethynynaphthalen-1-yl)-5-(3-(trifluoromethyl)-3H-diazirin-3-yl)benzo[d]oxazole **4**



Diazirine **4** was obtained according to General Procedure G, using diazirine **26** (200 mg, 0.465 mmol), bis(triphenylphosphine)palladium(II) dichloride (48.9 mg, 69.7 μmol), copper(I) iodide (8.86 mg, 46.5 μmol), NEt₃ (1.50 mL) and trimethylsilylacetylene (78.2 μL, 0.558 mmol) in THF (10 mL). The reaction was worked up after 6 h, although starting material was still present. The TMS-protected alkyne intermediate formed was purified by flash column chromatography (PE : EtOAc, 1:0 → 99:1), then deprotected with TBAF (0.93 mL, 1 M in THF) in THF (5 mL). The reaction was complete after 30 min. The crude product was purified by flash column chromatography (pentane : toluene, 19:1) to yield alkyne **4** (58.9 mg, 0.156 mmol, 34%) as an off-white solid.

R_f (0.16, pentane : toluene, 19:1); **v_{max}** (cm⁻¹) 2981 (C-H), 1256 (C-F), 1154, 773; **mp** 87-89 °C; ¹HNMR (500 MHz, CDCl₃) δ_H 9.52 (1H, ddd, *J* = 8.6, 1.0, 1.0 Hz, H_{9'}), 8.64 (1H, ddd, *J* = 8.4, 1.1, 1.1 Hz, H_{4'}), 8.46 (1H, dd, *J* = 7.3, 1.3 Hz, H_{2'}), 7.85 (1H, dd, *J* = 7.1, 1.2 Hz, H_{7'}), 7.82 (1H, d, *J* = 1.7 Hz, H₆), 7.70 (1H, dd, *J* = 8.4, 7.3 Hz, H_{3'}), 7.65 (1H, dd, *J* = 8.7, 7.1 Hz, H_{8'}), 7.64 (1H, d, *J* = 8.7 Hz, H₃), 7.24 (1H, dd, *J* = 8.4, 1.9 Hz, H₂), 3.53 (1H, s, H_{12'}); ¹³CNMR (125 MHz, CDCl₃) δ_C 163.9 (C₇), 150.7 (C₄), 142.8 (C₅), 134.0 (C_{5'}), 131.9 (C_{7'}), 130.9 (C_{4'}), 130.5 (C_{2'}), 130.2 (C_{10'}), 127.4 (C_{9'}), 127.3 (C_{8'}), 125.9 (C_{3'}), 125.6 (C₁), 123.9 (C₂), 123.2 (C_{1'}), 122.3 (q, ¹J_{C-F} = 274.7 Hz, C₉), 120.6 (C_{6'}), 119.4 (C₆), 111.1 (C₃), 82.7 (C_{12'}), 81.5 (C_{11'}), 28.8 (q, ²J_{C-F} = 40.6 Hz, C₈); ¹⁹FNMR (376 MHz, CD₃OD) δ_F -65.4 (s); HRMS (CI⁺) Calc. for C₂₁H₁₀F₃N₃O [M⁺] 377.0770 found 377.0778.

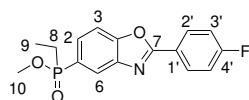
5-bromo-2-(4-fluorophenyl)benzo[d]oxazole **27**



4-fluorobenzoyl chloride (18.6 g, 0.12 mol) was added to a suspension of 2-amino-4-bromophenol (20.0 g, 0.11 mol) in xylenes (100 mL) and refluxed for 1 h. Then methanesulfonic acid (2.0 g, 0.02 mol) was added and the mixture was refluxed for a further 1 h. The reaction was cooled to RT, diluted with EtOAc (500 mL) and washed with water, sat. aq. NaHCO₃ and brine. The combined organic layers were dried over Na₂SO₄, filtered and concentrated *in vacuo*. The residue was recrystallized from petroleum ether/EtOAc (2:1) and filtered to afford the title compound (20.0 g, 90%).

mp 149-151 °C; **¹H NMR** (500 MHz, CDCl₃) δ 8.27 - 8.21 (2H, m, H_{2'}), 7.89 (1H, d, *J* = 1.6 Hz, H₆), 7.47 (1H, dd, *J* = 8.6, 1.7 Hz, H₂), 7.45 (1H, d, *J* = 8.5 Hz, H₃), 7.25 - 7.20 (2H, m, H_{3'}); **¹³C NMR** (125 MHz, CDCl₃) δ 165.20 (d, ¹*J*_{C-F} = 253.6 Hz, C_{4'}), 163.4 (C₇), 149.9 (C₄), 143.9 (C₅), 130.2 (d, ³*J*_{C-F} = 9.0 Hz, C_{2'}), 128.3 (C₂), 123.2 (C_{1'}), 123.1 (C₆), 117.5 (C₁), 116.5 (d, ²*J*_{C-F} = 22.2 Hz, C_{3'}), 111.9 (C₃); **¹⁹F NMR** (376 MHz, CDCl₃) xx; **HRMS** (ES⁺) Calc. for C₁₃H₈⁷⁹BrFNO [M + H]⁺ 291.9768, found 291.9769.

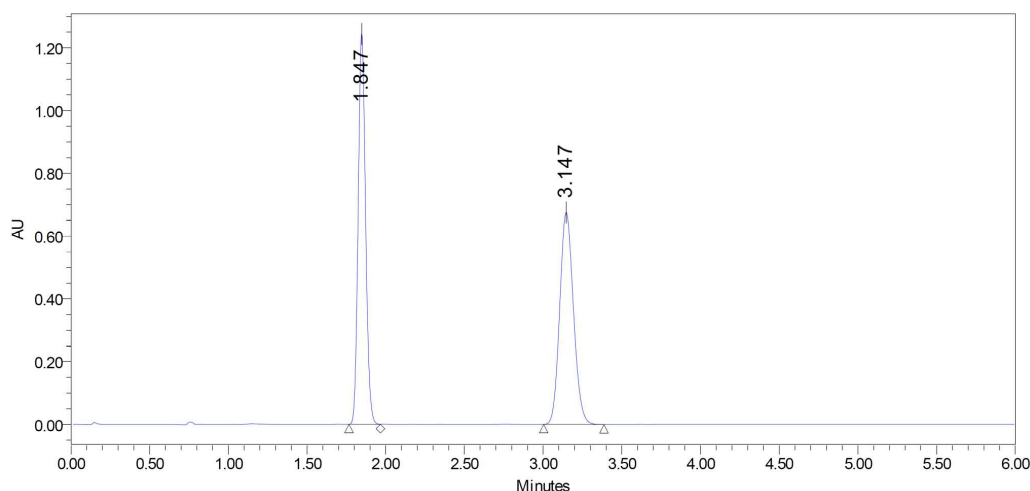
methyl ethyl(2-(4-fluorophenyl)benzo[*d*]oxazol-5-yl)phosphinate (SMT021256) 8



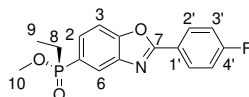
To a degassed solution of 5-bromo-2-(4-fluorophenyl)benzo[*d*]oxazole (20.0 g, 0.07 mol), ethylphosphinic acid (14.8 g, 0.14 mol) and DIPEA (25 mL, 0.14 mol) in DME (100 mL) and toluene (300 mL) Pd(OAc)₂ (0.92 g, 0.004 mol) and XantPhos (2.27 g, 0.004 mol) were added under N₂ and the reaction was stirred at 90°C for 2 h. The solvents were removed *in vacuo* and the residue partitioned between EtOAc and NaOH (1M). The aqueous layer was extracted into EtOAc, acidified with 1M HCl (pH 3) and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na₂SO₄, and the desired product was obtained by column chromatography (5% MeOH/DCM) as an off-white solid (18.9 g, 86%).

mp 90-2 °C; **¹H NMR** (500 MHz, (CD₃)₂SO) δ 8.32 - 8.25 (2H, m, H_{2'}), 8.16 - 8.10 (1H, m, H₆), 7.97 (1H, dd, *J* = 8.3, 2.3 Hz, H₃), 7.79 (1H, ddd, *J* = 10.8, 8.3, 1.4 Hz, H₂), 7.53 - 7.44 (2H, m, H_{3'}), 3.53 (3H, d, *J* = 10.9 Hz, H₁₀), 2.09 - 1.91 (2H, m, H₈), 0.97 (3H, dt, *J* = 18.9, 7.6 Hz, H₉); **¹³C NMR** (125 MHz, (CD₃)₂SO) δ 164.5 (d, ¹*J*_{C-F} = 250.8 Hz, C_{4'}), 162.7 (C₇), 152.7 (d, ⁴*J*_{C-P} = 3.4 Hz, C₄), 141.8 (d, ³*J*_{C-P} = 16.4 Hz, C₅), 130.3 (d, ³*J*_{C-F} = 9.4 Hz, C_{2'}), 128.9 (d, ²*J*_{C-P} = 11.3 Hz, C₂), 126.9 (d, ¹*J*_{C-P} = 121.1 Hz, C₁), 123.4 (d, ⁴*J*_{C-F} = 11.1 Hz, C_{1'}), 122.7 (d, ²*J*_{C-P} = 3.4 Hz, C₆), 116.7 (d, ²*J*_{C-F} = 22.1 Hz, C_{3'}), 111.7 (d, ³*J*_{C-P} = 13.5 Hz, C₃), 50.8 (d, ²*J*_{C-P} = 6.6 Hz, C₁₀), 21.2 (d, ¹*J*_{C-P} = 101.3 Hz, C₈), 5.8 (d, ²*J*_{C-P} = 4.7 Hz, C₉); **³¹P NMR {H}** (162 MHz, (CD₃)₂SO) δ 46.8 (s); **¹⁹F NMR** (376 MHz, (CD₃)₂SO) δ -106.8 (m); **LC-MS** (254 nm, 100%) R_T 2.34 min, MS (ES⁺) Calc. for C₁₆H₁₅FNO₃P [M + H]⁺ 320.1, found 320.1; **HRMS** (ES⁺) Calc. for C₁₆H₁₅FNO₃P [M + H]⁺ 320.0846, found 320.0843.

The two enantiomers were isolated by chiral separation. SMT021256 was dissolved in MeOH (100 mg/mL) and then purified by supercritical flash chromatography with a Lux C4 column (21.2 mm x 250 mm, 5 μm) and isocratic MeOH/CO₂ (35:65). From 10076.2 mg racemic mixture, 3647.3 mg of the first eluting enantiomer (R_T 1.85 min, 49.8%) were collected and assigned the name SMT022331 and 4962.1 mg of the second enantiomer (R_T 3.15 min, 50.2%) were collected and assigned the name SMT022332.

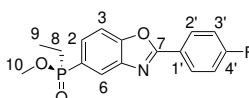


methyl (-)-ethyl(2-(4-fluorophenyl)benzo[d]oxazol-5-yl)phosphinate (SMT022331) 28



mp 88 °C. **¹H NMR** (500 MHz, (CD₃)₂SO) δ 8.32 - 8.25 (2H, m, H_{2'}), 8.16 - 8.10 (1H, m, H₆), 7.97 (1H, dd, *J* = 8.3, 2.3 Hz, H₃), 7.79 (1H, ddd, *J* = 10.8, 8.3, 1.4 Hz, H₂), 7.53 - 7.44 (2H, m, H_{3'}), 3.53 (3H, d, *J* = 10.9 Hz, H₁₀), 2.09 - 1.91 (2H, m, H₈), 0.97 (3H, dt, *J* = 18.9, 7.6 Hz, H₉); **¹³C NMR** (125 MHz, (CD₃)₂SO) δ 164.5 (d, ¹*J*_{C-F} = 250.8 Hz, C_{4'}), 162.7 (C₇), 152.7 (d, ⁴*J*_{C-P} = 3.4 Hz, C₄), 141.8 (d, ³*J*_{C-P} = 17.2 Hz, C₅), 130.3 (d, ³*J*_{C-F} = 9.7 Hz, C_{2'}), 128.9 (d, ²*J*_{C-P} = 11.2 Hz, C₂), 126.9 (d, ¹*J*_{C-P} = 120.9 Hz, C₁), 123.4 (d, ⁴*J*_{C-F} = 11.0 Hz, C_{1'}), 122.7 (d, ²*J*_{C-P} = 3.1 Hz, C₆), 116.7 (d, ²*J*_{C-F} = 22.1 Hz, C_{3'}), 111.7 (d, ³*J*_{C-P} = 13.7 Hz, C₃), 50.8 (d, ²*J*_{C-P} = 6.5 Hz, C₁₀), 21.2 (d, ¹*J*_{C-P} = 101.7 Hz, C₈), 5.8 (d, ²*J*_{C-P} = 4.6 Hz, C₉); **³¹P NMR {H}** (162 MHz, (CD₃)₂SO) δ 46.8. **¹⁹F NMR** (376 MHz, (CD₃)₂SO) δ -106.7 (m); **HRMS** (ES⁺) Calc. for C₁₆H₁₅FNO₃P [M + H]⁺ 320.0846, found 320.0845; [α_D²⁵] - 40.7[c1.00, THF].

methyl (+)-ethyl(2-(4-fluorophenyl)benzo[d]oxazol-5-yl)phosphinate (SMT022332) 7



mp 86-7 °C; **¹H NMR** (500 MHz, (CD₃)₂SO) δ 8.31 - 8.25 (2H, m, H_{2'}), 8.13 (1H, dd, *J* = 11.6, 1.4 Hz, H₆), 7.97 (1H, dd, *J* = 8.3, 2.3 Hz, H₃), 7.79 (1H, ddd, *J* = 10.8, 8.3, 1.4 Hz, H₂), 7.53 - 7.44 (2H, m, H_{3'}), 3.53 (3H, d, *J* = 10.9 Hz, H₁₀), 2.09 - 1.91 (2H, m, H₈), 0.97 (3H, dt, *J* = 18.9, 7.6 Hz, H₉); **¹³C NMR** (125 MHz, (CD₃)₂SO) δ 164.5 (d, ¹*J*_{C-F} = 251.5 Hz, C_{4'}), 162.7 (C₇), 152.7 (d, ⁴*J*_{C-P} = 3.4 Hz, C₄), 141.8 (d, ³*J*_{C-P} = 17.0 Hz, C₅), 130.3 (d, ³*J*_{C-F} = 9.3 Hz, C_{2'}), 128.9 (d, ²*J*_{C-P} = 11.0 Hz, C₂), 126.9 (d, ¹*J*_{C-P} = 121.6 Hz, C₁), 123.4 (d, ⁴*J*_{C-F} = 11.0 Hz, C_{1'}), 122.7 (d, ²*J*_{C-P} = 3.3 Hz, C₆), 116.7 (d, ²*J*_{C-F} = 22.0 Hz, C_{3'}), 111.7 (d, ³*J*_{C-P} = 13.6 Hz, C₃), 50.8 (d, ²*J*_{C-P} = 6.4 Hz, C₁₀), 21.2 (d, ¹*J*_{C-P} = 101.6 Hz, C₈), 5.8 (d, ²*J*_{C-P} = 4.6 Hz, C₉); **³¹P NMR {H}** (162 MHz, (CD₃)₂SO) δ 46.8; **¹⁹F NMR** (376 MHz, (CD₃)₂SO) δ -106.8 (m); **HRMS** (ES⁺) Calc. for C₁₆H₁₅FNO₃P [M + H]⁺ 320.0846, found 320.0846; [α_D²⁵] + 40.7[c1.00, THF].

Chemical and chiral purity of SMT022331 and SMT022332

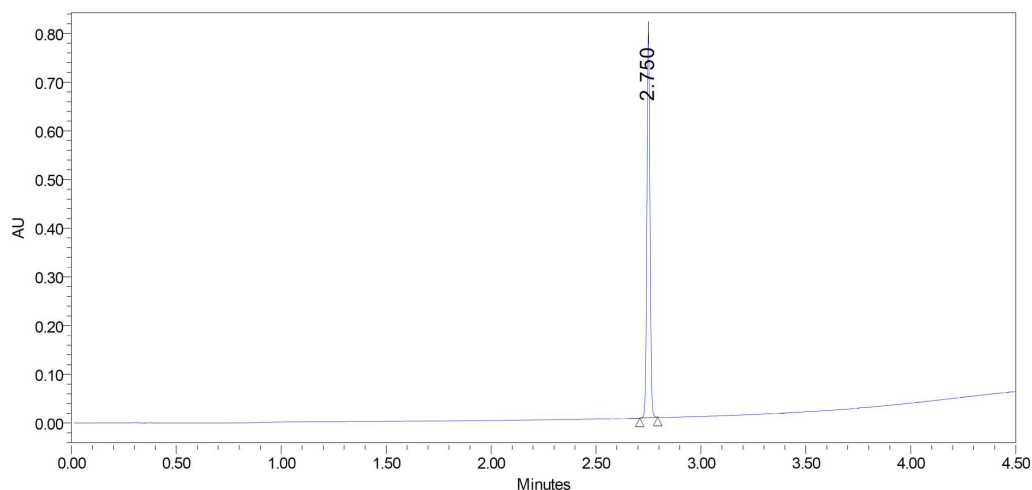
Chemical purity analysis conditions

Column Details	XSelect CSH C18 (50 x 2.1 mm, 1.7 μ m)		
Column Temperature	40 °C		
Flow Rate	0.6 mL/minute		
Detector Wavelength	240 nm		
Injection Volume	1.0 μ L		
Mobile Phase A	Water (0.1% v/v TFA)		
Mobile Phase B	MeCN (0.1% v/v TFA)		
Gradient Profile	Time (min)	%A	%B
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	4	3	97
	4.02	0	100
	4.5	0	100
	4.52	97	3
	6	97	3

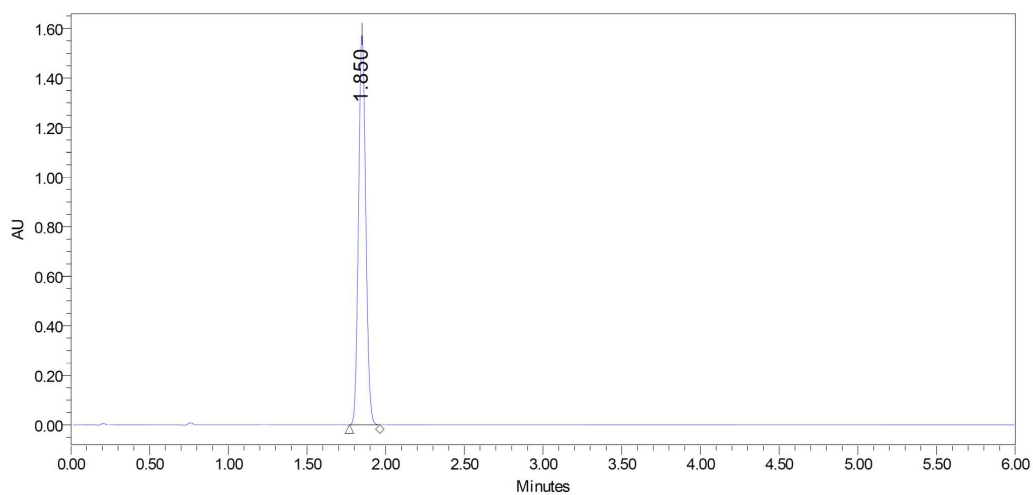
Chiral purity analysis conditions

Column Details	Lux C4 (4.6 mm x 250 mm, 5 μ m)
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Detector Wavelength	210-240 nm
Injection Volume	1.0 μ L
Isocratic conditions	36:65 MeOH/CO ₂

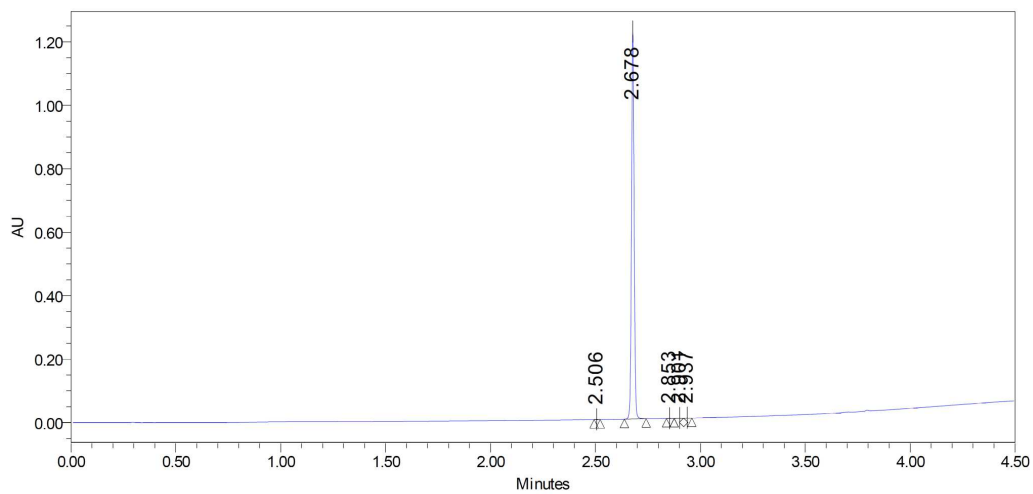
methyl (-)-ethyl(2-(4-fluorophenyl)benzo[d]oxazol-5-yl)phosphinate (SMT022331) Chemical purity (100%)



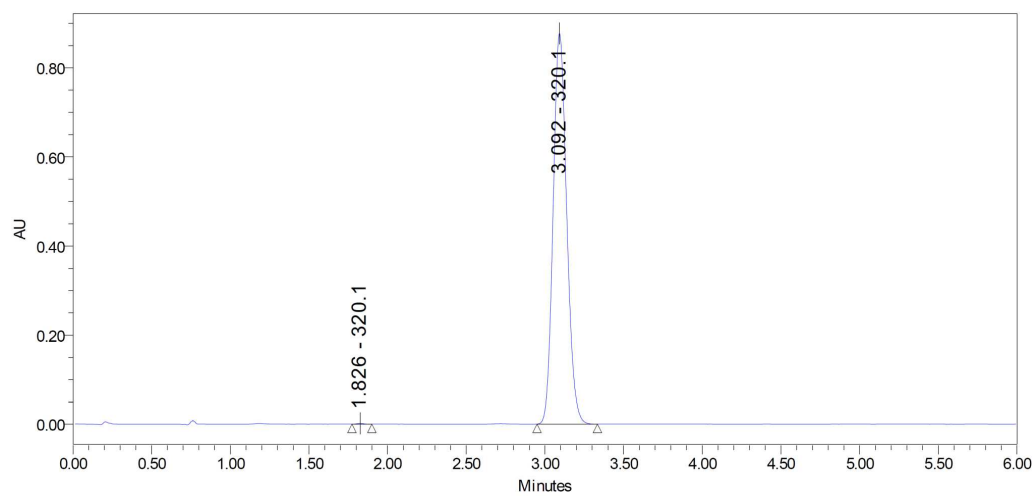
Chiral purity (100%)



methyl (+)-ethyl(2-(4-fluorophenyl)benzo[d]oxazol-5-yl)phosphinate (SMT022332)
Chemical purity (99.7%)

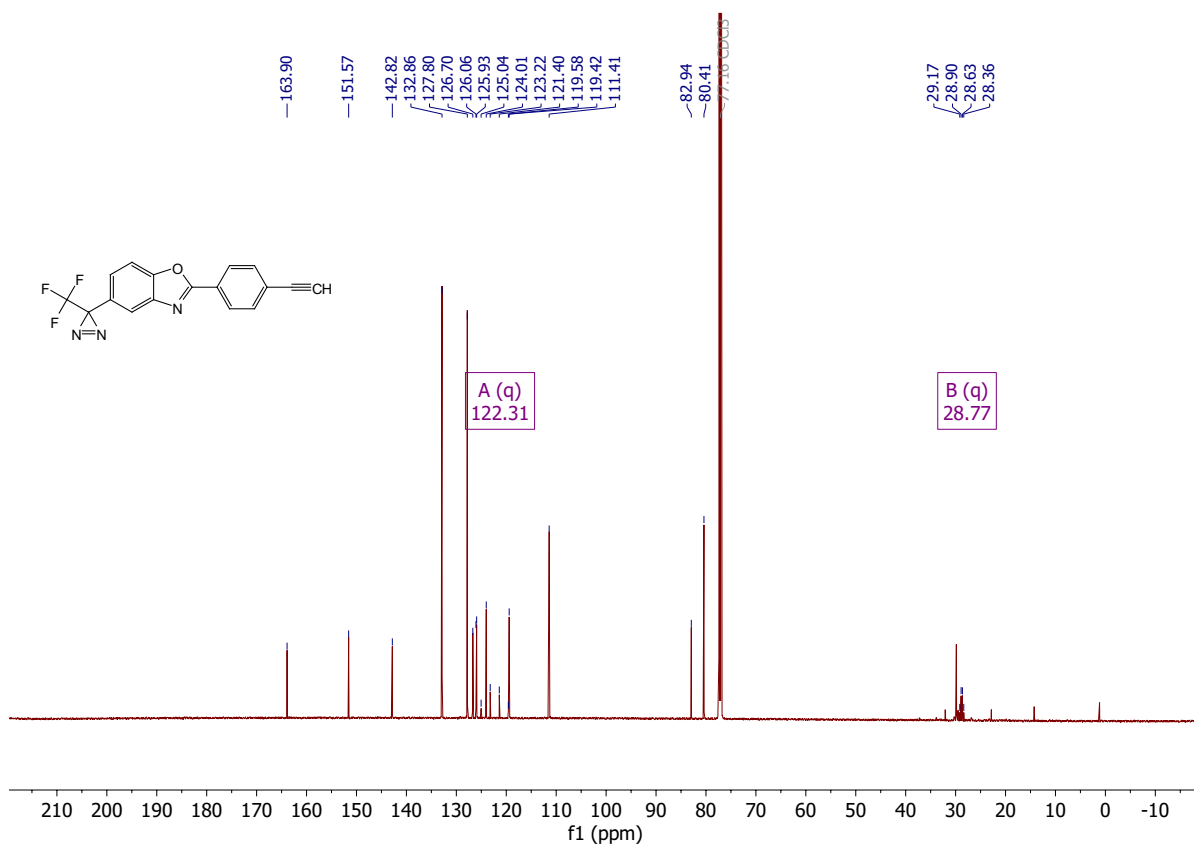
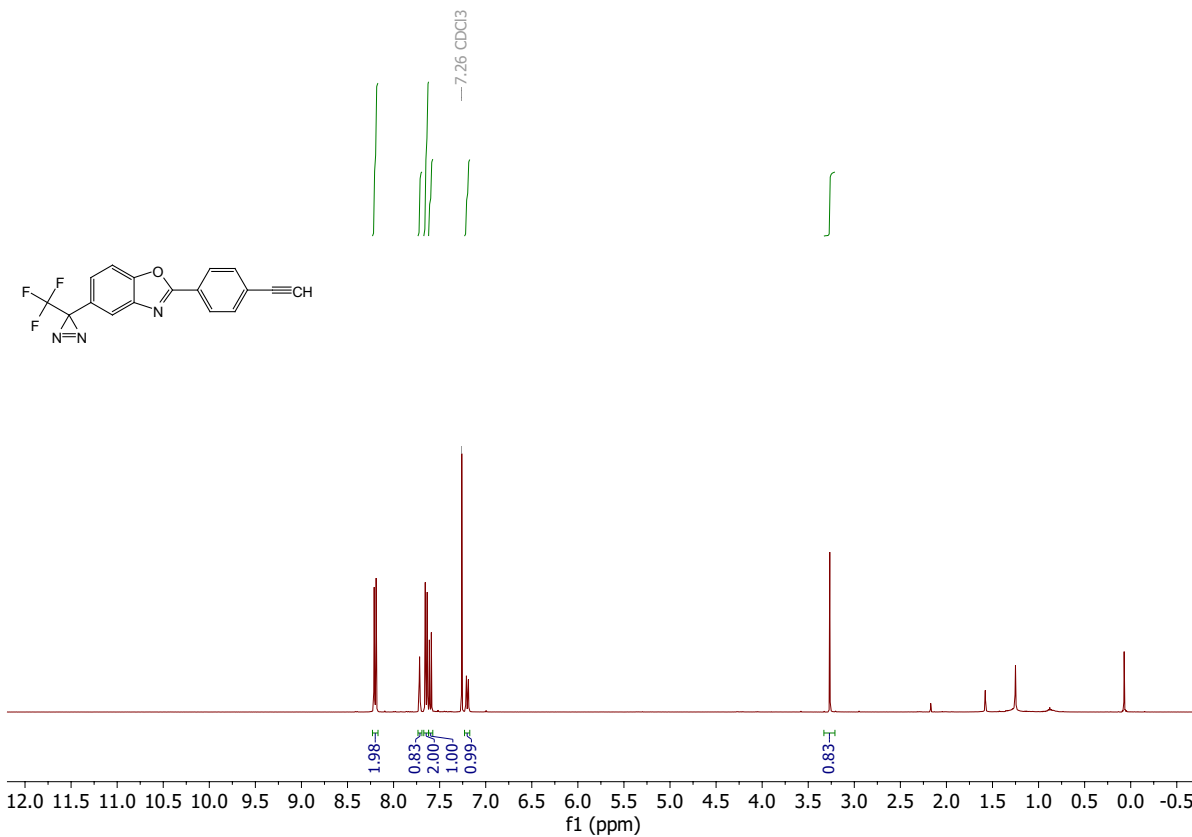


Chiral purity (99.9%)

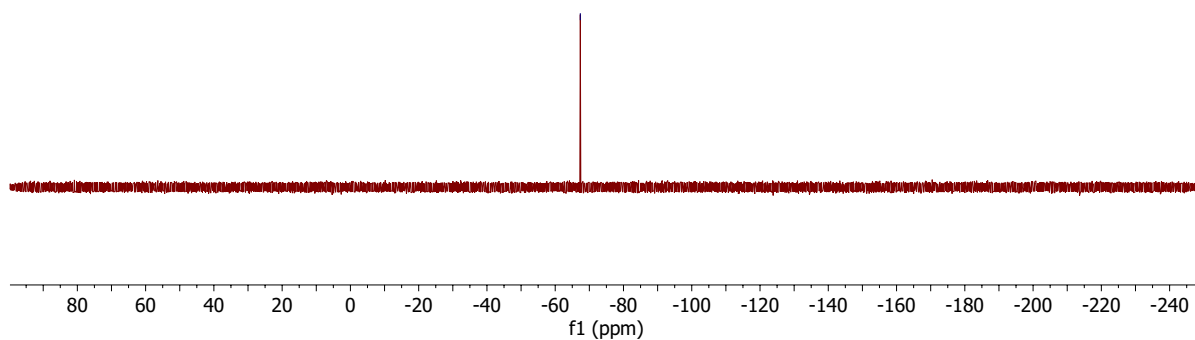
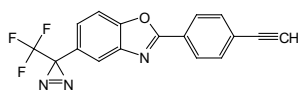


Spectra:

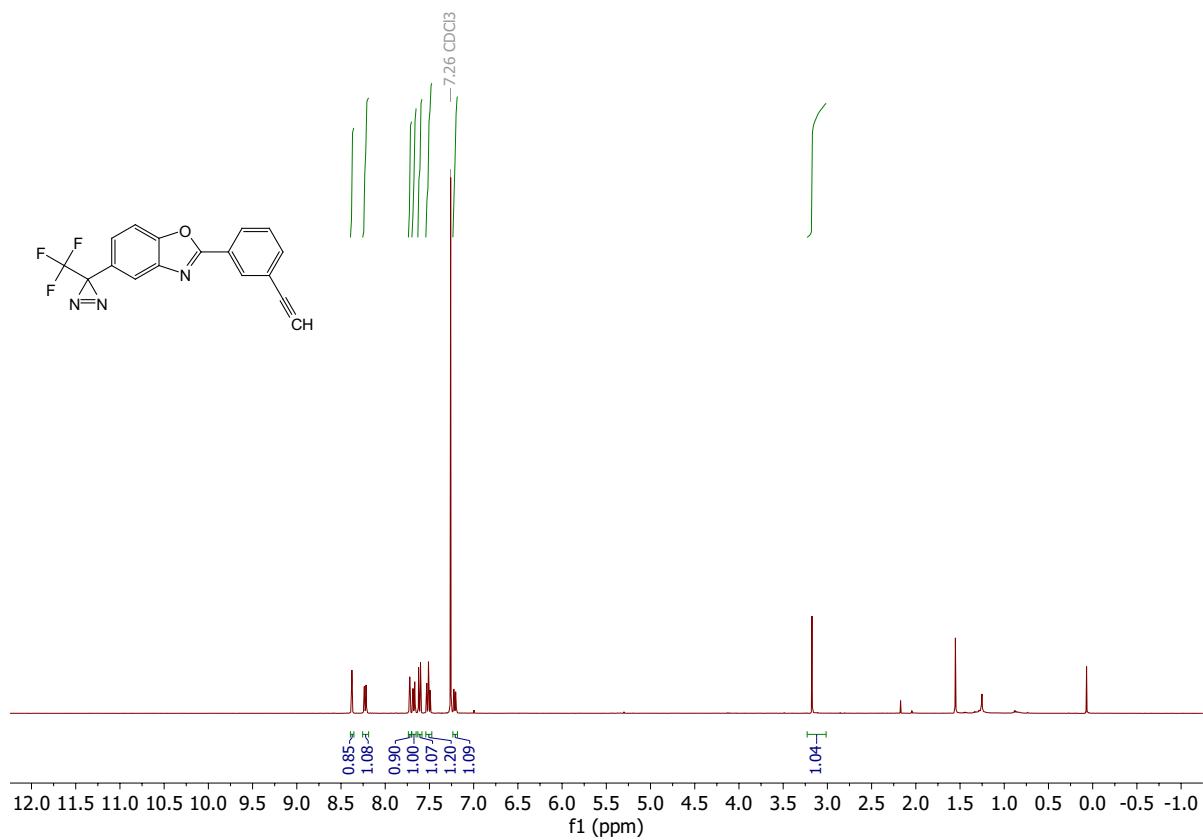
2-(4-ethynylphenyl)-5-(3-(trifluoromethyl)-3H-diazirin-3-yl)benzo[d]oxazole 3

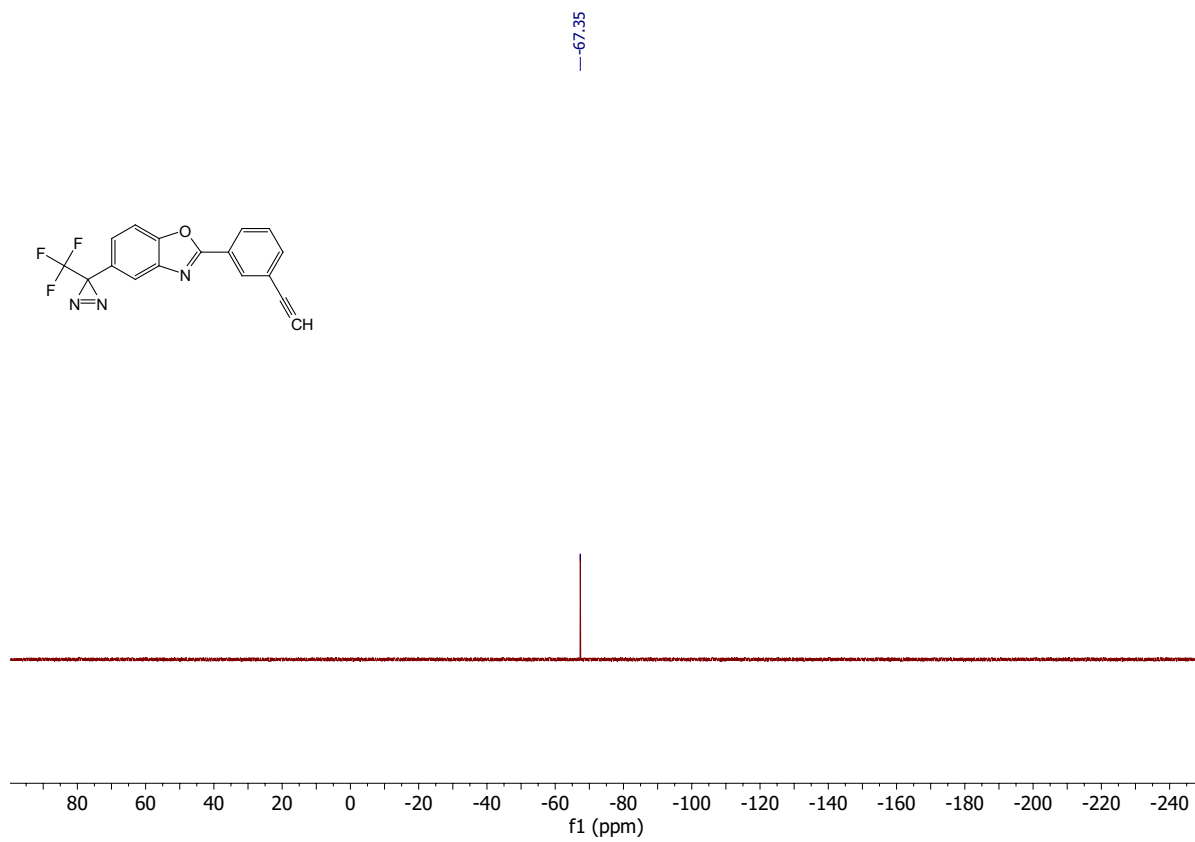
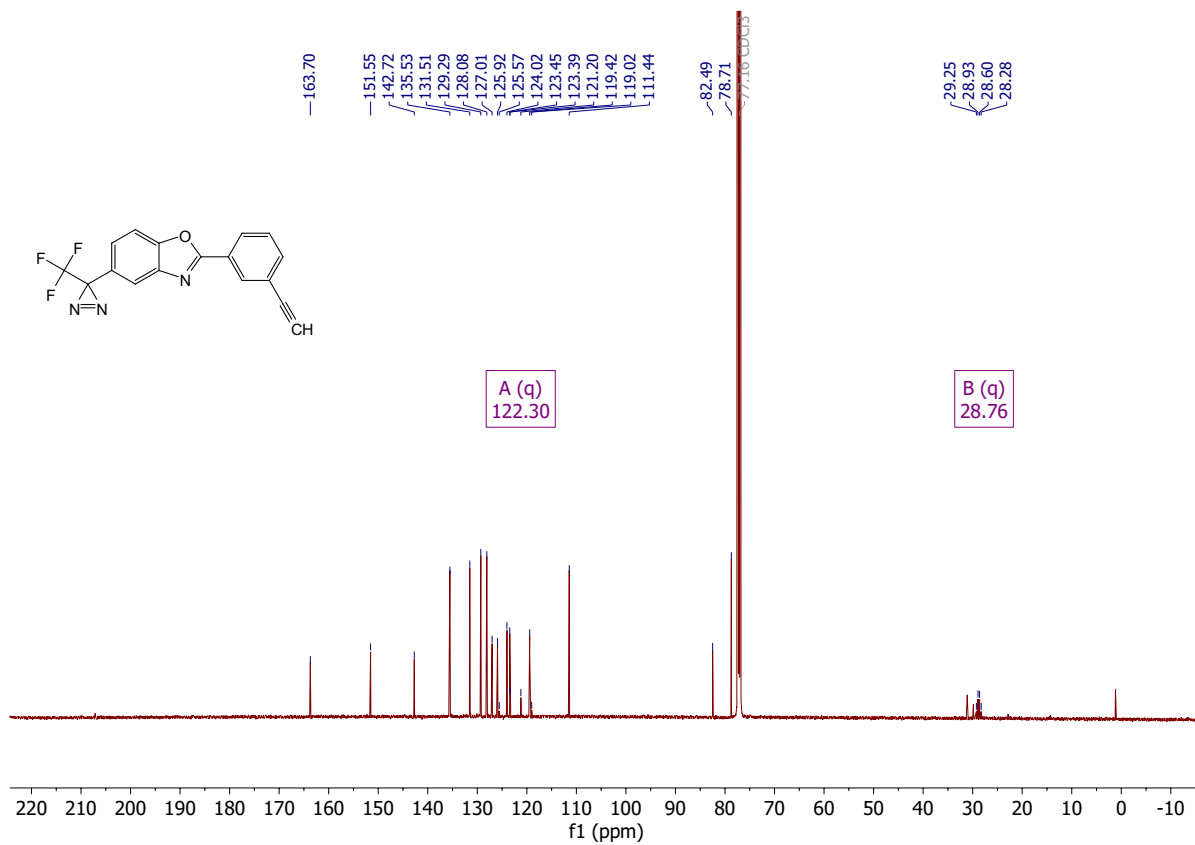


-67.35

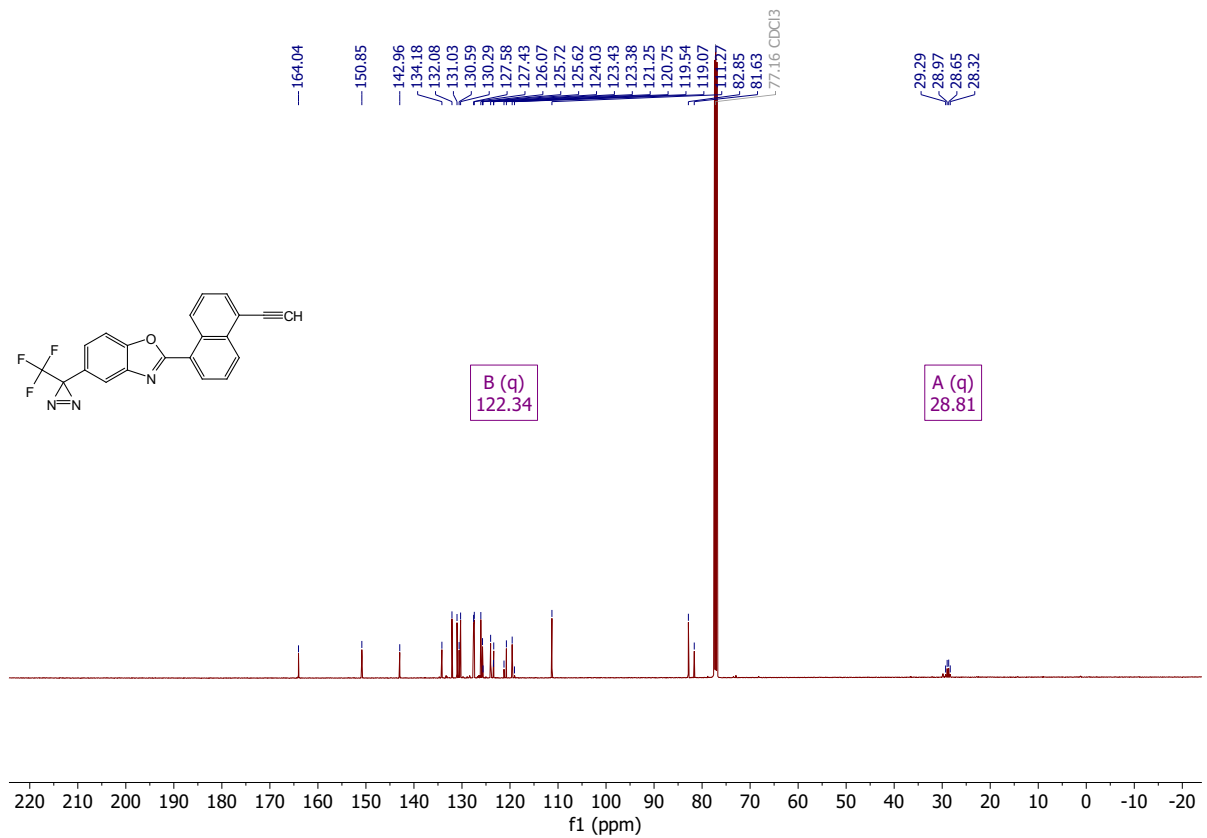
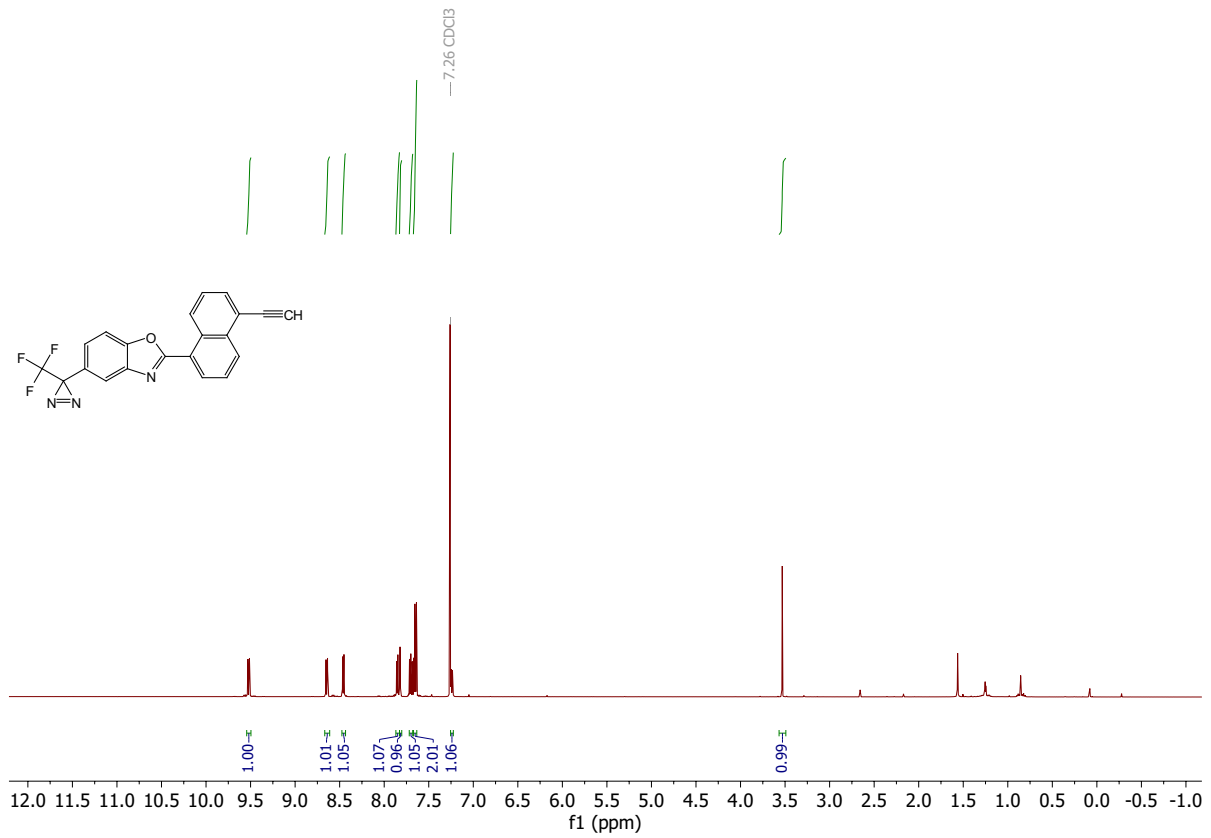


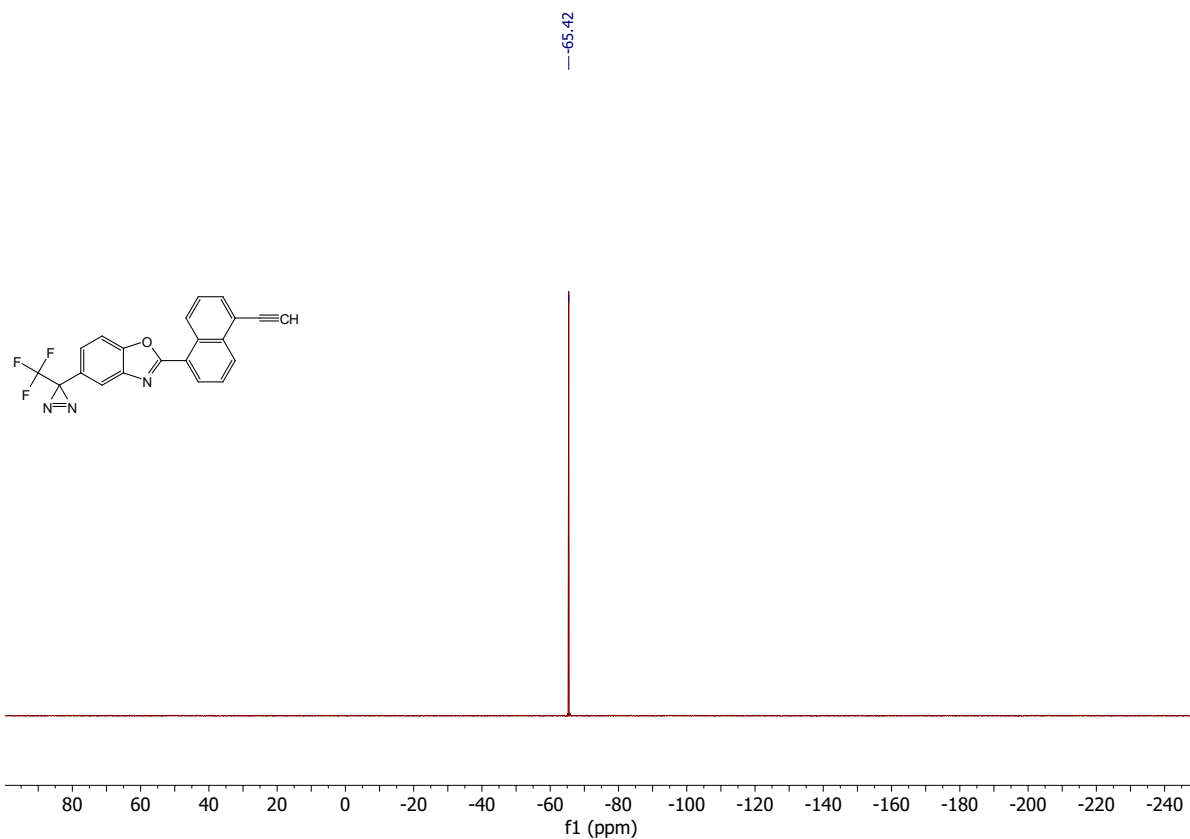
2-(3-ethynylphenyl)-5-(3-(trifluoromethyl)-3H-diazirin-3-yl)benzo[d]oxazole 2



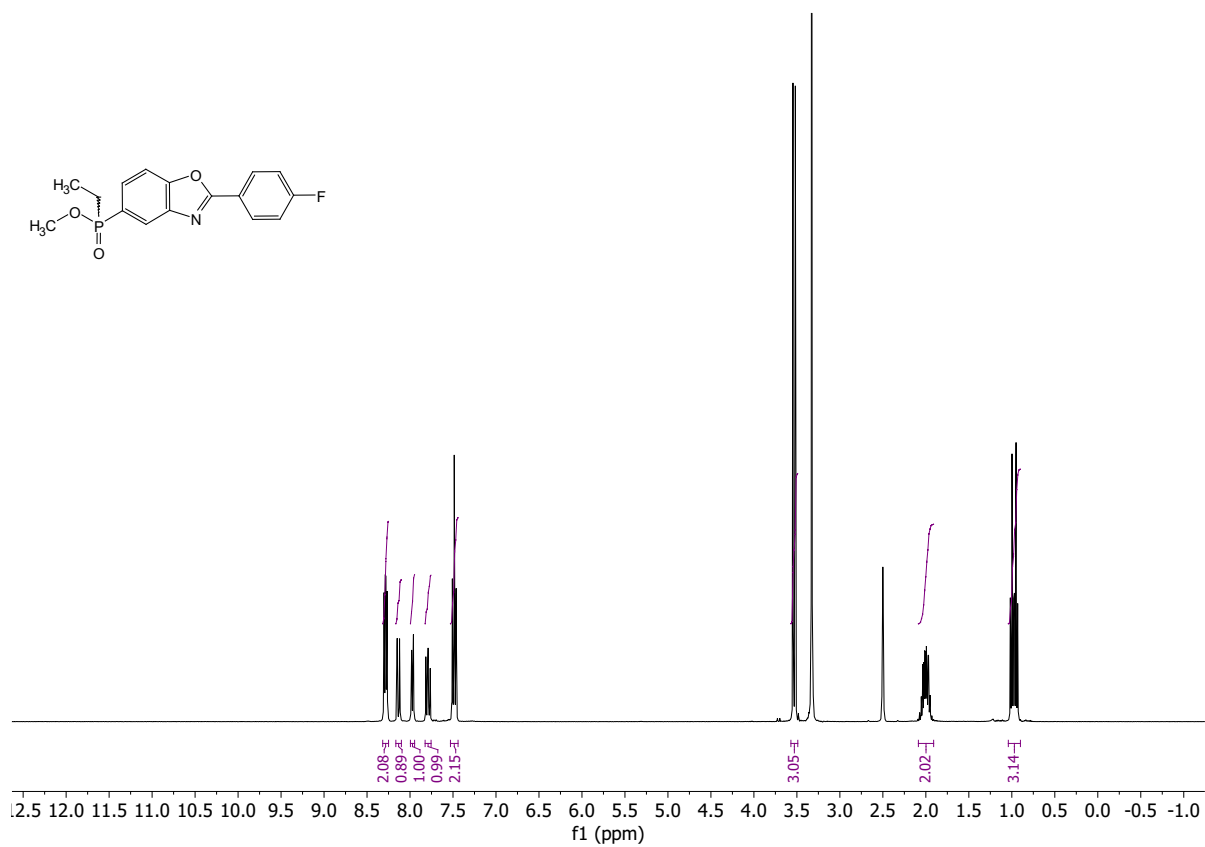


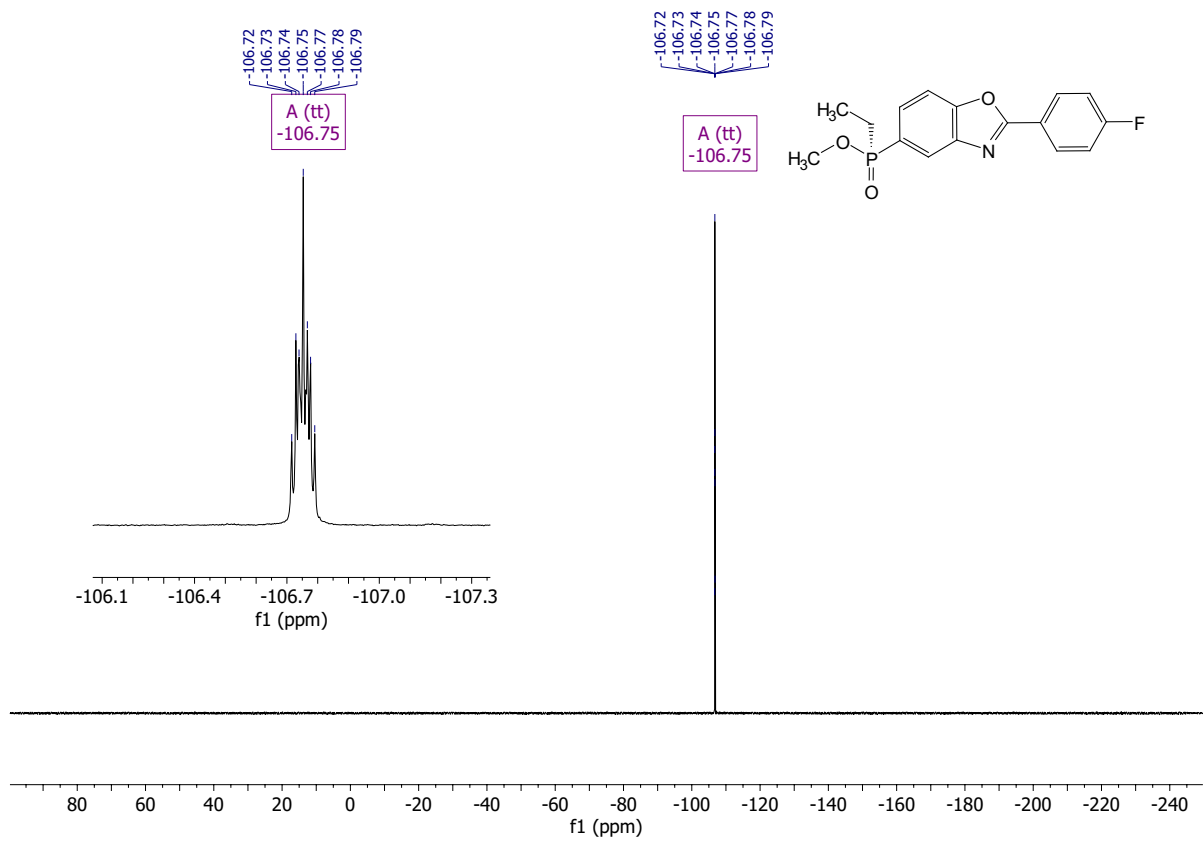
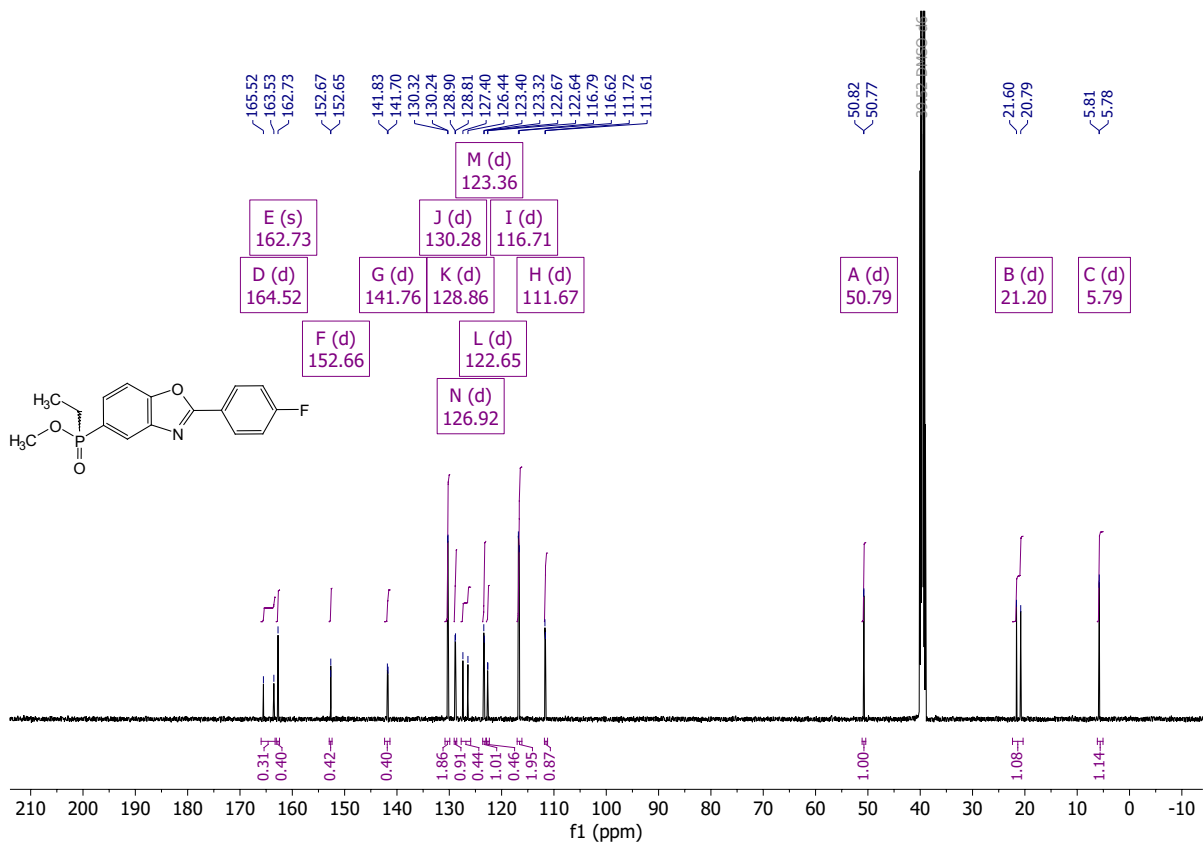
2-(5-ethynyl-naphthalen-1-yl)-5-(3-(trifluoromethyl)-3H-diazirin-3-yl)benzo[d]oxazole 4

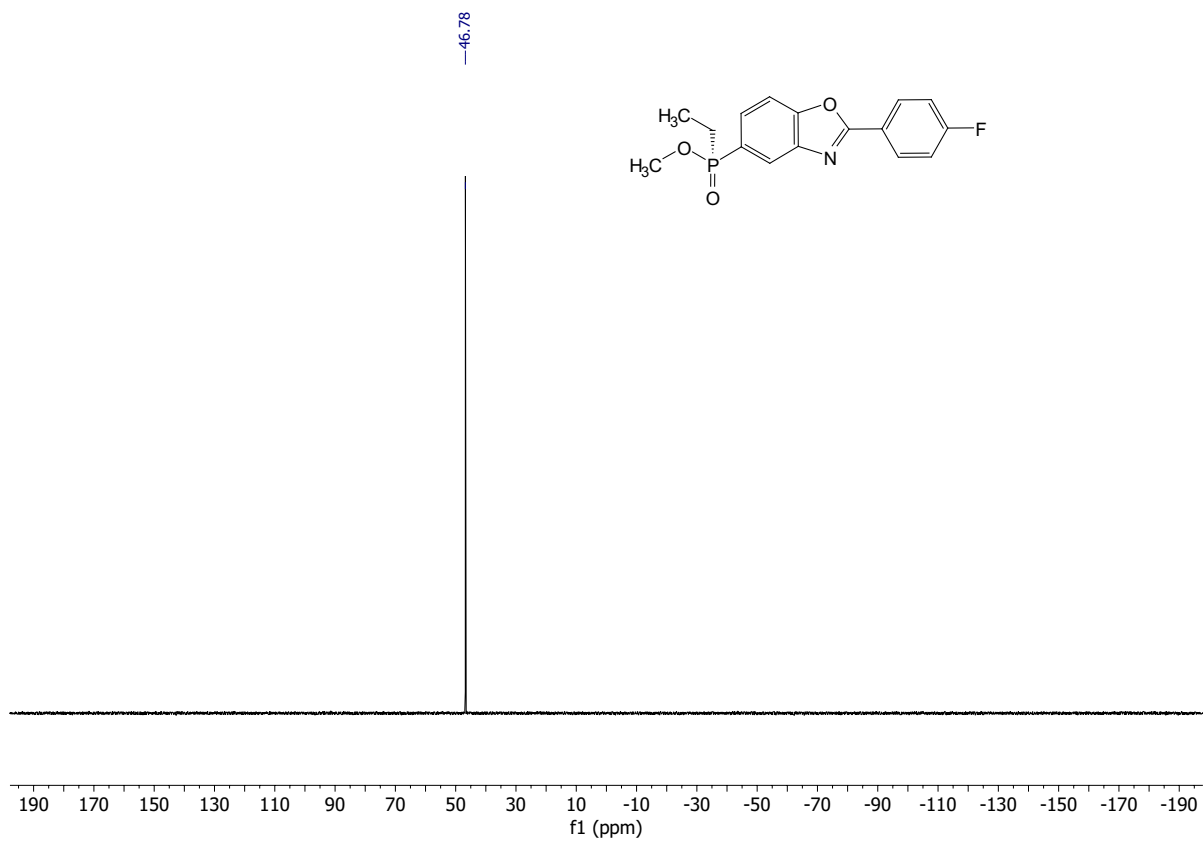




methyl (+)-ethyl(2-(4-fluorophenyl)benzo[d]oxazol-5-yl)phosphinate 7







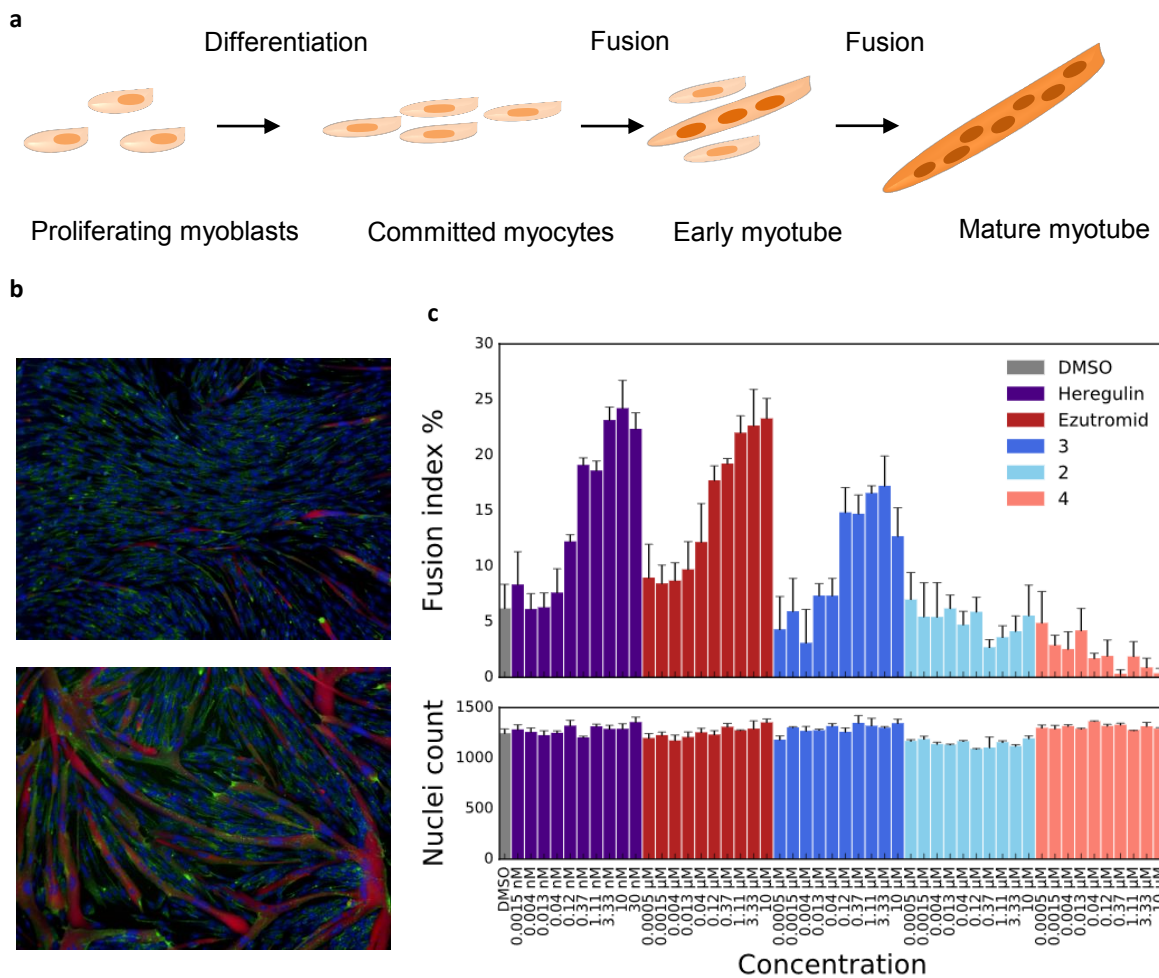
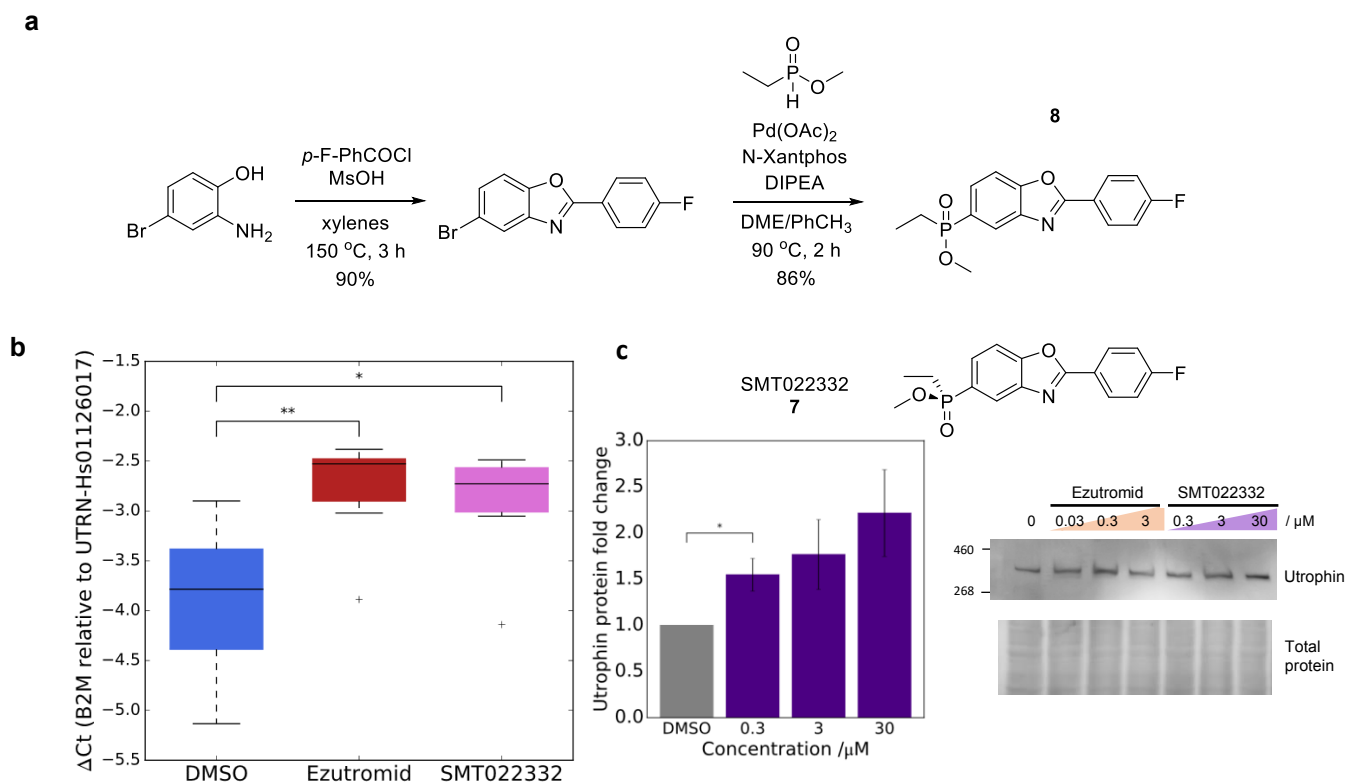


Figure S1. Utrophin modulators such as heregulin, ezutromid and probe 3 increase fusion of DMD myoblasts into mature myotubes. **a**) Schematic of the process of fusion of proliferating myoblasts into myotubes. **b**) Immortalised DMD myoblasts were treated with compound or vehicle (0.1% DMSO) during five days of differentiation, then fixed and stained for utrophin (green), myosin heavy chain (red) and DAPI (blue). Images taken with a Perkin Elmer Operetta high-content imaging system with a 10 × objective; top: vehicle control, bottom: 10 μM ezutromid. **c**) Dose-dependent increase in fusion of myoblasts to mature myotubes after 5 days observed after heregulin and ezutromid treatment is also observed after treatment with probe 3, but not 2 or 4. Fusion index is shown (top) as mean ± SD and nuclei count (bottom) mean ± SD, each n = 4.



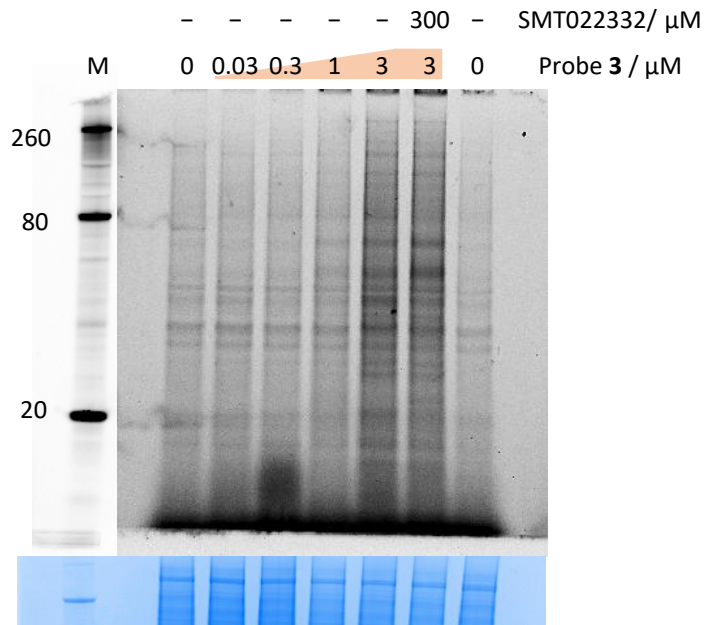


Figure S3. Probe 3 shows concentration-dependent labelling of protein targets. H2K *mdx* cells were treated with **3** (2 h) and irradiated (365 nm, 3 min, 0 °C) to trigger crosslinking. Probe labelled proteins were ligated to TAMRA, separated by SDS-PAGE and visualised by in gel fluorescence. M: protein standard, bottom: Coomassie staining as loading control.

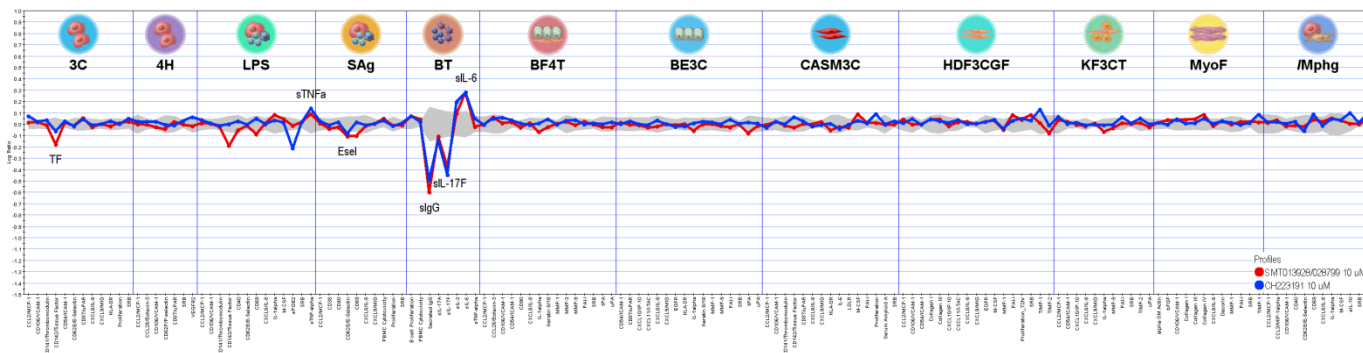
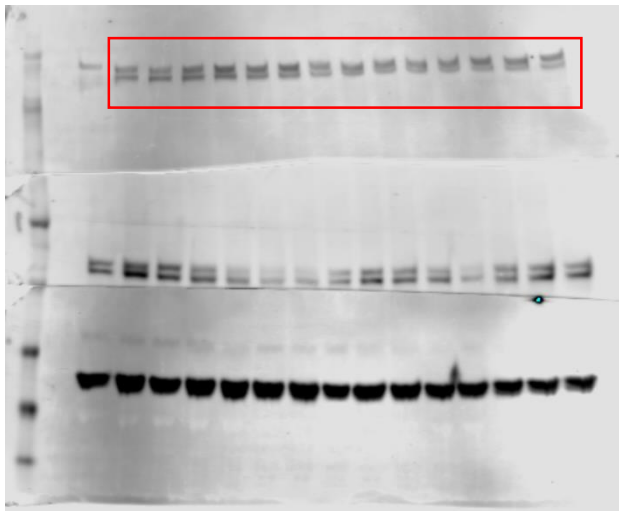


Figure S4. Ezutromid was profiled in the DiscoverX BioMap Diversity PLUS panel, which monitors changes in activity of 148 biomarkers across 12 different human primary cell-based co-culture systems upon compound treatment, and compares the signature with a reference database of compounds with known mechanism. The profile of ezutromid (10 μ M, red) best matched the profile of AhR antagonist CH223191 (10 μ M, blue), Pearson correlation of 0.854. Grey profiles represent baseline variation, biomarkers with activity deviating from the baseline are annotated.

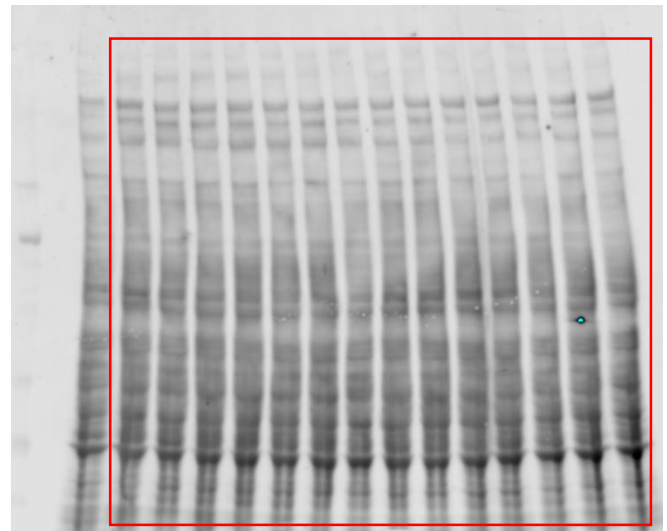
Figure S5. Uncropped blots from Figure 2

H2K *mdx* cell line

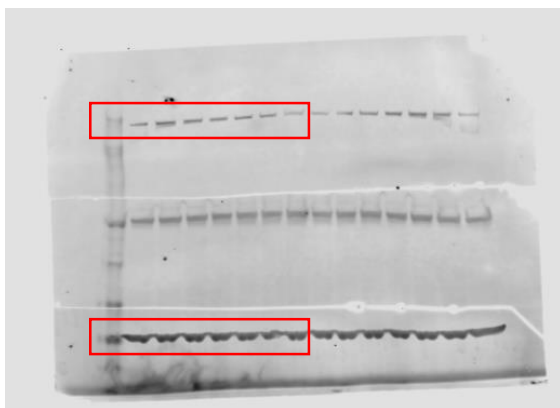
Utrophin



REVERT total protein stain.



Human DMD cell line



Utrophin

β -actin

Figure S6. Uncropped blot from Figure 4

Human DMD cell line

Anti-AhR antibody staining

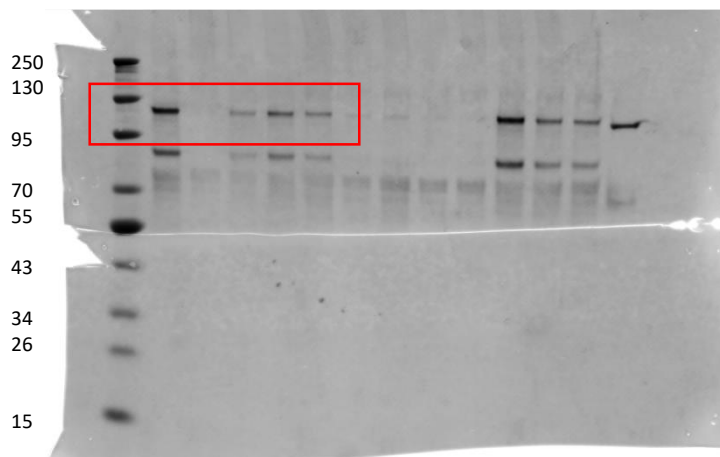
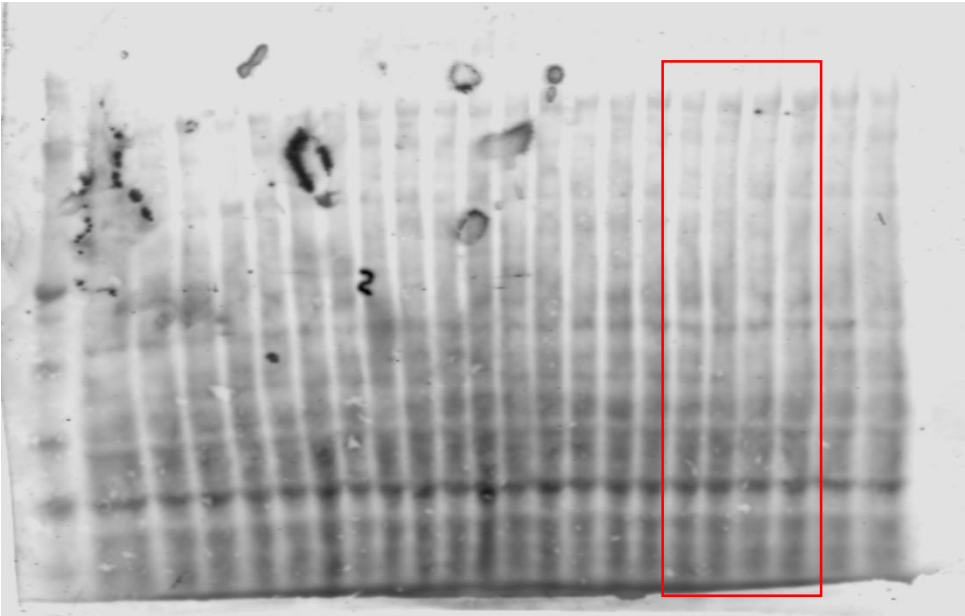
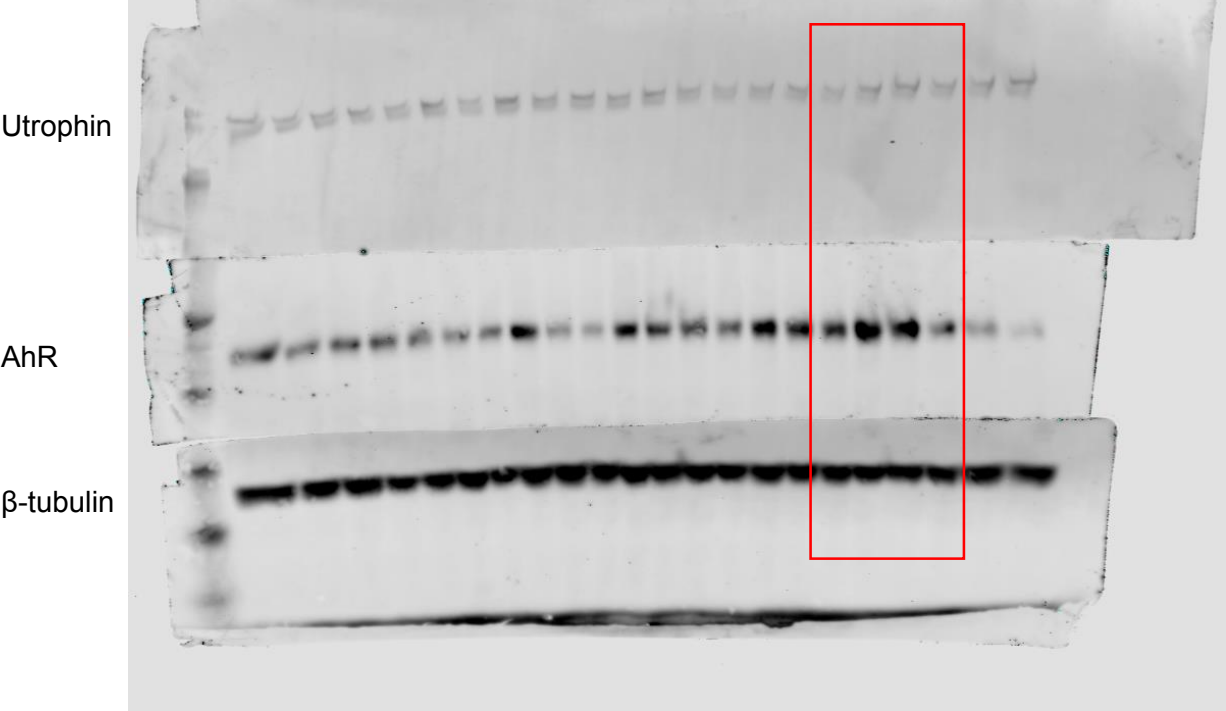


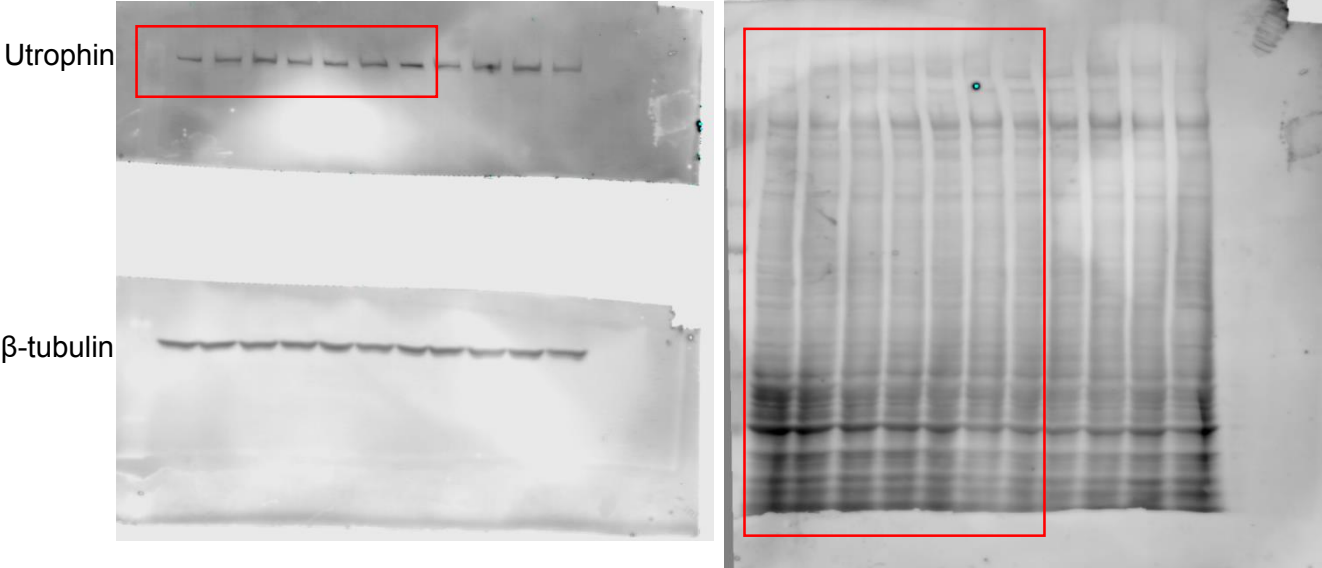
Figure S7. Uncropped blots from Figure 6

Human DMD cell line



REVERT total protein stain.

Figure S8. Uncropped blots from Supplementary Figure 2



REVERT total protein stain.

References

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Dync1h1	Cytoplasmic dynein 1 heavy chain 1	Q9JHU4	Q9JHU4	19.9095	20.6064	19.6306	22.5184	17.5	21.6579	17.5	17.5	17.5	4	4	1.6	1.6	532.04	0.19045000	5	0.117743	-0.509938	0.30321	2.54882			
Dync1i2	Cytoplasmic dynein 1 intermediate	Q88487;A28F8	Q88487;A28F8;Q3PT8;AJ	17.5	20.6201	26.5702	17.5	17.5	17.5	17.5	17.5	17.5	2	2	4.9	4.9	68.393	0.101e+08	1	0.699592	4.06343	0.699592	4.06343			
Ebp	3-beta-hydroxyysteroid-DeH8B)DeH1	P70245;AJ2C9	P70245;AJ2C9	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	1	1	5.7	5.7	26.215	0.004008	6980200	2	-3.44e-08	0.472743	-1.12076			
Eef1a1	Elongation factor 1-alpha 1	P02126;Q32H8	P02126;Q32H8;Q3Y268	26.9032	28.3132	28.8026	30.4943	28.8704	27.8008	28.8429	28.9332	28.9332	19	19	19	19	50.1113	0.78e+09	1	1.56829	-0.202695	0.147821	0.147821			
Eef1b;Eef1b2	Elongation factor 1-beta	Q70251;MQDQ1	Q70251;MQDQ5;MQDQW	17.5	18.1218	22.4995	21.6397	17.5	17.5	17.5	17.5	17.5	1	1	6.7	6.7	24.693	0.004115	2380000	0	0.0835356	0.49386	0.00380426	0.0281741		
Eef1d	Elongation factor 1-delta	P57776;P57776	P57776;P57776;P57776-3;D3YUQ9	17.5	21.3745	20.6711	17.5	17.5	17.5	17.5	23.1128	23.73	2	2	12.8	12.8	13.293	0.4359900	5	0.92058	2.34852	-1.59909	-1.59909			
Eef1g	Elongation factor 1-gamma	Q8D8N0	Q8D8N0	23.0111	24.5284	25.1005	26.0441	24.9351	24.6113	22.9432	24.468	25.8936	8	8	8	8	50.06	0.371e+08	5	0.574925	-0.981995	0.0730712	-0.220061			
Eef2	Elongation factor 2	P82852;O8881	P82852	24.3428	26.4848	26.6509	27.6161	26.9834	25.5138	25.3346	25.8784	27.5985	17	17	17	17	95.313	0.131e+09	113	0.380618	-0.87263	0.167321	-0.447318			
Eef2s1	Eukaryotic translation initiation factor G26Y66	Q6ZW66	Q6ZW66	20.1758	21.6619	17.5	22.0519	22.7397	23.7977	17.5	24.872	23.3962	2	2	2	2	36.108	0.5583000	4	1.00311	-2.90386	0.202703	-2.90386			
Eef2s2	Eukaryotic translation initiation factor G26Y67	Q6ZWK3	Q6ZWK3;E0CKJ3	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	2	2	2	2	38.092	0.004357	7851000	1	0.146033	-0.751216	0.147821			
Eef2s3;Eif2s3x	Eukaryotic translation initiation factor G20N02;Q920N1;Q920N2;Q920N1	Q920N1	Q920N1	17.5	17.5	22.0674	22.694	17.5	20.8507	17.5	17.5	21.5138	3	3	3	3	11.7	0.111	10.842000	3	0.243287	-1.32578	0.0036007	0.184526		
Eif3a	Eukaryotic translation initiation factor P23116	P23116	P23116	21.3824	22.613	22.8739	22.9042	20.9611	22.8029	17.5	20.4162	24.3273	5	5	5	5	4.2	0.16193	0.70824000	13	0.0288211	0.0669823	0.309855	1.5419		
Eif3b	Eukaryotic translation initiation factor Q81Z09	Q81Z09	Q81Z09	17.5	17.5	17.5	23.2217	24.2768	24.1109	21.3676	21.0752	25.0223	3	3	3	3	6.4	6.4	91.3669	0.179e+08	4	3.48479	-6.36979	1.76638	-4.98838	
Eif3c	Eukaryotic translation initiation factor Q8R184;MQCW	Q8R184	Q8R184	23.6889	24.1716	23.7284	24.4733	20.4159	22.9018	17.5	22.4658	23.5536	7	7	7	7	9	9	105.53	0.182e+08	23	0.424652	1.19262	0.628464	2.61647	
Eif3d	Eukaryotic translation initiation factor Q70194	Q70194	Q70194	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	1	1	1	1	4.6	4.6	63.988	0.0	0	1	-3.43e-08	0		
Eif3i	Eukaryotic translation initiation factor Q8Q2Y1	Q8Q2Y1	Q8Q2Y1	17.5	17.5	17.5	21.0982	17.5	21.9740	20.3968	17.5	17.5	1	1	1	1	2	2	66.612	0.004386	11212000	2	0.179878	-0.655686	0.179878	
Eif4a1;Eif4a2	Eukaryotic initiation factor 4A;Eif40k843;P10630	P60843;P10630;Q8BTU6;P	Q8BTU6;P	24.0024	25.9397	25.4677	25.452	24.6141	24.8227	17.5	23.7194	26.8507	8	8	8	8	29.3	29.3	46.153	0.433e+08	29	0.0799327	0.173657	0.363568	2.44656	
Eif4b	Eukaryotic translation initiation factor Q8BGD9	Q8BGD9	Q8BGD9	21.4504	22.2454	23.6393	22.1482	17.5	17.5	22.4879	22.3293	17.5	17.5	2	2	2.6	2.6	6.839	0.004193	51925000	6	0.947833	-0.395624	0.403264	1.6726	
Eif4g1	Eukaryotic translation initiation factor Q6N216;A0A019	Q6N216;A0A019;YU55;EPYV1	YU55;EPYV1	22.7295	23.4423	22.4435	25.5366	22.4874	25.2902	17.5	24.1822	24.5458	8	8	8	8	8.1	8.1	176.07	0.226e+08	16	0.698632	-1.56634	0.0698217	0.495742	
Eif4h	Eukaryotic translation initiation factor Q6WUK2;Q6WUK2	Q6WUK2	Q6WUK2	17.5	20.3496	22.4598	22.6603	17.5	22.0283	17.5	23.5755	24.4109	2	2	2	2	13.3	13.3	27.341	0.6565000	4	0.139968	-0.624438	0.264994	-1.7301	
Eif5a1;Eif5a2	Eukaryotic translation initiation factor P63242;Q8BG72	P63242;Q8BG72;A0A040M	A0A040M	20.6825	17.5	17.5	17.5	20.8304	17.5	17.5	17.5	24.1124	2	2	2	2	3.1	3.1	137.611	0.96131000	4	0.0105846	-0.0493056	0.17742	-1.14328	
Eif6	Eukaryotic translation initiation factor Q55135;A6WVZ	Q55135;A6WVZ	Q55135;A6WVZ	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	22.1585	1	1	1	1	7.3	7.3	26.511	0.19079000	2	-3.43e-08	0.427243	-0.55283		
Elav1	ELAV-like protein 1	P70372	P70372	19.3871	19.9126	20.9303	20.3393	17.5	22.123	17.5	20.6756	21.1576	1	1	1	1	3.4	3.4	36.169	0.003824	16438000	4	0.212117	0.0903619	0.0863072	0.300044
Eno1	Alpha-enolase	P17182;Q6PHC1	P17182;Q6PHC1;B0QZL1	25.9275	27.3236	26.8219	27.8397	26.8873	27.0115	25.6096	27.5835	28.5355	20	20	20	20	55.8	55.8	47.14	0.209e+09	103	0.47959	-0.555318	0.240087	-0.584727	
Epkh1	Eppiklike	Q8R8W0	Q8R8W0	17.5	17.5	17.5	20.5283	17.5	17.5	17.5	17.5	17.5	1	1	1	1	2.6	2.6	12.3	0.5617000	1	0.472743	-1.02094	0.4346	0	
Eprs	ER functional glutamyl-proline--	Q8R8C7	Q8R8C7	21.1198	22.8137	22.8137	22.8137	24.1039	22.8137	22.8137	22.8137	22.8137	12	12	12	12	2.5	2.5	0.5840000	0.0	0	7	-0.9947022	-0.483522	-2.54183	
Enh	Enhancer of rudimentary homeolo-	P84089	P84089	17.5	21.3157	22.4671	21.853	17.5	19.9333	17.5	17.5	20.9869	1	1	1	1	10.6	10.6	12.259	0.003861	17340000	1	0.124374	0.666166	1.7653	
Esd	5'-formylglutathione hydrolase	Q8R0P3;H3BL9	Q8R0P3;H3BL9;H3B1C6;H	21.3018	22.3129	23.1595	23.1494	21.3898	23.2624	17.5	20.6393	24.028	1	1	1	1	7.8	7.8	31.319	0.67565000	5	0.0136215	-0.0304521	0.213384	1.53567	
Fas	Fatty acid synthase	Q8R096	Q8R096	19.8905	24.2225	23.6084	24.3877	17.5	22.8152	20.4328	22.4234	25.1422	9	9	9	9	4.8	4.8	272.43	0.124e+08	16	0.135603	-1.002329	0.159573	-1.53729	
Flna	Filamin-A	Q8BTM6;B7FAU	Q8BTM6;B7FAU;B7FAU1	26.6317	28.2287	28.1887	29.3637	28.4194	29.2673	25.658	27.6399	29.6054	62	62	62	62	36.7	36.7	281.22	0.468e+09	374	1.03564	-1.34344	0.00786245	0.0300255	
Flnb	Filamin-B	Q8R092	Q8R092	22.5119	24.932	24.6428	26.9042	24.9422	27.7568	16.5357	24.379	27.0584	21	20	20	20	14.5	14.5	27.82	0.8049000	68	1.040668	-0.9961329	0.0961329		
Flncl	Filamin-C	Q8VHK6;Q8VHK6	Q8VHK6;Q8VHK6	23.6115	25.2705	24.3837	24.1303	24.9657	26.4391	22.5646	22.7336	26.7728	26	25	24	24	13.2	13.2	29.212	0.503e+08	61	0.963751	-1.48643	0.00794276	0.334956	
Fscn1	Fascin	Q61553;A0Q155	A0Q155;A0ADG2;DU7	22.2252	21.9395	22.5411	24.2527	22.9586	22.4539	21.8023	23.2845	24.474	4	4	4	4	12.6	12.6	54.507	0.106e+08	13	0.781142	-1.04412	0.322559	-0.651661	
Fxdy5	FXD domain-containing intran-	P97808;F6TWM	P97808;F6TWM;F78WJ1	17.5	24.5493	26.0718	17.5	23.8746	19.9363	17.5	23.6874	22.751	1	1	1	1	5.1	5.1	19.454	0.003876	1.41e+08	1	0.188994	1.60341	0.160146	-1.39421
Gadp2	Glyceraldehyde 3-phosphate de-	P16858;A0A00	P16858;A0A00;MQ2F6;S4R	25.7838	26.7976	27.9732	27.8606	28.2069	28.0599	25.9109	26.4636	28.4371	15	15	15	15	44.7	44.7	35.81	0.22e+09	90	0.86485	-1.19092	0.028969	-0.0865339	
Gab2	Interferon-induced gamma-este-	Q920E6	Q920E6	17.5	17.5	17.5	17.5	23.7884	23.7547	17.5	23.976	23.0162	2	2	2	2	3.7	3.7	66.739	0.77526000	7	0.935096	-0.48102	0.366408	-0.584727	
Rab GDP dissociation inhibitor	beta	Q51598	Q51598;Q51598-2	17.5	21.1484	17.5	22.5017	17.5	22.0839	17.5	22.0599	17.5	2	2	2	2	5.8	5.8	50.537	0.2049000	8	0.075772	-0.454568	0.258168	-1.17163	
Gfp1	Glutamine-fructose-6-phosphat	ap74856	ap74856;ap74856-2	17.5	17.5	17.5	21.8445	17.5	17.5	17.5	17.5	20.588	1	1	1	1	2.3	2.3	78.538	0.8190200	2	0.427243	-1.44715	0.427243	-1.02934	
Glu1d	Glutamate dehydrogenase 1,	mitocP26443	F7CFA5	P26443;F7CFA5	19.8764	17.5	17.5	22.9296	17.5	19.5879	17.5	17.5	1	1	1	1	3.8	3.8	61.336	0.15591000	2	0.397371	-1.50137	0.117224	-0.483901	
Gms41a	Guanine nucleotide-binding	Q61F28	Q61F28	23.1169	27.2321	30.319	25.3834	26.8819	24.9814	23.2842	26.8292	24.237	9	2	2	2	12.1	12.1	60.227	0.336e+09	50	0.203299	1.14046	0.377832	2.10591	
Gms2;Gnao1;Gnas;Gna3	Guanine nucleotide-binding	P08752;P18872	P08752;P18872;P63094;Q	19.0141	22.2829	17.5	22.7849	17.5	21.3459	17.5	17.5	21.0531	3	2	2	2	7.3	7.3	40.489	0.002212	24266000	5	0.16845</			

ligp1	Interferon-inducible GTPase 1	Q9Q285; Q3UED; Q9Q285	21.5097	24.4122	24.5503	25.3955	24.3218	25.8122	21.4445	23.5403	25.4777	7	7	7	24	24	24	47.571	0	2.88e+08	40	0.70859	-1.68572	0.000696886	0.00326856	
limpdh2	inosine-5-monophosphate dehydrogenase 2	P24547; A0A06 P24547; A0A06AY672	17.5	17.9902	17.5	17.4261	17.5	17.20942	17.5	17.5	17.20973	3	1	3	7.2	7.2	7.2	55.814	0	2.0515000	4	4.61288	-2.4034	0.212142	-1.10238	
lipo5	Impartin-5	QB8KCS; QB8KCS; QB8KCS; QB8KCS-2	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	1	1	1	1.5	1.5	1.5	123.59	0	0	1	4.34e-08	0	-4.34e-08	0	
lipo9	Impartin-9	Q91V65; Q91V65; Q91V65; Q91V65; Q91V65; Q91V65; Q91V65; Q91V65; Q91V65; Q91V65	17.5	17.5	22.2533	17.5	17.5	21.9324	17.5	17.5	21.9324	1	1	1	2	2	2	116.075	0	9419100	1	0.0232228	0	0.132928	0	1.61776
lqgap1	Ras GTPase-activating-like protein 1	Q9JFK1	20.5814	19.068	17.5	17.5	17.5	17.5	17.5	17.5	17.5	2	2	2	2.1	2.1	2.1	188.74	0	2.9923000	3	0.0883769	-0.572108	0.183698	0.620031	
Irgm1	Immunity-related GTPase family M p	Q60766; G5NCB1; Q60766; G5NCB5; Q60766-1	17.5	23.2947	23.4162	21.3827	22.2536	23.6146	17.5	21.6918	19.8899	3	3	3	9	9	9	46.551	0	5.3510000	11	0.188321	-1.0133	0.30247	1.70976	
Irtg1	Integrin beta-1	P09055; P09055; P09055; P09055-2	21.4053	21.8273	22.0607	22.5349	21.5	22.9887	17.5	17.5	22.6231	2	2	2	4.6	4.6	4.6	88.231	0	3.8131000	1	1.06055	0.756535	0.675884	2.55671	
Jup	Junctin glycoprotein	Q02257; Q02257; Q02257	29.0322	30.0735	32.2	28.4417	28.9022	26.9546	26.5041	29.4443	27.8458	2	2	2	42.4	42.4	42.4	81.8	0	1.13e+10	344	0.993023	0.259782	0.527632	2.50387	
Kars	Lysine-tRNA ligase	Q9D9M1	20.2145	21.6328	22.0436	21.7172	22.3414	21.9408	21.0366	21.4975	21.7043	1	1	1	2.5	2.5	2.5	8.839	0	3.9163000	7	0.530649	-0.702847	0.0687957	-0.11581	
Khsr9	Far upstream element-binding protein	Q9J4V1	22.3914	23.8471	24.107	22.606	22.0649	24.3949	20.7498	22.8519	24.4717	6	6	6	11	11	11	76.775	0	1.44e+08	11	0.0257168	0.0590988	0.274048	0.16176	
Kpn2	Importin subunit alpha-1	P52293; A2A600; P52293; A2A600; A2A601; A	20.4673	20.6091	21.1643	20.292	22.0659	22.6744	17.5	17.5	21.9151	3	3	3	8.3	8.3	8.3	57.927	0	2.4881000	4	0.525683	-0.930511	0.516186	1.76324	
Kpn1	Importin subunit beta-1	P70168	21.149	22.8993	21.3526	24.2172	22.8318	23.6622	19.8216	22.951	24.0688	4	4	4	6.1	6.1	6.1	97.183	0	9.6696000	20	2.12641	-1.77005	0.126978	-0.480134	
Krt27	Keratin, type I cytoskeletal 27	Q92320	17.5	20.6878	17.5	22.1141	17.5	17.5	17.5	17.5	17.5	2	2	2	2	2	2	49.104	0	1.6228700	1	0.0905591	-0.475437	0.427243	1.02621	
Krt76	Keratin, type II cytoskeletal 2 oral	Q3UV17	31.0281	31.5905	32.5898	30.7475	31.4087	29.5952	29.1806	31.1945	30.0894	17	2	2	14.6	14.6	14.6	29.944	0	2.66e+10	99	0.757399	1.15234	0.633224	3.58131	
Lap3	Cytosol aminopeptidase	Q9C9Y7; Q9C9Y7; Q9C9Y7; Q9C9Y7-2	17.5	17.5	17.5	17.1162	17.5	21.5057	17.5	17.5	21.8994	1	1	1	2.3	2.3	2.3	56.141	0.00426	1.0942000	1	0.934844	0	0.427243	-1.46645	
Lasp1	LM and SH3 domain protein 1	Q51792; A2AG65; Q51792; A2AG65; A2AG65H	25.3847	22.8213	22.923	22.9467	17.5	17.5	17.5	21.5556	24.6293	6	6	6	27	27	27	27	27	29.894	0	1.59e+08	5	1.03191	0.484348	2.48138
Ldha	L-lactate dehydrogenase A chain; l	P06151; A0A180 P06151; A0A180G9S; Q5G6	24.0309	25.397	25.2958	26.4855	25.7034	24.8878	25.9082	24.7444	26.4599	9	9	9	27.1	27.1	27.1	23.5	36.498	0.60e+08	9	5.44079	-0.784376	0.522398	-0.976291	
Lgal1	Galectin-1	P16045	20.0773	22.6776	22.5932	22.0898	17.5	17.3521	17.5	17.5	23.3823	1	1	1	13.3	13.3	13.3	14.866	0	5.5997000	5	0.151791	0.8021	0.470323	2.32195	
Lgal3	Galectin-3	P16110; Q8C253; P16110; Q8C253	17.5	17.8967	23.4251	21.809	17.5	17.5	17.5	17.5	21.7013	21	21	21	4.2	4.2	4.2	27.55	0.004073	3.3712000	4	0.36677	0.200428	0.119733	0.733878	
Lmna	Prefoldin-A/C; Lamin-A/C	P48678; P48678; P48678; P48678-2; P48678	25.9729	26.0056	26.5895	26.043	25.7161	24.4837	17.5	26.3877	26.37	19	19	19	34.7	34.7	34.7	24.737	0	7.36e+08	84	0.684003	0.77057	0.394423	2.77012	
Lnc59	Leucine-rich repeat-containing protein	Q92238	17.5	17.4683	25.8321	23.5401	20.1431	19.983	17.5	19.8986	20.9087	3	3	3	12.4	12.4	12.4	34.877	0.00232	8459000	5	0.0485234	0.370077	0.376606	2.32408	
Lrrfp1	Leucine-rich repeat flightless-interer	Q3U239; Q3U239; Q3U239; Q3U239-3	17.5	17.5	17.5	17.1971	17.5	17.5	17.5	17.0975	21.953	1	1	1	4.3	4.3	4.3	79.248	0.004167	8287500	3	0.427243	-1.23238	0.923665	-0.629305	
Luc7/2	Putative RNA-binding protein Luc7	Q7TNC4; EQ715; Q7TNC4; EQ715; Q7TNC4-2	21.1396	21.8737	22.6307	23.3597	21.051	21.7887	17.5	21.9077	24.6604	5	5	5	15.6	15.6	15.6	46.582	0	1.56e+08	11	0.091331	-0.203171	0.087628	-2.52304	
Luc7/3	Luc7-like protein 3	Q5SU72; Q5SU72; Q5SU72; Q5SU72-3; Q5SU72	20.6796	17.5	23.5385	20.173	17.5	20.4683	17.5	17.5	22.1159	23.4488	5	5	5	2	2	2	13	51.45	0.93135000	15	0.00521978	0.0395857	0.0527778	-0.379541
Ly1/1, Ly2/2	Lyzozyme C-1; Lyzozyme C-2	P17897; P08905; P17897; P08905	22.1381	23.933	25.1281	24.0457	17.5	17.5	20.3862	24.2608	24.6291	2	2	2	14.2	14.2	14.2	16.794	0	1.79e+08	23	0.796912	0.405117	0.148071	0.641027	
Makp4	Microtubule-associated protein 4	NV P27546; P27546; P27546; P27546; P27546	17.5	17.5	17.5	17.4869	17.5	17.5	17.5	17.5	17.5	2	2	2	2.3	2.3	2.3	117.43	0.004133	1715000	2	0.427243	-1.32898	0.917556	-0.570716	
Mark3	Microtubule-associated protein C-kinase	P28645	28.5	29.661	17.5	17.5	17.5	17.5	17.5	23.196	28.65	10	10	10	28.5	28.5	28.5	29.661	0	1.31e+08	10	0.427243	0.0590988	0.274048	0.16176	
Mark3L1	MARCKS-related protein	P28667	21.8622	20.6345	17.5	22.1318	17.5	21.8092	20.2397	22.784	20.141	2	2	2	27.5	27.5	27.5	27.5	0	6.5424000	9	0.0887011	-0.492443	0.507568	-0.20469	
Mars	Methionine-tRNA ligase, cytoplasm	Q68FL6; EQ80B2; Q68FL6; EQ80B2	17.5	17.5	17.5	17.7121	17.5	17.7606	17.5	17.5	20.6558	3	3	3	5.1	5.1	5.1	101.43	0	9.603800	3	0.935074	-2.82722	0.427243	-1.05193	
Mat2a	S-adenosylmethionine synthase isoform	Q3TH56; A0A0U1 Q3TH56; A0A0U1RNT6; A0A1	17.5	17.5	17.5	17.1927	17.5	17.5	17.5	17.5	21.3707	2.455	2	2	7.6	7.6	7.6	43.688	0	1.3216000	4	0.427243	1.23089	0.68201	-1.711	
Matr3	Matrin-3	Q8K130; A0A087 Q8K130; A0A087SPT7; A0A	17.5	17.5	17.5	17.1722	21.2393	20.675	17.5	20.9298	22.5349	2	2	2	3.9	3.9	3.9	94.629	0.00566	14587000	3	4.41828	-3.52888	0.885332	-2.82158	
Mcc1	Nucleosyltransferase CoA carboxylase	Q92238	18.833	28.3745	28.9881	27.6604	28.3045	28.0596	23.3378	18.7549	23.0882	27	27	27	45.3	45.3	45.3	79.343	0	1.74e+09	108	0.627574	-2.69665	0.429445	3.61513	
Mcm3	DNA replication licensing factor	P25206	17.5	17.5	20.7799	17.5	17.5	21.2638	17.5	17.5	21.7682	2	2	2	3.9	3.9	3.9	91.545	0	7.8902000	3	0.0327153	-0.16182	0.063816	-0.329444	
Mcm4	DNA replication licensing factor	MCP P49717	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	22.5388	1	1	1	3.1	3.1	3.1	96.735	0.003884	6093300	1	-4.34e-08	0	0.427243	-1.6796	
Mdh2	Malate dehydrogenase, mitochondrion	P08249; A0A002 Q08249	22.0254	23.2411	24.7587	25.5899	21.6423	25.2982	23.7261	22.6858	26.0941	5	5	5	20.4	20.4	20.4	35.611	0	2.68e+08	17	0.217181	-0.835065	0.265689	-0.826939	
Mif	Macrophage migration inhibitory factor	P34884	21.1735	18.7858	23.3108	23.6469	17.5	17.8997	20.2435	24.1166	22.1731	2	2	2	15.7	15.7	15.7	12.504	0	7.7553000	9	0.0109314	0.0745099	0.334719	-1.42106	
Moin	Moesin	P26041; P26043; P26041	23.8322	24.4018	24.436	25.8035	23.3901	25.6917	18.2949	21.7089	27.3593	19	19	19	31.7	31.7	31.7	67.766	0	4.61e+08	40	0.632987	-0.737747	0.269546	1.80259	
Mpp	5-methyl-5-thioadenosine phosphotransferase	Q9C065	17.5	17.5	20.2169	17.5	20.6958	17.5	17.5	21.2062	17.5	2	2	2	12.4	12.4	12.4	31.062	0	1.2802000	2	0.0477066	0.183929	0.062804	0.31742	
Mthf1	C-1-methylhydrofolate synthase, cytosol	Q922D8	17.5	20.6006	17.5	21.4243	17.5	17.8768	17.5	17.5	19.9685	3	3	3	3.6	3.6	3.6	101.2	0	13226000	6	1.29178	-2.92107	0.055023	0.210712	
Mtpn	Mp2774	P62774	21.7067	22.232	22.83	22.9199	17.5	17.5	17.5	20.9865	23.8841	2	2	2	30.5	30.5	30.5	12.861	0	1.8287000	6	0.736274	2.94957	1.46601	1.64601	
Myadm	Myoid-associated differentiation n	Q35682; A0A00N Q35682; A0A00N5W94	20.9968	23.0301	23.312																					

Prdx6	Peroxisredoxin-6	O08709;A0AAE	O08709;A0AAE	17.5	22.0556	17.5	22.5659	17.5	22.0982	17.5	17.5	22.8952	1	1	1	9.4	9.4	9.4	24.87	0.36154000	4	0.313886	-1.70283	0.0404389	-0.279853	
Prp2	Prolyl endopeptidase	OQUR6	OQUR6	17.5	17.5	17.5	22.6799	17.5	17.5	17.5	17.5	22.8954	2	2	2	4.5	4.5	4.5	80.751	0.21946000	3	0.427243	-1.72663	-1.79846		
Prp21	DNA primase large subunit	P33610	P33610	25.6557	26.1555	28.0001	24.9167	24.7042	25.5249	28.2007	24.9322	17.5	2	2	2	4.8	4.8	4.8	58.408	0.0039314	8.026408	4	1.35139	2.34182	0.100781	
Prp38a	Pre-mRNA splicing factor 38A	O04F66;O4F66	O4F66;O4F66	20.3008	17.5	17.5	22.7865	17.5	20.9515	17.5	17.5	22.2455	1	1	1	5.3	5.3	5.3	28.532	0.19671000	6	0.438989	-0.132328	0.128012	-0.637871	
Prpf40a	Pre-mRNA processing factor 40b	OQ1C7;OQ1C1	OQ1C7;OQ1C1	17.5	17.5	17.5	20.5751	17.5	17.5	17.5	17.5	17.5	1	1	1	1.7	1.7	1.7	108.48	0.20232000	2	0.427243	-1.02502	-4.34E-08	0	
Psm1a	Proteasome subunit alpha type-1	OQR1P4	OQR1P4	20.5372	21.0204	17.5	20.85	17.5	17.5	17.5	17.5	17.5	1	1	1	5.7	5.7	5.7	29.546	0.5538600	2	0.273334	-1.0692	1.28585	0	
Psm3a	Proteasome subunit alpha type-3	O70435;EDC23	O70435;EDC23	21.5416	21.7751	17.5	21.4407	17.5	21.8466	17.5	17.5	21.6966	1	1	1	7.5	7.5	7.5	28.405	0.24768000	3	0.00163637	0.00983556	0.280501	1.37336	
Psm3b	Proteasome subunit alpha type-3	OQUM9;EDC18	OQUM9;EDC18	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	23.7713	1	1	1	7.3	7.3	7.3	27.372	0.21704000	3	-4.34E-08	0	-0.427243	-2.09044	
Psm3c	Proteasome subunit alpha type-3	OQUM9;EDC18	OQUM9;EDC18	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	23.7713	1	1	1	7.3	7.3	7.3	27.372	0.21704000	3	-4.34E-08	0	-0.427243	-2.09044	
Psm3d	Proteasome subunit alpha type-3	OQUM9;EDC18	OQUM9;EDC18	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	23.7713	1	1	1	7.3	7.3	7.3	27.372	0.21704000	3	-4.34E-08	0	-0.427243	-2.09044	
Psm3e	Proteasome subunit alpha type-3	OQUM9;EDC18	OQUM9;EDC18	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	23.7713	1	1	1	7.3	7.3	7.3	27.372	0.21704000	3	-4.34E-08	0	-0.427243	-2.09044	
Psm3f	Proteasome subunit alpha type-3	OQUM9;EDC18	OQUM9;EDC18	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	23.7713	1	1	1	7.3	7.3	7.3	27.372	0.21704000	3	-4.34E-08	0	-0.427243	-2.09044	
Psm3g	Proteasome subunit alpha type-3	OQUM9;EDC18	OQUM9;EDC18	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	23.7713	1	1	1	7.3	7.3	7.3	27.372	0.21704000	3	-4.34E-08	0	-0.427243	-2.09044	
Psm3h	Proteasome subunit alpha type-3	OQUM9;EDC18	OQUM9;EDC18	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	23.7713	1	1	1	7.3	7.3	7.3	27.372	0.21704000	3	-4.34E-08	0	-0.427243	-2.09044	
Psm3i	Proteasome subunit alpha type-3	OQUM9;EDC18	OQUM9;EDC18	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	23.7713	1	1	1	7.3	7.3	7.3	27.372	0.21704000	3	-4.34E-08	0	-0.427243	-2.09044	
Psm3j	Proteasome subunit alpha type-3	OQUM9;EDC18	OQUM9;EDC18	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	23.7713	1	1	1	7.3	7.3	7.3	27.372	0.21704000	3	-4.34E-08	0	-0.427243	-2.09044	
Psm3k	Proteasome subunit alpha type-3	OQUM9;EDC18	OQUM9;EDC18	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	23.7713	1	1	1	7.3	7.3	7.3	27.372	0.21704000	3	-4.34E-08	0	-0.427243	-2.09044	
Psm3l	Proteasome subunit alpha type-3	OQUM9;EDC18	OQUM9;EDC18	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	23.7713	1	1	1	7.3	7.3	7.3	27.372	0.21704000	3	-4.34E-08	0	-0.427243	-2.09044	
Psm3m	Proteasome subunit alpha type-3	OQUM9;EDC18	OQUM9;EDC18	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	23.7713	1	1	1	7.3	7.3	7.3	27.372	0.21704000	3	-4.34E-08	0	-0.427243	-2.09044	
Psm3n	Proteasome subunit alpha type-3	OQUM9;EDC18	OQUM9;EDC18	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	23.7713	1	1	1	7.3	7.3	7.3	27.372	0.21704000	3	-4.34E-08	0	-0.427243	-2.09044	
Psm3o	Proteasome subunit alpha type-3	OQUM9;EDC18	OQUM9;EDC18	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	23.7713	1	1	1	7.3	7.3	7.3	27.372	0.21704000	3	-4.34E-08	0	-0.427243	-2.09044	
Psm3p	Proteasome subunit alpha type-3	OQUM9;EDC18	OQUM9;EDC18	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	23.7713	1	1	1	7.3	7.3	7.3	27.372	0.21704000	3	-4.34E-08	0	-0.427243	-2.09044	
Psm3q	Proteasome subunit alpha type-3	OQUM9;EDC18	OQUM9;EDC18	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	23.7713	1	1	1	7.3	7.3	7.3	27.372	0.21704000	3	-4.34E-08	0	-0.427243	-2.09044	
Psm3r	Proteasome subunit alpha type-3	OQUM9;EDC18	OQUM9;EDC18	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	23.7713	1	1	1	7.3	7.3	7.3	27.372	0.21704000	3	-4.34E-08	0	-0.427243	-2.09044	
Psm3s	Proteasome subunit alpha type-3	OQUM9;EDC18	OQUM9;EDC18	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	23.7713	1	1	1	7.3	7.3	7.3	27.372	0.21704000	3	-4.34E-08	0	-0.427243	-2.09044	
Psm3t	Proteasome subunit alpha type-3	OQUM9;EDC18	OQUM9;EDC18	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	23.7713	1	1	1	7.3	7.3	7.3	27.372	0.21704000	3	-4.34E-08	0	-0.427243	-2.09044	
Psm3u	Proteasome subunit alpha type-3	OQUM9;EDC18	OQUM9;EDC18	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	23.7713	1	1	1	7.3	7.3	7.3	27.372	0.21704000	3	-4.34E-08	0	-0.427243	-2.09044	
Psm3v	Proteasome subunit alpha type-3	OQUM9;EDC18	OQUM9;EDC18	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	23.7713	1	1	1	7.3	7.3	7.3	27.372	0.21704000	3	-4.34E-08	0	-0.427243	-2.09044	
Psm3w	Proteasome subunit alpha type-3	OQUM9;EDC18	OQUM9;EDC18	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	23.7713	1	1	1	7.3	7.3	7.3	27.372	0.21704000	3	-4.34E-08	0	-0.427243	-2.09044	
Psm3x	Proteasome subunit alpha type-3	OQUM9;EDC18	OQUM9;EDC18	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	23.7713	1	1	1	7.3	7.3	7.3	27.372	0.21704000	3	-4.34E-08	0	-0.427243	-2.09044	
Psm3y	Proteasome subunit alpha type-3	OQUM9;EDC18	OQUM9;EDC18	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	23.7713	1	1	1	7.3	7.3	7.3	27.372	0.21704000	3	-4.34E-08	0	-0.427243	-2.09044	
Psm3z	Proteasome subunit alpha type-3	OQUM9;EDC18	OQUM9;EDC18	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	23.7713	1	1	1	7.3	7.3	7.3	27.372	0.21704000	3	-4.34E-08	0	-0.427243	-2.09044	
Psm4	Proteasome non-ATPase regulat	QD8W5;Q317H	QD8W5;Q317H	19.2911	20.5845	17.5	21.3734	17.5	17.5	17.5	17.5	22.0991	1	1	1	4.6	4.6	4.6	52.895	0.002331	9423000	1	0.0747117	0.334082	0.0172508	0.0922057
Psm5	Proteasome non-ATPase regulat	QD8W5;Q317H	QD8W5;Q317H	17.5	17.5	17.5	22.2864	17.5	21.8914	19.8828	17.5	24.312	4	4	4	6.1	6.1	6.1	100.2	0.38367000	8	0.398139	-1.84851	0.324898	-1.84851	
Psm6	Proteasome non-ATPase regulat	P14685	P14685	17.5	17.5	17.5	22.2838	17.5	22.0587	17.5	17.5	23.3091	1	1	1	4.6	4.6	4.6	28.718	0.003953	33684000	2	0.312828	-1.64545	0.0645096	-0.467374
Psm7	Proteasome non-ATPase regulat	OQ914	OQ914	17.5	17.5	17.5	21.8596	17.5	17.5	17.5	17.5	22.7264	1	1	1	4.4	4.4	4.4	45.536	0.004338	14170000	3	0.427243	-1.45321	0.427243	-1.74213
Psm8	Proteasome non-ATPase regulat	P26516	P26516	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	2	2	2	15	15	15	36.539	0.10522000	2	-4.34E-08	0	-4.34E-08	0	
Psm9	Proteasome activator complex sub	P97372;G3X9V	P97372;G3X9V	17.5	21.0407	24.6751	22.0788	17.5	17.5	17.5	17.5	21.6948	1	1	1	9.6	9.6	9.6	5.27057	0.42660000	5	0.252698	-2.01633	0.363007	1.27366	
Ptp1	Polypyrimidine tract-binding protein	Q8C858;Q8C58	Q8C58;Q8C58	17.5	21.1386	23.0559	24.0157	17.5	21.1129	17.5	21.2908	24.4916	4	4	4	11	11	11	52.63	0.56412000	6	0.0425994	-3.15469	0.0714076	-0.529277	
Ptgs2	Prostaglandin synthase 2	OQ90Q7;D3Z7C	OQ90Q7;D3Z7C	17.5	17.5	17.5	22.0465	17.5	20.4465	17.5	17.5	21.0616	1	1	1	6.2	6.2	6.2	18.721	0.004184	6348200	1	-4.34E-08	0	-0.427243	
Ptgs2	Prostaglandin synthase 2	OQ5769	OQ5769	17.5	17.5	22.4135	17.5	17.5	17.5	17.5	17.5	21.0939	3	3	3	7.3	7.3	7.3	69.012	0.14867000	3	0.427243	-1.63784	0.075888	0.438174	
Ptma	Prothymosin alpha/Prothymosin al	P26350;A0A087	P26350;A0A087	23.2352	21.2731	17.5	20.0613	17.5	23.4507	17.5	17.5	23.2666	2	2	2	15.3	15.3	15.3	12.254	0.55253000	6	0.0470216	0.32071	0.186442	1.24723	
Ptth2	Peptidyl-tRNA hydrolase 2, mitocho	Q8R2Y8	Q8R2Y8	17.5	17.5	17.5	23.0983	17.5	17.5	17.5	17.5	22.7879	1	1	1	7.7	7.7	7.7</								

S100a14	Protein S100-A14	Q8D2Q8	Q9D208	22.3832	23.672	26.5714	22.5768	22.5101	21.1555	21.3558	23.1284	22.7287	3	3	3	40.4	40.4	40.4	11.599	0	1.84e+08	13	0.738011	2.12803	0.59821	1.80455	
S100a4	Protein S100-A4	P07091;A0A0G2 P07091;A0A0G2JGD2		17.5	17.5	22.0067	17.5	17.5	17.5	17.5	17.5	23.0378	2	2	2	15.8	15.8	11.721	0.004107	2406300	2	0.427243	1.50222	0.0495603	-0.343709		
S100a6	Protein S100-A6	P14069	P14066	24.8318	25.3756	25.8433	26.0618	25.4993	25.0233	22.4841	25.126	26.2506	3	3	3	25.8	25.8	10.051	0	2.44e+08	18	0.159293	-0.177896	0.250758	-0.279978		
Sec1	Syntaxin-1	P18828;P18828;P18828;P18828-2		17.5	17.5	17.5	17.5	21.0314	17.5	17.5	21.409	17.739	1	1	1	6.4	6.4	32.904	0.00565	10977000	2	0.427243	-1.17789	0.272759	-1.68447		
Sec22b	Vesicle-trafficking protein Sec22b	O08547;E9G6R3;O08547;E9G6R3		17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	23.3687	1	1	1	6.5	6.5	6.5	24.74	0.00431	5415800	1	-4.34e-08	0.427243	-1.62291		
Sec61a1	Protein transport protein Sec61 sub P61620;O91R1.1;P61620			17.5	22.1997	24.327	22.6536	17.5	17.5	17.5	17.5	21.7386	3	3	3	6.7	6.7	6.7	52.264	0.0238000	9	0.0984997	0.705683	0.420541	1.34879		
Sec61b	Protein transport protein Sec61 sub O9CQ58		Q9CQ58	17.5	17.5	17.5	23.8147	24.0446	24.1332	22.6797	17.5	24.0814	1	1	1	15.6	15.6	15.6	9.9583	0.0360000	5	6.56418	-6.4975	0.145583	-3.92037		
Serb1p	Plasminogen activator inhibitor 1 R	O9CYS58;O9CYS58;O9CYS58;O9CYS58-2;O9CYS58		23.3648	24.2961	24.1251	24.3176	17.5	17.5	17.5	24.2345	26.0052	7	7	7	24.6	24.6	44.714	0	2.35e+08	21	0.589261	2.66541	0.191884	1.34879		
Serp1h1	Serpin H1	P19324;A0A104 P19324;A0A104;A0LH94		23.1398	23.1219	23.618	23.8929	23.237	26.1195	17.5	24.5931	25.2621	3	3	3	9.4	9.4	46.533	0	2.83e+08	15	0.578317	-1.55661	0.112951	0.820411		
Ser1	Serpin H1	P18828;P18828;P18828;P18828-2		17.5	17.5	17.5	17.5	21.0314	17.5	17.5	21.409	17.739	1	1	1	6.4	6.4	32.904	0.00565	10977000	2	0.427243	-1.17789	0.272759	-1.68447		
Sfl1	Splicing factor 1	Q64213;Q64213;Q64213;Q64213-2;Q3VYH4		20.1958	17.5	17.5	23	17.5	17.5	17.5	17.5	22.3978	1	1	1	2	2	70.402	0.004367	18944000	1	0.188709	-0.994761	0.162665	-0.794012		
SfB3a	Splicing factor 3B subunit 3	Q921M3-2;Q921M3-2;Q921M3-2		17.5	20.8428	21.0762	22.6139	17.5	22.6861	17.5	17.5	24.4231	3	3	3	3.7	3.7	125.31	0	436500000	9	0.211172	-1.12701	0.00553073	-0.00438372		
SfB3b	Splicing factor 3B subunit 4	Q8Q2Y9	Q8Q2Y9	17.5	17.5	17.5	20.3055	17.5	20.3766	17.5	17.5	20.2715	1	1	1	3.3	3.3	3.3	44.355	0.004301	3922800	2	0.934874	-1.89403	0.427243	-0.923834	
Sfqa	Splicing factor, proline and arginine	O8V106	O8V106	17.5	17.5	22.9156	22.8742	17.5	23.7767	17.5	17.5	23.0273	1	1	1	2.4	2.4	75.441	0.002268	497590000	4	0.31978	-2.07844	0.00473083	-0.037262		
Shm22	Serine hydroxymethyltransferase	Q8C2N7	Q8C2N7	17.5	17.5	17.5	21.7804	22.1813	17.5	17.5	21.4867	21.7965	1	1	1	2.2	2.2	55.758	0.002262	149400000	6	0.932241	0	0.932302	-2.76108		
Slc25a24	Calcium-binding mitochondrial carrier	O8BM08	O8BM08	17.5	20.8594	21.7315	21.0615	19.9074	17.5	17.5	17.5	20.0294	1	1	1	2.7	2.7	27	52.901	0.009191	10907000	4	0.118414	0.540658	0.174816	1.168124	
Slc25a3	Phosphate carrier protein, mitochondrion	O8VEM8;O5E902;O8VEM8;O5E902		23.2333	25.7729	26.5332	26.4896	26.1274	24.3102	24.3683	23.7907	25.4253	6	6	6	15.7	15.7	15.9	39.632	0	5.12e+08	33	0.142411	-0.462566	0.230943	0.615668	
Slc25a5;Slc25a4	ADP/ATP translocase 2;ADP/ATP translocase 2	P51881;P48962;P51881;P48962		21.4488	25.0432	27.3265	25.3832	26.2366	26.1901	24.4862	23.8905	26.5299	10	10	10	30.9	30.9	30.9	32.931	0	6.34e+08	33	0.318333	-1.32046	0.1604402	-0.335691	
Slc39a7	Zinc transporter SLC39A7	Q31125	Q31125	17.5	17.5	17.5	21.5106	17.5	17.5	17.5	17.5	17.5	2	2	2	7.1	7.1	7.1	50.656	0.004098	4989300	2	0.427243	-1.33685	-1.34e-08	0	
Slc3a2	4F2 cell-surface antigen heavy chain P10852;A0A0U1 P10852;A0A0U1;R0K4;P101			21.2414	23.0014	17.5	17.5	17.5	21.8418	17.5	17.5	17.5	1	1	1	3.2	3.2	58.336	0.003906	22821000	3	0.306138	1.63366	0.884943	3.08094		
Smarc5	SWI/SNF-related matrix-associated 1	Q912N3	Q912N3	17.5	17.5	17.5	17.5	23.1096	17.5	17.5	17.5	17.5	1	1	1	1.4	1.4	121.63	0	90505000	1	0.472243	1.85986	0	-4.34e-08		
Snd1	Staphylococcal nuclease domain	Q78P77;Q3TJ56;Q78P77;Q3TJ56		19.8867	21.36	24.0102	23.1683	22.0479	21.8732	17.5	19.6766	23.533	6	6	6	8.9	8.9	8.9	102.09	0	60132000	6	0.182669	-0.610853	0.126842	0.752075	
Snrnp27	U4/U6/U5 small nuclear ribonucleoprotein	Q8K194;O8K194;O8K194;O8K194-2		19.9923	20.7534	23.151	22.2076	17.5	20.9262	17.5	20.5577	22.7009	3	3	3	17.4	17.4	17.4	18.885	0	40542000	8	0.254533	0.22976	1.04603	0	
Snrnp70	U1 small nuclear ribonucleoprotein	Q62376;A0A10C Q62376;A0A10C;R0GR44;Q62		17.5	17.5	17.5	21.7209	17.5	17.5	17.5	17.5	17.5	1	1	1	2.2	2.2	51.991	0.005639	3456500	1	0.427243	-1.40696	0	-4.34e-08		
Srk1	Splicing regulatory glutamine/lysine	Q8B2K4;A0A10C Q8B2K4;A0A10C;B0G584;A0A1		17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	22.1921	1	1	1	2.8	2.8	56.763	0	7.560100	1	-4.34e-08	0.427243	-1.56403	-1.56403		
Srk1	Serine/arginine repetitive matrix protein	Q524H8;A2A9V9;Q524H8;A2A9V9;Q524H8;A2A9V9		17.5	20.901	23.909	17.5	17.5	22.0847	17.5	22.5568	22.9841	5	5	5	8.2	8.2	106.86	0	1.34e+08	19	0.293896	1.74178	0.3204682	-0.245955		
Srk1	Serine/arginine repetitive matrix protein	Q47639;O8B178;O8B178;O8B178-2;Q8B178		24.7639	24.7215	25.2262	24.7318	24.0135	23.2547	24.598	24.9748	24.77	14	14	14	7.1	7.1	294.84	0	2.84e+08	10	-0.817525	0.427243	0.427243	0.427243		
Srf1	Serine/arginine-rich splicing factor	Q1G6PM2;H7BX9;Q1G6PM2;H7BX9;Q1G6PM2		20.8976	25.5236	25.2165	25.5603	20.8744	19.8612	25.3977	26.2301	10	10	10	42.3	42.3	42.3	27.744	0	5.82e+08	53	0.310664	2.21212	0.335544	1.71574		
Srf10	Serine/arginine-rich splicing factor	Q1G6PM2;H7BX9;Q1G6PM2;H7BX9;Q1G6PM2		17.5	23.6571	17.5	24.3261	17.5	21.5294	17.5	17.5	23.6337	3	3	3	17.9	17.9	31.3	0	1.02e+08	3	0.213104	-1.56612	0.00087872	0.00786014		
Srf11	Serine/arginine-rich splicing factor	Q1G6PM2;H7BX9;Q1G6PM2;H7BX9;Q1G6PM2		17.5	19.6865	20.2643	19.5814	17.5	17.5	17.5	17.5	22.0179	4	4	4	13.9	13.9	13.9	53.102	0	3.8726000	9	0.356433	0.956484	0.0280938	0.144307	
Srf2	Serine/arginine-rich splicing factor	Q262093	Q262093	25.2969	24.1565	25.3819	25.3009	22.8313	24.7067	23.5441	25.6588	26.1373	4	4	4	21.7	21.7	21.7	25.476	0	6.69e+08	33	0.324378	0.665464	0.124292	-0.271677	
Srf3;Gm12355	FACT complex subunit SSRP1	P84104;P84104;P84104;P84104-2;A2A4W6		26.7015	17.5	17.5	26.4498	27.4138	23.9852	27.4889	23.6125	27.8876	28.2125	8	7	7	2.8	2.8	80.855	0	10704000	77	0.327262	0.123449	0.0847626	-0.455384	
Srf4	Serine/arginine-rich splicing factor	Q8V897;Q52V3 Q8V897;Q52V3		17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	22.7158	2	2	2	4.5	4.5	2.7	2.7	55.979	0	42365000	2	-4.34e-08	0.917869	-1.33554	
Srf5	Serine/arginine-rich splicing factor	Q35326;Q08D85;Q35326;Q08D85		21.6073	22.5718	17.5	24.1349	17.5	24.1017	17.5	23.2227	26.4748	2	2	2	10.8	10.8	7.4	7.4	30.891	0	2.55e+08	13	0.196304	-1.38585	0.235871	-1.83947
Srf6	Q3TWW8;A0A01T;Q3TWW8			24.1733	22.2738	23.825	24.5989	23.3479	21.9195	22.8099	24.2511	24.5535	5	5	5	2	2	14.5	11.8	39.025	0	2.08e+08	25	0.0478048	0.135291	0.129389	-0.447427
Srf7	Serine/arginine-rich splicing factor	Q8BL97;Q8BL97;Q8BL97;Q8BL97-3;Q8BL97		24.5967	26.8513	22.9902	26.5516	19.741	24.083	22.0616	23.252	26.1262	6	6	6	24.7	24.7	30.17	0	5.18e+08	22	0.060568	0.35419	0.0390938	-0.165792		
Srpf	Translocase-associated protein subunit	Q9DC99;Q9DC99;Q9DC99;Q9DC99-2		17.5	17.5	17.5	21.4366	17.5	17.5	17.5	17.5	21.1165	1	1	1	7.6	7.6	21.6	21.064	0.003795	5112600	1	0.427243	-1.3222	0.427243	-1.20552	
Stat1	FACT complex subunit SSRP1	Q8V897;Q52V3 Q8V897;Q52V3		17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	22.7158	2	2	2	4.5	4.5	2.7	2.7	55.979	0	42365000	2	-4.34e-08	0.917869	-1.33554	
Stat1	Signal transducer and activator of transcription 4	P44225;Q8C3V4;P44225;Q8C3V4;A0A08R7W		17.5	22.1229	22.0769	23.6786	17.5	21.4147	19.9913	20.1899	21.9712	4	4	4	6.1	6.1	6.1	87.196	0	33378000	5	0.0428824	-0.297858	0.00946441	0.0491371	
Stip1	Stress-induced-phosphoprotein 1	Q08064	Q08064	21.3147	22.453	22.6916	22.4733	21.9115	23.2055	19.9801	23.1369	23.5343	2	2	2	4.2	4.2	4.2	62.581	0	170196000	11	0.256921	-0.376979	0.017674	-0.063996	
Stmn1	Stathmin	P54227;D3Z128;P54227;D3Z128;D3Z5N2		22.3172	17.5	22.24	21.8737	17.5	23.7985	17.5	17.5	25.0083	2	2	2	18.1	18.1	17.274	0	1.36e+08	7	0.025978	-0.376974	0.0806876	0.677649		
Stmn2	Stathmin-2	P55821	P55821	17.5	20.4403	17.5	21.2255	17.5	20.7097	17.5	17.5	17.5	1	1	1	5.6	5.6	5.6	20.828	0.004237	16669000	3	0.365305	-1.33164	0.427243	0.990101	
Str3a	Dolichyl-diphosphooligosaccharin transferase	P46978	P46978	17.5	20.8441	21.6713	20.4666	17.5	17.5	17.5	17.5	21.5762	1	1	1	1.6	1.6	10.897	0.004384	11662000	1	0.13104	1.74178	0.3204682	1.8005		
Sumo2;Sumo3	Small ubiquitin-related modifier 2;SUMO2;SUMO3	P61957;Q92172;P61957;Q92172;G3UJZ6;H		22.1115	22.1229	22.3459	22.4638	17.5	17.5	17.5																	

Zyx	Zyxin	Q7TQE2;Q62523;Q7TQE2;Q62523;A0A0N451	24.123	24.6724	23.0673	25.0872	17.5	24.1897	20.9685	24.8638	25.4445	4	4	4	10.7	10.7	10.7	57.026	0	2.89E+08	14	0.279552	1.69526	0.045019	0.195285
	UPF0444 transmembrane protein C	Q9DAM7	17.5	17.5	24.4654	24.3808	17.5	21.7552	17.5	17.5	23.2242	1	1	1	22.6	22.6	11.549	0.002222	90384000	4	0.1714	-1.3902	0.047135	0.413747	
		ADA140LI4	17.5	22.6036	23.4242	17.5	17.5	21.3576	21.7948	22.418	17.5	2	2	2	0.6	0.6	516.94	0.004049	43918000	1	0.457096	2.39006	0.0891578	0.604989	