



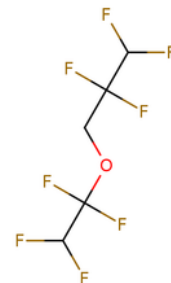
## FLUORINATED MATERIALS FOR BATTERY & ELECTROLYTE RESEARCH

SynQuest Laboratories provides specialty fluorinated compounds for research and development, including electrolyte salts, fluorinated solvents, and advanced materials for battery applications.

### 1,1,2,2-Tetrafluoroethyl 2,2,3,3-tetrafluoropropyl ether (TTE)

CAS: [16627-68-2], PN# 2107-3-56

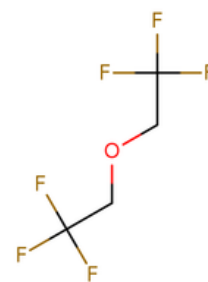
- Fluorinated ether used as a co-solvent or diluent in advanced electrolyte formulations.
- Helps enable high-voltage and high-performance systems by supporting favorable solvation behavior and interphase stability.



### Bis(2,2,2-trifluoroethyl) ether (BTFE)

CAS: [333-36-8], PN# 2107-3-18

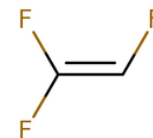
- Fluorinated ether of interest for localized high-concentration and other advanced electrolyte systems.
- Used in formulation work aimed at improving stability, lowering viscosity, and supporting overall electrochemical performance.



### Trifluoroethylene

CAS: [359-11-5], PN# 1300-3-05

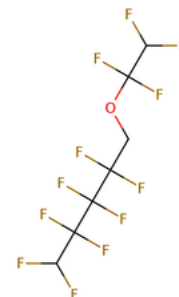
- Fluorinated olefin used as a building block for fluoropolymer materials.
- Well suited for applications involving binders, separators, and other chemically demanding environments.



### 1H,1H,5H-Octafluoropentyl 1,1,2,2-tetrafluoroethyl ether

CAS: [16627-71-7], PN# 2107-3-45

- Fluorinated ether diluent used in localized high-concentration electrolyte development.
- Supports safer, more stable formulations through improved thermal stability and favorable solvation structure.





## FEATURED FLUORINATED SOLVENTS & INTERMEDIATES

SynQuest Laboratories offers specialty fluorinated solvents and intermediates designed to support advanced chemical synthesis, materials development, and research applications.

### Trifluoromethanesulfonic acid (Fluorinated Intermediate)

CAS: [1493-13-6], PN# 6164-3-02

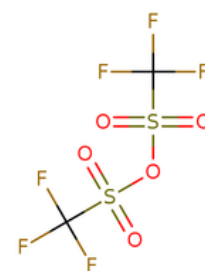
- Strong fluorinated organic acid used as a reagent and intermediate in advanced synthesis.
- Useful where highly acidic functionality is needed for activation, cleavage, or further transformation.



### Trifluoromethanesulfonic anhydride

CAS: [358-23-6], PN# 6164-2-13

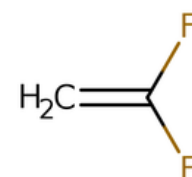
- Widely used activating reagent for converting hydroxyl-containing compounds to triflates.
- Valuable for introducing triflate functionality and driving transformations that require strong electrophilic activation.



### 1,1-Difluoroethylene

CAS: [75-38-7], PN# 1300-3-06

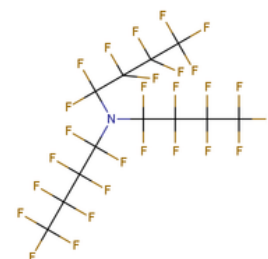
- Fluorinated olefin used as a key monomer for vinylidene fluoride-based fluoropolymers.
- Applied in development of high-performance materials requiring chemical resistance and thermal stability.



### Perfluorotributylamine, MS Grade

CAS: [311-89-7], PN# 3132-2-04

- Chemically inert perfluorinated tertiary amine with high fluorine content and strong thermal stability.
- Used in specialty applications where a stable fluorinated fluid is desired for analytical, electronic, or research-related work.





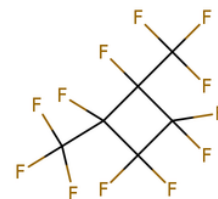
## FEATURED FLUORINATED SOLVENTS & INTERMEDIATES

SynQuest Laboratories offers specialty fluorinated solvents and intermediates designed to support advanced chemical synthesis, materials development, and research applications.

### Perfluorodimethylcyclobutane

CAS: [2994-71-0], PN# 1200-2-03

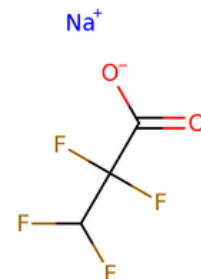
- Fully fluorinated cyclic compound with high chemical stability and distinctive fluorocarbon properties.
- Useful in specialty fluorine chemistry and in development of advanced fluorinated materials.



### Sodium 2,2,3,3-tetrafluoropropionate

CAS: [22898-01-7], PN# 2122-3-14

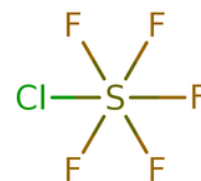
- Fluorinated carboxylate salt used as an intermediate in preparation of specialty fluorinated compounds.
- Suitable for synthesis routes that require incorporation of fluorinated acid functionality.



### Sulfur chloropentafluoride

CAS: [13780-57-9], PN# M016-6-01

- Reactive fluorinated sulfur compound used in preparation of specialty sulfur-containing fluorinated materials.
- Valuable in synthesis where sulfur fluoride functionality is needed for further chemical transformation.



### 1,2-Difluoroethylene

CAS: [1691-13-0], PN# 1300-3-02

- Fluorinated olefin suited for advanced research and chemical development work.
- Low-boiling fluorochemical intermediate for laboratory and process development applications.





thermo scientific

This  
is more  
than a  
**chemical**

Drug discovery

# Increasing success rates in your drug discovery research

High-throughput screening  
and fragment libraries

Find it at [fishersci.eu](https://fishersci.eu)

 **fisher scientific**  
part of Thermo Fisher Scientific

# Introduction

The search for bioactive molecules in early-stage drug discovery using rapid compound screening and fragment-based design should not be like looking for a needle in a haystack.

The Thermo Scientific™ collection is widely recognized for its market leading diversity and quality. A highly diverse library of compounds that have the right chemical properties is much more likely to provide successful results than larger less diverse libraries with less suitable chemical properties.

In compound screening the size of your library is not as important as its diversity! After all why would you screen larger numbers of compounds at greater cost with less chance of getting positive results?

Thermo Scientific™ libraries are designed to provide a high probability of discovering “hits” and thus accelerate your discovery campaigns!

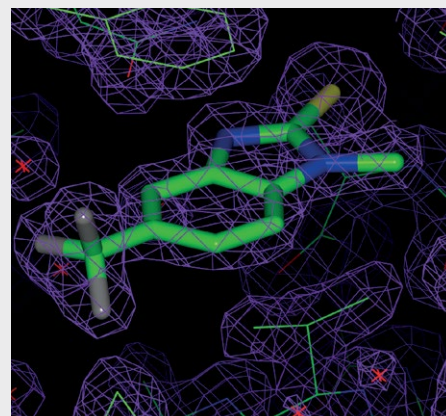
## Index

### High-throughput screening libraries

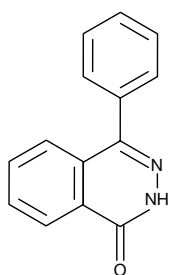
- HitDiscover library
- HitFinder library
- HitCreator library
- Specialty Libraries: Antiviral, Antibacterial, PPI, GPCR, Kinase

### Fragment Collections

- Fragment library
- Fluoro-fragment library
- 19F-fragment library
- Bromo-fragment library
- Pre-Fragment library

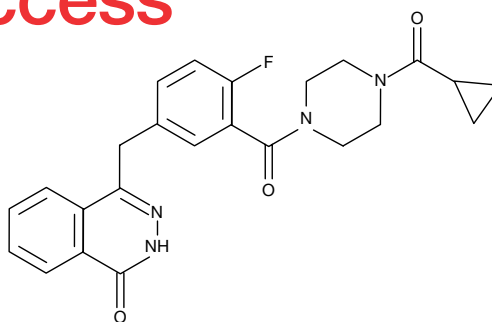


## Track Record of Success



### Thermo Scientific Screening Compound

Olaparib, trade name Lynparza was approved by the FDA in December of 2014 for the treatment of ovarian cancer. The compound from which this drug was developed came from the Maybridge Screening Collection. It is an inhibitor of poly ADP ribose polymerase (PARP), an enzyme involved in DNA repair. It acts against cancers in people with hereditary BRCA1 or BRCA2 mutations, which includes many ovarian, breast, and prostate cancers. This is the fourth drug that has been identified as being developed from the Maybridge Screening Collection.



### Olaparib (Lynparza)

In 2019 the drugs advisory body NICE, the National Institute for Health and Care Excellence, said using olaparib at an earlier stage in treatment of ovarian cancer would bring the greatest benefit “and may have the potential to cure the disease”.

Lynparza is now also a “first-line” maintenance treatment for BRCA-mutated Metastatic Pancreatic cancer reducing the risk of disease progression or death by 47% in patients whose disease had not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen.

# Screening Libraries

Thermo Scientific Screening Collection: A highly diverse set of over 53,000 hit-like and lead-like molecules widely acknowledged as a critical tool in screening campaigns.

## HitDiscover: the entire Screening Collection pre-plated

A ready to screen collection of ~53,000 Thermo Scientific screening compounds in dry film format the compounds are of minimum 90% purity and pre-plated as 1 $\mu$ mol dry films in 96 well plate format offering exceptional diversity and outstanding value! Immediate re-supply is available on the majority of the compounds.

## HitFinder: representing the diversity of the entire Screening Collection

HitFinder Compounds are selected from the Thermo Scientific screening collection using a clustering algorithm employing standard Daylight fingerprints with the Tanimoto similarity index (J.Chem.Inf.Comput.Sci.,1999, 39, 747-750), clustering at 0.7 similarity. All compounds fit Lipinski guidelines for "Drug-likeness" (ClogP  $\leq$ 5, H-bond acceptors  $\leq$ 10, H-bond donors  $\leq$ 5,

Molecular Weight  $\leq$ 500), and all have purity greater than 90%.

Each plate represents a unique sample from this selection, is diverse in its own right and available pre-plated at 1 $\mu$ mol in 96-well plates or .25 $\mu$ mol in 384-well plates.

## HitCreator: The ultimate diversity screening library!

This library takes away the need to choose between different libraries by providing the ultimate coverage of drug-like chemical space with a single library. Building on over 50 years of expertise in designing industry leading screening libraries the pre-plated HitCreator represents the diversity of a 500,000 compound library distilled to 14,000 molecules. Each HitCreator is conveniently supplied as dry films in 96 shallow-well plates or 384-well microplates.

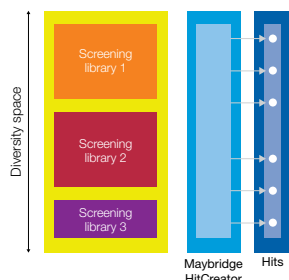


Figure 1. Importance of diversity in finding hits

The figure left illustrates how a highly diverse screening library will provide a greater hit probability than larger, but less diverse libraries.

## Other specialty screening libraries available under the Thermo Scientific brand in close collaboration with an external partner include:

- **Antiviral library:** over 8000 compounds chosen to facilitate the discovery of novel chemical entities with profound antiviral activity and improved safety profiles
  - **Antibacterial library:** over 8,000 compounds that form a unique compound library for antibacterial research based on the proprietary natural product like scaffolds that provide great skeletal diversity combined with the presence of polar functional groups and multiple stereogenic centers.
  - **Protein protein Interaction (PPI) library:** over 11,000 compounds selected through analysis of the PPI relevant chemical space and development of several strategies for building PPI-focused chemical libraries
  - **GPCR library:** over 10,000 compounds selected for screening against G-Protein Coupled Receptors
  - **Kinase library:** over 6,000 compounds chosen to facilitate the discovery of novel kinase inhibitors by providing access to our advanced collection of small molecules, fragments and macrocycles
- Other focused libraries are available on request.**

# Success story

There are a great many success stories of our customers accelerating their drug discovery programs with Maybridge Screening Libraries, one example is shown below:

**Antimicrob Agents Chemother. 2012 Sep;56(9):4718-28. doi: 10.1128/AAC.00957-12. Epub 2012 Jun 25.**

**Severe Acute Respiratory Syndrome Coronavirus Replication Inhibitor That Interferes with the Nucleic Acid Unwinding of the Viral Helicase nucleic acid unwinding of the viral helicase.**

**Adedeji AO1, Singh K, Calcaterra NE, DeDiego ML, Enjuanes L, Weiss S, Sarafianos SG.**

Severe acute respiratory syndrome (SARS) is a highly contagious disease, caused by SARS coronavirus (SARS-CoV), for which there are no approved treatments. We report the discovery of a potent inhibitor of SARS-CoV that blocks replication by inhibiting the unwinding activity of the SARS-CoV helicase (nsp13). We used a Förster resonance energy transfer (FRET)-based helicase assay to screen the Thermo Scientific Hitfinder chemical library. We identified and validated a compound (SSYA10-001) that specifically blocks the double-stranded RNA (dsRNA) and dsDNA unwinding activities of nsp13, with 50% inhibitory concentrations (IC<sub>50</sub>s) of 5.70 and 5.30  $\mu$ M, respectively. This compound also has inhibitory activity (50% effective concentration [EC<sub>50</sub>] = 8.95  $\mu$ M) in a SARS-CoV replicon assay, with low cytotoxicity (50% cytotoxic concentration [CC<sub>50</sub>] = >250  $\mu$ M), suggesting that the helicase plays a still unidentified critical role in the SARS-CoV life cycle.

Hence, it is possible that SSYA10-001 inhibits unwinding by nsp13 by affecting conformational changes during the course of the reaction or translocation on the nucleic acid. SSYA10-001 will be a valuable tool for studying the specific role of nsp13 in the SARS-CoV life cycle, which could be a model for other nidoviruses and also a candidate for further development as a SARS antiviral target.

# Thermo Scientific libraries contain diverse and hit-like compounds

The collection was mapped against the 400,000 known theoretical pharmacophores in the World Drug Index (WDI), by Oxford Molecular and it was found that ca. 87% are expressed in this collection therefore providing a far-reaching spread of active moieties, which can generate great value in screening programmes.

An independent study carried out by McGregor and Pallai comparing the diversity of 10 commercially available collections and the Available Chemicals Directory (ACD), showed that out of those that were produced in-house, Thermo Scientific had the most diverse library i.e. the most singletons (clusters with one member), and the highest number of clusters.

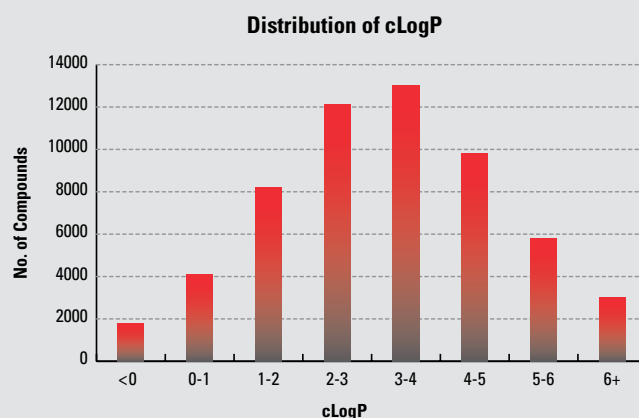
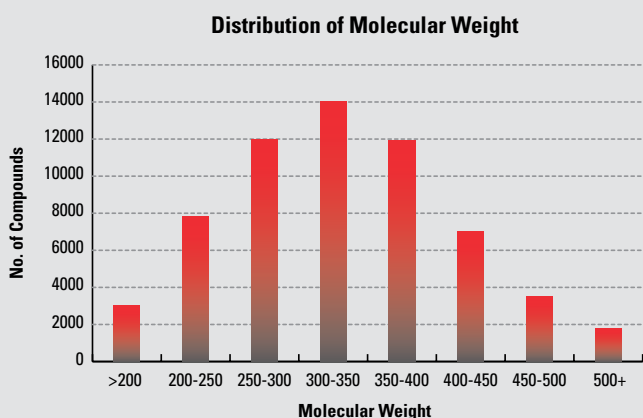
(Journal of Chemical Information and Computer Sciences; 1997; 37(3); 443-448.)

The Thermo Scientific collection also has a high degree of 'hit-like' compounds. The paper by Teague et al\*, summarises that the ideal hit profile of a compound is clogP 1-3 and molecular weight 100-350. The information in the table below illustrates that a large portion of the Screening Collection complies with these hit-like characteristics.

(\* S.J. Teague et al., *Angew. Chem. Int. Edn.*, 1999, 38, No.24, pp3743-3748)

## Benefits

- **Diverse** – A highly diverse library will provide a greater probability of obtaining "hits"
- **Hit-Like** – compounds containing the right chemical properties provide more successful results
- **Reliable** – High quality compounds ensure the hits you discover are an excellent starting point to accelerate your discovery campaigns



The collection also demonstrates classic characteristics of drug-like molecules, as defined by Lipinski's so-called 'Rule of 5'. These rules are essentially a pragmatic reduction of the common features of the drugs represented by the WDI. The collection is highly compliant with Lipinski's guidelines as the table shows.

## Lipinski Rule\*\* Thermo Scientific Screening Collection

< 5 H-bond donors 99.7% <5  
< 10 H-bond acceptors 99.8% <10  
cLog P <5 mean log P 2.83, 95% in range -0.11 to 6.3  
Mol. Weight <500 mean mol. weight 308, 95% in range 146-498

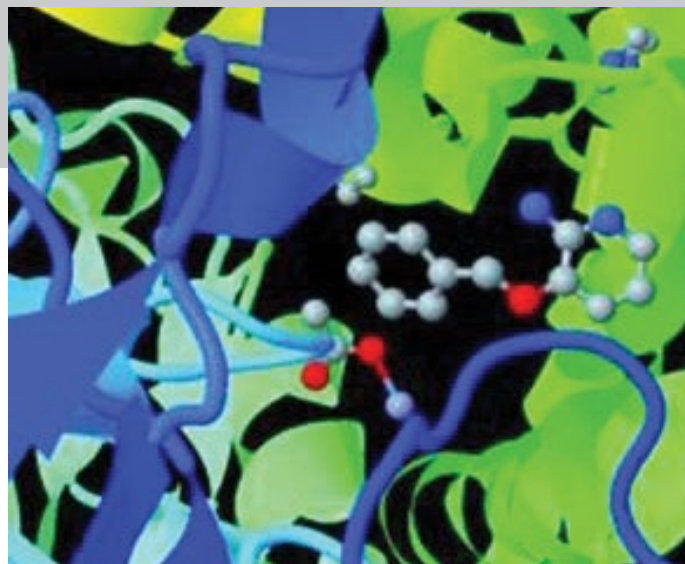
(\*\* Lipinski, C.A., Lombardo, F., Dominy, B.W. and Feeney, P.J. (1996). Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. *Advanced Drug Delivery Reviews* 23 3-25.)

# Fragment Libraries

## Fragment Library: the industry leading library for fragment-based drug screening

Fragment screening has become a method of choice in the quest for rapid identification of new lead molecules in drug discovery due to the higher hit probability and fewer fragments needing to be screened.

The fragment library is a proven, industry-leading library due to its diversity, pharmacophoric content and novelty.



## Key Features and Benefits

- **Rule of Three (Ro3) compliance** delivers superior ADME attributes
- **Exceptional diversity** – Tanimoto similarity index of 0.66 based on standard Daylight fingerprinting
- **PAINS Free** – The library has been filtered to remove pan assay interference compounds (PAINS) avoiding false hits
- **Experimentally measured solubility** – guaranteed solubility of fragments in PBS buffer (1mM) ensures robust screening data and minimizes candidate attrition
- **Assured quality of >95%**, NMR spectrum available for each of the 2,500 compounds in DMSO **AND Aqueous conditions**
- **Optimised for SPR** – in collaboration with GE Healthcare a “Clean Screen” was run on a Biacore instrument to remove promiscuous binders
- **Chemically “clean”** – filtered to remove toxic and reactive groups
- **Pharmacophore rich**, but not too complex to allow simpler interpretation of the results

Fragment hopping is facilitated with the entire Maybridge portfolio, for the full range visit [thermofisher.com/maybridge](http://thermofisher.com/maybridge)

## Leading the way in fragment library design since 2005

2005

### Fragment Library

One of the first commercially available fragment libraries.

- 500 compounds cherry picked from the pharmacophore-rich Maybridge building block portfolio

### Ro3 Fragment Library

The first commercially available Ro3-compliant library.

- 1,000 compounds computationally selected to provide:
  - > Full “Rule of Three” compliance
  - > High structural diversity
  - > Pharmacophore-rich fragments containing “linkerfriendly” groups for hit evolution

### Fragment Collection

- 30,000+ compounds
- Convenient access to the extensive Thermo Scientific portfolio
- Powerful tool for building bespoke fragment screening libraries or searching for hit

### Ro3 Fragment Library Solubility Upgrade

The first commercially available fragment library with assured solubility.

- Experimental solubility data acquired for each of the 1,000 Ro3 library compounds
- Each member of the library has been shown to dissolve in:
  - > DMSO at 200mM
  - > PBS buffer (0.5% DMSO) at 1mM
- The solubility assurance is an additional benefit to the Ro3 and diversity advantages of the original library

### Ro3 Diversity Fragment Library

Developed with fragment screening practitioners to provide the most practical and powerful fragment library available.

- 1,500 compounds selected from the Maybridge and Acros Organics portfolios to provide:
  - > Improved structural diversity
  - > Access to a broader pool of analogues for “fragment hopping”
  - > “Linker-friendly” groups allow for rapid hit evolution
  - > Full “Rule of Three” compliance
  - > Experimental solubility assurance for each compound in the library

### Expansion of the Ro3 Diversity Fragment Library

As the number of fragments that can be screened during assays increases due to the development of higher throughput biophysical techniques such as surface plasmon resonance, we have added additional fragments.

This has enabled us to:

- Increase the diversity by 30%
- Redesign the library to maximize the diversity across all the subsets
- Offer a greater number of high quality fragments for custom selection

2020

### Redesigned the Ro3 Library to be PAINS free

PAINS free – filtered to remove pan assay interference compounds

- Aqueous NMR for every compound
- Data for 5 fragment cocktails
- Optimized for Surface Plasmon Resonance (SPR) – clean screen carried out on 3 different probes

## The Thermo Scientific Fragment Library is available in the following formats

Available format	Comments
<b>Entire library</b> with <b>2,500</b> compounds	Highly recommended. It provides the highest probability to find a hit.
A <b>core set</b> the entire library with <b>1000</b> compounds	It encompasses the diversity of the entire library. Suitable for rapid and exploratory work.
A <b>supplement set</b> of the entire library with <b>1,500</b> compounds	For those who have screened the core set. It provides an additional probability to identify more hits.
<b>Customised set</b>	A selection of any number of fragments. Our searchable database allows rapid selection of fragments based on substructure and calculated Ro3 parameters.
<b>Complete convenience</b>	Custom weighed to your requirements in milligram or micromolar quantities, neat, in DMSO, in D6DMSO, in plates or vials.

## Success story

The Ro3 Fragment library has been the source of many successful fragment screening projects, for example:

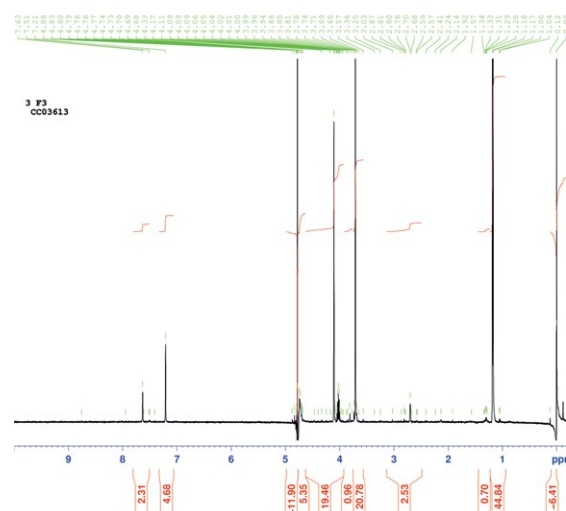
**Antimicrob Agents Chemother.** 2018 Mar; 62(3): e01571-17.

**Negatu DA1,2,3, Liu JJJ2, Zimmerman M4, Kaya F4, Dartois V4, Aldrich CC5, Gengenbacher M6,4, Dick T7,4.**

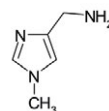
Tuberculosis (TB) remains a global health threat, killing 1.34 million people in 2016. The high prevalence of drug-resistant *Mycobacterium tuberculosis* strains is a medical urgency and calls for the development of new drugs active against TB.

Several key antituberculosis drugs, including pyrazinamide, with a molecular mass of 123.1 g/mol, are smaller than the usual drug-like molecules. Current drug discovery efforts focus on the screening of larger compounds with molecular masses centered around 400 to 500 g/mol. Fragment (molecular mass < 300 g/mol) libraries have not been systematically explored for antitubercular activity. Here we screened a collection of 1,000 fragments, present in the Ro3 library, for whole-cell activity against *Mycobacterium tuberculosis*.

Twenty-nine primary hits showed dose-dependent growth inhibition equal to or better than that of pyrazinamide. The most potent hit, indole propionic acid [IPA; 3-(1H-indol-3-yl)propanoic acid], a metabolite produced by the gut microbiota, was profiled in vivo. The molecule was well tolerated in mice and showed adequate pharmacokinetic properties. In a mouse model of acute *M. tuberculosis* infection, IPA reduced the bacterial load in the spleen 7-fold. Our results suggest that IPA should be evaluated as an add-on to current regimens and that fragment libraries should be further explored to identify antimycobacterial lead candidates.



**Figure 1.** An example of an NMR spectra in PBS with the chemically encoded shift data of all of the compounds in the Fragment Library.



**CC03613:**  
(1-Methyl-1H-imidazol-4-yl) methylamine

<sup>1</sup>H-NMR spectra in aqueous conditions is available on request and accelerates your screening workflow by avoiding having to run an <sup>1</sup>H-NMR baseline

## Other specialty fragment libraries include:

### The Fluoro-Fragment Collection

More than 5,300 fluorine containing fragments ideal for  $^{19}\text{F}$  NMR based fragment screening a diverse set of which is offered as the Maybridge  $^{19}\text{F}$  Fragment Library

### $^{19}\text{F}$ Fragment Library - with $^{19}\text{F}$ NMR spectra for every compound

A fluorine labelled fragment library of 480 compounds, designed based on the Thermo Scientific collection of fluorinated compounds. This library has been developed in collaboration with Argenta and the University of Kent and has been shown to have appropriate properties for fragment screening using biophysical methods.

### The Bromo-Fragment Collection

More than 1,500 bromine containing fragments for X-ray based fragment screening.

### The Pre-Fragment Collection

A valuable source of reactive "pre-fragments" for synthesising your own fragments or evolving your hits.

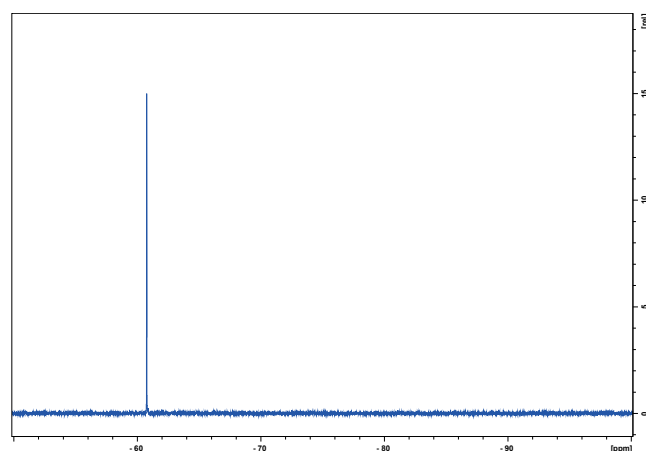
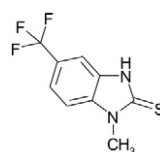


Figure 2. An example of a  $^{19}\text{F}$  NMR spectra.



#### TG00013:

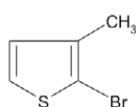
1-Methyl-5-(trifluoromethyl)-2,3-dihydro-1Hbenzo[d]imidazole-2-thione

$^{19}\text{F}$  NMR spectra simplifies the interpretation of the spectra and thus facilitates the use of 'cocktailing' allowing multiple compounds to be screened together

## Examples of Fragments

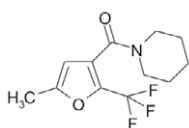
### 1. SPB08396:

2-Bromo-3-methylthiophene



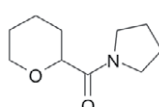
### 2. MO08143:

1-[5-Methyl-2-(trifluoromethyl)-3-furoyl]piperidine



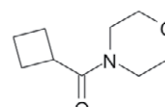
### 3. MO08161:

1-(Tetrahydropyran-2-ylcarbonyl)pyrrolidine



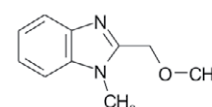
### 4. MO08170:

4-(Cyclobutylcarbonyl)morpholine



### 5. MO08563:

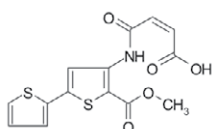
2-(Methoxymethyl)-1-methyl-1H-benzimidazole



## Examples of hits from high-throughput screening compounds

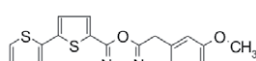
### 1. HTS01037:

4-[[2-(Methoxycarbonyl)-5-(2-thienyl)-3-thienyl]amino]-4-oxo-2-butenoic acid



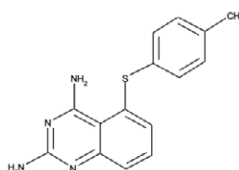
### 2. HTS11125:

2-(3-Methoxybenzyl)-5-[5-(2-thienyl)-2-thienyl]-1,3,4-oxadiazole



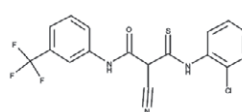
### 3. MWP01127:

5-[[4-Methylphenyl]thio]quinazoline-2,4-diamine



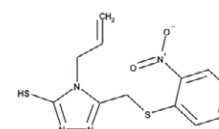
### 4. DP00477:

N1-[3-(Trifluoromethyl)phenyl]-3-(2-chloroanilino)-2-cyano-3-thioxopropanamide



### 5. DSHS00884:

4-Allyl-5-[[2-nitrophenyl]thio]methyl}-4H-1,2,4-triazole-3-thiol





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