MAYBRIDGE

The Maybridge Ro3 Fragment Library

Specifically designed and computationally clustered to provide a rich source of optimizable hits for your fragment screening programs

Fragment based screening is a rapidly developing means of expediting the drug discovery process. The **Maybridge Ro3 Fragment Library** combines forty-five years experience of delivering pharmacophorically-rich compounds through innovative heterocyclic chemistry with industry standard chemometrics to bring you a premier diverse fragment offering engineered to meet Rule of Three (Ro3) criteria.[1] The result is a unique tool for efficiently probing structural space within your target protein.

Advantages of fragment based screening [2,3,4,5]

- A much smaller library of premier compounds is required to produce multiple hits than might be achieved with a traditional HTS approach.
- Efficient probing of the target site can lead to novel hits at proteins intractable to HTS approaches with standard screening libraries.
- Fragment hits are more likely to generate selective, compact and ligand-efficient lead drug candidates, which may reduce attrition rates attributable to poor ADME profiles.

The success of fragment-based screening relies heavily on the quality of the fragment library.

The **Maybridge Ro3 Fragment Library** builds on the success of the earlier Maybridge Fragment Library, integrating many new compounds from the rapidly expanding Maybridge portfolio.

Rigorous pre-filtering and application of standard Daylight fingerprint algorithms has resulted in a library of 1000 desirable fragments of quantifiable structural diversity and complete Rule of Three compliance.

This offering provides a convenient and cost-effective source of pre-selected high quality fragments, weighed and packed to your specific requirements.

Key features of the Maybridge Ro3 Fragment Library

> 'Rule of Three' compliant
ALL of our fragments satisfy widely accepted 'Rule of Three' parameters. Fragment hits with these physicochemical limits allow greater scope for development of leads with superior ADME attributes.

> Chemically Clean
Structural filtering excludes undesirable reactive functionalities, whilst retaining 'linker-friendly' groups such as amines, acids and hydroxyls to allow rapid evolution of hits into larger drug-like leads.[6]

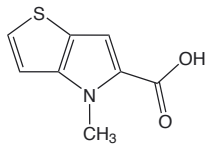
> Quantifiable Diversity
Established clustering software was used to select a highly diverse collection with a Tanimoto similarity index of 0.68 based on standard Daylight fingerprinting.[7]

> Pharmacophoric Enrichment
For 45 years our focus has been the design of novel heterocyclic compounds, the cornerstone of pharmaceutical SAR. This library taps into that rich vein of small molecules many of which are exclusive to the Maybridge portfolio.

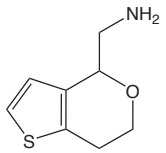
> Quality Assured
All Maybridge Ro3 Fragments are >95% purity for full confidence in your hits. Full analytical data are supplied, including NMR spectra of all 1000 compounds.

> Access to Analogues
With over 500 new building blocks added to the Maybridge range each year, many Ro3 Fragments and close analogues are available in multigram quantities, often providing a range of functional groups to aid synthetic work following a hit. To see the full range visit **www.maybridge.com**.

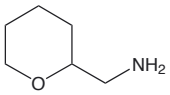
Examples of Unique Maybridge Ro3 Fragments



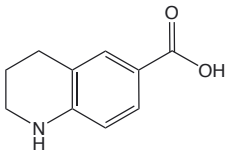
CC40901
4-methyl-4H-thieno[3,2-b]-pyrrole-5-carboxylic acid



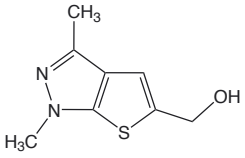
CC61114
(6,7-dihydro-4H-thieno-[3,2-c]pyran-4-ylmethyl)amine



CC41213
(tetrahydropyran-2-ylmethyl)amine



MO00019
1,2,3,4-tetrahydro-6-quinolinecarboxylic acid



CC22909
(1,3-dimethyl-1H-thieno-[2,3-c]pyrazol-5-yl)methanol

Library Construction

The 1,000 fragments in the Maybridge Ro3 Fragment Library have been chosen from the Maybridge portfolio of over 70,000 compounds following a meticulous selection process. First, exclusion filters were applied to remove undesirable reactive functionalities. Further filtering on the basis of purity (≥95%) and physicochemical properties ensured a compound dataset which achieves our high quality specifications and observes the 'Rule of Three' standard for reduced chemical complexity (Table 1).

TABLE 1	Rule of Three Criteria[1]	Maybridge Ro3 Fragments RANGE OF VALUES	Maybridge Ro3 Fragments AVERAGE VALUE
MW	≤ 300	93.1 - 298.4	178.3
cLogP	≤ 3.0	-2.5 - 3.0	1.5
H-Bond Acceptors	≤ 3	0 - 3	2.4
H-Bond Donors	≤ 3	0 - 2	0.9
Rotatable bonds (Flexibility Index)	≤ 3	0 - 3	0.9
Polar Surface Area	≤ 60Å²	4.9 - 69.1Å² (99% < 60Å²)	37.0Å²

Additionally, calculated LogS values predict aqueous solubility in excess of 1 millimolar for all members of the library.

The majority of Maybridge Ro3 Fragments are functionalized ready for fragment linking and rapid lead evolution. Unique capped fragments, such as carboxamides and sulfonamides (many specifically synthesized for this library using Maybridge Reactive Intermediates), have also been included as valuable fragments with scope for analoguing.

The dataset of pre-selected, pre-filtered fragments was subjected to standard Daylight fingerprint analysis and clustered to a Tanimoto similarity coefficient of 0.68, producing the 427 cluster centroids and 563 singletons that make up the final selection.[7] The outcome of this scientifically rigorous process is The Maybridge Ro3 Fragment Library – the perfect tool to help you accelerate your lead generation programs.

Download structures and physicochemical properties of all the compounds in the library at **www.maybridge.com**.

The Maybridge Ro3 Fragment Library is available custom weighed to your requirements, in milligram (≥10mg) or micromolar (≥50µmol) quantities per compound.

Please contact us for a quotation at **maybridge.sales@thermofisher.com**.

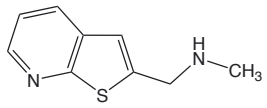
Also available:

Chemistry Services for Drug Discovery:
Utilize Maybridge medicinal and heterocyclic chemistry expertise to quickly optimize your fragment screening hits into leads.

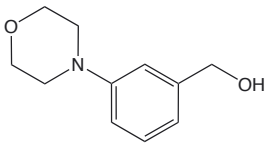
The Maybridge Screening Collection:
Over 56,000 compounds of market leading diversity with high Lipinski compliance.

The HitFinder™ Collection:
14,400 compound selection representing the overall diversity of the collection.

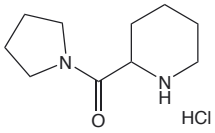
Examples of Unique Maybridge Ro3 Fragments



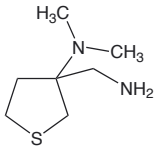
CC05646
N-methyl-(thieno[2,3-b]-pyridin-2-ylmethyl)amine



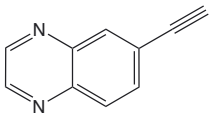
CC33809
3-morpholinophenylmethanol



MO01175
2-piperidyl(1-pyrrolidinyl) methanone hydrochloride



MO00687
[3-(dimethylamino)tetrahydro-thien-3-ylmethyl]amine



CC11747
6-ethynylquinoxaline

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