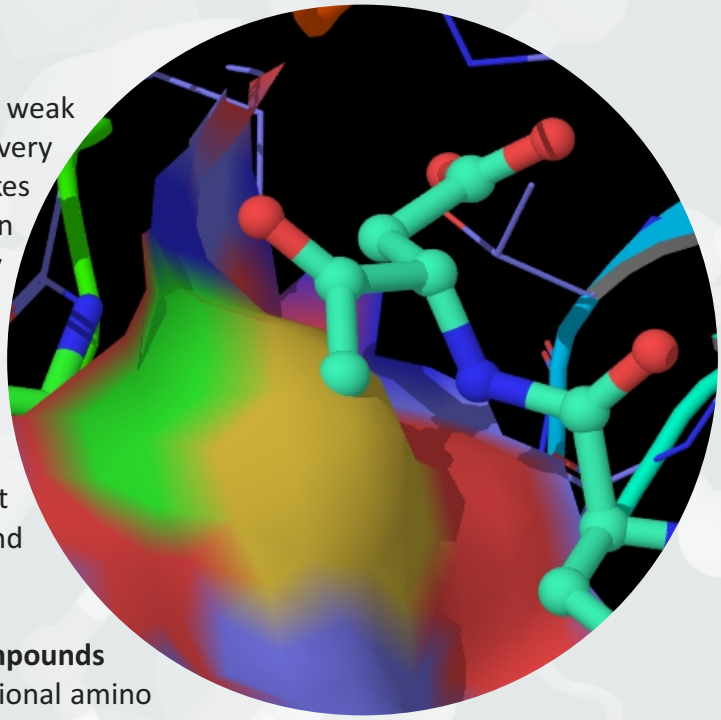
Reaxense

Covalent Fragment Library



The major limitation in fragment-based screening is the weak binding affinity of fragment hits, which not only necessitates very sensitive biophysical detection methods but also makes progressing hits to potency difficult and expensive. In particular, it requires a large compound series with typically ambiguous structure–activity relationships, because no method to date can reliably rationalize which are the dominant interactions of the original fragment. Screening covalent fragments addresses these limitations. Covalent binders are easy to detect by mass spectrometry, because the dominant interaction is unambiguous (namely, the covalent bond), which simplifies the design of follow-up series, and because the primary hits are already potent [1].

Reaxense's **Covalent Fragment Library** consists of **2,506 compounds for FBDD** which are able to form covalent bonds with functional amino acid residues (such as Tyr, Ser, His, Lys, Cys) of drug targets. A subset of this library comprising only mild electrophile fragments is available separately on request.

Features:

- **2,506 reactive fragment molecules for FBDD**
- **Each fragment contains at least 1 covalent bond-forming group**
- **Full Ro3 compliance over the library**
- **Separate subset of mildly electrophilic fragments is available**
- **High diversity over the library**
- **Purity >90%; spectral data available**

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Selection Criteria:

Parameter	Value
Molecular Weight (MW)	≤ 300
Number of Hydrogen Bond Donors (HBD)	≤ 3
Number of Hydrogen Bond Acceptors (HBA)	≤ 3
Octanol/Water Partition Coefficient (LogP)	≤ 3
Number of Rotatable Bonds (RB)	≤ 3
Topological Polar Surface Area (TPSA)	≤ 60 $Å^2$

Functional groups (explicit hydrogen and substitution sensitive)

- α,β-unsaturated ketones
- α-halomethylketones
- isothiocyanates
- alkynes
- nitriles
- thiols
- epoxides
- aziridines
- 2,5-derivatives of 1,4-benzoquinone
- vinylsolfones
- α,β-unsaturated amides
- β-substituted α,β-unsaturated ketones
- aldehydes
- boronic acid derivatives (except ethers)
- carbamates
- esters
- α-ketoamides
- carbamide(urea) derivatives

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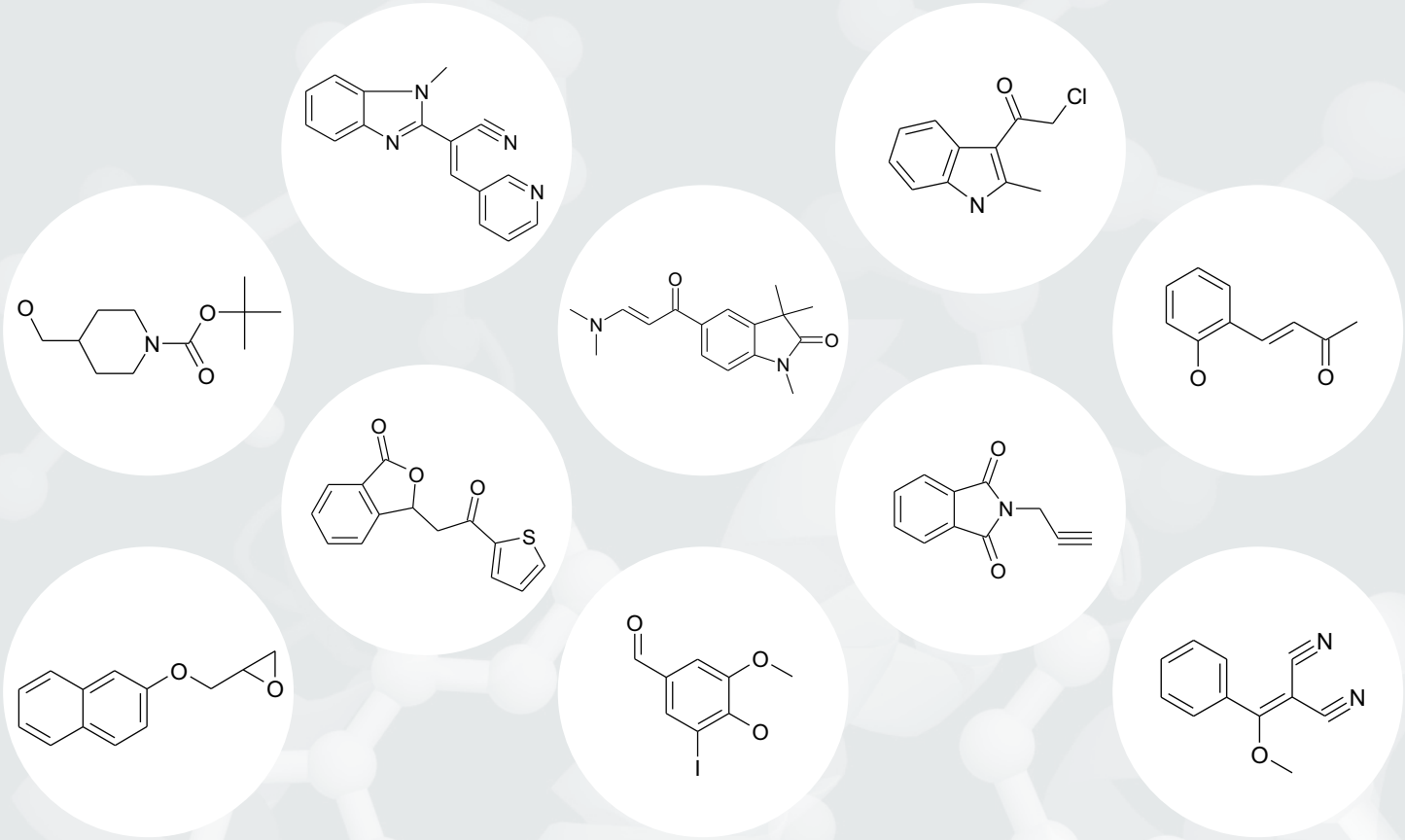
Structure examples:



Publications:

1. *J. Am. Chem. Soc.* 2019, 141, 22, 8951-8968

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