Covalent Screening Library

Covalent chemical probes remain in high demand in drug discovery. By 2020, there were at least 50 FDA-approved drugs that act as covalent inhibitors. Continuous research focused on the development of irreversible inhibitors, especially for cancer targets, is reported [1].

Taking into account the only-growing interest in covalent inhibitors as drugs, Life Chemicals has designed a proprietary collection of **34,700** potential covalent binders to support covalent screening projects in drug discovery (Fig. 1).

These small-molecule screening compounds were selected from the Life Chemicals HTS Compound Collection by specific structural moieties (functional groups), sometimes referred to as "covalent warheads", that are known to form covalent bonds with amino acid residues (e.g., Cys, Ser, Lys, Tyr) in binding sites of target proteins.

The following chemical classes and structural features were used for the selection of possible covalent binding irreversible inhibitors:

- β-lactams
- Alkyl halides
- Epoxides, aziridines
- Michael acceptors:
  - α,β-unsaturated ketones, -nitriles, -esters;
  - maleimide-like compounds;
  - activated vinyl derivatives
- Cyanoacrylamides
- Sulfonate esters
- Sulfonyl fluorides
- Thioles
- Rodanides
- Thiourea and thioketones
- *o*-quinones
- *p*-quinones
- Ketales
- Acetales
- Disulfides
- Terminal acetylenes
- Sulfoalkenes
- Aromatic nitriles
- Phenol benzoate derivatives

You can cherry-pick compounds or focus on a specific class of covalent modifiers.

Separate focused sets of covalent binders targeting each of the indicated amino acid residues (Cysteine, Serine, Lysine, Tyrosine) can be provided on request.

Please, contact us at orders@lifechemicals.com for any additional information and price quotations.

You can also be interested in our related products:

- Covalent Fragment Library
- Cysteine Focused Covalent Inhibitor Library
- Serine Focused Covalent Inhibitor Library

Moreover, the screening molecules that are considered as potential covalent agents against specific amino acid residues according to published data [1-8] were also included in this screening set. Therefore, it should be pointed out that some cysteine and serine covalent modifiers from Cysteine Focused Covalent Inhibitor Library, Serine Focused Covalent Inhibitor Library, respectively, may not necessarily include the traditional warheads but were demonstrated to be covalent inhibitors when in a complex with target proteins.

For a specific protein drug target needed, please, feel free to contact us and our molecular design team will be happy to assist you in structure optimization of potential irreversible binders, as well as in performing virtual covalent docking.

In addition, a new **Diversity Screening Set** of **4,800** most-promising covalently binding molecules containing a high variety of covalent warheads was designed to be used as a convenient starting point for covalent screening projects. These structurally-diverse screening compounds were shown to be optimal in terms of reactivity and essential stability, being compliant with our in-house MedChem and PAINS structural filters.

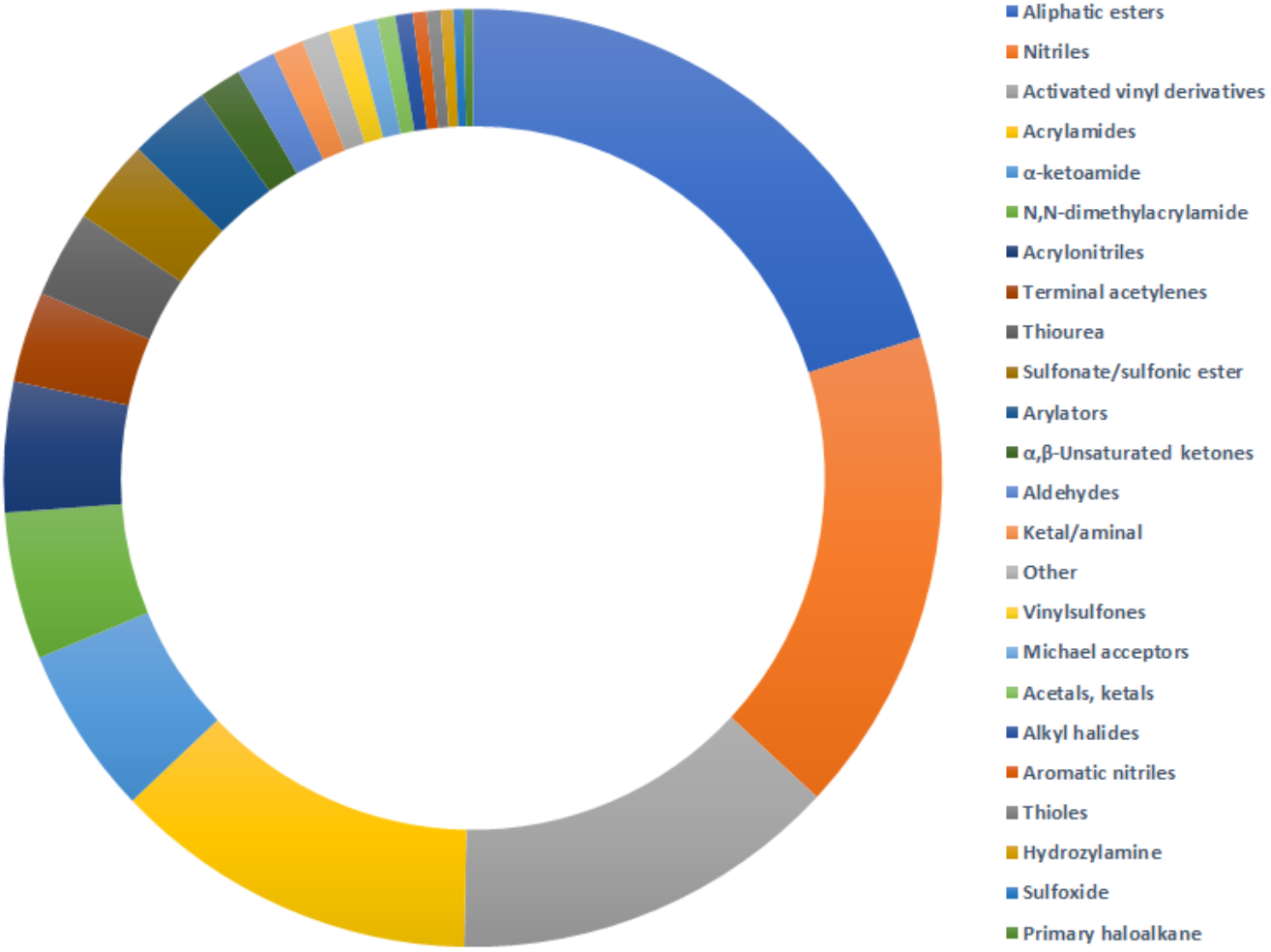

Figure 1. Screening compound distribution by the type of the covalent warhead in the Covalent Screening Library.

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