

New Covalent Fragment Libraries by parallel synthesis

T. Matviyuk, T. Savchenko, A. Zhemera, D. Radchenko, Y. Moroz, V. Ivanov

Introduction and Aim

REAL concept

Ar-OH + ONSN-SO₂F

Creation of REAL array

In stock Building Blocks

+ 0H R

25,000 in stock O ,R1 HN R2 42,000 in stock NH2 or CO2H

Establishment of new synthesis scheme

R1 NH+ ⊖ R2 TfOH N−SO2F parallel synthesis REAL criteria

REAL Array

93 compounds 95% success rate

O 81 compounds 25-58% yield 93% success rate

 Smart selection of reagents
Enumeration of the library
Physicochemical, structural filtering
High success rate

Expansion of REAL array

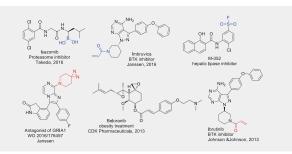
Careful choice of the building blocks and elaboration of specific reaction

conditions and purification procedures has allowed synthesis of different novel

Synthesis of new covalent probes

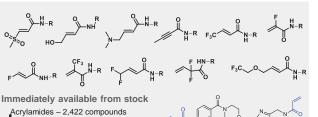
covalent fragments, not yet represented by commercial proposal.

Covalent chemical probes have become a hot topic in drug discovery within last few years. To be efficient for early stage drug discovery, covalent modifiers have to integrate novel scaffolds and easy, potentially enumerated setups. To address continuously growing interest in this field and bring new high level of novelty we elaborated parallel chemistry approaches to synthesize series of new covalent binders. Herein, we describe our approach to parallel synthesis of various covalent modifiers, that resulted in enumeration of arrays of REAL compounds – covalent fragments available for cherry-picking and reliable supply within only 3 weeks, and high success rate.



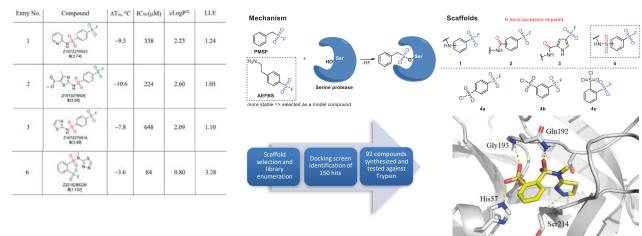
Advanced acrylamides

Enamine specially synthesized series of acrylic-like building blocks for synthesis of new covalent libraries. Fluorinated acrylamides can also be used for F19 NMR contrscreen. Synthesis of corresponding amides was validated by parallel chemistry



Acrylamides – 2,422 compounds Boronic Fragments – 860 compounds Sulfonyl Fluorides – 745 compounds Chloroacetamides – 2,210 compounds Exopxyde Fradments – 350 compounds Vinyl Sulfones – 470 compounds $\begin{array}{c} \stackrel{\circ}{\downarrow}_{H^{-R}} \\ \stackrel{\circ}{\to}_{3} \\ \stackrel{\circ}{\leftarrow} \\ \stackrel{\circ}{\to} \\ \stackrel{\circ}{$

Case Study: N-aryIsulfonyl fluorides as inhibitors of serine proteases



Contact

Tatiana Matviyuk, PhD

t.matviyuk@enamine.net, Enamine Ltd, www.enamine.net 78 Chervonotkatska St, 02660 Kyiv, Ukraine