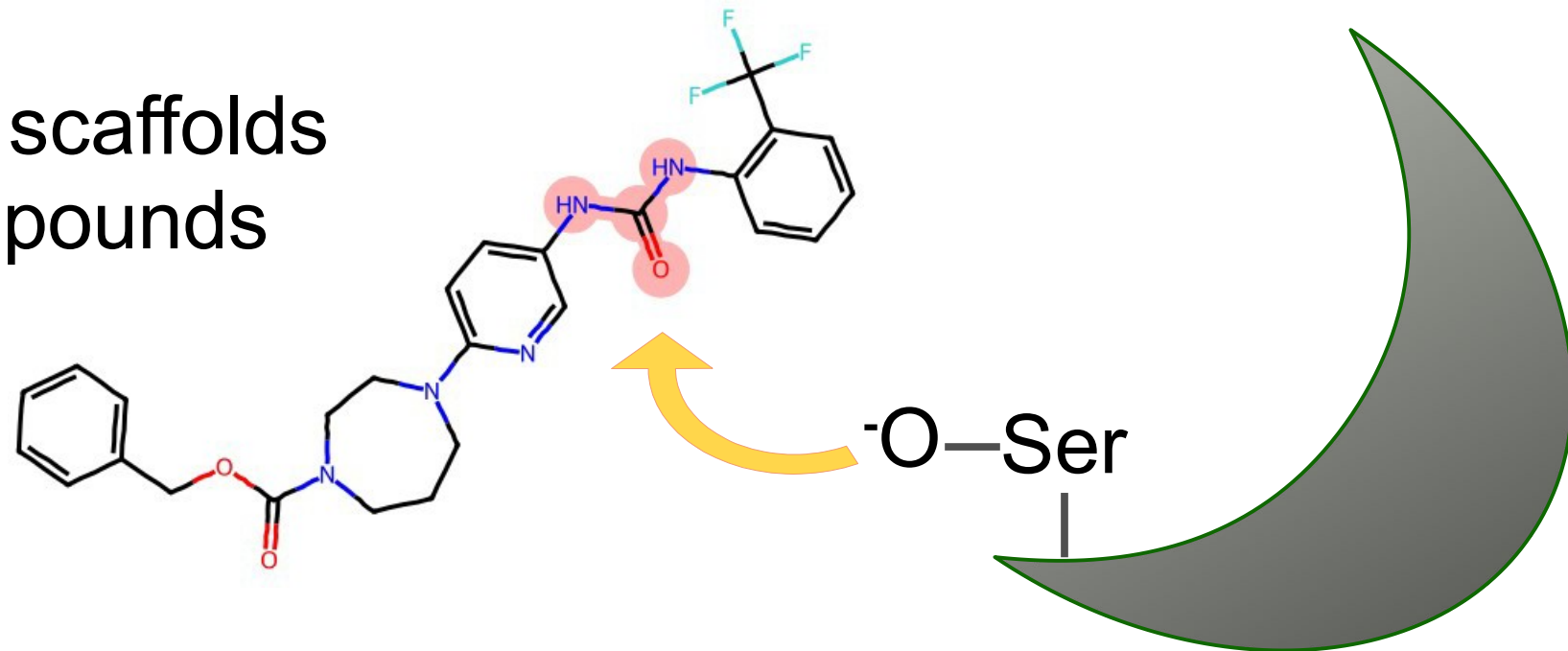


# Ковалентно серин- связывающие библиотеки

## Covalent serine binder library

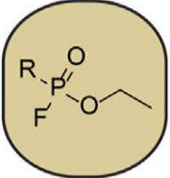
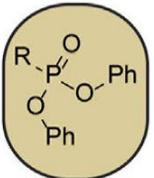
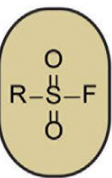
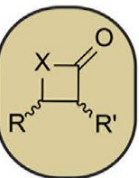
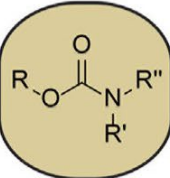
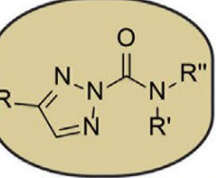
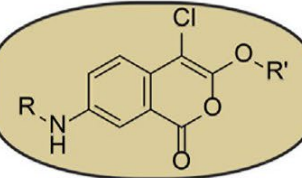
10 warhead scaffolds  
4 400 compounds



MedChem compatible, REOS filtered

# The core idea of library design

Take warhead scaffolds known to be rather selective to serine binding

Warhead Scaffold							
Warhead	Fluoro-phosphonate	Diphenyl-phosphonate	Sulfonyl Fluoride	$\beta$ -lactam $\beta$ -lactone	Carbamate	Triazole Urea	4-chloro-isocoumarin
Synthetic Tractability	Difficult	Moderate	Easy	Moderate	Easy	Easy	Easy
Serine Selectivity	High	High	Poor	Poor	Moderate	Moderate	High
Hydrolase Preference	Broad-spectrum	Proteases	Proteases	$\beta$ -lactamases	Lipases	Peptidases, Lipsases	Broad
Diversity of Leaving Group	Fluoride	Broad	Fluoride	N.A.	Broad	Broad	Chloride

\*Several warhead examples taken from: Faucher, F., et al. (2020) // Cell chemical biology, 27(8), 937-952.

## The preparation algorithm:

1. Prepare a set of SMARTS queries that capture literature extracted warheads selective to serine binding – 10 SMARTS patterns prepared\*
2. Apply REOS filter to the entire 1.6M ChemDiv inventory to rule out the most MedChemically undesirable structural motifs
3. Find structures in the filtered inventory that obey warhead SMARTS patterns
4. Within each warhead scaffold set apply diversity picking (MaxMin algo):
  - a. The internal set similarity is no more than 0.4 (Tanimoto, ECFP4 2048)
  - b. The most diverse structures are retained, the rest similar structures can be ordered to establish SAR for the promising hits at hand

\*Warhead pattern sources:

1. Faucher, F. et al. (2020) // Cell chemical biology, 27(8), 937-952.
2. Bachovchin, D. A. et al. (2012). // Nature reviews Drug discovery, 11(1), 52-68.
3. Adibekian, A. et al. (2011) // Nature chemical biology, 7(7), 469-478.

# Covalent serine binder library



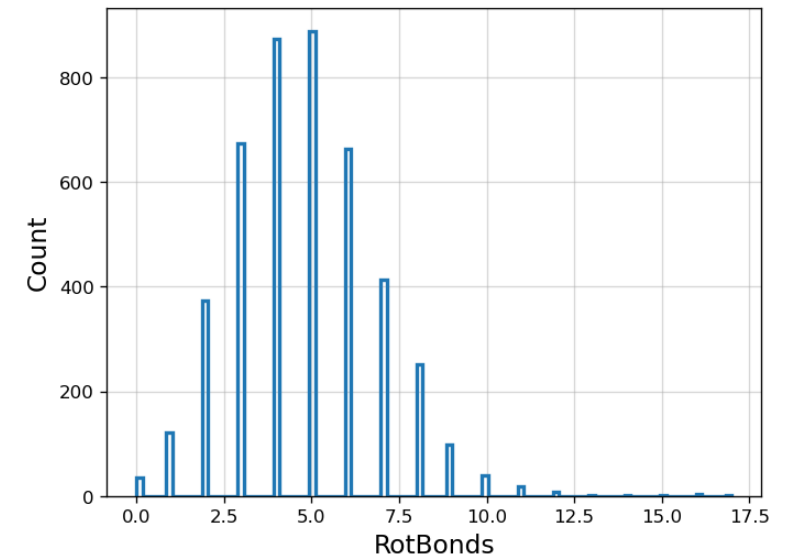
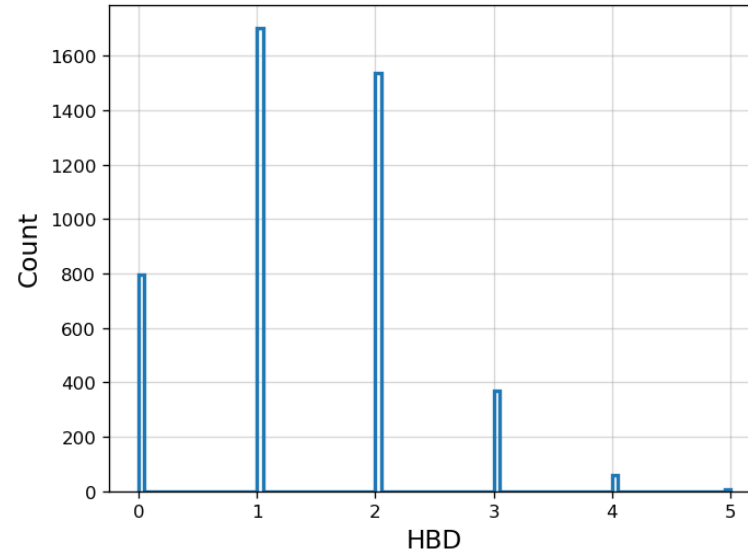
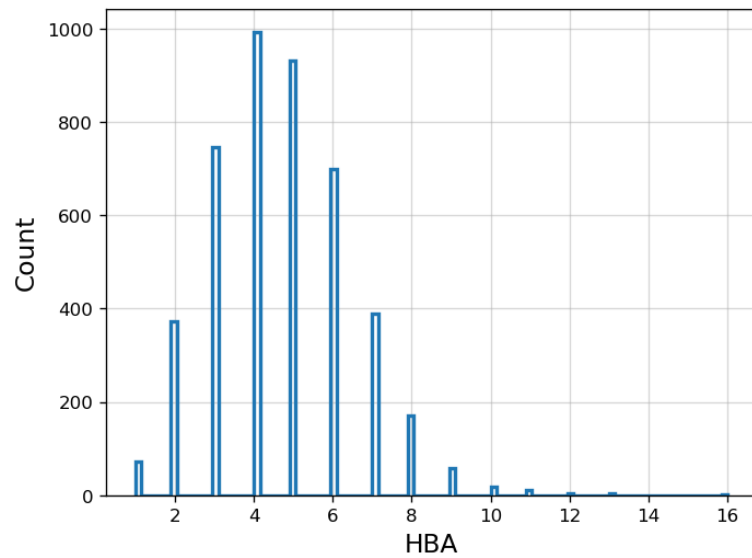
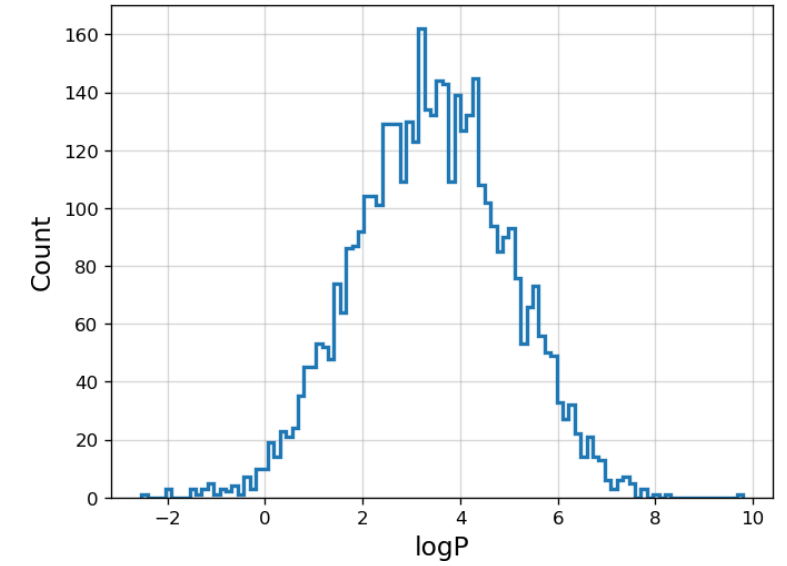
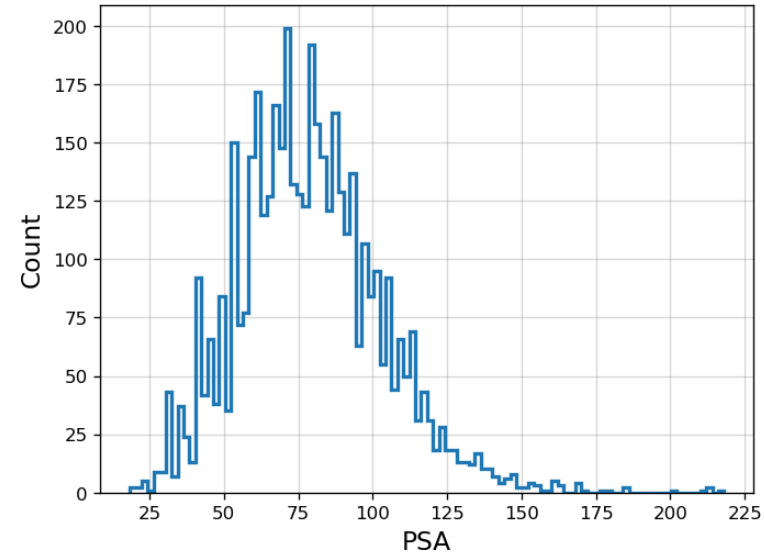
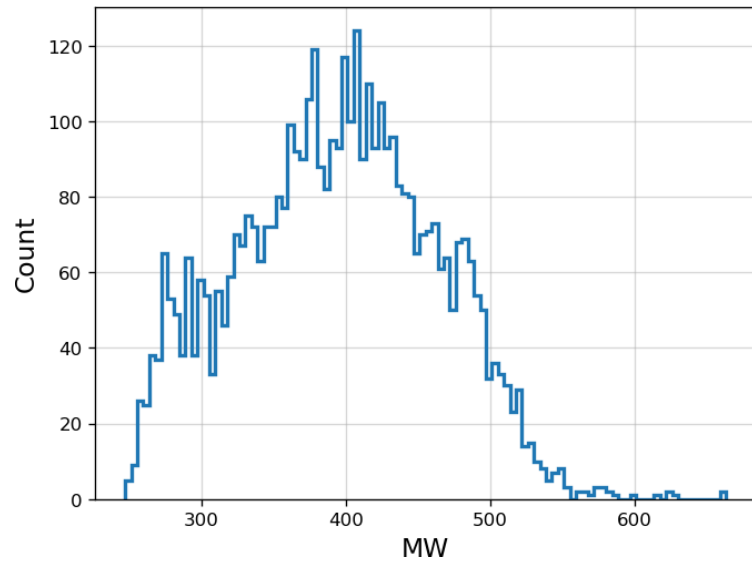
The library properties:

1. In total 4468 MedChem tolerable compounds, not containing the most active REOS
2. 10 warhead patterns with 3 to 3000 representative molecules in each
3. Highly diverse structures are within each warhead pattern retained

# Covalent serine binder library



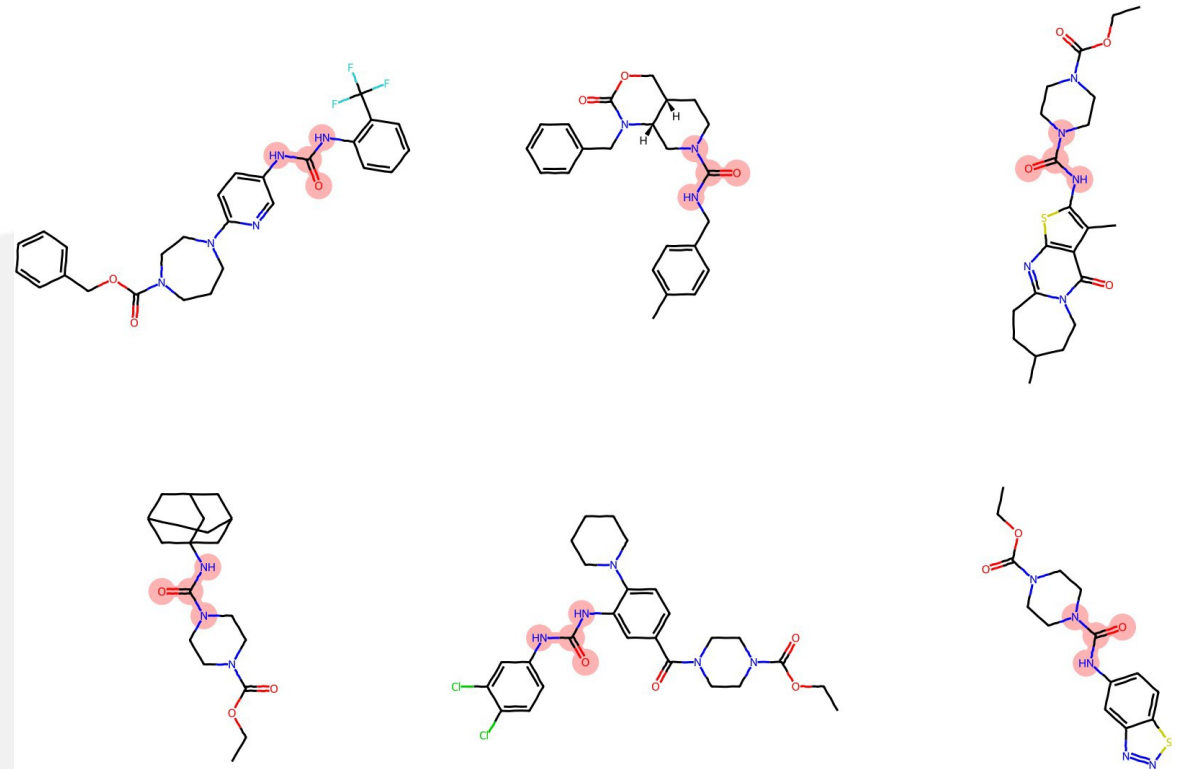
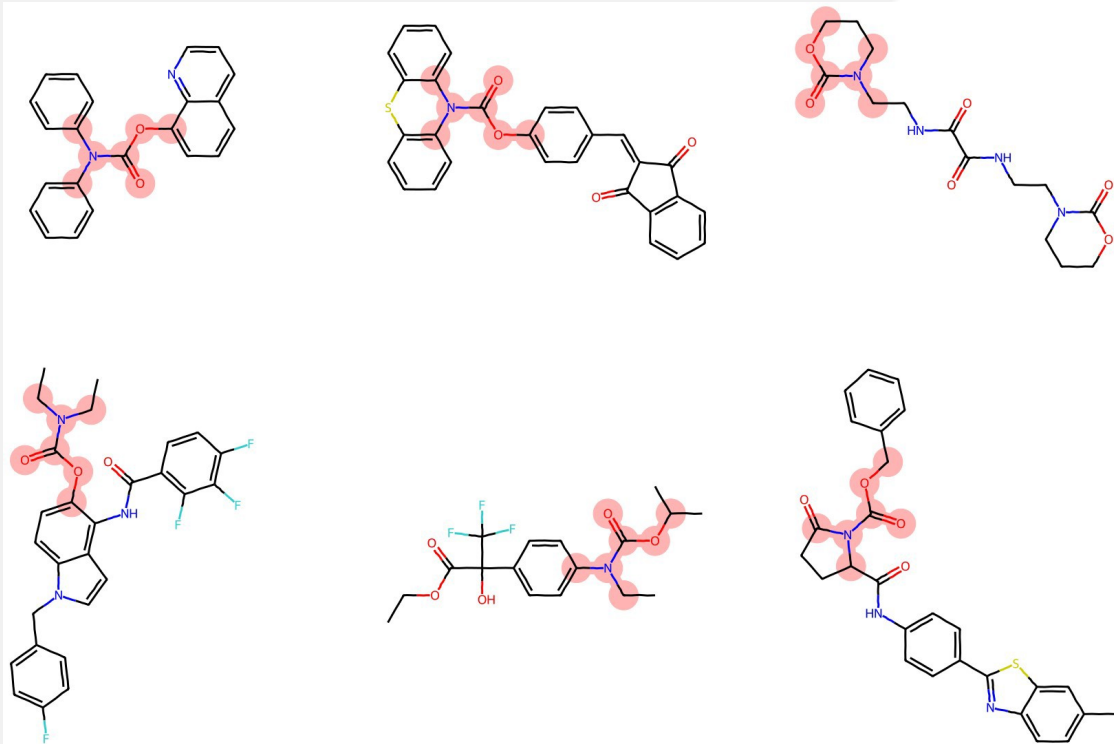
## Distribution of Phys-Chem Properties



# Covalent serine binder library

## Examples of Structures with warheads

### Carbamates



### Ureas



# Благодарим за внимание

Инструкция по заказу соединений из библиотеки «ХимРар»:

Наш сайт: <https://chemrar.ru/library-full-list/>

Направьте список интересующих соединений на email: [vvk@chemrar.ru](mailto:vvk@chemrar.ru)

В соответствии с вашим запросом менеджер выполнит подборку соединений и направит информацию о наличии. Имеется возможность сделать поиск по структуре/буквенному идентификатору (ID, CAS, MFCD), а также импортировать файл в различных форматах: SMILE, sdf, txt.