Synthetic organic compounds

for research and drug discovery

OTAVA chemicals

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www.otavachemicals.com

2018

Compounds for HTS

Quantities as well as quality of compound libraries are key factors in high-throughput screening (HTS). Using OTAVAchemicals HTS libraries is a unique opportunity to enrich your company's collection of compounds for screening purposes. Our libraries were developed to meet the needs of researchers by harnessing the quality and structural diversity you have come to expect from OTAVAchemicals products.

Screening Compounds For Prompt Delivery

OTAVAchemicals screening collection contains about **260,000 compounds for prompt delivery.** All compounds in this library have undergone quality control to confirm their chemical structures and are ready-to-use. We offer the possibility to re-supply compounds purchased from us.

Tangible Screening Compounds

Our company offers a collection of Tangible Screening Compounds and it includes about **6,050,000 compounds** where "tangible" denotes structures with a high likelihood of being synthesized. Any compound ordered from this library can be delivered within 4 weeks.

Drug-Like Green Collection

This collection is prepared on the basis of in-house stock library and pre-formatted using Lipinski's Rules of Five to select drug-like compounds only. Compounds with reactive groups, biologically unstable compounds and compounds containing any atom different to O, N, C, H, Br, I, Cl, F, or S were removed from the library.

Lead-Like Library

This is a universal screening library which, comparing to Drug-Like Green Collection, has compounds with lower molecular weights (MW 160-400), smaller number of rotatable bonds (≤ 8) and number of hydrogen bond donors (≤ 4) and acceptors (≤ 8). The library is done to extend potential chemical space for further lead optimization.

CNS Library

Central Nervous System (CNS) Library from OTAVAchemicals is designed as a special screening library containing compounds with high probability to penetrate blood brain barrier (BBB). All compounds in this library possess physicochemical properties preferable for BBB penetration and they are simultaneously suitable for oral administration.

Diversity Libraries

Our Diversity Libraries are prepared by structure diversity sorting and characterized by the similarity (or dissimilarity) of molecules included in them. The purpose of our Diversity Libraries is to represent all the variety of compounds available from OTAVAchemicals.

Fragment Libraries

Understanding the increasing importance of the fragment-based approach for modern pharmaceutical industry, we designed a number of quality fragment libraries that provide small fragment binders suitable for any drug discovery project.

General Fragment Library

The OTAVAchemicals General Fragments library, comprising about **11,600 compounds**, has been designed based upon the commonly accepted "Rule-of-Three" and other physicochemical and structural properties. Reactive, pan-assay interference (PAINS), redox-active and aggregator compounds were removed from the library.

Solubility Fragment Library

The Solubility Fragment Library consists of about **1,000 low molecular fragments** with "Rule-of-Three" compliance and assured solubility in both DMSO (200mM) and PBS buffer (1mM). The library design included diversity filtering in order to provide chemical structure variety for your fragment screening program.

Fluorine Fragment Library

OTAVAchemicals new ^{19}F NMR Fluorine-containing Fragment Library comprises compounds that have at least one mono fluoro or mono trifluoromethyl group. This allows easier and faster identification of the fragment bound in the active site of a target by the highly sensitive ^{19}F NMR technique.

Chelator Fragment Library

Several small-molecule chelators have been shown to effectively inhibit metalloproteins, therefore the design, synthesis, and use of fragment libraries based on metal chelators for fragment-based lead discovery applications is of great interest. The OTAVAchemicals Chelator Fragment Library library contains fragments with chelating groups only.

Halogen-Enriched Fragment Library

Our Halogen-Enriched Fragment Library comprises brominated fragments that can explore binding sites for favorable halogen bond interactions to identify unique binding modes that are complementary to those obtained from classical fragment-based screening. The compounds contain at least one bromine atom.

Target-Focused Libraries

Targeted compound libraries comprise collections of compounds with in silico predicted affinity to a target protein or predicted biological activity. In order to design such libraries OTAVAchemicals applies different computational methods used in structure-based and ligand-based drug design. **More than 350** target-focused libraries are available.

Approach Used

Our proprietary method for receptor-based virtual screening of compounds includes powerful combination of drug-likeness filtering, molecular docking, re-scoring, key intermolecular hydrogen bond detection and, finally, visual inspection of ligand-receptor complexes (Fig.1). The approach used to design ligand-based targeted libraries (Fig.2) exploits pharmacophore modeling, Bayesian modeling, QSAR or their combinations. Compound training sets are carefully created using data taken from ChEMBL, TIMBAL and other knowledge databases.

Variety of the Libraries

OTAVAchemicals focuses its attention on the different targets: RNA, epigenetic targets, PPI, GPCR's, protein kinases, ion channels, proteases and others. Our company also offers focused libraries of compounds with certain biological activity: anticancer, antiviral, analgesic, antibacterial etc. All compounds are for prompt delivery.

Design your target-focused library!

If you are running screening projects for specific molecular targets, you could send us a request to design custom target-focused library using our in-stock compound collection.

Available Target-Focused Libraries:

- Disease-based libraries
- Phenotypic Screening Library
- RNA Binding
- SH2 Binding
- Protein-Protein Interaction
- Epigenetic targets
- Peptidomimetic
- Glycomimetic
- Protein Kinases
- Proteases
- GPCRs
- Nuclear Receptors
- Ion channels
- General activities
- Other

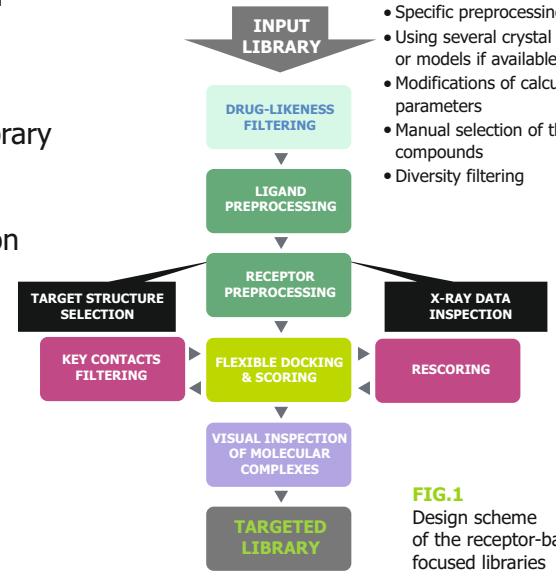


FIG.1
Design scheme of the receptor-based focused libraries

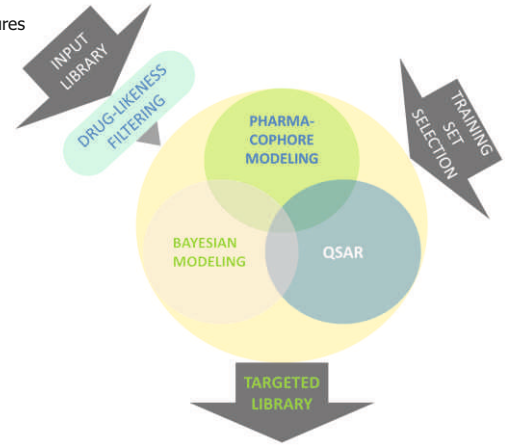


FIG.2
Design scheme of the ligand-based focused libraries

Chemical Building Blocks

Our company offers about **3,800,000 chemical building blocks** with many unique structures in multi-gram quantities. This collection of diverse compounds is used for high-throughput and combinatorial synthesis of pharmaceutical libraries, scale-up of lead compounds and it is also ideally suited for diversity-oriented syntheses.

Chemical Building Blocks for Prompt Delivery

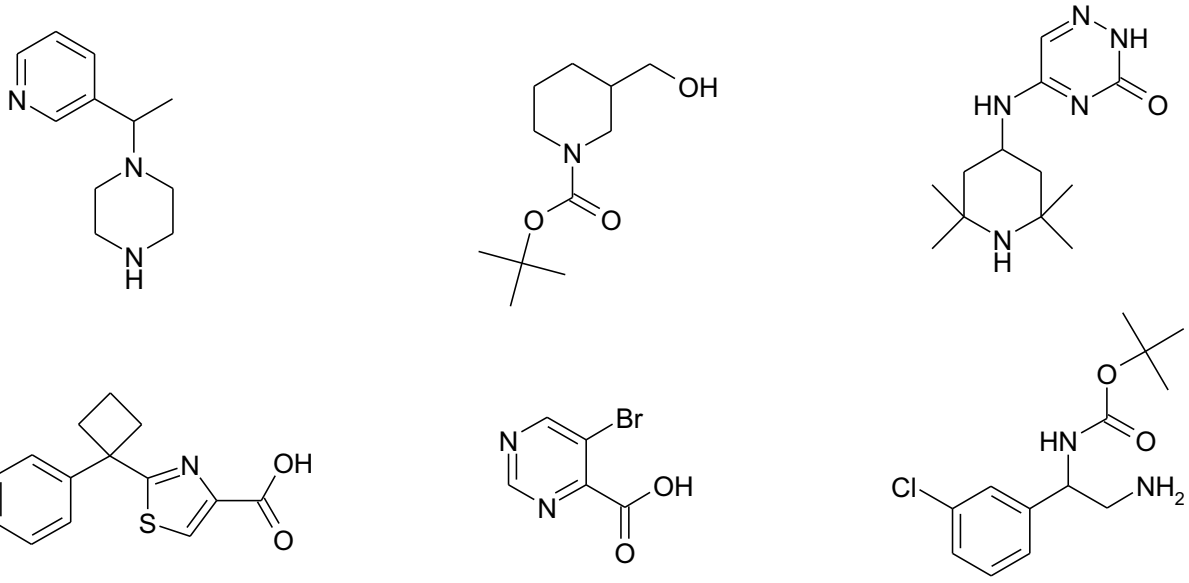
OTAVAchemicals offers collection of Chemical Building Blocks for prompt delivery. All compounds have undergone quality control to confirm their chemical structures and have purity higher than 95%.

Virtual Chemical Building Blocks

OTAVAchemicals Virtual Chemical Building Blocks are chemically feasible compounds that could be synthesized and delivered within 4-12 weeks (this is estimated lead time which could be changed during the synthesis). Typically, the synthesis is carried out "from scratch" according to the methodologies for chemical analogs synthesized by us previously or described in literature. This constantly growing compound collection is a unique opportunity to order new chemical building blocks that are not available from other suppliers.

Request to synthesize a molecule!

If you are looking for custom synthesis services, please send us single or multiple structures directly from our web-site or by e-mail.



Representative chemical building blocks from OTAVA's collection

Custom Synthesis

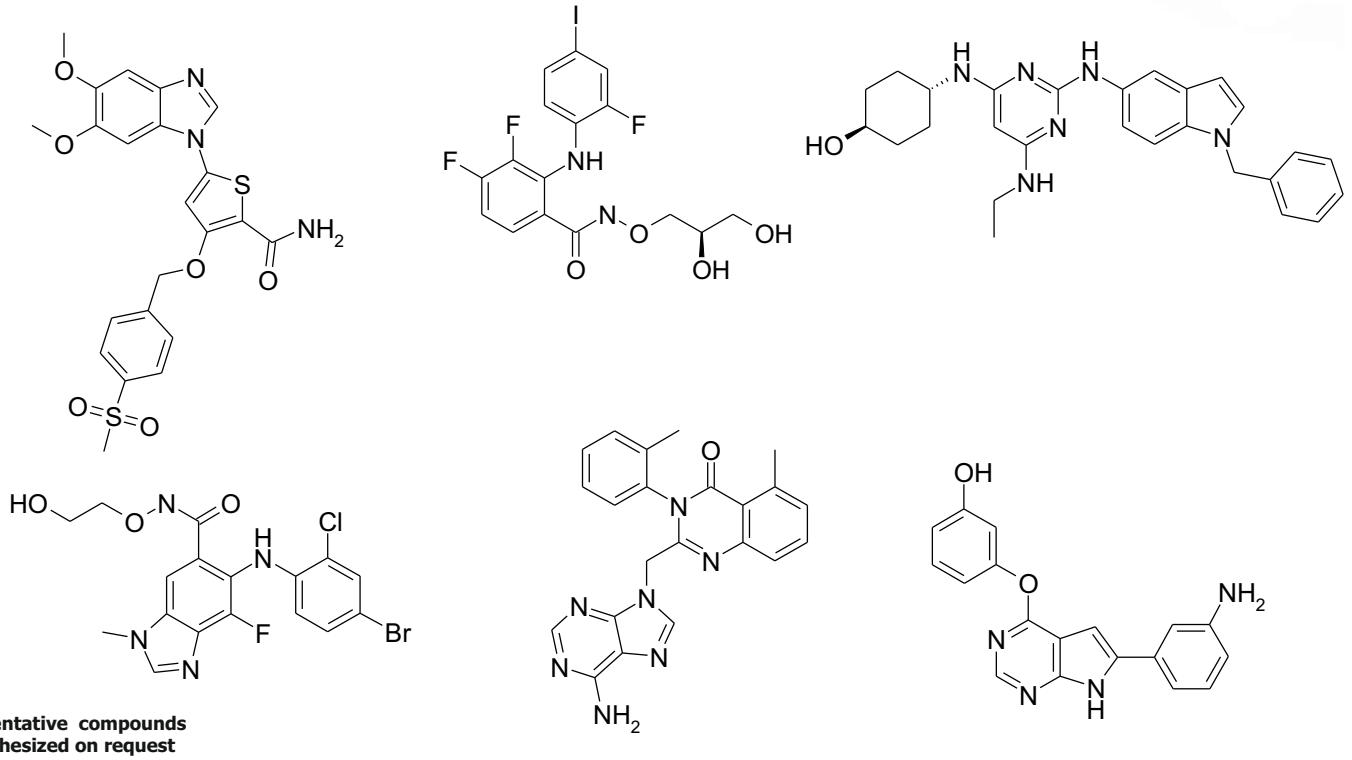
Our small-scale and large-scale chemistry capabilities are able to undertake your projects and work with them right from idea to final production at any scale. The synthetic work can involve extensive application of proprietary cheminformatics, molecular modeling and computational chemistry procedures as well as virtual screening and QSAR in order to select/design compounds for various drug discovery projects.

The service includes synthesis of the following:

- Starting materials, intermediates, and/or final products
- Advanced intermediates in drug synthesis
- Combinatorial chemistry templates
- Chemical building blocks
- Reference compounds
- Hit-to-lead custom libraries
- Literature and non-literature compounds
- R&D of synthetic pathways for research & commercial molecules and intermediates

We also offer custom synthesis on the basis of our rare scaffolds. Our unique scaffold database was prepared using comparative analysis of worldwide suppliers of compound libraries.

This is your opportunity to get novel compounds for screening purposes!



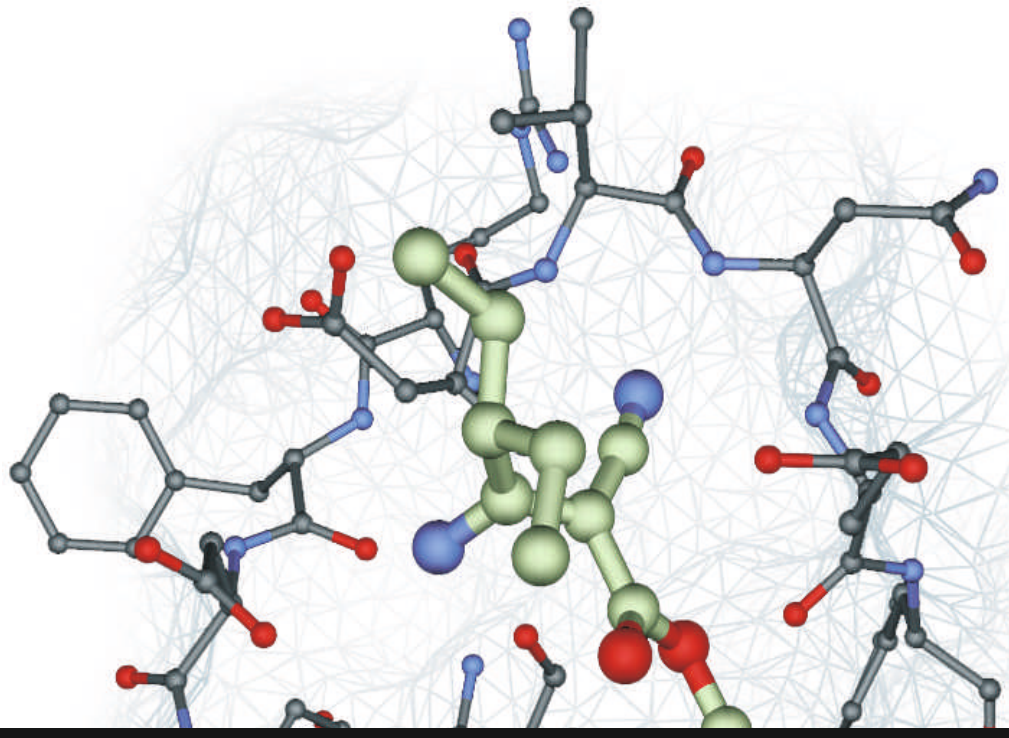
Representative compounds we synthesized on request

Drug Discovery Services

We provide high quality, efficient and cost-effective integrated computational drug discovery services and will design any target-specific set of compounds for your screening program with the aid of state-of-the-art molecular modeling and computational chemistry methods. Structural optimization and synthetic chemistry support is also available.

The Variety of Our Services Includes:

- Rational design of small organic ligands against biological target of interest within efficient infrastructure of molecular modeling, biochemical screening and organic synthesis facilities.
- Computational chemistry services (drug-likeness prediction, diversity calculations, compound filtering by any physico-chemical properties)
- Pharmacophore search and scaffold hopping
- Preparation of custom target-focused libraries
- Receptor-based virtual screening and design (molecular docking)
- Ligand-based activity prediction (QSAR, Bayesian modeling)
- Target structure comparative modeling
- Hit-to-lead optimization (improvement of compounds' activity, selectivity and ADME properties)
- Molecular dynamics simulation of macromolecules and their complexes with small molecule ligands



Contract Research

The quality and reliability we offer is established from the company's long-standing experience of over 20 years in the industry. We have developed a reputation as a trustworthy and experienced outsourcing partner and have a strong background in organic and medicinal chemistry, biochemistry and molecular modeling. We would be glad to respond to any project proposal, and are ready to sign a non-disclosure agreement prior to any discussions.

Selected Publications

Our company has extensive experience in the area of custom synthesis/contract research and guarantees quality results, competitive pricing, and a fast turn-around time. We already collaborate with many companies and academic institutions in Europe, the U.S. and Canada; we hope you will consider working with us for your next project.

OTAVAchemicals molecular modeling facilities and organic synthesis capabilities are intensively used for internal and collaborative research and drug discovery projects. Our approach works and here is a list of our selected publications:

- Niefind K, Bischoff N, Golub AG, Bdzhola VG, Balanda AO, Prykhod'ko AO, Yarmoluk SM (2017) Structural Hypervariability of the Two Human Protein Kinase CK2 Catalytic Subunit Paralogs Revealed by Complex Structures with a Flavonol- and a Thieno[2,3-d]pyrimidine-Based Inhibitor. Pharmaceuticals (Basel) 10(1), 9; doi:10.3390/ph10010009.
- Gudzera OI, Golub AG, Bdzhola VG, Volynets GP, Lukashov SS, Kovalenko OP, Kriklivyi IA, Yaremchuk AD, Starosyla SA, Yarmoluk SM, Tukalo MA (2016) Discovery of potent anti-tuberculosis agents targeting leucyl-tRNA synthetase. Bioorg Med Chem 24(5):1023-1031.
- Ostrynska OV, Balanda AO, Bdzhola VG, Golub AG, Kotey IM, Kukharenko OP, Gryshchenko AA, Briukhovetska NV, Yarmoluk SM (2016) Design and synthesis of novel protein kinase CK2 inhibitors on the base of 4-aminothieno[2,3-d]pyrimidines. Eur J Med Chem 115:148-60.
- Starosyla SA, Volynets GP, Lukashov SS, Gorbatiuk OB, Golub AG, Bdzhola VG, Yarmoluk SM (2015) Identification of apoptosis signal-regulating kinase 1 (ASK1) inhibitors among the derivatives of benzothiazol-2-yl-3-hydroxy-5-phenyl-1,5-dihydro-pyrrol-2-one. Bioorg Med Chem 23(10):2489-2497.
- Guerra B, Bischoff N, Bdzhola VG, Yarmoluk SM, Issinger OG, Golub AG, Niefind K (2015) A note of caution on the role of halogen bonds for protein kinase/inhibitor recognition suggested by high- and low-salt CK2α complex structures. ACS Chem Biol 10(7):1654-1660.
- Gryshchenko AA, Bdzhola VG, Balanda AO, Briukhovetska NV, Kotey IM, Golub AG, Ruban TP, Lukash LL, Yarmoluk SM (2015) Design, synthesis and biological evaluation of N-phenylthieno[2,3-d]pyrimidin-4-amines as inhibitors of FGFR1. Bioorg Med Chem 23(9):2287-2293.