

Chemoinformatic tools for prioritization of the synthetic projects in CRO and chemical suppliers industry

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Prioritizing what should be synthesized is one of the central practical tasks of modern synthetic chemistry. In pharmaceutical discovery, computational prioritization is usually discussed as selection of the most promising analogues for array synthesis. For a contract research organization and chemical supplier, however, the same question becomes broader: which screening compounds, fragments or building blocks should be produced so that they are not only novel and synthetically accessible, but also relevant to current medicinal chemistry demand? Using Enamine's experience as a case study, this lecture will show how chemical space analysis can support product strategy and catalogue expansion. The analyses of supplier libraries showed that commercially available collections have improved in drug-likeness but remain unevenly distributed in chemical space, with both overpopulated regions and persistent "white spots". [1,2]

The workflow combines market-aware evaluation of commercially available space, comparison of supplier collections with biologically relevant reference spaces, and synthon-based analysis of building blocks. GTM maps and ISIDA descriptors provide a practical way to visualize gaps and compare vendor libraries with ChEMBL-like bioactive space. For building blocks, the Synthl toolkit enables fragmentation, synthon generation and classification, and quality assessment, including medicinal chemistry-oriented constraints such as the Rule-of-Two. Several Enamine examples will be discussed: expansion of medicinally relevant building block classes, identification of underrepresented synthons, and prioritization of reaction-development targets such as (het)arylacetic acid, thiol and boronic-acid/boronate motifs. The general message is a shift from a purely synthetic "what can we make?" logic to a chemoinformatics-guided "what is needed?" logic, where chemical-space diagnostics guide synthesis, reaction optimization and catalogue design. [3–5]

Bibliography:

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