

NatDiverse™: Diverse Semi-synthetic Chiral Libraries

NatDiverse™: There is a Need for Highly Diverse Chiral Libraries!

Definition: A tailor-made synthetic compound library of highly diverse, nitrogen containing, natural product like molecules with gram-scale resupply opportunities and feasible lead generating chemistry that covers the chemical space of your target.

With the introduction of combinatorial chemistry and parallel synthesis, a new era of drug discovery began. Suddenly, it was feasible to quickly generate thousands of new compounds with relatively simple synthetic efforts. Concurrently, an increasing number of druggable targets emerged from the human genome project; achievements which seemed to form a powerful alliance to address unmet medical needs. The promise of new chemical entities (NCE) seemed to appear on the horizon.

Despite this tremendous technical progress, the expected flood of NCEs did never materialise, presumably because synthetic molecules often lack diversity and 3-dimensionality required for complex binding action. This is simply due to a limited number of applicable reaction pathways and building blocks in the hands of synthetic chemists. Nature it seems is the better chemist providing us with enzymatically engineered and biologically validated small molecules called natural products (NP).

As a matter of fact, the enormous potential of NP's to generate new drugs (more than 40% of all blockbuster drugs are NPs or their derivatives) is unquestioned in the drug discovery community. It is only because of logistical problems; a lack of sufficient numbers of discrete natural product molecules for HTS, unsatisfactory resupply when a hit is identified, and complex, time consuming medicinal chemistry which caused pharmaceutical companies to simply avoid the effort required to fully access nature's pool of diversity. Now, AnalytiCon Discovery has removed these obstacles by creating NatDiverse™ libraries.

NatDiverse™: When modern synthetic chemistry meets nature!

With NatDiverse™, AnalytiCon Discovery marries the diversity of nature with the power of modern parallel synthesis. Chiral, nitrogen containing, natural compound-like molecules can be quickly reproduced in accordance with state-of-the-art medicinal chemistry rules to generate molecules that are druglike.

NatDiverse™ enables drug discovery departments to access a huge number of natural carriers of pharmacophore groups with an extraordinary high level of patentability. Medicinal chemistry complications, resupply problems and scale-up restrictions belong to an earlier era of traditional natural extract screening.

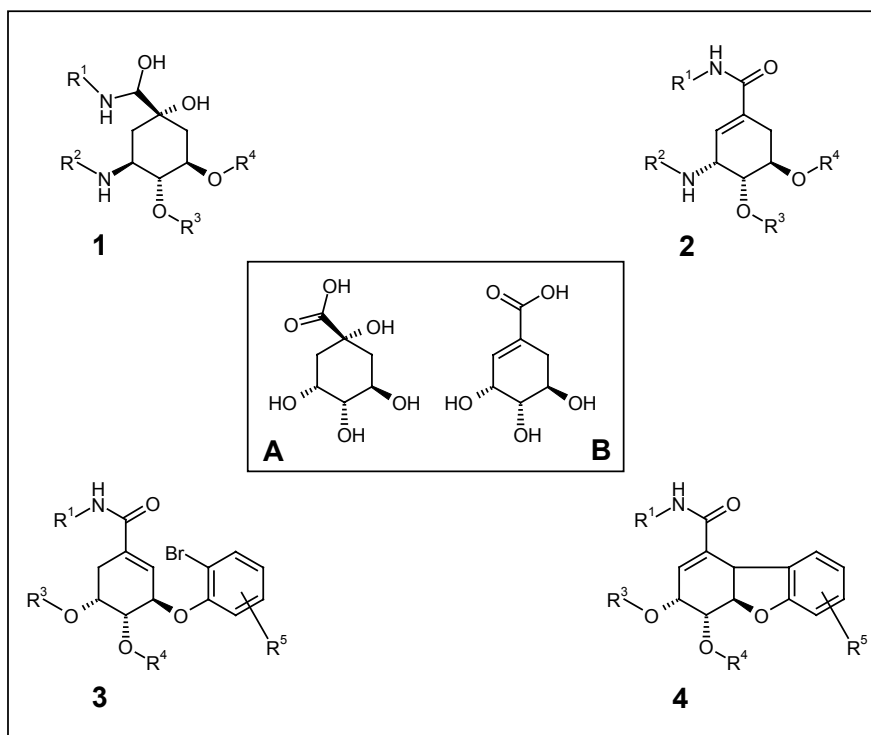
AnalytiCon's carefully selected natural small molecules scaffolds share four main selection criteria that form the basis of each NatDiverse™ library design:

- Scaffold quantities greater than 200g
- Scaffold to contain two or more chiral centres
- Scaffold to contain two or more functional groups
- A molecular weight less than 350 Da (leading to final products with a weight less than 650)

With this approach, AnalytiCon takes into account that the drug discovery chain has to be fed

with more and more amounts of a compound when moving upstream; i.e. the production of molecules must be scalable. Furthermore, NatDiverse™ compounds provide an excellent platform for subsequent lead generation chemistry.

A selected scaffold undergoes a substantial synthetic transformation process leading to 6 up to 8 templates (see example). In a subsequent decoration step approx. 100 to 300 novel chiral compounds with exactly defined stereochemistry will sprout from each of these templates.



Example: NatDiverse™ NAT2-library based on scaffolds quinic acid (A) and shikimic acid (B) leading to 4 templates.

NatDiverse™: Off the shelf opportunities.

AnalytiCon currently offers three sets of NatDiverse™ libraries for sale: Nat1, Nat2 and Nat3. The libraries contain unpublished as well as public domain compound libraries of highest quality available for immediate delivery. CD-ROMs containing structures, detailed library set-ups and calculated relevant descriptors of each molecule are available for review. The libraries are described as follows:

Nat1 - macrocycles

Nat2 - based on scaffolds of quinic acid and shikimic acid

Nat3 - nitrogen rich mono- and oligocycles

NatDiverse™ : Tailor your target orientated library.

NatDiverse™ libraries can also be tailored to a client's needs. Clients may either select suitable NP scaffolds stocked at AnalytiCon or propose their own scaffolds. AnalytiCon then develops virtual library designs with client input. The application of reaction pathways leading to the templates is achieved by allowing as much client's influence on library design as

chemically possible. Even the choice of side chains to form final compounds can be determined by the client. In this way a target's software model can be turned into chemical reality. The degree of synthesis success tells a good story: more than 75% of a library's virtually designed molecules will be delivered.

Further Information:

AnalytiCon Discovery GmbH

Dr. Dietmar Wolf

Hermannswerder Haus 17

D-14473 Potsdam

Tel.: +49-(0)-331-2300-300 Fax: +49-(0)-331-2300-333

d.wolf@ac-discovery.com

www.ac-discovery.com