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Diversity-Oriented Synthesis of Multiscaffold Alkaloid

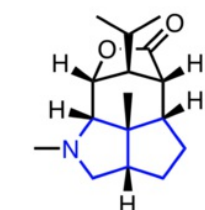
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Libraries

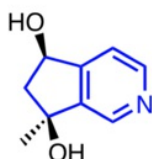
[News & Events](#)

[Open Positions](#) Polycyclic Alkaloid and Terpenoid Natural Products

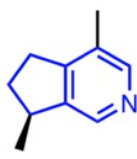
Rigid, densely functionalized scaffolds are derived from simple starting materials



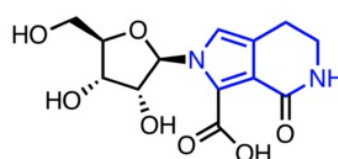
dendrobine
analgesic, antipyretic



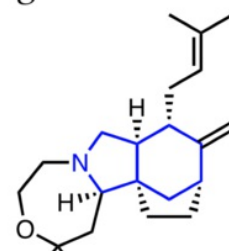
oxerine
contraceptive



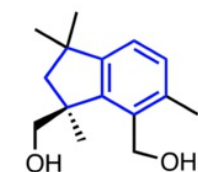
actinidine
cat attractant



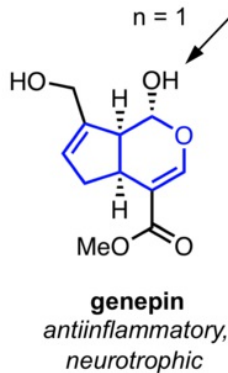
**N-1-β-D-ribofuranosyl-
makaluvic acid C**
anticancer



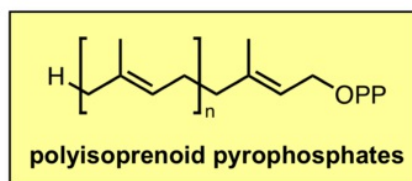
concavine
antibacterial



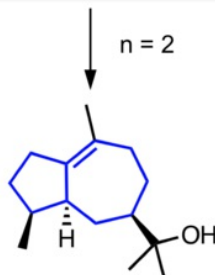
dehydrobotydienol
phytotoxic



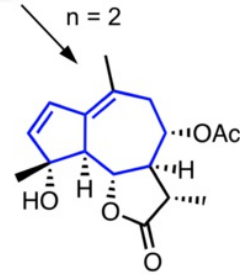
genepin
antiinflammatory,
neurotrophic



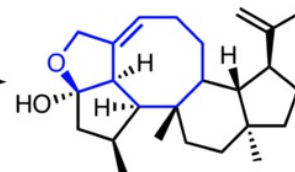
polyisoprenoid pyrophosphates



bulnesol
fragrance



matracin
antiinflammatory



variecolol
immunosuppressant,
antiretroviral

[Alkaloid and Terpenoid Diversity in Natural Products](#)

Complex polycyclic structures are found in nearly every biosynthetic class of natural products. In particular, an amazing range of

rigid densely functionalized polycyclic compounds are formed from simple polyisoprenoid precursors during terpenoid biosynthesis. Related strategies are used in alkaloid biosynthesis, leading to diverse polycycles with nitrogen functionalities.

We have developed a diversity-oriented synthesis in which multiple polycyclic scaffolds are synthesized from a small set of relatively simple starting materials. A variety of cyclization reactions are then used to generate diverse polycyclic molecules related to alkaloid and terpenoid natural products. The *t*-butyl sulfonamide moiety was identified as a versatile lynchpin in this synthetic approach, and solid-phase synthesis of a 190-membered multiscaffold library has been completed.

Recently, in collaboration with Dr. Lisa Marcaurelle and colleagues at the [Broad Institute Chemical Biology Platform](#), we have synthesized second-generation libraries based on these polycyclic alkaloid scaffolds that incorporate functionally diverse appendages and computational strategies for building block selection. We are currently following up upon promising hits that have been identified in screens of these libraries.

Publications

Solid-phase synthesis and chemical space analysis of a 190-membered alkaloid/terpenoid-like library.

Moura-Letts, G.; DiBlasi, C. M.; Bauer, R. A.; Tan, D. S.* *Proc. Natl. Acad. Sci. USA* 2011, *108*, 6745–6750.

[[Abstract](#) | [PubMed](#) | [PMC](#)]

The *tert*-butylsulfonamide lynchpin in transition-metal-mediated multiscaffold library synthesis.

Bauer, R. A.; DiBlasi, C. M.; Tan, D. S.* *Org. Lett.* 2010, *12*, 2084–2087.

[[Abstract](#) | [PubMed](#) | [PMC](#)]

An acid-stable *tert*-butyldiarylsilyl (TBDAS) linker for solid-phase organic synthesis.

DiBlasi, C. M.; Macks, D. E.; Tan, D. S.* *Org. Lett.* 2005, *7*, 1777–1780.

[[Abstract](#) | [PubMed](#)]

(Highlighted in [Lett. Org. Chem.](#) [[PDF](#)])

News Articles

08/02/2009

Trends in Chemical Biology 2009

NYAS eBriefing

The year-end meeting of the Chemical Biology Discussion Group, held June 1, 2009, highlighted the diverse spokes of chemical biology around a central theme: biomolecular recognition.

[[Overview \(free\)](#) | [Meeting report \(membership req'd\)](#)]

Renato Bauer's seminar: Asymmetric Synthesis of a Multiscaffold Library for Discovery Screening

[[Video \(membership req'd\)](#)]

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