

## The ISHC Bulletin

### Recent Publications of ISHC Members

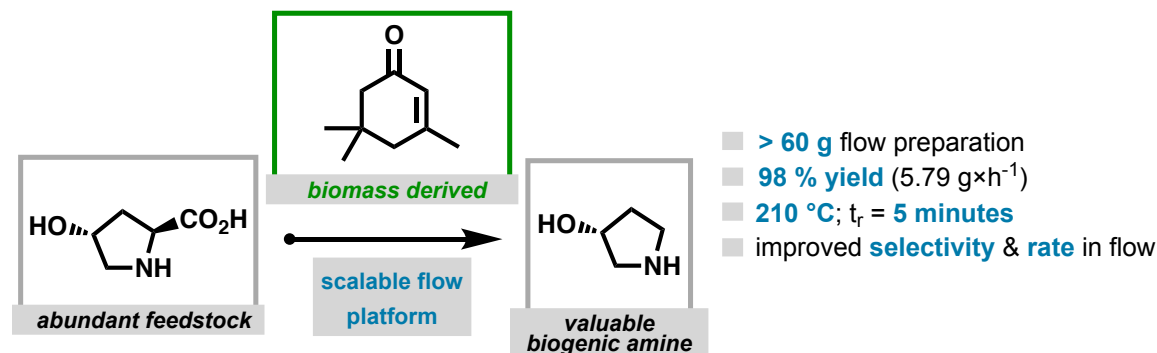
Issue 54; April 2021

#### Enone-Promoted Decarboxylation of *trans*-4-Hydroxy-L-Proline in Flow: A Side-by-Side Comparison to Batch

Rowan L. Pilkington, Madeleine A. Dallaston, G. Paul Savage, Craig M. Williams,\* and Anastasios Polyzos\* ([anastasios.polyzos@unimelb.edu.au](mailto:anastasios.polyzos@unimelb.edu.au) or [c.williams3@uq.edu.au](mailto:c.williams3@uq.edu.au))

*React. Chem. Eng.* **2021**, *6*, 486–493.

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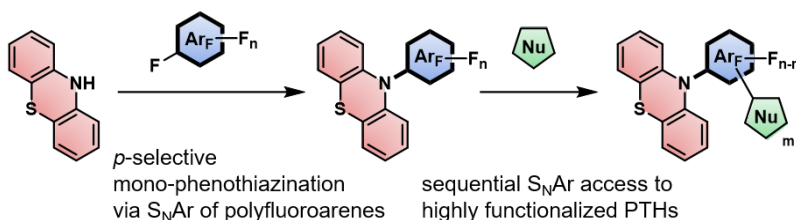
**Abstract:** The decarboxylation of natural and non-natural amino acids provides access to valuable amine substrates which are common in fragment libraries, drug discovery projects, and are important industrial starting materials. (*R*)-3-Hydroxypyrrolidine, used in the production of chiral catalysts and as a privileged motif in pharmaceutical agents, can be produced by decarboxylation of readily available feedstock *trans*-4-hydroxy-L-proline. However, typical amino acid decarboxylation techniques require high temperature and/or high pressure and can result in highly varied yields due to the heterogeneity of the reaction mixture and temperature sensitive nature of the product. Herein is reported a scalable, efficient, and reliable flow reactor method for the enone-assisted decarboxylation of *trans*-4-hydroxy-L-proline in homogeneous solution. The use of a biomass-derived enone and aqueous alcohol solvent system lays the foundations for renewable manufacturing of functionalised biogenic amines from abundant amino acid feedstock.

#### Nucleophilic Aromatic Substitution of Polyfluoroarene to Access Highly Functionalized 10-Penylphenothiazine Derivatives

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*Molecules* **2021**, *26*, 1365 (1–14).

DOI: 10.3390/molecules26051365



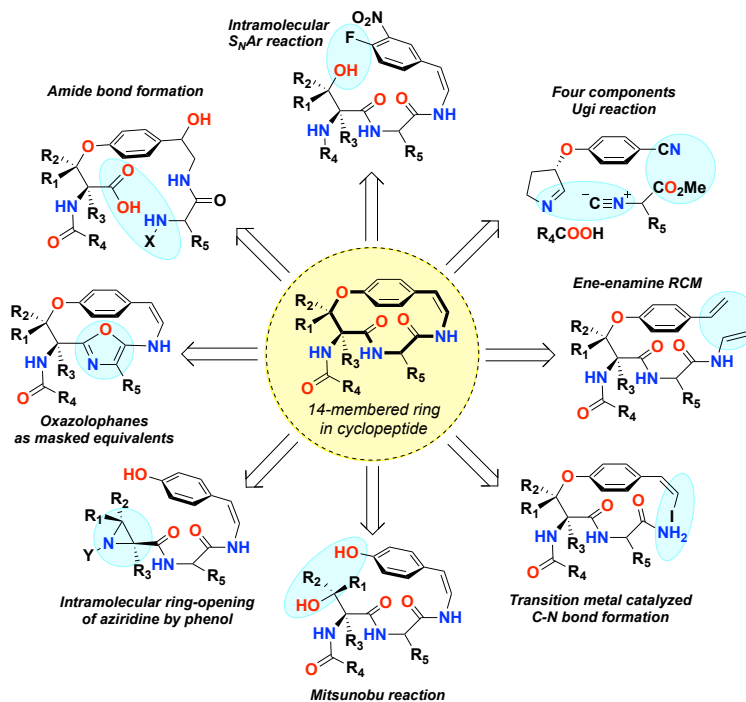
**Abstract:** Nucleophilic aromatic substitution ( $S_NAr$ ) reactions can provide metal-free access to synthesize monosubstituted aromatic compounds. We developed efficient  $S_NAr$  conditions for *p*-selective substitution of polyfluoroarenes with phenothiazine in the presence of a mild base to afford the corresponding 10-phenylphenothiazine (PTH) derivatives. The resulting polyfluoroarene-bearing PTH derivatives were subjected to a second  $S_NAr$  reaction to generate highly functionalized PTH derivatives with potential applicability as photocatalysts for the reduction of carbon–halogen bonds.

## Approaches to Cyclophane-Types of Cyclopeptide Alkaloids

Yuanhao Wang and Madeleine M. Joullie\* ([mjoullie@sas.upenn.edu](mailto:mjoullie@sas.upenn.edu))

*Chem. Rec.* **2021**, *21*, 1–19.

DOI: 10.1002/tcr.202100017



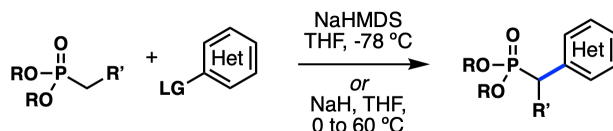
**Abstract:** The cyclopeptide alkaloids are cyclic depsipeptides incorporating cyclophanes with polyamide units 13-, 14- and 15-membered macrocyclic systems. Although various pharmacological activities have been ascribed to cyclopeptide alkaloids from plants of the *Rhamnaceae* family, these studies have been hampered by their low availability due to the lack of reasonable amounts distributed in nature. Therefore, novel and efficient synthetic approaches should be an important aim, which inspired us to examine how to diversely construct the unique structures of this type of natural products. In this account, several typical strategies are presented in terms of efficient, stereocontrolled and regioselective synthesis of cyclopeptide alkaloids.

## A Modular Approach for the Installation of Functionalized Phosphonates to Heterocycles

Zachary Shultz, Chuan Shan, Lukasz Wojtas, and Justin M. Lopchuk ([justin.lopchuk@moffitt.org](mailto:justin.lopchuk@moffitt.org))

*Arkivoc* **2021**, *part v*, 73–96.

DOI: 10.24820/ark.5550190.p011.486



- **Operationally simple**
  - **>20 examples - up to 91% yield**
  - **no transition metals required**
  - **Modular disconnection**
  - **Pharmaceutically-relevant heterocyclic scaffolds**
- [Biologically active analogs]*

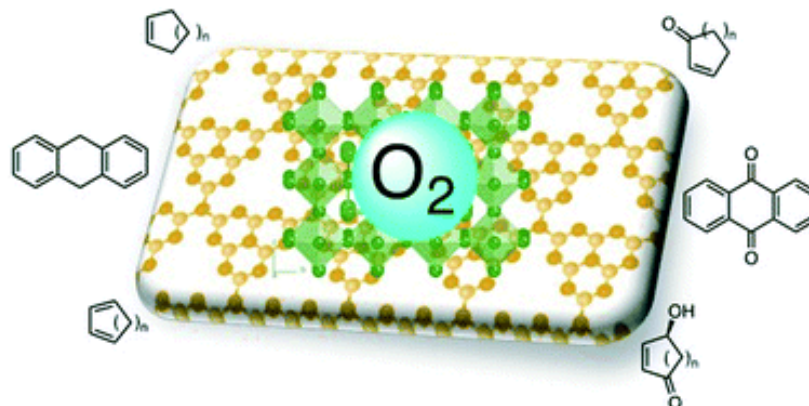
**Abstract:** Phosphonic acids and esters are pervasive throughout the discovery sciences, from medicine and agriculture, to materials and asymmetric synthesis. The ability to install and construct molecular architecture containing phosphonic functionality has led to the development of new medicines and catalyst systems in the field of organo- and organometallic catalysis. To continue the advancement in the field, improved synthetic access to phosphorous-containing motifs is required. In particular, heterocyclic phosphonates and their acid derivatives are so far underdeveloped. The method described herein provides a robust and operationally simple procedure for the installation of various phosphonates to a wide range of electrophilic heterocycles.

## g-C<sub>3</sub>N<sub>4</sub>/Metal Halide Perovskite Composites as Photocatalysts for Singlet Oxygen Generation Processes for the Preparation of Various Oxidized Synthons

Marco Corti, Rossella Chiara, Lidia Romani, Barbara Mannucci, Lorenzo Malavasi,\* and Paolo Quadrelli\* ([lorenzo.malavasi@unipv.it](mailto:lorenzo.malavasi@unipv.it) or [paolo.quadrelli@unipv.it](mailto:paolo.quadrelli@unipv.it))

*Catal. Sci. Technol.* **2021**, *11*, 2292–2298.

DOI: 10.1039/d0cy02352c



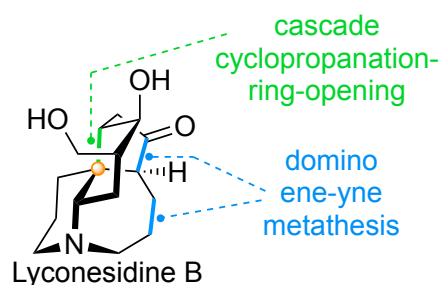
**Abstract:** g-C<sub>3</sub>N<sub>4</sub>/metal halide perovskite composites were prepared and used for the first time as photocatalysts for in situ <sup>1</sup>O<sub>2</sub> generation to perform hetero Diels–Alder, ene and oxidation reactions with suitable dienes and alkenes. The standardized methodology was made applicable to a variety of olefinic substrates. The scope of the method is finely illustrated and the reactions afforded desymmetrized hydroxy-ketone derivatives, unsaturated ketones and epoxides. Some limitations were also observed, especially in the case of the alkene oxidations, and poor chemoselectivity was somewhere observed in this work, which is the first application of MHP-based composites for in situ <sup>1</sup>O<sub>2</sub> generation. The experimental protocol can be used as a platform to further expand the knowledge and applicability of MHPs to organic reactions, since perovskites offer a rich variety of tuning strategies, which may be explored to improve reaction yields and selectivities.

## Total Synthesis of Lyconesidine B, a *Lycopeodium* Alkaloid with an Oxygenated, Amine-Type Fawcettimine Core

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*Org. Lett.* **2021**, *23*, 676–681.

DOI: 10.1021/acs.orglett.0c03816



**Abstract:** This report describes the total synthesis of the complex, oxygenated tetracyclic alkaloid, lyconesidine B. The key synthetic challenge involves diastereoselective generation of a decahydroquinoline ring with a quaternary carbon at the angular position *via* domino cyclopropanation, ring-opening, and reduction. Another crucial step is the domino ene-yne metathesis involving a quaternary ammonium ion, leading to the construction of a decahydroazaazulen framework.