Advanced Biocatalytic Methods for the Synthesis of Non-Canonical Amino Acids and Amine Derivatives

Tech ID: 34614 / UC Case 2025-367-0

BACKGROUND

Non-canonical amino acids (ncAAs) and secondary and tertiary alkyl primary amines have multiple market applications including applications protein engineering, biological imaging, and therapeutics. The sustainable synthesis of traditionally underexploited ncAAs have been extensively sought after by the pharmaceutical industry, and there is a need for efficient synthesis.

DESCRIPTION

Researchers at the University of California, Santa Barbara have developed several patent-pending technologies that synthesize ncAAs and amine derivatives using pyridoxal phosphate (PLP)-dependent enzyme variants. The products are used in pharmaceuticals, plastics, lubricants, fuel stabilizers, and other products. ncAAs constitute building blocks in biologically active products and clinically important peptide therapeutics, and processes that produce secondary and tertiary alkyl primary amines are of interest to multiple industries. These approaches overcome the limitations of traditional chemical synthesis and natural enzyme substrate scopes, offering improved potency, chemical stability, and conformational rigidity in peptide therapeutics and biocatalysts.

Compositions, Systems, and Methods for Stereoselective Synthesis of Amino Acids Using Nonheme Enzymes

UC Case No. 2025-367

Despite their potential, nonheme Fe enzymes remain largely underexploited in the development of new-to-nature biocatalytic reactions with significant synthetic utility. This new method for forming a non-canonical amino acid includes catalyzing a nitrogen migration reaction to form a non-canonical amino acid using an azanyl moiety-containing substrate and a metalloenzyme catalyst.

Systems, Compositions, and Methods for the Biocatalytic Synthesis of Non-Canonical Amino Acids
UC Case No. 2025-396

A cutting-edge process for forming a ncAA that utilizes an organoboron substrate, an amino acid, an enzyme, actinic radiation, a photocatalyst, and an oxidant to form a β-branched-α-tetrasubstituted non-canonical amino acids. The organoboron substrate, amino acid, enzyme, photocatalyst, and oxidant may be added separately, in any order, or

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OTHER INFORMATION

KEYWORDS

amino acids, non-canonical amino acids, ncAAs, amines, protein engineering, biological imaging, nonheme enzymes, enzymes, biocatalytic, biocatalytic synthesis, pharmaceuticals, novel peptide therapeutics, medicinal chemistry

CATEGORIZED AS

- **Materials & Chemicals**
  - Biological

RELATED CASES

2025-367-0

simultaneously. One or more non-canonical amino acids can be formed.

Systems, Compositions and Methods for Diversity-Oriented Three-Component Biocatalytic Synthesis
UC Case No. 2026-551

Diversity-oriented synthesis is a powerful strategy for addressing significant chemical and biological challenges by generating functional compound libraries with excellent skeletal, functional group, and stereochemical diversity. While enzymes can impose exceptional stereocontrol over challenging chemical reactions, using a single enzyme or a set of closely related enzyme mutants for diversity-oriented synthesis remains a challenge. This innovative radical C—C bond coupling strategy for forming a C—C bond from a from an α, β-unsaturated amino acid substrate, using a (PLP)-dependent enzyme variant.

Systems, Compositions and Methods for Biocatalytic Decarboxylative Synthesis of Non-canonical Amino Acids
UC Case No. 2026-552

Biocatalysis represents a promising alternative to traditional chemical synthesis, owing to its ability to provide excellent stereo-control. This novel approach to decarboxylative synthesis that utilizes a halocarbonyl, an amino acid substrate, a decarboxylative enzyme, a photocatalyst, and actinic radiation to form a first product using decarboxylative C—C coupling. This stereoselective synthesis of polysubstituted unnatural prolines established a new mode of radical pyridoxal enzymology by leveraging open-shell enamine catalysis, opening avenues for developing novel free radical reactions.

ADVANTAGES

- Efficient and stereoselective synthesis of complex ncAAs with tetrasubstituted α-stereocenters
- Protecting-group-free reaction conditions reduce synthesis complexity and waste
- Utilizes engineered enzymes evolved for improved activity and selectivity
- Enables enantioconvergent transformation of racemic organoboron substrates
- Alternative to toxic or harsh chemical synthesis methods
- Broad substrate scope and applicability for diverse ncAA building blocks

APPLICATIONS

- Pharmaceutical industry for production of macrocyclic peptide and glucagon-like peptide therapeutics
- Biocatalysis and synthetic biology for development of novel peptide therapeutics and biomolecules
- Chemical manufacturing for stereoselective amino acid synthesis
- Protein engineering and genetic code expansion technologies
- Research and development in asymmetric catalysis and medicinal chemistry

PATENT STATUS

Patent Pending

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Compositions, Systems, and Methods for Stereoselective Synthesis of Non-Canonical Amino Acids
- Compositions, Systems, and Methods for Stereoselective Decarboxylative Radical Cyclization

- Engineered Metalloenzymes for Stereocontrolled Atom Transfer Radical Addition
- Systems, Compositions And Methods Of Metalloprotein-Catalyzed Fluorination, Azidation, Thiocyanation and Hydroxylation
- Enzyme-Controlled Stereoselective Radical Cyclisation to Arenes Enabled by Metalloredox Biocatalysis

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