(SD2022-092) Cannabinoid production

Tech ID: 32980 / UC Case 2021-Z08-1

BACKGROUND

The implementation of ortho-quinone methide (o-QM) intermediates in complex molecule assembly represents a remarkably efficient strategy designed by Nature and utilized by synthetic chemists. o-QMs have been taken advantage of in biomimetic syntheses for decades, yet relatively few examples of o-QM-generating enzymes in natural product biosynthetic pathways have been reported. The biosynthetic enzymes that have been discovered thus far exhibit tremendous potential for biocatalytic applications, enabling the selective production of desirable compounds that are otherwise intractable or inherently difficult to achieve by traditional synthetic methods. Characterization of this biosynthetic machinery has the potential to shine a light on new enzymes capable of similar chemistry on diverse substrates, thus expanding our knowledge of Nature's catalytic repertoire.

TECHNOLOGY DESCRIPTION

Researchers from UC San Diego can convert cannabigerolic acid to cannabichromenic acid in vivo by incubating the substrate with overexpressed bacterial enzymes in vivo. This process also works with three derivatives of cannabigerolic acid, and can be successfully demonstrated using hundreds of milligrams in one bioconversion reaction.

APPLICATIONS

Production of cannabinoids in bacteria on an industrial scale.

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OTHER INFORMATION

KEYWORDS

Biocatalysis, Biological Products, Indolequinones, quinone methide, pharmaceuticals, Biosynthesis, Cyclization, Addition reactions, biomimetic synthese

CATEGORIZED AS

- **Biotechnology**
  - Other
- **Materials & Chemicals**
  - Agricultural
  - Biological
- **Medical**
  - New Chemical Entities, Drug Leads

RELATED CASES

2021-Z08-1

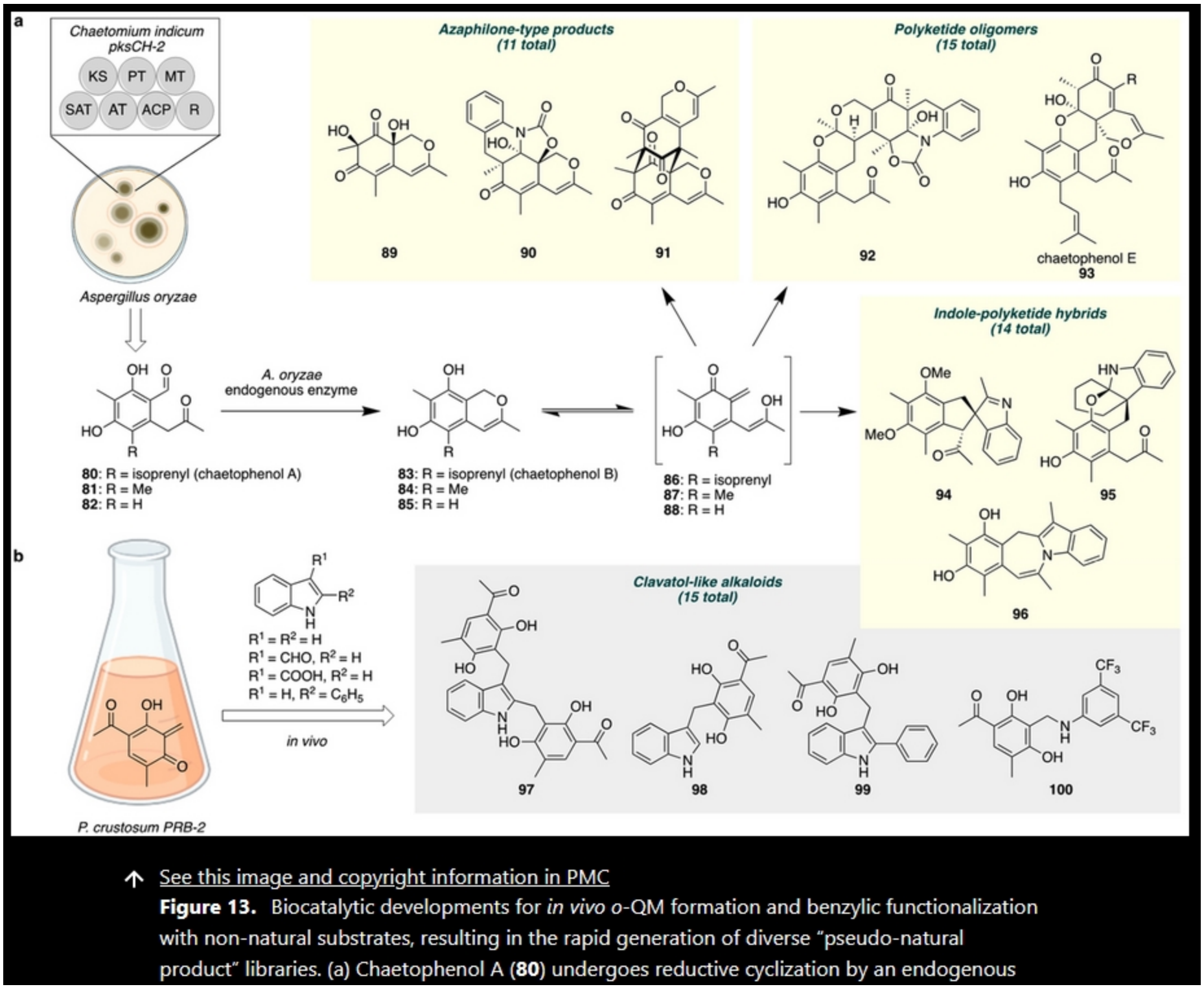

Figure 13. Biocatalytic developments for *in vivo* *o*-QM formation and benzylic functionalization with non-natural substrates, resulting in the rapid generation of diverse "pseudo-natural product" libraries. (a) Chaetophenol A (**80**) undergoes reductive cyclization by an endogenous

ADVANTAGES

STATE OF DEVELOPMENT

The most exciting prospect for these enzymes is their biomanufacturing potential to produce rare or unnatural cannabinoids in a bacterial heterologous system, a feat yet to be achieved with the plantderived cannabinoid synthases. Future work will focus on optimizing the reaction conditions by studying the effects of pH, temperature, substrate concentration, and then scaling up these conditions to confirm the structures of all the observed products.

Additional rational engineering studies may also improve the selectivity of these enzymes to produce desired cannabinoids.

INTELLECTUAL PROPERTY INFO

Patent pending. UC San Diego is seeking partners to commercialize this technology.

RELATED MATERIALS

▶ Purdy TN, Moore BS, Lukowski AL. Harnessing ortho-Quinone Methides in Natural Product Biosynthesis and Biocatalysis. J Nat Prod. 2022 Mar 25;85(3):688-701. doi: 10.1021/acs.jnatprod.1c01026. Epub 2022 Feb 2. - 02/02/2022

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