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Opinion

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Recent Developments in Chemoenzymatic Synthesis for Complex Molecule Construction

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DESCRIPTION

Chemoenzymatic synthesis, the integration of enzymatic and chemical catalysis, has emerged as a powerful strategy for the construction of complex molecules with high efficiency and selectivity. This approach leverages the versatility of enzymes to perform selective transformations under mild conditions, complemented by chemical catalysts to facilitate additional synthetic steps. Recent advancements in chemoenzymatic synthesis have expanded its scope and applicability, enabling the synthesis of diverse molecules including pharmaceuticals, natural products, and functional materials. Cascade reactions involve the sequential action of multiple enzymes to catalyze a series of transformations in a single pot, minimizing the need for intermediate purification steps and reducing waste generation. Recent advancements in cascade reactions include the development of new enzyme cascades for the synthesis of pharmaceutical intermediates, natural product derivatives, and fine chemicals.

Recent years have seen significant progress in enzyme discovery and engineering, enabling the identification and optimization of enzymes with tailored catalytic properties. Advances in genomics, bioinformatics, and directed evolution techniques have facilitated the discovery of novel enzymes capable of catalyzing specific chemical transformations. Moreover, enzyme engineering strategies, such as protein engineering and directed evolution, have been employed to enhance the catalytic efficiency, substrate specificity, and stability of enzymes for chemoenzymatic synthesis applications. These developments have expanded the enzymatic toolbox available to synthetic chemists, enabling the synthesis of complex molecules with unprecedented precision and efficiency.

Cascade reactions and multienzyme systems are key strategies in chemoenzymatic synthesis for the efficient assembly of complex molecules from simple precursors. Multienzyme systems, comprising multiple enzymes immobilized or encapsulated within a single reactor, enable the integration of incompatible enzymatic transformations and the recycling of cofactors, further enhancing the efficiency and scalability of chemoenzymatic synthesis. Biocatalytic redox reactions, which involve the transfer of electrons between enzymes and substrates, have emerged as versatile tools in chemoenzymatic synthesis for the construction of complex molecules. Enzymes such as oxidoreductases, dehydrogenases, and oxygenases catalyze a wide range of redox transformations, including oxidation, reduction, and hydroxylation reactions. Recent developments in biocatalytic redox reactions include the discovery of novel enzymes with unique catalytic properties, the engineering of enzymes for improved activity and stability under non-natural conditions, and the development of cofactor recycling systems to minimize cofactor usage and waste generation. Biocatalytic redox reactions enable the selective modification of complex molecules at specific sites, facilitating the synthesis of chiral intermediates, pharmaceuticals, and natural product analogs.

Enzyme-mediated conjugation reactions have gained attention in chemoenzymatic synthesis for the site-selective functionalization of biomolecules and synthetic intermediates. Enzymes such as ligases, transferases, and hydrolases catalyze the formation of covalent bonds between functional groups, enabling the synthesis of peptide conjugates, glycoconjugates, and nucleic acid conjugates. Recent advancements in enzyme-mediated conjugation reactions include the development of engineered enzymes with expanded substrate scopes, the discovery of novel enzyme classes capable of catalyzing specific conjugation reactions, and the optimization of reaction conditions for high efficiency and selectivity. Enzyme-mediated conjugation reactions offer a versatile and mild approach to functionalize complex molecules with diverse chemical functionalities, facilitating the synthesis of bioconjugates for biomedical applications. The integration of chemical catalysts with enzymes has emerged as a powerful strategy in chemoenzymatic synthesis for expanding the scope of enzymatic transformations and accessing new chemical space. Chemical catalysts such as transition metal complexes, organocatalysts, and photocatalysts can facilitate non-natural transformations that are not catalyzed by enzymes alone.

In conclusion, recent developments in chemoenzymatic synthesis have significantly expanded the synthetic capabilities available to chemists for the construction of complex molecules. Enzyme discovery and engineering, cascade reactions and multienzyme systems, biocatalytic redox reactions, enzyme-mediated conjugation reactions, and the integration of chemical catalysts represent key areas of innovation in chemoenzymatic synthesis. These advancements offer new opportunities for the efficient synthesis of pharmaceuticals, natural products, and functional materials with tailored properties and functionalities. Continued research and development in chemoenzymatic synthesis are expected to further advance the field and accelerate the discovery of novel molecules for diverse applications in science and technology.