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Enzymes of Halogenase for Synthesis Development

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Abstract

Halogenase enzymes have evolved in nature to regioselectively halogenate a wide range of biosynthetic precursors, with the halogens added often having a major impact on the biological activity of the resulting natural products. Synthetic seeks to create non-natural bioactive tiny molecules for use in medicine and cosmetics. A similar conclusion has been obtained in the field of agrochemicals. Organic compounds can be considerably improved by halogens, allowing them to regulate biological targets selectively in vivo. As a result, halogens can now be found in a wide range of pharmaceuticals and agrochemicals. Halogenated organic compounds are also common synthesis intermediates, and they're particularly beneficial in metal catalyst cross-coupling processes.

Introduction

Despite the potential benefit of organohalogens, traditional nonenzymatic halogenation chemistry uses toxic compounds and frequently lacks regiocontrol. Reliable, simple, and cleaner technologies for regioselective halogenation of organic molecules are required to provide cost-effective and ecologically acceptable commercial processes. One path to such strategies could be to use halogenase enzymes as biocatalysts, which are responsible for the manufacture of halogenated natural chemicals. The progress in producing halogenases for biocatalysis, as well as potential untapped sources of such biocatalysts, will be discussed in this review, as well as how additional optimization of these enzymes is required to attain the aim of industrial scale biohalogenation. Many pharmaceutical and agricultural products, as well as other useful materials, contain organohalogen moieties, which are widely employed in all sectors of the chemical industry in the form of synthetic intermediates. Because of the numerous C-C, C-F, C-N, and other C-heteroatom couplings that are possible, transition metal-catalyzed crosscoupling processes have become crucial tools for the synthesis of complex compounds possible. Because of their capacity to metalate C-X bonds, organohalogens are used in many of these reactions, and halogenated compounds are now common intermediates in organic synthesis. Furthermore, the addition of a halogen atom to a tiny molecule can have a significant impact on its bioactivity and physical properties. This property has been utilised in medicinal chemistry, with halogen atoms found in a substantial fraction of all medications in clinical trials or on the market. It has been proven that the halogen substituents are critical for antibacterial action in the antibiotic vancomycin, with dechlorovancomycin variants demonstrating considerably lower binding affinity for the biological target peptidoglycan. The halogen's unique effect on biological activity has extended to the design of agrochemicals, with many of the most popular herbicides, pesticides, and insecticides including halogen. Organohalogen compounds have also been discovered to have desirable characteristics in polymers, and as a result, they are

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garnering more consideration for future material generations. The effect of halogens on bioactivity and bioavailability was previously assumed to be mainly attributable to lipophilicity modulation and nonspecific hydrophobic interactions with protein targets. Carbonhalogen bonds, on the other hand, have recently been shown to form halogen bonds, which are directed intermolecular interactions with proteins. These are created by a halogen's electron-deficient "sigma-hole" in a CX bond, which allows halogens to engage with lone pairs of heteroatoms like as N, O, and S in protein targets in a fashion that is comparable to hydrogen bonding. As a result, utilising halogen atoms in medicinal chemistry is a well-established practise since it allows for the insertion of additional ligand target connections without needing significant alterations to the target's other contacts.