Drug discovery, Functional materials

Diastereodivergent Synthesis of 1,2-Diamines Enabled by Iodine Catalysis

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Researchmap https://researchmap.jp/read0185263?lang=en

Abstract

Iodine (the world's second-largest production), an element that Japan is proud of, which has few resources, is utilized as a catalyst for complete stereoselective *anti*- and *syn*-1,2-diamination of unfunctionalized carbon-carbon double bonds (alkenes). The combined use of the two potential methods provides access to all of the disastereomeric forms of 1,2-diamines in spite of the availability of *E*- and *Z*-alkenes (Fig. 1).

Background & Results

The 1,2-diamine substructure is a ubiquitous structural motif that is found in a number of natural products, biologically active compounds, ligands for metal-mediated catalysis. Among these, the method of introducing two amino group units into a carbon-carbon double bond (alkene) is the most direct and diverse method of synthesizing 1,2-diamines. From these points of view, the development of diamination of alkens has been energetically promoted worldwide for about 10 years. However, there are many drawbacks such as the lack of generality of raw alkenes, the peculiarity of the nitrogen unit to be introduced, and the uncontrolled stereochemistry when converting a planar alkene to a three-dimensional diamine. In order to overcome these issues, we succeeded in finding a synthetic strategy that permits various 1,2-diamine derivatives to be produced from unactivated alkenes. The substrates (nitrogen sources)-controlled stereospecific intermolecular *anti*- and *syn*-1,2-diamination was successfully achieved. Both *anti*- and *syn*-diaminations could be conducted in a stereospecific manner using this iodine catalysis, which are regarded as the catalytic aza-Prévost-Woodward reactions. The simplicity of this new method, *anti*-1,2-diamination is one of its more attractive aspects; the starting components nosylamide, $NaOCl{\cdot}5H_2O$ and iodine catalyst needed for the reaction are all commercially available and inexpensive.

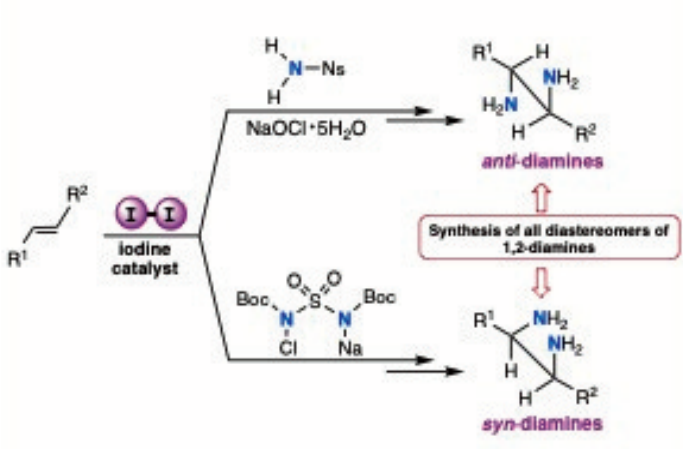

Fig. 1 Stereospeciflc 1,2-Diamination Enabled by I_2 Catelysls

Significance of the research and Future perspective

The 1,2-diamine skeleton is a very important partial structure contained in *anti*-influenza drugs such as Tamiflu® , Relenza® and Inavir® , natural products such as biotin and ligands for metal catalyst (Fig. 2). Therefore, the present methods, which can completely control the stereochemistry of this unit, is an extremely significant methodology for organic synthesis. In addition, this reaction does not use a rare transition metal catalyst, and the only by-products after the reaction are water and sodium chloride, which can contribute to a sustainable society as a manufacturing method. Among the currently used drugs including the above-mentioned *anti*-influenza drugs, many bioactive substances having a 1,2-diamine substructure are found. It is unclear whether this unit is needed for the currently coveted silver bullet for COVID-19, but the development of unprecedented reactions has enabled the rapid synthesis of new substances, a group of new drug candidate compounds.

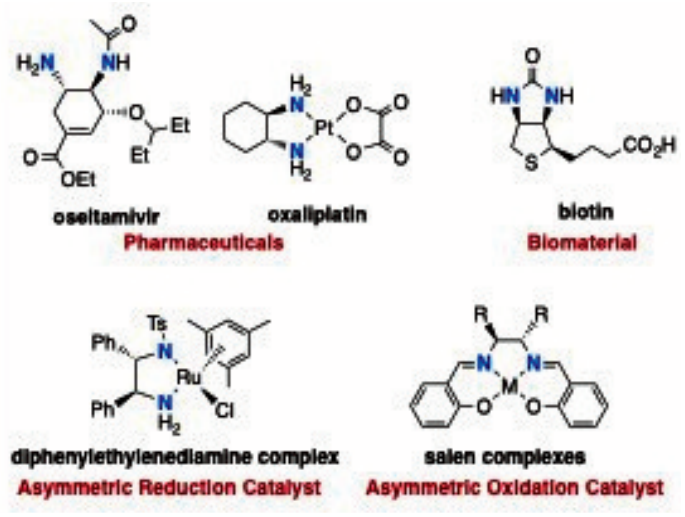

Fig. 2. Examples of Functional Materials Containing 1,2-Diamine Molety

Patent	
Treatise	Minakata, Satoshi; Miwa, Hayato; Yamamoto, Kenya et al. Diastereodivergent Intermolecular 1,2-Diamination of Unactivated Alkenes Enabled by Iodine Catalysis. J. Am. Chem. Soc. 2021; 143 (11): 4112-4118. doi: 10.1021/jacs.1c00228
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Keyword	1,2-diamines, iodine catalysis, stereospecificity, alkenes