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学位論文内容の要旨

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Bioorganic Studies on *cis*-Jasmone and Pyrethrins Biosynthesized via the OPDA Isomerizing Pathway

（OPDA異性化経路により生合成される*cis*-ジャスモン及びピレスリンに関する生物有機化学的研究）

The OPDA-isomerizing pathway was recently proposed, but its detail still remains unknown. It was assumed that *cis*-Jasmone (CJ) and pyrethrins might be biosynthesized through this pathway. CJ was isolated as one of the main fragrances from the essential oil of jasmine. Today, CJ is an important industrial material to produce many commodities, such as perfumes, cosmetics, and food additives. Pyrethrins are natural insecticides produced by pyrethrum (*Tanacetum cinerariifolium*). The history of pyrethrins is long, and pyrethrum plants have been used for pest control since medieval times. Today, industrial production of pyrethrins still relies on extraction from flowers of the plants. It is estimated that the world production of pyrethrum reaches or exceeds 30,000 metric tons, although the cost for extracting pyrethrins from the plants is extremely high. The purpose of this study was to clarify the importance of OPDA-isomerizing pathway, and to increase endogenous amounts of pyrethrins in pyrethrum plant to improve the productivity of pyrethrins.

1.　Establishment of a method for the synthesis of *iso*-OPDA

This chapter aimed to develop a synthetic route to *iso*-OPDA from (±)-methyl jasmonate (MeJA) for applying the method to synthesize [$^2H_1$-10, $^2H_2$-11, $^2H_3$-12]-*iso*-OPDA and deuterium labeled 4,5-didehydro-MeJA, and 3,7-didehydro-MeJA. The proposed synthetic strategy in this study composed three key processes. In the first process, the -CH_2-COOMe side chain was extended via a Horner–Wadsworth–Emmons reaction. Second process was ruthenium-catalyzed oxidative cleavage of an alkene combined with a Wittig reaction, which enabled incorporations of deuterium atoms into the pentenyl unit of target compounds. Third, a double bond was introduced into the outer side methylene carbons of the cyclopentanone ring, and subsequent migration of the double bond into inner side methyne carbons. At finally last, *iso*-OPDA was synthesized from MeJA in 10 steps with an overall yield of 6.9%, and the syntheses of [$^{2}H_{1}$-10, $^{2}H_{2}$-11, $^{2}H_{3}$-12]-*iso*-OPDA and other labeled compounds were accomplished according to the established synthetic scheme.

2. Investigation of CJ biosynthetic pathway in plants

The biosynthesis of CJ in plants has been proposed to proceed via two distinct pathways, the OPDA-reducing and the OPDA-isomerizing pathways, but remains controversial. In order to clear the ambiguous point, plants having ability to accumulate large amount of CJ were explored, and their biosynthetic pathways were investigated using deuterium-labeled compounds. GC-MS analysis revealed that CJ accumulates in the leaves of several Lamiaceae species. Finally, the leaves of apple mint (*Mentha suaveolens*) were used to perform the experiments, and it was found that deuterium labeled 3,7-didehydro-MeJA were metabolized into CJ, but labeled MeJA and 4,5-didehydro-MeJA were not into CJ, whose results strongly supported that CJ was biosynthesized via the OPDA-isomerizing pathway rather than the OPDA-reducing pathway.

3. Exploration of triggers that increased pyrethrin contents in pyrethrum plants

In this chapter, phytohormones and stress treatments that increase endogenous pyrethrin levels were investigated to improve industrial pyrethrin production and to contribute to the elucidation of the OPDA-isomerizing pathway. Treatments with MeJA and methyl salicylate, which are considered biotic stress signals such as herbivory and pathogen infection, did not lead to increase the endogenous pyrethrin levels. In contrast, abscisic acid (ABA) treatments, which are associated with responses to abiotic stresses such as drought and salinity, resulted in 3.5-fold increase in endogenous pyrethrin levels. Furthermore, treatments with PEG, NaCl, and EtOH, which are known to stimulate ABA biosynthesis in plants, led to 2.2-, 1.9-, and 1.7-fold increases in endogenous pyrethrin levels.