

CHEMO-ENZYMATIC HYBRID PROCESS FOR PRODUCTION OF MONATIN, A HIGH-INTENSITY SWEETENER

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Monatin, 4-hydroxy-4-(3-indolylmethyl)-glutamic acid, is a naturally occurring sweet amino acid isolated from the plant *Sclerochiton ilicifolius*, found in South Africa [1]. Monatin has two asymmetric centers at C2 and C4, the (2*R*,4*R*)-monatin isomer has been found to be the sweetest among its four stereoisomers. It is 2700 times sweeter than sugar and has a clean taste like sugar. Because of these properties, (2*R*,4*R*)-monatin has been expected as a new high-intensity sweetener [2]. However, industrial production process of (2*R*,4*R*)-monatin using inexpensive raw materials has not been established owing to the difficulty for optically specific synthesis. Here, we report a chemo-enzymatic hybrid process for production of (2*R*,4*R*)-monatin from L-tryptophan. In the steps of enzymatic reaction from L-tryptophan, L-amino acid deaminase and aldolase were used for production of 4-(Indole-3-ylmethyl)-4-hydroxy-2-oxoglutaric acid (IHOG) with pyruvic acid as co-substrate. The keto-form of (2*R*,4*R*)-monatin, (*R*)-IHOG, was specifically synthesized by using *R*-specific aldolase from *Shingomonas* sp. in the second reaction. In the next chemical reaction steps, (*R*)-IHOG was converted to the oxime form, reduced to (2*R*,4*R*) and (2*S*,4*R*)-monatin, and (2*R*,4*R*)-monatin salt was obtained from optical resolution by crystallization. By the combination of epimerization and crystallization, (2*R*,4*R*)-monatin was obtained specifically from the mixture of diastereomers. In this study, we established an efficient production process for (2*R*,4*R*)-monatin using both chemical and enzymatic reactions, and a large amount of (2*R*,4*R*)-monatin was prepared by the bench-scale production.

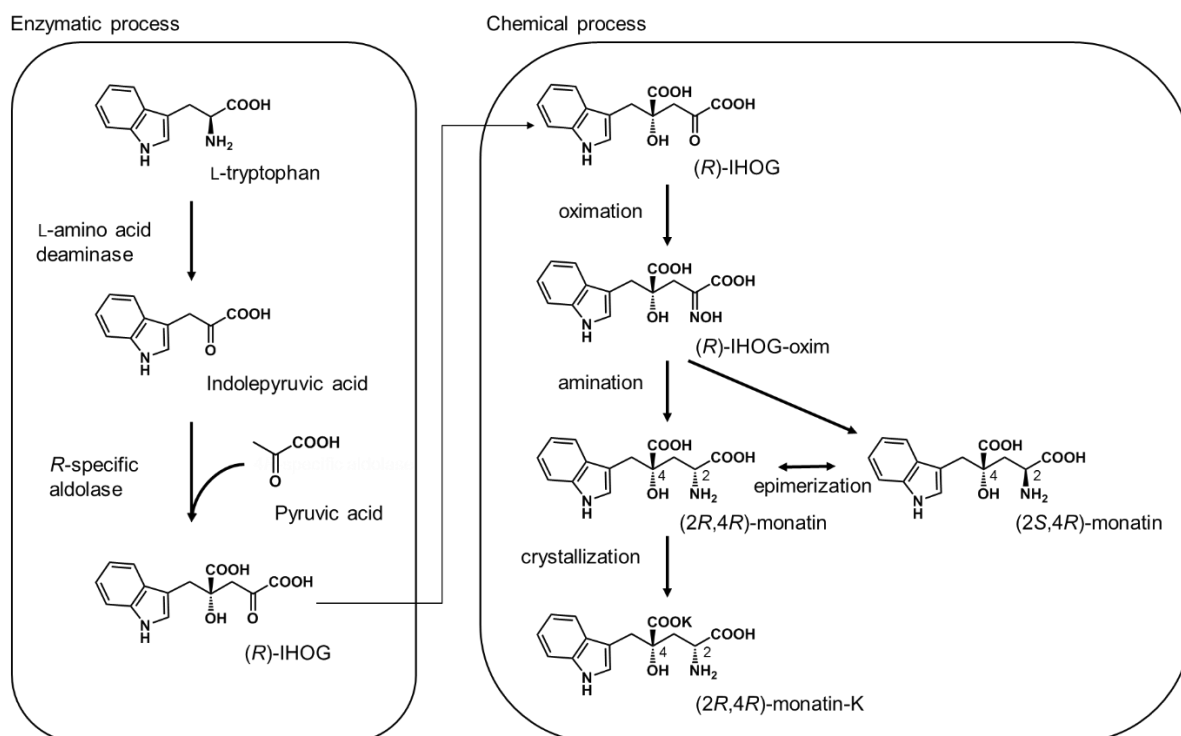


Figure 1 – Chemo-enzymatic synthesis of (2*R*,4*R*)-monatin from L-tryptophan.

References

- [1] R. Vlegaar et al., J Chem Soc., Perkin Trans., 1, 3095-3098 (1992)
- [2] Y. Amino et al., Chem Pharm Bull., 64, 1161-1171 (2016)