

Synthesis of β -amino acids using a modified Hydantoinase Process as an enzymatic reaction cascade

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The use of **β -amino acids** is of increasing importance in the pharmaceutical industry. They serve for instance as building blocks for β -peptides, which form very stable secondary structures and are therefore promising molecules for the application as peptidomimetics.^[1] Due to their specific structure, β -amino acids are also found as constituents of biologically active secondary metabolites like the antitumor drug Taxol™, which contains a modified β -phenylalanine moiety (Fig. 1).^[2] Since the **Hydantoinase Process** for the synthesis of optically pure D- α -amino acids from hydantoin derivatives is well-established in industry, a modified Hydantoinase Process for the synthesis of β -amino acids has been proposed (Fig. 2).^[3]

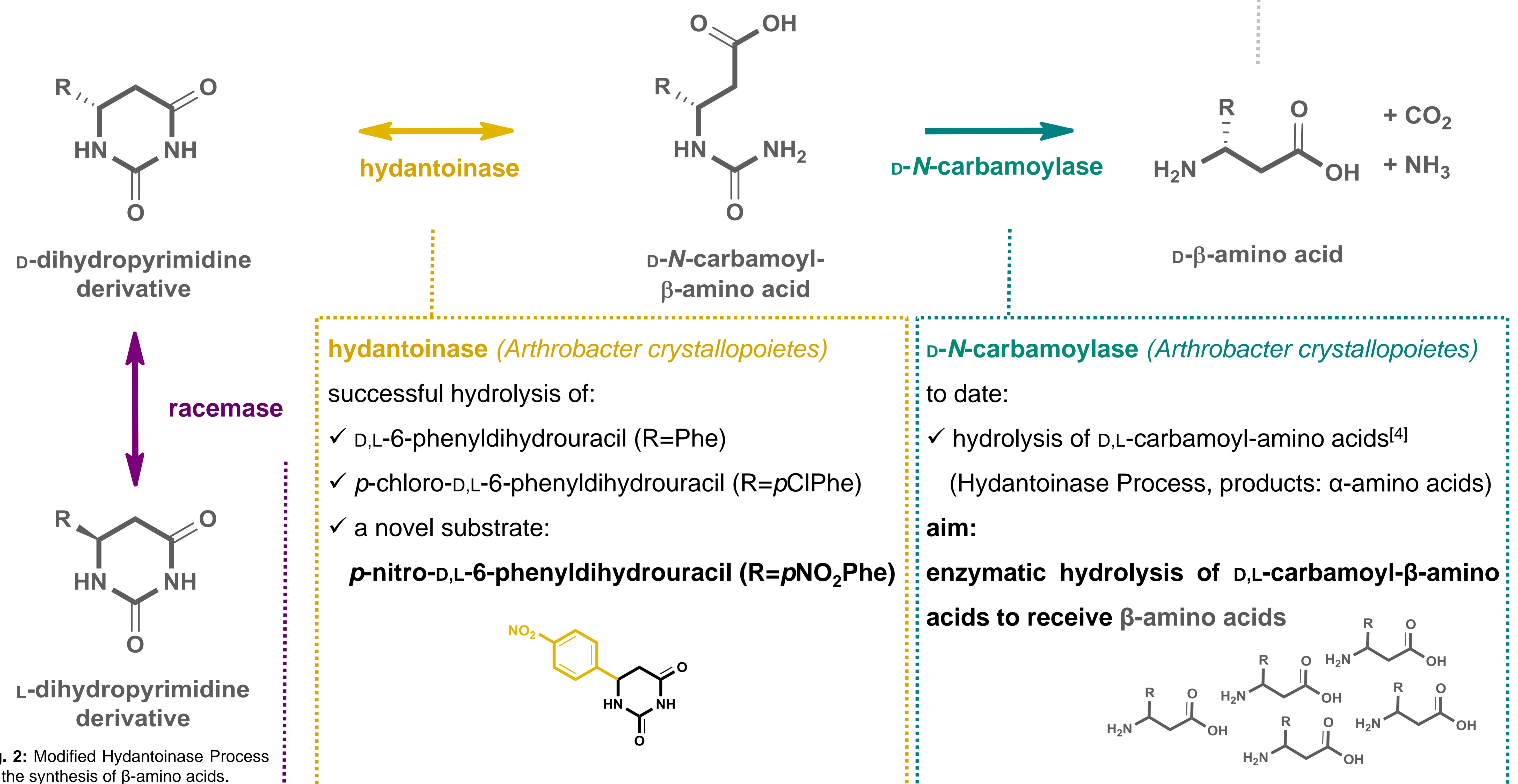
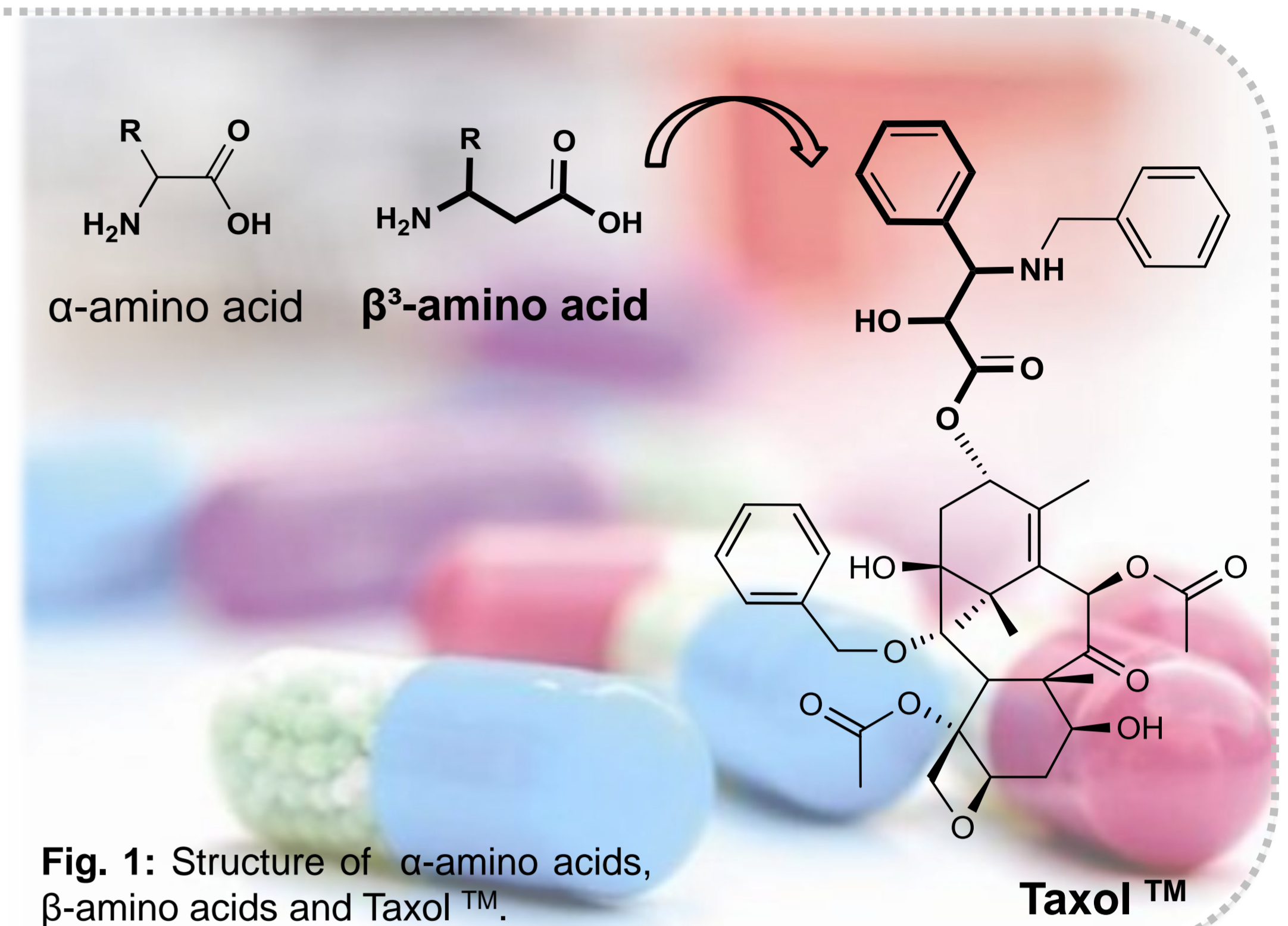


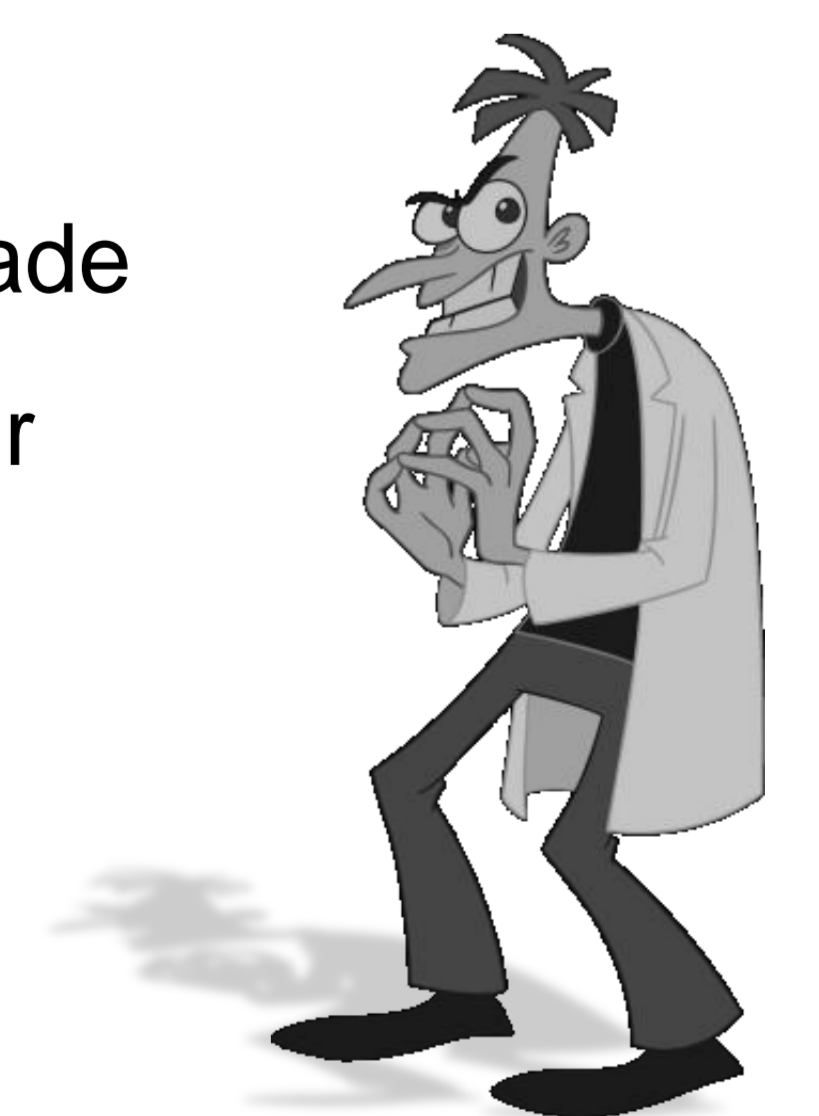
Fig. 2: Modified Hydantoinase Process for the synthesis of β -amino acids.

dynamic kinetic resolution

- enzymatically by racemase, theoretically:
- ✓ **100 % yield**
- ✓ **100 % enantiomeric excess**
- ✓ no enantiomeric separation necessary

outlook

- hydrolysis of D,L-carbamoyl- β -amino acids
- purification and characterization of enzymes involved in the cascade
- applications in microfluidic systems (continuous system with lower product inhibition)
- investigations toward reaction cascades with isolated enzymes in organic solvents



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[2] J. Parness, D. G. I. Kingston, R. G. Powell, C. Harracksingh, S. B. Horwitz, Structure-activity study of cytotoxicity and microtubule assembly by taxol and related taxanes. Biochem. Biophys. Res. Commun. 105(3), p. 1082-1089 (1982)

[3] U. Engel, C. Syldatk, J. Rudat, Stereoselective hydrolysis of aryl-substituted dihydropyrimidines by hydantoinases, Appl. Microbiol. Biotechnol. 94, p. 1221-1231 (2012)

[4] M. Werner, F. J. Las Heras Vazquez, C. Fritz, O. Vielhauer, M. Siemann-Herzberg, J. Altenbuchner, C. Syldatk, Cloning of D-specific Hydantoin Utilization Genes from *Arthrobacter crystallopoietes*. Eng. Life Sci. 4 (6), p. 563-572 (2004)