Iris Biotech

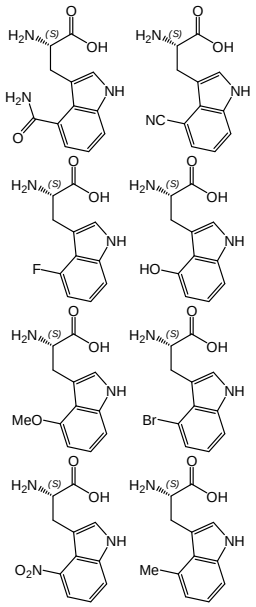
Empowering Peptide Innovation

NEW A Treasure Trove of **Tryptophan Analogues!**

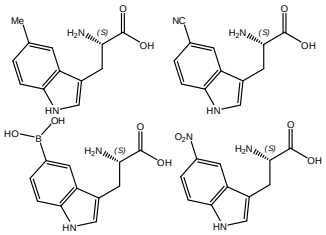
Variants of the TrpB enzyme catalyze the condensation of a substituted indole, indoline or isostructural analogue with a β-hydroxy amino acid, such as serine or threonine, yielding an enantiopure tryptophan analogue with water as the only byproduct. In addition to indoles, the enzyme accepts various nitrogen and sulfur nucleophiles to make other classes of noncanonical amino acids. A vast variety of compounds are now easily accessible with this methodology, both for research and industry.

- ✓ only one step from readily available precursors
- ✓ green synthesis conditions in water
- ✓ robust biocatalytic process with hyperthermostable enzymes, with high expression rates and cycle numbers
- ✓ no column purification necessary
- ✓ scalable to bulk production

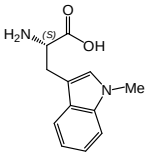
4-substitution



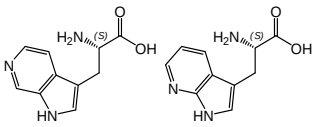
5-substitution

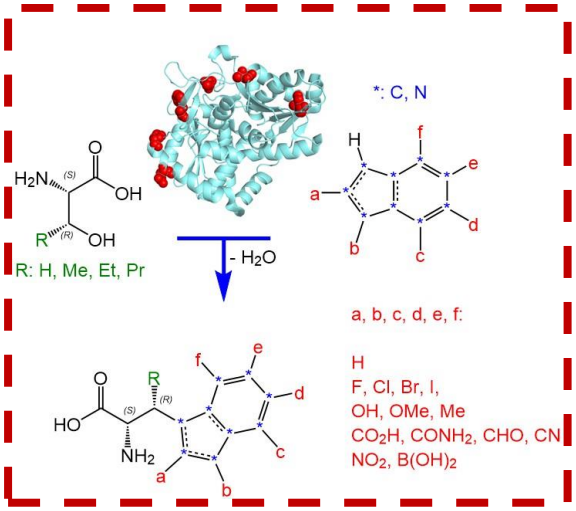


1- and 2-substitution

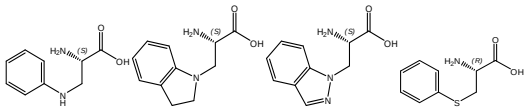


aza-substitution

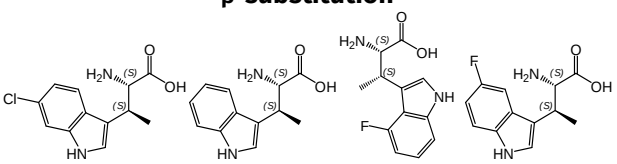




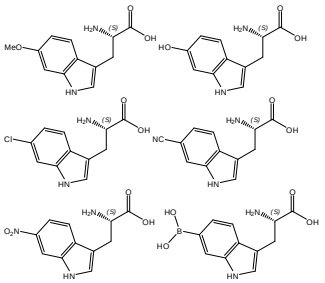
other classes of α-amino acids



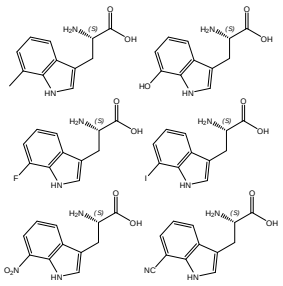
β-substitution



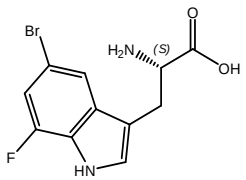
6-substitution



7-substitution



di-substitution



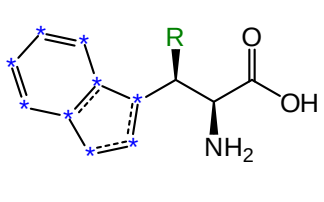
... and many more

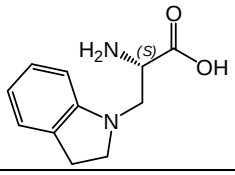
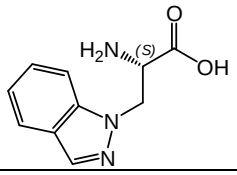
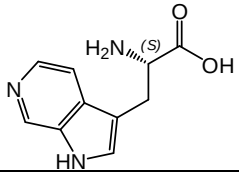
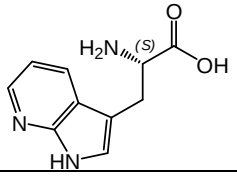
TrpB variant tolerates substrates which are isostructural to indole, such as indoline and indazole. Even molecules which are only somewhat similar to indole, like different kinds of pyrrolopyridines, can be used and yield in completely novel and unusual analogues.

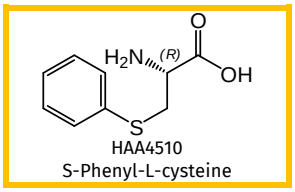
Iris BIOTECH GMBH

Empowering Peptide Innovation

Current Gems in our Tryptophan Treasure Trove

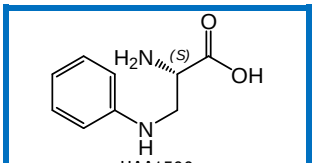


			
HAA4520 3-Indolyl-L-alanine	HAA4530 3-Indazolyl-L-alanine	HAA4460 6-Aza-L-tryptophan	HAA4470 7-Aza-L-tryptophan



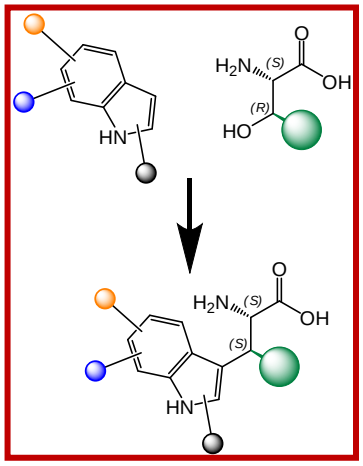
HAA4510
S-Phenyl-L-cysteine

In addition to indoles, the enzymes accept nitrogen and sulfur nucleophiles to make other classes of noncanonical amino acids accessible like unusually substituted cysteine and diamino-propionic acid derivatives.

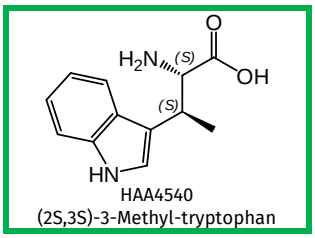


HAA4500
N-beta-Phenyl-
L-2,3-diaminopropionic acid

If threonine is used in place of serine β-methylated derivatives can be designed in high optical purity. β-Alkylation with defined stereochemistry and high optical purity otherwise is very laborious and costly to carry out.

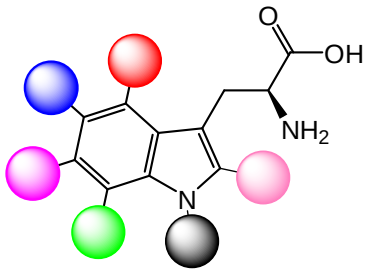


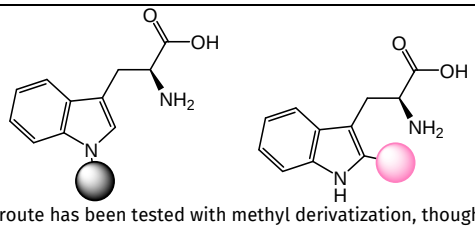
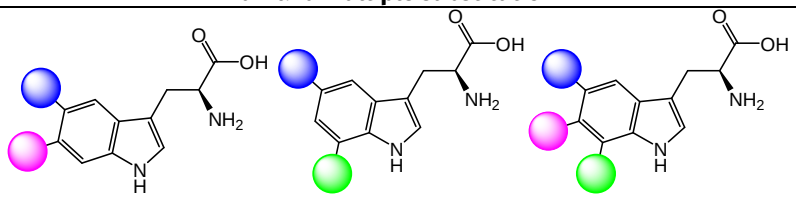
Noncanonical amino acids (ncAAs) with dual stereocenters at the α and β positions are valuable precursors to natural products and therapeutics. Despite the potential applications of such bioactive β-branched ncAAs, their availability is limited due to the inefficiency of the earlier multistep methods used to prepare them. A new engineered variant of *Pyrococcus furiosus* tryptophan synthase (*Pf*TrpB), *Pf*TrpB^{7E6} is an operationally simple and environmentally benign platform to provide in a stereoselective biocatalytic synthesis novel β-branched and bulky tryptophan analogues. Simply by using threonine instead of serine as starting material all potential β-methylated tryptophan analogues can very easily be prepared. Dual and multiple ring-substituted derivatives are also accessible with appropriate indole precursor molecules.



HAA4540
(2S,3S)-3-Methyl-tryptophan

A large number of substituted indole derivatives are accepted as substrate, yielding new structures of substituted tryptophans. Many of these were previously not available or were only accessible via multi-step laborious and expensive routes. Here are examples of available products, please suggest other products for testing.



1- and 2-substitution	di- and multiple substitution
 This route has been tested with methyl derivatization, though many more variations are possible. Suggest your indole derivative and it can be tested as substrate.	 Other substituted tryptophans are available, if the corresponding indole is accessible. We can try with your indole, whether it is tolerated by the current TrpB variant or by a new variant.

➔ Contact us for the Tryptophan Derivative of your choice!