Reference: TyrAcyl

SITE-SELECTIVE ACYLATION OF TYROSINE-CONTAINING PEPTIDES WITH ALDEHYDES

This invention identifies a new Pd-catalyzed technique for the production of non-proteogenic *ortho*-acylated tyrosine (Tyr) containing peptides.

TYPE OF DEVELOPMENT

Synthetic method.

DESCRIPTION

Site-selective functionalization of C–H bonds within a peptide framework poses a challenging task of capital synthetic relevance. This invention offers a robust, yet innovative, means for the radical functionalization of a wide range of Tyr-containing oligopeptides, thus expanding the landscape of peptide synthesis to forge heavily substituted peptide analogues containing aryl, heteroaryl and alkyl ketone residues.

The protocol relies on the introduction of a pyridine-containing group upon a Cu-catalyzed O-arylation of the corresponding Tyr unit within a peptide setting. The latter pyridyl ether motif (OPy) directs the subsequent *ortho*-C-H acylation in a selective fashion featuring the use of an aqueous solution of inexpensive *tert*-butyl hydroperoxide (TBHP) and a wide range of readily available aldehydes.

INDICATION

- Compatible with water as the sole solvent.
- Chemoselective towards Tyr units.
- Inexpensive oxidant & aldehydes.
- Scalable.
- Operational simplicity.
- Pd-catalyzed.

NOVELTY/ADVANTAGE

This procedure represents an unprecedented late-stage avenue for the straightforward assembly of non-natural Tyr-containing peptides, which often exhibit enhanced biological activities and improved pharmacokinetics compared with their native counterparts. The tolerance of the method with an aqueous environment is a salient feature of utmost significance toward protein engineering and bioconjugation. The compatibility of this C-H acylation platform with a number of oligopeptides of high structural complexity illustrates its many opportunities within the drug discovery space. Collectively, the library of oligopeptides rapidly assembled illustrates the vast potential of our catalytic manifold to introduce ketone motifs in a late-stage fashion to furnish densely decorated Tyr-containing peptides, thus providing access to new peptide entities beyond those found in native proteins.

EHU
Euskal Herriko Unibertsitatea
Universidad del País Vasco

Research group:
Sustainable Catalysis.

Main researcher:
Arkaitz Correa Navarro.

Contact:
Knowledge/Technology Transfer Office, iproperty.otri@ehu.eus

IPR STATUS

Patent Filling:
P202030131, PCTEP2021053723 (Granted)

Priority date:
17/02/2020

Applicant:
University of the Basque Country (EHU).

STAGE OF DEVELOPMENT

TRL4

COOPERATION GOAL

License agreement