Beijing Dilun Biotechnology Co., Ltd.
Specializes in R&D and manufacturing of peptide synthesis equipment, providing comprehensive technical solutions and services.
Web: www.peptidescientific.com. Email: chengchao.wei@dilunbio.com

Novel Hydrophobic Anchor for Efficient Liquid-Phase Peptide Synthesis

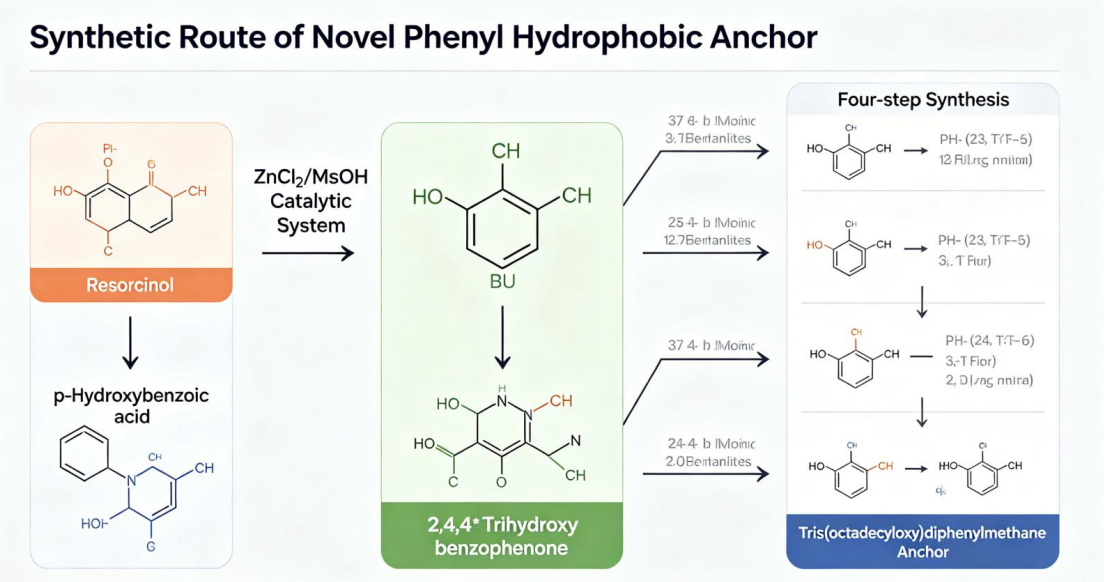
1.Research Background

Solid-phase peptide synthesis dominates mainstream peptide production, yet traditional liquid-phase synthesis (LPPS) is more cost-effective and easy to scale up, limited mainly by hard-to-remove intermediate impurities and cumbersome multi-step purification. Soluble hydrophobic anchor technology solves the above pain points: peptides bind onto lipophilic carriers to dissolve in low-polar organic solvents, and crude peptide can be precipitated out by adding polar solvent after each reaction cycle, drastically simplifying post-processing. Existing commercial long-chain alkoxy anchor has poor solubility in mixed solvent systems, restricting large-batch production of C-terminal amide peptides such as oxytocin and enkephalin. Against this backdrop, researchers develop a brand-new tris(octadecyloxy)benzophenone-derived anchor to upgrade LPPS practicability.

2.Research Purpose and Significance

The research first establishes a one-pot green synthetic route for

polyhydroxybenzophenone intermediates with $ZnCl_2$ /MsOH catalytic system without hydroxyl protection steps, then synthesizes novel phenyl-based hydrophobic anchor, compares its solubility with classic reference anchor under varied temperature and solvent conditions, and verifies application capacity via synthesis of Leu-enkephalin and oxytocin. The optimized anchor and synthetic process cut overall production cost of C-amidated bioactive peptides, provide mature technical route for industrial liquid-phase production of hormone peptide raw drugs.



3.Research Content

First, the team optimizes Friedel-Crafts reaction parameters including catalyst dosage, solvent amount and reaction temperature, realizing one-step preparation of multiple polyhydroxybenzophenone products without hydroxyl protection and deprotection, target products get high purity after simple water recrystallization, and the catalytic system features broad substrate compatibility. Based on core intermediate 2,4,4'-

trihydroxybenzophenone, four-step synthesis is carried out to obtain target tris(octadecyloxy) diphenylmethane anchor. Solubility test proves the new anchor has dramatically superior solubility than conventional docosyl-substituted counterpart: in DCM/DMF (9:1) mixed solvent at 40 °C, solubility is over 1000 times higher, which enables homogeneous peptide coupling under mild reaction condition. Afterwards, researchers adopt this anchor to synthesize Leu-enkephalin and oxytocin following standard Fmoc peptide assembly rules; after TFA cleavage and air oxidation for disulfide ring closure, target peptides reach qualified HPLC purity, confirming the anchor ' s reliable performance for practical peptide manufacturing.

4.Conclusion & Outlook

The newly developed benzophenone-type hydrophobic anchor possesses outstanding solvent solubility and chemical stability, the matched catalyst system realizes straightforward preparation of polyhydroxybenzophenone precursors, and successful synthesis of two classic bioactive peptides verifies its industrial application value; going forward, the research team will further modify anchor molecular structure to expand solvent adaptability, enrich applicable peptide types including cyclic peptide and long-chain therapeutic peptide, continuously optimize process parameters to reduce raw material consumption and impurity generation, accelerate the industrial promotion of liquid-phase peptide

synthesis technology for various polypeptide API production.