SOLID PHASE PEPTIDE SYNTHESIS PROCESSES AND ASSOCIATED SYSTEMS

RELATED APPLICATIONS

This application is a continuation-in-part of U.S. Patent Application Serial No. 13/833,745, filed March 15, 2013, and entitled "Solid Phase Peptide Synthesis Processes and Associated Systems," which is incorporated herein by reference in its entirety for all purposes.

TECHNICAL FIELD

Systems and processes for performing solid phase peptide synthesis are generally described.

BACKGROUND

Solid phase peptide synthesis is a process used to chemically synthesize peptides on solid supports. In solid phase peptide synthesis, an amino acid or peptide is bound, usually via the C-terminus, to a solid support. New amino acids are added to the bound amino acid or peptide via coupling reactions. Due to the possibility of unintended reactions, protection groups are typically used. To date, solid phase peptide synthesis has become standard practice for chemical peptide synthesis. The broad utility of solid phase peptide synthesis has been demonstrated by the commercial success of automated solid phase peptide synthesizers. Though solid phase peptide synthesis has been used for over 30 years, fast synthesis techniques have not yet been developed. Accordingly, improved processes and systems are needed.

SUMMARY

Solid phase peptide synthesis processes and associated systems are generally described. Certain examples relate to systems and methods which can be used to perform solid phase peptide synthesis quickly while maintaining high yield. In some examples, reagents can be heated, transported, and/or mixed in ways that reduce the amount of time required to perform solid phase peptide synthesis. The subject matter of the present disclosure involves, in some cases, interrelated products, alternative solutions

to a particular problem, and/or a plurality of different uses of one or more systems and/or articles.

In some examples, a process for adding amino acid residues to peptides is provided. The process, in certain examples, comprises heating a stream comprising amino acids such that the temperature of the amino acids is increased by at least about 1 °C; and exposing the heated amino acids to a plurality of peptides immobilized on a solid support, wherein the heating step is performed prior to and within about 30 seconds of exposing the heated amino acids to the peptides.

In one aspect, there is provided a process for adding amino acid residues to peptides, comprising: heating a stream comprising amino acids such that the temperature of the amino acids is increased by at least about 1 °C; and exposing the heated amino acids to a plurality of peptides immobilized on a solid support, wherein the heating step is performed prior to and within about 30 seconds of exposing the heated amino acids to the peptides.

In certain examples, the process comprises providing a plurality of peptides comprising protection groups, each peptide immobilized on a solid support; performing a first amino acid addition cycle comprising exposing amino acids to the immobilized peptides such that an amino acid residue is added to at least about 99% of the immobilized peptides; and performing a second amino acid addition cycle comprising exposing amino acids to the immobilized peptides such that an amino acid residue is added to at least about 99% of the immobilized peptides. In some examples, the total amount of time between the ends of the first and second amino acid addition cycles is about 10 minutes or less and the protection groups comprise fluorenylmethyloxycarbonyl protection groups and/or the total amount of time between the ends of the first and second amino acid addition cycles is about 5 minutes or less.

In certain examples, the process comprises providing a plurality of peptides immobilized on a solid support; and exposing activated amino acids to the immobilized peptides such that at least a portion of the activated amino acids are bonded to the immobilized peptides to form newly-bonded amino acid residues; wherein an amino acid residue is added to at least about 99% of the immobilized peptides within about 1 minute or less.

In certain examples, the process comprises flowing a first stream comprising amino acids; flowing a second stream comprising an amino acid activating agent; merging the first and second streams to form a mixed fluid comprising activated amino acids; and within about 30 seconds after merging the first and second streams to form the mixed fluid, exposing the mixed fluid to a plurality of peptides immobilized on a solid support.

In certain examples, the process comprises providing a plurality of peptides comprising protection groups, each peptide immobilized on a solid support; exposing a

deprotection reagent to the immobilized peptides to remove protection groups from at least a portion of the immobilized peptides; removing at least a portion of the deprotection reagent; exposing activated amino acids to the immobilized peptides such that at least a portion of the activated amino acids are bonded to the immobilized peptides to form newly-bonded amino acid residues; and removing at least a portion of activated amino acids that do not bond to the immobilized peptides. In some examples, an amino acid residue is added to at least about 99% of the immobilized peptides during the amino acids exposing step. In certain examples, the total amount of time taken to perform the combination of all of the deprotection reagent exposing step, the deprotection reagent removal step, the activated amino acid exposing step, and the activated amino acid removal step is about 10 minutes or less and the protection groups comprise fluorenylmethyloxycarbonyl protection groups and/or the total amount of time taken to perform the combination of all of the deprotection reagent exposing step, the deprotection reagent removal step, the activated amino acid exposing step, and the activated amino acid removal step is about 5 minutes or less.

Other advantages and novel features of the present disclosure will become apparent from the following detailed description of various non-limiting examplesof the disclosure when considered in conjunction with the accompanying figures. In cases where the present specification and a document incorporated by reference include conflicting and/or inconsistent disclosure, the present specification shall control.

BRIEF DESCRIPTION OF THE DRAWINGS

Non-limiting embodiments of the present invention will be described by way of example with reference to the accompanying figures, which are schematic and are not intended to be drawn to scale. In the figures, each identical or nearly identical component illustrated is typically represented by a single numeral. For purposes of clarity, not every component is labeled in every figure, nor is every component of each embodiment of the invention shown where illustration is not necessary to allow those of ordinary skill in the art to understand the invention. In the figures:

FIG. 1 is a schematic illustration of a system for performing peptide synthesis, according to one set of embodiments;

FIGS. 2A-2D are, according to certain embodiments, (A) an exemplary schematic diagram of a peptide synthesis system, (B) a photograph of an exemplary peptide

CLAIMS

1. A process for adding amino acid residues to peptides, comprising:

heating a stream comprising amino acids such that the temperature of the amino acids is increased by at least about 1 °C; and

exposing the heated amino acids to a plurality of peptides immobilized on a solid support,

wherein the heating step is performed prior to and within about 30 seconds of exposing the heated amino acids to the peptides.

2. The process of claim 1, wherein the solid support comprises polystyrene and/or polyethylene glycol.

3. The process of claim 1, wherein the solid support comprises a resin.

4. The process of claim 3, wherein the solid support comprises a microporous polystyrene resin.

5. The process of claim 1, wherein the solid support is contained within a packed column and/or a fluidized bed.

6. The process of claim 1, wherein an amino acid residue is added to at least about 99% of the immobilized peptides after exposing the heated amino acids to the immobilized peptides.

7. The process of claim 1, wherein multiple copies of the amino acid residue are bonded to fewer than about 1% of the immobilized peptides after exposing the heated amino acids to the immobilized peptides.

8. The process of claim 6, wherein adding an amino acid residue to the immobilized peptides comprises adding a single amino acid residue to the immobilized peptides.

9. The process of claim 6, wherein adding an amino acid residue to the immobilized peptides comprises adding a peptide comprising two or more amino acid residues to the immobilized peptides.

10. The process of claim 1, wherein the amino acids comprise activated amino acids.

11. The process of claim 1, wherein the amino acids comprise protection groups.

12. The process of claim 11, wherein amine groups of the amino acids are protected.

13. The process of claim 11, wherein the protection groups comprise fluorenylmethyloxycarbonyl protection groups.

14. The process of claim 11, wherein the protection groups comprise tert-butyloxycarbonyl protection groups.

15. The process of claim 11, wherein the protection groups comprise allyloxycarbonyl protection groups.

16. The process of claim 11, wherein the protection groups comprise carboxybenzyl protection groups.