Novel method to Efficiently Synthesize complex Carbohydrates

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ABSTRACT

Tumor Associated Carbohydrate Antigens (TACAs), have been in great demand due their use as target therapies and industrial relevance. Unfortunately, P^k trisaccharide, the precursor to the globo series of TACAs requires eleven steps to synthesize using current technologies, seven of which are used to develop an orthogonally protected lactose. This is a very costly and painstaking process. Researchers at the University of California, Davis, have developed a two-step method to synthesize orthogonally protected lactose from commercially available lactose, and a three step method to synthesize P^k, providing economic relief and time saving benefits for consumers and manufacturers of TACAs.

FULL DESCRIPTION

Lactose is a core structural unit of many complex carbohydrates including the globo series of tumor associated carbohydrate antigens (TACAs). Globotriaosyl ceramide (Gb3), Gb5, and Globo-H all share the structural feature resulting from galactosylation of the 4' hydroxyl of lactose giving rise to P^k trisaccharide. The carbohydrate backbone of P^k trisaccharide has attracted the attention of synthetic chemists, since most, if not all, synthesis of globo series intercept variously protected versions of the trisaccharide at some point during the synthesis. Currently, the gold standard requires a total of eleven steps, from commercially available lactose, for the synthesis of P^K, seven of these steps were focused on orthogonally protecting lactose for 4' galactosylation. In fact, all previously reported chemical syntheses of P^k trisaccharide require between 6-12 steps to prepare the lactosyl acceptor.

Researchers at the University of California, Davis have demonstrated that per-*O*-silylated monosaccharides undergo regioselective exchange of silicon for acyl protecting groups providing useful building blocks for organic synthesis in a single step. This ReSET technology has also been applied to disaccharides. The protecting groups are carefully selected such that they offset a glycosidic cleavage due to hydrolysis. The process not only results in the generation of orthogonally protected carbohydrates, but also circumvents the well documented problem of trans-acetylation associated with partially acylated pyranosides.

As opposed to using either alkyl glycosides or unfunctionlized sugars, the present invention is based on the selective exchange of electron donating trimethyl silyl ether moieties in protected disaccharide substrates to electron-withdrawing acetyl protecting groups. The extraordinary reactivity allows for the rapid preparation of carbohydrate derivatives such as orthogonally 4'- protected lactose, which can be readily transformed into P^k trisacharide. As such, the invention meets a long-standing need for synthetic intermediates that can be used for the protection of biologically and industrially important carbohydrate compounds.

APPLICATIONS

- Method to efficiently develop orthogonally protected lactose for use as therapeutics or research purposes
- Synthesis of biologically relevant complex glycosides that could ultimately be useful as therapeutic drugs

FEATURES/BENEFITS

- Quick. Easy, and Fast method to make orthogonally protected carbohydrates
- Environmentally friendly inexpensive method to develop otherwise costly materials

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	10,759,823	09/01/2020	2013-277
United States Of America	Issued Patent	10,100,074	10/16/2018	2013-277

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OTHER INFORMATION

KEYWORDS

TACA

CATEGORIZED AS

- **Biotechnology**
  - Health
  - Industrial/ Energy
- **Materials & Chemicals**
  - Biological
  - Chemicals
  - Polymers
- **Medical**
  - Disease: Cancer
  - New Chemical Entities, Drug Leads
  - Research Tools
  - Screening
  - Therapeutics
- **Research Tools**
  - Antibodies
  - Reagents

RELATED CASES

2013-277-0

- Method of Preparing Multivalent Single Chain Antibodies (scFv)
- Synthesis of Immunopotent Alpha Glycolipids via Glycosyl Iodides
- High-Throughput Screening of Neuraminidase Inhibitors
- Camellia Sinesis Rapid Growth Platform

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