Synthesis of Immunopotent Alpha Glycolipids via Glycosyl Iodides

Tech ID: 11301 / UC Case 2007-551-0

ABSTRACT

One-pot Synthesis for alpha glycolipids and their analogs using glycosyl iodide donors.

FULL DESCRIPTION

Alpha glycolipids have shown potent anti-tumor and anti-viral activities as well as potential for the treatment of certain autoimmune disorders via Natural Killer T (NKT) cell activation. Already in Phase I clinical trials for a variety of disease treatments that include cancer and diabetes, the structure of the glycolipid dictates the type as well as the extent of immunological activity.

Beta-linked glycolipids play important roles in various biological processes via lipid rafts (highly ordered structural domains serve as anchoring platforms for extracellular proteins). While some beta-linked glycolipids are commercially available, they are typically obtained from bovine brains and are sold as mixtures with respect to the lipid component making definitive and reproducible results sometimes problematic.

Current synthetic protocols afford either alpha/beta product mixtures, lack efficiency, or are limited by the reactivity of the reaction components. A readily accessible library of these alpha glycolipids is desirable for drug discovery and development while the stereoselective synthesis of pure beta-linked glycolipids is of great importance in understanding these and other biological processes.

Researchers at the University of California, Davis have developed novel glycosyl iodide chemistry for the fast, efficient, and stereoselective syntheses of alpha and beta linked glycolipids. This technology utilizes glycosyl iodides as donors and involves subsequent reaction with fully functionalized lipid acceptors in a one-pot endeavor.

APPLICATIONS

- Synthesis of libraries of alpha or beta-linked glycolipids
  - Alpha glycolipids - study of NKT activation, the immune response pathway, and clinical application for disease treatment
  - Beta glycolipids - study of cell-cell interactions as well as disease infection and progression.

FEATURES/BENEFITS

- Highly stereoselective and efficient
- Yields over 90%
- Exclusive formation of alpha glycolipids
- Beta glycolipids can also be synthesized in a stereoselective manner
- Does not require neighboring group participation, eliminates the numerous steps required for the installation and subsequent removal of protecting groups
- Mild reaction conditions which tolerate sensitive functionalities such as amides, esters and olefins

RELATED MATERIALS

- Sriram V, Du W, Gervay-Hague J & Brutkiewicz RR. 2005. Cell wall glycosphingolipids of Sphingomonas paucimobilis are CD1d-specific ligands for NKT cells. Eur J Immunol. 35(6):1692-701.
- Du W & Gervay-Hague J. 2005. Efficient synthesis of alpha-galactosyl ceramide analogues using glycosyl iodide donors. Org Lett. 7(10):2063-5.
- Du W, Kulkarni SS & Gervay-Hague J. 2007. Efficient, one-pot syntheses of biologically active alpha-linked glycolipids. Chem Commun (Camb). (23):2336-8.
- Brutkiewicz RR, Willard CA, Gillett-Heacock KK, Pawlak MR, Bailey JC, Khan MA, Nagala M, Du W, Gervay-Hague J & Renukaradhya GJ. 2007. Protein kinase C delta is a critical regulator of CD1d-mediated antigen presentation. Eur J Immunol. 37(9):2390-5.

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OTHER INFORMATION

KEYWORDS

alpha glycolipids, glycosyl, glycosyl iodides, natural killer T cells, NKT

CATEGORIZED AS

- **Medical**
  - Disease: Cancer
  - Therapeutics
- **Research Tools**
  - Reagents

RELATED CASES

2007-551-0, 2007-551-1, 2007-551-2

▶ Webb TJ, Litavecz RA, Khan MA, Du W, Gervay-Hague J, Renukaradhya GJ & Brutkiewicz RR. 2006. Inhibition of CD1d1-mediated antigen presentation by the vaccinia virus B1R and H5R molecules. Eur J Immunol. 36(10):2595-600.

▶ Renukaradhya GJ, Webb TJ, Khan MA, Lin YL, Du W, Gervay-Hague J & Brutkiewicz RR. 2005. Virus-induced inhibition of CD1d1-mediated antigen presentation: reciprocal regulation by p38 and ERK. J Immunol. 175(7):4301-8.

▶ Renukaradhya GJ, Sriram V, Du W, Gervay-Hague J, Van Kaer L & Brutkiewicz RR. 2006. Inhibition of antitumor immunity by invariant natural killer T cells in a T-cell lymphoma model in vivo. Int J Cancer. 118(12):3045-53.

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	9,586,984	03/07/2017	2007-551
United States Of America	Issued Patent	8,624,006	01/07/2014	2007-551

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Novel method to Efficiently Synthesize complex Carbohydrates
- Camellia Sinesis Rapid Growth Platform

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