[S4-2] [4/19/2002(Fri) 10:25-10:50/Hall B]

A Study on the Chemical Synthesis of Tetrasaccharide, Glc*N*Ac*p*-β-D-(1→3)-Gal*p* α-D-(1→2)-*alt*Hep*p*- α -D-(1→3)-Glc*N*Ac*p*-(1→*O*-chloroethyl, an *O*-Antigenic Repeating Unit from *C. jejuni* O:23 and O:36

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Campylobacter jejuni (*C. jejuni*) is a leading cause of acute gastroenteritis in humans and is increasingly recognized for its association with neurological complications of the Miller-Fisher (MFS) and Guillain-Barre syndromes (GBS) [1-5]. According to the genetic and biochemical studies of a *C. jejuni* lipopolysaccharide (LPS) biosynthesis, the differences in chemical structure of high-molecular-weight (HMW) LPS may be the importance factor in the development of GBS[6,7].

The chemical structure of LPS from several *C. jejuni* serotypes were elucidated by Aspinall *et al.*[8,9]. Particularly, *C. jejuni* serotypes O:23 and O:36 were known to contain HMW LPS, which include trisaccharide repeating units with three altroheptose variants. It was suggested that these heptose components must be related to serotypic discrimination, evading the immune response of the host, and permitting the infection to continue. In order to evaluate the immunological specificity and elucidate the role of *altro*heptopyranosyl residues in serotypic differences, it is necessary to synthesis various oligosaccharides containing the repeating unit of *C. jejuni* serotypes O:23 and O:36. Furthermore, oligosaccharides containing altroheptose are rarely found, and their synthesis must be an attractive challenge for a synthetic chemist.

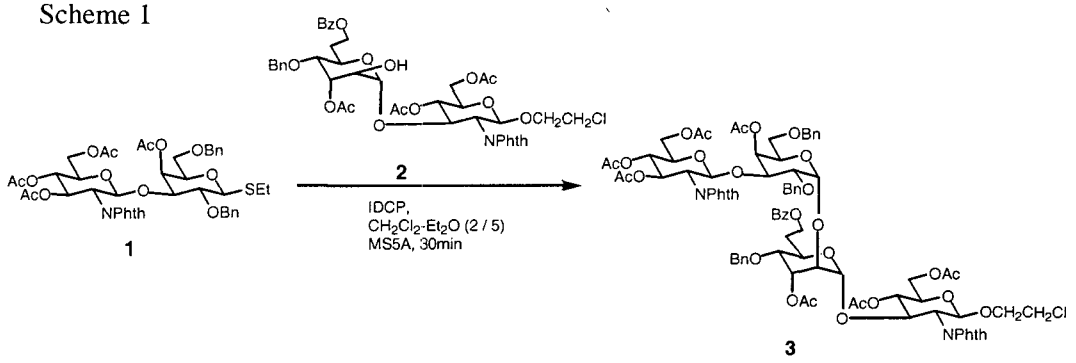
This report describes the stereoselective synthesis of tetrasaccharide as its corresponding chloroethyl glycoside, Glc*N*Ac*p*-β-D-(1→3)-Gal*p*-α-D-(1→2)*alt*hep*p*-α-D-(1→3)-Glc*N*Ac*p*-(1→*O*-chloroethyl (scheme 1). Tetraccharide 3 can be divided into two synthetic building blocks, a thio-glycosyl donor **1** and acceptor **2**. The ethylthio 4-*O*-acetyl-2, 6-di-*O*-benzyl-3-*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-*N*-phthalimido-β-D-glucopyranosyl)-β-D-galactopyranoside donor **1** was obtained by regio and stereoselective coupling of 3,4,6-tri-*O*-acetyl-*N*-phthalimido-D-glucopyranosyl bromide and ethylthio 2,6-di-*O*-benzyl-α-D-galactopyranoside in the presence of silver triflate, s-collidine, and molecular sieve (4 Å) in CH_2Cl_2 at -25℃ followed by acetylation of 4-OH by treating acetanhydride.

The 2'-cloroethyl *O*-(7-*O*-benzoyl-4-*O*-benzyl-6-deoxy-α-D-altroheptopyranosyl)-(1→3)-4,6-*O*-di-*O*-acetyl-2-deoxy-2-*N*-phthalimido-β-D-glucopyranoside donor **2**, which has an α-altro

glycosidic linkage, was efficiently synthesized by converting the configuration of 3-OH of the disaccharide product prepared from the coupling between ethylthio 2-*O*-allyl-7-*O*-benzoyl-4-*O*-benzyl-6-deoxy-3-*O*-*p*-methoxybenzyl-α-D-mannoheptopyranoside and 2'-chloroethyl 4,6-*O*-benzylidene-2-deoxy-2-*N*-phthalimido-β-D-glucopyranoside with IDCP as a promotor.

Finally, **1** and **2** was coupled in the presence of IDCP, and titled tetrasaccharide **3** was obtained in 68% yield.

Scheme 1



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