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学 位 論 文 要 旨

氏名： YI RUIQIN

題目：The synthetic study of inner-core oligosaccharides of lipopoly- and lipooligosaccharides produced by gram-negative bacteria: Construction of 4,5-branched 3-deoxy-D-*manno*-oct-2-ulosonic acid structure

（グラム陰性菌が産生するリポ多糖およびリポオリゴ糖の内部コア糖鎖の合成研究：4, 5で分岐した3-デオキシ-D-マンノオクト-2-ウロン酸の構築）

Lipopolysaccharides (LPSs) and lipooligosaccharides (LOSs) are the major glycolipds expressed in the outer membrane of gram-negative bacteria and play an important role in the pathogenesis of bacterial infections. LPS is composed of O-specific polysaccharide, a core oligosaccharide (core OS), and lipid A, whereas LOS lacks an O-antigen. The core OS, which is a significant target for vaccine development and diagnostics of pathogenic bacteria, can be further subdivided into the inner core and outer core. The inner core is composed of branched 3-deoxy-D-*manno*-2-octulosonic acid (Kdo) structures. However, there are few reports about the synthesis of branch Kdo structure. To synthesize this branch Kdo structure and extend our previous research, a new synthetic approach was developed.

In this study, chapter 2 described the synthesis of 2–4 linked Kdo disaccharide; chapter 3 showed a new synthetic approach to synthesize 4,5-branched Kdo trisaccharides using Kdo disaccharide as an acceptor; in chapter 4 more complex 4,5-branched Kdo structures were synthesized by using the same Kdo disaccharide as the acceptor; chapter 5 showed the conclusions.

In chapter 2, 2-4 linked Kdo disaccharide was obtained by glycosylation of glycosyl donor with 4,5-diol acceptor. To optimize the condition of this reaction, several types of glycosyl donors with different leaving groups were prepared from common

Kdo intermediate and were glycosylated with 4,5-diol acceptor. The results showed that all donors produced the α-glycoside as the main product and the stereoselectivity was not influenced by the type of leaving group. Moreover, the α-fluoride donor with $BF_3 \cdot OEt_2$ as the activator provided the best yield and α-selectivity of product.

In chapter 3, Kdo(α2-4)Kdo as an acceptor was glycosylated with L-*glycero*-D-*manno*-heptosyl, mannosyl, and 2-azido-2-deoxy-galactosyl imidates, respectively, and three corresponding 4,5-branched trisaccharides, Hep(α1-5)[Kdo(α2-4)]Kdo, Man(α1-5)[Kdo(α2-4)]Kdo and $GalN_3$(α1-5)[Kdo(α2-4)]Kdo, were successfully synthesized in good yield and high α-selectivity. These results confirmed that glycosylation at the 4-OH position of the Kdo acceptor followed by a second glycosylation at 5-OH position could produce the target 4,5-branched Kdo structures and this new synthetic strategy is different from Paulsen's method.

In chapter 4, to extend the utility of the new synthetic strategy, more complex 4,5-branched Kdo structures were synthesized by using the same Kdo disaccharide as the acceptor. To do it, firstly the L-*glycero*-D-*manno*-heptopyranose (Hep) units for the branched core oligosaccharide Ga(β1-4)Glc(β1-4)Hep and Hep(α1-3)Hep were prepared from the corresponding Hep building blocks. Then, the Hep units were glycosylated with the common acceptor Kdo(α2-4)Kdo to afford 4,5-branched core oligosaccharide structures. Three complex 4,5-branched inner-core OSs, Hep(α1-3)Hep(α1-5)[Kdo(α2-4)]Kdo, Gal(β1-4)Glc(β1-4)Hep(α1-5)[Kdo(α2-4)]Kdo and Gal(β1-4)Glc(α1-5)[Kdo(α2-4)]Kdo were successfully obtained.

In all, the new synthetic approach using Kdo(α2-4)Kdo as an intermediate is useful for the synthesis of 4,5-branched core OS structures including Kdo trisaccharides, Kdo tetrasaccharides and Kdo pentasaccharide.