8. Summary

The goal of this work was to investigate synthetic applications of the Claisen rearrangement to carbohydrate chemistry. To this end, syntheses of carbohydrate structures bearing a methylene group at the C-1 and C-6 positions were developed. Several synthetic pathways were investigated in the case of glucose. Initially, an allyl group was used to protect the 1-position and the moieties at the 6-position were varied. Benzylidene, *tert*-butyldiphenylsilyl and trityl protecting groups were each used to mask the glucopyranosyl C-6 position. The allyl group was cleaved from the benzylidene derivatives **85** and **86** under basic oxidative conditions, giving compound **87**, which could be converted to lactone **88** and then to enol ether **89**, by treatment with pyridinium chlorochromate. Opening the benzylidene ring of **89** did not lead to the expected enol ether **90** with a free 6-hydroxyl group, but rather to the *C*-glycoside **91**. The structure of this compound could be assigned using ^{1}H, ^{13}C and HMBC NMR experiments.

One variation of the synthetic pathway involved first deprotecting and modifying the 6-position. To this end, the benzylidene derivatives **85** and **86** and the tritylated compound **114** were converted to the deprotected compound **115**. Oxidation by treatment with dicyclohexylcarbodiimide and dimethylsulfoxide and olefination with triphenylphosphonium bromide and sodium amide lead to the formation of compound **117** in good yields. The deprotection of this substance with palladium(II)chloride under acid catalysis resulted in the cyclohexanone derivative **119**. The structural analysis of this compound involved ^{1}H and ^{13}C NMR experiments as well as MALDI-TOF mass spectroscopy. To determine whether or not the palladium/H^{+} system could catalyse a reaction analogous to a Ferrier-II rearrangement, the methyl glycoside **130**, which is analogous to compound **117**, was synthesised. All that could be observed in the case of compound **130** was the formation of the acetal. However, successful reaction using the palladium/H^{+} system could be observed when the starting material exhibits an unprotected 1-position, as in compound **117**. This is the first reported Ferrier-II analagous reaction of a compound possessing a methyl group at the 6-position such as **117**, which leads to a stereochemically pure product, in this case to compound **119**. The results achieved upon employment of the allyl protecting group made a change of the protecting group for the 1-position necessary.

One alternative was the use of the thioglycoside, thus a synthesis of the 6-unprotected thioglycoside **139**, made from glucose, was developed. This compound was thus available via both the benzylidene-masked derivate **138** and the trityl-protected compound **141**. With an

overall yield of 24%, the synthetic pathway using the trityl protecting group was superior and therefore preferable to the benzylidene protecting group alternative. Oxidation of the 6-position of **139** to aldehyde **142** by treatment with pyridinium chlorochromate was conducted in good yields. Subsequent Wittig olefination could be performed under standard conditions or by application of the ready-made reagent mixture (methyltriphenylphosphonium bromide/sodium amide). The yields in both instances were almost identical. Hydrolysis of the thioglycoside **143** was achieved using NBS and water, leading to compound **144**, which was unprotected at the 1-position. Oxidation and olefination with the Tebbe reagent gave the 1,7-octadienitol **146**. This could be converted to the chiral cyclooctenone **147** via a Claisen rearrangement. The structural analysis of **147** was performed using ^{1}H, ^{13}C and NO NMR spectroscopy as well as MALDI-TOF mass spectroscopy. Compound **147** exists in a boat-chair conformation.

An alternative synthetic pathway, which does not begin with glucose, involved application of the commercially available gluconic acid δ-lactone. This compound already has a carbonyl group at the 1-position. Synthesis of the enol ether **152** via the TMS-protected derivative proceeded in good yields. However, it was not possible to reach the completely protected compound **153**.

The synthesis of compound **178** began with galactose. The double bond at the 6-position was introduced early in the synthesis via the isopropylidene derivative **157**. To protect the 1-position, a TBDPS group was used. During the introduction of the benzyl ether protecting groups, the TBDPS group is cleaved and furanoside **171** was obtained and subjected to structural analysis with ^{1}H, ^{13}C and NO NMR and MALDI-TOF mass spectroscopy. One alternative synthesis involved employment of thioglycoside **170** as starting material. For the synthesis of **178**, the same reactions were applied as for the glucose derivative. During the thermal Claisen rearrangement, both the formation of the cyclooctenone **178** and the addition of water to the double bond at the 1-position could be observed. Structural analysis of the chiral cyclooctenone system was performed using ^{1}H, ^{13}C and NO NMR and MALDI-TOF mass spectroscopy. According to these results this compound was not present in a boat-chair conformation, but rather in a slightly skewed boat conformation. This clearly shows that the system reacts to a change of configuration at only one centre – the 4-position – in comparison to the glucose derivative – with a change in conformation.

The experience gathered during syntheses of the glucosyl and galactosyl derivatives could be applied to the synthesis of the manno-configured cyclooctenone system **192**. Thus, the trityl group was employed to selectively protect the 6-position, the thioglycoside was used as the

starting material and the same reactions and reagents as for the analogous glucosyl and galactosyl derivatives could be applied.

For the oxidation, application of pyridinium chlorochromate proved to be most advantageous. With this reagent, both the aldehyde at the 6-position and the lactone at the 1-position could be obtained. Olefination at the 6-position could be achieved using the ready-made reagent (methyltriphenylphosphonium bromide/sodium amide) in good to very good yields. For the olefination at the 1-position, the Tebbe reagent was ideal in all systems investigated. Thus, by applying these reactions, the chiral cyclooctenone **192** was obtained. The structure of this target moleule was established with ^{1}H, ^{13}C and NO NMR spectroscopy as well as MALDI-TOF mass spectroscopy. This molecule was present in the boat-chair conformation, as was compound **147**. Variation of the configuration at the 2-position (as compared to the glucose analogue) does not lead to a conformational change of the system in this instance.