Sometimes chemo- and bio-catalysis are in open competition (C_1-oxidation and -dehydrogenation, C_2-oxidation), in other oxidations (e.g. glycolic splitting) the choice is limited.

In carboxy-alkylation direct methods (carboxymethylation) as well as indirect routes (e.g. via the nitrile) are applied. This will be exemplified for inulin and model compounds.

Finally, anhydrides may be used to attach carboxylate groups to carbohydrates. As an example the addition of D-glucamine to DTPA-bisanhydride will be obtained. The Gd(III)-complex of the tricarboxylate obtained may serve as MRI contrast agent.

Quantification of Arabinose in Pectic Polysaccharides by FT-IR spectroscopy

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The sequential extraction of the cell wall material (CWM) of olive and orange pulps and its subsequent fractionation by ethanol precipitation and anion-exchange chromatography gave a wide range of fractions rich in cell wall polysaccharides. The fractions rich in pectic polysaccharides are characterized by the presence of uronic acid, rhamnose, arabinose and galactose monosaccharides released by acid hydrolysis. The FT-IR spectra in the 1200–850 cm^{-1} region allows the prediction of the amount of arabinose, as a molar percentage of the total sugars, in the pectic polysaccharide samples of the two distinct fruits. Regression models for the arabinose content were constructed. In order to highlight the selective wavenumbers for the determination of the arabinose present in the pectic polysaccharides, a selection of variables was made based on a mathematical method that uses the signal to noise ratio and a PLSI regression procedure. For the olive samples, the relevant wavenumbers, in decreasing order of importance, are: 1111, 1107, 1049, 1069, 1065, 1045, 1103, 1053, 1115, 1146, 1061, 1014, 1057 cm^{-1}; for the orange samples, the relevant wavenumbers are: 1049, 1065, 1115, 1045, 1061, 1053, 1041, 1111, 1057 cm^{-1}. For both systems, the absorbances in the regions 1115–1111 cm^{-1} and 1065–1045 cm^{-1} were found to be important for the prediction of the content of arabinose in the pectic samples. This study reports the potential of these regions to predict the amount of arabinose of pectic origin, as a quick evaluation, from different sources.

Recent Advances in the Synthesis of Carbohydrate Mimics

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C-disaccharides are close analogues of disaccharides in which the interglycosidic oxygen atom has been replaced by a methylene group. The major part of the lecture will deal with the detailed presentation of a flexible synthetic strategy based on a 8 or 9 *endo-trig* radical cyclisation reaction from two monosaccharides temporarily connected through a chemical tether. It will delineate the scope of the procedure, analyze variations on the theme, and describe some biological aspects.

Two novel reactions will also be described:

1. The one step stereoselective conversion of a sugar derivative into a highly substituted cyclopentane derivative.
2. The one step stereoselective conversion of a sugar derivative into a highly substituted cyclohexane derivative.

Sialyl Lewis^x and Synthetic Analogues Thereof as New Antiinflammatory Drugs

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Leukocyte influx from blood vessels into the surrounding tissue can be a beneficial response of the body to control infections and injuries. Excessive leukocyte influx, however, may result in an acute or chronic reaction as observed in reperfusion injuries or respiratory diseases.

The first step in the cascade of events which finally leads to the recruitment of leukocytes is their adhesion to the endothelial cell surface. It has been shown that an inducible set of calcium dependent adhesion molecules, the so-called selectins, are involved in this initial step. A possible strategy for preventing the negative effects of an excessive leukocyte influx is the inhibition of the leukocyte/selectin interactions. Therefore, intense efforts have been directed at defining the ligand of the three known selectins. It was found that the selectin ligands have a common epitope, which is the Sialyl Lewis^x tetrasaccharide.

Sialyl Lewis^x has served as a lead structure in our search for simplified and more potent selectin antagonists. Our strategy may be summarized as follows:

1. Elucidation of the structure/activity relationship of the lead structure (SAR study) and determination of its conformation bound to the selectin (bioactive conformation).
2. Development of molecular modeling tools for the rational design of new potential selectin antagonists.
3. Preparation of potential selectin antagonists by chemical and enzymatic synthesis.
4. Evaluation of the antagonists in appropriate *in vitro* assays (under static and flow conditions) and *in vivo* models (intravital microscopy, peritonitis).

Stereocommunication Through Glycosidic Linkages

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Glycosides are of paramount importance in chemistry and biology. They are ubiquitous in Nature and possess wide-ranging biological properties. Important low molecular weight glycosides include sucrose (a sweetening agent), digitoxin (a cardiotonic agent), streptomycin (an antibacterial agent) and adriamycin (an anticancer agent). Heightened by the discovery that glycoside domains of glyconjugates are involved in cell–cell, cell-bacterium and cell–virus interactions and the expectation that low molecular weight carbohydrate-related constructs may serve as drug-discovery leads, glycoside assembly is now a focus for synthetic chemists.

Glycosides with aglycones featuring stereogenic centres are traditionally assembled from sugars (in appropriately protected and anomerically activated forms) and aglycone alcohols (in protected forms if necessary). An alternative strategy, pursued in the author's group and the subject of this lecture, is the synthesis of glycosides with aglycone units that lack stereogenic centres and their subsequent elaboration into ones that possess them. Clearly, the success of such an approach depends critically upon the ability of the sugar units to

communicate stereoinformation to the diastereotopic faces of the aglycone units.

If diastereopure products emerge, an added opportunity becomes available. Because of their acetal nature, glycosidic linkages undergo hydrolysis under mildly acidic conditions. There is therefore the prospect of obtaining the free aglycone in a stereopure state. Overall, the sugar unit would fulfil a chiral auxiliary role and an enantioselective synthesis of the aglycone would be achieved. Because of the abundance, low cost and stereochemical variety of sugars, the technology could provide practical routes to enantiopure compounds, materials that are of particular importance to the pharmaceutical industry.

Glycosides derived from D-glucose – the cheapest monosaccharide available – will be the focus of this lecture. Specifically, the ability of the 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl unit to direct the facial reactivity of dienes in cycloaddition reactions (leading to the synthesis of anthracyclinones, monocarbadisaccharides, 5-arylpyranoses, disaccharides and piperazines) and of vinylogous esters/carbonates in hydrogenation, bromoalkoxylation and epoxidation reactions (leading to the synthesis of chirons bearing tertiary stereogenic centres with functional arms) will be addressed.

Stereoselective Synthesis of C-, S-, and N-glycosides of Therapeutic Potential from Levoglucosenone

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In continuing our research on the synthesis of (1-4)-inked C- and S- disaccharides from levoglucosenone, via Michael addition of nucleophiles, we expanded our study to other nucleophiles with strong reactivity. The advantage of the stereoselective, 1,4-addition is the exclusive formation of an *exo*-adduct *via* formation of the 1,4-C-linkage from the less hindered face of the molecule.

The shielding effect of the 1,6-anhydro bridge is sufficiently strong to direct any kind of nucleophilic attack exclusively from the *exo*-face of the molecule. The most direct way to prove the correct stereochemistry of the 1,4-adduct is to measure the coupling constants $J_{4,3ax}$ and $J_{4,3e}$, which are in the range 5.0–7.0 and 1.0–1.5 Hz respectively. Recently, we have demonstrated a facile procedure for the synthesis of (1-4)-S-thiodisaccharides. From the application of the procedure, we have achieved a facile systematic synthesis of a variety of other C-, S-, and N-disaccharides.

We now wish to present a new methodology of stereoselective synthesis of (1-2)-, S-, O-, linked disaccharides based on Michael addition carbohydrate thiols and other reactive nucleophiles to the new chiral synthon recently synthesized in our laboratory directly from levoglucosenone in three steps.

Stereoselective Synthesis of Optically Active, Highly Functionalized Carbocycles from Aldonolactones

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Highly functionalised cyclopentanes appear as structural elements in a number of biologically interesting compounds such as carbocyclic nucleosides, prostaglandines and glycosidase inhibitors. Our group has recently developed a short and efficient method for the stereo-selectively preparation of bicyclic cyclopentane derivatives from unsaturated bromodeoxy aldonolactones, which because of their bicyclic structure are versatile chiral synthons.

The bicyclic lactone 1(R),5(S)-7(R),8(R)-Dihydroxy-2-oxabicyclo[3.3.0]oct-3-one (**1**) can easily be prepared from commercially available D-*glycero*-D-*gulo*-heptone-1,4-lactone in five steps. Conversion of the diol **1** to the bromohydrin 1(R),5(R)-7(S)-Bromo-8(S)-hydroxy-2-oxabicyclo[3.3.0]oct-3-one (**2**) was regio- and stereospecifically performed in high yield using HBr/HOAc. Using **2** as the key synthon, amino hydroxy substituted bicyclic lactones could be obtained, either by reaction of **2** with ammonia or azide ions, or by conversion of **2** to the epoxide 1(R),5(S)-7(R),8(R)-Epoxy-2-oxabicyclo[3.3.0]oct-3-one (**3**). The latter in turn yielded similar products by regioselective opening with ammonia or with acetonitrile in the presence of BF_3 OEt_2 in a Ritter-type reaction. Furthermore the epoxide **3** could regioselectively be opened to a trans diol. Subsequent reduction of the lacton ring gave the substituted cyclopentanes 5-Deoxycarba-β-L-*xylo*-hexofuranose, 1-Amino-1,5-dideoxycarba-β-L-*xylo*-hexofuranose, tosylate, and 1-Amino-1,5-dideoxycarba-α-L-*xylo*-hexofuranose, tosylate. The compounds can be viewed as sugar mimics, and amino hydroxy cyclopentanes has been found to be glycosidase inhibitors.

Studies on the Structure of Glycoproteins

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Glycoproteins consist of a protein chain to which one or more carbohydrate chains are covalently attached. The carbohydrates are usually connected through N- or O-linkages, but also other types occur like C-glycosyl. In nature glycoproteins have a wide variety of biological functions. These functions may be dependent on the protein part, the carbohydrate part or on both. The most difficult aspect of the role of such compounds is the understanding of the structure-function relationship. This is in particular true for the carbohydrate moieties. The same glycan structure may be found on different glycoproteins, but involved in different types of function. The same glycoprotein can exhibit glycosylation patterns that change with the developmental stage of cell or organism. Our studies on Tamm-Horsfall glycoprotein have shown that an enormous amount of glycan structures occurs, even when the protein is obtained from a single donor. Comparison of the glycans derived from various donors suggests that a donor specificity exists.

The α-subunit of human chorionic gonadotropin contains two N-linked carbohydrate chains occurring at Asn-52 and -78, respectively. The glycan at Asn-52 is essential for hormonal activity. We investigated the structure of the free α-subunit in solution by using NMR spectroscopy. The two N-glycans behave differently as judged from the interaction with the protein backbone. Glycosylation beyond the Asn-linked GlcNAc-residue has no effect on the conformation of the free α-subunit. However, it could be shown that the protein moiety severely restricts the mobility of the inner three residues of the glycan at Asn-78. For the mobility of the two branches in the diantennary structure interesting observations were made.