non-linear parameter estimation, represent well the process behaviour. A process simulator for studies on computer-based operation should have the capacity to represent adequately both intrinsic process characteristics and practical features of process operation. This means, essentially – (i) processing of non-linear dynamical models, including sensors and final control elements, synchronised with real-time; (ii) efficient mathematical treatment of process non-linearities, such as dead-times; (iii) communications through standard analog and/or serial signals; (iv) simulation of noisy measurements; (v) interactivity in real-time with the operation. One such tool has been developed within the research group.

The theoretical non-linear dynamical model of the crystallization process, implemented in the process simulator, includes growth rate dispersion mechanisms and the characterisation of crystal size distribution (CSD) by its first six linear moments. Values of the state variables (internal temperature, brix, vacuum pressure and level), together with those of other key variables (feed and steam properties) are made available as standard analog output signals, as if they came from industrial sensors. Also, standard analog input signals, corresponding in practice to the commands to the control valves, are received and translated as inputs to the integration routines. Noises can be superimposed to the output signals. Process loads and process characteristic parameters can be changed on-line. With such standard communications and working synchronised with real-time, the simulator provides the environment to which any formal industrial control system can be linked. Or, simply, manual operation can be performed. Studies aiming at the development of new strategies for computer-based crystallizer operation and the relevant operator training on the use of new technologies are now possible at low cost and in a safe environment.

New Autocatalytic Oxidations of Primary Alcohols in Cellulose in Phosphoric Acid

Mario Pagliaro
Istituto di Chimica e Tecnologia dei Prodotti Naturali, CNR, via La Malfa 153, 90146 Palermo, Italy

Homogeneous oxidations at 4°C of cellulose dissolved in phosphoric acid with (i) sodium bromate with a small amount of sodium bromide, (ii) sodium chlorate with a small amount of sodium chloride and (iii) sodium chlorite have been studied. With these reaction systems the primary alcohol groups were completely (>95%) oxidised to carboxylic acids. Undesired ketones due to secondary alcohol groups oxidation were reduced with sodium borohydride. The selectivity observed is explained in terms of common autocatalytic oxidation mechanisms involving the positive hypohalous acidium ions, H_2OCl^+ and H_2OBr^+.

New Compounds From Microbiological Products of Sucrose

M.A. Clarke*[1], E.J. Roberts[1] and P.J. Garegg[2]
[1]Sugar Processing Research Institute, Inc., New Orleans, LA, USA and [2]Arrhenius Laboratory, Stockholm University, Stockholm, Sweden

A microbial product of sucrose, a high molecular weight levan, is readily made in high yield and high purity from commercial sucrose, sugarcane and sugarbeet juices and molasses.

Several derivatives of this levan have been synthesized. The characteristics and properties of these polymeric derivatives are described. Applications and uses of the compounds are outlined.

New Synthetic Pathways to C-glycosides

Paul H. Gross
Department of Chemistry, University of the Pacific, Stockton, CA 95211, USA

C-glycopyranosyl compounds exhibit antimicrobial, antifungal, and antitumor activities, most probably based on enzyme inhibition, or interference with cell surface recognition and differentiation processes.

C-glycosidic analogues of that component would be metabolically stable, and thus offer enhanced therapeutic value. Synthesis of a configurational variety of e.g. amino (glyco-pyranosyl) methanes is thus an important synthetic goal. The amino group would allow linking the C-glycoside to a variety of scaffolds.

Our first approach has been to C-link a C-N synthon (HCN or CH_3NO_2) to the anomeric carbon of a natural carbohydrate. We have realised this with cyanide on glycal, on per-O-acetyl sugars and on cyclic acetal protected glycosyl fluorides, prepared by a novel method. The catalytic hydrogenation of glycosyl cyanides presented challenges and new synthetic possibilities. With CH_3NO_2, and 4,6-O-alkylidene protected D-glucose or D-mannose derivatives, we obtained very good yields of cyclic Henry condensation products in THF with a novel catalytic procedure.

The novel reduction of the resulting nitro (4,6-O-benzylidene-b-D-glycopyranosyl) methane with Fe°/Ni° in THF/H_2O/CO_2 readily supplied amino (4,6-O-benzylidene-b-D-glycopyranosyl) methane, which was diasterodiversified into D-allo, D-manno, and D-altro C-glycosides. These approaches fail, however, if prerequisite natural carbohydrate precursors are not available in a given case. Thus, a total synthesis scheme was also initiated.

Phtalimido acetaldehyde diethylacetal and 4-penten-2-ol, with $TiCl_4$, form 2-methyl-4-chloro-6-phtalimido-methyl tetrahydropyran, which was functionalized into phtalimido (6-deoxy-b-D,L-hexopyranosyl) methanes. Chiral extensions of this method are possible.

C-"disaccharides" became available from the Ferrier "dimerisation" of glycals, and from the hydrogenation of glycosyl cyanides.

Oxidized and Carboxy-alkylated Carbohydrates and Some Potential Applications

H. van Bekkum
Laboratory of Organic Chemistry and Catalysis, Delft University of Technology, Julianalaan 136, 2628 BL Delft, The Netherlands

Converting carbohydrates into carboxylates or polycarboxylates is an obvious way of upgrading renewables. The (poly)carboxylates obtained may display unique properties or may enter the competition with fossil-based materials such as poly-acrylates.

Methods to introduce carboxylate groups include carbohydrate oxidation and carboxy-alkylation.

Progress in oxidation is still substantial. Some old methods are revised (noble metal catalysis, nitrate/nitrite oxidation) and new methods come to the fore. Here, the amazingly selective TEMPO-catalyzed 6-oxidation of low and high molecular mass pyranose systems will be discussed.

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

Manuel A. Coimbra[1]*, Mário Barros[1], António Barros[2], Douglas Rutdledge[2] and Ivonne Delgadillo[1]

[1]Department of Chemistry, University of Aveiro, 3810 Aveiro, Portugal and [2] Laboratory of Analytical Chemistry, INA, Paris Grignon, France

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

Pierre Sinaø

Ecole Normale Supérieure, Département de Chimie, URA CNRS 1686, 24 rue Lhomond, 75231 Paris Cédex 05, France

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

Beat Ernst

Novartis Pharma Ltd., CH-4002 Basel, Switzerland

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

R.J. Stoodley

Department of Chemistry, UMIST, PO Box 88, Manchester M60 1QD, UK

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