2003
06 CARBOHYDRATE CHEMISTRY
SYNOPSIS AND KEY CONCEPTS
AGM Barrett

(A) "Open Chain" Carbohydrate Chemistry

Nomenclature; pentose, hexose, etc. aldose, ketose; chemistry of the carbonyl group: *via* oxidation of aldoses to -onic acids and -aric acids; reduction; hydrazone and osazone formation; thioacetal formation; homologation (ascent) by the Kiliani method; degradation (descent) by the Weerman method; structural correlations by these methods

(B) Cyclisation of Carbohydrates - Hemiacetal Formation

(1) Mutarotation of D-glucose - □ and □ pyranose and furanose forms in equilibrium. Pyranose form is usually favoured with most hexoses. Anomeric Centre

(2) Glycoside Formation (Glycosidation) under kinetic control both □ and □ methyl furanosides are formed. Under thermodynamic control the □ pyranoside is the major isomer. The anomeric effect is explained in terms of lone pair-lone pair repulsion, dipole-dipole interactions and by M.O. theory. Glycosides are stable in neutral or basic solution but readily hydrolysed to the free sugar with dilute aqueous acid. Modern methods of glycoside synthesis: trichloroacetimidate activation.

(3) Reactions of Carbohydrates - Selective hydroxyl protection and neighbouring group participation

- (a) Acetylation to give the □ and □ pyranose forms of the penta- acetate; preparation of □-glycosyl halides and their conversion to glycosides and formation of glycals; reactions of glycals e.g. with dilute aqueous acid to give 2-deoxy-sugars and with peracids to give epoxides
- (b) Etherification
    - (i) MeI/NaH methyl ethers - difficult to remove
    - (ii) Benzyl ethers - cleaved by H_2/Pd or Na/NH_3
    - (iii) Silyl ethers - volatile for mass spectral studies, very readily cleaved by H_3O^+/ or KF/H_2O, variable reactivity depending on bulk
    - (iv) Allyl ethers - acid stable, isomerisation with KO^tBu or $(Ph_3P)_3RhCl$ to give acid labile vinyl ethers
    - (v) Triphenylmethyl ethers, "trityl" ethers - selective for primary OH. Removed by dilute acid
- (c) Acetal and ketal formation - ketones prefer to form 5 membered ring ketals-1,2 diol protection. Aldehydes prefer to form 6 membered ring acetals-1,3 diol protection.
- (d) Sulfonate esters - preparation and selectivity for primary hydroxyl; intermolecular nucleophilic displacement reactions and their problems;

deoxygenation *via* free radical chain reaction of xanthate esters with tri-n-buylstannane; intramolecular nucleophilic displacement reactions give ethers and epoxides (anhydro sugars); ring opening of epoxides and glycoside synthesis

(e) Keto sugars - best prepared by oxidation of alcohol with DMSO/Ac_2O or DMSO/P_4O_{10}; nucleophilic attack from the least hindered side

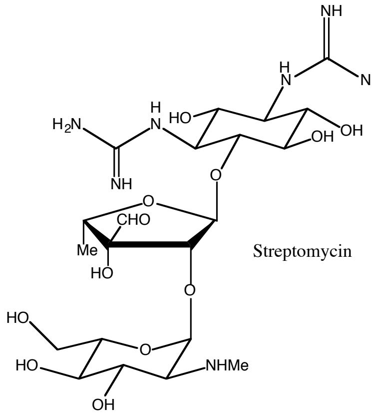
(f) Unsaturated sugars - the Corey-Winter Olefin synthesis (thiocarbonates + trimethyl phosphite); reduction of ditosylates with sodium iodide and zinc

(g) Amino sugars - tosylate displacement with azide followed by $LiAlH_4$ reduction; epoxide ring opening by ammonia; reduction of ketoximes with $LiAlH_4$

(4) Use of Carbohydrates

(a) Fermentation

(b) Aminoglycosides are important in antibiotics e.g. erythromycin, streptomycin.



Streptomycin

For a review of the preparation and reaction of aminoglycosides see: *Topics in Antibiotic Chemistry* Vol 1, p 1; Sammes, P.G., Ed.; John Wiley and Sons, **1977**.

(c) In non-carbohydrate natural product synthesis carbohydrates belong to the "Chiral Pool" i.e. they are a very cheap source of starting materials for organic synthesis which contain chiral functionality.

Bibliography

Hanessian, S. *Acc. Chem. Res.* **1979**, *12*, 159.

Fraser-Reid, B. *Acc. Chem. Res.* **1975**, *8*, 192.

"Monosaccharide Chemistry" Hough, L. and Richardson, A.C. in "Comprehensive Organic Chemistry", Ed. Barton, D.H.R.; Ollis, W.D.; Haslam, E.; Pergamon Press, Oxford, **1979**, vol. 5, p. 687-753.

"Synthsis of Glycosides" Schmidt, R.R. in "Comprehensive Organic Synthesis", Ed. Trost, B.M.; Fleming, I.; Winterfeldt, E.; Pergamon Press, Oxford, **1991**, vol. 6, p. 33-64.

"Exploration with Sugars How Sweet it Was" Lemieux, R.U. *American Chemical Society*, Washington, D.C., **1990**.

"Carbohydrate Chemistry" Kennedy, J.F. Claredon Press, Oxford, **1988**.