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# Book review

*Glycopeptides and Related Compounds*: *Synthesis Analysis and Applications* Large, David G. and Warren, Christopher D. (eds): New York: Marcel Dekker. 1997 766 pp ISBN 08247-9531-8.

Until recently the synthesis of glycopeptides was generally regarded as a monumental exercise in carbohydrate chemistry. It was only undertaken by a few laboratories and generally produced a restricted number of compounds with great effort and in low yield. Recent advances, prompted in part by a growing interest in possible therapeutic applications, seem set to change this view. This book presents a good introduction to such advances and seeks to present them in the context of biological and biomedical applications. The addition of material on the historical background, analysis and future potential makes this a most comprehensive and up to date reference text on this subject.

In the introductory chapter Christopher Warren and David Large outline the challenges which the synthesis of glycopeptides present. They also give an insight into the biomedical applications which give impetus to the search for new approaches to overcome these problems. The different types of approach adopted are outlined and a view of the future of research is given showing how a combination of chemical and enzymatic approaches can lead to a reduction in the complexity and hence reduce the cost and improve the yield of the synthesis. The contribution expected from molecular biology is also discussed. This chapter sets the scene and is a good introduction to the rest of the work.

The next two chapters give extensive detail on the routes of enzymatic and chemical synthesis respectively. The chapter by Yoshitaka Ichikawa covers most of the transferases which are likely to be useful in synthesis with details of their specificities and examples of their application. The use of glycosidases is also discussed. The particular problems of large scale enzymatic synthesis are explained and many useful examples of continuous regeneration of the sugar neucleosides, which makes this kind of approach an economic possibility, are given. In the accompanying chapter by Sabine Flitsch and Gregory Watt on chemical synthesis the various different routes that may be employed with regard to protecting groups and the stereochemistry of the reactions are clearly presented. Finally, examples of complete synthesis of relatively large oligosacchardies are given.

The use of supports for synthesis is covered in the next chapter by David Large and Ian Bradshaw which shows different supports that may be used and types of linker employed. The use of both insoluble and soluble supports is covered. These types of approach give the possibility of automated synthesis and production of glycopeptide libraries for biomedical studies. Relative merits of different supports and numerous examples of their use are given. This theme is taken up and expanded in the next chapter where David Large and Ian Bradshaw show examples of synthesis of the peptide portion of the glycopeptide, reviewing different approaches which have been taken. The particular restraints which the presence of glycosylation places on the peptide chemistry are discussed and the relative merits of construction from glycoamino acids or from pre-formed peptide and oligosaccharide considered. The problems encountered during peptide elongation which may lead to modification of the attached oligosaccharide are also covered. The remaining barriers to routine synthesis are then discussed and the combination of strategies which are likely to lead to success shown.

The next chapter deals with the synthesis of the complex glycolipid moieties, the glycosylphosphatidylinositol (GPI) anchor linkages, found in some membrane glycoproteins. The particular problems of such syntheses and the relative merits of different approaches taken by the various groups working on this are covered. Numerous examples are given of the different stages in the synthesis leading to the complete anchor with full details of the synthetic schemes provided. Synthesis of GPI anchors is also related to the analysis of such molecules and this is covered by Malcolm McConville and Julie Ralton in the next chapter. The particular methodologies used for GPI characterisation are reviewed and compared. Techniques for the analysis of the intact glycopeptide and also the release of the anchor and subsequent analysis of glycolipid and of the glycan backbone are given. Finally, analysis of the lipid moiety is covered. This chapter is a comprehensive review of methodology employed in this specialised area.

The synthesis of another type of glycoconjugate, namely the biosynthetic intermediates of the dolichol pathway in N-glycan biosynthesis, is covered in the next chapter by Vladimir Shibaev and Leonid Dabnilov. They review the role of this class of compounds in the biosynthetic pathways of a number of species and then give details of the various approaches to the synthesis of the key intermediates in these pathways. These important compounds for the study of the biosynthetic pathways are not easily obtainable from natural sources so synthesis is frequently the only source of material. A large number of synthetic routes are presented and some of the applications in which they are used are given. The related topic of inhibitors of various processes in

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the biosynthetic pathways is covered by Michael Williams. The various types of inhibitors which have been used are described and the specific steps at which they act are shown. The potentially important topic of inhibitors of various glycosyl transferases by modification of the natural substrate is also covered and some of the applications mentioned.

The next three chapters are concerned with the various analytical techniques employed to study glycopeptides and it is useful to have this information in the same source as that of the chapters dealing with their synthesis. In the first of these chapters Steven Levery covers the topic of permethylation analysis by gas chromatography mass spectrometry (GC-MS) which remains the only technique available for the unequivocal assignment of linkage analysis in many oligosaccharides. The reactions of permethylation are covered and this is followed by a detailed account of the way in which linkage analysis is carried out on these derivatives. Various other related topics are also covered and the chapter provides a useful update on the recent advances in this relatively long established technique.

The next chapter by David Harvey covers the rapidly expanding field of mass spectrometric analysis concentrating on the protein-bound oligosaccharides. The development of instrumentation in this area has been increasingly rapid and this has made the techniques increasingly affordable and available to a much larger number of laboratories. The features of the various forms of instrumentation are described in clear detail which shows how information can be derived from the measurements. The various ways in which mass spectrometry is applied to the determination of oligosaccharide structure are then presented showing techniques for release of the oligosaccharides and the usefulness of exoglycosidases in structure determination. All currently available technology is described in an understandable manner, this is a valuable addition to the chapters on synthesis.

Another essential technique in structural determination is described in the next chapter by Elizabeth Hounsell and David Bailey. They describe how the technology of nuclear magnetic resonance spectroscopy (NMR) has proved crucial to the determination of certain oligosaccharide structures. After a brief summary of the essential types of NMR analysis, details of their application to a wide variety of O-linked glycans are given covering such biologically important molecules as proteoglycans and mucins. Details are given on how the measurements are interpreted and how the data is converted into images describing the structures present. The final section of the role of glycoconjugates in immune activation serves to show the relevance of the technique to investigation of biological systems. This is further developed in the following chapter by Trevor Rutherford who shows how NMR can prove invaluable in conformational studies of glycans associated with glycoproteins. The chapter describes techniques of multi-dimensional NMR in a readily understandable manner and how these are used to provide information on the conformations adopted by the oligosaccharides. This leads on to a description of how this data is used in molecular modelling calculations to give simulations of the conformations likely to be adopted.

In the final chapter an insight is given into the medical application of glycoprotein synthesis by Rao Koganty, Mark Reddish and Michael Longenecker from one of the new companies exploiting the synthetic technology described in this book. The target chosen is that of cancer where changes in glycosylation of the MUC-1 mucin are closely correlated with the progression of many cancers including breast cancer and adenocarcinomas. The strategy involves synthesis of glycopeptide for immune therapy, by stimulation of a response by synthetic glycopeptides related to MUC-1. Details are given of the synthetic approaches and the ways in which their efficacy is measured. This is certainly an area of great scientific and commercial interest and the results of clinical trials of the glycopeptides must be eagerly awaited.

In conclusion this book presents a most comprehensive and well rounded account of the synthesis, analysis and application of glycopeptides and is a most useful and timely addition to the literature in this field.

Tony Merry
*BioMed Labs*
*Ponteland*
*Newcastle upon Tyne*
*NE20 9PS*