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INTRODUCTION

SYNTHETIC CARBOHYDRATE CHEMISTRY OF THE 1980s

Various earlier dedicated issues of *Carbohydrate Research* have presented collections of papers selected to bring together modern developments in specific new or expanding areas of the subject, or have been prepared in order to recognise the contributions of senior chemists in the attainment of personal milestones; otherwise, conference papers have been published in combined sets. This special issue aims to illustrate developments in synthetic methods and achievements which are largely characteristic of the decade that has just finished. In a somewhat random way they identify a rapidly changing field which is in a position to diverge further and penetrate deeper with the objectives of developing the simplest, cheapest, most selective and efficient ways to a myriad of increasingly complex biologically and commercially important substances, both carbohydrate and non-carbohydrate in character. Nature sets the ultimate standards and challenges, and as understanding of biological processes and the role of the carbohydrates in them increases, so do the demands on the synthetic chemist.

Since the specific choice of the material presented in this issue lay primarily with the authors, it cannot be suggested that its illustrative character is systematically representative of the period in focus, but it selectively and forcefully shows how strange, from the current vantage point, seems the conviction held by so many for so long that the chemistry of the monosaccharides was "worked out", in the senses of being both complete and understood, more than fifty years ago.

Modern separatory and spectrometric methods — especially modern n.m.r. procedures and increasingly X-ray diffraction analysis — have been the keystones to the advances, but recent progress has also been facilitated greatly by the ending of the over-long era of the carbohydrates' special and somewhat isolated niche in organic chemistry. Chemists of carbohydrate lineage now recognise the wealth of modern organic chemistry applicable in the field and, with no less significance and nicely reciprocally, organic chemists whose primary experience is outside sugar chemistry now clearly recognise the synthetic value of the sugars — especially as inexpensive sources of manageable functionality and chirality. It is salutary to note how some of the most prominent synthetic organic chemists have contributed entirely new vision, insight and achievement to the field — almost as if they had been spared the traditional wisdom relating to the well-nigh impossibility of working with sugars. Along with these facilitating factors have gone the synthetic challenges posed by increasing understanding of the complex compounds of biology, and science's increasing understanding of the subtleties of their functions at the molecular level. The highly sophisticated needs of the pharmaceutical and agricultural chemical industries have especially stimulated research in the field of synthetic carbohydrate chemistry, which is now vibrant, rich, and more ecumenical than could have been imagined even ten brief years ago.

Basic work continues to reveal new protecting groups such as complex silyl ethers and selective deprotecting procedures (and hence better routes to specifically substituted compounds), new simple derivatives such as 1,3-anhydrohexopyranoses which have extremely important analogues in prostaglandin chemistry, and means of manipulating sugars such as interchanging the terminal functions of the aldoses. The decade is more notable, however, for the extension of the study of sugar-derived carbonium ions and especially for the introduction of work on analogous carbanions and free-radical intermediates. While the former of these have brought to light opportunities presented by monosaccharide organometallic derivatives, the latter have changed the status of single-electron species from that of uncontrollable reaction intermediates (both in the formation and reaction sense) to that of specifically reactive species the advantages of which have already been shown to represent one of the most powerful new developments in synthesis. Work with both carbanions and radicals has led to new and controllable routes to such important classes of compounds as *C*-glycosyl derivatives, poly-branched-chain compounds, and carbocyclic derivatives and thence a range of complex and chiral non-carbohydrate systems of biological significance. Carba-sugars ("pseudo-sugars") and cyclopentane derivatives are amongst many classes of compounds which have received special attention.

A permanent challenge in carbohydrate synthesis is the simple, efficient and selective preparation of oligosaccharides and natural products having oligosaccharide components — especially those such as Lipid A and various glycopeptides of importance in biological processes. Refinements and simplifications of glycosylation procedures remain to be made, but the introduction of glycosyl imidate derivatives, glycosyl fluorides, and both *S*-aryl and *S*-alkyl thioglycosides as glycosylating agents represent real advances, as do studies of stereoselective reactions which depend for their selectivity on chelation control. Such has been the rate of progress in this area that, whereas at the beginning of the 1980s the preparation of a tetrasaccharide was a notable achievement, chemists are now using chemical methods to put together specific hetero-oligosaccharides containing a dozen monosaccharide units. Analogues having sulphur, nitrogen, or carbon in place of oxygen as inter-unit linking atoms clearly are of interest as modified enzyme substrates, and we appear to be on the threshold of major developments in this area.

At the interface of carbohydrate chemistry and "orthodox" synthesis has been research into means by which many complex natural products (palytoxin being an extreme example) have been elaborated at least partially from sugars as starting materials, and multifunctional macrocycles, aminoglycoside antibiotics, anthracyclines, and a host of other compounds structurally too different from the monosaccharides to permit mention in general remarks, can now be obtained in enantiomerically pure state by this approach.

Chemical syntheses of enantiomerically pure sugars and derivatives, such as those which occur naturally in antibiotics developed well over the decade, as has research into the use of enzymes in such syntheses and in selective substitution of carbohydrates and selective hydrolysis of their ester derivatives. Synthetic carbohydrate chemistry of the 1990s seems poised to press the advantages of combining organic and enzymic procedures, and the present decade may well be the age of bio-organic carbohydrate synthetic chemistry.

Warm thanks are expressed to all the authors for contributing to this special project.

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