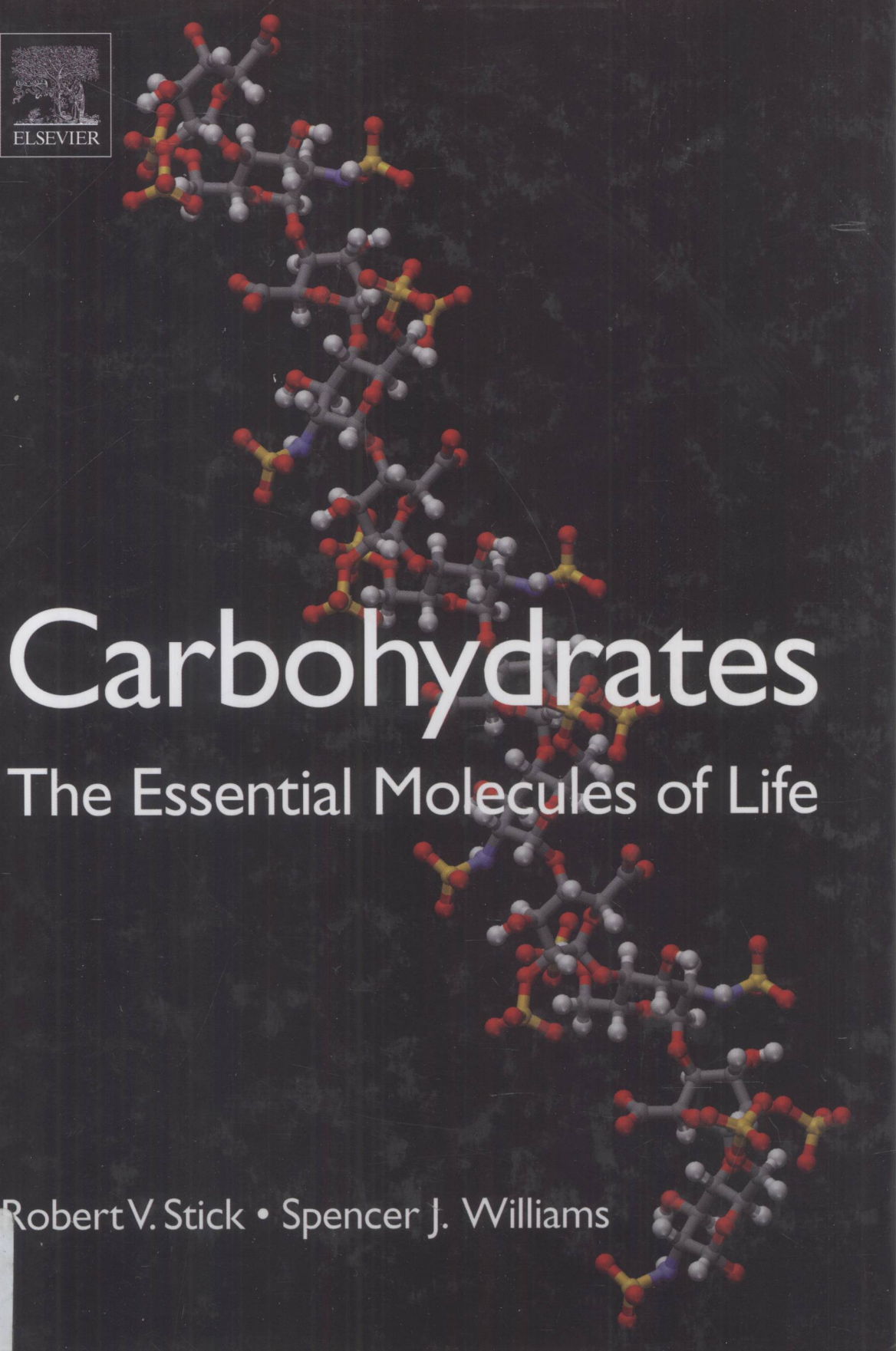
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Carbohydrates
The Essential Molecules of Life
Robert V. Stick • Spencer J. Williams

Carbohydrates:
The Essential Molecules of Life

Second Edition

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The front cover shows a representation of the solution structure of a heparin fragment, determined by NMR spectroscopy (Protein Data Bank code: 1hpn).

For Rob,
unrealized artist

Also, in memory of Bruce Stone and his beloved 1,3-β-glucans and wattle-bloom arabinogalactan proteins

Preface and Acknowledgements

The year 2000 marked a watershed in the sciences with the sequencing of the human genome. Along with other sequencing efforts, we now know the blueprint for life in an ever-increasing number of organisms. Not unexpectedly, whole new areas of science have flourished: genomics, ribonomics, proteomics, metabolomics and, not to be left out, glycomics. Glycomics has been defined as 'the functional study of carbohydrates in living organisms' (de Paz, J. L. and Seeberger, P. H. *QSAR Comb. Sci.*, 2006, **25**, 1027).

Glycomics would not have even been considered a century ago because carbohydrates and, in particular the sugars, were viewed simply as essential molecules for the survival of most organisms. For example, sucrose and glucose provided energy, starch stored energy, and cellulose was responsible for structure and strength. Decades of research then provided novel carbohydrate structures where the function was not always obvious. What were these molecules doing in the world of biology, often being present on the surface of bacteria, viruses and cancer cells, the vanguard of these life forms?

Well, these molecules have a function, and it is now recognized that carbohydrate–protein and even carbohydrate–carbohydrate interactions are of fundamental importance in modulating protein structure and localization, signalling in multicellular systems and cell–cell recognition, including bacterial and viral infection processes, inflammation and aspects of cancer. Some of these carbohydrates have high molecular weights and, not surprisingly, complex chemical structures that challenge the chemists, biochemists and biologists. A pertinent example would be that of the N-glycans, complex molecules in which the carbohydrate is linked, through nitrogen, to a peptide chain (thus forming a glycopeptide or glycoprotein); a small change in the structure of the carbohydrate can lead to all sorts of human diseases.

This book will provide all of the background for a successful study of carbohydrates. Also, it will give a taste for the subject of glycobiology, concentrating especially on the structures and the biosynthesis of carbohydrates and glycoconjugates, and to a lesser extent on their function. A question often asked is 'Why study carbohydrate chemistry?'. The answer is simple: 'It is fundamental to the study of biology'. An organic chemist trained in carbohydrates will move smoothly into the

worlds of biochemistry, molecular biology and cell biology; the reverse is much more difficult.

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Robert Stick and Spencer Williams

Abbreviations

Ac	acetyl
AIBN	2,2′-azobis(isobutyronitrile)
All	allyl (prop-2-enyl)
AMP/ADP/ATP	adenosine 5′-mono/di/triphosphate
Ar	aryl
ATIII	antithrombin III
BMS	*tert*-butyldimethylsilyl
Bn	benzyl (phenylmethyl)
Boc	*tert*-butoxycarbonyl
BPS	*tert*-butyldiphenylsilyl
Bz	benzoyl
CAN	cerium(IV) ammonium nitrate
Cbz	benzyloxycarbonyl
C_6H_{11}	cyclohexyl
ClAc	chloroacetyl
CMP/CDP/CTP	cytidine 5′-mono/di/triphosphate
CoA	coenzyme A
CSA	camphor-10-sulfonic acid
DABCO	1,4-diazabicyclo[2.2.2]octane
DAST	(diethylamino)sulfur trifluoride
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCC	*N,N′*-dicyclohexylcarbodiimide
DCE	1,2-dichloroethane
DDQ	2,3-dichloro-5,6-dicyanobenzoquinone
DEAD	diethyl azodicarboxylate
DIAD	diisopropyl azodicarboxylate
DMAP	4-(dimethylamino)pyridine
DMDO	dimethyldioxirane
DME	1,2-dimethoxyethane
DMF	dimethylformamide
DMSO	dimethyl sulfoxide
DMTST	dimethyl(methylthio)sulfonium triflate

DNP	2,4-dinitrophenyl
DTBMP	2,6-di-*tert*-butyl-4-methylpyridine
DTBP	2,6-di-*tert*-butylpyridine
DTPM	(dimethyltrioxopyrimidinylidene)methyl
DTT	1,4-dithiothreitol
ER	endoplasmic reticulum
ERAD	endoplasmic reticulum–associated degradation
FADH	flavin adenine dinucleotide
Fmoc	9-fluorenylmethoxycarbonyl
GAG	glycosaminoglycan
GH	glycoside hydrolase
GMP/GDP/GTP	guanosine 5′-mono/di/triphosphate
GPI	glycosylphosphatidylinositol
GT	glycosyltransferase
HIT	heparin-induced thrombocytopenia
HIV	human immunovirus
HMPA	hexamethylphosphoramide
IDC	iodonium dicollidine
Im	1-imidazolyl
IPTG	isopropyl 1-thio-β-D-galactopyranoside
KLH	keyhole limpet hemocyanin
LDA	lithium diisopropylamide
Lev	levulinyl (4-oxopentanoyl)
LPG	lipophosphoglycan
LPS	lipopolysaccharide
*m*CPBA	3(*meta*)-chloroperbenzoic acid
Ms	mesyl (methanesulfonyl)
NADH	nicotinamide adenine dinucleotide
NADPH	nicotinamide adenine dinucleotide phosphate
NBS	*N*-bromosuccinimide
NIS	*N*-iodosuccinimide
NMO	*N*-methylmorpholine *N*-oxide
Ns	4-nitrobenzenesulfonyl
PAPS	3′-phosphoadenosine-5′-phosphosulfate
PCC	pyridinium chlorochromate
PDC	pyridinium dichromate
PEG	poly(ethylene glycol)
PEP	phosphoenolpyruvate
Ph	phenyl
Phth	phthalyl
PI	phosphatidylinositol
Piv	pivalyl (2,2-dimethylpropanoyl)

PLP	pyridoxal-5′-phosphate
*p*MB	4(*para*)-methoxybenzyl
*p*NP	4(*para*)-nitrophenyl
*p*TSA	4(*para*)-toluenesulfonic acid
py	pyridine
rt	room temperature
SF	selectfluor {1-chloromethyl-4-fluoro-1,4-diazoniabicyclo [2.2.2]octane bis(tetrafluoroborate)}
TBP	2,4,6-tri-*tert*-butylpyridine
TCP	tetrachlorophthalyl
TDS	thexyldimethylsilyl
TEMPO	2,2,6,6-tetramethylpiperidine-1-oxyl
Tf	triflyl (trifluoromethanesulfonyl)
THF	tetrahydrofuran
THP	tetrahydropyran-2-yl
TIPS	triisopropylsilyl
TMP	2,2,6,6-tetramethylpiperidide
Tol	tolyl (4-methylphenyl)
TPAP	tetrapropylammonium perruthenate
Tr	trityl (triphenylmethyl)
Ts	tosyl (4-toluenesulfonyl)
TTBP	2,4,6-tri-*tert*-butylpyrimidine
UMP/UDP/UTP	uridine 5′-mono/di/triphosphate

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