



Universiteit
Leiden

The Netherlands

Structure-reactivity relationships in glycosylation chemistry

Hengst, J.M.A. van

Citation

Hengst, J. M. A. van. (2023, December 7). *Structure-reactivity relationships in glycosylation chemistry*. Retrieved from <https://hdl.handle.net/1887/3665922>

Version: Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/3665922>

Note: To cite this publication please use the final published version (if applicable).

Structure-reactivity relationships in glycosylation chemistry

Proefschrift

ter verkrijging van

de graad van doctor aan de Universiteit Leiden,

op gezag van rector magnificus prof. dr. ir. H. Bijl

volgens besluit van het college voor promoties

te verdedigen op donderdag 7 december 2023

klokke 11:15 uur

door

Jacobus Meindert Antonius van Hengst

geboren te Rotterdam

in 1993

Promotores:

prof. dr. J.D.C. Codée

prof. dr. G.A. van der Marel

Promotiecommissie:

prof. dr. M. Ubbink

prof. dr. H.S. Overkleeft

dr. S. van der Vorm

dr. M.T.C. Walvoort (Rijksuniversiteit Groningen)

prof dr. C.-C. Wang (Academia Sinica, Taipei, Taiwan)

Cover design by Maaïke de Wit

Printed by Proefschriftspecialist

Printed on recycled paper

Dedicated to Desiree van Gastel

11-04-1958 / 03-05-2023

Contents

<i>Abbreviations</i>	5
<i>Chapter 1: General introduction</i>	7
<i>Chapter 2: Stereoselectivity of S_N1-like reactions of all eight diastereoisomeric pyranosyl and 6-deoxy pyranosyl donors with D- or C-nucleophiles</i>	33
<i>Chapter 3: Acceptor nucleophilicity – Glycosylation stereoselectivity mapping for all eight diastereomeric pyranosyl donors</i>	83
<i>Chapter 4: How configuration and protecting group pattern influence glycosyl acceptor reactivity</i>	113
<i>Chapter 5: Influence of N-protecting groups on the reactivity of glycosyl acceptors</i>	263
<i>Chapter 6: Mapping the reactivity of 2,3-di-N-acetyl glucuronic acid and 2,4-di-N-acetyl bacillosamine building blocks in the synthesis of a highly N-acetylated Acinetobacter Baumannii LUH5554 tetrasaccharide</i>	301
<i>Chapter 7: summary and future prospects</i>	339
<i>Samenvatting in het Nederlands</i>	362
<i>List of Publications</i>	368
<i>Academic CV</i>	370
<i>Acknowledgments</i>	371

Abbreviations

A.	Acinetobacter	ddt	doublet of double triplets
Ac	acetyl	DFE	difluoroethanol
ACN	acetonitrile	DFT	density function theory
AIBN	2,2'-azobis(2-methyl- propionitrile)	DIAD	diisopropyl azocarboxylate
APT	attached proton test	DIPEA	diisopropylethylamine
aq.	aqueous	DLNPO	domain-based local pair natural orbital
Arom	aromatic	DMAP	4-dimethylaminopyridine
B	boat	DMBA	1,3-Dimethylbarbituric acid
B3LYP	Becke, 3-parameter, Lee-Yang- Parr	DMF	<i>N,N</i> -dimethylformamide
BAIB	(diacetoxyiodo)benzene	DMP	Dess-Martin periodinane
Bn	benzyl	DMSO	dimethylsulfoxide
bs	broad singlet	dq	double quartet
Bu	butyl	dt	double triplet
Bz	benzoyl	dtd	doublet of triple doublets
C	chair	DTBS	di-tert-butylsilylidene
cal	calorie	E	energy
calcd	calculated	<i>E</i>	envelope
cat.	Catalytic	EDC(I)	1-Ethyl-3-(3- dimethylaminopropyl) carbodiimide
CCSDT	coupled cluster single-double- triple	eq.	molar equivalent
CEL	conformational energy landscape	Et	ethyl
CIP	contact ion pair	E-X	electrophilic activator system
COSY	correlation spectroscopy	gg	gauche-gauche
C _q	quaternary carbon atom	gt	gauche-trans
CSA	camphor-10-sulfonic acid	GATED	proton decoupling applied only during relaxation
δ	chemical shift	GlcNAc3NAcA	2,3-di- <i>N</i> -acetyl-D- glucuronic acid
d	doublet	h	hour(s)
DBTO	dibutyltin oxide	<i>H</i>	half-chair
DCE	1,2-dichloroethane	HFIP	hexafluoro-iso-propanol
DCM	dichloromethane	HMBC	heteronuclear multiple-bond correlation spectroscopy
dd	double doublet	HMDS	hexamethyldisilazane
ddd	doublet of double doublets	HRMS	high-resolution mass spectroscopy
dddd	double doublet of double doublets		
DDQ	2,3-Dichloro-5,6-dicyano-1,4- benzoquinone		

HSQC	heteronuclear single quantum coherence	rt	room temperature
IR	infrared	rxn	reaction
IRIS	infrared ion spectroscopy	s	singlet
<i>J</i>	coupling constant	<i>S</i>	skew boat
LAH	lithium aluminium hydride	sat.	saturated
Lev	Levulinoyl	<i>S_N1</i>	uni-molecular nucleophilic substitution
LG	leaving group	<i>S_N2</i>	bi-molecular nucleophilic substitution
M	molar	SSIP	solvent-separated ion pair
m	multiplet	SAR	structure-activity-relationships
m.s.	molecular sieves	t	triplet
m/z	mass over charge ratio	<i>t</i>	<i>tert</i>
min	minute(s)	T	twist
Me	methyl	<i>tg</i>	trans-gauge
MFE	monofluoroethanol	TBA	tetrabutylammonium
M.S.	molecular sieves	TBS	<i>tert</i> -butyldimethylsilyl
Ms	methanesulfonyl	TBDMS	<i>tert</i> -butyldimethylsilyl
Nap	2-methylnaphthyl	TBDPS	<i>tert</i> -butyldiphenylsilyl
NIS	N-iodosuccinimide	TCA	trichloroacetyl
NMR	nuclear magnetic resonance	TES	triethylsilyl
NOESY	nuclear Overhauser effect spectroscopy	TEMPO	2,2,6,6-tetramethylpiperidine 1-oxyl
Nu	nucleophile	TFA	trifluoroacetic acid
p	para	TFAA	trifluoroacetic anhydride
PG	protection group	TFE	trifluoroethanol
PCM	polarizable continuum model	Tf	trifluoromethanesulfonyl
Ph	phenyl	THF	tetrahydrofuran
PMB	4-methoxybenzyl	TIPS	tri-isopropylsilyl
ppm	parts per million	TLC	thin layer chromatography
PTFAI	2,2,2-Trifluoro- <i>N</i> -phenylacetimidoyl	TMS	trimethylsilyl
PTSA	para-toluenesulfonic acid	TOCSY	total correlation spectroscopy
q	quartet	Ts	4-methylbenzene-1-sulfonyl
qd	quartet of doublets	TS	transition state
QuiNAc ₄ NAc	2,4-di- <i>N</i> -acetyl-D-quinovose	td	triple doublet
R ² or r ²	coefficient of determination	tt	triple triplet
R _f	retention factor	TTBP	2,4,6-tri- <i>tert</i> -butylpyrimidine
RRV	relative reactivity value	UV	ultraviolet
		VT	variable temperature