Contents

List of Contributors *xi*
Preface *xv*

Part I Introduction *1*

1 Stereoselective Glycosylations – Additions to Oxocarbenium Ions *3*
Bas Hagen, Stefan van der Vorm, Thomas Hansen, Gijs A. van der Marel, and Jeroen D.C. Codée
1.1 Introduction *3*
1.2 Stability, Reactivity, and Conformational Behavior of Glycosyl Oxocarbenium Ions *4*
1.3 Computational Studies *10*
1.4 Observation of Glycosyl Oxocarbenium Ions by NMR Spectroscopy *14*
1.5 Oxocarbenium Ion(-like) Intermediates as Product-Forming Intermediates in Glycosylation Reactions *15*
1.6 Conclusion *24*
References *26*

2 Application of Armed, Disarmed, Superarmed, and Superdisarmed Building Blocks in Stereocontrolled Glycosylation and Expeditious Oligosaccharide Synthesis *29*
Mithila D. Bandara, Jagodige P. Yasomanee, and Alexei V. Demchenko
2.1 Introduction: Chemical Synthesis of Glycosides and Oligosaccharides *29*
2.2 Fraser-Reid's Armed–Disarmed Strategy for Oligosaccharide Synthesis *31*
2.3 Many Reactivity Levels Exist between the Armed and Disarmed Building Blocks *33*
2.4 Modes for Enhancing the Reactivity: Superarmed Building Blocks *35*
2.5 Modes for Decreasing the Reactivity: Superdisarmed Building Blocks *38*
2.6 Application of Armed and Disarmed Building Blocks in Stereocontrolled Glycosylation *41*
2.7 Application of Armed/Superarmed and Disarmed Building Blocks in Chemoselective Oligosaccharide Synthesis *46*
2.8 Conclusions and Outlook *54*
References *55*

3 Solvent Effect on Glycosylation *59*
KwoK-Kong Tony Mong, Toshiki Nokami, Nhut Thi Thanh Tran, and Pham Be Nhi
3.1 Introduction *59*
3.2 General Properties of Solvents Used in Glycosylation *60*
3.3 Polar and Noncoordinating Solvents in Glycosylation *62*
3.4 Weakly Polar and Noncoordinating Solvents in Glycosylation *63*
3.5 Polar and Coordinating Solvents in Glycosylation *64*
3.6 Weakly Polar and Coordinating Solvents in Glycosylation *68*
3.7 Solvent Effect of Ionic Liquid on Glycosylation *71*
3.8 Solvent Effect on Electrochemical Glycosylation *73*
3.9 Molecular Dynamics Simulations Studies on Solvent Effect *73*
3.10 Conclusions *74*
References *75*

Part II Stereocontrolled Approaches to Glycan Synthesis *79*

4 Intramolecular Aglycon Delivery toward 1,2-*cis* Selective Glycosylation *81*
Akihiro Ishiwata and Yukishige Ito
4.1 Introduction *81*
4.2 Ketal Type Tethers *82*
4.3 Silicon Tethers *82*
4.4 2-Iodoalkylidene Acetals as Tether *84*
4.5 Benzylidene Acetals as Tether *86*
4.6 IAD through Hemiaminal Ethers *93*
4.7 Conclusions *93*
References *94*

5 Chiral Auxiliaries in Stereoselective Glycosylation Reactions *97*
Robin Brabham and Martin A. Fascione
5.1 Introduction *97*
5.2 Neighboring Group Participation of O-2 Chiral Auxiliaries *97*
5.3 Neighboring Group Participation of O-2 Achiral Auxiliaries *103*
5.4 Preconfigured Chiral Auxiliaries *106*
5.5 Conclusion *111*
References *112*

6 Glycosylation with Glycosyl Sulfonates *115*
Luis Bohé and David Crich
6.1 Introduction *115*
6.2 Formation of Glycosyl Sulfonates *115*
6.3 Evidence for Glycosyl Sulfonates *118*
6.4 Location of the Glycosyl Sulfonates in the General Glycosylation Mechanism *119*
6.5 Applications in *O*-Glycoside Synthesis *123*
6.6 Applications in *S*-Glycoside Synthesis *128*
6.7 Applications in *C*-Glycoside Synthesis *128*

6.8 Polymer-Supported Glycosylation with Sulfonates *129*
6.9 Conclusion *130*
References *130*

Part III Catalytic Activation of Glycosides *135*

7 Stereoselective C-Glycosylation from Glycal Scaffolds *137*
Kim Le Mai Hoang, Wei-Lin Leng, Yu-Jia Tan, and Xue-Wei Liu
7.1 Introduction *137*
7.2 Classification of *C*-Glycosylation Reactions *138*
7.3 Ferrier-Type Rearrangement *138*
7.4 Pd-Catalyzed Heck-Type *140*
7.5 Tsuji–Trost-Type *C*-Glycosylation *145*
7.6 Sigmatropic Rearrangement *147*
7.7 NHC-Catalyzed *C*-Glycosylations *149*
7.8 Conclusion *151*
References 151

8 Brønsted- and Lewis-Acid-Catalyzed Glycosylation *155*
David Benito-Alifonso and M. Carmen Galan
8.1 Introduction *155*
8.2 Chiral Brønsted Acids *155*
8.3 Achiral Brønsted Acids *159*
8.3.1 Homogeneous Brønsted Acid Catalysis *159*
8.3.2 Heterogeneous Brønsted Acid Catalysis *161*
8.4 Lewis-Acid-Catalyzed Glycosylations *161*
8.4.1 Synthesis of O-Glycosides *161*
8.4.2 Conformationally Constraint Glycosyl Donors *163*
8.4.3 Synthesis of O-Glycoside Mimics *164*
8.5 Metals as Lewis Acids *165*
8.5.1 Gold *165*
8.5.2 Cobalt *167*
8.5.3 Nickel *168*
8.5.4 Iron *168*
8.6 Synthesis of C-Glycosides *169*
8.7 Conclusions and Outlook *170*
References *170*

9 Nickel-Catalyzed Stereoselective Formation of 1,2-*cis*-2-Aminoglycosides *173*
Eric T. Sletten, Ravi S. Loka, Alisa E. R. Fairweather, and Hien M. Nguyen
9.1 Introduction *173*
9.2 Biological Importance of 1,2-*cis*-Aminoglycosides *173*
9.3 Use of Nonparticipatory Groups to Form 1,2-*cis*-Aminoglycosides *175*
9.4 Nickel-Catalyzed Formation of 1,2-*cis*-Aminoglycosides *178*
9.5 C(2)-*N*-Substituted Benzylidene Glycosyl Trichloroacetimidate Donors *180*
9.5.1 Comparison to Previous Methodologies *182*

9.5.2 Expansion of Substrate Scope *183*
9.6 Studies of C(2)-*N*-Substituted Benzylideneamino Glycosyl *N*-Phenyl Trifluoroacetimidate Donors *187*
9.6.1 Synthetic Advantage of *N*-Phenyltrifluoroacetimidate Donors *189*
9.7 1,2-*cis*-Amino Glycosylation of Thioglycoside Acceptors *190*
9.8 Application to the Synthesis of Biologically Active Glycans *194*
9.8.1 Mycothiol *196*
9.8.2 GPI Anchor *197*
9.8.3 *O*-Polysaccharide Component of Gram-Negative Bacteria *S. enterica* and *P. rustigianii* *200*
9.8.4 T_N Antigen *201*
9.8.5 Heparin *204*
9.9 Conclusion *206*
References *207*

10 Photochemical Glycosylation *211*
Justin Ragains
10.1 Introduction *211*
10.2 Photochemistry Basics *212*
10.3 Photosensitized O-Glycosylation with Chalcogenoglycoside Donors *214*
10.4 Photochemical *O*-Glycosylation with Other Donors *223*
10.5 Photosensitized C-Glycosylation *224*
10.6 Conclusions *228*
References *229*

Part IV Regioselective Functionalization of Monosaccharides *231*

11 Regioselective Glycosylation Methods *233*
Mark S. Taylor
11.1 Introduction *233*
11.2 Substrate Control: "Intrinsic" Differences in OH Group Reactivity of Glycosyl Acceptors *234*
11.3 Substrate Control: Modulation of Acceptor OH Group Reactivity by Variation of Protective Groups *239*
11.4 Substrate Control: Glycosyl Donor/Acceptor Matching in Regioselective Glycosylation *241*
11.5 Reagent-Controlled, Regioselective Glycosylation *243*
11.6 Enzyme-Catalyzed Regioselective Glycosylation *246*
11.7 Synthetic Catalysts for Regioselective Glycosylation *248*
11.8 Summary and Outlook *250*
References *252*

12 Regioselective, One-Pot Functionalization of Carbohydrates *255*
Suvarn S. Kulkarni
12.1 Introduction *255*

12.2 Regioselective, Sequential Protection/Functionalization of Carbohydrate Polyols *256*
12.3 Regioselective, One-Pot Protection of Sugars via TMS Protection of Polyols *262*
12.4 Orthogonally Protected D-Glycosamine and Bacterial Rare Sugar Building Block via Sequential, One-Pot Nucleophilic Displacements of O-Triflates *268*
12.5 Summary and Outlook *273*
References *273*

Part V Stereoselective Synthesis of Deoxy Sugars, Furanosides, and Glycoconjugate Sugars *277*

13 Selective Glycosylations with Deoxy Sugars *279*
Clay S. Bennett
13.1 Introduction *279*
13.2 Challenges in 2-Deoxy-Sugar Synthesis *281*
13.3 Protecting Group Strategies *283*
13.4 Addition to Glycals *284*
13.5 Additions to Glycosyl Halides *285*
13.6 Latent Glycosyl Halides *287*
13.7 Reagent-Controlled Approaches *289*
13.8 Umpolung Reactivity *291*
13.9 Conclusion *293*
References *293*

14 Selective Glycosylations with Furanosides *297*
Carola Gallo-Rodriguez and Gustavo A. Kashiwagi
14.1 Introduction *297*
14.2 Construction of the Furanose Template *299*
14.3 Stereoselective Glycosylation with Furanoside Donors *300*
14.3.1 1,2-*trans* Furanosides *300*
14.3.2 1,2-*cis* Furanosides *303*
14.3.2.1 Flexible Donors *303*
14.3.2.2 Conformationally Restricted Donors *307*
14.3.2.3 Indirect Methods *314*
14.3.2.4 Oxidation–Reduction *318*
14.4 Reactivity Tuning of Furanosides for Oligosaccharide Synthesis *319*
14.5 Conclusion *321*
References *321*

15 *De novo* Asymmetric Synthesis of Carbohydrate Natural Products *327*
Pei Shi and George A. O'Doherty
15.1 Introduction *327*
15.2 Danishefsky Hetero-Diels–Alder Approach *328*
15.3 MacMillan Proline Aldol Approach *330*

15.4 The O'Doherty Approaches *334*
15.4.1 O'Doherty Iterative Dihydroxylation Approach *334*
15.4.2 O'Doherty Achmatowicz Approach *335*
15.4.3 *De novo* Use of the Achmatowicz Approach to Pyranose *336*
15.4.4 *De novo* Access to Monosaccharide Natural Products *337*
15.4.5 *De novo* Access to Oligosaccharide Natural Products *341*
15.5 Conclusion *347*
References *347*

16 Chemical Synthesis of Sialosides *353*
Yu-Hsuan Lih and Chung-Yi Wu
16.1 Introduction *353*
16.2 Chemical Synthesis of Sialosides *354*
16.3 Conclusions *366*
References *367*

Index *371*