Available online at www.sciencedirect.com
ScienceDirect
Carbohydrate Research 342 (2007) 374–406
Carbohydrate RESEARCH

Review

Recent trends in the synthesis of *O*-glycosides of 2-amino-2-deoxysugars

Aileen F. G. Bongat and Alexei V. Demchenko*

Department of Chemistry and Biochemistry, University of Missouri—St. Louis, One University Blvd., St. Louis, MO 63121, USA

Received 14 July 2006; received in revised form 13 October 2006; accepted 20 October 2006
Available online 27 October 2006

Dedicated to the memory of Professor Nikolay K. Kochetkov

Abstract—The discovery of new methods for stereoselective glycoside synthesis and convergent oligosaccharide assembly has been critical for the area of glycosciences. At the heart of this account is the discussion of the approaches for stereoselective synthesis of glycosides of 2-amino-2-deoxysugars that have emerged during the past two decades. The introductory part provides general background information and describes the key features and challenges for the synthesis of this class of compounds. Subsequently, major approaches to the synthesis of 2-amino-2-deoxyglycosides are categorized and discussed. Each subsection elaborates on the introduction (or protection) of the amino functionality, synthesis of glycosyl donors by introduction of a suitable leaving group, and glycosidation. Wherever applicable, the deprotection of a temporary amino group substituent and the conversion onto the natural acetamido functionality is described. The conclusions part evaluates the current standing in the field and provides a perspective for future developments.

Keywords: 2-Amino-2-deoxysugars; Stereoselective glycosylation; Protecting groups; Carbohydrates; Oligosaccharide synthesis

Contents

* Corresponding author. E-mail: demchenkoa@umsl.edu

0008-6215/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.carres.2006.10.021

1. Introduction

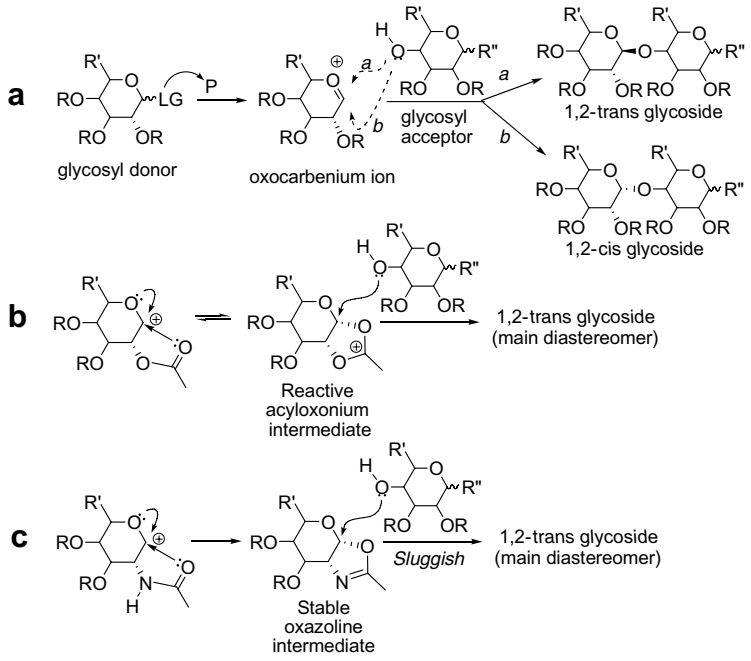
Elucidation of the exact mechanisms of carbohydrate involvement in pathogenesis of human diseases is difficult due to the complexity and relatively low availability of natural glycostructures. The main conceptual difference between oligosaccharides and other natural biopolymers, that is, proteins and DNA, is in the complexity of the bonds connecting the monomeric units. The glycosidic bond represents a new chirality center and often brings along an obstacle associated with its stereoselective synthesis. The necessity to form either 1,2-cis or 1,2-trans glycosidic linkage with complete stereoselectivity and in high yields is the main reason for which oligosaccharides remain amongst the major synthetic challenges.

Glycosides of 2-amino-2-deoxysugars are present in the most important classes of glycoconjugates and naturally occurring oligosaccharides, in which they are connected to other residues *via* either 1,2-cis or, more frequently, 1,2-trans glycosidic linkage.[1–3] In particular, 2-*N*-acetamido-2-deoxyglycosides, most commonly of the D-glucose and D-galactose series, are widely distributed in living organisms as glycoconjugates (glycolipids, lipopolysaccharides, glycoproteins),[1] or glycosaminoglycans (heparin, heparin sulfate, dermatan sulfate, chondroitin sulfate, hyaluronic acid),[4] and in blood group oligosaccharides[5–7] Aminosugars on cell surfaces play an important role as receptor ligands for protein molecules such as enzymes,[8] antibodies,[9] and lectins,[10,11] and participate in antibody-antigen interactions.[12] As appreciation for the biological importance of 2-amino sugars has increased, so have efforts to develop chemical methods for the synthesis of oligosaccharides containing these residues. Special efforts for the synthesis of glycosyl donors of 2-amino-2-deoxysugars have been focusing on the development of simple, efficient, regio-, and stereoselective procedures.

Generally, a promoter-assisted departure of the leaving group of regular (O-2) glycosyl donors results in the formation of the glycosyl cation, which is stabilized by resonance from O-5 *via* flattened oxocarbenium ion (Scheme 1a). Hence, the nucleophilic attack is almost equally possible from either the top (trans, β- for the D-gluco series) or the bottom face (cis, α-) of the ring. Even though the α-product is thermodynamically favored (anomeric effect),[13] a substantial amount of the kinetic β-linked product is often obtained. Various factors such as temperature, protecting groups, conformation, solvent, promoter, steric hindrance, or leaving groups may influence the glycosylation outcome.[14,15] If the use of a base-labile ester-protecting group is permitted, 1,2-trans glycosides can be reliably prepared with the assistance of a neighboring participating group at C-2.[16,17] These glycosylations proceed primarily *via* a reactive bicyclic acyloxonium ion intermediate directing the nucleophilic attack mainly to the top face of the ring and allowing stereoselective formation of a 1,2-trans glycoside (Scheme 1b). Many traditional glycosyl donors such as halides, thioglycosides, or *O*-trichloroacetimidates provide excellent stereoselectivity and high yields.[18,19]

Since a vast majority of naturally occurring 2-amino-2-deoxysugars are N-acetylated, from the synthetic point of view, a 2-acetamido-2-deoxy-substituted glycosyl donor would be desirable to minimize protecting group manipulations. For this type of glycosyl donors however, the oxocarbenium ion rearranges rapidly into an oxazoline intermediate (Scheme 1c). Even under harsh Lewis acid catalysis, this highly stable oxazoline intermediate does not exert strong glycosyl donor properties. Although the synthesis of 1,2-trans glycosides is possible with the use of this type of glycosyl donors, the synthesis of 1,2-cis glycosides is a burden. As a matter of fact, the participating nature of the *N*-acetyl moiety presents an obvious hindrance when the formation of the α-linkage is desired. A minimal requirement for the synthesis of 1,2-cis glycosides would be the use of a C-2 non-participating moiety.

Nowadays, a variety of synthetic approaches to the synthesis of 2-amino-2-deoxyglycosides have been developed and the progress in this area has been previously



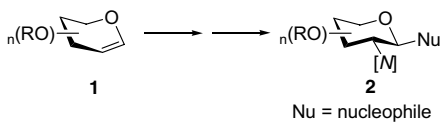
R = protecting group; LG = leaving group; R' = H (pentose) or CH_2OR (hexose); P = promoter; R'' = temporary or permanent anomeric substituent

Scheme 1.

reviewed.[20,21] These syntheses start from either a glycosamine directly or by introduction of the nitrogen functionality to glycose or glycal derivatives. To this end, various glycosamine donors with modified functionalities have been investigated, in particular, those bearing an N-2 substituent capable of either efficient participation *via* acyloxonium, but not (2-methyl)oxazoline, intermediate for 1,2-trans glycosylation or a non-participating moiety for 1,2-cis glycosylation. The aim of this account is to summarize the progress toward the establishment of reliable methods for the efficient preparation of differently protected 2-amino-2-deoxyglycosyl donors, their application to oligosaccharide synthesis, and transformation of the protected aminosugars into the natural acetamido derivatives. A particular attention is focused on the recent work.

2. Synthesis of 2-amino-2-deoxyglycosides from glycals

Glycals (1,2-dehydro sugar derivatives, **1**, Scheme 2) are often employed as versatile building blocks in synthetic carbohydrate chemistry.[22–24] Glycals were found to be excellent starting materials for the synthesis of 2-amino-2-deoxysugars by way of N-functionalization at C-2 accompanied by C-1 bond formation. Over the last few decades, a variety of methods have been developed for the nitrogen transfer to glycals (**1**→**2**, Scheme 2) and are discussed in the following section.



Scheme 2.

2.1. Introduction of the 2-azido moiety to glycals

The advantages of employing azide as an amine protecting group in general synthetic applications include lower steric hindrance, greater solubility, lack of rotamer formation, and the absence of a hydrogen or carbon nuclei to complicate NMR spectra.[25] In addition, participating usefulness of the 2-azido moiety of glycosyl donors in carbohydrate chemistry is in its non participating effect during glycosylation reactions, allowing for the synthesis of 1,2-cis glycosidic linkage. To date, the most common methods for the preparation of azide derivatives are as follows.

2.1.1. *Via* the radical mechanism. In 1971, Trahanovsky and Robbins reported the formation of α-azido-β-nitroalkanes on treating alkenes with sodium azide and ceric ammonium nitrate (CAN) in moist acetonitrile.[26] Since the products obtained were consistent with the reaction being initiated by addition of an azide radical (anti-Markovnikov route), Lemieux and Ratcliffe anticipated that the azide radical-induced addition to glycals would provide 2-azido-2-deoxyglycosyl

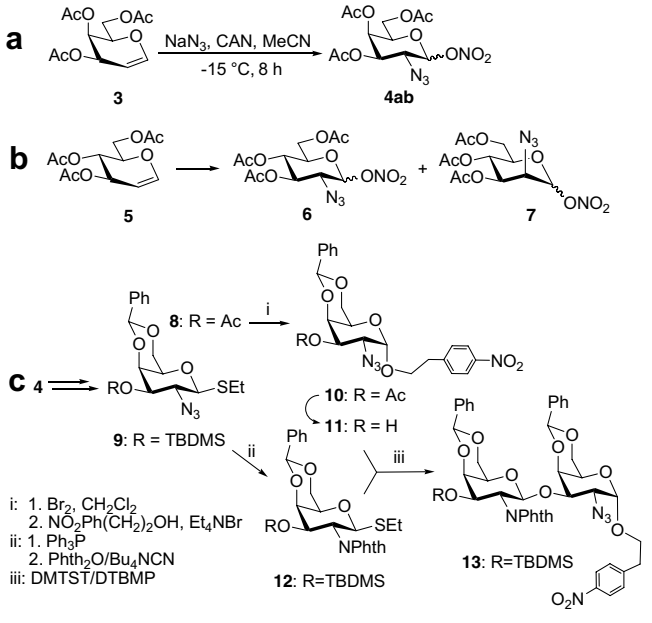
nitrates. This gave rise to the development of the azidonitration protocol.[27] As in the original procedure, the azido radical is generated from sodium azide and CAN. High regioselectivity of this process is an important advantage, yet, very commonly, epimeric mixtures of 2-azido-2-deoxy-1-*O*-nitropyranoses are obtained. The ratio of the epimers formed is strongly dependent on the structure of the glycal substrate. For example, for the *lyxo*-glycal **3** ('galactal', Scheme 3a), the 2-equatorial product is highly favored, leading to 2-azido-deoxygalactose nitrates **4a**,**b** in 85% yield.[27] Differently, for the *arabino*-glycal **5** ('glucal'), mixtures of 2-azido-2-deoxy-D-gluco **6**[28] and D-manno derivatives **7** result (Scheme 3b).[20,29,30] This higher regioselectivity can be explained by the increased steric hindrance of the top face of the D-galactal derivative **3** in comparison to that of the D-glucal derivative **5**.

Transformation of the 2-azido-2-deoxy-1-nitro-pyranose intermediate into a suitable glycosyl donor can be achieved in a number of ways. Conversions to hemiacetal,[31–33] halides,[27,34,35] acetate,[36] trichloroacetimidate,[33,37,38] pentenyl glycoside,[39] phosphate,[40,41] thioglycosides,[42–44] and xanthate[36] are amongst the most common approaches that have been efficiently applied in the synthesis of oligosaccharides (Scheme 3c). Thus far, the azidonitration method has been employed in the synthesis of *N*-acetylhyalobiuronic acid,[45] Lewis Y determinants,[46] gangliosides,[47] aminoglycoside antibiotics,[48] tunicaminyl-uracil,[49] hexosamine inositol phosphates,[50] and mucin-related Tn and TF O-linked antigens,[51] among many others.

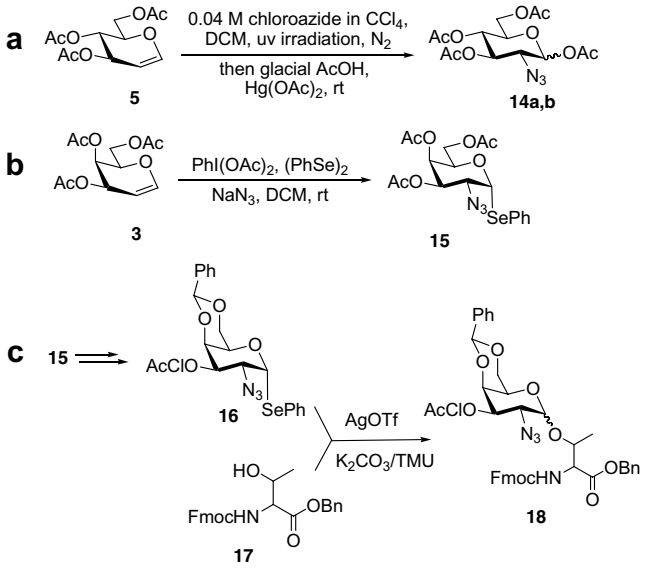
The azido moiety can then be reduced under a variety of reaction conditions amongst which are catalytic hydrogenation (H_2, Pd/C),[52–54] treatment with 1,3-propanedithiol,[55] Staudinger ligation (Ph_3P in THF/H_2O),[56,57] or Birch reduction (Na/liquid NH_3).[58,59] The free amine can then be converted into acetamido or other NHR or NR_2 derivatives by simple protecting group chemistry. Direct conversion of azido to acetamido moiety has also been accomplished *via* reductive acetylation using neat thiolacetic acid.[51,60] Depending on the strategy employed, the azide deprotection can be achieved either prior or after the glycosylation step (Scheme 3c). On the one hand this approach allows the synthesis of 1,2-cis glycosides *via* direct glycosidation of a 2-azido donor, as for example for glycosidation of thioglycoside **8** (R = Ac)[42] with 2-(*p*-nitrophenyl)ethanol to obtain **10** in 70% yield. On the other hand, 1,2-trans glycosides can also be obtained *via* transformation of the azido moiety in **9** (R = TBDMS) into a 2-*N*-participating group, such as 2-phthalimido, as for example for the synthesis of glycosyl donor **12**. The latter compound is suitable for 1,2-trans glycosylation, which is evident from the dimethyl(thiomethyl)sulfonium triflate (DMTST)-promoted glycosylation of glycosyl acceptor **11**, obtained from **10** by deacetylation, to afford 1,2-trans-linked disaccharide **13** in 76% yield (Scheme 3c). Apparently, this approach requires the use of either a stable leaving group or a temporary anomeric substituent that would tolerate conditions associated with the azide reduction.

In the course of their studies, Lemieux and Ratcliffe have also tried to generate the azide radical *via* halogen-azides.[27] These studies were abandoned after a reaction involving chloroazide and sulfuryl chloride (radical initiator) detonated with violence. Two years after, Khorlin and co-workers found an easier solution to the dilemma by developing a so-called azidochlorination protocol. This reaction features the addition of chloroazide to glucal **5** under UV irradiation in inert atmosphere.[61] Advantageously, this reaction proceeds regio- and stereoselectively to furnish mainly 2-azido-2-deoxy-D-glucopyranosyl chloride, subsequent treatment of which with glacial acetic acid and mercuric acetate provides stable tetra-*O*-acetyl derivatives **14a** and **14b** in 66% combined yield (Scheme 4a).

As mentioned above, potent glycosyl donors from azidonitrates are usually obtained after additional synthetic steps. With the goal of streamlining these operations, and bearing in mind excellent glycosyl donor properties of selenoglycosides,[62] the azidophenylselenation protocol initially developed for aliphatic alkenes[63] was introduced in sugar chemistry.[64,65] In this one-pot procedure, the azide radical is generated from the reaction of the glycal with diacetoxyiodobenzene, sodium azide, and diphenyl diselenide in dichloromethane (Scheme 4b). The reaction yields α-azidoselenides (e.g., **15**) with complete anti-Markovnikov regioselectivity as shown in Scheme 4b. A downside to this protocol,



Scheme 3.



Scheme 4.

however, is the heterogeneity of the reaction media due to the insolubility of sodium azide in dichloromethane. This complicates the generation of the azide radical and leads to by-product formation and, as a result, low yields.[66–68] To overcome this problem, Nifantiev and co-workers proposed using a soluble azide donor, trimethylsilylazide ($TMSN_3$), instead of NaN_3.[69]

One application to glycosylation is illustrated in Scheme 4c. Glycosyl donor **16**, obtained by simple protecting group sequence from **15**, was reacted with amino acid acceptor **17** in the presence of AgOTf, K_2CO_3, and tetramethylurea (TMU) to afford glycoside **18** in 87% yield. The high α-stereoselectivity of this reaction (α/β = 7.2/1) was attributed to a possible participating effect of TMU. This observation is supported by the fact that reactions without TMU provided no selectivity (α/β = 1–1.3/1).[66]

2.1.2. *Via* the azide ion. While the azidophenylselenation protocol described above works well for peracetylated glycals, attempts to apply the same procedure to perbenzylated glycals were less successful.[64,65] Czernecki et al. reasoned that this could be due to the oxidative cleavage of the benzyl groups.[65] Since the redox potential of the azide ion[70] and benzyl groups[71] are close, it appeared problematic to selectively generate the azido radical in the presence of the benzyl groups.

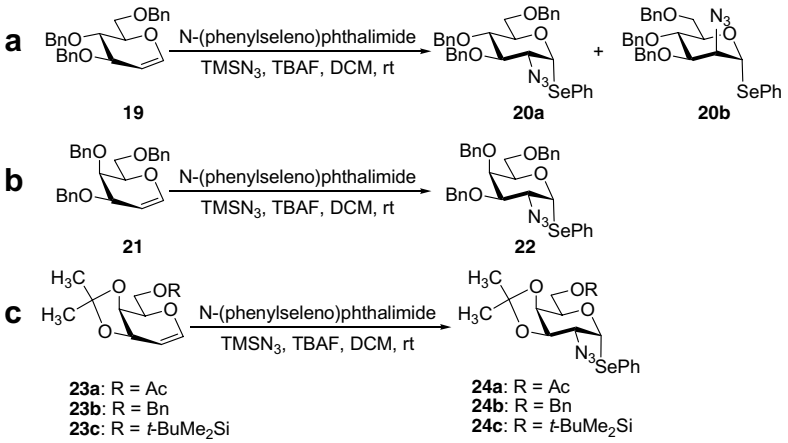
Hence, based on the ionic mechanism proposed by Hassner and Hamarasekara,[63] Czernecki and co-workers introduced a different route to the azidophenylselenation of glycals.[65] In this procedure, the transformations were carried out using *N*-(phenylseleno)phthalimide, azidotrimethylsilane, and tetra-*n*-butylammonium fluoride (TBAF) in CH_2Cl_2, under argon (Scheme 5). Under these reaction conditions, the perbenzylated glucal **19** gave an inseparable mixture of phenyl 2-azido-2-deoxy-1-seleno-α-D-gluco- and mannopyranosides (**20a** and **20b**, respectively) in a total yield of 82%. For the perbenzylated galactal **21** on the other hand, the α-galacto isomer **22** was obtained exclusively in 75% yield (Scheme 5b). The usefulness of this technique and its compatibility with many classes of protecting groups were further exemplified with diversely protected D-galactal derivatives **23a–c** (Scheme 5c), which afforded the corresponding selenoglycosides **24a–c** in 60–76% yields.

2.2. Nitration of glycals followed by Michael addition

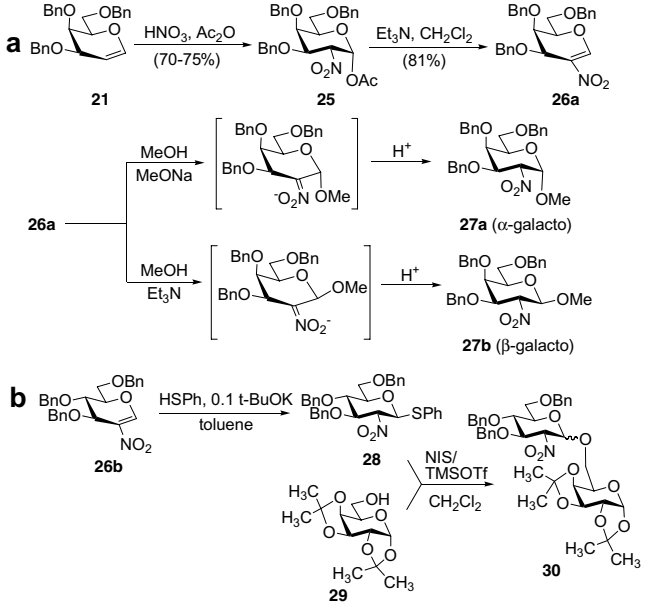
Lemieux's seminal publications describe the transformation of tri-*O*-acetyl glucal **5** into the corresponding 2-nitroglucal and, subsequently, by the Michael addition of methanol, into methyl 2-deoxy-2-nitro-D-glucopyranosides.[72,73] Since then, only scattered studies involving reactions of this type had been conducted.[74–76] In 1998, Das and Schmidt reasoned that Michael-type additions to 2-nitro-D-galactal derivatives could be particularly rewarding if the alcohol addition could be selectively guided to either α- or β-galactopyranoside formation.[77] Subsequent nitro group reduction to the corresponding amine and N-acetylation would furnish the desired glycosides. To this end, the perbenzylated galactal **21** (Scheme 6a) was treated with acetyl nitrate, generated in situ by the addition of nitric acid to acetic anhydride under strict temperature control, to afford 2-deoxy-2-nitrogalactopyranoside **25** in good yield.[72,73,78] Addition of triethylamine to the solution of **25** in CH_2Cl_2 gave the elimination product, 2-deoxy-2-nitrogalactal **26a**, in 81% yield.

For stereoelectronic reasons, addition of nucleophiles to **26a** in the $^4H_5$ conformation should occur from the bottom face (α).[79] Accordingly, the addition of 0.1 M NaOMe in MeOH to a solution of **26a** in THF at room temperature gave predominantly the expected methyl α-galactoside **27a** in 92% yield (α/β = 8:1, Scheme 6). Conversely, if the same reaction was carried out using excess methanol in the presence of triethylamine as a base, β-galactoside **27b** was predominantly obtained (90%, α/β = 1:8). According to Das and Schmidt, these results imply that, in the presence of an amine base, addition from the top face of the ring (β) of **26a** is kinetically favored.[77]

Consequently, Barroca and Schmidt applied these observations to the synthesis of 2-nitro-1-thioglycoside donors.[80] Thus, base-catalyzed glycosylation of 2-nitroglucal **26b** with thiophenol and 0.1 equiv of potassium *tert*-butoxide gave 2-nitrothioglycoside **28** in 70% yield. As expected, glycosylation of soft nucleophiles, such as thiophenol, in the presence of a strong base yields mainly the β-anomer. To demonstrate the potential of this approach, glycosyl donor **28** was glycosidated with



Scheme 5.



Scheme 6.

various acceptor alcohols. While glycosylation of highly reactive 2-propanol provided the β-glycoside stereoselectively, in case of the less reactive acceptors such as **29**, the β-selectivity was conserved but not exclusive (Scheme 6). Thus, disaccharide **30** was obtained in 82% yield as a mixture of α,β-anomers (1/2). It is possible that the presence of a nitro group at C-2 directed the glycosidation to favor the β-anomer as the major product.

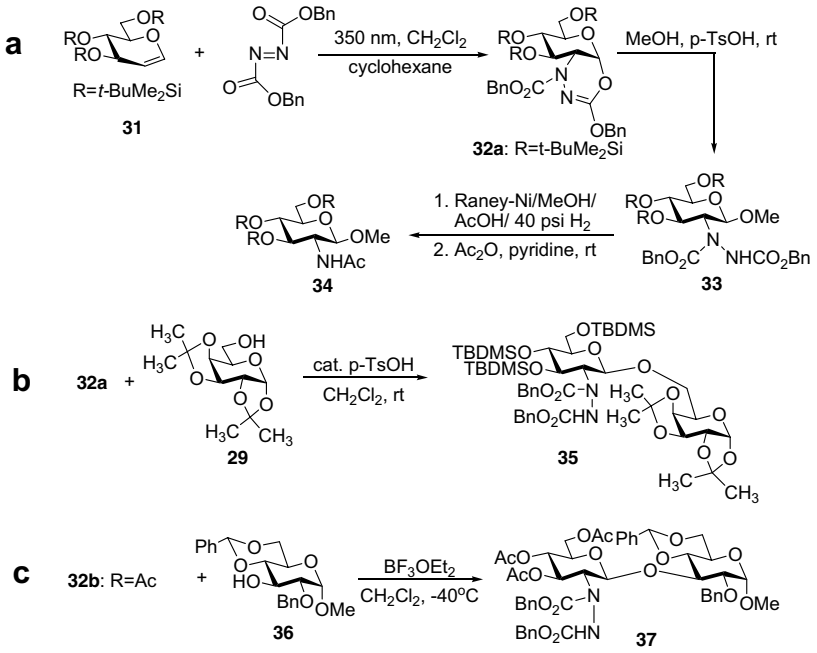
2.3. Cycloaddition reactions

Cycloaddition reaction is amongst the most important tools employed in mainstream organic chemistry.[81,82] It has been applied to a tremendous number of modern syntheses of natural products and medicinally relevant substances. These reactions are often used to create multiple chirality centers with excellent regio and stereocontrol. There are several important types of cycloaddition reactions in carbohydrate chemistry.[83] Herein, the application of the cycloaddition chemistry to the synthesis of 2-amino-2-deoxyglycosides is discussed.

2.3.1. Formation of pyrano-oxadiazines. The cycloaddition of azadicarboxylates with simple vinyl ethers was first reported in 1969 to give [4+2] or [2+2] adducts depending on the substrate.[84–89] Based on the published mechanistic studies of this reaction with simple substrates, Leblanc and co-workers reasoned that the diastereoselectivity of the cycloadducts would be most readily attainable with a rigid substrate having an appropriately placed substituent—for example, allyl-substituted cyclic vinyl ethers.[90] Since glycals fit this criterion, Leblanc et al. explored the possibility of applying this reaction to the synthesis of 2-aminosugars from glycals.[90–93]

Thus, irradiation with UV light at 350 nm of a solution of tri-O-silylated glucal **31** with dibenzyl azadicarboxylate in cyclohexane led to the single [4+2] cycloadduct **32a** in 70% yield (Scheme 7a).[92] This initially surprising diastereoselectivity was attributed to the preference of the trisilylated glucal to adopt a $^1C_4$ or a half-boat conformation. As such, the axial C-3 silyl ether would hinder the cycloaddition from the top face of the molecule. Treatment of cycloadduct **32a** with a catalytic amount of *p*-TsOH in MeOH gave the corresponding methyl glycoside **33** in 88% yield. Hydrogenolysis of the protected hydrazine **33** followed by acetylation gave methyl 2-acetamido-2-deoxyglycoside **34** in 72% yield.

Since the treatment of **32a** with *p*-TsOH in MeOH gave stereospecific opening at C-1 with inversion of stereochemistry, it was assumed that pyrano-oxadiazines may provide entry to more complex 2-aminoglycosides.[91,93]

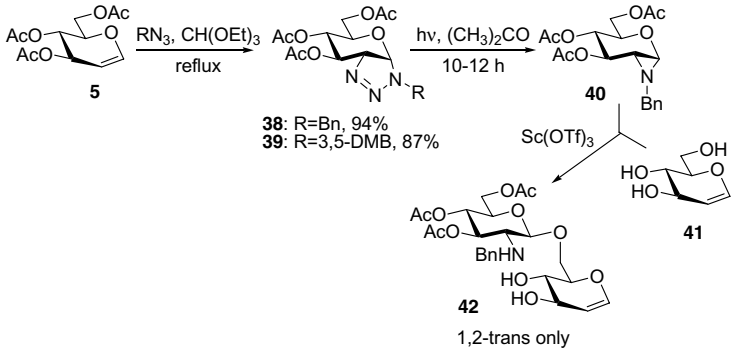


Scheme 7.

Thus, to demonstrate the utility of this protocol in oligosaccharide synthesis, the variably substituted pyrano-oxadiazines **32a** and **32b** were glycosylated with primary and secondary glycosyl acceptors **29** and **36**, respectively (Scheme 7b and c). The reactions proceeded as expected affording the corresponding disaccharide derivatives **35** and **37** in 95% and 65% yield, respectively.

2.3.2. Formation of triazolines. In the same manner, the applicability of dipolar cycloaddition reactions to the synthesis of 2-aminoglycosides from glycals has been investigated.[94] These studies demonstrated that tri-*O*-acetyl glucal **5** readily engages in dipolar cycloadditions with alkyl azides such as benzyl azide, 3,5-dimethoxybenzyl azide, and 1-adamantyl azide, at elevated temperatures. It was also found that the choice of the reaction solvent is critical to the outcome of the reaction. For instance, if the cycloaddition is carried out at high temperature in trimethyl- or triethylchloroformate, the unstable triazoline intermediates (**38** or **39**) were isolated in good yields with little or no purification required (Scheme 8).

Initial attempts to convert the isolated triazolines **38** or **39** into a reactive aziridine and, consequently, 2-aminoglycosides under acidic conditions led to poor yields of the corresponding aminoglycosides. Whereas these reactions were accompanied by extensive elimination, photochemical conversion of triazoline **38** to the corresponding aziridine **40** was clean and efficient, provided the photolysis was carried out in acetone. Subsequent $Sc(OTf)_3$-promoted glycosidations of aziridine **40** with a range of nucleophiles gave the β-aminoglycoside derivatives exclusively. For example, glycosylation of acceptor **41** afforded disaccharide **42** in 74% yield (Scheme 8).



Scheme 8.

2.4. Amidation of glycals

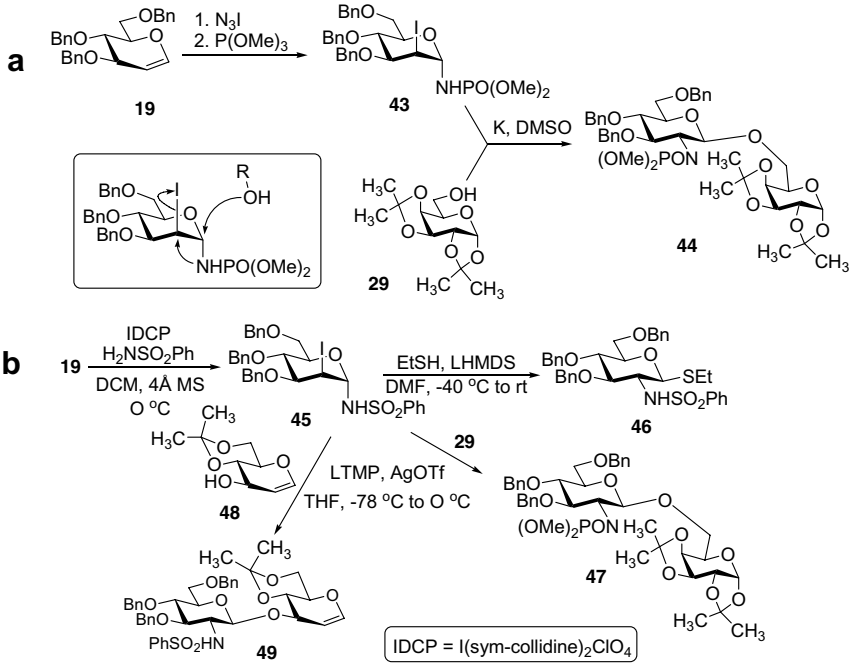
The increased strain and unique reactivity attributed to three-membered rings make aziridine derivatives useful intermediates for the synthesis of 2-aminoglycosides. As demonstrated above, nucleophilic ring opening[94] and cycloaddition reactions[95] have harnessed the synthetic utility of these intermediates. Although direct synthesis of 1,2-aziridines from glycal precursors has not yet emerged, it is believed that a variety of approaches, among which are products of amidation procedures described herein, proceed through aziridines.

2.4.1. Phosphoramidation. The elaboration of activated 1,2-aziridines for the synthesis of 2-aminosugars by direct insertion was developed by Lafont and Descotes.[96,97] Thus, the reaction of tri-*O*-benzyl glucal **10** with iodoazide, followed by Staudinger reaction led to the formation of the trans-diaxially substituted 2-deoxy-2-iodomannopyranosyl phosphoroamidate **43** in 58% yield. Along with the main product of the D-mannose series, a 2-iodo phosphoroamidate of β-D-glucose series was obtained in 34% yield. The reaction of **43** with a glycosyl acceptor, for example, **29**, under basic conditions resulted in the inversion of configuration at C-1 and C-2. As a result, disaccharide **44** was obtained in 28% yield (Scheme 9a).

Overall, this approach was found to be significantly more efficient for simple alcohol substrates, for example, reaction of **43** with NaOMe/MeONa allowed the corresponding β-methyl glucoside in 92% yield. It was proposed that the glycosylations proceeded *via* the aziridine intermediate.

2.4.2. Sulfonamidoglycosylation. Inspired by the pyrano-oxadiazine[90–93] and phosphoramidation[97] procedures described above, Griffith and Danishefsky explored another possibility for the azaglycosylation of glycals.[98] It was assumed that substitution of the nitrogen with an electron-withdrawing group would significantly enhance the glycosidating potential of the aziridine linkage, and thereby allow glycosylation of unreactive glycosyl acceptors, a major limitation of the previously introduced techniques. Thus, the reaction of tri-*O*-benzyl glucal **19** with iodonium (di-sym-collidine) perchlorate (IDCP) and benzenesulfonamide gave the trans-diaxial iodosulfonamide **45** in 78% yield (Scheme 9b).

Both oxygen and sulfur nucleophiles were investigated for subsequent glycosidations of **45**. For example, the sulfonamide migration reaction in the presence of lithium ethanethiolate produced thioglycoside **46** in 85% yield. O-Glycosidation of **45** with diacetone galactose **29** in the presence of lithium tetramethyl-piperidine (LTMP) and AgOTf in THF at −78 °C, followed by warming to 0 °C, gave disaccharide **47** in 57% yield (Scheme 9b). This result is favorably compared to the synthesis of **44** achieved in a similar fashion *via* the phosphoroamidation protocol. A secondary glycosyl acceptor **48** was also efficiently glycosylated, providing a 1,2-trans-linked disaccharide **49** in 64% yield.[98] It was also demonstrated that 2-sulfonamidoglucosides can be readily converted into natural 2-acetamido



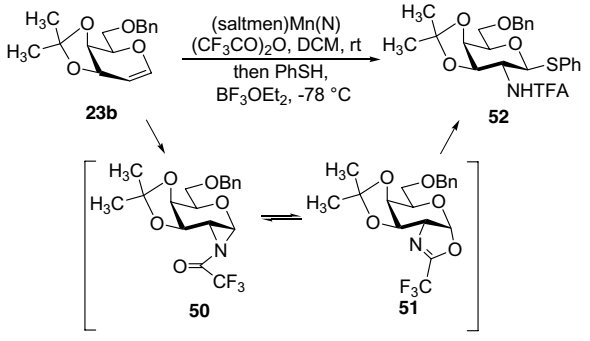
Scheme 9.

derivatives by the treatment with excess sodium in ammonia followed by N-acetylation.

Additionally, disaccharide **49** can be employed in iterative elongation of the oligosaccharide sequence, since the double bond could be sulfonamidated followed by glycosidation, etc. To date, the potency and versatility of the sulfonamide glycosylation reaction has been applied to the synthesis of sialyl Lewis X antigen and antigenic determinants,[99,100] asparagine-linked N-protected glycopeptides and N-linked glycopeptides,[101,102] stage-specific embryonic antigen-3 (SSEA-3),[103] allosamidin,[104] human breast tumor (Globo-H) antigen,[105] asialo GM_1,[106] KH-1 (adenocarcinoma) antigen,[107] mucin-related F1α antigen,[108] and the core pentasaccharide of N-linked[109] glycoproteins.

2.4.3. Transition metal-mediated amidation. In 1997, Carreira and co-workers introduced a transition metal-mediated approach to amidation of glycal substrates that leads to the formation of 2-deoxy-2-trifluoroacetylamido derivatives.[110] The impetus for this project was provided by previous studies showing that easily accessible salen-derived nitride manganese complexes, when reacted with trifluoroacetic anhydride, transferred a CF_3CON unit to electron-rich silyl enol ethers.[111–115] Thus, activation of (saltmen)Mn(N)[116] with TFAA and transfer of the CF_3CON group to variably substituted glycals, for example, **23b**, gave 2-*N*-trifluoroacetamido derivatives in good yields and excellent diastereoselectivity. The stereochemical outcome at C-2 of this reaction is controlled by the proximal stereocenter at C-3. As illustrated in Scheme 10, sequential treatment of the **23b**-(saltmen)Mn(N)–TFAA solution with thiophenol and BF_3–OEt_2 afforded the desired thioglycoside **52** with complete β-stereoselectivity.

2.4.4. 2-Acetamido glycosylation. As a means of providing direct access to 2-acetamido-2-deoxyglycosides in one pot, Gin and co-workers introduced the so-called C-2-amidoglycosylation procedure.[117,118] This protocol involved the use of a new sulfonium reagent derived from thianthrene-5-oxide, which, in combination with Tf_2O, generates the thianthrene bis(triflate) in situ



Scheme 10.

(Scheme 11). Electrophilic activation of the glucal donor **19**, followed by nitrogen transfer, resulted in the formation of glycosyl imidate **53**. Subsequent intramolecular displacement of thianthrene by the nitrogen with concomitant N-desilylation generated glycosyl *N*-acylaziridine **54**, which then underwent rearrangement to afford oxazoline **55**.[119] Finally, acid-mediated ring opening with isopropanol afforded the 2-acetamido-2-deoxyglycoside **56** in 73% yield.

Synthesis of a series of disaccharides was performed using this procedure. Thus, acetamidoglycosylation of glycosyl donors **19**, **59**, and **61** with the primary acceptor methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (**57**) led to the formation of the corresponding 2′-acetamido-2′-deoxy disaccharides **58**, **60**, and **62** (Table 1). Synthesis of **62** illustrated the propensity of the thianthrene sulfoxide/triflic anhydride reagent to selectively react with the glycal enol ether functionality in the presence of simple alkenes (allyl substituent).

Gin and co-workers also demonstrated that by varying the sulfoxide reagent, this protocol can be applied to the diastereoselective synthesis of 2-amino-2-deoxymannopyranosides.[120] Thus, treatment of the glucal with the reagent combination of 2,8-dimethyldibenzothiophene-5-oxide (DMDBTO) and Tf_2O, followed by nitrogen transfer and acid-mediated glycosylation, provides the corresponding 2-acetamido-2-deoxymannopyranosides with good to excellent diastereoselectivity.

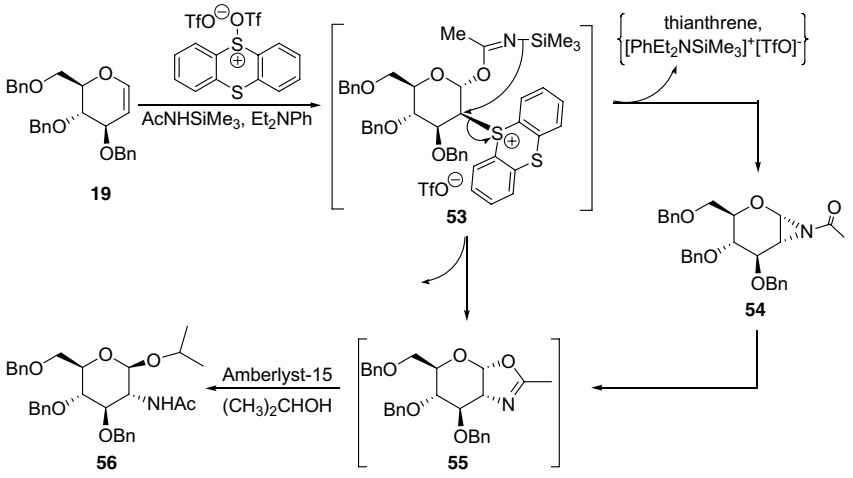
In brief, although traditional glycal approach to the synthesis of 2-aminoglycosides is somewhat cumbersome, the latter two examples described herein clearly demonstrate that there are other possibilities for more rapid or straightforward access to the glycosyl donors (Scheme 10) or even to glycosides directly (Scheme 11).

3. Synthesis of 2-amino-2-deoxyglycosides *via* the nucleophilic displacement at C-2

The nucleophilic displacement reaction of appropriately activated derivatives is an indispensable tool for the introduction of substituents into the sugar framework. These reactions proceed *via* the bimolecular mechanism and result in the inversion of configuration. The efficiency of the displacement strongly depends on the site of substitution, the nature of the nucleophile, the leaving group, the polarity of the solvent, and other factors. Other common reactions of this class include introduction of oxygen, sulfur, and halogen substituents.[121] The application of displacement reactions to the synthesis of 2-amino-2-deoxysugars is discussed hereafter.

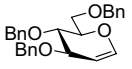
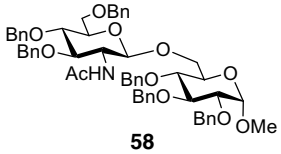
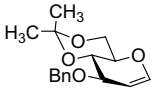
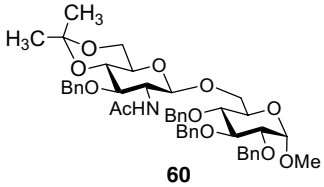
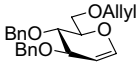
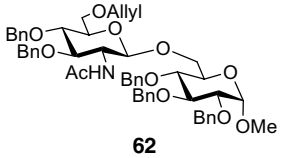
3.1. From *O*-sulfonyl derivatives

For sulfonic acid esters of most organic compounds, substitution reactions occur under relatively mild condi-



Scheme 11.

Table 1. 2-Acetamido glycosidation of variably protected glucal donors **19**, **59**, and **61**

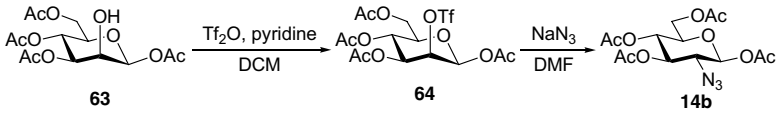
Entry	Donor	Product	% Yield
1	 **19**	 **58**	60
2	 **59**	 **60**	45
3	 **61**	 **62**	55

tions. In carbohydrate chemistry, however, displacement reactions with less reactive sulfonic acid esters (mesyl, tosyl) are often limited to the more accessible primary carbon atoms.[122–125] In contrast, if highly reactive carbohydrate triflates are employed as the substrates, substitution reactions at either primary or secondary carbon atoms are usually accomplished under mild reaction conditions. Overall, based on the extensive research that has been done on carbohydrate-derived sulfonate esters, the S_N2 displacement of a suitable triflate glycosyl derivative with the azide ion appears to be a viable alternative to the existing technologies for the preparation of 2-azido-2-deoxyglycosides.[126–134]

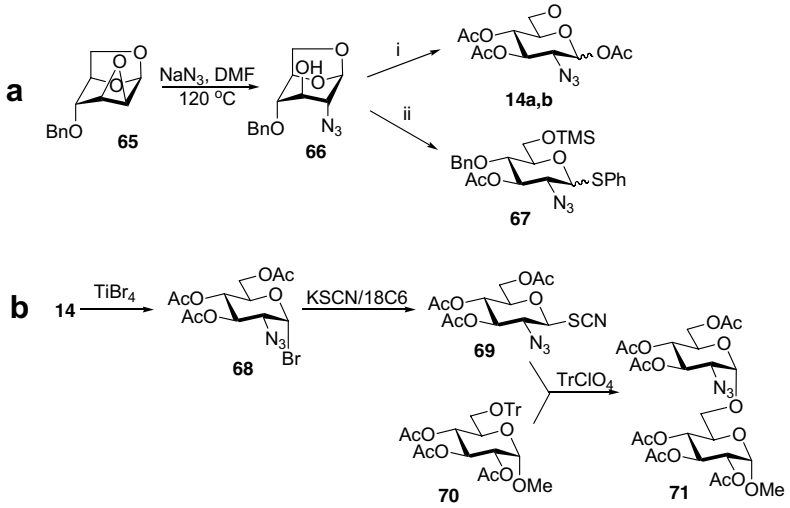
The triflate moiety is typically introduced by reaction of an alcohol with Tf_2O and pyridine in dichloromethane, see for example, the synthesis of 2-*O*-triflate **64** from 2-hydroxyl derivative **63** (Scheme 12).[135–145] As to the triflate displacement reaction, many modifications have emerged[135–152] since the pioneering work by van Boom and co-workers.[153] For example, the treatment of **64** with NaN_3 in DMF afforded **14b** in 86% yield.[136] Apparently, the 2-azido-2-deoxy derivative **14b** can then be converted into a suitable glycosyl donor and used in subsequent glycosylations. Amongst a variety of reaction conditions employed for the azide displacement of the triflyl moiety are the following: LiN_3 in DMF,[141,153] NaN_3 in DMF,[135–137,142,146,148,149,151,152] Bu_4NN_3 in benzene,[139,140,143,144] or $TMSN_3$ and TBAF in THF.[145,147,150,154]

3.2. From epoxides

Amongst synthetic precursors suitable for nucleophilic displacement reactions, arguably, a series of epoxide



Scheme 12.



Scheme 13. Reagents and conditions: (i) Ac_2O, AcOH, H_2SO_4; (ii) (a) Ac_2O/pyridine; (b) TMSSPh, ZnI_2.

derivatives developed by Černý and Stanek occupy an important niche.[155] First reported in the 1970s, Černý epoxides,[156–159] for example, **65** (Scheme 13), have served as useful synthons for the synthesis of many biologically important derivatives. It was demonstrated that the ring opening of **65** with NaN_3 could be readily achieved in 9:1 DMF–water at 120 °C to afford **66** in high yield of 80%.[160] Recently introduced modified one-pot procedures further enhance the usefulness of this protocol.[161,162]

The 1,6-anhydro ring of **66** can be opened either under acetolysis conditions to afford **14a**,**b** or with TMSSPh to provide a simple and direct access to thioglycosides, see, for example, the synthesis of **67** (Scheme 13).[163] Derivative **14a**,**b** could also be converted into a glycosyl donor, for example, glycosyl thiocyanate. This approach, developed by Kochetkov et al., provided complete α-stereoselectivity of glycosylation even in dichloromethane, a reaction solvent that does not typically favor α-glycosylations.[164] For example, coupling of thiocyanate **69**, obtained from bromide **68**, with 6-O-tritylated glycosyl acceptor **70** in the presence of $TrClO_4$ provided α-linked disaccharide **71** in 81% yield (Scheme 13).

To date, the anhydrosugar approach to 2-aminoglycosides has been applied to the synthesis of glycosaminoglycans,[162] GPI-anchored peptide, lipid A disaccharides,[165,166] *N*-acetyllactosamines,[167] and umbelliferone glycosides of *N*-acetyl glucosamine and chitobiose,[168] among others.

4. Synthesis of glycosides from 2-amino-2-deoxysugars *via* the introduction of an amine protecting group

As mentioned earlier, naturally occurring 2-amino-2-deoxy glycopyranosides are often N-acetylated and are linked *via* 1,2-trans-glycosidic linkages. The use of N-acetylated donors, however, is often impractical. On the one hand, glycosidation of such donors often leads to the formation of relatively unreactive oxazoline intermediate that often remains as a major by-product. On the other hand, high nucleophilicity of the lone pair of electrons on nitrogen of the acetamido group also presents a complication by attracting electrophilic species (such as promoters of glycosylation) that often results in decreased reactivity and/or additional by-products.

A common way to decrease the reactivity of the amino group is to temporarily convert it into an electron-withdrawing amide, carbamate, or imide. The carbonyl group(s) effectively withdraw the electron density from the nitrogen atom and render it less reactive. The drawback of this indirect approach is in the necessity to perform a number of additional steps that are required for the synthesis of the glycosyl donor and the conversion of the temporary substituent into the acetamido moiety. These additional synthetic manipulations significantly decrease the overall efficiency and yields.

The choice of an amine protecting group for C-2 of aminosugars is also influenced by the fact that the protecting group at C-2 can directly influence the stereochemical outcome of the glycosylation reactions (see

Scheme 1). Thus, for a 1,2-trans glycosidic linkage, it would be desirable if the amine function on C-2 would be capable of providing anchimeric assistance to the oxocarbenium ion that forms. Conversely, for the synthesis of 1,2-cis glycosides, it is necessary to have a non-participating group at C-2. It should be noted that the use of the non-participatory moiety alone does not guarantee 1,2-cis selectivity; for example, the use of 2-azido 1-phosphate donors provided excellent 1,2-trans selectivity even in the presence of a non-participating solvent.[40] Overall, the ideal amine protecting group should be stable to a wide range of reaction conditions while also being able to impart sufficient reactivity, stereoselectivity, and high yield in glycosylation reactions. Moreover, it should be readily removed under mild reaction conditions. The progress in this area is described hereafter.

4.1. Monosubstituted 2-amino-2-deoxyglycosyl donors

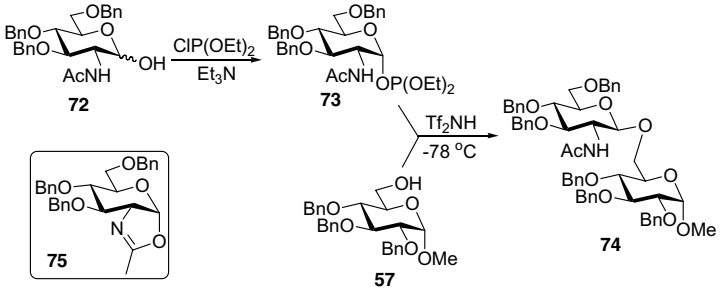
4.1.1. Acetamido derivatives. As mentioned earlier, the use of N-acetylated donors is often impractical due to the formation of relatively unreactive oxazoline intermediate. In early days, 1,2-*O*,*N*-oxazoline derivatives have been thoroughly investigated and reviewed;[20] nowadays, the application of these derivatives as glycosyl donors is mainly limited to glycosylation of highly reactive simple alcohols or primary glycosyl acceptors. However, the attempts to create an efficient method that would allow glycosidation of 2-acetamido glycosyl donors never cease.[169–171] Recent reports in this area dealing with the glycosidation of furanosyl oxazoline derivatives[172] and direct glycosidation of 2-acetamido derivatives with a phosphite leaving group[173] may open new exciting perspectives for the future development of this attractive concept (Scheme 14). For example, glycosidation of the glycosyl phosphate donor **73**, obtained from hemiacetal **72**, with glycosyl acceptor **57** in the presence of triflimide at −78 °C afforded the corresponding disaccharide **74** in 93% yield. In some experiments, oxazoline **75** was formed as the major by-product. Interestingly, model glycosidations of **75** with acceptor **57** under the same reaction conditions resulted in no product formation. This result was used in an argument that this reaction proceeds directly from the glycosyl phosphite donor with no oxazoline intermediate formation.[173]

4.1.2. Haloacetamido derivatives. Simple amides are generally prepared from the acid chloride or the anhydride. Many amides are stable toward mild acidic or basic hydrolysis and are classically hydrolyzed by heating in strongly acidic or basic solutions.[174] Among simple amides, hydrolytic stability increases from formyl to acetyl to benzoyl. Lability of the haloacetyl derivatives to mild acid hydrolysis increases with substitution: acetyl < chloroacetyl < dichloroacetyl < trichloroacetyl < trifluoroacetyl.[175]

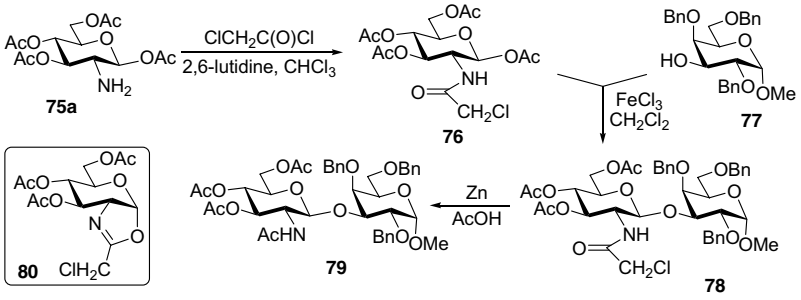
The use of 2-chloroacetamido-2-deoxyglycopyranosyl donors was introduced by Kiso and Anderson in 1985, who reasoned that halogen-substituted 2-acetamides will form weaker, and therefore more reactive, oxazoline intermediates (see compound **80**, Scheme 15) by virtue of electron withdrawal.[176] As a result, glycosyl donors of this type would be better electrophiles, and hence, more reactive in glycosidation. To this end, 2-chloroacetamido derivative **76** was synthesized from **75a** using chloroacetyl chloride in the presence of 2,6-lutidine in $CHCl_3$ (Scheme 15). To demonstrate the effectiveness of monochloroacetyl derivatives as glycosyl donors, **76** was then glycosidated with various primary and secondary glycosyl acceptors.[175,177]

Thus, $FeCl_3$-promoted glycosidation of **76** with glycosyl acceptor **77** gave disaccharide **78** in 80% yield. When acetate **76** was treated with $FeCl_3$ in CH_2Cl_2 in the absence of the glycosyl acceptor, the oxazoline derivative **80** was isolated as a proof that the glycosylation reaction proceeds *via* an oxazoline intermediate. It was demonstrated that the treatment of **78** with zinc and acetic acid in refluxing oxolane reduces the *N*-chloroacetyl group (see the synthesis of **79**, Scheme 15).

2-Deoxy-2-dichloroacetamido derivatives were introduced as glycosyl donors with the purpose to address another challenge associated with the use of 2-acetamido derivatives as glycosyl donors. Thus, a glycosyl donor 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl bromide was found to be easily transformed



Scheme 14.



Scheme 15.

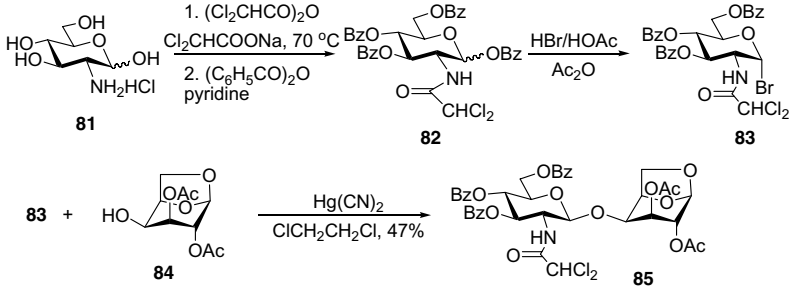
into a relatively unreactive 1-acetyl-2-amino-2-deoxy hydrobromide derivative by an $N \rightarrow O$-acyl migration *via* oxazoline.[178] Therefore, it was believed that the powerful electron-attracting dichloroacetyl group has the appropriate structure to address this challenge.[179] For this purpose, glucosamine hydrochloride **81** was reacted with dichloroacetic anhydride and sodium dichloroacetate followed by O-benzoylation to afford 2-deoxy-2-dichloroacetamido sugar **82** in 68% yield (Scheme 16). Bromination of **82** with HBr/HOAc gave glycosyl donor **83**, which was reacted with glycosyl acceptor **84** under Helferich conditions to afford disaccharide **85** in 47% yield.[179,180] Hydrolysis of the amide group was effected by adding 1 N methanolic barium methoxide and water to a solution of **78** in methanol.[179]

2-Deoxy-2-trichloroacetamido derivatives have also been investigated, initially in the synthesis of nucleosides under acidic conditions.[181] Unfortunately, the main product of this glycosylation was found to be stable trichloromethyl oxazoline, which was the reason to abandon these studies. Three decades later, Beau and co-workers noted that, as a matter of fact, (2-trichloromethyl)oxazoline resembles an intramolecular trichloroacetimidate.[182] Since glycosyl trichloroacetimidates are excellent glycosyl donors,[183,184] this bicyclic derivative could serve as a potentially reactive glycosyl donor for the synthesis of 1,2-trans 2-amino-2-deoxyglycosides.

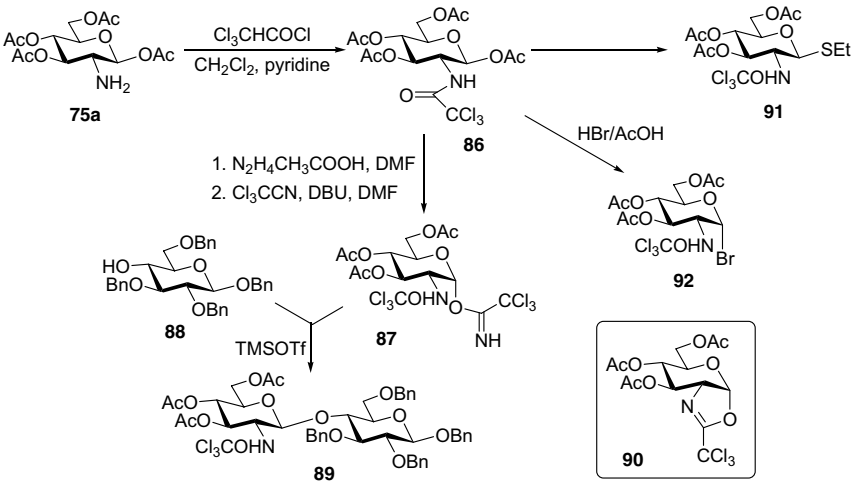
To this end, 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranose **86** was prepared from D-glucosamine tetraacetyl derivative **75a** as illustrated in Scheme 17.[181,185] Anomeric deacetylation of **86** with hydrazine acetate in DMF followed by reaction with trichloroacetonitrile in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) afforded the trichloroacetimidate derivative **87** in 79% yield. Glycosyl donor **87** was then glycosidated with **88** in the presence of TMSOTf to afford 1,2-trans-linked disaccharide **89** in 82% yield. The complete stereoselectivity achieved supports the intermediacy of an oxazolinium species. This conclusion was confirmed when treatment of **87** with TMSOTf followed by workup furnished oxazoline **90** as the major product (Scheme 17). Thus, it seems that the electron-withdrawing effect of the trichloromethyl group in the intermediary oxazolinium ion greatly increases the electrophilic character of the anomeric carbon, as compared to its methyloxazoline counterpart.

Other classes of glycosyl donors with the 2-deoxy-2-trichloroacetamido moiety have been investigated.[182,186–188] Amongst the derivatives investigated, glycosyl donors **91** and **92** serve as a clear illustration of the versatility of 2-trichloroacetamido derivatives in terms of their application to oligosaccharide synthesis. In this connection, Donohoe et al. found that 2-(trichloroacetyl)oxazoline derivatives of allosamines and talosamines are also excellent glycosyl donors.[189]

Another advantage to the use of *N*-trichloroacetyl derivatives is the ease of their deprotection. This canbe achieved under a variety of reaction conditions, amongst which are tributylstannane-azobisisobutyronitrile



Scheme 16.

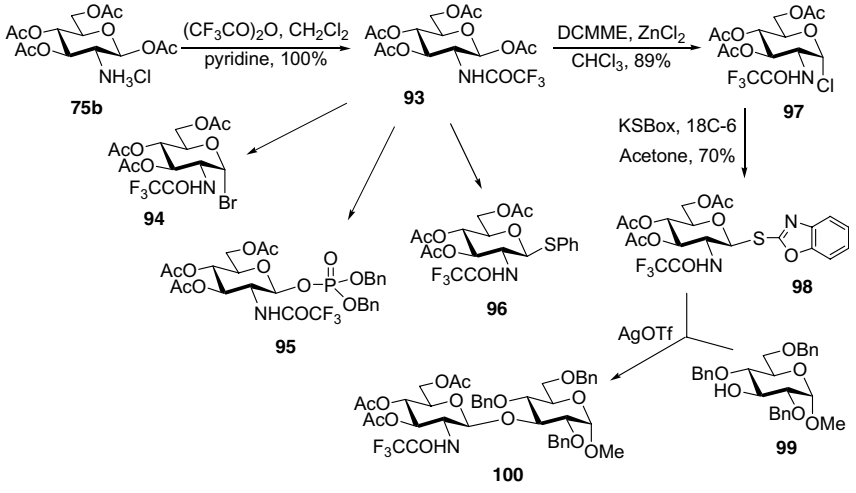


Scheme 17.

(AIBN) in refluxing benzene,[182] hydrogenolysis (H_2, Et_3N, PtO, AcOEt, 55 psi),[190] or cleavage with NaOH followed by reacetylation.[189,191]

The early application of 2-deoxy-2-trifluoroacetamido (TFA) derivatives was to the synthesis of steroid glycosides using glycosyl bromides as donors.[181,192,193] The precursor for this synthesis, derivative **75b**, was obtained in three steps from D-glucosamine *via* sequential treatment with anisaldehyde in 1 N NaOH, acetylation with acetic anhydride, and hydrolysis of the *N*,*N*-anisylidene moiety with 5 N HCl.[194,195] Reaction of **75b** with trifluoroacetic anhydride gave the *N*-trifluoroacetyl derivative **93** quantitatively (Scheme 18). A variety of glycosyl donors with a suitable anomeric leaving group have been prepared. Amongst the reported glycosyl donors bearing the *N*-trifluoroacetyl moiety on C-2 are the acetates (such as **93**),[196,197] bromides (**94**),[181,193,198–203] phosphates (**95**),[204–207] thioglycosides (**96**) and their corresponding sulfoxides,[208] 4-*tert*-butylthiophenyl glycosides,[209] phenylselenides,[210] etc. Very recently, the anomeric acetyl moiety was converted into chloride **90** and then into *S*-benzoxazolyl (SBox) glycosyl donor **98** (Scheme 18).[211] The latter derivative showed potent glycosyl donor properties; for example, glycosylation of the glycosyl acceptor **99** in the presence of AgOTf provided 1,2-trans-linked disaccharide **100** in 89% yield.

To convert the *N*-trifluoroacetyl moiety back to the free amine, various methods have been employed. Amongst these are the use of HCl in MeOH,[212] NaOH in acetone–water,[201,213] or LiOH[208] in THF–MeOH. It should be noted that these conditions allow for the orthogonal deprotection of the *N*-trifluoroacetyl group over other amine protecting groups.[208] Glycosyl donors of this class have been employed in the synthesis of chiro-inositols,[198] didemnin B analogues,[214] *C*-glycosyl phosphonates,[204] globotriosylceramide,[215] diosgenin derivatives,[202] bacterial polysaccharide fragments,[216] and Lipid A analogues.[217]



Scheme 18.

4.1.3. Alkoxycarbamoyl derivatives. 2-Alkoxycarbamoyl-2-deoxy derivatives have found widespread use as glycosyl donors due to their ease of formation and the orthogonality or chemoselectivity of N-deprotection.[20] Protection is usually accomplished by condensation of the free amine and the appropriate chloroformate in the presence of a mild base.[218] Conditions for removal, however, depend on the moiety employed, that is, benzyl carbamate (NHCbz or NHZ) is cleaved by catalytic hydrogenolysis; allyl carbamate (NHAlloc) is readily cleaved by Pd-catalyzed isomerization; while trichloroethyl carbamate (NHTroc) is readily cleaved by acidic hydrolysis or reduction with Zn.[174] Other carbamates, for example, *N*-methoxycarbonyl,[219–224] *N*-(*tert*-butyl)oxycarbonyl (*t*Boc),[218] and *N*-(*p*-nitrobenzyl)oxycarbonyl (PNZ)[225] have been used in oligosaccharide synthesis, yet only commonly employed carbamate moieties are discussed in this subsection.

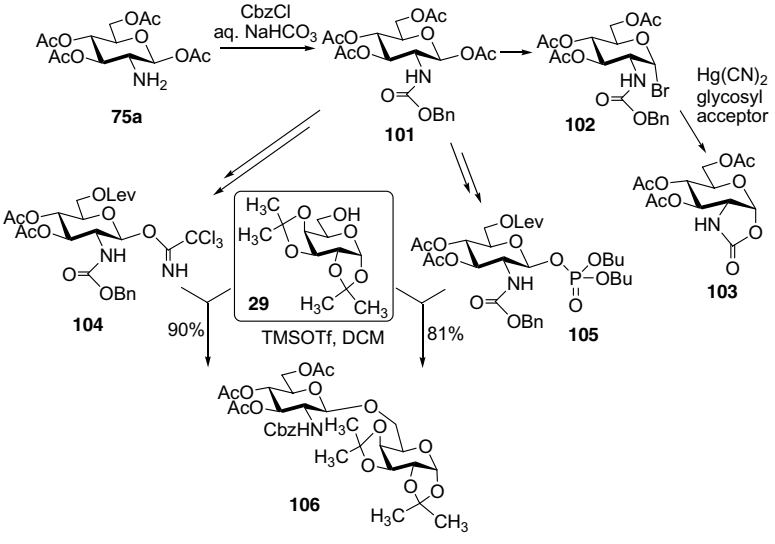
Dating back to the 1930s,[194,226] the use of benzylchloroformate (CbzCl) in the presence of a suitable base is still the method of choice for installing the *N*-benzyloxycarbonyl moiety on the free amine function.[30,218,227–230] Tetraacetate **101** can be easily prepared from either unprotected glucosamine[226] or from 2-amino tetraacetate **75a**.[218] The latter approach is preferred if the synthesis of **101** in anomerically pure β-form is required (Scheme 19). It has been effectively used in the synthesis of glycopeptide[231] and glycolipid derivatives.[232] Cbz-protected glycosamines can also be obtained by consequent reprotection of azido or another carbamate-protected glucosamine.[160,227]

The first reported glycosylations with 2-*N*-benzyloxycarbonyl amino sugars involved the activation of bromides.[233,234] Unfortunately, the $Hg(CN)_2$-promoted reaction of glycosyl bromide **102** with glycosyl acceptors gave the oxazolidinone derivative **103** with migration of the benzyl group to the aglycone.[233] Silver salt-promoted condensation of simple alcohols with 2-NHCbz chloride was more successful. Yet, β-glycosides were isolated in only moderate yields (42–46%) despite the use of a large excess of alcohol.[235] When applied to the synthesis of simple aminosugar–pyrimidine nucleosides, however, 2-NHCbz chlorides gave the 4-methoxypyrimidinone nucleoside in 84% yield.

Over the years, more potent glycosyl donors bearing the 2-NHCbz moiety have been developed including dimethylphosphinothioates,[236] phosphorodiamidimidothioate,[237] trichloroacetimidates,[160] 4-pentenyl glycosides,[238] and phosphates.[238] For example, glycosylation of glycosyl acceptor **29** with glycosyl donors **104** or **105** in the presence of TMSOTf provided disaccharide **106** in 90% and 81% yield, respectively (Scheme 19).[238] These glycosyl donors were prepared in a few steps using conventional synthetic manipulations *via* stable *O*-pentenyl moiety as a temporary anomeric substituent.

As mentioned, catalytic hydrogenolysis cleaves the carbobenzoxy moiety to afford the free amine. Reported deprotection conditions include H_2/Pd in EtOH,[239] H_2/Pd in dioxane/water,[30] and H_2/Pd in MeOH/H_2O,[240,241] along with the chemoselective N-deprotection reported by Hasegawa et al.[242] using H_2/Pd in the presence of MeOH, HBr, and dioxane. The efficacy of these glycosyl donors has been demonstrated in the synthesis of nucleosides[243] inner core of lipopolysaccharides,[244] heparin derivatives,[240,245–247] dibekacin,[248] Lipid A derivatives,[249] glycosidic lignan variants,[250] neoglycoconjugates,[227] solid-phase peptide synthesis,[231] and antibacterial amino glycosides,[251] among others.

Versatile applications of the allyloxycarbamoyl (Alloc) protective group[252,253] prompted Boullanger et al. to investigate its participating properties in 1,2-trans glycosylation reactions.[254] For this purpose, glucosyl

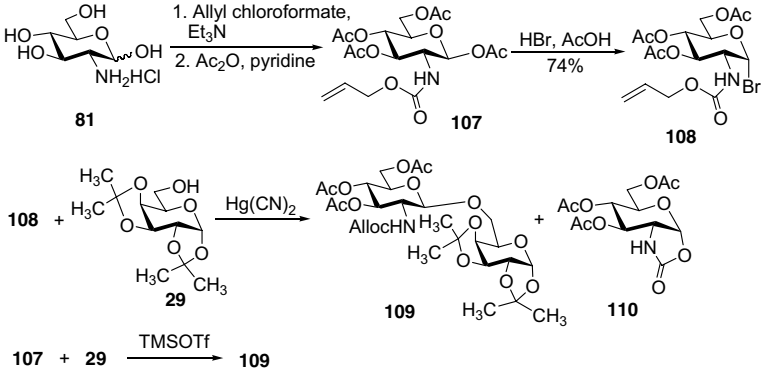


Scheme 19.

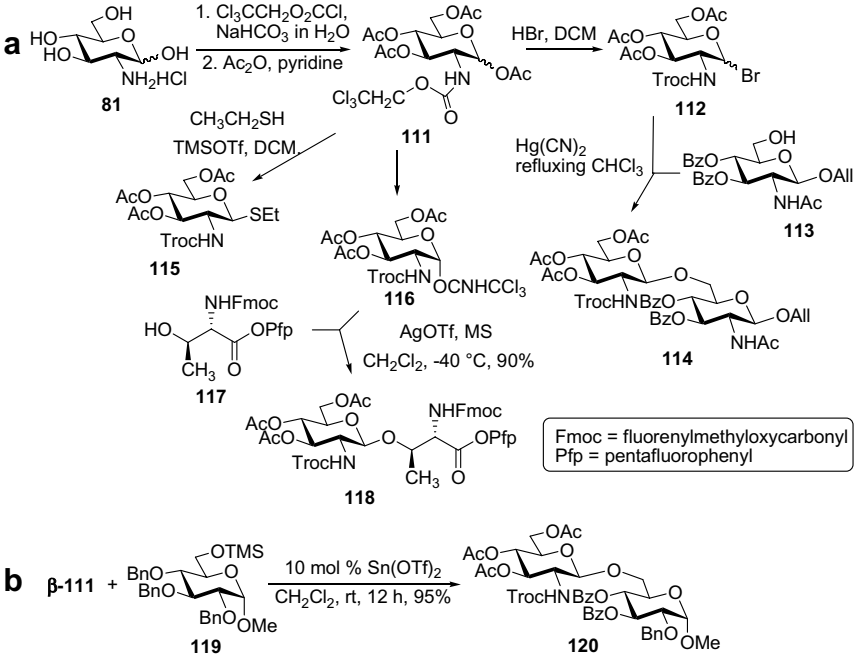
bromide **108** was prepared in 74% overall yield from D-glucosamine hydrochloride **81** by sequential treatment with allylchloroformate and Et_3N at 50 °C, followed by acetylation (Ac_2O, pyridine) and bromination with 33% HBr in AcOH (Scheme 20).[255] The reaction of 2-*N*-allyloxycabonyl bromide **108** with galactosyl acceptor **29** promoted by $Hg(CN)_2$ gave the β-linked disaccharide **109** in 86% yield along with the oxazolidinone derivative **110**.[255] In contrast, glycosidation of β-acetate **107** with glycosyl acceptor **29** in the presence of trimethylsilyl triflate (TMSOTf) provided disaccharide **109** in 82% yield with no formation of side product **110**.[254]

In an attempt to improve the reactivity as well as to expand the scope of applications, a variety of leaving groups with a 2-*N*-allyloxycarbonyl moiety have been developed over the years, for example, trichloroacetimidates[256] and thioglycosides.[257] The derivatives of 2-*N*-allyloxycarbonyl sugars have been applied to the synthesis of peptidoglycan partial structures,[258] glycopeptide assemblies,[256,259] 1,6-anhydro derivatives,[260] neoglycolipid analogues,[261] *N*-acetylneuraminic acid derivatives,[257] and surfactants.[262] The deprotection of the *N*-allyloxycarbonyl group is achieved using any of the following methods: reductive cleavage,[263] treatment with $Ni(CO)_4$,[264] basic hydrolysis,[257] homogeneous palladium catalysis using $Pd(PPh_3)_4$,[254,258,265–267] or Pd-catalyzed hydrogenolytic cleavage with formic acid in the presence of an allyl acceptor.[268] The allyl acceptor can be dimedone,[265] 2-ethylhexanoic acid,[266] tributyl tin hydride,[256,267] dimethyl malonate,[254,261] or AcOH.[258]

The use of 2-*N*-trichloroethoxycarbonyl (Troc) derivatives in aminoglycoside synthesis was first introduced by Kusumoto and co-workers in 1985.[269] In their report, *N*-Troc bromide **112** was synthesized from commercially available compound **81** in quantitative yield over three steps (Scheme 21a). Glycosylation of glucosyl acceptor



Scheme 20.



Scheme 21.

113 with bromide **112** gave disaccharide **114** in good yield and complete β-selectivity. This method was used extensively in the synthesis of *Escherichia coli* Lipid A and analogues thereof, as well as the synthesis of *O*- and *S*-linked glycopeptides.[249,270–276] Another typical procedure for the preparation of the NHTroc derivatives is *via* temporary *N*,*N*-anisylidene protection.[218] The resulting intermediate **111** can serve as a suitable precursor for the preparation of a range of excellent glycosyl donors.

Schultz and Kunz converted intermediate β-**111** into thioglycoside donor **115**, thiophilic activation of which with DMTST gave the desired β-linked glycopeptides.[259] Trichloroacetimidate **116**, obtained from acetate **111** *via* conventional two-step protocol,[184] provided high yields in the synthesis of glycopeptides. For example, AgOTf-promoted reaction of **116** with glycosyl acceptor **117** provided 1,2-trans glycoside **118** (Scheme 21a).[277] Moreover, Mukaiyama and Matsubara showed that tetraacetate β-**111** can be useful in tin(II) trifluoromethanesulfonate-catalyzed glycosylations with alkyl trimethylsilyl ethers.[278,279] Under these conditions, β-glycosides were typically obtained in 80–99% yields. For example, the synthesis of disaccharide **120** was accomplished in 95% yield from building blocks β-**111** and **119** (Scheme 21b).

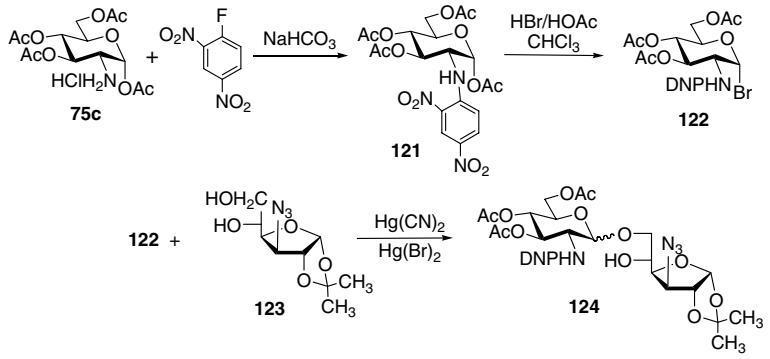
Over the years, these and other classes of 2-NHTroc glycosyl donors have been used in glycoside and oligosaccharide synthesis: as trichloroacetimidates,[165,238,258,277,280–303] for the synthesis of pyruvated saccharide fragments,[280,304] Lipid A derivatives,[165,281,288,290,294,297,298,305,306] glycopeptides,[277,284,285] lactosaminyl donors,[282,307] Re-type lipopolysaccharides,[289] sialyl Lewis^{x} glycolipids,[291,301] gangliosides,[292] peptidoglycan partial structures,[258,308] thiooligosaccharide analogues[286] of Nod factors, carbohydrate antigens,[295,302] sialyl-trimeric-Lewis X,[300] hyaluronan trisaccharides,[309] meonomycin A analogues,[310] and ceramidated GLA-60[293] derivatives; as fluorides,[282,311,312] for the synthesis of lactosaminyl donors, glycosylamines,[312] and tumor-associated antigen[311] Globo-H; as chlorides;[313] as thioglycosides,[283,286,314–331] for the synthesis of carbohydrate antigens,[315,325,327–329,333] globotetraose tetrasaccharides,[316] lactosamine donors,[318] glycopeptide partial structures,[321,324] *N*-acetyllactosamine oligomers,[332] thiooligosaccharide analogues of Nod factors,[286] vancomycin,[326] gangliosides,[334] and glycosyl amino acids;[323] as sulfoxides, for the preparation of 2-aminoglycals;[223,319] and more recently, as thioimidate derivatives.[211]

The Troc group has been found to be stable under a wide range of standard conditions typically used in carbohydrate synthesis.[314] Its sensitivity to alcoholysis under basic conditions permits convenient transformations into other carbamates. Removal of the Troc group to liberate the primary amine is typically accomplished by reductive elimination using Zn in AcOH,[259,270,271,277,280,282,283,285,290–292] Zn–Cu alloy in AcOH,[258,288,289,297,298,308,335] Zn and acidic buffer,[293,336] Cd–Pb in AcOH,[309,331,337] or more recently, using $(Bu_3Sn)_2$[338] in DMF. The use of Zn–*N*-methylimidazole,[339] in particular, allows selective deprotection of Troc in the presence of reducible and acid-sensitive functionalities.

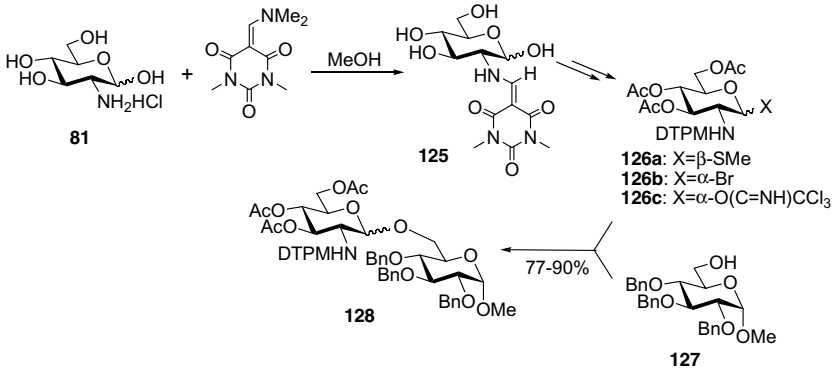
4.1.4. Miscellaneous monosubstituted derivatives. On account of their crystalline properties and distinctive color, the use of *N*-2,4-dinitrophenyl (DNP) derivatives of glycosamines was introduced in the 1950s to separate aminosugars from biological isolates.[340–342] A decade later, Lloyd and Stacey[343] investigated the possibility of using these derivatives for 2-amino glycoside synthesis. To this end, 2-DNP derivatives were prepared either from unprotected glucosamine or from **75c** with 1-fluoro-2,4-dinitrobenzene and sodium bicarbonate. The latter example is illustrated in Scheme 22. The resulting tetraacetate **121** can then be brominated under standard conditions to give **122**,[343,344] glycosidation of which with glycosyl acceptor **123** under Helferich conditions gave the corresponding disaccharide **124** in 50% yield (α:β = 3:1).[199] The anomeric mixture of predominantly α-linked disaccharide indicates the non-participatory nature of this protecting group and makes it a possible candidate for 1,2-cis glycoside synthesis. Removal of the DNP group can be easily effected by alkaline hydrolysis.[343]

Another monovalent amine protecting group that has been developed recently is 1,3-dimethyl-2,4,6-(1*H*,3*H*,5*H*)-trioxopyrimidine-5-ylidene methyl (DTPM) amine type moiety. DTPM protection can be achieved in high yield by reacting D-glucosamine **81** with inexpensive reagent 1,3-dimethyl-5-[(dimethylamino)methylene]-2,4,6-(1*H*,3*H*,5*H*)-trioxopyrimidine-5-ylidene methyl to give the NHDTPM derivative **125** in 90% yield (Scheme 23).[345] Consequent studies on donors of this type, for example, **126a**–**c**, showed weakly participatory nature of the DTPM moiety at C-2. Thus, glycosylations of glycosyl acceptor **127** with 2-NHDTPM thioglycoside **126a**, bromide **126b**, or trichloroacetimidate **127c** gave anomeric mixtures (β mainly, α/β = 1/1–8) of the corresponding disaccharide **128** in 77–90% yields.[346]

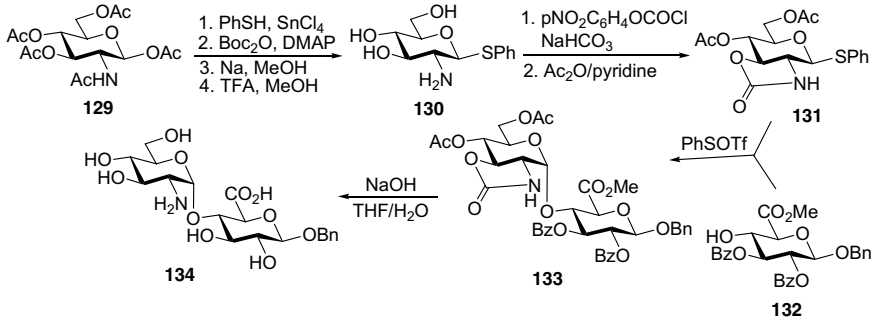
The 2,3-*N*,*O*-carbamate protecting group[347] was investigated in glycosylation reactions by Kerns and co-workers.[317,348] Their approach to the synthesis of this bicyclic derivative involved sequential thioglycosylation with PhSH and transformation of the acetamido moiety in **129** into 2-*N*-benzyloxycarbonylacetamido derivative, which was globally deprotected in two steps to afford **130** (Scheme 24). The cyclocarbamate moiety was then introduced using *p*-nitrophenylchloroformate; subsequent O-acetylation led to the glycosyl donor **131**. Gly-



Scheme 22.



Scheme 23.



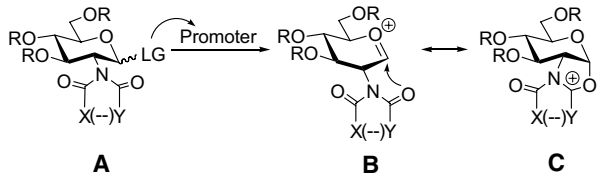
Scheme 24.

cosylation of acceptor **132** with glycosyl donor **131** in the presence of phenylsulfenyltriflate at −78 °C afforded a 1,2-cis-linked disaccharide derivative **133** in 75% yield. It was demonstrated that the 2,3-carbamoyl moiety can be removed with NaOH in aqueous THF with concomitant cleavage of ester moieties. Thus, deprotected disaccharide **134** was obtained in 80% yield.[317] In contrast, glycosidation of similar ethylthio glycoside in the presence of NIS/AgOTf provided complete 1,2-trans selectivity.[349] Analogous N-acetylated derivatives and their application will be discussed below in Section 4.2.3.

The oxazolidinone moiety was also investigated in glycosyl acceptors.[350] Amongst other developments in the area of 2-N-monosubstituted derivatives are *N*-formyl[351] and *N*-pentenoyl derivatives.[352] The *N*-pentenoyl moiety could be orthogonally removed in the presence of the TCP functionality, an especially beneficial property in the synthesis of oligosaccharides containing multiple aminosugar residues such as Lipid-A derivatives.[353]

4.2. Disubstituted 2-amino-2-deoxyglycosyl donors

As mentioned above, the most attractive means for the establishment of a 1,2-trans-glycosidic linkage would be through the formation of cationic species from a derivative of the sugar with participation of the



Scheme 25.

neighboring substituent at C-2 (Scheme 1). The latter substituent should be so chosen that its engagement does not lead to products other than the desired 1,2-trans-β-glycoside, that is, the formation of stable 1,2-oxazolines or oxazolidinones seen above. In this regard, blocking the amino function with two monovalent protecting groups or a bivalent cyclic group seems to be a reasonable recourse. Thus, electrophilic activation of the bivalently protected glycosyl donor **A** yields an oxocarbenium ion **B**, which can form an oxazolinium intermediate **C** (Scheme 25). The reactive intermediate **C** can only be attacked from the β-face by a nucleophile, and more importantly, cannot form a stable oxazoline. Various 2-amino-2-deoxyglycosyl donors of this type have been developed over the years. Their preparation, activation, N-deprotection and model glycosidations will be discussed hereafter.

4.2.1. Phthalimido and tetrachlorophthalimido derivatives. In 1954, Baker et al. prepared 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranose and observed that treatment of this compound with HBr/HOAc gave 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl bromide.[354] Six years later, Akiya and Osawa utilized the latter in glycosylations of simple alcohols and obtained the desired β-glycosides in high yields.[355] Hence in 1976, Lemieux et al. proposed the use of 2-phthalimido glycopyranosyl halides for the development of a generally useful preparation of 2-amino-2-deoxy oligosaccharides.[356] It was anticipated that engagement of the phthalimido group in charge delocalization at the anomeric center to form a strongly delocalized intermediate **C** (Scheme 25) will strongly influence the formation of a 1,2-trans linkage. Since then, 2-deoxy-2-phthalimido-protected glycosyl donors have been extensively studied and arguably became the method of choice for the preparation of 1,2-trans-linked glycosides and oligosaccharides of 2-amino-2-deoxy-sugars.[20]

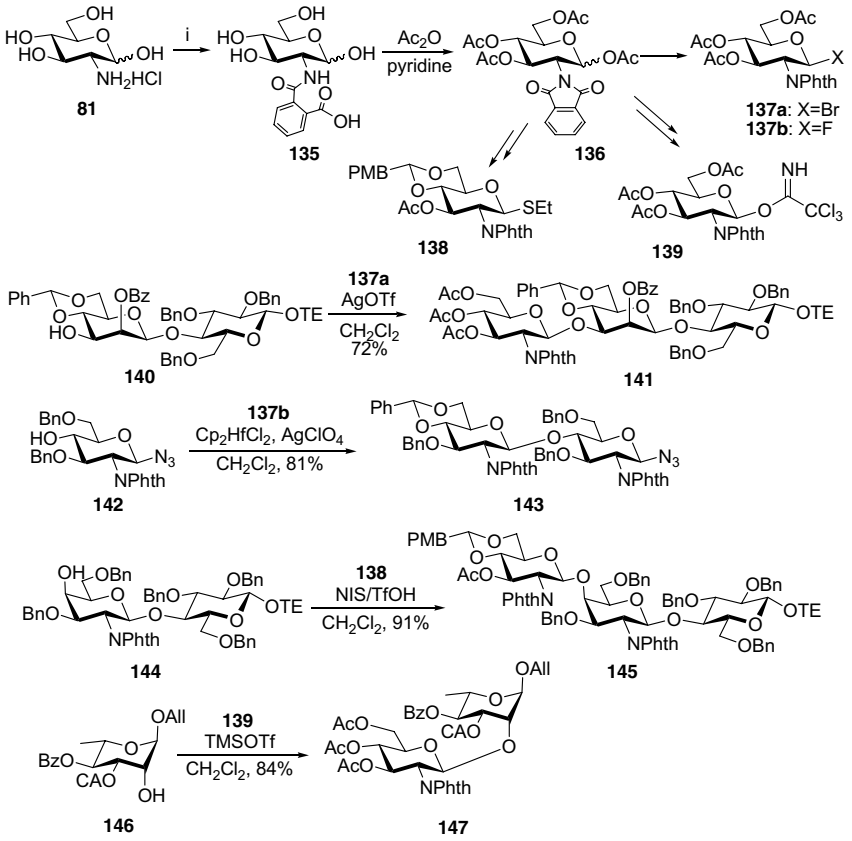
Preparation of 2-deoxy-2-phthalimido glycopyranosyl derivatives is usually accomplished by treatment of the corresponding 2-amino-2-deoxy sugar precursor **81** with phthalic anhydride in the presence of a base. Acetylation of the monosubstituted intermediate **135** results in the formation of the peracetylated derivative **136** that was obtained by Kochetkov et al. (conditions A)[357] or Lemieux et al. (conditions B)[356] in 69% and 79% yields, respectively (Scheme 26). Starting from precursor **136**, a range of glycosyl donors, including halides, trichloroacetimidates, thioglycosides, and thioimidates, have been synthesized. The progress in this area since a comprehensive report by Banoub et al.[20] will be discussed herein.

The chemical synthesis and properties of both the anomeric forms of 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-D-glucopyranosyl halides, for example, **137a**, as well as their 1-chloro and 1-iodo counterparts, have been described by Lemieux and contrary to the premise of the anomeric effect, they found that the β-form was more stable.[356] Initially, as described in the synthesis of O-specific polysaccharides of *Shigella flexneri*,[358,359] asialo-GM1 and -GM2,[360] 1,6-anhydromuramyl peptides,[361] and cell-surface glycans,[362] 2-phthalimido bromides were more commonly used in glycosylations under Koenigs–Knorr or Helferich conditions.

A representative example is shown in Scheme 26; thus, reaction of the bromide donor **137a** with glycosyl acceptor **140** resulted in the formation of trisaccharide **141** in 72%.[363] The greater stability of the chloride counterpart, however, started a change in the trend and resulted in a number of syntheses employing this building block; for example, blood-group antigens,[364] peptidoglycans,[365] and disaccharide analogues of meonomycin.[366]

Highly stable 2-phthalimidoglycosyl fluorides also found application in aminosugar synthesis.[367] For example, 2-phthalimidoglucopyranosyl fluoride **137b**, obtained from **136** by a protecting group sequence followed by treatment with dimethylaminosulfur trifluoride (DAST) in THF, was reacted with glycosyl acceptor **142**.[368] Amongst the activating conditions developed, Cp_2HfCl_2–$AgClO_4$ (Suzuki's et al. protocol)[369] was chosen, providing disaccharide **143** in 81% yield.[368]

2-Phthalimido thioglycosides have also been widely employed in oligosaccharide synthesis. Amongst these are *methyl thioglycosides*, used in the synthesis of novel sulfated GM1b analogues (Scheme 26b),[370,371] ganglioside GD2 and GQ1b,[372–374] and galactosyl globosides;[375] *ethyl thioglycosides*, used in the synthesis of blood-group antigens,[376–378] capsular polysaccharides of bacterial pathogens,[43,379] glycoprotein[380] residues, and peptidoglycan[381,382] residues; *phenyl thioglycosides*, used in the synthesis of blood-group determinants and antigens,[383–385] chitin oligosaccharides,[386] lactosamine[318] donors, glycan residues,[387] oligosaccharides from respiratory mucins,[388] selectin ligands,[389,390] and bacteriohopanetetrol[391] derivatives; *p-methylphenyl thioglycosides*, used in the synthesis of α-Gal epitopes,[392,393] synthetic aminoglycosides,[394] and synthetic heparan sulfate[60] ligands; and *isopropyl thioglycosides*, used in the synthesis of immunostimulants[395] buffalo milk pentasaccharide derivatives,[396] and anticancer agents.[397–399]



Scheme 26. Reagents and conditions: (i) (A) phthalic anhydride, $NaHCO_3$, H_2O; or (B) 1. NaOMe, MeOH; 2. $Phth_2O$, Et_3N, MeOH.

The introduction of the thioalkyl/aryl leaving group is generally accomplished by condensation of the appropriate acetate precursor with the corresponding thiol,[314,389,395,400,401] stannane,[362,402] or silyl ether[403–405] in the presence of Lewis Acids such as BF_3OEt_2,[314,389,395,400] $TiCl_4$,[406] TMSOTf,[404,407] $FeCl_3$,[401] ZnI_2,[405] and $SnCl_4$.[362,408] Nucleophilic displacement of an anomeric halide with the salt of the thiol is also a viable route.[409–411] Glycosidation of thioglycosides can be achieved with the use of a variety of acceptors.[412] For example, NIS/TfOH-promoted reaction of glycosyl donor **138** with glycosyl acceptor **144** afforded oligosaccharide **145** in 91% yield (Scheme 26).[413]

The use of 2-deoxy-2-phthalimido trichloroacetimidates in aminosugar synthesis was introduced by Grundler and Schmidt in 1983.[414] Thus, the β-imidate **139** was obtained by reaction of carbohydrate hemiacetals with trichloroacetonitrile in the presence of a base (Scheme 26). Typical glycosylations using trichloroacetimidates are performed in CH_2Cl_2 as a solvent, using a sub-stoichiometric amount of the promoter, usually BF_3OEt_2[414–418] or TMSOTf.[284,419–422] For example, the synthesis of disaccharide **147** from glycosyl donor **139** and glycosyl acceptor **146** was accomplished in 84% yield.[421] To date, this method has been applied to the synthesis of bacterial antigenic polysaccharides,[415,416,421,422] tumor-associated antigens,[424] chitosan polysaccharides,[425] buffalo milk polysaccharides,[396] mucin-type[417] core units,[284] hyaluronic acid,[418] and E-selectin ligands,[426] among others.

While the above glycosyl donors have proved to be potent and efficient, other glycosyl donors, such as phenylselenides,[62,427] trifluoroacetimidates,[428,429] and thioimidates,[211] have also been investigated. Deprotection of the phthaloyl group can be achieved with hydrazine hydrate in MeOH or EtOH,[370,371,388,430] alcoholic methylamine,[431,432] ethylenediamine in BuOH or EtOH,[368,376,380,433–435] ammonia in MeOH,[398] sodium borohydride,[401,436] and hydrazine acetate,[437] to form a free amine.

The strongly basic conditions described and the high temperature required to carry out the cleavage of *N*-phthaloyl moiety present the biggest drawback of the phthalimido procedure in target synthesis. This excludes its application to the synthesis of a broad range of targets, including various families of glycopeptides and glycolipids where numerous base-sensitive groups such as esters and α-amino acid residues exist.[21] Thus, Fraser-Reid and co-workers[352] and Castro-Palomino and Schmidt[438] reasoned that the presence of electron-withdrawing groups on the aromatic ring would enable

cleavage under less demanding conditions. It was pointed out, however that the remote withdrawal of electron density should not inhibit neighboring group participation.[352] This led to the introduction of readily available tetrachlorophthalimido (TCP) derivatives as building blocks for aminosugar synthesis. Application of the 4,5-dichlorophthalimido moiety to glycoside and oligosaccharide synthesis has also been investigated.[438–441]

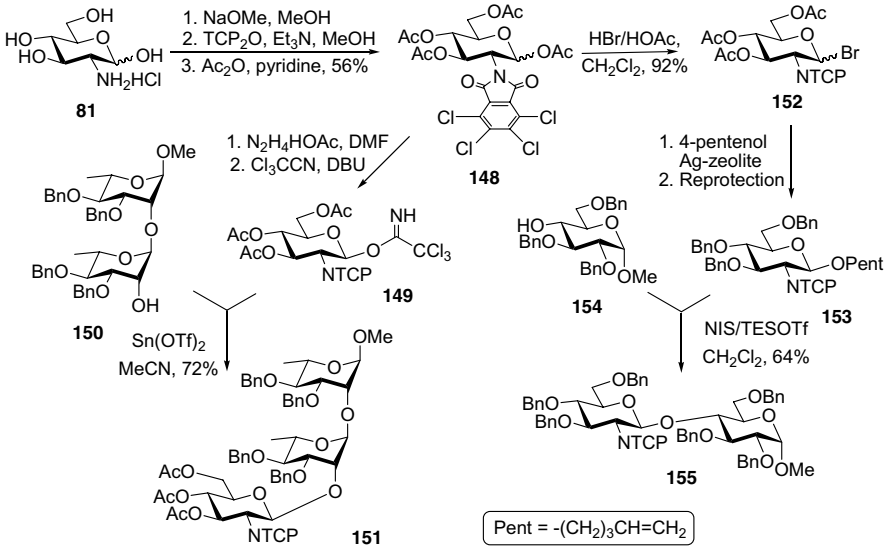
The TCP derivatives can be readily prepared using Lemieux's classic procedure for the synthesis of 2-phthalimido derivatives.[356] Thus, starting from precursor **81**, the tetra-acetyl 2-tetrachlorophthalimido derivative **148** is obtained in 56% yield over three steps (Scheme 27).[443] Precursor **148** can then be modified accordingly into potent glycosyl donors such as bromides,[202,444,445] fluorides,[441] pentenyl ethers,[352,353,443,446] trichloroacetimidates,[438,447] or thioglycosides.[448–450] Herein, the synthesis and application of trichloroacetimidate **149** and *O*-pentenyl glycoside **153** synthesized *via* bromide **152** will be discussed. Thus, the reaction of trichloroacetimidate **149** with glycosyl acceptor **150** in the presence of tin(II) triflate afforded trisaccharide **151** in 72% yield.[447] Glycosylation of glycosyl acceptor **154** with *O*-pentenyl glycoside **153** led to the corresponding disaccharide **155** in a yield of 64% (Scheme 27).[352]

Among other applications, TCP glycosyl donors have been used for the synthesis of nodulation factors,[443] Lipid A derivatives,[353] saponins,[202] mucin oligosaccharide chains,[449] and blood-group antigens.[451] Removal of the TCP group either by ethylene diamine,[352,353,452,453] or by $NaBH_4$ in isopropanol,[452] followed by acetylation affords the corresponding *N*-acetyl derivative.

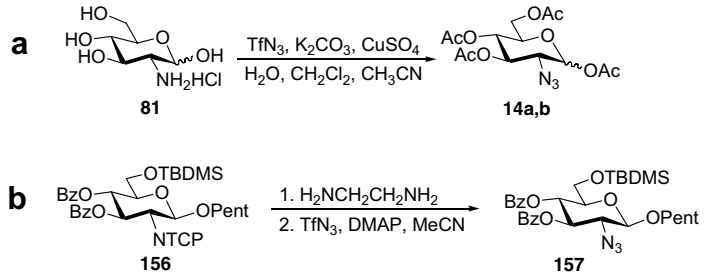
4.2.2. Diazotransfer reactions (2-azido derivatives). As mentioned above, 2-azido-2-deoxy derivatives of glycopyranoses, useful building blocks for the synthesis of 1,2-cis glycosides, can be stereo- and regioselectively obtained from glycals and hexoses in a number of different ways. These methods have proven to be extremely useful in the synthesis of expensive precursors of the D-galactosamine and D-mannosamine series. For the synthesis of the D-glucosamine derivatives, however, there is no cheaper and vastly available starting material than D-glucosamine. Thus, a method allowing the direct transformation of glucosamine to 2-azido-2-deoxy derivatives would be a useful tool in oligosaccharide synthesis.

In 1967, Fischer and Anselme[454] showed that the reaction of an arylamine anion and *p*-toluenesulfonyl azide gave the azide derivative of the amine. Five years later, Cavender and Shiner[455] showed that the use of trifluoromethanesulfonyl (triflyl) azide (TfN_3) can promote the same reaction more efficiently. After it was shown that this method can be used to make azides from aliphatic amines[455] and amino acids,[456] Vasella et al.[457] applied Shiner's procedure to the synthesis of 2-azido-2-deoxy glycopyranose derivatives. For this purpose, a solution of TfN_3 in CH_2Cl_2 was added to a solution of amine **81** in MeOH. Standard acetylation of the resulting intermediate gave anomeric mixture of 1,3,4,6-tetra-*O*-acetyl-2-azido-deoxy glucopyranose **14a**,**b** (Scheme 28). Alternative approaches are also possible *via* mild temporary amino group substituents. For example, selective removal of the TCP group in **156**, followed by the installation of the azido group with TfN_3, provided 2-azido-2-deoxy intermediate **157** that could be applied to the synthesis of various glycosyl donors.[458]

Due to the unpredictability of this reaction as well as the inherent explosiveness of TfN_3 when dried, various modifications to this procedure have been published since. Accordingly, it has been shown that diazotransfer reactions with TfN_3 can be promoted by a variety of



Scheme 27.



Scheme 28.

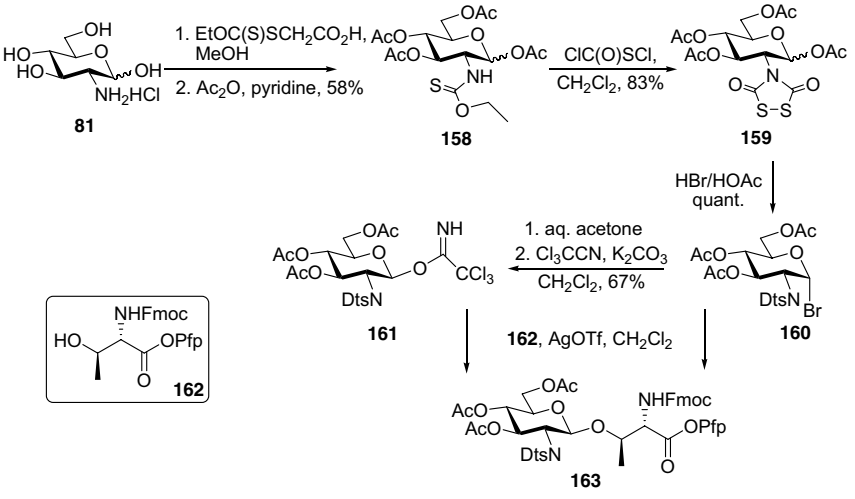
bases including DMAP (Scheme 13b),[257,457–460] K_2CO_3 (Scheme 13a),[462,463] Et_3N,[25] *t*-BuOK,[464] and $NaHCO_3$, depending on the substrate. It was also found that the presence of catalytic amounts of $CuSO_4$ can enhance product conversion as well as the reaction rate.[462,463,465,466] Moreover, the judicious choice of solvent was also found to greatly affect the rate and efficiency of the conversion. Thus, solvent combinations of water, MeOH, *t*-BuOH, CH_2Cl_2, toluene, pyridine, and CH_3CN were found to have a distinct influence on the reaction.[25,257,464,467] As a testament to its synthetic utility, the diazotransfer reaction has been employed in the synthesis of biologically important targets including heparan sulfate fragments,[466] aminoglycoside antibiotics,[464] neomycin analogues,[468] heparin fragments,[461,463] hyaluronan neoglycopolymers,[460] and *N*-acetylneuraminic acid[257] derivatives.

An alternative synthesis of 2-azido-2-deoxy derivatives from D-glucosamine was reported by Dasgupta and Garegg.[469]

4.2.3. Miscellaneous disubstituted derivatives. As mentioned, arguably the biggest drawback to the use of the phthalimido moiety for β-selective coupling is the relatively harsh conditions required for its removal. The high temperature and strongly basic conditions are incompatible with base-labile groups such as esters and α-amino acid residues. Hence, for glycopeptide synthesis, an orthogonal amine protecting group that can be easily removed is highly desirable.

One such candidate was the *N*-dithiasuccinoyl (Dts) function, which was found to be compatible with the Fmoc/Pfp protecting group strategy for the effective synthesis of glycopeptides and readily removed under mild conditions by thiolysis or other reductive methods.[470–472] Originally developed by Barany and Merrifield,[470] NDts derivatives had been heavily applied in peptide synthesis for many years before it was utilized as an orthogonally removable *N*-amino-protecting group of D-glucosamine derivatives.[473]

Following Barany and Merrifield's approach,[470] NDts derivatives can be prepared by treating ethoxythiocarbonyl intermediates with anhydrous chlorocarbonylsulfenyl chloride. To this end, the ethoxythiocarbonyl glucosamine intermediate **158** was obtained by treatment of **81** with *S*-carboxymethyl *O*-ethyl dithiocarbonate in methanol[473] or bis(ethoxythiocarbonyl) sulfide in aqueous ethanol,[474] followed by per-acetylation with acetic anhydride in pyridine (Scheme 29). Upon condensation of intermediate **158** with (chlorocarbonyl)sulfenyl



Scheme 29.

chloride, a rapid and clean cyclization occurs to form the *N*-dithiasuccinoyl derivative **159**. The latter can then be transformed into a suitable glycosyl donor, such as bromide **160**[473,474] or trichloroacetimidate **161**.[473,475] Reaction of either glycosyl donor **160** or **161** with the threonine acceptor **162** in the presence of AgOTf afforded stereoselectively β-glycoside **163** in 85% or 71% yield, respectively.[473,474]

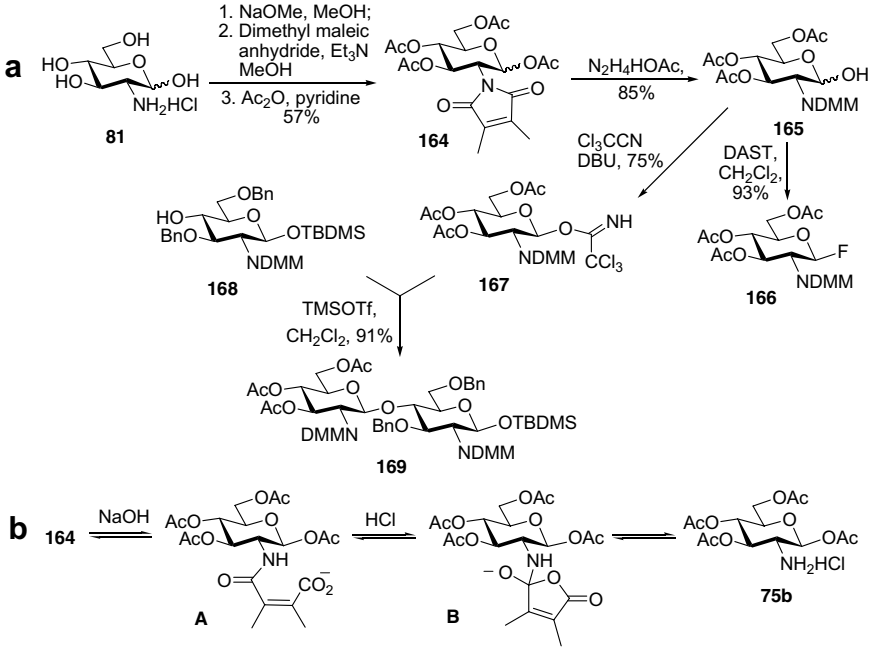
The Dts group can be removed by thiols through an open-chain carbamoyl disulfide intermediate,[21] which reacts further to give the free amine. To date, *N*-Dts derivatives have been successfully transformed into the free amine using β-mercaptoethanol (BME), *N*-methyl-mercaptoacetamide (MAc), and dithiothreitol (DTT).[473,474] Moreover, addition of tertiary amines like *N*,*N*-diisopropylethylamine was also found to greatly accelerate the thiolytic cleavage of the Dts group.

In 1998, Schmidt and co-workers introduced the use of *N*-dimethylmaleoyl (DMM) derivatives for the synthesis of 2-aminoglycosides.[476] Aside from its reported ease of introduction and cleavage under weakly aqueous basic then acidic conditions, the DMM moiety also provides anchimeric assistance to enforce the β linkage, and more importantly, is stable in the presence of acids and non-nucleophilic bases and thereby compatible with a wide array of functional group interconversions.[476]

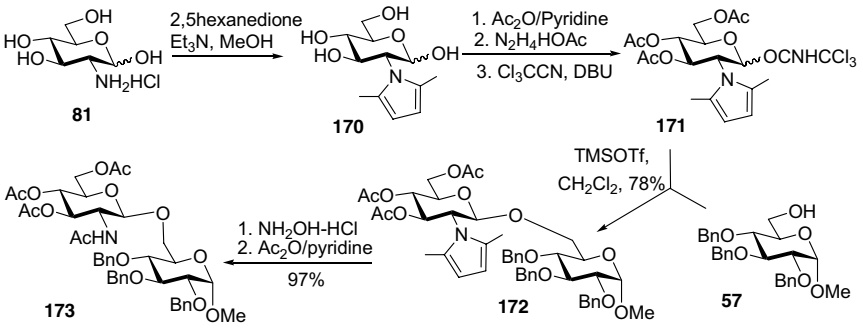
Adopting Lemieux's classic procedure for the synthesis of 2-phthalimido derivatives,[356] 2-NDMM derivatives can be easily synthesized from glucosamine hydrochloride **81** in three steps, as shown in Scheme 30a.[476] The first step liberates the free amine while the next step forms the amide bond upon nucleophilic attack of the amine on the carbonyl of the anhydride. Acetylation by acetic anhydride in pyridine protects all the hydroxyls and cyclizes the amide into the dimethylmaleoyl moiety to afford the tetraacetyl 2-NDMM derivative **164**. The anomeric acetate can then be readily removed by treatment with hydrazine acetate to form hemiacetal **165**, which can be converted accordingly into glycosyl donors, that is, fluorides, such as **166**, iodides, and more commonly, trichloroacetimidates (**167**).[476–478]

Glycosyl donors bearing the 2-NDMM moiety have been applied to the synthesis of *N*-glycan derivatives,[477,479] lacto-*N*-hexaose analogues,[480,481] glycopeptides,[482,483] glucosamine–glycerophospholipids,[484] and human milk[485] oligosaccharides. For example, TMSOTf-promoted glycosidation of trichloroacetimidate **167** with glycosyl acceptor **168** afforded chitodisaccharide **169** in 91% yield.[476] The cleavage of the DMM moiety in **164** is outlined in Scheme 30b.[476] Thus, base hydrolysis leads to ring-opened intermediate **A**, which, in the presence of an acid, is in equilibrium with butenolide **B**. Protonation of the basic nitrogen atom of the amide acetal moiety leads to generation of DMMA and amine hydrochloride **75b**, which can then be transformed into the 2-acetamido derivative by N-acetylation.

Boons and co-workers developed the 2,5-dimethylpyrrole group, which was found to be compatible with many reaction conditions employed in carbohydrate chemistry.[486] It was installed by the reaction of D-glucosamine **81** with 2,5-hexanedione in the presence of Et_3N in methanol to afford intermediate **170**, which was then conventionally converted into the trichloroacetimidate



Scheme 30.



Scheme 31.

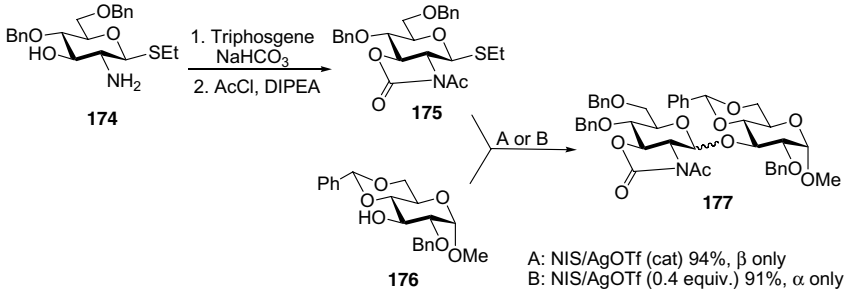
derivative **171** (Scheme 31). Glycosylation of acceptor **57** with glycosyl donor **171** in the presence of TMSOTf was entirely stereoselective affording disaccharide **172** in 78% yield. Since the dimethylpyrrole moiety is not capable of anchimeric assistance, the high 1,2-trans diastereoselectivity of this glycosylation was attributed to a hindered access to the bottom face of the ring resulting from its steric bulk. It was also demonstrated that the dimethylpyrrole moiety in **172** can be converted in natural 2'-acetamido derivative **173** by treatment with hydroxylamine followed by acetylation. Importantly, the dimethylpyrrole moiety was found to be stable toward conditions for the 2-phthalimido group removal.

The 2-*N*,*N*-dibenzylamino moiety, introduced by benzylation of the free amine with BnBr in the presence of NaH in DMF, was also found to be 1,2-trans stereodirecting.[487] This stereoselectivity was proposed to be governed by the formation of the dibenzyl aziridine intermediate (similar to intermediate **40**, see Scheme 8). Arguably, a steric bulkiness rationale could be applied herein as well. Advantageously, this moiety can be removed by hydrogenation with concomitant removal of *O*-benzyl substituents.

As mentioned earlier, 2,3-carbamate protected glycosyl donors provide excellent 1,2-cis selectivity.[317] However in a number of cases, when the nitrogen atom of the oxazolidinone ring was additionally acetylated, good 1,2-trans stereoselectivity was achieved.[488] It should be noted that at this stage, there has been a certain degree of inconsistency in the results obtained with 2-acetamido-2,3-*N*,*O*-carbonyl derivatized glycosyl donors. In a variety of cases, good or even entire 1,2-cis stereoselectivity has been detected.[488] An interesting promoter-dependent stereoselectivity was observed by Oscarson and co-workers.[349] Thus, glycosyl donor **175**, efficiently prepared from the free amine precursor **174**, was reacted with glycosyl acceptor **176** (Scheme 32). If the reaction was performed in the presence of NIS and a catalytic amount of AgOTf, 1,2-trans linked disaccharide β-**177** was obtained exclusively in 94% yield. If the amount of AgOTf was increased to 0.4 equiv, only the 1,2-linked disaccharide α-**177** was obtained in 91% yield.[349]

The nature of this remarkable observation remains to be understood; it was proposed however that the increased β-selectivity of the N-acetylated oxazolidinone derivatives was not due to the anchimeric assistance of the *N*-acetyl moiety. Rather, its steric bulk hindered access to the bottom face of the ring.[488] Conveniently, the disaccharides obtained can be transformed into their 2′-acetamido counterparts by simple removal of the carbamate moiety in the presence of NaOMe.[349] In contrast, MeONa treatment of a similar derivative described by Wei and Kerns led to the removal of the *N*-acetyl group while the carbonate moiety remained untouched.[489]

2-*N*-(*p*-Methoxy)benzylidene (anisylidene) derivatives have been extensively investigated.[490] Various glycosyl donors of this class have been prepared and applied to the synthesis of both 1,2-cis and 1,2-trans glycosides, hence the non-participatory character of this moiety



Scheme 32.

has not yet been verified. While this protecting moiety has been primarily used lately as a temporary protection and as a convenient entry to other classes of protected 2-amino derivatives, its early application in glycosyl donors has been thoroughly overviewed.[20] Removal of the *N*-anisylidene moiety can be accomplished by mild acid hydrolysis.

A variety of other disubstituted 2-amino-2-deoxy derivatives and their application to oligosaccharide synthesis were reported by Schmidt's group.[491] Amongst these, *N*-acetylacetamido derivatives have been investigated most extensively.[492,493] Although it is conceptually a simple way to access natural acetamido derivatives by deacetylation, the relatively low stability of the secondary acetate decreases the yields of the glycosylation products and somewhat limits the application of this approach. However, 5-acetylacetamido derivatives were found to be very useful building blocks for the synthesis of oligosaccharides containing neuraminic acid.[494,495]

2,4-Dimethoxybenzyl (Dmob) was used as an amide protecting group for 2-acetamido glycosyl imidates and acetates as donors.[496] It was noted that the 2-acetamido-2-*N*-Dmob glucosyl acetate donor gave higher glycosylation yields than its 2-acetamido counterpart.

5. Summary

The discovery of new methods and strategies for stereoselective glycoside synthesis and convergent oligosaccharide assembly has been critical for the area of glycosciences. Herein, we discussed only a fairly narrow topic dealing with the synthesis of *O*-glycosides of 2-amino-2-deoxysugars. As evident from the recent accomplishments, in spite of the recent progress, no universal approach for the synthesis of this class of compounds has yet been developed. A variety of excellent participating moieties are available for the synthesis of 1,2-trans glycosides. Amongst these, *N*-phthaloyl moiety is arguably the most commonly employed. However, in recent years, new excellent participating groups (especially NTroc) that can be removed under mild reaction conditions have been rapidly emerging. On the other hand, the synthesis of 1,2-cis glycosides, requiring the use of a non-participatory moiety at C-2, has been mainly limited to the glycosidation of 2-azido-2-deoxy derivatives. Indeed, these compounds deliver excellent properties to the glycosyl donor, yet cumbersomeness of their preparation often results in lengthy synthetic sequences. In this context, perhaps the next decade will witness the development of new non-participating groups for the synthesis of 1,2-cis glycosides. Virtually all leaving groups that have been employed in the synthesis of regular saccharides have been employed in the synthesis of the glycosides of 2-amino-2-deoxysugars. Amongst these, such common leaving groups as trichloroacetimidoyl, alkyl/arylthio, acetyl, or halogeno are the most commonly seen in these applications. Anomeric halides or acetates offer the most reliable glycosyl donors for the preparation of glycosides of simple alcohols. Thioglycosides and imidates are often the leaving groups of choice when more complex hindered sugar glycosyl acceptors are glycosylated.

Acknowledgment

The authors thank the American Heart Association (AHA0660054Z) for the financial support of this work.

References

1. Dwek, R. A. *Chem. Rev.* **1996**, *96*, 683–720.
2. Herzner, H.; Reipen, T.; Schultz, M.; Kunz, H. *Chem. Rev.* **2000**, *100*, 4495–4537.
3. Rai, R.; McAlexander, I.; Chang, C. W. T. *Org. Prep. Proced. Int.* **2005**, *37*, 337–375.
4. Casu, B. *Adv. Carbohydr. Chem. Biochem.* **1985**, *43*, 51–134.
5. Lemieux, R. U. *Chem. Soc. Rev.* **1978**, *7*, 423–452.
6. Varki, A. *Glycobiology* **1993**, *3*, 97–130.
7. *Essentials of Glycobiology*; Varki, A., Cummings, R., Esko, J., Freeze, H., Hart, G., Marth, J., Varki, A., Cummings, R., Esko, J., Freeze, H., Hart, G., Marth, J., Eds.; Cold Spring Harbor Laboratory Press: Cold Spring Harbor, NY, 1999.
8. Schauer, R. *Adv. Carbohydr. Chem. Biochem.* **1982**, *40*, 131–234.
9. Hakomori, S. *Annu. Rev. Immunol.* **1984**, *2*, 103–126.
10. Shibuya, N.; Goldstein, I. J.; Broekaert, W. I.; Nsimba-Lubaki, M.; Peters, B.; Pennemans, W. J. *J. Biol. Chem.* **1987**, *262*, 1596–1601.
11. Ravindranash, M. H.; Higer, H. H.; Cooper, E. Z.; Paulson, J. C. *J. Biol. Chem.* **1985**, *260*, 8850–8856.
12. Feizi, T. *Trends Biochem. Sci.* **1981**, *6*, 333–335.
13. Tvaroska, I.; Bleha, T. *Adv. Carbohydr. Chem. Biochem.* **1989**, *47*, 45–123.
14. Demchenko, A. V. *Synlett* **2003**, 1225–1240.
15. Demchenko, A. V. *Curr. Org. Chem.* **2003**, *7*, 35–79.
16. Nukada, T.; Berces, A.; Zgierski, M. Z.; Whitfield, D. M. *J. Am. Chem. Soc.* **1998**, *120*, 13291–13295.
17. Goodman, L. *Adv. Carbohydr. Chem. Biochem.* **1967**, *22*, 109–175.
18. Toshima, K.; Tatsuta, K. *Chem. Rev.* **1993**, *93*, 1503–1531.
19. Nicolaou, K. C.; Mitchell, H. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 1576–1624.
20. Banoub, J.; Boullanger, P.; Lafont, D. *Chem. Rev.* **1992**, *92*, 1167–1195.
21. Debenham, J.; Rodebaugh, R.; Fraser-Reid, B. *Liebigs Ann. Recl.* **1997**, 791–802.
22. Danishefsky, S. J.; Bilodeau, M. T. *Angew. Chem., Int. Ed.* **1996**, *35*, 1380–1419.
23. Seeberger, P. H.; Bilodeau, M. T.; Danishefsky, S. J. *Aldrichim. Acta* **1997**, *30*, 75–92.
24. Priebe, W.; Grynkiewicz, G. In *Glycoscience: Chemistry and Chemical Biology*; Fraser-Reid, B., Tatsuta, K., Thiem, J., Eds.; Springer: Berlin–Heidelberg–New York, 2001; Vol. 1, pp 749–783.

25. Nyffeler, P. T.; Liang, C.-H.; Koeller, K. M.; Chi-Huey, W. *J. Am. Chem. Soc.* **2002**, *124*, 10773–10778.
26. Trahanovsky, W. S.; Robbins, M. D. *J. Am. Chem. Soc.* **1971**, *93*, 5256–5258.
27. Lemieux, R. U.; Ratcliffe, R. M. *Can. J. Chem.* **1979**, *57*, 1244–1251.
28. Seeberger, P.; Roehrig, S.; Schell, P.; Wang, Y.; Christ, W. J. *Carbohydr. Res.* **2000**, *328*, 61–69.
29. Paulsen, H. *Chem. Soc. Rev.* **1984**, *13*, 15–45.
30. Paulsen, H.; Lorentzen, J. P.; Kutschker, W. *Carbohydr. Res.* **1985**, *136*, 153–176.
31. Gauffery, F.; Marra, A.; Shi Shun, L. K.; Sinay, P.; Tabeur, C. *Carbohydr. Res.* **1991**, *219*, 237–240.
32. Toyokuni, T.; Cai, S.; Dean, B. *Synthesis* **1992**, 1236–1238.
33. Grundler, G.; Schmidt, R. R. *Justus Liebigs Ann. Chem.* **1984**, 1826–1847.
34. Paulsen, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 155–173.
35. Forsgren, M.; Norberg, T. *Carbohydr. Res.* **1983**, *116*, 39–47.
36. Marra, A.; Gauffeny, F.; Sinay, P. *Tetrahedron* **1991**, *47*, 5149–5160.
37. Allen, J. R.; Harris, C. R.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2001**, *123*, 1890–1897.
38. Lee, S.; Rosazza, J. P. N. *Org. Lett.* **2004**, *6*, 365–368.
39. Svarovsky, S. A.; Barchi, J. J. *Carbohydr. Res.* **2003**, *338*, 1925–1935.
40. Tsuda, T.; Nakamura, S.; Hashimoto, S. *Tetrahedron Lett.* **2003**, *44*, 6453–6457.
41. Tsuda, T.; Nakamura, S.; Hashimoto, S. *Tetrahedron* **2004**, *60*, 10711–10737.
42. Paulsen, H.; Rauwald, W.; Weichert, U. *Liebigs Ann. Chem.* **1988**, 75–86.
43. Hansson, J.; Garegg, P. J.; Oscarson, S. *J. Org. Chem.* **2001**, *66*, 6234–6243.
44. Codee, J. D. C.; Litjens, R. E. J. N.; Heeten, R.; Overkleeft, H. S.; van Boom, J. H.; van der Marel, G. A. *Org. Lett.* **2003**, *5*, 1519–1522.
45. Wang, L. X.; Sakairi, N.; Kuzuhara, H. *Carbohydr. Res.* **1991**, *219*, 133–148.
46. Kinzy, W.; Low, A. *Carbohydr. Res.* **1993**, *245*, 193–218.
47. Sabesan, S.; Lemieux, R. U. *Can. J. Chem.* **1984**, *62*, 644–654.
48. Tatsuta, K.; Akimoto, K.; Takahashi, H.; Hamatsu, T.; Annaka, M.; Kinoshita, M. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 529–538.
49. Danishefsky, S.; Barbachyn, M. *J. Am. Chem. Soc.* **1985**, *107*, 7761–7762.
50. Berlin, W. K.; Zhang, W. S.; Shen, T. Y. *Tetrahedron* **1991**, *47*, 1–20.
51. Kuduk, S. D.; Schwartz, J. B.; Chen, X. T.; Glunz, P. W.; Sames, D.; Ragupathi, G.; Livingston, P. O.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1998**, *120*, 12474–12485.
52. Crossman, A.; Smith, T. K.; Ferguson, M. A. J.; Brimacombe, J. S. *Tetrahedron Lett.* **2005**, *46*, 7419–7421.
53. Moitessier, N.; Henry, C.; Aubert, N.; Chapleur, Y. *Tetrahedron Lett.* **2005**, *46*, 6191–6194.
54. de Oliveira, R. N.; Cottier, L.; Sinou, D.; Srivastava, R. M. *Tetrahedron* **2005**, *61*, 8271–8281.
55. Bayley, H.; Standring, D. N.; Knowles, J. R. *Tetrahedron Lett.* **1978**, *19*, 3633–3634.
56. Kohn, M.; Breinbauer, R. *Angew. Chem., Int. Ed.* **2004**, *43*, 3106–3116.
57. Yashunsky, D. V.; Borodkin, V. S.; Ferguson, M. A. J.; Nikolaev, A. V. *Angew. Chem., Int. Ed.* **2006**, *45*, 468–474.
58. Birch, A. J. *Pure Appl. Chem.* **1996**, *68*, 553–556.
59. Hederos, M.; Konradsson, P. *J. Org. Chem.* **2005**, *70*, 7196–7207.
60. Fan, R.-H.; Achkar, J.; Hernandez-Torres, M. J.; Wei, A. *Org. Lett.* **2005**, *7*, 5095–5098.
61. Bovin, N. V.; Zurabyan, S. E.; Khorlin, A. Y. *Carbohydr. Res.* **1981**, *98*, 25–35.
62. Mehta, S.; Pinto, B. M. *J. Org. Chem.* **1993**, *58*, 3269–3276.
63. Hassner, A.; Amarasekara, A. S. *Tetrahedron Lett.* **1987**, *28*, 5185–5188.
64. Santoyo-Gonzales, F.; Calvo-Flores, F. G.; Garcia-Mendoza, P.; Hernandez-Mateo, F.; Isac-Garcia, J.; Robles-Diaz, R. *J. Org. Chem.* **1993**, *58*, 6122–6125.
65. Czernecki, S.; Ayadi, E.; Randriamandimby, D. *J. Org. Chem.* **1994**, *59*, 8256–8260.
66. Jiaang, W. T.; Chang, M. Y.; Tseng, P. H.; Chen, S. T. *Tetrahedron Lett.* **2000**, *41*, 3127–3130.
67. Yamago, S.; Yamada, T.; Hara, O.; Ito, H.; Mino, Y.; Yoshida, J. *Org. Lett.* **2001**, *3*, 3867–3870.
68. Tseng, P.-H.; Jiaang, W.-T.; Chang, M.-Y.; Chen, S.-T. *Chem. Eur. J.* **2001**, *7*, 585–590.
69. Mironov, Y. V.; Sherman, A. A.; Nifantiev, N. E. *Tetrahedron Lett.* **2004**, *45*, 9107–9110.
70. Alfassi, Z. B.; Harriman, A.; Huie, R. E.; Mosseri, S.; Neta, P. *J. Phys. Chem.* **1987**, *91*, 2120–2122.
71. Mayeda, E. A.; Miller, L. L.; Wolf, J. F. *J. Am. Chem. Soc.* **1972**, *94*, 6812–6816.
72. Lemieux, R. U.; Nagabushan, T. L.; O'Neill, I. K. *Tetrahedron Lett.* **1964**, *5*, 1909–1916.
73. Lemieux, R. U.; Nagabushan, T. L.; O'Neill, I. K. *Can. J. Chem.* **1968**, *46*, 413–418.
74. Takamoto, T.; Sudoh, R.; Nakagawa, T. *Carbohydr. Res.* **1973**, *27*, 135–140.
75. Sakakibara, T.; Tachimori, Y.; Sudoh, R. *Tetrahedron Lett.* **1982**, *23*, 5545–5548.
76. Holzapfel, C. W.; Marais, C. F.; van Dyk, M. S. *Synth. Commun.* **1988**, *18*, 97–114.
77. Das, J.; Schmidt, R. R. *Eur. J. Org. Chem.* **1998**, 1609–1613.
78. Kogan, T. P.; Gaeta, F. C. A. *Synthesis* **1988**, 706–707.
79. Deslongchamps, P. *Stereolectronic Effects in Organic Chemistry*; Pergamon Press: Oxford, 1983.
80. Barroca, N.; Schmidt, R. R. *Org. Lett.* **2004**, *6*, 1551–1554.
81. Carruthers, W. *Cycloaddition Reactions in Organic Synthesis*; Pergamon: Elmsford, NY, 1990.
82. *Cycloaddition Reactions in Organic Synthesis*; Kobayashi, S., Jorgensen, A. K., Eds.; Wiley-VCH: Weinheim, Germany, 2002.
83. *Cycloaddition Reactions in Carbohydrate Chemistry*; Giuliano, R. M., Ed.; Amer. Chemical Soc.: Washington, DC, 1992.
84. Firl, J.; Sommer, S. *Tetrahedron Lett.* **1969**, *10*, 1133–1136.
85. Firl, J.; Sommer, S. *Tetrahedron Lett.* **1971**, *12*, 4193–4196.
86. Firl, J.; Sommer, S. *Tetrahedron Lett.* **1972**, *13*, 4713–4716.
87. von Gustorf, E. K.; White, D. V.; Kim, B.; Hess, D.; Leitich, J. *J. Org. Chem.* **1970**, *35*, 1155–1165.
88. Firl, J.; Sommer, S. *Tetrahedron Lett.* **1970**, 1929–1932.
89. von Gustorf, E. K.; White, D. V.; Leitich, J.; Henneberg, D. *Tetrahedron Lett.* **1969**, 3113–3116.

90. Fitzsimmons, B. J.; Leblanc, Y.; Rokach, J. *J. Am. Chem. Soc.* **1987**, *109*, 285–286.
91. Leblanc, Y.; Fitzsimmons, B. J. *Tetrahedron Lett.* **1989**, *30*, 2889–2892.
92. Leblanc, Y.; Fitzsimmons, B. J.; Springer, J. P.; Rokach, J. *J. Am. Chem. Soc.* **1989**, *111*, 2995–3000.
93. Fitzsimmons, B. J.; Leblanc, Y.; Chan, N.; Rokach, J. *J. Am. Chem. Soc.* **1988**, *110*, 5229–5231.
94. Dahl, R. S.; Finney, N. S. *J. Am. Chem. Soc.* **2004**, *126*, 8356–8357.
95. Hedley, S. J.; Moran, W. J.; Prenzel, A. H. G. P.; Price, D. A.; Harrity, J. P. A. *Synlett* **2001**, 1596–1598.
96. Lafont, D.; Descotes, G. *Carbohydr. Res.* **1987**, *166*, 195–209.
97. Lafont, D.; Descotes, G. *Carbohydr. Res.* **1988**, *175*, 35–48.
98. Griffith, D. A.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1990**, *112*, 5811–5819.
99. Danishefsky, S. J.; Gervay, J.; Peterson, J. M.; McDonald, F. E.; Koseki, K.; Oriyama, T.; Griffith, D. A.; Wong, C. H.; Dumas, D. P. *J. Am. Chem. Soc.* **1992**, *114*, 8329–8331.
100. Danishefsky, S. J.; Gervay, J.; Peterson, J. M.; McDonald, F. E.; Koseki, K.; Griffith, D. A.; Oriyama, T.; Marsden, S. P. *J. Am. Chem. Soc.* **1995**, *117*, 1940–1953.
101. Danishefsky, S. J.; McDonald, F. E. *J. Org. Chem.* **1992**, *57*, 7001–7002.
102. Roberge, J. Y.; Beebe, X.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1998**, *120*, 3915–3927.
103. Park, T. K.; Lim, I. J.; Danishefsky, S. J. *Tetrahedron Lett.* **1995**, *36*, 9089–9092.
104. Griffith, D. A.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1996**, *118*, 9526–9538.
105. Park, T. K.; Kim, I. J.; Hu, S.; Bilodeau, M. T.; Randolph, J. T.; Kwon, O.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1996**, *118*, 11488–11500.
106. Kwon, O.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1995**, *120*, 1588–1599.
107. Deshpande, P. P.; Kim, H. M.; Zatorski, A.; Park, T. K.; Ragupathi, G.; Livingston, P. O.; Live, D.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1998**, *120*, 1600–1614.
108. Chen, X.-T.; Sames, D.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1998**, *120*, 7760–7769.
109. Dudkin, V. Y.; Miller, J. S.; Danishefsky, S. J. *Tetrahedron Lett.* **2003**, *44*, 1791–1793.
110. Du Bois, J.; Tomooka, C. S.; Hong, J.; Carreira, E. M. *J. Am. Chem. Soc.* **1997**, *119*, 3179–3180.
111. Du Bois, J.; Hong, J.; Carreira, E. M.; Day, M. W. *J. Am. Chem. Soc.* **1996**, *118*, 915–918.
112. Groves, J. T.; Takahashi, T. *J. Am. Chem. Soc.* **1983**, *105*, 2073–2074.
113. Evans, D. A.; Faul, M. M.; Bilodeau, M. T. *J. Am. Chem. Soc.* **1993**, *116*, 2742–2753.
114. Li, Z.; Conser, K. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1993**, *115*, 5326–5327.
115. Evans, D. A.; Faul, M. M.; Bilodeau, M. T.; Anderson, B. A.; Barnes, D. M. *J. Am. Chem. Soc.* **1993**, *115*, 5328–5329.
116. Nagano, T.; Itoh, M.; Matsumura, K. *J. Am. Chem. Soc.* **1953**, *75*, 2770–2771.
117. Di Bussolo, V.; Liu, J.; Huffman, L. G. J.; Gin, D. Y. *Angew. Chem., Int. Ed.* **2000**, *39*, 204–207.
118. Liu, J.; Gin, D. Y. *J. Am. Chem. Soc.* **2002**, *124*, 9789–9797.
119. Nishiguchi, T.; Tochio, H.; Nabeya, A.; Iwakura, Y. *J. Am. Chem. Soc.* **1969**, *91*, 5835–5841.
120. Liu, J.; Di Bussolo, V.; Gin, D. Y. *Tetrahedron Lett.* **2003**, *44*, 4015–4018.
121. Binkley, E. R.; Binkley, R. W. In *Preparative Carbohydrate Chemistry*; Hanessian, S., Ed.; Marcel Dekker: New York, 1997; pp 87–104.
122. Reist, E. J.; Spencer, R. R.; Baker, B. R. *J. Org. Chem.* **1959**, *24*, 1618–1619.
123. Richardson, A. C. *Carbohydr. Res.* **1969**, *10*, 395–402.
124. Ball, D. H.; Parrish, F. W. *Adv. Carbohydr. Chem. Biochem.* **1968**, *23*, 233–280.
125. Ball, D. H.; Parrish, F. W. *Adv. Carbohydr. Chem. Biochem.* **1969**, *24*, 139–197.
126. Ambrose, M. G.; Binkley, R. W. *J. Org. Chem.* **1983**, *48*, 674–677.
127. Binkley, R. W.; Hehemann, D. G. *J. Org. Chem.* **1978**, *43*, 3244–3245.
128. Binkley, R. W.; Hehemann, D. G. *Carbohydr. Res.* **1979**, *74*, 337–340.
129. Binkley, R. W.; Ambrose, M. G.; Hehemann, D. G. *J. Org. Chem.* **1980**, *45*, 4387–4391.
130. El Nemr, A.; Tsuchiya, T. *Tetrahedron Lett.* **1995**, *36*, 7665–7668.
131. El Nemr, A.; Tsuchiya, T.; Kobayashi, Y. *Carbohydr. Res.* **1996**, *293*, 31–59.
132. El Nemr, A.; Tsuchiya, T. *Carbohydr. Res.* **1997**, *301*, 77–87.
133. El Nemr, A.; Tsuchiya, T. *Carbohydr. Res.* **1997**, *303*, 267–281.
134. El Nemr, A.; Tsuchiya, T. *Carbohydr. Res.* **2001**, *330*, 205–214.
135. Pozsgay, V.; Glaudemans, C. P. J.; Robbins, J. B.; Schneerson, R. *Tetrahedron* **1992**, *48*, 10249–10264.
136. Pavliak, V.; Kovac, P. *Carbohydr. Res.* **1991**, *210*, 333–337.
137. Pozsgay, V. *J. Org. Chem.* **1999**, *64*, 7277–7280.
138. Knapp, S.; Kukkola, P. J.; Sharma, S.; Dhar, T. G. M.; Naughton, A. B. J. *J. Org. Chem.* **1990**, *55*, 5700–5710.
139. Koto, S.; Asami, K.; Hirooka, M.; Nagura, K.; Takizawa, M.; Yamamoto, S.; Okamoto, N.; Sato, M.; Tajima, H.; Yoshida, T.; Nonaka, N.; Sato, T.; Zen, S.; Yago, K.; Tomonaga, F. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 765–777.
140. Karpiesiuk, W.; Banaszek, A.; Zamojski, A. *Carbohydr. Res.* **1989**, *186*, 156–162.
141. Kloosterman, M.; De Nijs, M. P.; van Boom, J. H. *J. Carbohydr. Chem.* **1986**, *5*, 215–233.
142. Bruce, I.; Fleet, G. W. J.; Girdhar, A.; Haraldsson, M.; Peach, J. M.; Watkin, D. J. *Tetrahedron* **1990**, *46*, 19–32.
143. Sato, K.-i.; Yoshitomo, A. *Chem. Lett.* **1995**, *1*, 39–40.
144. Cipolla, L.; Lay, L.; Nicotra, F. *J. Org. Chem.* **1997**, *62*, 6678–6681.
145. Anilkumar, G.; Nair, L. G.; Olsson, L.; Daniels, J. K.; Fraser-Reid, B. *Tetrahedron Lett.* **2000**, *41*, 7605–7608.
146. Knapp, S.; Naughton, A. B. J.; Jaramillo, C.; Pipik, B. *J. Org. Chem.* **1992**, *57*, 7328–7334.
147. Soli, E. D.; DeShong, P. *J. Org. Chem.* **1999**, *64*, 9724–9726.
148. Hung, S.-C.; Thopate, S. R.; Chi, F.-C.; Chang, S.-W.; Lee, J.-C.; Wang, C.-C.; Wen, Y.-S. *J. Am. Chem. Soc.* **2001**, *123*, 3153–3154.
149. Lee, J.-C.; Chang, S.-W.; Liao, C.-C.; Chi, F.-C.; Chen, C.-S.; Wen, Y.-S.; Wang, C.-C.; Kulkarni, S. S.; Puranik, R.; Liu, Y.-H.; Hung, S.-C. *Chem. Eur. J.* **2004**, *10*, 399–415.
150. Lu, J.; Jayaprakash, K. N.; Schlueter, U.; Fraser-Reid, B. *J. Am. Chem. Soc.* **2004**, *126*, 7540–7547.

151. Popelova, A.; Kefurt, K.; Hlavackova, M.; Moravcova, J. *Carbohydr. Res.* **2005**, *340*, 161–166.
152. Dasgupta, F.; Garegg, P. J. *Synthesis* **1988**, 626–628.
153. Vos, J. N.; van Boom, J. H.; van Boeckel, C. A. A.; Beetz, T. J. *J. Carbohydr. Chem.* **1984**, *3*, 117–124.
154. Soli, E. D.; Manoso, A. S.; Patterson, M. C.; DeShong, P.; Favor, D. A.; Hirschmann, R.; Smith, A. B., III. *J. Org. Chem.* **1999**, *64*, 3171–3177.
155. Černý, M.; Stanek, J., Jr. *Adv. Carbohydr. Chem. Biochem.* **1977**, *34*, 23–177.
156. Černý, M.; Trnka, T.; Beran, P.; Pacak, J. *Collect. Czech. Chem. Commun.* **1969**, *34*, 3377–3382.
157. Černý, M.; Julakova, O.; Pacak, J. *Collect. Czech. Chem. Commun.* **1974**, *39*, 1391–1396.
158. Trnka, T.; Černý, M. *Collect. Czech. Chem. Commun.* **1971**, *35*, 2216–2225.
159. Stanek, J.; Černý, M. *Synthesis* **1972**, 698–699.
160. Tailler, D.; Jacquinet, J. C.; Noiret, A. M.; Beau, J. M. *J. Chem. Soc., Perkin Trans. 1* **1992**, *23*, 3163–3164.
161. Xue, J.; Guo, Z. *Tetrahedron Lett.* **2001**, *42*, 6487–6489.
162. Arndt, S.; Hsieh-Wilson, L. C. *Org. Lett.* **2003**, *5*, 4179–4182.
163. Wang, L. X.; Sakairi, N.; Kuzuhara, H. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1677–1682.
164. Kochetkov, N. K.; Klimov, E. M.; Malysheva, N. N.; Demchenko, A. V. *Carbohydr. Res.* **1993**, *242*, C7–C10.
165. Oikawa, M.; Shintaku, T.; Sekljic, H.; Fukase, K.; Kusumoto, S. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 1857–1867.
166. Demchenko, A. V.; Wolfert, M. A.; Santanam, B.; Moore, J. N.; Boons, G. J. *J. Am. Chem. Soc.* **2003**, *125*, 6103–6112.
167. Nishimura, S.; Murayama, S.; Kurita, K.; Kuzuhara, H. *Chem. Lett.* **1992**, *8*, 1413–1416.
168. Ganguli, A. R. S.; Coward, J. K. *Tetrahedron: Asymmetry* **2005**, *16*, 411–424.
169. Wittmann, V.; Lennartz, D. *Eur. J. Org. Chem.* **2002**, 1363–1367.
170. Mohan, H.; Gemma, E.; Ruda, K.; Oscarson, S. *Synlett* **2003**, 1255–1256.
171. Crasto, C. F.; Jones, G. B. *Tetrahedron Lett.* **2004**, *45*, 4891–4894.
172. Cai, Y.; Ling, C. C.; Bundle, D. R. *Org. Lett.* **2005**, *7*, 4021–4024.
173. Arihara, R.; Nakamura, S.; Hashimoto, S. *Angew. Chem., Int. Ed.* **2005**, *44*, 2245–2249.
174. Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed.; Wiley: New York, 1999.
175. Goody, R. S.; Walker, R. T. *Tetrahedron Lett.* **1967**, *4*, 289–291.
176. Kiso, M.; Anderson, L. *Carbohydr. Res.* **1985**, *136*, 309–323.
177. Dasgupta, F.; Garegg, P. J. *Carbohydr. Res.* **1990**, *202*, 225–238.
178. Micheel, F.; Petersen, H. *Chem. Ber.* **1959**, *92*, 298–304.
179. Shapiro, D.; Acher, A. J.; Rachaman, E. S. *J. Org. Chem.* **1967**, *32*, 3767–3771.
180. Acher, A. J.; Shapiro, D. *J. Org. Chem.* **1969**, *34*, 2652–2654.
181. Wolfrom, M. L.; Bhat, H. B. *J. Org. Chem.* **1967**, *32*, 1821–1823.
182. Blatter, G.; Beau, J.-M.; Jacquinet, J.-C. *Carbohydr. Res.* **1994**, *260*, 189–202.
183. Schmidt, R. R.; Jung, K. H. In *Preparative Carbohydrate Chemistry*; Hanessian, S., Ed.; Springer: New York, 1997; pp 283–312.
184. Schmidt, R. R.; Jung, K. H In *Carbohydrates in Chemistry and Biology*; Ernst, B., Hart, G. W., Sinay, P., Eds.; Wiley-VCH: Weinheim, New York, 2000; Vol. 1, pp 5–59.
185. Dempsey, A. M.; Hough, L. *Carbohydr. Res.* **1975**, *41*, 63–76.
186. Coutant, C.; Jacquinet, J. C. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1573–1581.
187. Sherman, A. A.; Yudina, O. N.; Mironov, Y. V.; Sukhova, E. V.; Shashkov, A. S.; Menshov, V. M.; Nifantiev, N. E. *Carbohydr. Res.* **2001**, *336*, 13–46.
188. Takano, Y.; Habiro, M.; Someya, M.; Hojo, H.; Nakahara, Y. *Tetrahedron Lett.* **2002**, *43*, 8395–8399.
189. Donohoe, T. J.; Logan, J. G.; Laffan, D. D. P. *Org. Lett.* **2003**, *5*, 4995–4998.
190. Armstrong, P. L.; Coull, I. C.; Hewson, A. T.; Slater, M. J. *Tetrahedron Lett.* **1995**, *36*, 4311–4314.
191. Das, S. K.; Reddy, K. A.; Abbineni, C.; Roy, J.; Rao, K. V. L. N.; Sachwani, R. H.; Iqbal, J. *Tetrahedron Lett.* **2003**, *44*, 4507–4509.
192. Weygand, F.; Csendes, E. *Angew. Chem.* **1952**, *64*, 136.
193. Strachan, R. G.; Ruyle, W. V.; Shen, T. Y.; Hirschmann, R. *J. Org. Chem.* **1966**, *31*, 507–509.
194. Bergmann, M.; Zervas, L. *Ber.* **1931**, *64B*, 975–980.
195. Horton, D. *J. Org. Chem.* **1964**, *29*, 1776–1782.
196. Cheung, A. W.-H.; Sidduri, A.; Garofalo, L. M.; Goodnow, R. A., Jr. *Tetrahedron Lett.* **2000**, *41*, 3303–3307.
197. Lin, H.; Walsh, C. T. *J. Am. Chem. Soc.* **2004**, *126*, 13998–14003.
198. Berlin, W. K.; Wang, S. N.; Shen, T. Y. *Tetrahedron Lett.* **1990**, *31*, 1109–1112.
199. Meyer-zu-Reckendorf, W.; Vassiliadou-Micheli, N. *Chem. Ber.* **1970**, *103*, 1792–1796.
200. Paquet, A.; Layne, D. S. *Can. J. Chem.* **1973**, *51*, 3855–3859.
201. Abramson, H. N.; Banning, J. W.; Nachtman, J. P.; Roginski, E. T.; Sardessai, M.; Wormser, H. C.; Wu, J.; Nagia, Z.; Schroeder, R. R.; Bernardo, M. M. *J. Med. Chem.* **1986**, *29*, 1709–1714.
202. Bednarczyk, D.; Kaca, W.; Myszka, H.; Serwecinska, L.; Smiatacz, Z.; Zaborowski, A. *Carbohydr. Res.* **2000**, *328*, 249–252.
203. Fialova, P.; Weignerova, L.; Rauvolfova, J.; Prikrylova, V.; Pisvejcova, A.; Ettrich, R.; Kuzma, M.; Sedmera, P.; Kren, V. *Tetrahedron* **2004**, *60*, 693–701.
204. Junker, H.-D.; Fessner, W.-D. *Tetrahedron Lett.* **1998**, *39*, 269–272.
205. Busca, P.; Martin, O. R. *Tetrahedron Lett.* **1998**, *39*, 8101–8104.
206. Tai, V. W.-F.; O'Reilly, M. K.; Imperiali, B. *Bioorg. Med. Chem.* **2001**, *9*, 1133–1140.
207. Busca, P.; Martin, O. R. *Tetrahedron Lett.* **2004**, *45*, 4433–4436.
208. Silva, D. J.; Wang, H. M.; Allanson, N. M.; Jain, R. K.; Sofia, M. J. *J. Org. Chem.* **1999**, *64*, 5926–5929.
209. Weiss, H.; Unverzagt, C. *Angew. Chem., Int. Ed.* **2003**, *42*, 4261–4263.
210. SanMartin, R.; Tavassoli, B.; Walsh, K. E.; Walter, D. S.; Gallagher, T. *Org. Lett.* **2000**, *2*, 4051–4054.
211. Bongat, A. F. G.; Kamat, M. N.; Demchenko, A. V. submitted for publication.
212. Wolfrom, M. L.; Bhat, H. B. *Chem. Commun.* **1966**, *6*, 146.
213. Myszka, H.; Bednarczyk, D.; Najder, M.; Kaca, W. *Carbohydr. Res.* **2003**, *338*, 133–141.

214. Ramanjulu, J. M.; Joullie, M. *J. Carbohydr. Chem.* **1996**, *15*, 371–381.
215. Hansen, H. C.; Magnusson, G. *Carbohydr. Res.* **1999**, *322*, 190–200.
216. Lemanski, G.; Ziegler, T. *Eur. J. Org. Chem.* **2006**, 2618–2630.
217. Shiozaki, M.; Watanabe, Y.; Iwano, Y.; Kaneko, T.; Doi, H.; Tanaka, D.; Shimozato, T.; Kurakata, S.-I. *Tetrahedron* **2005**, *61*, 5101–5122.
218. Boullanger, P.; Jouineau, M.; Bouammali, B.; Lafont, D.; Descotes, G. *Carbohydr. Res.* **1990**, *202*, 151–164.
219. Kobayashi, Y.; Tsuchiya, T.; Ohgi, T.; Taneichi, N.; Koyama, Y. *Carbohydr. Res.* **1992**, *230*, 89–105.
220. Klemer, A.; Wilbers, H. *Liebigs Ann. Chem.* **1985**, *12*, 2328–2341.
221. Mostowicz, D.; Belzecki, C.; Chmielewski, M. *Synthesis* **1991**, *4*, 273–274.
222. Adamski-Werner, S. L.; Yeung, B. K. S.; Miller-Deist, L. A.; Petillo, P. A. *Carbohydr. Res.* **2004**, *339*, 1255–1262.
223. Liu, J.; Huang, C.-Y.; Wong, C.-H. *Tetrahedron Lett.* **2002**, *43*, 3447–3448.
224. Nishiyama, T.; Ichikawa, Y.; Isobe, M. *Synlett* **2004**, 89–92.
225. Liao, W.; Piskorz, C. F.; Locke, R. D.; Matta, K. L. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 793–795.
226. Chargaff, E.; Bovarnick, M. *J. Biol. Chem.* **1937**, *118*, 421–426.
227. Ichikawa, Y.; Matsukawa, Y.; Isobe, M. *J. Am. Chem. Soc.* **2006**, *128*, 3934–3938.
228. Paulsen, H.; Stiem, M.; Unger, F. M. *Carbohydr. Res.* **1988**, *172*, 11–25.
229. Bodner, R.; Marcellino, B. K.; Severino, A.; Smenton, A. L.; Rojas, C. M. *J. Org. Chem.* **2005**, *70*, 3988–3996.
230. Yasuda, N.; Matsuda, K.; Tsutsumi, H.; Takaya, T. *Carbohydr. Res.* **1986**, *146*, 51–61.
231. Kyas, A.; Feigel, M. *Helv. Chim. Acta* **2005**, *88*, 2375–2396.
232. Bazin, H. G.; Bess, L. S.; Livesay, M. T.; Ryter, K. T.; Johnson, C. L.; Arnold, J. S.; Johnson, D. A. *Tetrahedron Lett.* **2006**, *47*, 2087–2092.
233. Heyns, K.; Harrison, R.; Paulsen, H. *Chem. Ber.* **1967**, *100*, 271–279.
234. Kulkarni, S. R.; Zimmerman, H. K. J. *Liebigs Ann. Chem.* **1965**, *684*, 223–226.
235. Lessard, J.; Driguez, H.; Vermes, J. P. *Tetrahedron Lett.* **1970**, *56*, 4887–4890.
236. Inazu, T.; Yamanoi, T. *Chem. Lett.* **1989**, 69–72.
237. Hashimoto, S.; Honda, T.; Ikegami, S. *Tetrahedron Lett.* **1991**, *32*, 1653–1654.
238. Melean, L. G.; Love, K. R.; Seeberger, P. H. *Carbohydr. Res.* **2002**, *337*, 1893–1916.
239. Westphal, O.; Stadler, R. *Angew. Chem.* **1963**, *75*, 452.
240. Chiba, T.; Jacquinet, J. C.; Sinay, P.; Petitou, M.; Choay, J. *Carbohydr. Res.* **1988**, *174*, 253–264.
241. Leder, I. G. *J. Carbohydr. Chem.* **1988**, *7*, 583–592.
242. Hasegawa, A.; Sakurai, T.; Hasegawa, N. *Carbohydr. Res.* **1975**, *45*, 19–27.
243. Stevens, C. L.; Nagarajan, K. *J. Med. Pharm. Chem.* **1962**, *5*, 1124–1148.
244. Paulsen, H.; Stiem, M.; Unger, F. M. *Liebigs Ann. Chem.* **1987**, *4*, 273–281.
245. Beetz, T.; van Boeckel, C. A. A. *Tetrahedron Lett.* **1986**, *27*, 5889–5892.
246. Paulsen, H.; Huffziger, A.; Van Boeckel, C. A. A. *Liebigs Ann. Chem.* **1988**, *5*, 419–426.
247. Petitou, M.; Duchaussoy, P.; Lederman, I.; Choay, J.; Jacquinet, J. C.; Sinay, P.; Torri, G. *Carbohydr. Res.* **1987**, *167*, 67–75.
248. Yoshikawa, M.; Torihara, M.; Nakae, T.; Cha, B. C.; Kitagawa, I. *Chem. Pharm. Bull.* **1987**, *35*, 2136–2139.
249. Imoto, M.; Yoshimura, H.; Shimamoto, T.; Sakaguchi, N.; Kusumoto, S.; Shiba, T. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 2205–2214.
250. Saito, H.; Nishimura, Y.; Kondo, S.; Takeuchi, T.; Umezawa, H. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 1259–1263.
251. Francois, B.; Szychowski, J.; Adhikari, S. S.; Pachamuthu, K.; Swayze, E. E.; Griffey, R. H.; Migawa, M. T.; Westhof, E.; Hanessian, S. *Angew. Chem., Int. Ed.* **2004**, *43*, 6735–6738.
252. Kloosterman, M.; Van Boom, J. H.; Chatelard, P.; Boullanger, P.; Descotes, G. *Tetrahedron Lett.* **1985**, *26*, 5045–5048.
253. Hayakawa, Y.; Kato, H.; Uchiyama, M.; Kajino, H.; Noyori, R. *J. Org. Chem.* **1986**, *51*, 2400–2402.
254. Boullanger, P.; Banoub, J.; Descotes, G. *Can. J. Chem.* **1987**, *65*, 1343–1348.
255. Boullanger, P.; Descotes, G. *Tetrahedron Lett.* **1986**, *27*, 2599–2602.
256. Vargas-Berenguel, A.; Meldal, M.; Paulsen, H.; Bock, K. *J. Chem. Soc., Perkin Trans. 1* **1994**, *18*, 2615–2619.
257. Laurent, N.; Lafont, D.; Boullanger, P.; Mallet, J. M. *Carbohydr. Res.* **2005**, *340*, 1885–1892.
258. Inamura, S.; Fukase, K.; Kusumoto, S. *Tetrahedron Lett.* **2001**, *42*, 7613–7616.
259. Schultz, M.; Kunz, H. *Tetrahedron Lett.* **1992**, *33*, 5319–5322.
260. Bouali, A.; Boullanger, P.; Lafont, D.; Fenet, B. *Carbohydr. Res.* **1992**, *228*, 81–93.
261. Lafont, D.; Bouchu, M.-N.; Girard-Egrot, A.; Boullanger, P. *Carbohydr. Res.* **2001**, *336*, 181–194.
262. Boullanger, P.; Chevalier, Y.; Croizier, M.-C.; Lafont, D.; Sancho, M.-R. *Carbohydr. Res.* **1995**, *278*, 91–101.
263. Stevens, C. M.; Watanabe, R. *J. Am. Chem. Soc.* **1950**, *72*, 725–727.
264. Corey, E. J.; Suggs, J. W. *J. Org. Chem.* **1973**, *38*, 3223–3224.
265. Kunz, H.; Unverzagt, C. *Angew. Chem.* **1984**, *96*, 426–427.
266. Jeffrey, P. D.; McCombie, S. W. *J. Org. Chem.* **1982**, *47*, 587–590.
267. Guibe, F.; Dangles, O.; Balavoine, G. *Tetrahedron Lett.* **1986**, *27*, 2365–2368.
268. Hey, H.; Arpe, H. J. *Angew. Chem.* **1973**, *85*, 986–987.
269. Imoto, M.; Kusumoto, S.; Shiba, T.; Rietschel, E. T.; Galanos, C.; Luederitz, O. *Tetrahedron Lett.* **1985**, *26*, 907–908.
270. Imoto, M.; Yoshimura, H.; Sakaguchi, N.; Kusumoto, S.; Shiba, T. *Tetrahedron Lett.* **1985**, *26*, 1545–1548.
271. Takahashi, T.; Nakamoto, S.; Ikeda, K.; Achiwa, K. *Tetrahedron Lett.* **1986**, *27*, 1819–1822.
272. Imoto, M.; Kusunose, N.; Kusumoto, S.; Shiba, T. *Tetrahedron Lett.* **1988**, *29*, 2227–2230.
273. Paulsen, H.; Krogmann, C. *Liebigs Ann. Chem.* **1989**, *12*, 1203–1213.
274. Szabo, L.; Polt, R. *Carbohydr. Res.* **1994**, *258*, 293–297.
275. Zhu, X.; Pachamuthu, K.; Schmidt, R. R. *J. Org. Chem.* **2003**, *68*, 5641–5651.
276. Zhu, X.; Pachamuthu, K.; Schmidt, R. R. *Org. Lett.* **2004**, *6*, 1083–1085.

277. Meinjohanns, E.; Meldal, M.; Bock, K. *Tetrahedron Lett.* **1995**, *36*, 9205–9208.
278. Mukaiyama, T.; Matsubara, K. *Chem. Lett.* **1992**, *9*, 1755–1758.
279. Matsubara, K.; Mukaiyama, T. *Chem. Lett.* **1993**, *12*, 2145–2148.
280. Ziegler, T. *Liebigs Ann. Chem.* **1995**, *1995*, 949–955.
281. Fukase, K.; Liu, W. C.; Suda, Y.; Oikawa, M.; Wada, A.; Mori, S.; Ulmer, A. J.; Rietschel, E. T.; Kusumoto, S. *Tetrahedron Lett.* **1995**, *36*, 7455–7458.
282. Kaji, E.; Lichtenthaler, W. F.; Osa, Y.; Zen, S. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 1172–1179.
283. Dullenkopf, W.; Castro-Palomino, J. C.; Manzoni, L.; Schmidt, R. R. *Carbohydr. Res.* **1996**, *296*, 135–147.
284. Mathieux, N.; Paulsen, H.; Meldal, M.; Bock, K. *J. Chem. Soc., Perkin Trans. 1* **1997**, *16*, 2359–2368.
285. Qiu, D.; Koganty, R. R. *Tetrahedron Lett.* **1997**, *38*, 45–48.
286. Auzanneau, F.-I.; Bennis, K.; Fanton, E.; Prome, D.; Defaye, J.; Gelas, J. *J. Chem. Soc., Perkin Trans. 1* **1998**, *21*, 3629–3636.
287. Fukase, K.; Fukase, Y.; Oikawa, M.; Liu, W. C.; Suda, Y.; Kusumoto, S. *Tetrahedron* **1998**, *54*, 4033–4050.
288. Sakai, Y.; Oikawa, M.; Yoshizaki, H.; Ogawa, T.; Suda, Y.; Fukase, K.; Kusumoto, S. *Tetrahedron Lett.* **2000**, *41*, 6843–6847.
289. Yoshizaki, H.; Fukuda, N.; Sato, K.; Oikawa, M.; Fukase, K.; Suda, Y.; Kusumoto, S. *Angew. Chem.* **2001**, *113*, 1523–1528.
290. Watanabe, Y.; Mochizuki, T.; Shiozaki, M.; Kanai, S.; Kurakata, S.-i.; Nishijima, M. *Carbohydr. Res.* **2001**, *333*, 203–231.
291. Gege, C.; Oscarson, S.; Schmidt, R. R. *Tetrahedron Lett.* **2001**, *42*, 377–380.
292. Sawada, N.; Ito, M.; Ishida, H.; Kiso, M. *Tetrahedron Lett.* **2001**, *42*, 1745–1747.
293. Nakamura, T.; Shiozaki, M.; Kurakata, S.-i. *Carbohydr. Res.* **2002**, *337*, 1343–1349.
294. Jiaang, Z.-H.; Budzynski, W. A.; Skeels, L. N.; Krantz, M. J.; Koganty, R. R. *Tetrahedron* **2002**, *58*, 8833–8842.
295. Bedini, E.; Barone, G.; Unverzagt, C.; Parrilli, M. *Carbohydr. Res.* **2004**, *339*, 393–400.
296. Oikawa, M.; Tanaka, T.; Fukuda, N.; Kusumoto, S. *Tetrahedron Lett.* **2004**, *45*, 4039–4042.
297. Zamyatina, A.; Sekljic, H.; Brade, H.; Kosma, P. *Tetrahedron* **2004**, *60*, 12113–12137.
298. Fukase, K.; Ueno, A.; Fukase, Y.; Oikawa, M.; Suda, Y.; Kusumoto, S. *Bull. Chem. Soc. Jpn.* **2003**, *76*, 485–500.
299. Biskup, M. B.; Mueller, J. U.; Weingart, R.; Schmidt, R. R. *ChemBioChem* **2005**, *6*, 1007–1015.
300. Koeller, K. M.; Wong, C.-H. *Chem. Eur. J.* **2000**, *6*, 1243–1251.
301. Gege, C.; Geyer, A.; Schmidt, R. R. *Chem. Eur. J.* **2002**, *8*, 2454–2463.
302. Gege, C.; Geyer, A.; Schmidt, R. R. *Eur. J. Org. Chem.* **2002**, 2475–2485.
303. Yang, G.; Mansourova, M.; Hennig, L.; Findeisen, M.; Oehme, R.; Giesa, S.; Welzel, P. *Helv. Chim. Acta* **2004**, *87*, 1807–1824.
304. Ziegler, T.; Eckhardt, E.; Birault, V. *J. Org. Chem.* **1993**, *58*, 1090–1099.
305. Fukase, K.; Nakai, Y.; Kanoh, T.; Kusumoto, S. *Synlett* **1998**, 84–86.
306. Fujimoto, Y.; Kimura, E.; Murata, S.; Kusumoto, S.; Fukase, K. *Tetrahedron Lett.* **2006**, *47*, 539–543.
307. Xue, J.; Khaja, S. D.; Locke, R. D.; Matta, K. L. *Synlett* **2004**, 861–865.
308. Inamura, S.; Fujimoto, Y.; Kawasaki, A.; Shiokawa, Z.; Woelk, E.; Heine, H.; Lindner, B.; Inohara, N.; Kusumoto, S.; Fukase, K. *Org. Biomol. Chem.* **2006**, *4*, 232–242.
309. Yeung, B. K. S.; Hill, D. C.; Janicka, M.; Petillo, P. A. *Org. Lett.* **2000**, *2*, 1279–1282.
310. Yang, G.; Hennig, L.; Findeisen, M.; Oehme, R.; Giesa, S.; Welzel, P. *Helv. Chim. Acta* **2004**, *87*, 1794–1806.
311. Zhu, T.; Boons, G. J. *Angew. Chem., Int. Ed.* **1999**, *38*, 3495–3497.
312. Nakano, J.; Ichiyanagi, T.; Ohta, H.; Ito, Y. *Tetrahedron Lett.* **2003**, *44*, 2853–2856.
313. Johnson, D. A.; Keegan, D. S.; Sowell, C. G.; Livesay, M. T.; Johnson, C. L.; Taubner, L. M.; Harris, A.; Myers, K. R.; Thompson, J. D.; Gustafson, G. L.; Rhodes, M. J.; Ulrich, J. T.; Ward, J. R.; Yorgensen, Y. M.; Cantrell, J. L.; Brookshire, V. G. *J. Med. Chem.* **1999**, *42*, 4640–4649.
314. Ellervik, U.; Magnusson, G. *Carbohydr. Res.* **1996**, *280*, 251–260.
315. Nilsson, K. G. I. *Tetrahedron Lett.* **1997**, *38*, 133–136.
316. Bhattacharyya, S.; Magnusson, B. G.; Wellmar, U.; Nilsson, U. J. *J. Chem. Soc., Perkin Trans. 1* **2001**, *8*, 886–890.
317. Benakli, K.; Zha, C.; Kerns, R. J. *J. Am. Chem. Soc.* **2001**, *123*, 9461–9462.
318. Yan, F.; Mehta, S.; Eichler, E.; Wakarchuk, W. W.; Gilbert, M.; Schur, M. J.; Whitfield, D. M. *J. Org. Chem.* **2003**, *68*, 2426–2431.
319. Chen, M.-Y.; Patkar, L. N.; Chen, H.-T.; Lin, C.-C. *Carbohydr. Res.* **2003**, *338*, 1327–1332.
320. Imamura, A.; Ando, H.; Korogi, S.; Tanabe, G.; Muraoka, O.; Ishida, H.; Kiso, M. *Tetrahedron Lett.* **2003**, *44*, 6725–6728.
321. Reipen, T.; Kunz, H. *Synthesis* **2003**, 2487–2502.
322. Chen, M.-Y.; Patkar, L. N.; Lin, C.-C. *J. Org. Chem.* **2004**, *69*, 2884–2887.
323. Tanaka, H.; Adachi, M.; Takahashi, T. *Tetrahedron Lett.* **2004**, *45*, 1433–1436.
324. Wittmann, V.; Seeberger, S. *Angew. Chem., Int. Ed.* **2000**, *39*, 4348–4352.
325. Burkhart, F.; Zhang, A.; Wacowich-Sgarbi, S.; Wong, C. H. *Angew. Chem., Int. Ed.* **2001**, *40*, 1274–1277.
326. Ritter, T. K.; Mong, K.-K. T.; Liu, H.; Nakatani, T.; Wong, C.-H. *Angew. Chem., Int. Ed.* **2003**, *42*, 4657–4660.
327. Zhu, T.; Boons, G. J. *Org. Lett.* **2001**, *3*, 4201–4203.
328. Buskas, T.; Li, Y.; Boons, G. J. *Chem. Eur. J.* **2004**, *10*, 3517–3524.
329. Zhu, T.; Boons, G.-J. *J. Am. Chem. Soc.* **2000**, *122*, 10222–10223.
330. Zhu, T.; Boons, G.-J. *Chem. Eur. J.* **2001**, *7*, 2382–2389.
331. Nitz, M.; Bundle, D. R. *J. Org. Chem.* **2000**, *65*, 3064–3073.
332. Mong, T. K.-K.; Huang, C.-Y.; Wong, C.-H. *J. Org. Chem.* **2003**, *68*, 2135–2142.
333. Ellervik, U.; Grundberg, H.; Magnusson, G. *J. Org. Chem.* **1998**, *63*, 9323–9338.
334. Mong, T. K.-K.; Lee, H.-K.; Duron, S. G.; Wong, C.-H. *Proc. Natl. Acad. Sci. U.S.A.* **2003**, *100*, 797–802.
335. Fukase, K.; Hasuoka, A.; Kinoshita, I.; Aoki, Y.; Kusumoto, S. *Tetrahedron* **1995**, *51*, 4923–4932.
336. Just, G.; Grozinger, K. *Synthesis* **1976**, 457–458.
337. Dong, Q.; Anderson, C. E.; Ciufolini, M. A. *Tetrahedron Lett.* **1995**, *36*, 5681–5682.

338. Tokimoto, H.; Fukase, K. *Tetrahedron Lett.* **2005**, *46*, 6831–6832.
339. Somsak, L.; Czifrak, K.; Veres, E. *Tetrahedron Lett.* **2004**, *45*, 9095–9097.
340. Kent, P. W.; Lawson, G.; Senior, A. *Science* **1951**, *113*, 354–355.
341. Meyer, K. H.; Schwartz, D. E. *Helv. Chim. Acta* **1950**, *33*, 1651–1662.
342. Annison, E. F.; James, A. T.; Morgan, W. T. J. *Biochem. J.* **1951**, *48*, 477–482.
343. Lloyd, P. F.; Stacey, M. *Tetrahedron* **1960**, *9*, 116–124.
344. Lloyd, P. F.; Roberts, G. P. *J. Chem. Soc.* **1963**, 2962–2971.
345. Dekany, G.; Bornaghi, L.; Papageoegiou, J.; Taylor, S. *Tetrahedron Lett.* **2001**, *42*, 3129–3132.
346. Singh, L.; Seifert, J. *Tetrahedron Lett.* **2001**, *42*, 3133–3136.
347. Miyai, K.; Gross, P. H. *J. Org. Chem.* **1969**, *34*, 1638–1642.
348. Kerns, R. J.; Zha, C.; Benakli, K.; Liang, Y.-Z. *Tetrahedron Lett.* **2003**, *44*, 8069–8072.
349. Boysen, M.; Gemma, E.; Lahmann, M.; Oscarson, S. *Chem. Commun.* **2005**, *24*, 3044–3046.
350. Crich, D.; Vinod, A. U. *Org. Lett.* **2003**, *5*, 1297–1300.
351. Trumtel, M.; Tavecchia, P.; Veyrieres, A.; Sinay, P. *Carbohydr. Res.* **1989**, *191*, 29–52.
352. Debenham, J. S.; Madsen, R.; Roberts, C.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1995**, *117*, 3302–3303.
353. Griffiths, S. L.; Madsen, R.; Fraser-Reid, B. *J. Org. Chem.* **1997**, *62*, 3654–3658.
354. Baker, B. R.; Joseph, J. P.; Schaub, R. E.; Williams, J. H. *J. Org. Chem.* **1954**, *19*, 1786–1792.
355. Akiya, S.; Osawa, T. *Chem. Pharm. Bull.* **1960**, *8*, 583–587.
356. Lemieux, R. U.; Takeda, T.; Chung, B. Y. *ACS Symp. Ser.* **1976**, *39*, 90–115.
357. Kochetkov, N. K.; Byramova, N. E.; Tsvetkov, Y. E.; Backinowsky, L. V. *Tetrahedron* **1985**, *41*, 3363–3375.
358. Byramova, N. E.; Tsvetkov, Y. E.; Bakinovskii, L. V.; Kochetkov, N. K. *Carbohydr. Res.* **1985**, *137*, C8–C13.
359. Gomtsyan, A. R.; Byramova, N. E.; Bakinovskii, L. V.; Kochetkov, N. K. *Carbohydr. Res.* **1985**, *138*, C1–C4.
360. Paulsen, H.; Paal, M. *Carbohydr. Res.* **1985**, *137*, 39–62.
361. Paulsen, H.; Himpkamp, P.; Peters, T. *Liebigs Ann. Chem.* **1986**, 664–674.
362. Sadozai, K. K.; Ito, Y.; Nukada, T.; Ogawa, T.; Kobata, A. *Carbohydr. Res.* **1986**, *150*, 91–101.
363. Ohtsuka, I.; Hada, N.; Ohtaka, H.; Sugita, M.; Takeda, T. *Chem. Pharm. Bull.* **2002**, *50*, 600–604.
364. Maranduba, A.; Veyrieres, A. *Carbohydr. Res.* **1986**, *151*, 105–119.
365. Kantoci, D.; Keglevic, D.; Derome, A. E. *Carbohydr. Res.* **1987**, *162*, 227–235.
366. Garneau, S.; Qiao, L.; Chen, L.; Walker, S.; Vederas, J. C. *Bioorg. Med. Chem.* **2004**, *12*, 6473–6494.
367. Mukaiyama, T.; Takeuchi, K.; Jona, H.; Maeshima, H.; Saitoh, T. *Helv. Chim. Acta* **2000**, *83*, 1901–1918.
368. Hojo, H.; Watabe, J.; Nakahara, Y.; Nakahara, Y.; Ito, Y.; Nabeshima, K.; Toole, B. P. *Tetrahedron Lett.* **2001**, *42*, 3001–3004.
369. Suzuki, K.; Maeta, H.; Matsumoto, T. *Tetrahedron Lett.* **1989**, *30*, 4853–4854.
370. Ito, H.; Ishida, H.; Collins, B. E.; Fromholt, S. E.; Schnaar, R. L.; Kiso, M. *Carbohydr. Res.* **2003**, *338*, 1621–1639.
371. Komori, T.; Kondo, S.; Ando, H.; Ishida, H.; Kiso, M. *Carbohydr. Res.* **2002**, *337*, 1679–1686.
372. Ishida, H.; Ohta, Y.; Tsukada, Y.; Isogai, Y.; Ishida, H.; Kiso, M.; Hasegawa, A. *Carbohydr. Res.* **1994**, *252*, 283–290.
373. Matsuzaki, Y.; Nunomura, S.; Ito, Y.; Sugimoto, M.; Nakahara, Y.; Ogawa, T. *Carbohydr. Res.* **1993**, *242*, c1–c6.
374. Ishida, H. K.; Ishida, H.; Kiso, M.; Hasegawa, A. *Carbohydr. Res.* **1994**, *260*, c1–c6.
375. Nilsson, U.; Magnusson, G. *Carbohydr. Res.* **1995**, *272*, 9–16.
376. Wang, Z.-G.; Zhang, X.; Visser, M.; Live, D.; Zatorski, A.; Iserloh, U.; Lloyd, K. O.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 1728–1732.
377. Chernyak, A.; Oscarson, S.; Turek, D. *Carbohydr. Res.* **2000**, *329*, 309–316.
378. Reddy, G. V.; Jain, R. K.; Locke, R. D.; Matta, K. L. *Carbohydr. Res.* **1996**, *280*, 261–276.
379. Soderman, P.; Widmalm, G. *Eur. J. Org. Chem.* **2001**, 3453–3456.
380. Soderman, P.; Larsson, E. A.; Widmalm, G. *Eur. J. Org. Chem.* **2002**, 1614–1618.
381. Agoston, K.; Kerekgyarto, J.; Hajko, J.; Batta, G.; Lefeber, D. J.; Kamerling, J. P.; Vliegenthart, J. F. G. *Chem. Eur. J.* **2002**, *8*, 151–161.
382. Chowdhury, A. R.; Siriwardena, A.; Boons, G. J. *Tetrahedron Lett.* **2002**, *43*, 7805–7807.
383. Kanie, O.; Ito, Y.; Ogawa, T. *Tetrahedron Lett.* **1996**, *37*, 4551–4554.
384. Huang, B.-G.; Jain, R. K.; Locke, R. D.; Alderfer, J. L.; Tabaczynski, W. A.; Matta, K. L. *Tetrahedron Lett.* **2000**, *41*, 6279–6284.
385. Mehta, S.; Whitfield, D. M. *Tetrahedron* **2000**, *56*, 6415–6425.
386. Robina, I.; Gomez-Bujedo, S.; Fernandez-Bolanos, J. G.; Fuentes, J.; Spaink, H. P. *Tetrahedron* **2002**, *58*, 521–530.
387. Litjens, R. E. J. N.; Heeten, R.; Timmer, M. S. M.; Overkleeft, H. S.; Marel, G. A. *Chem. Eur. J.* **2005**, *11*, 1010–1016.
388. Xia, J.; Srikrishnan, T.; Alderfer, J. L.; Jain, R. K.; Piskorz, C. F.; Matta, K. L. *Carbohydr. Res.* **2000**, *329*, 561–577.
389. Liao, W.; Locke, R. D.; Matta, K. L. *Chem. Commun.* **2000**, *5*, 369–370.
390. Otsubo, N.; Ishida, H.; Kannagi, R.; Kiso, M. *Tetrahedron: Asymmetry* **2005**, *16*, 1321–1327.
391. Pan, W.; Zhang, Y.; Liang, G.; Vincent, S. P.; Sinay, P. *Chem. Commun.* **2005**, 3445–3447.
392. Wang, Y.; Yan, Q.; Wu, J.; Zhang, L. H.; Ye, X. S. *Tetrahedron* **2005**, *61*, 4313–4321.
393. Wang, Y.; Huang, X.; Zhang, L. H.; Ye, X. S. *Org. Lett.* **2004**, *6*, 4415–4417.
394. Fridman, M.; Belakhov, V.; Lee, L. V.; Liang, F.-S.; Wong, C.-H.; Baasov, T. *Angew. Chem., Int. Ed.* **2005**, *44*, 447–452.
395. Yang, F.; He, H.; Du, Y. *Tetrahedron Lett.* **2002**, *43*, 7561–7563.
396. Gu, G.; Du, Y.; Pan, J. *Carbohydr. Res.* **2002**, *337*, 1313–1317.
397. Yang, F.; Du, Y. *Carbohydr. Res.* **2003**, *338*, 495–502.
398. Yang, F.; Hua, Y.; Du, Y. *Carbohydr. Res.* **2003**, *338*, 1313–1318.
399. Chen, Q.; Yang, F.; Du, Y. *Carbohydr. Res.* **2005**, *340*, 2476–2482.

400. Pozsgay, V.; Jennings, H. J. *Carbohydr. Res.* **1988**, *179*, 61–75.
401. Dasgupta, F.; Garegg, P. J. *J. Carbohydr. Chem.* **1988**, *7*, 701–707.
402. Sato, S.; Ito, Y.; Ogawa, T. *Tetrahedron Lett.* **1988**, *29*, 4759–4762.
403. Pozsgay, V.; Jennings, H. J. *Tetrahedron Lett.* **1987**, *28*, 1375–1376.
404. Jain, R. K.; Piskorz, C. F.; Matta, K. L. *Carbohydr. Res.* **1993**, *243*, 385–391.
405. Takahashi, S.; Terayama, H.; Sakairi, N.; Kuzuhara, H. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 288–290.
406. Lonn, H. *Carbohydr. Res.* **1985**, *139*, 105–113.
407. Pozsgay, V.; Jennings, H. J. *Tetrahedron Lett.* **1987**, *28*, 1375–1376.
408. Macmillan, D.; Daines, A. M.; Bayrhuber, M.; Flitsch, S. L. *Org. Lett.* **2002**, *4*, 1467–1470.
409. Nicolaou, K. C.; Caulfield, T. J.; Kataoka, H.; Stylianides, N. A. *J. Am. Chem. Soc.* **1990**, *112*, 3693–3695.
410. Cai, Y.; Roberts, B. P.; Tocher, D. A. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1376–1386.
411. Mukherjee, C.; Tiwari, P.; Misra, A. K. *Tetrahedron Lett.* **2006**, *47*, 441–445.
412. Garegg, P. J. *Adv. Carbohydr. Chem. Biochem.* **1997**, *52*, 179–205.
413. Takeda, Y.; Horito, S. *Carbohydr. Res.* **2005**, *340*, 211–220.
414. Grundler, G.; Schmidt, R. R. *Carbohydr. Res.* **1985**, *135*, 203–218.
415. Joosten, J. A. F.; Kamerling, J. P.; Vliegenthart, J. F. G. *Carbohydr. Res.* **2003**, *338*, 2611–2627.
416. Yan, F.; Wakarchuk, W. W.; Gilbert, M.; Richards, J. C.; Whitfield, D. M. *Carbohydr. Res.* **2000**, *328*, 3–16.
417. Horie, R.; Hara, K.; Nakano, K. *Carbohydr. Res.* **1992**, *230*, C11–C15.
418. Slaghek, T. M.; Hyppoenen, T. K.; Ogawa, T.; Kamerling, J. P.; Vliegenthart, F. G. *Tetrahedron Lett.* **1993**, *34*, 7939–7942.
419. Halcomb, R. L.; Huang, H.; Wong, C.-H. *J. Am. Chem. Soc.* **1994**, *116*, 11315–11322.
420. Ochiai, H.; Ohmae, M.; Kobayashi, S. *Carbohydr. Res.* **2004**, *339*, 2769–2788.
421. Ma, Z.; Zhang, J.; Kong, F. *Carbohydr. Res.* **2004**, *339*, 43–49.
422. Zhang, J.; Kong, F. *Carbohydr. Res.* **2003**, *338*, 19–27.
423. Love, K. R.; Andrade, R. B.; Seeberger, P. H. *J. Org. Chem.* **2001**, *66*, 8165–8176.
424. Li, Q.; Li, H.; Li, Q.; Lou, Q.-H.; Su, B.; Cai, M.-S.; Li, Z.-J. *Carbohydr. Res.* **2002**, *337*, 1929–1934.
425. Liew, S.-T.; Wei, A. *Carbohydr. Res.* **2002**, *337*, 1319–1324.
426. Halcomb, R. L.; Huang, H. M.; Wong, C. H. *J. Am. Chem. Soc.* **1994**, *116*, 11315–11322.
427. Santhanam, B.; Wolfert, M. A.; Moore, J. N.; Boons, G.-J. *Chem. Eur. J.* **2004**, *10*, 4798–4807.
428. Adinolfi, M.; Iadonisi, A.; Ravida, A. *Synlett* **2006**, 583–586.
429. Sun, J.; Han, X.; Yu, B. *Carbohydr. Res.* **2003**, *338*, 827–833.
430. Nilsson, U.; Magnusson, G. *Carbohydr. Res.* **1995**, *272*, 9–16.
431. Matsuzaki, Y.; Nunomura, S.; Ito, Y.; Sugimoto, M.; Nakahara, Y.; Ogawa, T. *Carbohydr. Res.* **1993**, *242*, C1–C6.
432. Vermeer, H. J.; Kamerling, J. P.; Vliegenthart, J. F. G. *Tetrahedron: Asymmetry* **2000**, *11*, 539–547.
433. Martin-Lomas, M.; Flores-Mosquera, M.; Chiara, J. L. *Eur. J. Org. Chem.* **2000**, 1547–1562.
434. Matsuo, I.; Ito, Y. *Carbohydr. Res.* **2003**, *338*, 2163–2168.
435. Hansson, J.; Garegg, P. J.; Oscarson, S. *J. Org. Chem.* **2001**, *66*, 6234–6243.
436. Ito, Y.; Sato, S.; Mori, M.; Ogawa, T. *J. Carbohydr. Chem.* **1988**, *7*, 359–376.
437. Lee, H. H.; Schwartz, D. A.; Harris, J. F.; Carver, J. P.; Krepinsky, J. J. *Can. J. Chem.* **1986**, *64*, 1912–1918.
438. Castro-Palomino, J. C.; Schmidt, R. R. *Tetrahedron Lett.* **1995**, *36*, 5343–5346.
439. Shimizu, H.; Ito, Y.; Matsuzaki, Y.; Iijima, H.; Ogawa, T. *Biosci., Biotechnol., Biochem.* **1996**, *60*, 73–76.
440. Lergenmuller, M.; Ito, Y.; Ogawa, T. *Tetrahedron* **1998**, *54*, 1381–1394.
441. Jona, H.; Maeshima, H.; Mukaiyama, T. *Chem. Lett.* **2001**, 726–727.
442. Yamada, T.; Kinjyo, S.; Yoshida, J.; Yamago, S. *Chem. Lett.* **2005**, *34*, 1556–1557.
443. Debenham, J. S.; Rodebaugh, R.; Fraser-Reid, B. *J. Org. Chem.* **1997**, *62*, 4591–4600.
444. Roe, B. A.; Boojamra, C. G.; Griggs, J. L.; Bertozzi, C. R. *J. Org. Chem.* **1996**, *61*, 6442–6445.
445. Mulard, L. A.; Clement, M.-J.; Segat-Dioury, F.; Delepierre, M. *Tetrahedron* **2002**, *58*, 2593–2604.
446. Debenham, J. S.; Fraser-Reid, B. *J. Org. Chem.* **1996**, *61*, 432–433.
447. Mulard, L. A.; Guerreiro, C. *Tetrahedron* **2004**, *60*, 2475–2488.
448. Olsson, L.; Kelberlau, S.; Jia, Z. J.; Fraser-Reid, B. *Carbohydr. Res.* **1998**, *314*, 273–276.
449. Clinch, K.; Evans, G. B.; Furneaux, R. H.; Rendle, P. M.; Rhodes, P. L.; Roberton, A. M.; Rosendale, D. I.; Tyler, P. C.; Wright, D. P. *Carbohydr. Res.* **2002**, *337*, 1095–1111.
450. Khiar, N.; Fernandez, I.; Araujo, C. S.; Rodriguez, J. A.; Suarez, B.; Alvarez, E. *J. Org. Chem.* **2003**, *68*, 1433–1442.
451. Ellervik, U.; Magnusson, G. *J. Org. Chem.* **1998**, *63*, 9314–9322.
452. Castro-Palomino, J. C.; Schmidt, R. R. *Tetrahedron Lett.* **1995**, *36*, 5343–5346.
453. Debenham, J. S.; Debenham, S. D.; Fraser-Reid, B. *Bioorg. Med. Chem.* **1996**, *4*, 1909–1918.
454. Fischer, W.; Anselme, J. P. *J. Am. Chem. Soc.* **1967**, *89*, 5284–5285.
455. Cavender, C. J.; Shiner, V. J., Jr. *J. Org. Chem.* **1972**, *37*, 3567–3569.
456. Zaloom, J.; Roberts, D. C. *J. Org. Chem.* **1981**, *46*, 5173–5176.
457. Vasella, A.; Witzig, C.; Chiara, J. L.; Martin-Lomas, M. *Helv. Chim. Acta* **1991**, *74*, 2073–2077.
458. Olsson, L.; Jia, Z. Z. J.; Fraser-Reid, B. *J. Org. Chem.* **1998**, *63*, 3790–3792.
459. Buskas, T.; Garegg, P. J.; Konradsson, P.; Maloisel, J.-L. *Tetrahedron: Asymmetry* **1994**, *5*, 2187–2194.
460. Iyer, S.; Rele, S.; Grasa, G.; Nolan, S.; Chaikof, E. L. *Chem. Commun.* **2003**, *13*, 1518–1519.
461. Haller, M. F.; Boons, G.-J. *Eur. J. Org. Chem.* **2002**, 2033–2038.
462. Alper, P. B.; Hung, S.-C.; Wong, C.-H. *Tetrahedron Lett.* **1996**, *37*, 6029–6032.
463. Orgueira, H. A.; Bartolozzi, A.; Schell, P.; Litjens, R. E. J. N.; Palmacci, E. R.; Seeberger, P. H. *Chem. Eur. J.* **2003**, *9*, 140–169.

464. Pathak, R.; Bottger, E. C.; Vasella, A. *Helv. Chim. Acta* **2005**, *88*, 2967–2985.
465. Titz, A.; Radic, Z.; Schwardt, O.; Ernst, B. *Tetrahedron Lett.* **2006**, *47*, 2383–2385.
466. Gavard, O.; Hersant, Y.; Alais, J.; Duverger, V.; Dilhas, A.; Bascou, A.; Bonnaffe, D. *Eur. J. Org. Chem.* **2003**, 3603–3620.
467. Yan, R.-B.; Yang, F.; Wu, Y.; Zhang, L.-H.; Ye, X.-S. *Tetrahedron Lett.* **2005**, *46*, 8993–8995.
468. Seeberger, P. H.; Baumann, M.; Zhang, G.; Kanemitsu, T.; Swayze, E. E.; Hofstadler, S. A.; Griffey, R. H. *Synlett* **2003**, 1323–1326.
469. Dasgupta, F.; Garegg, P. J. *J. Chem. Soc., Chem. Commun.* **1989**, 1640–1641.
470. Barany, G.; Merrifield, R. B. *J. Am. Chem. Soc.* **1977**, *99*, 7363–7365.
471. Barany, G.; Merrifield, R. B. *J. Am. Chem. Soc.* **1980**, *102*, 3084–3095.
472. Albericio, F.; Barany, G. *Int. J. Pept. Protein Res.* **1987**, *30*, 177–205.
473. Meinjohanns, E.; Meldal, M.; Paulsen, H.; Bock, K. *J. Chem. Soc., Perkin Trans. 1* **1995**, 405–415.
474. Jensen, K. J.; Hansen, P. R.; Venugopal, D.; Barany, G. *J. Am. Chem. Soc.* **1996**, *118*, 3148–3155.
475. Meinjohanns, E.; Meldal, M.; Schleyer, A.; Paulsen, H.; Bock, K. *J. Chem. Soc., Perkin Trans. 1* **1996**, 985–993.
476. Aly, M. R. E.; Castro-Palomino, J. C.; Ibrahim, E.-S. I.; El Ashry, E. S. H.; Schmidt, R. R. *Eur. J. Org. Chem.* **1998**, 2305–2316.
477. Chiesa, M. V.; Schmidt, R. R. *Eur. J. Org. Chem.* **2000**, 3541–3554.
478. Miquel, N.; Vignando, S.; Russo, G.; Lay, L. *Synlett* **2004**, 341–343.
479. Jonke, S.; Liu, K.-g.; Schmidt, R. R. *Chem. Eur. J.* **2006**, *12*, 1274–1290.
480. Knerr, L.; Schmidt, R. R. *Eur. J. Org. Chem.* **2000**, 2803–2808.
481. Aly, M. R. E.; Ibrahim, E.-S. I.; El-Ashry, E.-S. H. E.; Schmidt, R. R. *Eur. J. Org. Chem.* **2000**, 319–326.
482. Halkes, K. M.; Gotfredsen, C. H.; Grotli, M.; Miranda, L. P.; Duus, J. O.; Meldal, M. *Chem. Eur. J.* **2001**, *7*, 3584–3591.
483. Kajihara, Y.; Suzuki, Y.; Yamamoto, N.; Sasaki, K.; Sakakibara, T.; Juneja, L. R. *Chem. Eur. J.* **2004**, *10*, 971–985.
484. Bartolmas, T.; Heyn, T.; Mickeleit, M.; Fischer, A.; Reutter, W.; Danker, K. *J. Med. Chem.* **2005**, *48*, 6750–6755.
485. Knuhr, P.; Castro-Palomino, J.; Grathwohl, M.; Schmidt, R. R. *Eur. J. Org. Chem.* **2001**, 239–4246.
486. Bowers, S. G.; Coe, D. M.; Boons, G. J. *J. Org. Chem.* **1998**, *63*, 4570–4571.
487. Jiao, H.; Hindsgaul, O. *Angew Chem., Int. Ed.* **1999**, *38*, 346–348.
488. Wei, P.; Kerns, R. J. *J. Org. Chem.* **2005**, *70*, 4195–4198.
489. Wei, P.; Kerns, R. J. *Tetrahedron Lett.* **2005**, *46*, 6901–6905.
490. Marra, A.; Sinay, P. *Carbohydr. Res.* **1990**, *200*, 319–337.
491. Aly, M. R. E.; Schmidt, R. R. *Eur. J. Org. Chem.* **2005**, 4382–4392, and references cited therein.
492. Castro-Palomino, J. C.; Schmidt, R. R. *Tetrahedron Lett.* **1995**, *36*, 6871–6874.
493. Saha, U. K.; Schmidt, R. R. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1855–1860.
494. Demchenko, A. V.; Boons, G. J. *Tetrahedron Lett.* **1998**, *39*, 3065–3068.
495. Boons, G. J.; Demchenko, A. V. *Chem. Rev.* **2000**, *100*, 4539–4565.
496. Kelly, N. M.; Jensen, K. J. *J. Carbohydr. Chem.* **2001**, *20*, 537–548.