Abstract

Oligosaccharide derivatives, particularly glycosylated oligosaccharides, are important compounds in living systems, exhibiting multifunctional characteristics in various kinds of life phenomena. The development of an efficient synthetic method is demanded to supply sufficient quantities of oligosaccharide-glycomaterials for basic research. Although many chemical or chemo-enzymatic processes for constructing glycosidic bonds have resulted from rapid advances in modern organic synthesis and biotechnology, these processes involve the use of protecting groups. This review presents an overview of recent advances in protecting group-free chemical and chemo-enzymatic processes for synthesis of oligosaccharide-glycosides.

Keywords: oligosaccharide, protecting group-free glycosylation, sugar epoxide, sugar oxazoline

Introduction

In recent years, there has been great interest in carbohydrates.1) Almost all of the carbohydrates that exist in nature are glycosidic compounds that result from dehydrative condensation of hemiacetals (OH group at the reducing end) and aglycones.2) In general, the sugar parts are soluble in water due to the friendly relationship between water and saccharide moieties.3) If one has to prepare glycosidic compounds in a test tube, the best reaction solvent would be water. However, dehydrative condensation reactions in aqueous media are extremely disadvantageous due to the large negative values of standard Gibbs energy of formation for the hydrolysis of glycosidic bonds. It is, therefore, necessary to activate the hemiacetal by introducing an appropriate leaving group into the reducing end.

During recent years, there has been growing interest in artificial oligosaccharide materials such as glycosylated liposomes,4) DNA-sugar complexes,5) glycolipids,6) sugar chips,7) and glycopolymers,8) owing to their biochemical and pharmacological importance (Figure 1). In order to construct a glycosidic bond between the oligosaccharide and aglycon moiety, regiospecific activation of the hemiacetal in the oligosaccharide part is indispensable. Much effort has been devoted to glycoside synthesis, and many efficient methods have been developed using various kinds of activated oligosaccharides as glycosyl donors, where protecting groups play the key role in achieving the regio- or stereo-selectivity of the reactions.9) This review describes protection-free protocols for chemical and chemo-enzymatic glycosylations using oligosaccharide glycosyl donors, focusing on the newly developed strategies in our laboratory.
Protecting group-free synthesis of alkyl oligosaccharide-glycosides through dialkoxytriazine-type glycosyl donors

Alkyl oligosaccharide-glycosides have their own demanding issues as useful building blocks in the construction of complex glycomaterials.\textsuperscript{10} The most simple and direct route for the synthesis of unprotected alkyl glycosides was first reported by Emil Fischer in 1893.\textsuperscript{11} An unprotected monosaccharide was condensed with an alcohol in the presence of HCl, usually at elevated temperatures, resulting in substitution at the anomeric position by the alcohol through an oxonium ion intermediate.\textsuperscript{12} Fischer glycosylation has remained one of the most popular methods due to its simplicity and versatility, and only modifications such as the use of trifluoromethanesulfonic acid, Lewis acids, microwave radiation, and ammonium chloride have been adopted.\textsuperscript{13}

Despite the great utility of Fischer’s method, the use of a strong acid causes side reactions. For example, when employing oligosaccharides as starting sugars such as acid-labile melibiose, acetal exchanges of the inner glycosidic bonds take place due to protonation of the inner glycosidic oxygens (Figure 2 (A)). In order to avoid these unproductive interactions, a site-specific protonation at the reducing end is indispensable (Figure 2 (B)). However, such a chemical event has not been realized so far because the regiospecific modification of the reducing end of an unprotected oligosaccharide is extremely difficult. The development of a new glycosylation process that involves the specific anomeric activation of unprotected sugars has, therefore, been strongly demanded. Many researchers have tackled this problem, and direct synthetic processes for $O$-aryl glycosides,\textsuperscript{14a,b} $O$-alkyl glycosides,\textsuperscript{14c-l} glycosyl azides,\textsuperscript{14g} and nucleosides\textsuperscript{14m} have been developed by careful design of the structure of the glycosyl donors.

![Figure 2](image.png)

Figure 2. (A) Acetal exchange of the inner glycosidic bonds catalyzed by a proton under Fischer’s conditions. (B) Regiospecific introduction of $X,Y-H^+$ moiety into the reducing end of oligosaccharides. Examples of melibiose having an acid-labile 1,6-glycosidic bond are shown.

In 2008 we reported that 4,6-dialkoxy-1,3,5-triazine-type glycosyl donors can be prepared directly from the corresponding unprotected oligosaccharides.\textsuperscript{15} For example, an aqueous solution of glucose was treated with 2-chloro-4,6-dibenzyloxy-1,3,5-triazine (CDBT)\textsuperscript{16} and the resulting precipitates were filtered, giving rise to 4,6-dibenzyloxy-1,3,5-triazin-2-yl glucoside (DBT-glucoside) in good yield. The reaction proceeds in aqueous media without using any protecting groups, and the experimental procedure is very simple. Addition of an acetonitrile solution of CDBT to an aqueous solution of glucose followed by the filtration of the resulting precipitates gave β-type DBT-glucose (Figure 3). The formation of the β-product can be explained by the higher nucleophilicity of β-glucose compared to that of α-glucose.
Glycosylation of DBT-β-glycosides was carried out in various alcohols under palladium/carbon-catalyzed hydrogenolysis conditions (Figure 4). The glycosylation with DBT-melibioside as a glycosyl donor was demonstrated in which no cleavage of the acid-labile inner glycosidic bond was observed. When primary alcohols were used, the corresponding α-glycosides were formed preferentially, whereas the use of secondary alcohols afforded anomeric mixtures. When alcohols having a C-C double bond or a C-C triple bond were used, selective debenzylation was achieved with triethylsilane as the reductant without affecting the multiple bonds.

Figure 3. Synthesis of DBT-glucoside donor in aqueous media without protection.

Figure 4. Glycosylation using DBT-melibioside as glycosyl donor under hydrogenolytic conditions.

Figure 5. Plausible mechanism for activation of the nitrogen on the triazine ring of DBT donor by intermolecular hydrogen bonding with solvent alcohol (A) and hexafluoroisopropanol as additive (B).
The reductive debenzylolation reaction generates an acidic OH group whose acidity is close to that of the OH of cyanuric acid. It is estimated that the resulting OH can participate in a hydrogen bond network including the glycosyl acceptor of the alcohol, effectively protonating the triazine ring-nitrogen (Figure 5 (A)). The preferential formation of the α-glycosidic bond when using primary alcohols suggests that the reaction proceeds in a stereospecific manner (SN2 type). When secondary alcohols with lower nucleophilicity were employed, the contribution of the SN1 type reaction via an oxocarbenium ion intermediate may become larger, giving rise to a mixture of α- and β-glycosides. In this context, some hydrogen-bonding additives can be employed to offer a stronger H-bond interaction (Figure 5 (B)). Improved reaction efficiency and α-selectivity were noted with assistance of chloral hydrate or hexafluoro-2-propanol. Some experimental evidence for the hydrogen-bonding effect was obtained by an NMR study and DFT calculations.\(^1\)

In reference to the proton-promoted reaction with the DBT-glycosyl donor, Tanaka’s group revealed that 4,6-dimethoxy-1,3,5-triazin-2-yl glycosides prepared in one step were stereospecifically converted to the corresponding 1,2-cis-glycosides catalyzed by various kinds of metal catalysts.\(^2\)

Chemo-enzymatic glycosylation, particularly glycosylation catalyzed by glycosidases, is a promising technology, because glycosidases are stable, inexpensive and available on an industrial scale.\(^3\) In order to prepare a glycosyl donor starting from an unprotected sugar, it is necessary to protect the hydroxy groups, activate the anomeric center, introduce a leaving group, and deprotect the hydroxy groups, in a laborious process. In this review, a completely new approach that involves no protection/deprotection will be described.

There are several requirements of glycosyl donors for chemo-enzymatic glycosylations. Glycosyl donors must be stable enough to store, soluble in water, and easily prepared from the corresponding unprotected sugars. In addition, the glycosyl donors must be recognized by an enzyme (Figure 6 (A)), and the liberated leaving group must not inhibit the enzyme catalyst. Taking these requirements into consideration, we have designed dialkoxytriazine glycosides (DAT-glycosides) (Figure 6 (B)). The triazine ring has three nitrogen atoms that may increase the solubility in water. Additionally, DAT-glycosides possess many lone pairs on the nitrogen atoms and oxygen atoms such that one of these lone pairs can be protonated by the acid point in the active site of a glycosidase.

**Figure 6.** Design of endoglycosidase-catalyzed glycosylation using DAT-oligosaccharide-glycosyl donor. (A) Site-specific generation of glycosyl cation equivalent in the active site of an endoglycosidase. Both glycosyl donor and glycosyl acceptor (ROH) are recognized in the active site, leading to the perfect control of regio- and stereo-selectivities. (B) Structure of 4,6-alkoxy-triazin-2-yl oligosaccharide-glycosyl donor.
Finally, the alkoxy groups can be replaced by other alkoxy groups, which enable the control of the basicity of the nitrogen atom of the glycosyl donors.

When unprotected sugars were treated with 2-chloro-4,6-dimethoxy triazine (CDMT) or 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride (DMT-MM) in the presence of N-methylmorpholine (NMM) or 2,6-lutidine in aqueous media, the corresponding 4,6-dimethoxy triazin-2-yl glycosides (DMT-glycosides) were obtained in good yields (Table 1). In the case of 2-acetamido sugars, the corresponding α-type DMT-glycosides were obtained stereoselectively.

Our next concern was to determine whether these DMT-derivatives could be recognized by a glycosidase. In aqueous solution, the concentration of DMT-substrates remained steady, indicating that these compounds were extremely stable in water. When the corresponding enzyme in Table 1 was added to the solution, the concentration of DMT-glycoside decreased rapidly and reached zero within several hours. These results clearly indicated that DMT-glycosides were recognized by the enzyme to give an enzyme-substrate intermediate.

In the field of food science and woody biomass utilization, it is extremely important to determine kinetic parameters for endoglucanases, hydrolytic enzymes of polysaccharides. The use of naturally occurring polysaccharides as substrates is disadvantageous because the structure of polysaccharides is not homogeneous and their molecular weights change during the course of enzymatic hydrolysis reactions. Nitrophenyl glycosides have frequently been used for kinetic studies of glycosidases, because the liberated nitrophenol species exhibit yellowish colors. Various nitrophenyl glycosides can be chemically prepared starting from the corresponding unprotected sugars. However, these syntheses are problematic when applied to oligosaccharides with higher degrees of polymerizations. The syntheses require multi-step reactions including the protection and deprotection of the hydroxyl groups. In addition, the introduction of a nitrophenyl moiety at the anomeric center usually requires severe reaction conditions, resulting in cleavage of the inner glycosidic bonds of the oligosaccharide moiety.

It is well known that endo-β-1,4-glucanase III from Trichoderma reesei (EGIII) is able to hydrolyze naturally occurring xyloglucan into the oligoxyloglucan (XXXG or XLLG). In order to elucidate substrate recognition of EGIII in more detail, kinetic analysis using oligoxyloglucans carrying a chromophore as their aglycon moiety was performed. Kinetic parameters of EGIII using a one-step preparable DMT-oligoxyloglucan, DMT-β-XLLG, as a novel sugar substrate could be determined. These results indicate that the existence of the 4,6-dimethoxy-1,3,5-triazine moiety is essential for the terminal glycosidic bond at the reducing end to be cleaved in the catalytic site of the enzyme. It is well understood from the viewpoint of stereoelectronic effect theory that the conformation of the pyranose ring, located in the −1 subsite with a C1 conformation, must change to a distorted conformation.

### Table 1. One-step preparation of DMT-glycosides

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**DMT-oligosaccharide as a novel substrate for studying action of endo-β-1,4-glucanase**

In the field of food science and woody biomass utilization, it is extremely important to determine kinetic parameters for endoglucanases, hydrolytic enzymes of polysaccharides. The use of naturally occurring polysaccharides as substrates is disadvantageous because the structure of polysaccharides is not homogeneous and their molecular weights change during the course of enzymatic hydrolysis reactions. Nitrophenyl glycosides have frequently been used for kinetic studies of glycosidases, because the liberated nitrophenol species exhibit yellowish colors. Various nitrophenyl glycosides can be chemically prepared starting from the corresponding unprotected sugars. However, these syntheses are problematic when applied to oligosaccharides with higher degrees of polymerizations. The syntheses require multi-step reactions including the protection and deprotection of the hydroxyl groups. In addition, the introduction of a nitrophenyl moiety at the anomeric center usually requires severe reaction conditions, resulting in cleavage of the inner glycosidic bonds of the oligosaccharide moiety.

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such that the orientation of the cleaving β-glycosidic bond becomes antiperiplanar to one of the lone pairs on the ring oxygen atom of the pyranose (Figure 8 (B)). This conformational change may be caused by a strong interaction between the dimethoxytriazine ring and specific amino acids in the vicinity of the +1 subsite.

The present DMT-method would be a convenient analytical tool for studying the action of glycosyl hydrolases due to the extremely simple synthetic process. Despite the drawback that the hydrolytic product of DMT-glycosides, 2-hydroxy-4,6-dimethoxy-1,3,5-triazine (DMT-OH), is colorless, unlike pNP-glycoside, DMT-glycosides are attractive substrates for kinetic studies of glycosidases from the viewpoints of synthetic organic chemistry and biomolecular engineering since they are easy to prepare, possess tailor-made characteristics and have higher activities.

![Figure 7. Novel substrate for studying action of endo-β-1,4-glucanase.](image)

![Figure 8. Conformational change of DMT-glucoside unit in the −1 subsite of endoglycanase.](image)

(A) Chair conformation (C1) where none of the lone pairs is antiperiplanar to ODMT.

(B) Distorted conformation where one of the lone pairs is antiperiplanar to ODMT. Skew-boat conformation (S3) is shown here.
**DMT-oligosaccharide as a novel donor for enzymatic glycosylation**

Encouraged by the above results, we attempted endoglycanase-catalyzed transglycosylations using DMT-glycosides as glycosyl donors (Figure 9). When DMT-β-lactoside was mixed with a glycosyl acceptor in the presence of EGIII in an acetate buffer (pH 5.5) at 30 °C (donor/acceptor ratio = 2.5/1), the corresponding glycosylated products were obtained in a regio- and stereo-selective manner (21-95%). Since the glycosyl donor can be prepared in water, this is the first demonstration of a one-pot chemo-enzymatic glycosylation process that requires no protection and deprotection.15, 23)

The present method using a DMT-glycoside as a substrate for a hydrolytic enzyme in organic/water mixed solvent has enabled us to prepare various kinds of oligosaccharide derivatives such as artificial xylol glucans,24) the α-linked N-acetylgalactosamine galactose disaccharide unit form gastric mucin,27) N-acetylgalactosamine amino acids,28) β-glucosaminides,26) β xylopyranosides,25) chito-oligosaccharides,33) and lacto-N-biose.34) Furthermore, this basic research provided an entryway to the aqueous one-pot synthesis of glycopolymers having important biological functions.35-37)

![Figure 9. Enzymatic transglycosylation through one-step preparable DMT-glycosyl donors.](image)

**Protecting group-free synthesis of glycosyl compounds using formamidinium agents**

Although the protecting group-free one-pot synthesis of glycosides in aqueous media has successfully been demonstrated through the dialkoxytriazine (DAT) intermediates, there still remained the problem that the DAT-intermediates must be activated by an acid catalyst such as a protonic or Lewis acid (Figure 10 (A)). A new synthetic process for dehydrative glycosylation that consists of two elemental reactions, intramolecular dehydration and subsequent intermolecular addition reaction, has been proposed (Figure 10 (B)). The first step is the enhancement of intramolecular dehydration which is entropically more favorable than intermolecular reactions. The second step is an intermolecular addition reaction with a nucleophile, RYH (Y = O, S, etc.), where dehydration is no longer necessary because it has already been achieved in the first step.

![Figure 10. Concept of dehydrative process in water. The OH and XH in the substrate denote hemiacetal and nucleophilic groups at the 2-position of the pyranose ring, respectively.](image)

- **(A)** Dehydrative process through DAT-intermediate where XH group does not participate. DAT-Cl represents 2-chloro-4,6-dialkoxytriazine.
- **(B)** Dehydrative process through cyclic intermediate formed by intramolecular participation of the XH group.
We postulated that the use of a more powerful dehydrative agent than the dialkoxytriazine derivatives would lead to the formation of a more reactive species, from which a cyclic intermediate like a 1,2-anhydro sugar or sugar oxazoline could be easily formed in situ. On the basis of this hypothesis, we screened cation-type formamidinium salts as an appropriate candidate for the more reactive reagents (Figure 11).

**First detection of unprotected 1,2-anhydro sugars**

The existence of unprotected 1,2-anhydro sugars has been wrapped in mystery for nearly a hundred years. The intramolecular dehydration between the anomeric hydroxy group and the 2-hydroxy group of unprotected saccharides has been achieved in aqueous media using 2-chlorodimethyl imidazolinium chloride (DMC) \(^{38}\) or 2-chlorodimethyl benzimidazolium chloride (CDMBI) \(^{39}\) as dehydrative agents. \(^{40}\) The formation of the 1,2-epoxide ring was confirmed by detecting signals assignable to C1 and C2 at ca. 15 ppm higher magnetic fields compared with those of aldopyranose using low-temperature \(^{13}\)C NMR spectroscopy. The first characterization of unprotected sugar epoxides can be attributed to the mildness of the reaction conditions of the intramolecular dehydration reaction in aqueous media through the use of the formamidinium-type agent. With the direct anomeric activation technique using DMC in hand, subsequent research focused on the selection of appropriate nucleophiles for glycosylation in aqueous media through unprotected 1,2-anhydro sugar intermediates (Figure 12). \(^{41}\)

**Protecting group-free synthesis of S-glycoside derivatives**

Thioglycosides \(^{42}\) and glycosyl thiols \(^{43}\) have been synthesized from the corresponding unprotected sugars without protection of the hydroxy groups by the use of DMC as a dehydrative condensation agent (Figure 12 (A)). According to the present method, not only unprotected monosaccharides but also unprotected oligosaccharides such as cello-oligosaccharides, chito-oligosaccharides, malto-oligosaccharides, and glucosamine oligomers, can be converted to the corresponding thioglycosidic compounds, which would greatly expand the utility of thioglycosides in sugar chemistry. These fundamental technologies have been successfully applied to the preparation of various glycomaterials such as artificial glycoproteins, \(^{44a}\) labeled oligosaccharides, \(^{44b}\) and glycopolymers. \(^{44c}\)
Glycosyl Bunte salt as a new class of intermediate for sugar chemistry

S-Glycosyl thiosulfates have been discovered as a new class of synthetic intermediates in sugar chemistry, named “glycosyl Bunte salts” after 19th-century German chemist, Hans Bunte (Figure 12 (B)).45) The synthesis was achieved by direct condensation of unprotected sugars and sodium thiosulfate using DMC in a water-acetonitrile mixed solvent. Glycosyl Bunte salts were used as an efficient glycosyl donor for S-glycoside synthesis,46) site-selective peptide/protein modification,47) and preparation of glycopolymer-coated microbeads.48)

Protecting group-free synthesis of glycosyl dithiocarbamates

The three-component one-pot synthesis of glycosyl dithiocarbamates starting from unprotected sugars, carbon disulfide, and secondary amines has been demonstrated with DMC as a condensing agent in aqueous media (Figure 12 (C)).49) Based on this reaction, the first protection-free process for 1-deoxy sugars50) and α-C-glycosides 51) through glycosyl radical species has been achieved.

Protecting group-free synthesis of glycosyl azides

The recent developments in “click chemistry”52) have dramatically increased the potential of sugars possessing an azide function as precursors of glycoarrays and glycoconjugates. Various β-glycosyl azides have been synthesized directly in water by the reaction of unprotected sugars and sodium azide mediated by DMC (Figure 12 (D)).53) It is noteworthy that the present method could successfully be applied to a disialo complex-type disaccharide having two N-acetylneuraminic acid moieties at the non-reducing ends, giving rise to the corresponding azide derivative without cleaving the inner glycosidic bonds.

Protecting group-free synthesis of 1,6-anhydro sugars

Various 1,6-anhydro sugars have been synthesized directly from the corresponding unprotected glycopyranoses in excellent yields using DMC as a dehydrative condensing agent (Figure 12 (E)).54) The conventional method that uses pyrolysis of polysaccharides can only be applied to the synthesis of 1,6-anhydro monosaccharides, because it is difficult to control the pyrolytic conditions to obtain a 1,6-anhydro oligosaccharide product selectively. The present method employing DMC in aqueous media would be a practical tool for synthesis of 1,6-anhydro oligosaccharides.

First one-step synthesis of sugar oxazolines with formamidinium reagents

In 1996, it was found that sugar oxazolines can behave as substrates for N-acetylgalactosaminidases.55) Since this discovery, there have been many reports on enzymatic transglycosylations using sugar oxazolines as glycosyl donors.56) Since sugar oxazolines can be regarded as intramolecularly dehydrated compounds, we sought to find an appropriate dehydrating agent that can be used in aqueous solutions.57) In 2009, we discovered a direct method for the synthesis of sugar oxazoline derivatives from the corresponding N-acetyl-2-amino sugars in aqueous media using DMC (Figure 13),58) and further improved the structure of the dehydrative agent by introducing a benzene ring to give CDMBI (2-chloro-1,3-dimethyl-1H-benzimidazole-3-ium chloride).59)

Protecting group-free synthesis of chito-oligosaccharide derivatives

The synthesis of chitoheptaose has been achieved using chito-oligosaccharide oxazolines as glycosyl donors and chito-oligosaccharides as glycosyl acceptors catalyzed by a mutant chitinase.59) The combined use of one-step preparable oxazoline derivatives and an enzyme with a low hydrolytic activity enables the specific synthesis of chitoheptaose. Chitoheptaose is known to behave as an elicitor for the plant immune system.60)
Chemo-enzymatic synthesis of glycoproteins with a homogeneous glycan

An efficient method for synthesizing homogenous glycoproteins is essential for producing some therapeutic glycoproteins or elucidating the role of glycans of glycoproteins. The discovery of the direct synthesis of sugar oxazolines has accelerated the progress of synthetic research on glycoproteins with a homogeneous glycan. Various N-glycans were transferred from the corresponding oxazolines to the GlcNAc residue on glycoproteins using a mutant endoglycosidase.61) The one-step preparation of sugar oxazolines also enabled the preparation of an antibody drug conjugate (ADC) in the field of pharmaceutical sciences.62)

![Chemistry of sugar oxazolines](image)

Figure 13. Chemistry of sugar oxazolines.

Conclusion

One of the most important purposes of glycotechnology has been to support investigators in glycoscience through supplying basic tools. In this article, the protection-free glycosylating process based on the new concept of “Direct Anomeric Activation in Water” has been described.63) In the first part, chemistry of 4,6-dialkoxy-1,3,5-triazin-2-yl glycosides (DAT-glycosides) was summarized. Various unprotected oligosaccharides were converted to the corresponding DAT derivatives in water without using any protecting groups. The resulting DAT derivatives were further converted to the corresponding O-glycosides both chemically and enzymatically. One of the most significant characteristics of the resulting DAT-glycosides was that various functional groups could be introduced at the 4 and 6 positions of the triazine ring using nucleophilic aromatic substitutions. It was possible to control the reactivity of these DAT-glycosides as glycosyl donors by changing the type of alkyl groups at the 4 and 6 positions.

In the second part, the DMT-mediated chemistry of 1,2-anhydro sugars and sugar oxazolines was described. Various glycosidic compounds like S-glycosides, glycosyl azides, 1,6-anhydro sugars, and glycoproteins were successfully prepared without protection/deprotection through 1,2-anhydro sugars and sugar oxazolines.

Acknowledgement

I would like to thank all the present and past collaborators for their contributions to the development of new glycosylation reactions described herein. Our work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Sports, Science and Technology, Industrial Technology Research Grant Program in 2006 from NEDO of Japan, and the International Center of Research & Education for Molecular Complex Chemistry in 2007 from Tohoku University Global COE Program.
References and Notes


18) A capital G represents an unsubstituted glucopyranose bond, and a capital L represents a glucopyranose residue.

19) A capital G represents an unsubstituted glucopyranose residue, a capital X represents a glucopyranose residue substituted with a xylopyranose through an α-1,6-glycosidic bond, and a capital L represents a glucopyranose residue substituted with a galactopyranosyl β(1-2)xylopyranosyl through an α-1,6-glycosidic bond.


Author Information

Shin-ichiro Shoda graduated from The University of Tokyo, Department of Chemistry in 1976, and received his Ph.D. degree from the University of Tokyo in 1981 under the supervision of Professor Teruaki Mukaiyama in the field of synthetic organic chemistry, where he developed the glycosyl fluoride method as a novel glycosylating technology. After spending three years working as an Assistant Professor at the University of Tokyo, he conducted his postdoctoral fellowship at ETH-Zuerich (from 1984 till 1986) with Professor Dieter Seebach. In 1986, he moved to Tohoku University and joined the lab of Professor Shiro Kobayashi in the field of polymer synthesis, where he developed new chemo-enzymatic glycosylations using glycosyl fluorides and sugar oxazolines as glycosyl donors. In 1999, he was promoted to Full Professor at Tohoku University (Functional Macromolecular Chemistry Laboratory).

His research interests include synthesis of carbohydrates, development of novel glycosylations, macromolecular architecture and precision synthesis of well-designed functional oligo- and polysaccharides. He has been a Member of the Research Center for Science System at the Japan Society for the Promotion of Science (2003 - 2005). He received the Award of the Chemical Society of Japan for Young Chemists (1986), Science and Technology Institute Award for New Invention (1993), the Cellulose Society of Japan Award (2002), and Synthetic Organic Chemistry Award, Japan (2013), as well as the Ichimura Prize in Science for Distinguished Achievement (2019).

Related Products
2,4-Bis(benzylxyloxy)-6-chloro-1,3,5-triazine (= CDBT)
Triethylsilane
4-(4,8-Dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium Chloride (= DMT-MM)

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