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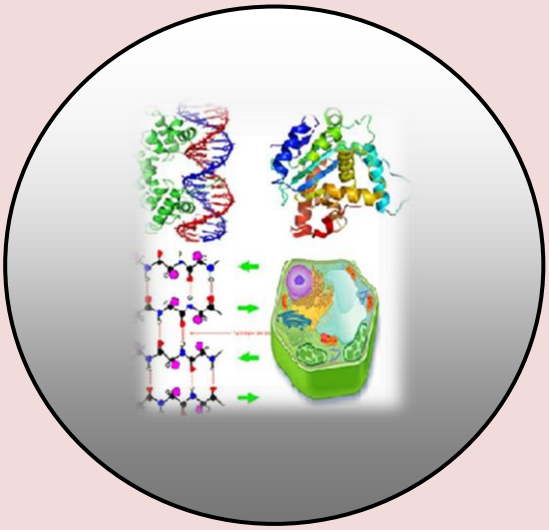
ISSN 2319-3077 Online/Electronic
ISSN 0970-4973 Print

Index Copernicus International Value
IC Value of Journal 82.43 Poland, Europe (2016)
Journal Impact Factor: 4.275
Global Impact factor of Journal: 0.876
Scientific Journals Impact Factor: 3.285
InfoBase Impact Factor: 3.66



J. Biol. Chem. Research
Volume 40 (2), 2023 Pages No. 1-20

Journal of Biological and Chemical Research

An International Peer Reviewed / Referred Journal of Life Sciences and Chemistry

Indexed, Abstracted and Cited in various International and National Scientific Databases

Published by Society for Advancement of Sciences®

J. Biol. Chem. Research. Vol. 40, No. 2, 1-20, 2023
(An International Peer Reviewed / Refereed Journal of Life Sciences and Chemistry)
Ms 40/02/19/2023

ISSN 2319-3077 (Online/Electronic)
ISSN 0970-4973 (Print)

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RESEARCH PAPER

Received: 01/07/2023 Revised: 08/09/2023 Accepted: 09/09/2023

Protecting and Deprotecting Strategies in Glycoside and Oligosaccharide Synthesis - A Review

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ABSTRACT

Oligosaccharides are medically efficacious organic molecules with structural specificities. The synthesis of these molecules is a real challenge for a carbohydrate chemist, which is due to the presence of primary and secondary hydroxyl groups with varied orientation i.e. axial and equatorial. Their vicinity and proximity also play a definite role in their synthesis. Since they are made up of monosaccharide building blocks, it is necessary to synthesize acceptors and donors by protecting and deprotecting the hydroxyl groups involving regio and stereo selective reagents. While selecting the protecting reagents we must consider that these reagents should be easily incorporated and removed with good percentage of yield. In the present review the authors have described the protection and deprotection strategies incorporating several regioselective and stereo specific reagents and different anomeric protection strategies along with glycosidation techniques have been discussed.

Keywords: Oligosaccharide synthesis, Protecting groups, Deprotecting groups, Regioselectivity and Stereospecificity.

INTRODUCTION

Oligosaccharides of natural origin are important class of bioactive compounds and are used for biological, synthetic, medicinal and technological purposes. A number of higher plants, fungi, algae, lichen, milk and bacteria serve as rich sources of biologically active oligosaccharides. The cell-surface carbohydrates serve as attachment sites for infectious bacteria, viruses and toxins resulting in pathogenesis. So the synthesis of structurally defined glycoconjugates provides the opportunity to probe and intervene in critical biological process. The synthesis of the partial structure of these oligosaccharides provide a demanding challenge as these structure act as tumor-associated and cancer-associated antigens, which occur as free oligosaccharides in human milk.

The tumor-associated carbohydrate structure can only be obtained in small amounts from tumor cells, although they are generally absent or present in undetectable levels in normal cells (Xu et al. 2005; Kannagi, 2003). Therefore currently human milk oligosaccharides are used for studying the biosynthesis of antigen-I, and antigen-i and Lewis blood group related oligosaccharide (Yurievet al. 2005, Ugorskiet al. 2004). Significantly oligosaccharides isolated from buffalo milk have been found immunostimulant (Saxena et al. 1999) and this isolated oligosaccharide was synthesized by Chinese workers (Gu et al. 2002). The oligosaccharides isolated from donkey's milk (Ranjan et al. 2016) have also shown high degree of immunostimulant activity and proposed to be very helpful in cure of AIDS patient. Since isolation of these oligosaccharides from their various natural sources provides a very meager quantity of the oligosaccharide. It is therefore of paramount importance to synthesize them in larger quantity using various stereo- and regio-selective synthetic strategies.

The synthesis of oligosaccharides required the preparation of two polyfunctional partners. One partner acts as acceptor and other acts as donor. A major problem in the synthesis of carbohydrate is the presence of several reactive hydroxyl groups in each sugar residue. So to achieve unambiguous synthesis, it is necessary to protect those hydroxyl groups of the monosaccharide that are not to be involved in the reaction. These protecting groups are also important as they influence the reactivity requirements, so various regio and stereoselective protecting groups and strategies have to be taken into consideration. A great deal of care should be taken while selecting the protecting groups for these hydroxyl groups.Some important factors that must be taken into consideration are:-

Protection /Deprotection Strategies

a) The protecting group must be introduced easily in high yield.
b) It should be stable under a variety of reaction conditions.
c) It should be easily cleavable in high yield at the appropriate time.
d) It should be readily separated after deprotection from the deprotected molecule.

Over the years a host of protecting groups for masking the hydroxy groups has been introduced by taking advantage of the re-activities of the respective protecting groups. Even more importantly, a variety of anomeric groups that allow for high yielding, selective and reliable formation of many glycosidic linkages have been developed.

A large number of protecting groups and strategies are currently available. Some of the more common protecting groups are shown in Table 1.

SYNTHESIS OF DEOXY SUGARS

The replacement of sugar hydroxyls by hydrogen, the preparation of deoxy sugar is important in carbohydrate chemistry (Table 2) where deoxy sugars are frequently encountered as constituents of bacterial O-polysaccharide (Bock et al. 1983, Bock et al. 1984) and milk oligosaccharides (Dua et al. 1985). The major difficulty in deoxygenation of secondary hydroxyl groups arises because SN2 processes are generally hindered at these carbons both sterically and through dipolar affect.

Table 1.

S.No.	O-protecting group	Usual method of attachment to Su-OH	Removal/ Remarks	Ref.
1.	a) –Ac	a) Ac2O or AcCl/Pyr b) N-acylthiazolidine-2 -thiones/pyr/NaH/ c) DMAP d) NaOAc/Ac2O	a) Good reactivity for neighboring –OH b) Method (b) of attachment is extremely selectively for O-6. c) Can be removed by NaOMe/MeOH or MeOH/HCl d) Converts to halide under proper conditions. e) Undergoes selective deprotection at anomeric position with Bu_2SuOMe or NH_2NHAc or bis (tributyltin) oxide/KOH/or KCN.	Wolform et al. 1963
2.	-Bz	BzCl/Pyr	a) Decreases reactivity for neighboring –OH b) Usual removal by NaOMe/MeOH	Guo et al. 2010
3.	-Bn	BnBr/NaOH or NaH	a) Increase reactivity for neighboring-OH b) “Persistent” blocking group. c) Can be hydrogenolysed by H_2/Pd.	Gigg et al. 1983
4.	-All	All-Br/NaH	a) Wide variation in ease of removal allows flexible strategies. b) Removalby$(Ph_3P)_3RhCl$, DBO,HgO,$HgCl_2$.	Gigg et al. 1983
5.	-Tr	Tr-Cl/pyr	a) Highly selective for O-6. b) “Transient” blocking group. c) Usual removal by mild acid.	Kovak et al. 1983
6.	-Si(R)2Bu^t R=Me/Ph	$Bu^t(R)_2Si$-Cl	a) Good O-6 selectivity. b) Can be removed by H_2O-Pyr or Bu_4NF.	Nashed et al. 1987
7.	-Piv	Piv-Cl/BF_3-OEt_2	a) Stable protecting group and stable under mild acidic conditions. b) Removal by NaOMe/MeOH.	Codee et al. 2011

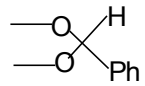
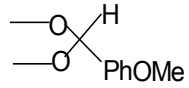
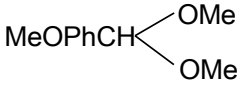
8.	-SEM	SEM-Cl/N,N-diisopropylamine	a) Compatible to various protection/deprotection condition. b) Undergoes removal by mild acid.	Chandra et al. 2010
9.	-MMT	MMT-Cl/Pyr	a) Extremely selective for O-6. b) Can be removed by mild acid.	Srivastava et al. 1988
10.	-DEIPS	DEIPS-Cl/imidazol	a) Highly selective in removal under mild acidic conditions. b) Usual removal by mildacid.	Toshima et al. 1989
11.		2,2DMP/An/PTSA/ (cis-vic-diol)	a) Cyclic ketal b) Usual removal under mild acid.	Barili et al. 1986
12.		a) PhCHO/PTSA b) α,α-dimethoxy toluene/ tetrefluoro boric acid/ (cis-vic-diol)	a) Cyclic acetal. b) Usual removal by mild acid. c) Opens regioselectively with $NaCNBH_3/AlCl_3$ giving free 4-OH and free 6-OH with $LiAlH_4/AlCl_3$.	Clode et al. 1979
13.		 PTSA/cis-vic-diol	a) Cyclic acetal. b) Opens regioselectivity with $NaCNBH_3/CF_3COOH$ giving free 4-OH and free 6-OH with $NaCNBH_3$/TMS-Cl.	Lee et al. 1986
14.	-MPM	a) MPM-trichloroacetimidate/TfOH/Su-OH. b) Bu2SuO/TBAB/R-X/cis-Vic-diol. R=MPM,All,Bn,Me, X=ClBr.	Usual removal by $[Ce(NH_4)_2(NO_3)_6]$ or DDQ when R=MPM.	Johansson et al. 1984
15.	-TBDPS	TBDPSCl/Imidazole/ N,N-DMF	a) Highly selective for O-6. b) Can be removed by mild acid	Khan et al. 1994

Table 2.

S.No.	O-Protecting Group	Usual method of attachment to Su-OH	Removal/ Remarks	Ref.
1.	O-Ts	TsCl/Pyr	a) Selective for primary- OH. b) Reduced to 6-deoxy sugar by $LIAlH_4$, in ether	Liptak A. 1982

2.	O-CS-SMe	Mel/CS/NaH/ Imidazole/THF	Reduced to deoxy sugar with tributyl tin hydride in presence of AIBN catalyst	Barton et al. 1975
3.	Tosyl hydra-zone	p-toluene sulphonyl hydrazine(ketosugar)	Reduced by $NaCNBH_3$/N,N-DMF	Hutchins et al. 1973
4.	Triflate	Triflicanhydride/ DMP/CH_2Cl_2	$NaBH_4$ /CH_3CN	Barrette et al. 1984

SOME COMMONLY USED O-PROTECTING GROUPS

ANOMERIC PROTECTING GROUPS IN CARBOHYDRATE CHEMISTRY

The choice of the anomeric protection in the synthetic carbohydrates is important for several reasons (Jansson et al. 1990).

a) It should be compatible with a series of different reaction conditions that are to be utilized in the synthesis.
b) It should be removable without affecting the remaining glycosidic bonds of the oligosaccharides.

SOME COMMON ANOMERIC PROTECTING GROUPS IN CARBOHYDRATE CHEMISTRY

S. No.	**Anomeric Protecting group**	**Usual methods of attachment**	**Remarks**	**Ref.**
1.	-Me	a) MeOH/H+/Su-OH b) MeOH/H+/Su-X X=Cl,Br	Converts to acetate With Ac_2O/AcOH/H_2SO_4	Codee et al. 2011
2.	-Vinyl	Bis (formylmethyl) mercury/SuX. X=Cl,Br.		Pétursson et al. 1997
3.	-Bn	a) Bn-OH/H+Su-OH b) Bn-OH/H+Su-X X=Cl,Br	a) Converts to halide by BF3OEt2/NaBr/NaI. b) Converts to acetate with NBS/HMPA. c) Undergoes deprotection with H2/Pd.	Hashimoto et al. 1987
4.	-All	a) All-OH/H+Su-OH b) All-OH/H+Su-X X=Br,Cl	a) Converts to halide with b) TBAB/TBAI/BF_3-OEt_2 or c) NaBr/NaI/BF_3-OEt_2 d) Converts to halide with Ac_2O/AcOH/H_2SO_4. e) Removal by $[(Ph_3P)_3RhCl]$, DBO,HgO,$HgCl_2$.	Brennan et al. 1989

5.	-TMSET	TMS-EtOH/HgO/ $HgBr_2$/$CaSO_4$/Su-OH.	a) Converts to halide with DCMMe/$ZnBr_2$. b) Converts to acetate with BF_3-OEt_2/Ac_2O. c) Undergoes deprotection with CF_3COOH.	Kartha et al. 1990
6**.**	-SR R=Ph, Et, Me, Ac	a) Gives SMe with methyltrimethyl silane BF_3-OEt_2/Su-OAc or CH_3SH/TMS-OTf or CH_3SH/BF_3-OEt_2/Su-OAc. b) Gives SET with EtSH/$FeCl_3$/Su-OAc orEtSH/BF_3-OEt_2/Su-OAc. c) Gives SPh with phenylthio trimethylsilane /TMS-OTf/SuOAc. d) Gives SuOAc with $AlCl_3$/thioaceticacid/ SuoAc.	a) Some converts to estersand hemiacetals under proper conditions. b) Converts to oligosaccharides and other natural products or to1-haloderivatives in a one-step reaction.	Sakonsinsiri et al. 2018
7**.**	TMS	Hexamethyldisilazane/ chloromethylsilane/ Pyr/Su-orTMS-OTf/Su-OH.	Reacts with acetals to yield1,1-diacetal structures.	Nashed et al. 1989

MILK OLIGOSACCHARIDE SYNTHESIS (Saksena et al. 1990, Baytas et al., 2004, Guofeng et al. 2004, Rencrosi et al. 2004)

The growing significance of glycosides and oligosaccharides as constituents biologically important compounds such as glycoprotiens, glycolipid, and antibiotics has sparked considerable interest in expeditious methods for the stereo controlled construction of the glycosidic linkages. So chemical synthesis of carbohydrates include protecting group manipulation to differentiate several hydroxyl groups of similar reactivity, complicated stereo-selective glycosylations and long overall routes. With the advent of various stereo and regio-selective reagents, convergence orthogonal strategies and diverse protection/deprotection routes, any desired oligosaccharide moiety can be synthesize from easily available monosaccharide. However, the glycosidation is still a major problem in organic synthesis as no universal method has been devised for the construction of glycosidic linkage and each individual oligosaccharide possesses a new challenge for the organic chemist.

The chemical synthesis of oligosaccharide is quite complicated than the synthesis of other biopolymer such as peptides and nucleic acids. In addition the glycosidic linkages have to be introduced stereo specifically. To date there are no general applicable methods or strategies for oligosaccharide synthesis and consequently the preparation of oligosaccharide is very time consuming. Nevertheless, contemporary carbohydrate chemistry makes it now possible to execute complex multistep synthetic sequences that give oligosaccharide consisting of as many as twenty monosaccharide units. The preparation of oligosaccharide of this size is only possible when a synthetic strategy is highly convergent. In such a glycosylation strategy, most of the synthetic effort is directed towards the preparation of monomeric glycosyl donors and acceptors. The assembly of these units to an oligomer should involve a minimum number of synthetic steps and each reaction step should proceed with high stereo selectivity and high yield. Furthermore, an efficient synthetic strategy should make optimal use of common intermediates and oligosaccharide building blocks. Further for the synthesis of the complex oligosaccharide core unit will be elongated by addition of different sugar units at required position by different glycosidation methods i.e. Koenigs-Knorr, Helferich, Imidate, thioglycosidation, Pyridyl-1-thio glycoside etc.

Konings Knorr and Helferich Method of Glycosidation Utilizing Glycosyl Halides as Donor

Konings Knorr and Helferich method of glycosidation require glycosyl halides as active donors. The halide is removed from the glycosyl donor by the free hydroxyl group on the acceptor in the presence of heavy metal salt catalysts viz silver and mercury salts during formation of the glycoside bond. The reactivity of the glycosyl donor can be controlled to some extent through the choice of halide, protecting groups and the promotors used and the order of reactivity among common catalysts is AgOTf / Ag_2CO_3> $AgClO_4$/ Ag_2CO_3> $HgBr_2$>$Hg(CN)_2$. The neighboring groups also participate during bond formation and play a vital role in determining the stereoselectivity.

BF_3-OEt and TMS-OTf Method of Glycosidation

Trichloroacetimidates have become the most commonly used glycosyl donors among the wide array of glycosylating agents due to their versatility, high yields and excellent selectivity in glycosidation reactions. The glycosyl trichloroacetimidates are prepared from hemiacetal sugar on reaction with trichloroacetonitrile in the presence of bases such as NaH, K_2CO_3 or DBU giving a stereo-selective kinetic or thermodynamic product (α or β) depending upon the catalyst taken. For the reaction of these O-glycosyl trichloroacetimidates with various alcohol components an acid is required as a catalyst. For this purpose Lewis acids such as BF_3-OEt_2 or TMS–OTf are used as catalyst. Presence of participating groups on the neighboring (i.e. C-2-OH) triggers the formation of 1, 2-trans products, while the presence of non-participating groups at this position leads to formation of product having an opposite anomeric configuration to that of the starting trichloroacetimidates. These donors can also be activated under very mild conditions by catalytic amounts of some other triflates likes dibutyl boron triflate (DBBOTf). This agent was introduced to prevent acceptor silylation sometimes encountered with silyl triflates. The synthesis of the partial structure of these oligosaccharides provides a demanding challenge as these structures act as tumor-associated and cancer-associated antigens, which occur as free oligosaccharides in human milk (Kitgawa et al. 1993).

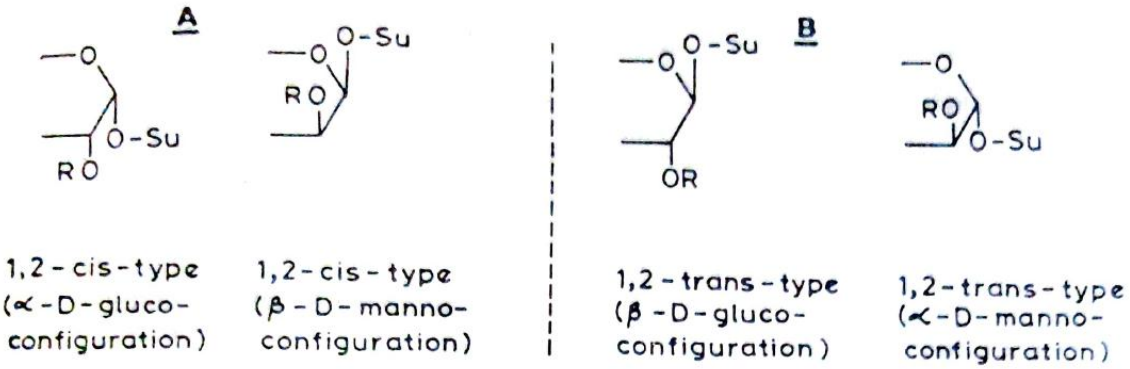
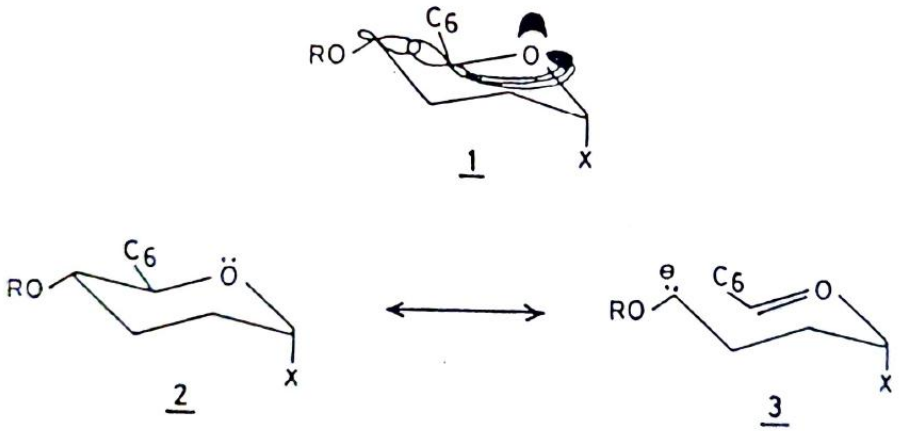


FIG. 1



1 : Orbital interaction indicating electron withdrawl from the ring Oxygen atom by delocalization.

2 & 3 : Resonance structures indicating electron withdrawl from the ring.

FIG. 2

However, the glycosidation is still a major problem in organic synthesis as no universal method has been devised for the construction of glycosidic linkage and each individual oligosaccharide possesses a new challenge for the organic chemist. The chemical synthesis of oligosaccharides is quite complicated than the synthesis of other biopolymers such as peptides and nucleic acids. The difficulties in the preparation of complex oligosaccharides are a result of greater number of possibilities for the combination of monomeric units to form oligosaccharides. In addition the glycosidic linkages have to be introduced stereo specifically.

To date there are no general applicable methods or strategies for oligosaccharide synthesis and consequently the preparation of oligosaccharide is very time consuming Nevertheless, contemporary carbohydrate chemistry makes it new possible to execute complex multistep synthetic sequences that give oligosaccharide consisting of as many as twenty monosaccharide units. The preparation of oligosaccharides of this size is only possible when a synthetic strategy is highly convergent. In such a glycosylation strategy, most of the synthetic effort is directed towards the preparation of monomeric glycosyl donors and acceptors. The assembly of these units to an oligomer should involve a minimum number of synthetic steps and each reaction step should proceed with high stereoselectivity and high yield. Furthermore, an efficient synthetic strategy should make optimal use of common intermediates and oligosaccharide building blocks (Unverzagt et al. 1994).

Glycosyl donors act as an electrophile upon activation with suitable configuration activating reagents, the anomeric protecting group or the hemiacetal has to be converted into a better leaving group. The electrophile so generated is then condensed with the nucleophile (Su-OH) resulting in the synthesis of glycosides. In addition, the saccharide coupling step should occur stereoselectively with respect to the formation of an α- or β- linkage.

In case of 1,2-cis-glycosides (A) it is an α glycoside in D-gluco-configuration and β-glycoside in D-manno-configuration. On the other hand, in case of 1,2-transglycoside (B), it is a β-glycoside in D-gluco-configuration and an α-glycoside in the D-manno-configuration (Fig. 1).
The reactivity of a leaving group attached to an anomeric carbon atom for example, a halogen atom in glycosyl halide is a function of several factors, including the type of protecting groups present in the molecule. Acetoxy, benzoyloxy and other electron withdrawing groups tend to decrease the reactivity, of the leaving group while reactivity is increased by O-alkyl ethers and similar electron donating groups. Neighboring group participation by substituents attached to C-2 represents the most important influence exerted by a protecting group, however, contribution of substituents at relatively remote positions in a ring system is attributable, atleast in part, to through bond interactions (Goodman et al. 1967). For example, electron withdrawing C-4 substituents inhibit ionization at C-1 in a glycosyl halide by removal of electron density from ring oxygen atom through delocalization (Fig 2).

This delocalization reduces the ability of the oxygen atom to assist in stabilizing a developing positive charge at C-1, that is, the relative importance of the resonance contributor 3 is increased by an electron withdrawing R group. Increased importance of 3 makes the departure of a leaving group from C-1 more difficult to produce a positive charge on this carbon atom.
New glycosylation strategies for the facile preparation of saccharide building blocks are now known and are as follows:

LINEAR GLYCOSYLATION STRATEGIES

Inter-glycosidic bond formation is generally achieved by condensing a completely protected glycosyl donor, which bears a leaving group at its anomeric centre, with a suitably protected glycosyl acceptor that contains often only one free hydroxyl group (Toshima et al. 1993).

Traditionally, the most widely used methods utilize 1-bromo or 1-chloro derivatives of carbohydrates as glycosyl donors and by careful selection of the reaction conditions and type of protection, both α- and β-glycosidic linkages can be prepared with high stereoselectivity. Formation of glycosidic linkage involves displacement of a halide from the glycosyl donor by a free hydroxyl group of the acceptor in the presence of heavy metal salts in Koenigs-Knorr (Koenigset al. 1901) reaction (silver salt) and Helferich procedure(Helferich et al. 1956)(mercury salt). The presence or absence of neighboring group participation by the substituent at 2-OH has a major influence on the diastereoselectivity in the coupling reaction with the acceptor. The order of reactivity among common catalysts is $AgOTf/Ag_2CO_3$>$AgClO_4$/ Ag_2CO_3>$HgBr_2$>$Hg(CN)_2/HgBr_2$> $Hg(CN)_2$. The ester groups at C-2-OH such as acetyl, benzoyl, amido, imido, etc. participate in determining the stereo-selectivity byinteracting with the initially formed cation to produce an acetoxonium ion. If the sugar alcohol approaches the acetoxonium ion from the side of the molecule opposite to that containing the participating group, a 1,2-trans glycoside is formed. On the other hand, if the approach of sugar alcohol is from the side containing the participating group, an orthoesteris formed. However, 1-halo glycosides often Suffer from instability and require relatively drastic conditions for their preparation.

CONVERGENT BLOCK SYNTHESIS

The introduction of the ortho-ester (Kochetkov et al. 1971) and imidate (Sinay et al. 1978) procedures were the first attempts to find alternatives to the glycosyl halide methodologies. Since then, many other leaving groups for the anomeric centre have been reported. However, from amongst these glycosyl donors, the fluorides. Trichloroacetimidates and thioglycosides have been applied most widely in glycosidic bond synthesis. Schmidt et al. (Toepfer et al. 1992) reported that O-glycosyl trichloroacetimidates have been prepared from hemiacetal sugar on reactions with trichloroacetonitrile in presence of bases such as NaH. K_2CO_3 or DBU giving a stereoselective kinetic or a thermodynamic product (α or β) depending upon the catalyst used (Schmidtet al. 1984). The reaction of O-glycosyl trichloroacetimidates with various alcohol components leading to oligosaccharides is catalyzed by Lewis acid catalysts such as BF_3-OEt_2 or TMS-OTf (Grundler et al. 1826) The participating group at C-2, gives 1,2-trans products while in the case of donors bearing a non-participating group at C-2, products of opposite anomeric configuration to that of the starting trichloroacetimidates are formed. Furthermore, stronger catalysts TMS-OTf has been found to lead to the formation ofthermodynamically more stable 1,2-cis product.

Kochetkov et al. reported a method of O-glycosylation using 1,2-o-alkyl-orthoesters of sugars as glycosylating agents which lead stereospecifically to 1.2-transglycosides (Kochetkov et al. 1977). Thus the condensation of 3,4,6-tri-o-acetyl-1,2-o-ethyl-orthoacetyl-α-D-glucopyranose with 1,2 3,4-Di-O-isopropylidene-α-D-galactopyranose in presence of $HgBr_2$ using nitromethane as a solvent gave 1,2,3,4-Di-O-isopropylidene-6-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-α-D-galactopyranose exclusively. Glycosyl fluorides (Araki et al. 1989) have recently shown considerable utility as synthetic intermediates in O-, N- and C-glycosylations. In addition to their synthetic utility these compounds have been studied as substrate analogs for enzymes that have an effect at the anomeric centre of carbohydrates. Kunz et al. achieved stereoselective glycosylation of alcohols and silyl ether using O-alkyl, O-aryl and acetal-protected glycosyl fluorides of the pyranose and furanose series using catalytic amount of BF_3-OEt_2 in dichloromethane.

Thioglycosides are stable and versatile derivatives that allow flexible strategies for synthesis of complex carbohydrates (Haelgren et al. 1992). Recent investigations have shown that thioglycoside can be conveniently and reproducibly activated in two ways:
1. Two step activation which involves first forming a glycosyl halide and then further activated this with a halophilic reagent (Fugedi et al. 1987).
2. One step activation with a thiophilic reagent such as methyltriflate or dimethyl (methylthio) sulphonium triflate (DMTST) (Backmann et al. 1982).

1. Van Boom et al. reported a stereospecific synthesis of 2-deoxy α- or β-glycosides by NIS/TfOH promoted glycosidation of ethyl (phenyl) thioglycosides having a trans-oriented phenoxy thiocarbonyl group at C-
2. Shun-ichi et al. 1990 synthesized disaccharides containing 1.2-cis glycosidic linkages by an efficient stereo-controlled two-step process involving a silicon tethering step to a dimethylsilyl acetal followed by intramolecular glycosidation with N-iodo succinimide in nitromethane. Comparative studies by Hanessian et alon the proton activation by pyridin-2-yl-thioglycopyranosides demonstrated the dramatic effect of the hetero atom (remote activation) as a base anchor for the proton and as a better leaving group, resulting from the negative inductive effect. The above anomeric leaving groups can be introduced under mild reaction conditions and are sufficiently stable to be purified and stored for a considerable period of time. Furthermore, they can undergo glycosylations under mild conditions and by selecting the appropriate reaction conditions, high yields and good α/β ratios can often be obtained. These favorable features allow the use of these glycosyl donors in elegant block synthesis. The favorable properties of the trichloroacetimidate methodology were exploited in the block synthesis of the prominent tumor- associated antigen Lewis X (Le^x). Using similar approach, a spacer containing dimeric Lewis X antigen has also been reported (Danishefskiet al. 1995). Recently (Nakagawa et al. 1994) the synthesis of an unnatural cyclodextrin containing five glucopyranoside units was reported. Ole et. al. has reported per-o-trimethylsilyl-α-L-fucopyranosyl iodide as a novel glycosylating agent for terminal α-L-fucosylation. This promoter reacts with alcohols to give α-L-fucopyranosides.

SELECTIVE AND TWO-STAGE ACTIVATION AND ORTHOGONAL GLYCOSYLATION STRATEGIES

Notwithstanding the attractive features of the abovementioned block synthesis, the conversion of a common building block into a glycosyl donor requires several manipulations at the anomeric center presenting a drawback (e.g. removal of anomeric protecting group followed by introduction of a leaving group) which is especially undesirable when performed on larger fragments. The possibility of epimerisation at C-2 of a 1-hydroxyl intermediate should not be excluded. Ideally, the anomeric substituent of an oligosaccharide building block should be sufficiently stable to withstand protecting group manipulations i.e. acts as a protecting group), but also have an adequate reactivity to permit its use as a glycosyl donor (i.e. acts as a leaving group). Furthermore, if these substituents are stable to conditions required to activate other types of leaving groups then they may also be used as glycosyl acceptors. Thioglycosides (Lonn, 1985) and n-pentenyl glycosides (Fraser-Reidet al. 1992) possess these features. They are stable under many different chemical conditions but can readily be activated and used as donors in glycosidic bond synthesis.

Mario Pinto et al. reported the armed and disarmed phenyl selenoglycosides. These are versatile donors and acceptors that provide the desired selectivity in glycosidation reactions. Thus their selective activation over thioglycosides together with their inertness under conditions in which glycosyl halides and trichloroacetimidates may be activated offer a significant and powerful addition to the repertoire of the synthetic oligosaccharide chemist. Pinto et al. showed that selenoglycosyl donors can be coupled with ethylthioglycosyl acceptors. It was observed that a selenoglycoside can be activated with silver triflate in the presence of an inorganic base (K_2CO_3).

Recently (Shedrecht et al. 1994), another two stage activation strategy was reported which employed anomeric sulfoxides as donor and thioglycosides as acceptor molecules. This approach is based on the fact that anomeric sulfoxides can be activated by Lewis acids and that thioglycosides are stable under these conditions. An orthogonal glycosylation strategy in which manipulations at the oligosaccharide steps are further reduced was proposed by Ogawa et al. (1994). In this approach, two anomeric groups (X& Y) are used which both act as anomeric protecting group as well as leaving group. Recently orthogonal (Ogawa et al. 1996) strategy was applied for synthesis of extended blood type B determinant I of a novel glycolipid.

CHEMOSELECTIVE GLYCOSYLATION REACTIONS

The orthogonal glycosylation strategy relies on the orthogonal properties of two different anomeric groups (Mootoo et al. 1985). Fraser-Reid et al. have introduced a chemoselective glycosylation strategy (armed-disarmed glycosylation strategy) in which a C-2 ether protected pentenyl glycoside can be coupled chemoselectively to a benzoylated pentenyl glycoside. Thus, in this strategy only one type of anomeric group is required. The chemoselective glycosylation relies on the fact that C-2 esters deactivate (disarm) and C-2 ethers activate (arm) the anomeric centre e.g., coupling of armed donor with disarmed acceptor in the presence of the mild activator iodonium di-collidine perchlorate (IDCP), gave the dimer as an anomeric mixture in a good yield. The disarmed dimer could be further glycosylated with an acceptor using the more powerful activating system N-iodosuccinimide /catalytic triflic acid (NIS/TfOH) to yield the trisaccharide (Madsen et al. 1995).

LATENT-ACTIVE GLYCOSYLATION STRATEGIES

Recently (Roy et al. 1992), latent-active concept for the convergent synthesis of oligosaccharide was proposed. In this strategy a stable anomeric group can be converted into a good leaving group by a simple chemical inter-conversion. It was anticipated that p-nitrophenyl thioglycosides are inert towards thiophilic reagents but the electron-withdrawing nitro- substituent should be easily convertible into an electron donating N-acetyl group (latent active) and it should be possible to condense the 'active' thioglycoside with a 'latent p-nitrophenyl thioglycoside. Next, the nitrophenyl substituent of the obtained condensed product can be activated by a repetition of this procedure. A novel approach based on a similar type of glycosylation reaction has been developed (Boons et al. 1996). This strategy relies on the isomerization of substituted allyl glycosides to give the corresponding vinyl glycosides, which can subsequently be used in Lewis acid mediated glycosidations. This isomerization reaction was performed by a rhodium catalyst obtained by treating tris (triphenylphosphine) rhodium (I) chloride with n-butyllithium.

This catalyst has many advantageous properties over the use of conventional Wilkinson's catalyst. The glycosylation reactions have high yields for both primary and secondary sugar alcohols, and the anomeric selectivity could be controlled by the constitution of the glycosyl donor and reaction conditions. The new isomerization and glycosidation approach enables complex oligosaccharides of biological importance to be prepared in a highly convergent manner.

ONE-POT MULTI-STEP GLYCOSYLATION

Recently, several methods have been reported to perform sequential glycosylations as a one-pot procedure Kahne et al. (1989) described a glycosylation method that is based on activation of anomeric sulfoxides with triffic anhydride (Tf_2O) or triflic acid (TfOH). Mechanistic studies revealed that the rate-limiting step in this reaction is triflation of the sulfoxide. Therefore the reactivity of the glycosyl donor could be influenced by the substituent in the para position of the phenyl ring and the following reactivity order was established OMe> H> NO_2. Ley et al. (1994) reported a facile one-pot two step synthesis of a trisaccharide unit which is derived from the common polysaccharide antigen of a group *B streptococci*.

Takahashi described (Yamada et al. 1994) a similar one-pot two-step-glycosylation but now the difference in reactivity between glycosyl donors and acceptors was accomplished by use of two types of anomeric leaving groups with different reactivities, for example in this case glycosyl bromide could be coupled with thioglycoside in presence of silver triflate to give the dimer For the preparation of an elicitor-active hexaglycoside the difference in reactivity between a trichloroacetimidate and thioglycoside was exploited (Yamada et al. 1994).

SOLID-PHASE OLIGOSACCHARIDE SYNTHESIS

Inspired by the success of solid phase peptide and oligonucleotide syntheses, in the early seventies several research groups attempted to develop methods for solid supported oligosaccharide synthesis. However, since no powerful methods for glycosidic bond formation were available, the successes of these methods were limited and only simple di- and trisaccharides could be obtained. In 1987, Veeneman et al. (1987) reported the solid supported synthesis of α D-galactofuranosyl heptamer, and Yan et al. (1994) described the solid supported synthesis of oligosaccharides using anomeric sulfoxides as donors. In both the procedures, the anomeric centre of a saccharide is linked to the solid support and glycosyl donors are added to the growing chain. Recently, Danishefsky et al. (1993) reported an inverse approach using the incoming sugars as glycosyl acceptor. The synthesis of an oligosaccharide is initiated by attaching suitably protected glycal to a solid support (polystyrene). The double bond of the glycalis then activated by epoxidation and glycosidation occurs between a solution based glycal acceptor and the epoxide linked to the solid support. The last sugar can be introduced as a non-glycal to terminate the process and the oligosaccharide can be released from the solid support by tetra- n-butylammonium fluoride (TBAF) treatment. The rates of reactions on a solid support are generally reduced compared to solution based methods. Douglaset al. (1991) addressed this problem by polymer-supported solution synthesis of oligosaccharides. This strategy is based on the fact that a polyethylene polymer supported saccharide is soluble under conditions of glycosylation but insoluble during the work-up procedure.

Poly(ethylene glycol) mono methyl ether (PEG) was coupled through a succinic (SU) ester linkage to a carbohydrate hydroxyl group. The progress of the glycosylation could be monitored by NMR spectroscopy. The PEG-succinimide linkage could be cleaved by DBU-catalysedmethanolysis in dichloromethane. An efficient and stereo controlled solid-phase chemical synthesis of oligosaccharides using a new type of insoluble support (a copolymer of polyethylene glycol and polystyrene) has recently been reported (Adinolfi et al. 1996). The polymer supported based glycosylation methods eliminate time-consuming work-up procedures and purification steps. Polymer supported synthesis of oligosaccharides using dibutylborontrifiate as promoter of glycosylations with glycosyl trichloroacetimidates has also been reported. Zhang et al. (1996) have reported the synthesis of a universal allyl linker for solid-phase synthesis that has a reactive terminal double bond. Since allyl linker extends the range of post-synthetic manipulations that can be carried out without cleavage from the support.

ENZYMATIC AND SEMI-SYNTHETIC GLYCOSYLATION STRATEGIES

The need for increasingly efficient methods for oligosaccharide synthesis has stimulated the development of enzymatic methods and two basic approaches are available (Wong et al. 1995). In the first approach, glycosyl transferases and sugar nucleotide diphosphate are used for glycosidic bond formation. This method is very powerful especially when the sugar nucleotides are regenerated in situ. The enzymatic method bypasses the need for protecting groups since the enzymes control both the regio- and stereoselectivity of glycosylation. Recently, a combined sequential use of a glycosidase together with a glycosyltransferase and co-factor regeneration was used for the preparation of Sialyl T-antigens. A convenient synthesis of di- and trisaccharide units, related to molecular recognition, by employing enzymic regioselective transgalactosylation, trans-N-acetylglucosaminidation, transfucosylation and transmannosylation (Usui et al. 1996).

In order to overcome problems associated with chemically and enzymatically based methods, combined approaches have been developed (Compston et al. 1993). In such an approach glycosidic linkages which are very difficult to introduce chemically are introduced enzymatically and vice-versa. This approach has proven to be extremely valuable for the introduction of neuraminic acid units in an oligosaccharide. Enzymatic oligosacchride synthesis has also been performed on solid supports (Schuster et al. 1994).

ACKNOWLEDGEMENTS

Authors are thankful to CSIR-New Delhi and UGC-New Delhi for financial assistance.

REFERENCES

Xu, Y., Sette, A., Sidney, J., Gendler, S.J. and Franco, A. (2005). Tumor-associated carbohydrate antigens: A possible avenue for cancer prevention. *Immunology and Cell Biology*, 83(4), 440-448.

Kannagi, R. (2003). Carbohydrate-Based Treatment of Cancer Metastasis. *Carbohydrate-Based Drug Discovery*, 803-829.

Yuriev, E., Farrugia, W., Scott, A.M. and Ramsland, P.A. (2005). Three-dimensional structures of carbohydrate determinants of Lewis system antigens: implications for effective antibody targeting of cancer. *Immunology and cell biology*, 83(6), 709-717.

Ugorski, M. and Laskowska, A. (2002). Sialyl Lewis a: a tumor-associated carbohydrate antigen involved in adhesion and metastatic potential of cancer cells. *Acta Biochimica Polonica*, 49(2), 303-311.

Saksena, R., Deepak, D., Khare, A., Sahai, R., Tripathi, L.M. and Srivastava, V.M.L. (1999). A novel pentasaccharide from immunostimulant oligosaccharide fraction of buffalo milk. *Biochimica Et Biophysica Acta (BBA)-General Subjects*, 1428(2-3), 433-445.

Gu, G., Du, Y. and Pan, J. (2002). Concise synthesis of a buffalo milk pentasaccharide derivative. *Carbohydrate research*, 337(14), 1313-1317.

Ranjan, A.K., Rathore, R.S., Deepak, D., Khare, A., Sahai, R. and Srivastava, V.M.L. (2016). Immunostimulant fractions of novel hexa and heptasaccharide from Donkey's milk. *AsianJournal of Organic and Medicinal Chemistry*, 1(2), 55-60.

Wolform, M.L. and Whistler, R.L. (1963). Method in Carbohydrate Chemistry, Volume 2, Reaction of Carbohydrate, *Academic Press Inc*, New York, 211.

Guo, J. and Ye, X.S. (2010). Protecting Groups in Carbohydrate Chemistry: Influence on Stereoselectivity of Glycosylations. *Molecules,* 15(10), 7235–7265.

Gigg, R., Payne, S. and Conant, R. (1983). The Allyl Group for Protection in Carbohydrate Chemistry, Part 14.1 Synthesis of 2, 3-Di-O-Methyl-4-O-(3, 6-Di-O-Methyl-β-D-Glucopyranosyl)-L-Rhamnopyranose (and its α-Propyl Glycoside): A Haptenic Portion of the Major Glycolipid from Mycobacterium Leprae. *Journal of Carbohydrate Chemistry*, 2(3), 207-223.

Kováč, P. and Edgar, K.J. (1990). Synthesis of a series of methyl β-glycosides of (1→ 6)-β-d-galacto-oligosaccharides having one residue deoxygenated at position 3. *Carbohydrate Research*, 201(1), 79-93.

Nashed, E.M. and Glaudemans, C.P. (1987). Selective silylation of. beta.-D-galactosides. A new approach to the synthesis of (1. fwdarw. 6)-. beta.-D-galactopyranooligosaccharides. *The Journal of Organic Chemistry*, 52(23), 5255-5260.

Codée, J.D.C., Ali, A., Overkleeft, H.S. and van der Marel, G.A. (2011). Novel protecting groups in carbohydrate chemistry. *Comptes Rendus Chimie*, 14(2-3), 178–193.

Chandra, T., Broderick, W.E. and Broderick, J.B. (2010). An Efficient Deprotection ofN-Trimethylsilylethoxymethyl (SEM) Groups from Dinucleosides and Dinucleotides. *Nucleosides, Nucleotides and Nucleic Acids,* 29(2), 132–143.

Srivastava, O.P., Hindsgaul, O., Shoreibah, M. and Pierce, M. (1988). Recognition of oligosaccharide substrates by N-acetylglucosaminyltransferase-V. *Carbohydrate Research*, 179, 137-161.

Toshima, K., Mukaiyama, S., Kinoshita, M. and Tatsuta, K. (1989). The diethylisopropylsilyl group: A new protecting group for alcohols. *Tetrahedron letters*, 30(46), 6413-6416.

Barili, P. L., Berti, G., Catelani, G., Colonna, F. andMarra, A. (1986). New results in the isopropylidenation of galactopyranosides. Useful intermediates for the synthesis of galactose derivatives. *Tetrahedron Letters*, 27(20), 2307-2310.

Clode, D.M. (1979). Carbohydrate cyclic acetal formation and migration. *Chemical Reviews,* 79(6), 491–513.

Lee, H.H., Schwartz, D.A., Harris, J.F., Carver, J.P. and Krepinsky, J.J. (1986). Syntheses of model oligosaccharides of biological significance. 7. Synthesis of a fucosylated N, N'-diacetylchitobioside linked to bovine serum albumin and immunochemical characterization of rabbit antisera to this structure. *Canadian Journal of Chemistry*, 64(9), 1912-1918.

Johansson, R. and Samuelsson, B. (1984). Regioselective reductive ring-opening of 4-methoxybenzylidene acetals of hexopyranosides. Access to a novel protecting-group strategy. Part 1. *Journal of the Chemical Society*, Perkin Transactions 1, 2371.

Khan, S.H., Piskorz, C.F. and Matta, K.L. (1994). Synthetic Antigens: Synthesis of 4-Aminophenyl O-α-D-Mannopyranosyl-(1→ 2)-O-α-D-mannopyranosyl-(1→ 6)-O-α-D-Mannopyranoside and A Related Di-and A Trisaccharide. *Journal of Carbohydrate Chemistry*, 13(7), 1025-1035.

Bock, K. and Meldal, M. (1983). Synthesis of Disaccharides Related to the O-Specific Polysaccharide of Salmonella typhimurium. *Acta Chem. Scand. B*, 37(7).

Bock, K. and Al, M.M. (1984). Synthesis of Tetrasaccharides Related to the 0-Specific Determinants of Salmonella Serogroups A, B and Dt. *Acta Chem. Scand. B*, 38, 255-266.

Dua, V.K., Goso, K., Dube, V.E. and Bush, C.A. (1985). Characterization of lacto-N-hexaose and two fucosylated derivatives from human milk by high-performance liquid chromatography and proton NMR spectroscopy. *Journal of Chromatography* A, 328, 259-269.

Liptak, A. (1982). Synthesis of 2-O-methyl-d-rhamnose, a constituent of a bacterial lipopolysaccharide. *Carbohydrate Research,* 107(2), 300–302.

Barton, D.H. and McCombie, S.W. (1975). A new method for the deoxygenation of secondary alcohols. *Journal of the Chemical Society, Perkin Transactions* 1, (16), 1574-1585.

Hutchins, R.O., Milewski, C.A.and Maryanoff, B.E. (1973). Selective deoxygenation of ketones and aldehydes including hindered systems with sodium cyanoborohydride. *Journal of the American Chemical Society*, 95(11), 3662-3668.

Barrette, E.P. and Goodman, L. (1984). Convenient and stereospecific synthesis of deoxy sugars. Reductive displacement of trifluoromethylsulfonates. *The Journal of Organic Chemistry*, 49(1), 176-178.

Jansson, K., Noori, G. and Magnusson, G. (1990). 2-(Trimethylsilyl)ethyl glycosides. Transformation into glycopyranosyl chlorides. *The Journal of Organic Chemistry,* 55(10), 3181–3185.

Pétursson, S. (1997). Protecting Groups in Carbohydrate Chemistry. *Journal of Chemical Education,* 74(11), 1297.

Hashimoto, H., Kawa, M., Saito, Y., Date, T., Horito, S. and Yoshimura, J. (1987). A convenient one-pot preparation of glycosyl bromides as well as glycosyl acetates from benzyl glycosides using N-bromosuccinimide. *Tetrahedron Letters*, 28(30), 3505-3508.

Brennan, P.J. (1989). Structure of mycobacteria: recent developments in defining cell wall carbohydrates and proteins. *Reviews of Infectious Diseases*, 11(Supplement_2), S420-S430.

Kartha, K.R. and Jennings, H.J. (1990). A facile, one-step procedure for the conversion of 2-(trimethylsilyl) ethyl glycosides to their glycosyl chlorides. *Tetrahedron Letters*, 31(18), 2537-2540.

Sakonsinsiri, C. and Turnbull, W.B. (2018). Protecting Groups at the Anomeric Position of Carbohydrates. *Protecting Groups,* 145–168.

Gangwar, L., Sahu, S. and Deepak, D. (2018). Synthesis of Reverse Building blocks of Milk Oligosaccharides. *Chemistry & Biology Interface*, 8(3), 162-176.

Rina Saksena, Desh Deepak and AnakshiKhare (1999). Synthesis of disaccharides related to human milk of antigenic properties. *Indian Journal of Chemistry*, 38(B), 795-799.

Baytas, S.N. and Linhardt, R.J. (2004). Combinatorial carbohydrate synthesis. *Mini-Reviews in Organic Chemistry*, 1(1), 27-39.

Gu, G., Du, Y. and Pan, J. (2002). Concise synthesis of a buffalo milk pentasaccharide derivative. *Carbohydrate Research*, 337(14), 1313-1317.

Anna Rencrosi, Laura Poletti, Marco Guerrini, Giovanni Russo and Luigi Lay (2002). Human milk oligosaccharides: an enzymatic protection step simplifies the synthesis of 3'- and 6'-O- sialyllactose and their analogues. *Carbohydrate Research,* 337, 473-483.

Kitagawa, H., Nakada, H., Fukui, S., Funakoshi, I., Kawasaki, T., Yamashina, I. and Inagaki, F. (1993). Novel oligosaccharides with the sialyl-Lea structure in human milk. *The Journal of Biochemistry*, 114(4), 504-508.

Unverzagt, C. (1994). Synthesis of a biantennary heptasaccharide by regioselective glycosylations. *Angewandte Chemie International Edition in English*, 33(10), 1102-1104.

Goodman, L. (1967). Neighboring-Group Participation in Sugars. *Advances in Carbohydrate Chemistry,* 109–175.

Toshima, K. and Tatsuta, K. (1993). Recent progress in O-glycosylation methods and its application to natural products synthesis. *Chemical Reviews*, 93(4), 1503-1531.

Koenigs, W. and Knorr, E. (1901). Uebereinige Derivate des Traubenzuckers und der Galactose. *Berichte der deutschenchemischen Gesellschaft*, 34(1), 957-981.

Lichtenthaler, F.W. (1987). Karl Freudenberg, Burckhardt Helferich, Hermann OL Fischer A centennial tribute. *Carbohydrate Research*, 164, 1-22.

Singh, Y., Geringer, S.A. and Demchenko A.V. (2022). Synthesis and Glycosidation of Anomeric Halides: Evolution from Early Studies to Modern Methods of the 21st Century. *Chem Rev*. 13; 122(13), 11701-11758.

Sinay, P.E. (1978). Recent advances in glycosylation reactions. *Pure and Applied Chemistry IXth*, 50(11-12), 1437-1452.

Toepfer, A. and Schmidt, R.R. (1992). An efficient synthesis of the Lewis x (Lex) antigen family. *Tetrahedron Letters*, 33(36), 5161-5164.

Schmidt, R.R. and Michel, J. (1984). Direct O-glycosyl trichloroacetimidate formation, nucleophilicity of the anomeric oxygen atom. *Tetrahedron Letters*, 2*5*(8), 821-824.

Schmidt, R.R. (1986). New Methods for the Synthesis of Glycosides and Oligosaccharides—Are There Alternatives to the Koenigs-Knorr Method?[New Synthetic Methods (56)]. *Angewandte Chemie International Edition in English*, 25(3), 212-235.

Kochetkov, N.K., Backinowsky, L.V. and Tsvetkov, Y.E. (1977). Sugar thioorthoesters as glycosylating agents. *Tetrahedron Letters*, 18(41), 3681-3684.

Araki, Y., Mokubo, E., Kobayashi, N., Nagasawa, J.I. and Ishido, Y. (1989). Structural elucidation and a novel reductive cleavage of ribofuranosyl ring C-1-O bond of the intramolecular C-arylation product of tri-O-benzyl-β-D-ribofuranosyl fluoride. *Tetrahedron Letters*, 30(9), 1115-1118.

Kunz, H. and Sager, W. (1985). Stereoselective glycosylation of alcohols and silyl ethers using glycosyl fluorides and boron trifluoride etherate. *Helvetica Chimica Acta*, 68(1), 283-287.

Crich, D., Sun, S. and Brunckova, J. (1996). Chemistry of 1-Alkoxy-1-glycosyl Radicals: The Manno-and Rhamnopyranosyl Series. Inversion of α-to β-Pyranosides and the Fragmentation of Anomeric Radicals. *The Journal of Organic Chemistry*, 61(2), 605-615.

Fügedi, P., Garegg, P.J., Lönn, H. and Norberg, T. (1987). Thioglycosides as glycosylating agents in oligosaccharide synthesis. *Glycoconjugate Journal*, 4, 97-108.

Bowen, R.D. and Williams, D.H. (1978). Potential energy profiles for unimolecular reactions of organic ions: C4H9O+. *Journal of the American Chemical Society*, 100(24), 7454-7459.

Zuurmond, H.M., Van der Klein, P.A.M., Van Der Marel, G.A. and Van Boom, J.H. (1993). A stereospecific approach towards the synthesis of 2-deoxy α-and β-glycosides based on a 1, 2-ethyl (phenyl) thio group migration. *Tetrahedron*, 49(29), 6501-6514.

Shun-ichi, H., Takeshi, H. and Shiro, I. (1990). An extremely mild and general method for the stereo controlled construction of 1,2-cis-glycosidic linkages via S-glycopyranosylphosphorodiamidimidothioates. *Tetrahedron Letters,* 31(33), 4769–4772.

Hanessian, S., Bacquet, C. and Lehong, N. (1980). Chemistry of the glycosidic linkage. Exceptionally fast and efficient formation of glycosides by remote activation. *Carbohydrate Research*, 80(2), C17-C22.

Danishefsky, S.J., Gervay, J., Peterson, J.M., McDonald, F.E., Koseki, K., Griffith, D.A. and Marsden, S.P. (1995). Application of glycals to the synthesis of oligosaccharides: Convergent total syntheses of the Lewis x trisaccharide sialyl Lewis x antigenic determinant and higher congeners. *Journal of the American Chemical Society*, 117(7), 1940-1953.

Nakagawa, T., Ueno, K., Kashiwa, M. and Watanabe, J. (1994). The stereoselective synthesis of cyclomaltopentaose. A novel cyclodextrin homologue with DP five. *Tetrahedron Letters*, 35(12), 1921-1924.

Uchiyama, T. and Hindsgaul, O. (1996). Per-O-trimethylsilyl-α-l-fucopyranosyl iodide: a novel glycosylating agent for terminal α-l-fucosylation. *Synlett*, (06), 499-501.

Lönn, H. (1985). Synthesis of a tri-and a hepta-saccharide which contain α-L-fucopyranosyl groups and are part of the complex type of carbohydrate moiety of glycoproteins. *Carbohydrate Research*, 139, 105-113.

Fraser-Reid, B., Udodong, U.E., Wu, Z., Ottosson, H., Merritt, J.R., Rao, C.S. and Madsen, R. (1992). n-Pentenyl glycosides in organic chemistry: a contemporary example of serendipity. *Synlett*, (12), 927-942.

Mehta, S.and Pinto, B.M. (1993). Novel glycosidation methodology. The use of phenyl selenoglycosides as glycosyl donors and acceptors in oligosaccharide synthesis. *The Journal of Organic Chemistry*, *58*(12), 3269-3276.

Sliedregt, L.A.J.M., Van der Marel, G.A. and Van Boom, J.H. (1994). Trimethylsilyl triflate mediated chemoselective condensation of arylsulfenyl glycosides. *Tetrahedron Letters*, 35(23), 4015-4018.

Kanie, O., Ito, Y. and Ogawa, T. (1994). Orthogonal glycosylation strategy in oligosaccharide synthesis. *Journal of the American Chemical Society*, 116(26), 12073-12074.

Kanie, O., Ito, Y. and Ogawa, T. (1996). Orthogonal glycosylation strategy in synthesis of extended blood group B determinant. *Tetrahedron Letters*, 37(26), 4551-4554.

Mootoo, D. R., Konradsson, P., Udodong, U. and Fraser-Reid, B. (1988). Armed and disarmed n-pentenyl glycosides in saccharide couplings leading to oligosaccharides. *Journal of the American Chemical Society*, 110(16), 5583-5584.

Madsen, R., Udodong, U.E., Roberts, C., Mootoo, D.R., Konradsson, P. and Fraser-Reid, B. (1995). Studies related to synthesis of glycophosphatidylinositol membrane-bound protein anchors. 6. Convergent assembly of subunits. *Journal of the American Chemical Society*, 117(5), 1554-1565.

Roy, R., Andersson, F.O. and Letellier, M. (1992). "Active" and "latent" thioglycosyl donors in oligosaccharide synthesis. Application to the synthesis of α-sialosides. *Tetrahedron Letters*, 33(41), 6053-6056.

Boons, G.J. and Isles, S. (1996). Vinyl glycosides in oligosaccharide synthesis. 2. The use of allyl and vinyl glycosides in oligosaccharide synthesis. *The Journal of Organic Chemistry*, 61(13), 4262-4271.

Kahne, D., Walker, S., Cheng, Y. and Van Engen, D. (1989). Glycosylation of unreactive substrates. *Journal of the American Chemical Society*, 111(17), 6881-6882.

Grice, P., Ley, S.V., Pietruszka, J., Osborn, H.M., Priepke, H.W. and Warriner, S.L. (1997). A New Strategy for Oligosaccharide Assembly Exploiting Cyclohexane-1, 2-diacetal Methodology: An Efficient Synthesis of a High Mannose Type Nonasaccharide. *Chemistry–A European Journal*, 3(3), 431-440.

Yamada, H., Harada, T., Miyazaki, H. and Takahashi, T. (1994). One-pot sequential glycosylation: a new method for the synthesis of oligosaccharides. *Tetrahedron Letters*, 35(23), 3979-3982.

Yamada, H., Harada, T. and Takahashi, T. (1994). Synthesis of an elicitor-active hexaglucoside analog by a one-pot, two-step glycosidation procedure. *Journal of the American Chemical Society*, 116(17), 7919-7920.

Veeneman, G.H., Notermans, S., Liskamp, R.M.J., Van Der Marel, G.A. and Van Boom, J.H. (1987). Solid-phase synthesis of a naturally occurring β-(1→ 5)-linked D-galactofuranosyl heptamer containing the artificial linkage arm L-homoserine. *Tetrahedron Letters*, 28(52), 6695-6698.

Yan, L., Taylor, C.M., Goodnow Jr, R. and Kahne, D. (1994). Glycosylation on the Merrifield resin using anomeric sulfoxides. *Journal of the American Chemical Society*, 116(15), 6953-6954.

Danishefsky, S.J., McClure, K.F., Randolph, J.T. and Ruggeri, R.B. (1993). A strategy for the solid-phase synthesis of oligosaccharides. *Science*, 260(5112), 1307-1309.

Douglas, S.P., Whitfield, D.M. and Krepinsky, J.J. (1991). Polymer-supported solution synthesis of oligosaccharides. *Journal of the American Chemical Society*, 113(13), 5095-5097.

Adinolfi, M., Barone, G., De Napoli, L., Iadonisi, A. and Piccialli, G. (1996). Solid phase synthesis of oligosaccharides. *Tetrahedron Letters*, 37(28), 5007-5010.

Zhang, X. and Jones, R.A. (1996). A universal allyl linker for solid-phase synthesis. *Tetrahedron Letters*, 37(22), 3789-3790.

Wong, C.H., Halcomb, R.L., Ichikawa, Y. and Kajimoto, T. (1995). Enzymes in organic synthesis: Application to the problems of carbohydrate recognition (part 2). *Angewandte Chemie International Edition in English*, 34(5), 521-546.

Usui, T. and Murata, T. (1996). Preparation of oligosaccharide units library. *Journal of Synthetic Organic Chemistry, Japan*, 54(7), 607-615.

Compston, C.A., Condon, C., Hanna, H.R. and Mazid, M.A. (1993). Rapid production of a panel of blood group A-active oligosaccharides using chemically synthesized di-and tri-saccharide primers and an easily prepared porcine (1→ 3)-α-N-acetyl-D-galactosaminyltransferase. *Carbohydrate Research*, 239, 167-176.

Schuster, M., Wang, P., Paulson, J.C. and Wong, C.H. (1994). Solid-phase chemical-enzymic synthesis of glycopeptides and oligosaccharides. *Journal of the American Chemical Society*, 116(3), 1135-1136.

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