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Recent Developments in Stereoselective Chemical Glycosylation

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Abstract

Because of their pivotal biological functions, attention to sugars and glycobiology has grown rapidly in recent decades, leading to increased demand for homogeneous oligosaccharides. The stereoselective preparation of oligosaccharides by chemical means remains challenging and continues to be a vivid research area for organic chemists. In the past decade, new approaches and reinvestigated traditional methods have transformed the field. These developments include novel catalyses, various types of glycosylation modulators and the use of photochemical energy to facilitate glycosylation. This Minireview presents a brief overview of the latest trends in chemical glycosylation, with emphasis on the stereoselective synthetic protocols developed in the past decade.

Graphical Abstract

Keywords

glycosylation; diastereoselectivity; oligosaccharides; glycosides; carbohydrates

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Dedicated to Professor Chi-Huey Wong on the occasion of his 70th birthday

Conflict of interest

The authors declare no conflict of interest.

1. Introduction

Carbohydrates are versatile biological compounds involved in numerous vital processes, such as the immune response, cell-cell recognition, and cell signaling.^[1] However, unlike other biological polymers (e.g. nucleic acids and peptides), the selective chemical synthesis of oligosaccharides remains a difficult challenge. This is the result of both the vast structural diversity of sugars, as well as the potential formation of diastereomers during glycosylation reactions. This challenge has spurred an increasing interest in developing newer, more selective protocols for the assembly of monosaccharides into complex carbohydrates. While a universal glycosylation method has yet to be discovered, tremendous progress has been made in this field over the course of the past decade. This article aims to highlight the latest trends and developments in selective chemical glycosylation within the last decade. We classify these synthetic protocols into four groups: transition metal catalysis, organocatalysis, photochemical reactions, and reactions in the presence of modulators designed to control selectivity. The review is meant to focus on new concepts in chemical glycosylation, and for a more comprehensive treatment the reader is directed to several recent reviews and monographs.^[2] Furthermore, the review will not cover reactions of glycals, as well as glycosylations directed by chiral auxiliaries, as these subjects have been reviewed extensively.^[2d,f] Similarly, reactions of amino sugars^[2a] will only be discussed when deemed relevant.

2. Transition Metal Catalysis

Transition metals have been extensively employed in organic synthesis, and their versatility has also attracted carbohydrate chemists. Recently, several catalytic glycosylation using transition metals such as gold, nickel, palladium and zinc have been reported. This section will highlight several recent developments in this field.

2.1. Gold

The excellent alkynophilicity of gold complexes has been widely exploited in synthetic chemistry.^[3] The first gold(III)-catalyzed glycosylation was reported by Hotha and Kashyap in 2006 (Scheme 1).^[4] In this protocol, perbenzylated donors such as propargyl glycoside **1** were employed. While excellent yields were achieved when simple, non-sugar acceptors were employed, this reaction required high temperatures and proceeded with low stereoselectivity. The authors attributed the need for elevated temperatures to the formation of strained aglycone byproduct **4** in the proposed mechanism, which lowered its leaving group ability.

Around the same time, the Yu's group reported the first gold(I)-catalyzed glycosylation, using glycosyl *ortho*-alkynylbenzoates **5** as the donors.^[5] This protocol employs gold(I) complexes (Primarily PPh₃AuOTf) as the catalysts. The activation of **5** is facile, as the aglycone byproduct **6** produced is aromatic and stable. Hence, this method is highly versatile and mild, with selective glycosylations demonstrated on the more challenging substrates like 2-deoxy sugars as well as sialic acid donors (Scheme 2A). Notably, β -mannosylation, a major challenge in chemical glycosylation, is also possible for mannosyl α -*ortho*-alkynylbenzoates such as donor α -**7** (Scheme 2B).^[6] Glycosylations with both primary and

secondary acceptors were shown to be highly β -selective. Extensive mechanistic studies have been performed on the reaction, which supports a mechanism shown in Scheme 3.^[6–7] The utility of this protocol has been demonstrated by its applications in the total syntheses of natural products including periploside A,^[8] acremomannolipin A,^[9] and trioxacarcins.^[10]

To address the need for elevated temperatures in their gold promoted activation of propargyl glycosides, Hotha's group later developed orthoester **8**,^[11] acetal **9**,^[12] and carbonate **10**^[13] as alternative donors (Figure 1). The authors suggested that both **9** and **10** exploit the Thorpe-Ingold effect to facilitate the activation of the aglycones. The addition of silver hexafluoroantimonate/triflate was found to further improve the efficiency of the reactions.^[12] These improved protocols allowed this group to synthesize a branched heneicosafuranosyl arabinogalactan.^[14]

Gold-catalyzed glycosylation of alkynyl thioglycosides have also been established. The Yu group reported the glycosylation of *ortho*-alkynylphenyl thioglycosides in 2012, though the scope was narrower than their ester counterparts.^[15] Later, Zhu and co-workers described the use of alkynyl thioglycosides **11** as glycosyl donors (Scheme 4).^[16] While deoxy sugars underwent glycosylations smoothly with very high yields and α -selectivities, fully substituted and 2-amino-2-deoxy sugars required higher catalyst loadings. Yields were usually higher when *gem*-dimethyl substituted aglycones (R=Me, Scheme 4) were used, presumably owing to the Thorpe-Ingold effect.

The role of gold is not limited to the activation of alkynes. In 2015, Peng and Schmidt reported a gold(III) chloride-promoted activation of trichloroacetimidate **12** (Scheme 5).^[17] This reaction proceeded with moderate to excellent β -selectivities. The authors proposed that the catalyst ligates with the hydroxyl group on the acceptor to form an adduct with enhanced nucleophilicity, which then attacks the donor. Comparable results were obtained when gold(I) chloride was used.

2.2. Nickel and Palladium

In 2009, Nguyen and co-workers described a chelation approach to control stereoselectivity in glycosylations. Using Pd(PhCN)₂Cl₂ to activate glycosyl trichloroacetimidates **13**, the authors were able to obtain products in high β -selectivities (Scheme 6).^[18] It was proposed that the palladium chelated with both the trichloroacetimidate oxygen and the ethereal oxygen at C2 position as in activated complex **14**, directing a S_N2-like attack to produce the β -anomers. This mechanistic proposal is supported with results of 2-deoxy and TIPS-protected 2-OH donors, which showed decreased β -selectivities.

The same group also demonstrated the stereoselective glycosylation of 2-aminoglycosyl trichloroacetimidates **15** (Scheme 7).^[19] This reaction is catalyzed by a Ni(II) complex, and proceeds in a highly α -selective fashion. Notably, this approach provides facile access to difficult structures, such as the tumor-associated T_N antigen.^[20] The authors proposed a mechanism based on chelation of the 1,2-*cis* substituents, which also included the involvement of the acceptor in the activated complex.

2.3. Zinc

Very recently, Walczak's group reported the oxidative glycosylation of glycosyl stannanes facilitated by $\text{Zn}(\text{OTf})_2$ (Scheme 8).^[21] In this protocol, β -stannanes **16** were employed as donors. These stannanes underwent glycosylation neatly to generate β -linked sugars exclusively, which the authors attribute to the intermediacy of a glycosyl tosylate, based on the comparison to work by Bennett and co-workers (*vide infra*). Interestingly, the free hydroxyl group at the C2 position is necessary for this reaction to proceed. The authors suggested its role in ligand exchange with the iodine oxidant, which supports the oxidative cleavage of the stannyl group.

3. Organocatalysis

Organocatalysts, with their versatility and mildness, have attracted many carbohydrate chemists in the past decade. Among them, thioureas are the most thoroughly studied. Other catalysts such as phosphoric acids and organoboron reagents have also been reported.

3.1. Thiourea/Urea

In 2013, Schmidt's group reported the glycosylation of glucosyl and galactosyl trichloroacetimidates could be catalyzed by both phosphoric acid **17** and thiourea **18** (Schreiner's thiourea,^[22] Scheme 9).^[23] The reaction is β -selective, which the authors suggested arises through the cooperative action of both catalysts in the transition state. Later, Shaw *et al.* described a glycosylation catalyzed by pyridinium bromide-thiourea combination that is very similar to Schmidt's system.^[24]

In 2016, Ye and co-workers reported that activating perbenzyl glycosyl chlorides with urea **19** resulted in glycosylation reactions that proceeded with low to high α -selectivity (Scheme 10).^[25] After screening several additives the authors found that excess phosphine **20** improved the α -selectivity for more challenging substrates. The authors attribute the increased selectivity to the phosphine blocking the β -face of the molecule, a phenomenon first described by West and Schuerch in 1973.^[26]

More recently, the Jacobsen group reported glycosylation catalyzed by macrocyclic bis-thioureas.^[27] In this reaction, α -glycosyl chlorides undergo selective glycosylation in the presence of catalytic bis-thiourea **21** to produce β -glycosides (Scheme 11). High β -selectivities were observed for challenging substrates, such as mannosyl and 2-deoxyglycosyl donors. Computational studies suggested the coordination of the thiourea moieties to the chloride ion activates the donor, and the amide group on **21** concomitantly enhances the nucleophilicity of the acceptor in the transition state. Glycosylations of glycosyl phosphate, using a similar bis-thiourea catalyst, have also been reported.^[28]

Very recently, Xu and Loh described the use of strained glycosyl donors to prepare 2-deoxy-2-alkyl furanosides (Scheme 12).^[29] This glycosylation is highly efficient, as it only requires a very low loading of either Schreiner's thiourea **18** or thiourea **22**. In addition, the stereoselectivity is dependent on the donor. Based on a series of NMR and kinetic experiments, the authors proposed that the thioureas catalyze the formation of donor-

acceptor ion pair **23**, which breaks down into the product. While this catalysis is also applicable to strained pyranose donors, side products formation is often observed.

3.2. Brønsted Acids

In 2010, Fairbanks and co-workers demonstrated that the chiral phosphoric acid **24** could be used to activate galactosyl trichloroacetimidate **25** for glycosylation (Scheme 13).^[30] While both enantiomers are effective, stereoselectivities of the (*S*)-**24**-catalyzed reactions are generally higher. Furthermore, the reaction was also found to be sensitive to the protecting group pattern on the donor, and benzylidene acetal protected donors reacted to form products with attenuated selectivity.

In 2017, the Nagorny group described the use of chiral phosphoric acids to control both the stereoselectivity and regioselectivity of glycosylations with complex polyol acceptors **26** and **27**.^[31] The stereo- and regioselectivity of the reaction appeared to be dependent on the catalyst backbone. For example, while reaction of 6-deoxyglycosyl donor **28** with **26** catalyzed by (*S*)-**24** resulted in glycosylation predominantly at the C-5 alcohol of **26**, the use of SPINOL phosphoric acid (*R*)-**30** led to a reversal of regioselectivity in the glycosylation between **29** and **27**, affording glycosylation at C-3 as the major product (Scheme 12). Structural changes in the donors and acceptors have profound effect to the selectivity. Thus, when *ent*-**29** was used, the β -selectivity of the glycosylation dropped significantly under the same reaction conditions. This observation is in line with results from the Bennett^[32] and Toshima labs,^[33] who reported that stereochemical match and mismatch played a role in chiral phosphoric acid-catalyzed glycosylations. Later, the Nagorny group applied the chiral phosphoric acid in the regioselective synthesis of aminoglycosides.^[34]

3.3. Organoboron Catalysts

In 2011, Schmidt and co-workers reported that catalytic phenyl-boron difluoride or diphenylboron fluoride would activate trichloroacetimidates for glycosylation (Scheme 15).^[35] The authors suggested that the reactions proceed in a S_N2 -like manner, with α -donors generating β -glycosides selectively, and vice versa. It is proposed that the boron reagent forms a nucleophilic adduct **31** with the acceptor, which undergoes glycosylation with the donor in a concerted manner, not unlike the gold catalysis described earlier (Section 2.1). Later, the group also reported a similar glycosylation using silicon fluorides catalysts.^[36] Similarly, the Kandasamy group developed a tris(pentafluorophenyl)borane-promoted glycosylation, and observed high β -selectivities when α -imidates were used as donors.^[37]

In 2011, Taylor's group reported the first catalytic borinic acid-catalyzed glycosylation.^[38] In this reaction, partially protected acceptors **32**, which have 1,2-*cis* diols, are activated by borinic acid **33** as "ate" complexes. These latter complexes react with α -glycosyl halides to produce β -glycosides exclusively at the equatorial alcohol (Scheme 16). The formation of "ate" complex was later confirmed by kinetic studies.^[39] Selectivity in the reaction was attributed to the ability of the silver salt to block the α -face of the donor, a proposal first put forth by Wulff and Röhle in 1974.^[40] The group later expanded the reaction scope to 2-deoxy sugars, and have applied the protocol in their total synthesis of a saponin fragment.^[41]

In 2016, the same group reported the dehydrative version of this borinic acid catalysis.^[42] As shown in Scheme 17, the hemiacetal donors are converted to glycosyl mesylates, which are attacked in situ by the “ate” complexes formed from acceptors **32** and borinic acid **34**. Under these conditions glucoand galactopyranosides react in a highly β -selective fashion. Reaction progress kinetic analysis^[43] confirmed the crucial presence of **34** in promoting a S_N2 -like pathway in the reaction.

Toshima and co-workers elegantly demonstrated the generation of 1,2-*cis* glycosides by using 1,2-anhydroglycosides donors with boronic acid catalysis. In this approach, 1,2-*cis* diol **32** or 1,3-diol **35** are subjected to partial boronic ester formation with **36**. The resulting boronic ester then attacks epoxides **37** to form the 1,2-*cis* glycosides as products (Scheme 18).^[44] In addition to the excellent α -stereoselectivities, regioselectivities for these partially protected acceptors are also good. The use of diols is not necessary when boronic acid is replaced with borinic acid. With the use of borinic acid **38**, this protocol is later expanded to the challenging synthesis of β -mannosides and β -rhamnopyranosides.^[45] The β -mannosylation, with **39** as the donor, is illustrated in Scheme 19 as an example.

Very recently, the Toshima's group further expanded the reaction to unprotected sugar acceptors using boronic acid **40** as the catalyst (Scheme 20).^[46] Under these conditions, the addition of water is crucial to suppress side product formation. The regioselectivity of the reaction depends on the configuration of the donor: 1,4-regiomers are usually favored in α -glycosylation, while 1,6-regiomers predominate in β -mannosylation.

Using a combination of kinetic isotope effect (KIE) studies and computation, the authors proposed the mechanism depicted in Scheme 21 using acceptor **32** as example.^[45b,46] Here, the boronic acid reacts with **32** to generate boronic ester **41**. This boronic ester then chelates to the oxirane moiety of the donor, forming a boronate complex, in which the acceptor opens the epoxide in a possible S_Ni mechanism to afford **42** as the intermediate.^[47] This intermediate subsequently undergoes hydrolysis/transesterification to afford the glycoside product. A similar mechanism can be drawn for borinic acid-catalyzed glycosylation.

4. Photochemical Reactions

Chemists have long utilized ultraviolet (UV) light irradiation to perform glycosylation. The light energy either cleaves the aglycone directly to activate the donor, or is harvested by a photosensitizer for further activation.^[2b,48]

In 2016, the Toshima group described a photoinduced glycosylation using Schreiner's thiourea **18** as a photoacid (Scheme 22).^[49] Energized by irradiation, compounds at excited states are more prone to heterogenous bond dissociation, leading to the enhanced acidity. Here, the group exploited the increased acidity of **18** under UV light irradiation to catalyze the glycosylation between glucosyl trichloroacetimidate **12** and pyranose acceptors. This reaction proceeded with moderate to high yields. Very recently, Zhao and Wang also demonstrated the activation of photoacids by visible light in their glycosylation protocol for 2-deoxyglycosides.^[50]

It has also been demonstrated that, under suitable conditions, glycosylation can also be performed under visible light, even without transition metal photosensitizers. In 2016, Ragains and co-workers reported the glycosylation of thioglycosides **43**.^[51] The donors underwent trifluoromethylation with Umemoto's reagent under blue light irradiation, forming sulfonium **44** as a reactive intermediate. As shown in Scheme 23, glycosylations with various acceptors produced disaccharides in moderate to good yields. Excellent β -selectivities achieved were through neighboring group participation (NGP). Similarly, Yang *et al.* demonstrated the photocatalyzed glycosylation of thiosialosides **45**, with moderate to high α -selectivities, using a combination of Ru(bpy)₃PF₆ and Umemoto's reagent (Scheme 24).^[52] Glycosylation using iridium photocatalysts has also been reported by Wever *et al.*^[53]

5. Stereoselective Glycosylation Modulators

While traditional glycosyl donors such as halides, sulfides and trichloroacetimidates remain popular among carbohydrate chemists, novel external modulators are constantly developed to improve selectivity and efficiency. In addition, chemists have begun to re-examine historical donors and realize their potentials in synthesis. In all cases these studies aim to provide a selective, reagent-controlled glycosylation with a general scope.

5.1. Amide/Imide Modulators

In 2011, Mong and co-workers revitalized the idea of using dimethylformamide (DMF) as an α -selective glycosylation modulator.^[54] While the use of dialkylamides to effect an α -selectivity was first described by Koto *et al.* in the early 1980s,^[55] Mong's group were the first to systematically exploit the nucleophilicity of DMF to control stereoselectivity of glycosylation, and extensively characterized the imidinium intermediates (Scheme 25). In their proposed mechanism, thioglycosides **46** are activated with NIS/TMSOTf and react with DMF to produce a reactive imidinium intermediate. The more stable α -imidinium was observed by NMR spectroscopy. The authors proposed that this species exists in equilibrium with the more reactive β -imidinium (not detected by NMR in this study, but is detectable when disarmed donors are used^[56]), which reacts in an S_N2-like fashion to afford α -linked products. Nevertheless, this α -selectivity can be overridden by NGP at the C2 position.^[56a] While DMF usually provides the best results, other amides may also be used. For example, the addition of excess *N*-formylmorpholine effectively facilitated the α -glycosylation of 2-azido-2-deoxyglycosyl donors.^[56b]

Similarly, Codée and co-workers reported high α -selectivity in amide-modulated glycosylation of glucosyl donors.^[57] In addition to thioglucoside donors, they also demonstrated that the glycosylations of glucosyl *N*-phenyl trifluoroacetimidates, modulated by DMF, achieve excellent α -selectivities for glucosyl secondary acceptors (An example, with donor **47** and acceptor **48**, is shown in Scheme 26). While poor selectivities are observed for the more reactive primary acceptors, they are improved when phosphine oxides are used as the modulators (vide infra).

The Demchenko group described an interesting chemistry of 3,3-difluoro-3*H*-indol-2-yl (OFox) imide donor in 2014. This imide is structurally similar to the *O*-benzoxazolyl "OBox"-imide, which was investigated by the same group in 2013 (Figure 2).^[58] Despite

the structural similarity, glycosylations of OFox-imidates are more selective; thus, high β -selectivities are observed for perbenzylated glucosyl OFox-imidate **50**, while α -selective glycosylations are achieved by the use of super-disarmed donor **51** (Scheme 27).^[59] More importantly, they also demonstrated that this glycosylation can be performed with catalytic amount of HOFox, the parent lactam of OFoximide.^[59a,60] An example is depicted in Scheme 28: perbenzylated thioglucoside **52** is first converted to glucosyl bromide **53** as a precursor. The bromide reacts in situ with HOFox to produce imidate **54**, which undergoes glycosylation with the acceptor to afford the product. The yield is similar to the stoichiometric imidate method, though the stereoselectivity decreases.

5.2. Phosphine Oxide Modulators

Stereoselective glycosylation that involves the possible inter-mediacy of a phosphonium halide intermediate was first introduced by the Mukaiyama laboratory in 2003.^[61] Codée and co-workers applied this strategy to rescue the poor selectivity of the glycosylation between perbenzylated glucosyl donors and primary glucosyl acceptors (Scheme 29).^[62] Here, the addition of excess triphenylphosphine oxide gives the best results in terms of stereoselectivity. In their mechanistic studies, the author also discovered the necessity of iodide for stereo-chemical control, which is consistent with the observation by the Mukaiyama group.^[61] Hence, they proposed the involvement of glycosyl phosphonium iodide **55** as the key intermediate, though direct observation of **55** was not provided.

Together with the DMF-modulated glycosylation with secondary acceptors, Codée's group successfully synthesized a *Mycobacterium tuberculosis* derived branched nonasaccharide.^[57] Very recently, a phosphonium-modulated glycosylation was also reported by Walczak's group, which achieved high α -selectivity with arabinose donors.^[62]

5.3. Sulfonate Modulators

The chemistry of glycosyl sulfonates was pioneered by Helferich and Gootz in 1929,^[63] and was investigated by the Schuerch group and Koto *et al.* in the 1970s and 80s.^[55b,64] By the turn of century, there was a renewed interest in glycosyl sulfonate chemistry after the discovery of stereoselective β -mannosylation of mannosyl triflates by Crich and co-workers, which remains one of the few reliable protocols for the construction of this challenging linkage.^[65] This triflate-modulated glycosylation was further developed by Crich's group^[66] as well as Gin's group,^[67] and the intermediacy of the glycosyl triflates were unambiguously confirmed by NMR characterization and mechanistic studies.

More recently, the Bennett group extended the sulfonate-modulated glycosylation to the synthesis of 2-deoxyglycosides by employing the more stable tosylates. In 2014, the group reported the β -selective dehydrative glycosylation of 2-deoxy sugars (Scheme 30).^[68] This protocol is an improvement of their previously reported glycosylation mediated by *N*-tosylimidazole.^[69] In this glycosylation, α -glycosyl tosylates are generated from hemiacetal donors **58**, which then react in situ with alkoxide acceptors to afford β -glycosides exclusively. Based on NMR studies, in which the quantitative formation of α -glycosyl tosylate is observed, the authors proposed a likely S_N2 pathway for this glycosylation. More

recently, this group has shown that the less expensive and more stable tosyl chloride is also a competent promoter in this reaction.^[70]

5.4. Miscellaneous Modulators

In 2016, Bennett and co-workers described the use of cyclopropenium cations as α -selective modulators in the glycosylation of 2-deoxyglycosides (Scheme 31).^[71] This dehydrative glycosylation, which is mediated by cyclopropenthione **59** and oxalyl bromide, is an improved version of their previously reported cyclopropenium/halide-mediated glycosylation,^[72] and is highly α -selective for a broad scope of 2,6-deoxy sugar donors. While the exact nature of the active intermediate remains to be determined, the authors suggest that this glycosylation proceeds via an S_N2 -like pathway, as indicated by the similar results obtained when *ent*-**60** was employed as the donor.

6. Conclusion

Chemical glycosylation is a promising method to produce large quantities of complex oligosaccharides with high purity. As the development of glycoscience hastens, the demand of stereo-selective protocols with general reaction scopes will only increase in the future.

In this focus review, we have summarized the latest trends in the advance of stereoselective glycosylation in the last decade. Organocatalysis and metal catalysis allow glycosylations to be performed under milder conditions and improve selectivity; however, these approaches frequently require the use of labile donors. The synthesis of difficult glycosides, such as 2-deoxy sugars and 1,2-*cis* glycosides, has become more facile through the development of new glycosyl modulators, which utilize stable donors such as thioglycosides and hemiacetals in the reaction. Furthermore, in line with other areas of organic synthesis, the application of photochemical energy, especially that from visible light, to facilitate glycosylation is also gaining in popularity. This may open new possibilities for selective synthesis of sugars.

Notably, modern research in glycosylation chemistry is aided by comprehensive mechanistic and computational studies. Lessons learned from these studies can provide invaluable insight for chemists who wish to further fine-tune the selectivity of glycosylation. These studies had in turn led to an increased reliance on reagent and catalyst controls to achieve predictable S_N2 -like reactivity for a broad scope of sugars. We can reasonably expect that mechanistic studies will become indispensable in the future development of selective glycosylation. Thus, while significant work needs to be done before a truly universal glycosylation protocol will be developed, the future of this exciting field looks very bright.

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Biographies

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Figure 1.
Other alkynyl donors employed by Hotha's group.

OBox-imidate **OFox-imidate**

Figure 2.
Demchenko's OBox- and OFox-imidates.

Proposed mechanism:

Scheme 1.
First gold(III)-catalyzed glycosylation

Scheme 2. Yu's gold(I)-catalyzed glycosylation of glycosyl α -alkynylbenzoates.

Scheme 3.

Proposed mechanism of gold(I)-catalyzed glycosylation.

Scheme 4.

Zhu's gold-catalyzed glycosylation of thioglycosides.

Proposed transition state:

Scheme 5.
Peng and Schmidt's gold-catalyzed glycosylation of trichloroacetimidates.

Scheme 6.
Pd(II)-catalyzed glycosylation of trichloroacetimidates.

Scheme 7.
Ni(II)-catalyzed glycosylation of trichloroacetimidates.

Scheme 8.
Oxidative glycosylation of glycosyl stannanes.

Scheme 9.

Schmidt's glycosylation by thiourea-Brønsted acid dual catalyst.

Scheme 10.

Ye's urea-catalyzed glycosylation of glycosyl chlorides.

Scheme 12.
Loh's glycosylation of strained furanosyl donors.

Scheme 13.

Fairbanks's glycosylation catalyzed by chiral BINOL phosphoric acid.

26: $R^1 = \text{Et}$, $R^2 = \text{H}$, $R^3 = \text{Me}$

27: $R^1 = \text{Me}$, $R^2 = \text{OH}$, $R^3 = \text{CH}_2\text{SPh}$

$\text{Ar} = 3,5\text{-F-Ph}$
(R)-30

Scheme 14.

Nagorny's glycosylation catalyzed by chiral BINOL phosphoric acid.

Formation of adduct:

Proposed transition state:

Scheme 15.

Glycosylation of glycosyl trichloroacetimidate catalyzed by boron catalysts.

Scheme 16.

Taylor's glycosylation of glycosyl halides catalyzed by borinic acid.

PMP:

1,2,2,6,6-
pentamethylpiperidine **34****Scheme 17.**

Borinic acid-catalyzed glycosylation of glycosyl mesylates.

Scheme 18.

1,2-*cis* glycosylation of anhydroglycosides **32** with boronic esters.

Scheme 19.1,2-*cis* glycosylation of anhydroglycosides **34** with borinic esters.

Scheme 20.

1,2-*cis* glycosylation of anhydroglycosides with boronic esters generated from unprotected sugars.

Scheme 21. Proposed mechanism of boronic acid-catalyzed 1,2-*cis* glycosylation

Scheme 22.
Toshima's photoacid glycosylation.

Scheme 23.
Ragains' photoredox-catalysed glycosylation.

Scheme 24.
Photocatalyzed glycosylation of thiosialosides.

Scheme 25.
Mong's DMF-modulated glycosylations.

Scheme 26.

Codée's glycosylations of glucosyl donor and acceptor.

Scheme 27.
Glycosylations of OFox imidate donors.

Scheme 28.

Regenerative glycosylations of perbenzylated glucosyl OFox imidate.

Scheme 29.

Phosphonium-modulated glycosylation of perbenzylated glucosyl donor and acceptor.

Scheme 30.

Bennett's tosylated-modulated glycosylation of 2-deoxy sugars.

Scheme 31.

Bennett's α-selective glycosylation of 2-deoxy sugars.