



Review

# ZnI<sub>2</sub>-Mediated *cis*-Glycosylations of Various Constrained Glycosyl Donors: Recent Advances in *cis*-Selective Glycosylations

 Akihiro Ishiwata <sup>1,\*</sup> , Xuemei Zhong <sup>2,3</sup>, Katsunori Tanaka <sup>1,4</sup>, Yukishige Ito <sup>1,5</sup> and Feiqing Ding <sup>2,\*</sup> 
<sup>1</sup> RIKEN Cluster for Pioneering Research, Wako 351-0198, Japan; kotzenori@riken.jp (K.T.); yukito@chem.sci.osaka-u.ac.jp (Y.I.)

<sup>2</sup> School of Pharmaceutical Sciences (Shenzhen), Shenzhen Campus of Sun Yat-sen University, Shenzhen 518107, China; zhongxm36@mail2.sysu.edu.cn

<sup>3</sup> Medical College, Shaoguan University, Shaoguan 512026, China

<sup>4</sup> Department of Chemical Science and Engineering, Tokyo Institute of Technology, Tokyo 152-8552, Japan

<sup>5</sup> Graduate School of Science, Osaka University, Toyonaka 560-0043, Japan

\* Correspondence: aishiwa@riken.jp (A.I.); dingfq3@mail.sysu.edu.cn (F.D.)

**Abstract:** An efficient and versatile glycosylation methodology is crucial for the systematic synthesis of oligosaccharides and glycoconjugates. A direct intermolecular and an indirect intramolecular methodology have been developed, and the former can be applied to the synthesis of medium-to-long-chain glycans like that of nucleotides and peptides. The development of a generally applicable approach for the stereoselective construction of glycosidic bonds remains a major challenge, especially for the synthesis of 1,2-*cis* glycosides such as  $\beta$ -mannosides,  $\beta$ -L-rhamnosides, and  $\beta$ -D-arabinofuranosides with equatorial glycosidic bonds as well as  $\alpha$ -D-glucosides with axial ones. This review introduces the direct formation of *cis*-glycosides using ZnI<sub>2</sub>-mediated *cis*-glycosylations of various constrained glycosyl donors, as well as the recent advances in the development of stereoselective *cis*-glycosylations.

**Keywords:** 1,2-*cis*-glycoside; stereoselective *cis*-glycosylation; oligosaccharides; ZnI<sub>2</sub>; constrained glycosyl donors



**Citation:** Ishiwata, A.; Zhong, X.; Tanaka, K.; Ito, Y.; Ding, F. ZnI<sub>2</sub>-Mediated *cis*-Glycosylations of Various Constrained Glycosyl Donors: Recent Advances in *cis*-Selective Glycosylations. *Molecules* **2024**, *29*, 4710. <https://doi.org/10.3390/molecules29194710>

Academic Editor: Juan M. Benito

Received: 23 July 2024

Revised: 11 September 2024

Accepted: 1 October 2024

Published: 4 October 2024

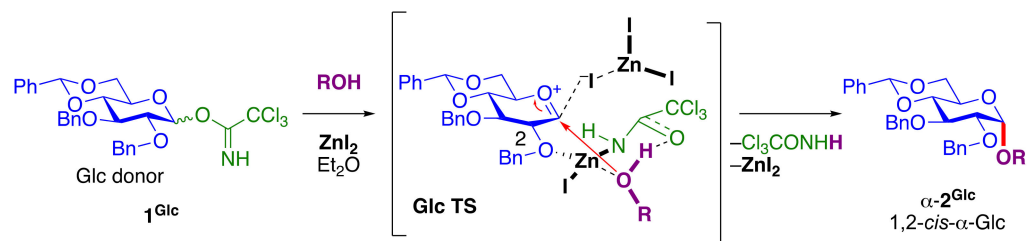


**Copyright:** © 2024 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

## 1. Introduction

Stereoselective 1,2-*cis* O-glycosylation is one of the most essential issues in synthetic carbohydrate chemistry for the construction of various glycans with biological functions [1–9]. The preparation of 1,2-*trans* O-glycoside became possible using a stereoselective glycosylation method based on the effect of neighboring group participation from acyl carbonyl functionality at the 2-position of the glycosyl donor [10–18]. By the activation of the glycosyl donor, the kinetically favored *cis*-participation of the acyl group at the 2-position of the donor to the anomeric carbon at the 1-position occurs, followed by the nucleophilic attack of the acceptor from the opposite side to afford the 1,2-*trans* O-glycoside stereoselectively. Compared to the 1,2-*trans* O-glycosylations, the highly stereoselective synthesis of 1,2-*cis* glycosides is far less straightforward. The stereochemical outcome of a chemical glycosylation reaction is influenced by multiple chemical and environmental factors, including the structure of the glycosyl donor, the type and position of protecting groups installed on the donor, the nucleophilicity of the acceptor, the solvent in which the reaction is performed, the concentration of substrates, and the reaction temperature, and is determined by the specific combination of these factors [19–29]. The 1,2-*cis*-configured O-glycosidic linkages, such as  $\alpha$ -glucopyranoside,  $\beta$ -mannopyranoside,  $\beta$ -L-rhamnopyranoside,  $\beta$ -D-arabinofuranosides, and 2-azido-2-deoxy- $\alpha$ -D-glucopyranoside, are found in natural glycans, especially in glycoconjugates (glycoproteins, glycolipids, proteoglycans, and microbial polysaccharides) and glycoside natural products [30–35]. Chemical glycosylation is a useful method to

obtain these glycosidic linkages as the alternative way of isolation from natural sources. However, the strictly controlled formation of these 1,2-*cis* glycosides is generally difficult, and the key factors controlling the stereoselectivity of glycosylation are not fully understood. This review introduces a direct formation of *cis* glycosides using recently developed ZnI<sub>2</sub>-mediated *cis* glycosylations of various constrained glycosyl donors [36–41] (Figure 1).



**Figure 1.** ZnI<sub>2</sub>-mediated 1,2-*cis*- $\alpha$ -D-glucopyranosylation. TS was obtained by DFT calculations (Section 2.8.1).

#### Recent Development of Stereoselective *cis* Glycosylations

In recent years, further progress has been made in the development of stereoselective *O*-glycosylation as well as orthogonal techniques using various methods [42,43] as stereoselective *C*-glycosylations have been extensively developed in recent publications [44–62]. Glycosyl iodide as an intermediate generated from glycosyl 2,2,2-trifluoro-*N*-phenylacetimidate [CF<sub>3</sub>C(=NPh)–O–] (**3**) with trimethylsilyl iodide (TMSI) could be complexed with triphenylphosphine oxide (Ph<sub>3</sub>P=O) [63] to afford *cis* glycosides (**6**,  $\alpha$ : $\beta$  = >20:1) through the direct interaction of Ph<sub>3</sub>P=O with the C1 position (4→5) [64,65] (Figure 2A). Glycosyl bromide generated from thioglycoside with Br<sub>2</sub> in the presence of silver trifluoromethanesulfonate (AgOTf) and 2,4,6-collidine afforded 1,2-*cis* glycoside which has been applied to a synthesis of a repeating unit of *Bacteroides fragilis* zwitterionic polysaccharide A1 [66]. Stereoselective glycosylations from 3,5-dimethyl-4-(2'-phenylethynylphenyl)phenyl glycoside (**7**) under *N*-iodosuccinimide (NIS)–trifluoromethanesulfonic acid (TfOH) conditions [67] (Figure 2B), as well as the Pd- or Cu-catalyzed activation system of donors through the cyclization of some aglycons [68,69], have been developed. For the synthesis of heparin pentasaccharide, [3+2] fragment coupling using the methodology of [67] has been applied to give the  $\alpha$ -selective formation of the pentasaccharide (**8**). The glycosylation of **7** proceeds via an unprecedented dearomative cyclization mechanism initiated by the activation of the triple bond with I<sup>+</sup>, resulting in side product **9**. Benzylthio/seleno glycosides (**10**) with an activation system using benzyne (**12**), generated in situ from *o*-TMS-phenol (**11**) with trifluoromethanesulphonate, KF, and 18-Crown-6 [70] (Figure 2C), have also been developed. The benzyne promotes the activation of the donor as well as the acceptor (ROH) through proposed intermediates (**14**→**16**) for an effective S<sub>N</sub>2 reaction. Gluco-, galacto-, and mannosyl as well as 2-deoxyglucosyl donors can be applied to afford S<sub>N</sub>2 products (**13**). Phenylseleno (PhSe-) 2-azidoglycosides (**17**) could be converted to 1,2-*cis* glycosides (**19**) with *N*-iodosuccinimide in the presence of a catalytic amount of Cu(OTf)<sub>2</sub> and *N,N*-bis-[(2,4-trifluoromethyl)phenyl]thiourea (**18**) [71] (Figure 2D). The reagent combination forming the metal–organocatalyst complex (**20**) can activate selenoglycoside by the liberation of iodonium ion. The resultant  $\alpha$ -selenonium salt analog ( $\alpha$ -**21**) is converted to  $\beta$ -isomer ( $\beta$ -**21**), which seems to be the key intermediate for *cis* glycosylation without neighboring group participation.

Recent developments were reported about the effective participation of solvents [72–77] and additives [78,79] as well as intramolecularly participating groups [79–83] to induce *cis* glycosides. The participation of special functionalities such as the 2-(diphenylphosphino)acetyl group (DPPA) with an acceptor has been shown to afford the *cis* glycoside (**24**) effectively through a participating intermediate (**23**) of the phosphine oxide (–Ph<sub>2</sub>P=O) functionality of donor (**22**) with the acceptor (ROH), as developed by Li [84,85] (Figure 2E).

By the action of  $M^{4+}$  Lewis acids such as  $SnCl_4$  and  $TiCl_4$ , the glycosylation of a 2,3,4,6-tetra-*O*-benzyl- $\alpha$ -D-glucopyranosyl trichloroacetimidate (**25**) afforded  $\alpha$ - and  $\beta$ -D-glucopyranoside (**27**) depending on the amount of  $M^{4+}$  (Figure 2F) [86]. When a catalytic amount of  $M^{4+}$  was used,  $\beta$ -D-glucopyranoside ( $\beta$ -**27**) was obtained predominantly through a proposed intermediate (**26**). The use of 3.0 equiv. of  $M^{4+}$  resulted in the formation of  $\alpha$ -D-glucopyranoside ( $\alpha$ -**27**) in one-pot from the donor (**25**). Since the initially obtained  $\beta$ -D-glucopyranoside ( $\beta$ -**27**) was isomerized to  $\alpha$ -D-glucopyranoside ( $\alpha$ -**27**) under  $M^{4+}$  conditions, the excess  $M^{4+}$  accelerated the anomerization through a proposed endo-cleavage intermediate (**28**), followed by cyclization to thermodynamically more stable  $\alpha$ -glucoside ( $\alpha$ -**27**). As reported by Santrsa et al., the  $ZnBF_4$ -catalyzed glycosylation of  $\alpha$ -imidate donor without 4,6-*O*-tethered structure in  $CH_2Cl_2$  at  $-78^\circ C$  also afforded the  $\beta$ -glycoside of various donor moieties, including D-Glcp, and D-Galp, through  $S_N2$  reaction without isomerization [87].

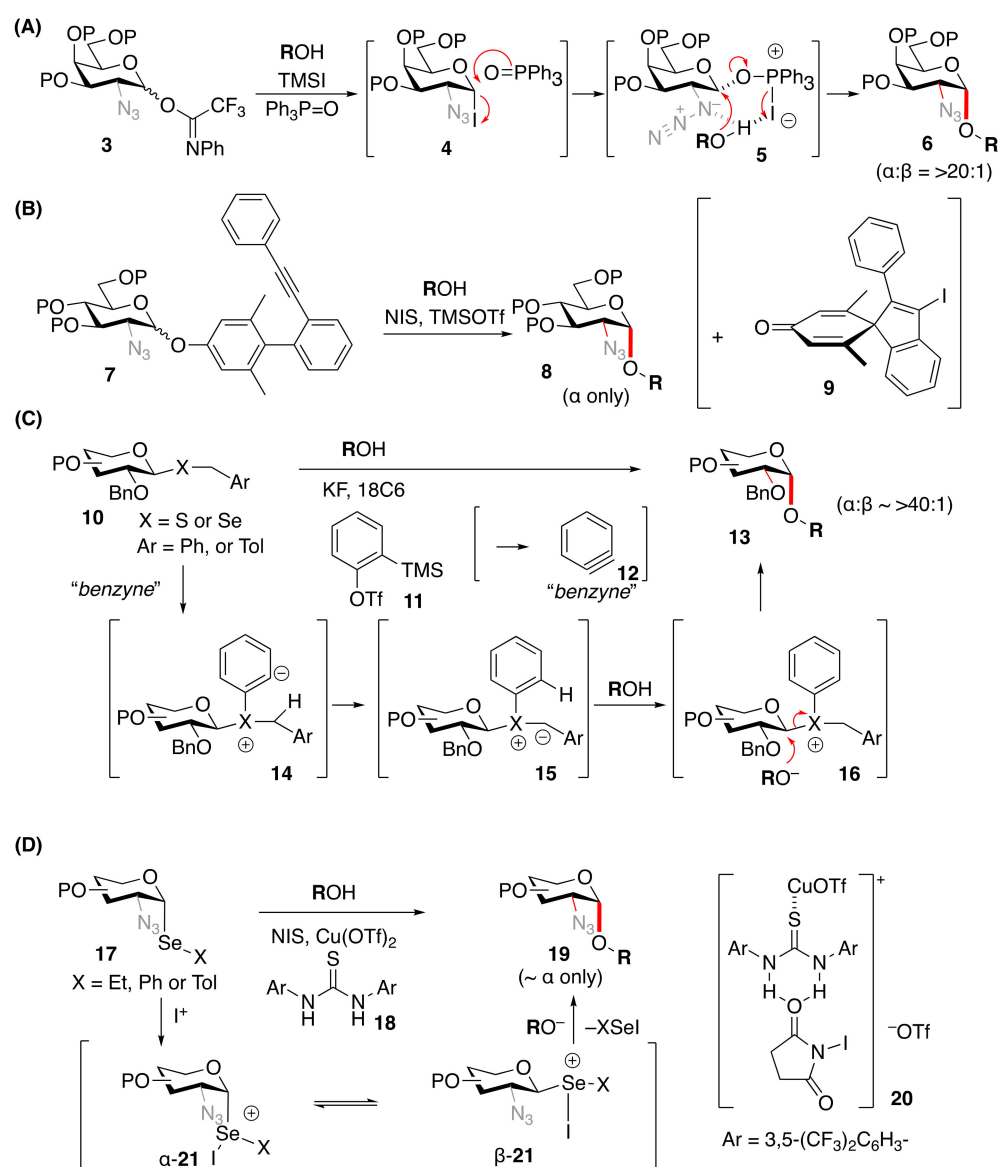
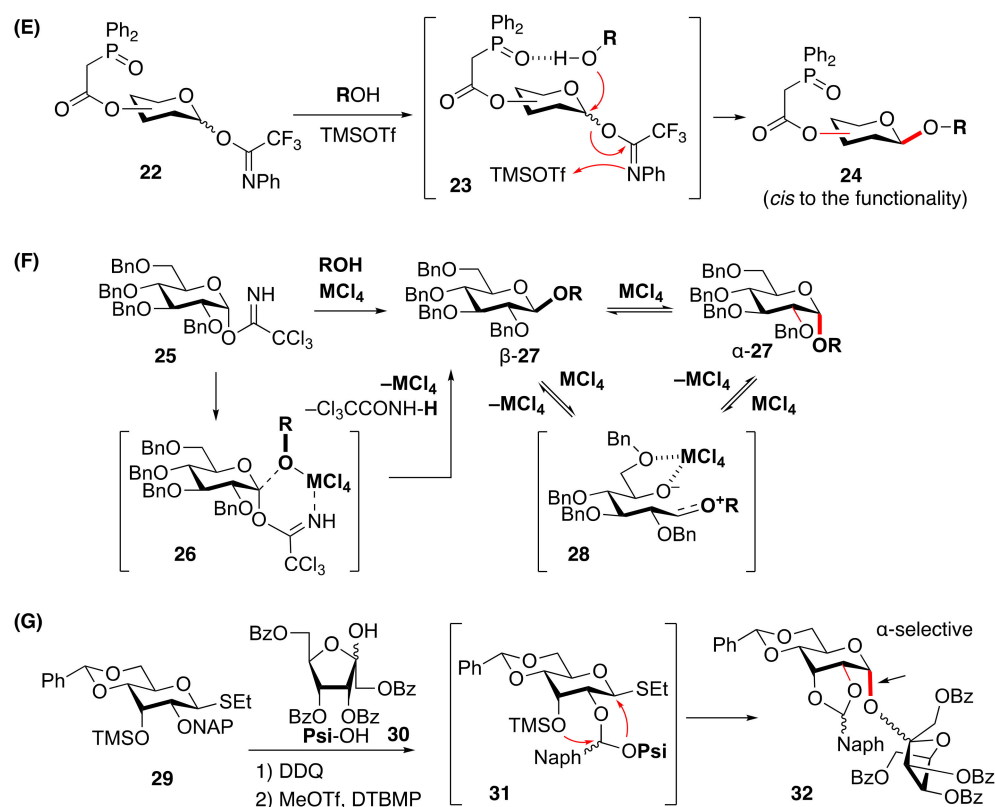


Figure 2. Cont.



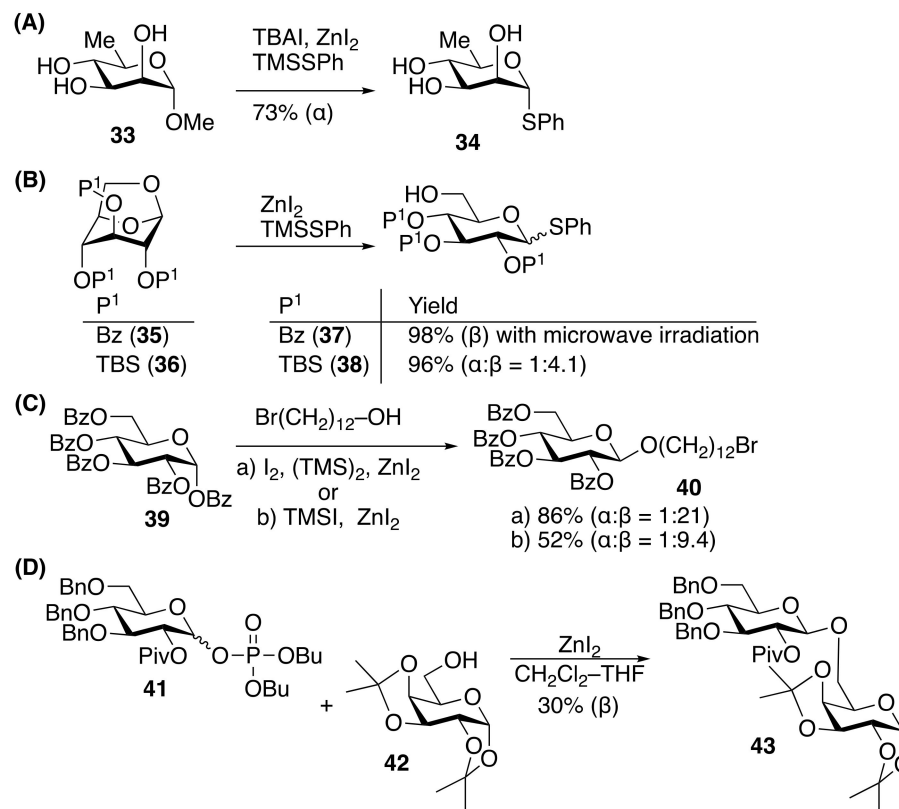
**Figure 2.** Recent progress on *cis* glycosylations. (A) Activation of glycosyl 2,2,2-trifluoro-*N*-phenylacetimidate by TMSI in the presence of  $Ph_3P=O$ ; (B) 3,5-Dimethyl-4-(2'-phenylethynylphenyl)-phenyl glycoside by NIS–TfOH; (C) activation of thio- and seleno-glycosides by using benzyne; (D) activation of seleno glycosides by using NIS– $Cu(OTf)_2$ –thiourea; (E) the remote participation of 2-(diphenylphosphinoyl)acetyl group; (F)  $SnCl_4$  or  $TiCl_4$ –mediated stereocontrolled one-pot glycosylations. TSs (**26**, **28**) were obtained by DFT calculations (Section 2.8.3). (G) 2-Naphthylmethyl ether-mediated intramolecular aglycon delivery to  $\alpha$ -D-altroside derivative with 1-OH of D-psicose acceptor. Red arrows and bonds indicate transfer of electron pairs and *cis*-linkages, respectively. Abbreviations: DDQ: 2,3-dichloro-5,6-dicyano-1,4-benzoquinone; MeOTf: methyl trifluoromethanesulfonate; DTBMP: 2,6-di-*t*-butyl-4-methylpyridine.

The combination of the donor, the leaving groups, and the reagent as a promoter [24,88] should be optimized. Recent progress on the orthogonal [89] one-pot procedure [90–97] using stereoselective glycosylation methods in combination with orthogonal activation systems [64,98–104] has afforded oligosaccharides containing 1,2-*cis* glycosidic linkages. Alternatively, 1,2-*cis* glycosylation using the naphthyl methyl ether-mediated intermolecular aglycon delivery (IAD) method [1,105–117] was applied to the selective 1,2-*cis*  $\alpha$ -D-allopyranosylation using the D-allopyranosyl donor (**29**) with the 1,3,4,6-tetra-*O*-benzoyl-D-psicofuranose acceptor (**30**) through a mixed acetal intermediate (**31**) [118], which is the first example of the synthesis of non-reducing disaccharides (**32**) comprising only rare D-sugars by IAD using protected ketose (Figure 2G).

## 2. $ZnI_2$ -Mediated Glycosylations

Zinc iodide ( $ZnI_2$ ) has been used as a catalyst in various organic reactions [119] such as the Simmons–Smith cyclopropanation [120]. In the field of carbohydrate chemistry, both methyl glycoside and 1-*O*-benzoate have been converted to thioglycoside by the action of  $ZnI_2$ , tetra-*n*-butyl ammonium iodide (TBAI), and alkylthiotrimethylsililane (TMSSR) [121–124], which are useful transformations for obtaining the key stable intermediate for glycosidic bond formation (Figure 3A,B). Methyl D-rhamnopyranoside (**33**) was treated with TMSSPh in the presence of  $ZnI_2$  and TBAI to give  $\alpha$ -thioglycoside

(34) in 73% [122] (Figure 3A). Benzoyl (Bz)- or tri-*t*-butyldimethylsilyl (TBS)-protected 1,6-anhydroglucose derivative (35, 36) could be used as the substrate to obtain thioglycoside (37, 38) by treatment under TMSSPh in the presence of  $ZnI_2$  without TBAI, respectively (Figure 3B).



**Figure 3.** Activation of glycosyl benzoate and phosphate by  $ZnI_2$ . (A) Glycosyl benzoate with TMSSR in the presence of TBAI for thioglycoside synthesis; (B) 1,6-Anhydroglucose derivative with TMSSR for thioglycoside synthesis; (C) Glycosyl benzoate with TMSI and acceptor for the synthesis of glycoside; (D) Glycosyl phosphate with  $ZnI_2$  and acceptor for the synthesis of glycoside.

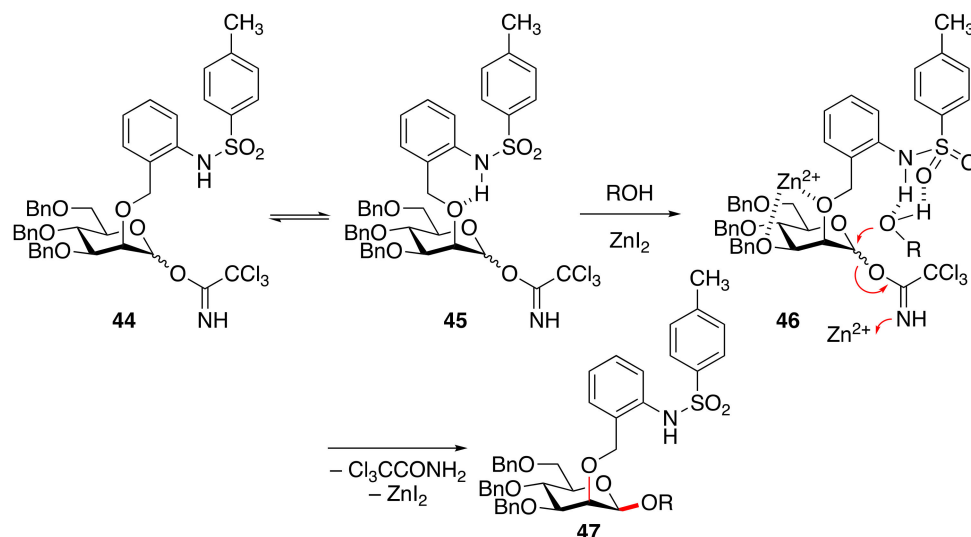
1-*O*-Benzoate and phosphate-protected glycosyl donors (39, 41) could be used for *O*-glycosylation activated by  $ZnI_2$  with  $I_2$ -(TMS)<sub>2</sub> [125,126] or TMSI [125,127] (Figure 3C), and  $ZnI_2$  [128] (Figure 3D), respectively, with glycosyl iodide as the intermediate [129]. The neighboring group participation effect of the 2-*O*-Bz group resulted in the predominant formation of 1,2-*trans* glycoside (40) (Figure 3C) [125]. During the screening of 1,2-*trans* glycosylation using dibutyl 2-*O*-pivaloyl-3,4,6-tri-*O*-benzyl-*D*-glucopyranosyl phosphate (41) reported by Seeberger and coworkers [128],  $ZnI_2$  in  $CH_2Cl_2$ -THF was indicated to afford β-glucoside (43) in 30% yield via the neighboring group participation of the 2-*O*-pivaloyl group, followed by the nucleophilic attack of an acceptor (42) (Figure 3D).

### 2.1. *cis*-Selective Glycosylations by the Action of $ZnI_2$

The 1-*O*-trichloroacetimidate moiety [7,130–133] can be used as a leaving group of a glycosyl donor by the action of a cheap and mild Lewis acid, such as  $ZnI_2$  for *cis* glycosylation [1,89,134,135], and  $Zn(BF_4)_2$  [136],  $B(C_6F_5)_3$  [137] and pyrylium salt [138] for 1,2-*trans* glycosylation. However, optimizations for the stereoselective construction of *cis* glycosides should be carried out. The conformational strain on the donor moiety caused by cyclic protective groups [139] is one of the important factors for *cis*-glycosylation [19–21]. There have been many recent advances in the development of  $ZnI_2$ -mediated *O*-glycosylation reactions especially for *cis*-selective glycosylations, including α-*D*-glucoside, β-*D*-mannoside, β-*D*-rhamnoside, β-*D*-galactoside, and 2-azido-2-deoxy-α-*D*-glucoside formation.

### 2.2. 1,2-*cis* Mannosylation Using C-2-*o*-TsNHbenzyl Ether (TAB)

When trichloroacetimidates are used as a convenient and common leaving group of the bimodal donor equipped with C-2-*o*-TsNHbenzyl ether (TAB) groups for gluco- [140,141], galacto- [140], and manno-sides [36], the examination of activators on the mannosylation suggested the proposed unique donor activation pathway with coordination to the donor (44 $\rightleftharpoons$ 45) by ZnI<sub>2</sub> for the stereo-direction toward 1,2-*cis* glycosidic bond formation [36] (Figure 4). Zn<sup>2+</sup> not only activates the donor leaving group but also coordinates to oxygens at the 2- and 3-positions to induce the effective interaction of TAB with an incoming nucleophile during 1,2-*cis*- $\beta$ -mannosylation (44 $\rightarrow$ 47).



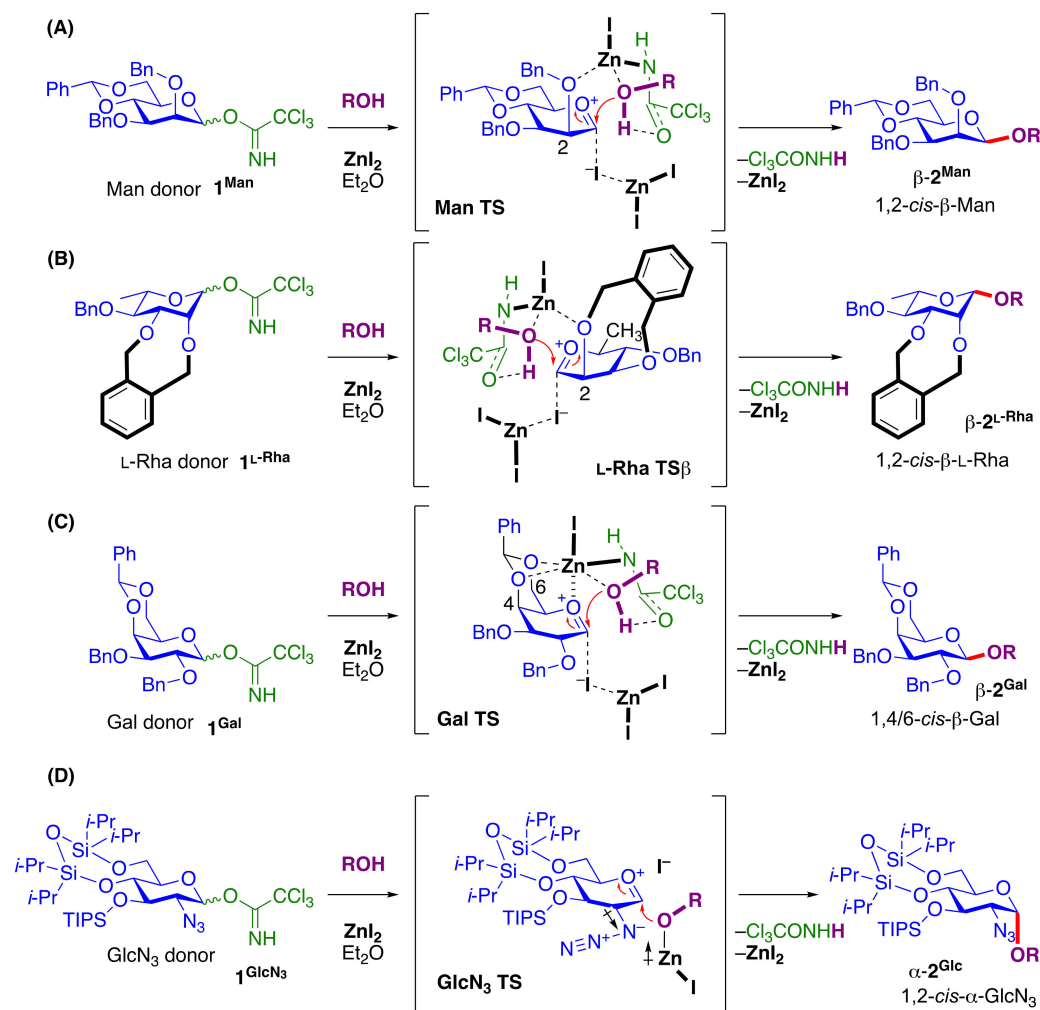
**Figure 4.** C-2-*o*-TsNHbenzyl ether (TAB)-protected mannosyl donor (44) under ZnI<sub>2</sub> activation conditions for 1,2-*cis*- $\beta$ -mannosylation.

### 2.3. ZnI<sub>2</sub>-Mediated 1,2-*cis* $\alpha$ -Glucosylation

Easily accessible and common 4,6-*O*-tethered glucosyl donors (**1**<sup>Glc</sup>) were found to be useful for highly stereoselective 1,2-*cis*  $\alpha$ -glucosylation mediated by ZnI<sub>2</sub> [37] (Figure 1). The 4,6-*O*-tethering constrains a pyranose ring of the glycosyl donors for stereoselective 1,2-*cis* glycosylation [19]. The versatility and effectiveness of the  $\alpha$ -glucosylation strategy was demonstrated successfully with various acceptors. This approach demonstrates the feasibility of the modular synthesis of  $\alpha$ -glucans with both linear and branched backbone structures. DFT calculations (vide infra) indicated that both the activation of trichloroacetimidate and the coordination between 2-*O* in the donor moiety and the hydroxy group in the acceptor could be carried out by Zn<sup>2+</sup>, and that 1,2-*cis* selective glycosylation proceeded through the proposed transition state (TS) structure (**Glc TS**) after activation to afford  $\alpha$ -glucoside ( $\alpha$ -**2**<sup>Glc</sup>).

### 2.4. ZnI<sub>2</sub>-Mediated 1,2-*cis* $\beta$ -D-Mannopyranosylation and $\beta$ -L-Rhamnopyranosylation

The ZnI<sub>2</sub>-mediated method could be applied to the synthesis of 1,2-*cis*  $\beta$ -glycosides such as  $\beta$ -D-mannopyranosides ( $\beta$ -**2**<sup>Man</sup>) [38] (Figure 5A) and  $\beta$ -L-rhamnopyranosides ( $\beta$ -**2**<sup>L-Rha</sup>) [39] which are 6-deoxy- $\beta$ -L-mannopyranosides [142] (Figure 5B). The 1,2-*cis*  $\beta$ -manno- and  $\beta$ -L-rhamno-sylation mediated by ZnI<sub>2</sub> employed easily accessible 4,6-*O*-tethered mannosyl and L-rhamnosyl trichloroacetimidate donors (**1**<sup>Man</sup> and **1**<sup>L-Rha</sup>). The versatility and effectiveness of this strategy were demonstrated with successful  $\beta$ -mannosylation of a wide variety of alcohol acceptors, including complex natural products, amino acids, and glycosides.



**Figure 5.** ZnI<sub>2</sub>-mediated *cis*-glycosylations. (A) 1,2-*cis* β-D-mannopyranosylation; (B) 1,2-*cis* β-L-rhamnopyranosylation; (C) 1,4/6-*cis* β-D-galactopyranosylation; (D) 1,2-*cis* 2-azido-2-deoxy-α-D-glucopyranosylation. TSs were obtained by DFT calculations (Sections 2.8.1 and 2.8.2).

Through iterative ZnI<sub>2</sub>-mediated mannosylation with a chitobiosyl azide acceptor, followed by the site-selective deprotection of the mannosylation product, this novel methodology enables the modular synthesis of a key intermediate trisaccharide with a β-D-Man-(1→4)-β-D-GlcNAc-(1→4)-β-D-GlcNAc linkage for *N*-glycan synthesis [38]. The core repeating tetrasaccharide unit with an α-L-Rhap-(1→2)-β-D-Galp-(1→4)-β-L-Rhap-(1→4)-α-D-Glcp linkage of the *Streptococcus pneumoniae* 23F capsule polysaccharide has been successfully synthesized using ZnI<sub>2</sub>-mediated 1,2-*cis* β-L-rhamnopyranosylation with a convergent [2 + 2] strategy [39].

DFT calculations also suggested similar activation and coordination via the key coordinated-intermediates (**Man TS** and **L-Rha TS**) in the aforementioned α-glucosylation. Theoretical investigations using DFT calculations (*vide infra*) delved into the mechanistic details of this β-selective glycosylation and elucidated the essential roles of two zinc cations as the activating agent of the donor and the principal mediator of the *cis*-directing intermolecular interaction [38,39].

### 2.5. ZnI<sub>2</sub>-Mediated 1,4/6-*cis* β-D-Galactopyranosylation

Although the ZnI<sub>2</sub>-mediated method has been applied to the synthesis of α-D-galactopyranosides, the β-anomer (β-2Gal) was obtained from the 4,6-*O*-tethered 2,3-di-*O*-benzyl-D-galactopyranosyl trichloroacetimidate donor (1Gal) in the presence of ZnI<sub>2</sub> in a 1,2-*trans* glycosylation fashion [40] (Figure 5C). The unexpected formation of

$\beta$ -D-galactopyranosides ( $\beta$ -2<sup>Gal</sup>) [143] could be explained by the favored coordination of  $Zn^{2+}$  to the conformationally fixed 4-O or 6-O of the galactopyranosyl donor instead of 2-O as in the expected cases. Suggested by DFT calculations (vide infra), the stability of the key intermediate for the stereodirection was proposed to be enhanced by the coordination of  $Zn^{2+}$  to 4-O or 6-O on the  $\beta$ -face that controlled the approach of the acceptor from the  $\beta$ -side. This  $\beta$ -D-galactopyranosylation should occur through 1,4/6-*cis* glycosylation under  $ZnI_2$  conditions via **Gal TS**. By using this  $ZnI_2$ -mediated  $\beta$ -galactosylation strategy, the tetrasaccharide fragment  $\beta$ -D-Galp-(1 $\rightarrow$ 6)-3-O-[ $\alpha$ -L-Araf-(1 $\rightarrow$ )]- $\beta$ -D-Galp-(1 $\rightarrow$ 6)- $\beta$ -D-Galp linkage of arabinogalactan, derived from the plant polysaccharide of *Stevia rebaudiana* and *Silybum marianum*, was synthesized efficiently with high stereoselectivity [40].

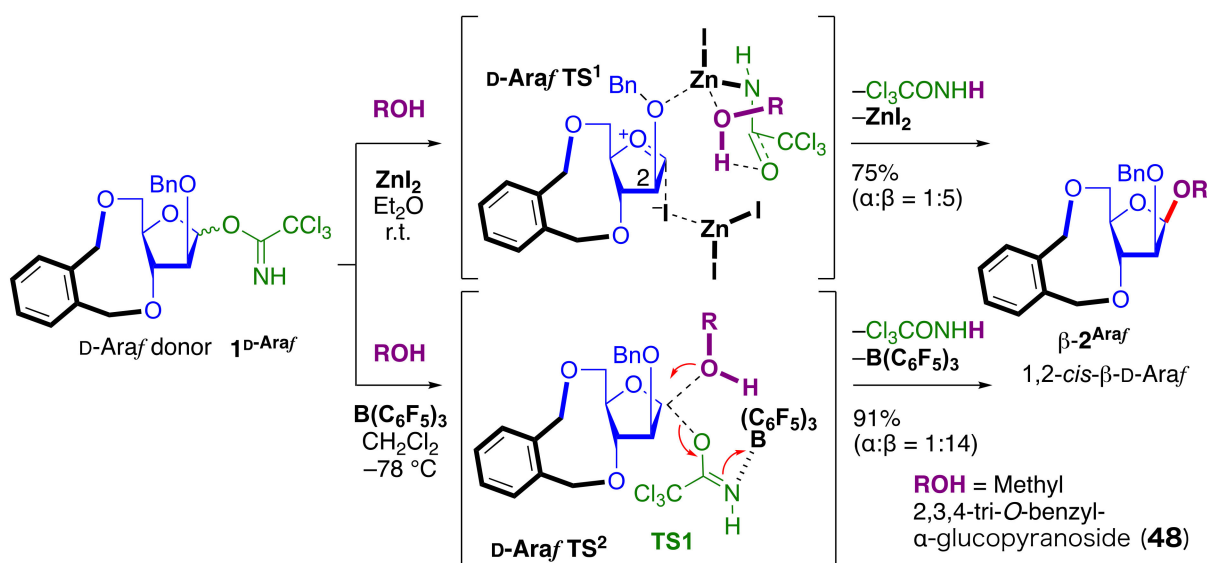
#### 2.6. $ZnI_2$ -Mediated 1,2-*cis* 2-azido-2-deoxy- $\alpha$ -D-Glucopyranosylation

The synthesis of the 1,2-*cis* 2-acetamido-2-deoxyglucoside (D-GlcNAc) core of the capsular polysaccharide (CPS) remains challenging. The tetraisopropylidisiloxane (TIPDS)-protected 2-azido-2-deoxy-D-glucosyl donor (**1<sup>GlcN<sub>3</sub></sup>**) afforded the  $\alpha$ -glycoside (**2<sup>GlcN<sub>3</sub></sup>**) ( $\alpha$ : $\beta$  = >20:1) predominantly in maximum yield [41] (Figure 5D). This approach applies to a wide acceptor substrate scope, including various aliphatic alcohols, sugar alcohols, and natural products. The reaction mechanism was explored by combined experimental variable-temperature NMR (VT-NMR) studies, mass spectrometry (MS) analysis, and DFT calculations (vide infra), and the results suggested the formation of a covalent  $\alpha$ -C1<sup>GlcN<sub>3</sub></sup>-iodide intermediate in equilibrium with a separated oxocarbenium-counter ion pair, followed by an  $S_N1$ -like  $\alpha$ -nucleophilic attack most likely from the separated ion pairs by the  $ZnI_2$ -activated acceptor complex under the influence of the 2-azido gauche effect [144] via **GlcN<sub>3</sub> TS**. The  $\alpha$ -D-GlcNAc-linked core structure of the CPS repeating fragments from *Acinetobacter baumannii* was synthesized by employing the developed reaction as the key step for constructing the 1,2-*cis* 2-azido-2-deoxy glycosidic linkage.

#### 2.7. $ZnI_2$ -Mediated 1,2-*cis* $\beta$ -D-Arabinofuranosylation

In the case of D-arabinofuranosylation using a D-arabinofuranosyl trichloroacetimidate as the donor, tris(pentafluorophenyl)borane [B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub>] conditions resulted in better 1,2-*cis* stereoselectivity compared to the  $ZnI_2$ -mediated reaction [145] (Figure 6). The reaction of D-arabinofuranosyl trichloroacetimidate (**1D-Araf**) under  $ZnI_2$  activation conditions proceeded 1,2-*cis* stereoselectively via the proposed TS structure (**D-Araf TS1**) when the donor was protected as an 8-membered 3,5-*O*-xylylene group [146–148] such as the 9-membered 3,5-*O*-tetra-*i*-propylidisiloxanylidene (TIPDS) group [149–151]. Since the 3,5-*O*-xylylene-protected donor gave higher yield, the optimization of the conditions including the promotor suggested that B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub> [142,152–155] could activate the  $\alpha$ -imidate and directly afford the glycosidic bond through an  $S_N2$ -like mechanism via **D-Araf TS2** from  $\alpha$ -D-arabinofuranosyl trichloroacetimidate at  $-78$  °C in CH<sub>2</sub>Cl<sub>2</sub>. This method was applied to the synthesis of  $\beta$ -D-Araf linkages with various acceptors including the acceptor for producing a non-reducing terminal structure of mycobacterial arabinan fragment (**2D-Araf**) [145,156].





**Figure 6.**  $B(C_6F_5)_3$ -promoted 1,2-*cis* D-arabinofuranosylations of 3,5-*O*-xylylene protected donor. TS was obtained by DFT calculations (Section 2.8.2).

## 2.8. Density Functional Theory (DFT) Calculations for $ZnI_2$ -Mediated Reactions

### 2.8.1. DFT Calculations for $ZnI_2$ -Mediated Glucosylation and Mannosylation

The TSs of each  $ZnI_2$ -mediated reaction were obtained by density functional theory (DFT) computations with Gaussian 16 software package [157] and the detailed conditions are as follows. For **GlcTS** (Figure 1) and **ManTS** (Figure 2A), structures of plausible reagents, products, and intermediates species were preoptimized at the PM6-d3 level of theory [158,159] at the gas phase, and then subjected to geometry optimization at the PBE0/def2-TZVP level of theory [160–162], with Grimme’s DFT-D3(BJ) empirical dispersion correction [163] applied to account for the dispersion interactions, and the implicit solvation model based on density (SMD) [164] applied to describe the solvent effect exerted by diethyl ether. A short intrinsic reaction coordinate scan with the local quadratic approximation [165] method and 0.1 Bohr step-size was performed on the optimized TS structures at the same level of theory for 30 steps on each side to ensure that the TS structures correspond to energy maxima along the reaction routes connecting the immediately reacting intermediates and product structures. The accurate electronic energy of the chemical species was calculated from the optimized structures with single-point calculation at the M06-2X/ma-def2-TZVPP/SMD (solvent = diethyl ether) level of theory [166–168] with an ultrafine integration grid, and the thermal energy terms associated with various thermal motions of the molecule as well as the solvation of the molecules in diethyl solvent were calculated from the frequency analysis output using Shermo [169], with scale factors [170] applied to adjust for the errors arising from the harmonic oscillation assumption. The Gibbs free energy of each chemical species was calculated as the sum of the accurate electronic energy and thermal energy terms.

### 2.8.2. DFT Calculations for $ZnI_2$ -Mediated L-Rhamnosylation, 2-azido-2-deoxy- $\alpha$ -D-Glucopyranosylation and for $B(C_6F_5)_3$ -Mediated D-Arabinofuranosylation

For **L-Rha TS**, **GlcN<sub>3</sub> TS** (Figure 5B,D) and **D-Araf TS<sup>2</sup>** (Figure 6), the geometries were optimized at the theory level of B3LYP [171,172] // BS1 (BS1 = 6-31G(d) [173,174] for main group elements and Lanl2dz [175] for Zn, Si, I, and Sn) in the gas phase. Solvation free energies were calculated using the SMD [164] solvation model (solvent = diethyl ether or DCM) under  $\omega$ B97XD [176] or M06 [177] // BS2 (BS2 = 6-311 + G\*\* [173,174] for main group elements and SDD [178] for Zn, Si, I, and Sn). The Gibbs free energy present in this paper is the sum of single-point energy at  $\omega$ B97XD [173] or M06 [174] // BS2, thermodynamic correction at B3LYP // BS1, and solvation free energy.

### 2.8.3. DFT Calculations for ZnI<sub>2</sub>-Mediated D-Galactopyranosylation

For **Gal TS** (Figure 5C), DFT computations at the TPSS/def-TZVP/SMD and diethyl ether [173–175] level of theory, with Grimme's empirical correction to account for dispersion D3(BJ) [163], were carried out.

## 3. Conclusions

For a 1,2-*trans* selective glycosylation, methodologies have been further developed using 2-(2-propylsulfinyl)benzyl 1,2-orthoester glycosides [179] activated by trifluoromethanesulfonic anhydride (Tf<sub>2</sub>O) with DTBMP, *N*-(1,1-dimethylpropargyl)carbamate by chloro[tris(2,4-di-*t*-butylphenyl)-phosphite]gold and AgOTf [180–182] and diphenyl phosphate by bis-thiourea type molecule catalyst with high site-selection [183].

There have been extremely valuable reports on the synthesis of large glycans with over 20 monosaccharide units [184] composed of pyranosides [185–192], furanosides [193–197], and both isomers [198]. Both the synthesis and the application of biosynthetic incorporation and selective labeling [199–201] of mycobacterial cell walls [202,203] related to tuberculosis [204,205] should be noted as recent advances in remodeling glycoconjugates containing *cis* glycosides.

This review summarizes recent stereoselective glycosylation methods including the very simple and efficient ZnI<sub>2</sub>-mediated *cis*-glycosylation methodology using constrained glycosyl trichloroacetimidate donors such as D-Glcp, D-Manp, L-Rhap, and 2-azido-2-deoxy-D-Glcp in a 1,2-*cis* selective manner, and D-Galp in a 1,4/6-*cis* selective manner. In addition, other findings for β-D-Araf formation using a constrained donor in the presence of B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub> instead of ZnI<sub>2</sub> as well as the synthesis of branched terminal D-arabanan hexasaccharide fragment using trichloroacetimidate donor-B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub> combination were also effective enough. These methodologies, mainly based on ZnI<sub>2</sub>-mediated *cis*-glycosylation with optimization, could be used in investigations focused on elucidating the biosynthetic pathways and function of these glycans, and conjugating them to a protein carrier for vaccine generation in the case of antigenic glycans from pathogenic bacteria. Further exploration of applications of this methodology for the synthesis of other complex oligosaccharides containing *cis* linkages is the focus of continuing investigation for synthetic carbohydrate chemists.

**Author Contributions:** Conceptualization and writing—original draft preparation, A.I. and F.D.; writing—review and editing, A.I., F.D., X.Z., K.T. and Y.I.; project administration, finalization, and revision for publication, A.I. and F.D.; supervision and funding acquisition, A.I., Y.I. and F.D. All authors have read and agreed to the published version of the manuscript.

**Funding:** This work was partly supported by JSPS KAKENHI for Scientific Research (JP19H00929 and JP24K01704 to A.I. and JP22H02196 to Y.I.) and for Transformative Research Areas (JP24H02269 to A.I.), by RIKEN Incentive Research Projects 2023, by the Shenzhen Science and Technology Program (No. GJHZ20220913142602004 to F.D.), and by the Guangdong Basic and Applied Basic Research Funding (No. 2024A1515010015 to F.D.).

**Data Availability Statement:** No new data were created or analyzed in this study. Data sharing is not applicable to this article.

**Acknowledgments:** We would like to thank Masayo Ohara for her kind technical assistance.

**Conflicts of Interest:** The authors declare no conflicts of interest.

## References

1. Ishiwata, A.; Tanaka, K.; Ao, J.; Ding, F.; Ito, Y. Recent advances in stereoselective 1,2-*cis*-O-glycosylations. *Front. Chem.* **2022**, *10*, 972429. [[CrossRef](#)] [[PubMed](#)]
2. Ishiwata, A.; Ito, Y. Development of highly efficient and stereocontrolled O-glycosylation methodologies and its application to the construction of bacterial glycans. *Trends Glycosci. Glycotechnol.* **2009**, *21*, 266–289. [[CrossRef](#)]
3. Nigudkar, S.S.; Demchenko, A.V. Stereocontrolled 1,2-*cis* glycosylation as the driving force of progress in synthetic carbohydrate chemistry. *Chem. Sci.* **2015**, *6*, 2687–2704. [[CrossRef](#)] [[PubMed](#)]
4. Takahashi, D.; Toshima, K. 1,2-*cis* O-glycosylation methods. *Compr. Glycosci.* **2021**, *2*, 365–412. [[CrossRef](#)]

5. Mukherjee, M.M.; Ghosh, R.; Hanover, J.A. Recent advances in stereoselective chemical *O*-glycosylation reactions. *Front. Mol. Biosci.* **2022**, *9*, 896187. [[CrossRef](#)]
6. Toshima, K.; Tatsuta, K. Recent progress in *O*-glycosylation methods and its application to natural products synthesis. *Chem. Rev.* **1993**, *93*, 1503–1531. [[CrossRef](#)]
7. Schmidt, R.R. New methods for the synthesis of glycosides and oligosaccharides—Are there alternatives to the Koenigs-Knorr method? [New Synthetic Methods (56)]. *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 212–235. [[CrossRef](#)]
8. Demchenko, A.V. Stereoselective chemical 1,2-*cis* *O*-glycosylation: From ‘Sugar Ray’ to modern techniques of the 21st century. *Synlett* **2003**, *2003*, 1225–1240. [[CrossRef](#)]
9. Mydock, L.K.; Demchenko, A.V. Mechanism of chemical *O*-glycosylation: From early studies to recent discoveries. *Org. Biomol. Chem.* **2010**, *8*, 497–510. [[CrossRef](#)]
10. Capon, B.; McManus, S.P. *Neighboring Group Participation*; Plenum: New York, NY, USA, 1976.
11. Capon, B. Mechanism in carbohydrate chemistry. *Chem. Rev.* **1969**, *69*, 407–4982. [[CrossRef](#)]
12. Bochkov, A.F.; Zaikov, G.E. *Chemistry of the O-Glycosidic Bond*; Pergamon: Oxford, UK, 1979.
13. Ernst, B.; Hart, G.W.; Sinaÿ, P. (Eds.) *Carbohydrates in Chemistry and Biology*; Wiley-VCH: Weinheim, Germany, 2000.
14. Fraser-Reid, B.; Tatsuta, K.; Thiem, J. (Eds.) *Glycoscience: Chemistry and Chemical Biology*; Springer: Berlin, Germany, 2001.
15. Demchenko, A.V. (Ed.) *Handbook of Chemical Glycosylation: Advances in Stereoselectivity and Therapeutic Relevance*; Wiley-VCH: Weinheim, Germany, 2008.
16. Green, L.G.; Ley, S.V. Protecting Groups: Effects on Reactivity, Glycosylation Stereoselectivity, and Coupling Efficiency. In *Carbohydrates in Chemistry and Biology*; Ernst, B., Hart, G.W., Sinaÿ, P., Eds.; Wiley-VCH: Weinheim, Germany, 2000; Volume 1, Chapter 17; pp. 427–448. [[CrossRef](#)]
17. Sinnott, M.L. (Ed.) *Carbohydrate Chemistry and Biochemistry: Structure and Mechanism*; RSC Publishing: Cambridge, UK, 2007. [[CrossRef](#)]
18. Crich, D.; Hu, T.; Cai, F. Does Neighboring Group Participation by Non-Vicinal Esters Play a Role in Glycosylation Reactions? Effective Probes for the Detection of Bridging Intermediates. *J. Org. Chem.* **2008**, *73*, 8942–8953. [[CrossRef](#)] [[PubMed](#)]
19. Crich, D.; Sun, S. Direct Formation of  $\beta$ -Mannopyranosides and Other Hindered Glycosides from Thioglycosides. *J. Am. Chem. Soc.* **1998**, *120*, 435–436. [[CrossRef](#)]
20. Crich, D.; Sun, S. Direct chemical synthesis of  $\beta$ -mannopyranosides and other glycosides via glycosyl triflates. *Tetrahedron* **1998**, *54*, 8321–8348. [[CrossRef](#)]
21. Weingart, R.; Schmidt, R.R. Can preferential  $\beta$ -mannopyranoside formation with 4,6-*O*-benzylidene protected mannopyranosyl sulfoxides be reached with trichloroacetimidates? *Tetrahedron Lett.* **2000**, *41*, 8753–8758. [[CrossRef](#)]
22. Imamura, A.; Ando, H.; Korogi, S.; Tanabe, G.; Muraoka, O.; Ishida, H.; Kiso, M. Di-*tert*-butylsilylene (DTBS) group-directed  $\alpha$ -selective galactosylation unaffected by C-2 participating functionalities. *Tetrahedron Lett.* **2003**, *44*, 6725–6728. [[CrossRef](#)]
23. Hao, T.; Feng, K.; Jin, H.; Li, J.; Zhou, C.; Liu, X.; Zhao, W.; Yu, F.; Li, T. Acceptor-reactivity-controlled stereoconvergent synthesis and immunological activity of a unique pentasaccharide from the cell wall polysaccharide of *Cutibacterium acnes* C7. *Angew. Chem. Int. Ed.* **2024**, *63*, e202405297. [[CrossRef](#)]
24. Leng, W.-L.; Yao, H.; He, J.-X.; Liu, X.-W. Venturing beyond donor-controlled glycosylation: New perspectives toward anomeric selectivity. *Acc. Chem. Res.* **2018**, *51*, 628–639. [[CrossRef](#)]
25. van der Vorm, S.; Hansen, T.; van Hengst, J.M.A.; Overkleef, H.S.; van der Marel, G.A.; Codée, J.D.C. Acceptor reactivity in glycosylation reactions. *Chem. Soc. Rev.* **2019**, *48*, 4688–4706. [[CrossRef](#)]
26. Gridley, J.J.; Osborn, M.I. Recent advances in the construction of  $\beta$ -D-mannose and  $\beta$ -D-mannosamine linkages. *J. Chem. Soc. Perkin Trans. 1* **2000**, 1471–1491. [[CrossRef](#)]
27. Davis, B.G. Recent developments in oligosaccharide synthesis. *J. Chem. Soc. Perkin Trans. 1* **2000**, 2137–2160. [[CrossRef](#)]
28. Cumpstey, I. Intramolecular aglycon delivery. *Carbohydr. Res.* **2008**, *343*, 1553–1573. [[CrossRef](#)] [[PubMed](#)]
29. Carmona, A.T.; Moreno-Vargas, A.J.; Robina, I. Stereoselective synthesis of 1,2-*cis*-glycosylic linkages. *Curr. Org. Synth.* **2008**, *5*, 33–63. [[CrossRef](#)]
30. Dwek, R.A. Glycobiology: Toward Understanding the Function of Sugars. *Chem. Rev.* **1996**, *96*, 683–720. [[CrossRef](#)] [[PubMed](#)]
31. Varki, A.; Cummings, R.; Esko, J.D.; Stanley, P.; Hart, G.W.; Aebi, M.; Mohnen, D.; Kinoshita, T.; Packer, N.H.; Prestegard, J.H. (Eds.) *Essentials in Glycobiology*; Cold Spring Harbor Laboratory Press: New York, NY, USA, 2022.
32. Kiessling, L.L. Chemistry-driven glycoscience. *Bioorganic Med. Chem.* **2018**, *26*, 5229–5238. [[CrossRef](#)]
33. Ohtsubo, K.; Marth, D. Glycosylation in Cellular Mechanisms of Health and Disease. *Cell* **2006**, *126*, 855–867. [[CrossRef](#)]
34. Zhao, X.; Huang, Y.; Zhou, S.; Ao, J.; Cai, H.; Tanaka, K.; Ito, Y.; Ishiwata, A.; Ding, F. Recent Chemical and Chemoenzymatic Strategies to Complex-Type *N*-Glycans. *Front. Chem.* **2022**, *10*, 880128. [[CrossRef](#)]
35. Ling, J.; Bennett, C.S. Recent Developments in Stereoselective Chemical Glycosylation. *Asian J. Org. Chem.* **2019**, *8*, 802–813. [[CrossRef](#)]
36. Ding, F.; Ishiwata, A.; Ito, Y. Stereodivergent mannosylation using 2-*O*-(*ortho*-tosylamido)benzyl group. *Org. Lett.* **2018**, *20*, 4833–4837. [[CrossRef](#)]
37. Zhou, S.; Zhong, X.; Guo, A.; Xiao, Q.; Ao, J.; Zhu, W.; Cai, H.; Ishiwata, A.; Ito, Y.; Liu, X.-W.; et al. ZnI<sub>2</sub>-directed Stereocontrolled  $\alpha$ -Glucosylation. *Org. Lett.* **2021**, *23*, 6841–6845. [[CrossRef](#)]

38. Zhong, X.; Zhou, S.; Ao, J.; Guo, A.; Xiao, Q.; Huang, Y.; Zhu, W.; Cai, H.; Ishiwata, A.; Ito, Y.; et al. Zinc(II) Iodide-directed  $\beta$ -Mannosylation: Reaction Selectivity, Mode and Application. *J. Org. Chem.* **2021**, *86*, 16901–16915. [[CrossRef](#)]
39. Ao, J.; Zhao, X.; Zhou, S.; Guo, Y.; Wang, G.; Fang, S.; Yao, X.; Liu, Y.; Ishiwata, A.; Tanaka, K.; et al. Construction of 1,2-*cis* Rhamnosidic Linkages and Synthesis of Tetrasaccharide Repeating Unit of Streptococcus pneumoniae Serotype 23F. *Org. Chem. Front.* **2023**, *10*, 5610–5615. [[CrossRef](#)]
40. Zhou, S.; Ao, J.; Guo, A.; Zhao, X.; Deng, N.; Wang, G.; Li, B.; Yang, Q.; Ishiwata, A.; Liu, X.-W.; et al. ZnI<sub>2</sub>-Mediated  $\beta$ -Galactosylation of C2-ether Type Donor. *Org. Lett.* **2022**, *24*, 8025–8030. [[CrossRef](#)]
41. Zhao, X.; Ding, H.; Guo, A.; Zhong, X.; Zhou, S.; Wang, G.; Liu, Y.; Ishiwata, A.; Tanaka, K.; Cai, H.; et al. Zinc(II)-mediated Stereoselective Construction of 1,2-*cis* 2-Azido-2-deoxy Glycosidic Linkage: Assembly of *Acinetobacter baumannii* K48 Capsular Pentasaccharide. *Chem. Sci.* **2024**, *15*, 12889–12899. [[CrossRef](#)] [[PubMed](#)]
42. Yamatsugu, K.; Kanai, M. Catalytic approaches to chemo- and site-selective transformation of carbohydrates. *Chem. Rev.* **2023**, *123*, 6793–6838. [[CrossRef](#)] [[PubMed](#)]
43. López, M.; de Parrodi, C.A.; Huelgas, G.; Lozada-Ramírez, J.D. Organocatalyzed stereoselective glycosylation: An overview of the last decade. *Mini-Rev. Org. Chem.* **2024**, *21*, 318–345. [[CrossRef](#)]
44. Takeda, D.; Yoritake, M.; Yasutomi, H.; Chiba, S.; Moriyama, T.; Yokoo, A.; Usui, K.; Hirai, G.  $\beta$ -Glycosyl trifluoroborates as precursors for direct  $\alpha$ -C-glycosylation: Synthesis of 2-deoxy- $\alpha$ -C-glycosides. *Org. Lett.* **2021**, *23*, 1940–1944. [[CrossRef](#)]
45. Shang, W.; Shi, R.; Niu, D. C-Glycoside synthesis enabled by nickel catalysis. *Chin. J. Chem.* **2023**, *41*, 2217–2236. [[CrossRef](#)]
46. Jiang, Y.; Zhang, Y.; Lee, B.C.; Koh, M.J. Diversification of glycosyl compounds via glycosyl radicals. *Angew. Chem. Int. Ed.* **2023**, *62*, e202305138. [[CrossRef](#)]
47. Shang, W.; Niu, D. Radical pathway glycosylation empowered by bench-stable glycosyl donors. *Acc. Chem. Res.* **2023**, *56*, 2473–2488. [[CrossRef](#)]
48. Xia, Y.; Wang, Y.; Zhang, Z.; Gulzar, T.; Lin, Y.; Wang, J.; Zhu, D.; Yu, B. Synthesis of 2-Indolyl C-Glycoside Neopetrosins A and C and Congeners via Ni-Catalyzed Photoreductive Cross-Coupling. *Org. Lett.* **2023**, *25*, 6741–6745. [[CrossRef](#)]
49. Ikazaki, T.; Ishikawa, E.; Tamashima, H.; Akiyama, H.; Kimuro, Y.; Yoritake, M.; Matoba, H.; Imamura, A.; Ishida, H.; Yamasaki, S.; et al. Ligand-Controlled Stereoselective Synthesis and Biological Activity of 2-Exomethylene Pseudo-Glycoconjugates: Discovery of Mincle-Selective Ligands. *Angew. Chem. Int. Ed.* **2023**, *62*, e202302569. [[CrossRef](#)] [[PubMed](#)]
50. Wang, S.; Chen, K.; Guo, F.; Zhu, W.; Liu, C.; Dong, H.; Yu, J.-Q.; Lei, X. C-H Glycosylation of Native Carboxylic Acids: Discovery of Antidiabetic SGLT-2 Inhibitors. *ACS Cent. Sci.* **2023**, *9*, 1129–1139. [[CrossRef](#)] [[PubMed](#)]
51. Guo, H.; Kirchhoff, J.-L.; Strohmman, C.; Grabe, B.; Loh, C.C.J. Exploiting  $\pi$  and Chalcogen Interactions for the  $\beta$ -Selective Glycosylation of Indoles through Glycal Conformational Distortion. *Angew. Chem. Int. Ed.* **2024**, *63*, e202316667. [[CrossRef](#)] [[PubMed](#)]
52. Moriyama, T.; Yoritake, M.; Kato, N.; Saika, A.; Kusuhara, W.; Ono, S.; Nagatake, T.; Koshino, H.; Kiya, N.; Moritsuka, N.; et al. Linkage-Editing Pseudo-Glycans: A Reductive  $\alpha$ -Fluorovinyl-C-Glycosylation Strategy to Create Glycan Analogs with Altered Biological Activities. *J. Am. Chem. Soc.* **2024**, *146*, 2237–2247. [[CrossRef](#)] [[PubMed](#)]
53. Wu, J.; Purushothaman, R.; Kallert, F.; Homöller, S.L.; Ackermann, L. Electrochemical glycosylation via halogen-atom-transfer for C-glycoside assembly. *ACS Catal.* **2024**, *14*, 11532–11544. [[CrossRef](#)]
54. Zhu, H.; Dang, Q.; Wang, Y.; Niu, D. Polarity-matched initiation of radical-polar crossover reactions for the synthesis of C-allyl glycosides with gem-difluoroalkene groups. *J. Org. Chem.* **2024**, *89*, 10175–10179. [[CrossRef](#)]
55. Sun, Y.; Ren, K.; Zhang, Z.; Li, Y.; Wang, N.; Zeng, H.; Huang, N.; Li, X.-X.; Deng, W.-Q.; Yao, H. Palladium-catalyzed O-glycosylation through  $\pi$ - $\pi$  interactions. *Org. Lett.* **2024**, *26*, 5396–5401. [[CrossRef](#)]
56. Lyu, M.-Y.; Jacobo, S.A.; Brown, M.K. Diverse synthesis of C-glycosides by stereoselective Ni-Catalyzed carboboration of glycals. *J. Am. Chem. Soc.* **2024**, *146*, 18866–18872. [[CrossRef](#)]
57. Zhang, C.; He, D.; Ma, Z.; Wang, M.; Zhu, Y.; Liu, Y.; Chen, J.; Guo, L.; Lv, G.; Wu, Y. Synthesis of nonclassical heteroaryl C-glycosides via decarboxylative C-H glycosylation. *J. Org. Chem.* **2024**, *89*, 10112–10126. [[CrossRef](#)]
58. Liu, D.-Y.; Wang, P.-F.; Ruan, Y.-J.; Wang, X.-L.; Hu, X.-Y.; Yang, Q.; Liu, J.; Wen, M.-M.; Zhang, C.-Z.; Xiao, Y.-H.; et al. Assembly of heterocyclic C-glycosides by Ru-catalyzed C-H activation/cyclization with carbonyl sulfoxonium ylide glyco-reagents. *Org. Lett.* **2024**, *26*, 5092–5097. [[CrossRef](#)]
59. Wu, X.; Li, S.; Chen, L.; Ma, S.; Ma, B.; Song, L.; Qian, D. Stereoselective construction of multifunctional C-glycosides enabled by nickel-catalyzed tandem borylation/glycosylation. *J. Am. Chem. Soc.* **2024**, *146*, 22413–22423. [[CrossRef](#)] [[PubMed](#)]
60. Shi, W.-Y.; Ma, J.-J.; Li, H.-Y.; Chen, D.; Liu, X.-Y.; Liang, Y.-M. Synthesis of C-alkyl glycosides from alkyl bromides and glycosyl carboxylic acids via Ni/photoredox dual catalysis. *J. Org. Chem.* **2024**, *89*, 11136–11147. [[CrossRef](#)] [[PubMed](#)]
61. Gan, Y.; Zhou, J.-F.; Li, X.; Liu, J.-R.; Liu, F.-J.; Hong, X.; Ye, B. Zirconaaziridine-mediated Ni-catalyzed diastereoselective C(sp<sup>2</sup>)-glycosylation. *J. Am. Chem. Soc.* **2024**, *146*, 16753–16763. [[CrossRef](#)] [[PubMed](#)]
62. Moritsuka, N.; Kiya, N.; Moriyama, T.; Koshino, H.; Yoritake, M.; Matoba, H.; Hirai, G. Linkage-editing of melibiosamine: Synthesis and biological evaluation of CH<sub>2</sub>- and CHF-linked analogs. *J. Org. Chem.* **2024**, *89*, 11909–11920. [[CrossRef](#)] [[PubMed](#)]
63. Oka, N.; Kajino, R.; Takeuchi, K.; Nagakawa, H.; Ando, K.  $\alpha$ -Selective ribofuranosylation of alcohols with ribofuranosyl iodides and triphenylphosphine oxide. *J. Org. Chem.* **2014**, *79*, 7656–7664. [[CrossRef](#)] [[PubMed](#)]
64. Wang, L.; Overkleeft, H.S.; van der Marel, G.A.; Codée, J.D.C. Reagent controlled stereoselective synthesis of  $\alpha$ -glucans. *J. Am. Chem. Soc.* **2018**, *140*, 4632–4638. [[CrossRef](#)]

65. Shou, K.; Zhang, Y.; Ji, Y.; Liu, B.; Zhou, Q.; Tan, Q.; Li, F.; Wang, X.; Lu, G.; Xiao, G. Highly stereoselective  $\alpha$ -glycosylation with GaN<sub>3</sub> donors enabled collective synthesis of mucin related tumor associated carbohydrate antigens. *Chem. Sci.* **2024**, *15*, 6552–6656. [[CrossRef](#)]
66. Pathan, E.K.; Ghosh, B.; Podilapu, A.R.; Kulkarni, S.S. Total synthesis of the repeating unit of *Bacteroides fragilis* zwitterionic polysaccharide A1. *J. Org. Chem.* **2021**, *86*, 6090–6099. [[CrossRef](#)]
67. Liu, W.; Hu, Z.; Xu, P.; Yu, B. Synthesis of anticoagulant pentasaccharide fondaparinux via 3,5-dimethyl-4-(2'-phenylethynylphenyl)phenyl glycosides. *Org. Lett.* **2023**, *25*, 8506–8510. [[CrossRef](#)]
68. Deng, L.-F.; Wang, Y.; Xu, S.; Shen, A.; Zhu, H.; Zhang, S.; Zhang, X.; Niu, D. Palladium catalysis enables cross-coupling-like SN2-glycosylation of phenols. *Science* **2023**, *382*, 928–935. [[CrossRef](#)]
69. Ghosh, B.; Alber, A.; Lander, C.W.; Shao, Y.; Nicholas, K.M.; Sharma, I. Catalytic stereoselective 1,2-*cis*-furanosylations enabled by enynal-derived copper carbenes. *ACS Catal.* **2024**, *14*, 1037–1049. [[CrossRef](#)]
70. Duong, T.; Valenzuela, E.A.; Ragains, J.R. Benzynes-promoted, 1,2-*cis*-selective O-glycosylation with genzylchalcogenoglycoside donors. *Org. Lett.* **2023**, *25*, 8526–8529. [[CrossRef](#)] [[PubMed](#)]
71. Li, Z.; Shen, W.; Cao, C.; Wang, Z.; Zhang, Y.; Xue, W. Thiourea-Cu(OTf)<sub>2</sub>/NIS-synergistically promoted stereoselective glycoside formation with 2-azidoselenoglycosides or thioglycosides as donors. *Org. Biomol. Chem.* **2024**, *22*, 2137–2144. [[CrossRef](#)] [[PubMed](#)]
72. Demchenko, A.V.; Rousson, E.; Boons, G.-J. Stereoselective 1,2-*cis*-galactosylation assisted by remote neighboring group participation and solvent effects. *Tetrahedron Lett.* **1999**, *40*, 6523–6526. [[CrossRef](#)]
73. Ishiwata, A.; Munemura, Y.; Ito, Y. Synergistic solvent effect in 1,2-*cis*-glycoside formation. *Tetrahedron* **2008**, *64*, 92–102. [[CrossRef](#)]
74. Ghosh, B.; Bhattacharjee, N.; Podilapu, A.R.; Puri, K.; Kulkarni, S.S. Total synthesis of the repeating units of O-specific polysaccharide of *Pseudomonas chlororaphis* subsp. *aureofaciens* UCM B-306 via one-pot glycosylation. *Org. Lett.* **2022**, *24*, 3696–3701. [[CrossRef](#)]
75. Shirsat, A.A.; Rai, D.; Ghotekar, B.K.; Kulkarni, S.S. Total synthesis of trisaccharide repeating unit of *Staphylococcus aureus* strain M. *Org. Lett.* **2023**, *25*, 2913–2917. [[CrossRef](#)]
76. Pradhan, K.; Paul, A.; Mishra, A.K.; Balhara, P.; Kulkarni, S.S. Total Synthesis of *Vibrio Cholerae* O43 Tetrasaccharide Repeating Unit. *J. Org. Chem.* **2024**, *89*, 4019–4030. [[CrossRef](#)]
77. Yang, X.; Zhang, H.; Zhao, Q.; Li, Q.; Li, T.; Gao, J. Total synthesis of the repeating iunits of highly functionalized O-antigens of *Pseudomonas aeruginosa* ATCC 27577, O10, and O19. *JACS Au* **2024**, *4*, 2351–2362. [[CrossRef](#)]
78. Behera, A.; Rai, D.; Kushwaha, D.; Kulkarni, S.S. Total synthesis of trisaccharide repeating unit of O-specific polysaccharide of *Pseudomonas fluorescens* BIM B-582. *Org. Lett.* **2018**, *20*, 5956–5959. [[CrossRef](#)]
79. Wang, L.; Zhang, Y.; Overkleeft, H.S.; van der Marel, G.A.; Codee, J.D.C. Reagent controlled glycosylations for the assembly of well-defined pel pligosaccharides. *J. Org. Chem.* **2020**, *85*, 15872–15884. [[CrossRef](#)] [[PubMed](#)]
80. Biswas, S.; Ghotekar, B.K.; Kulkarni, S.S. Total synthesis of the all-rare sugar-containing pentasaccharide repeating unit of the O-polysaccharide of *Plesiomonas shigelloides* strain 302–73 (Serotype O1). *Org. Lett.* **2021**, *23*, 6137–6142. [[CrossRef](#)] [[PubMed](#)]
81. Zhang, Y.; Chen, C.; Gao, Y.; Yang, M.; He, Z.; Zhang, B.; Gu, G.; Tang, B.; Cai, F.  $\beta$ -L-Rhamnosylation and  $\beta$ -D-mannosylation mediated by 4-O-ester groups in a weakly nucleophilic environment. *Org. Lett.* **2023**, *25*, 7120–7125. [[CrossRef](#)] [[PubMed](#)]
82. Chen, Z.; Xiao, G. Total synthesis of nona-decasaccharide motif from *Ganoderma sinense* polysaccharide enabled by modular and one-pot stereoselective glycosylation strategy. *J. Am. Chem. Soc.* **2024**, *146*, 17446–17455. [[CrossRef](#)] [[PubMed](#)]
83. Remmerswaal, W.A.; Elferink, H.; Houthuijs, K.J.; Hansen, T.; ter Braak, F.; Berden, G.; van der Vorm, S.; Martens, J.; Oomens, J.; van der Marel, G.A.; et al. Anomeric triflates versus dioxanium ions: Different product-forming intermediates from 3-acyl benzylidene mannosyl and glucosyl donors. *J. Org. Chem.* **2024**, *89*, 1618–1625. [[CrossRef](#)]
84. Liu, X.; Lin, Y.; Peng, W.; Zhang, Z.; Gao, L.; Zhou, Y.; Song, Z.; Wang, Y.; Xu, P.; Yu, B.; et al. Direct Synthesis of 2,6-dideoxy- $\beta$ -glycosides and  $\beta$ -rhamnosides with a stereodirecting 2-(diphenylphosphinoyl)acetyl group. *Angew. Chem. Int. Ed.* **2022**, *61*, e202206128. [[CrossRef](#)]
85. Tang, X.; Zhou, Y.; Wang, Y.; Lin, Y.; Pan, S.; Che, Q.; Sang, J.; Gao, Z.; Zhang, W.; Wang, Y.; et al. Direct Synthesis of  $\alpha$ - and  $\beta$ -2'-deoxynucleosides with stereodirecting phosphine oxide via remote participation. *J. Am. Chem. Soc.* **2024**, *146*, 8768–8779. [[CrossRef](#)]
86. Zhong, X.; Zhao, X.; Ao, J.; Huang, Y.; Liu, Y.; Zhou, S.; Li, B.; Ishiwata, A.; Cai, H.; Ding, F. An experimental and theoretical study on stereocontrolled glycosylations by "one-pot" procedure. *Org. Chem. Front.* **2022**, *9*, 4151–4157. [[CrossRef](#)]
87. Bharali, M.M.; Pramanik, S.; Santra, A. Zinc tetrafluoroborate catalyzed stereo- and regioselective O-glycosylation for the direct synthesis of  $\beta$ -glycosides from armed O-glycosyl trichloroacetimidates. *Chem. Asian J.* **2024**, *19*, e202400420. [[CrossRef](#)]
88. Morelli, L.; Compostella, F.; Panza, L.; Imperio, D. Unusual promoters and leaving groups in glycosylation reactions: The evolution of carbohydrate synthesis. *Carbohydr. Res.* **2022**, *519*, 108625. [[CrossRef](#)]
89. Kanie, O.; Ito, Y.; Ogawa, T. Orthogonal glycosylation strategy in oligosaccharide synthesis. *J. Am. Chem. Soc.* **1994**, *116*, 12073–12074. [[CrossRef](#)]
90. Wang, X.; Xiao, G. Recent chemical synthesis of plant polysaccharides. *Curr. Opin. Chem. Biol.* **2023**, *77*, 102387. [[CrossRef](#)]
91. Ma, Y.; Zhang, Y.; Huang, Y.; Chen, Z.; Xian, Q.; Su, R.; Jiang, Q.; Wang, X.; Xiao, G. One-Pot Assembly of mannose-capped lipoarabinomannan motifs up to 101-mer from the *Mycobacterium tuberculosis* Cell Wall. *J. Am. Chem. Soc.* **2024**, *146*, 4112–4122. [[CrossRef](#)] [[PubMed](#)]

92. Li, K.; Liu, B.; Wang, X.; Xiao, G. Highly Stereoselective Synthesis of Branched Fructooligosaccharides ABW90-1 and ABW50-1 from *Achyranthes bidentata* with Potent Antiosteoporosis Activities. *Org. Lett.* **2024**, *26*, 1468–1471. [[CrossRef](#)] [[PubMed](#)]
93. Sun, X.-C.; Chen, Z.; Yang, R.; Wang, M.; Wang, X.; Zhang, Q.; Xiao, G. Modular and Stereoselective One-pot Total Synthesis of Icosasaccharide motif from *Cordyceps sinensis* EPS-1A Glycan. *Org. Lett.* **2023**, *25*, 7364–7368. [[CrossRef](#)] [[PubMed](#)]
94. Li, P.; Fan, H.; Tan, Q.; Xiao, G. Highly Stereoselective Assembly of 1,2-*cis*-Arap Linkages. *Org. Lett.* **2023**, *25*, 2788–2792. [[CrossRef](#)]
95. Ma, Y.; Jiang, Q.; Wang, X.; Xiao, G. Total synthesis of *Cordyceps militaris* glycans via stereoselective orthogonal one-pot glycosylation and  $\alpha$ -glycosylation strategies. *Org. Lett.* **2022**, *24*, 7950–7954. [[CrossRef](#)]
96. Yang, R.; Sun, X.; Zhang, Y.; Xiao, G. The total synthesis of rhynchosporosides via orthogonal one-pot glycosylation and stereoselective  $\alpha$ -glycosylation strategies. *Org. Biomol. Chem.* **2022**, *20*, 6755–6758. [[CrossRef](#)]
97. Zhang, Y.; Hu, Y.; Liu, S.; He, H.; Sun, R.; Lu, G.; Xiao, G. Total synthesis of *Lentinus giganteus* glycans with antitumor activities via stereoselective  $\alpha$ -glycosylation and orthogonal one-pot glycosylation strategies. *Chem. Sci.* **2022**, *13*, 7755–7764. [[CrossRef](#)]
98. Yu, B.; Tao, H. Glycosyl trifluoroacetimidates. Part 1: Preparation and application as new glycosyl donors. *Tetrahedron Lett.* **2001**, *42*, 2405–2407. [[CrossRef](#)]
99. Yu, B.; Sun, J. Glycosylation with glycosyl *N*-phenyltrifluoroacetimidates (PTFAI) and a perspective of the future development of new glycosylation methods. *Chem. Commun.* **2010**, *46*, 4668–4679. [[CrossRef](#)] [[PubMed](#)]
100. Li, Y.; Yang, Y.; Yu, B. An efficient glycosylation protocol with glycosyl ortho-alkynylbenzoates as donors under the catalysis of Ph<sub>3</sub>PAuOTf. *Tetrahedron Lett.* **2008**, *49*, 3604–3608. [[CrossRef](#)]
101. Yu, B. Gold(I)-catalyzed glycosylation with glycosyl o-alkynylbenzoates as donors. *Acc. Chem. Res.* **2018**, *51*, 507–516. [[CrossRef](#)] [[PubMed](#)]
102. Shen, K.; Bai, B.; Liu, Y.H.; Lowary, T.L. Synthesis of a tridecasaccharide lipooligosaccharide antigen from the opportunistic pathogen *Mycobacterium kansasii*. *Angew. Chem. Int. Ed.* **2021**, *60*, 24859–24863. [[CrossRef](#)] [[PubMed](#)]
103. Yasomane, J.P.; Demchenko, A.V. Effect of remote picolinyl and picoloyl substituents on the stereoselectivity of chemical glycosylation. *J. Am. Chem. Soc.* **2012**, *134*, 20097–20102. [[CrossRef](#)]
104. Liu, Q.W.; Bin, H.C.; Yang, J.S.  $\beta$ -Arabinofuranosylation using 5-*O*-(2-quinolinecarbonyl) substituted ethyl thioglycoside donors. *Org. Lett.* **2013**, *15*, 3974–3977. [[CrossRef](#)]
105. Ishiwata, A.; Munemura, Y.; Ito, Y. NAP ether mediated intramolecular aglycon delivery: A unified strategy for 1,2-*cis*-glycosylation. *Eur. J. Org. Chem.* **2008**, *2008*, 4250–4263. [[CrossRef](#)]
106. Lee, Y.J.; Ishiwata, A.; Ito, Y. Stereoselective synthesis of  $\beta$ -L-rhamnopyranosides. *J. Am. Chem. Soc.* **2008**, *130*, 6330–6331. [[CrossRef](#)]
107. Ishiwata, A.; Lee, Y.J.; Ito, Y. Recent Advances in Stereoselective Glycosylation through Intramolecular Aglycon Delivery. *Org. Biomol. Chem.* **2010**, *8*, 3596. [[CrossRef](#)]
108. Ishiwata, A. Synthetic Study on Glycoconjugates Containing 1,2-*Cis* Glycoside and Their Application. *Trends Glycosci. Glycotechnol.* **2019**, *31*, SE53–SE54. [[CrossRef](#)]
109. Ishiwata, A.; Kaeohip, S.; Takeda, Y.; Ito, Y. Synthesis of Highly Glycosylated Hydrophilic Motif of Extensins. *Angew. Chem. Int. Ed.* **2014**, *53*, 9812–9816. [[CrossRef](#)] [[PubMed](#)]
110. Tamigney, M.; Blériot, K.Y.; Gauthier, C. Intramolecular aglycon delivery enables the synthesis of 6-deoxy- $\beta$ -D-manno-heptosides as fragments of *Burkholderia pseudomallei* and *Burkholderia mallei* capsular polysaccharide. *J. Org. Chem.* **2014**, *79*, 4615–4634. [[CrossRef](#)] [[PubMed](#)]
111. Yu, K.; Qiao, Y.; Gu, G.; Gao, J.; Cai, S.; Long, Z.; Guo, Z. Synthesis of the biological repeating unit of *Streptococcus pneumoniae* serotype 23F capsular polysaccharide. *Org. Biomol. Chem.* **2016**, *14*, 11462–11472. [[CrossRef](#)] [[PubMed](#)]
112. Jia, X.G.; Demchenko, A.V. Intramolecular glycosylation. *Beilstein J. Org. Chem.* **2017**, *13*, 2028–2048. [[CrossRef](#)] [[PubMed](#)]
113. Ishiwata, A.; Ito, Y. Intramolecular aglycon delivery toward 1,2-selective glycosylation. *Sel. Glycosylations Synth. Methods Catal.* **2017**, *4*, 79–96. [[CrossRef](#)]
114. Robinson, S.A.; Yau, J.; Terabe, M.; Berzofsky, J.A.; Painter, G.F.; Compton, B.J.; Larsen, D.S. Synthetic preparation and immunological evaluation of  $\beta$ -mannosylceramide and related *N*-acyl analogues. *Org. Biomol. Chem.* **2020**, *18*, 2739–2746. [[CrossRef](#)]
115. Fairbanks, A.J. Glycosylation through intramolecular aglycon delivery. *Compr. Glycosci.* **2021**, *2*, 413–434. [[CrossRef](#)]
116. Ishiwata, A.; Fujita, K.; Fushinobu, S.; Tanaka, K.; Ito, Y. Synthesis of naturally occurring  $\beta$ -L-arabinofuranosyl-L-arabinofuranoside structures towards the substrate specificity evaluation of  $\beta$ -L-arabinofuranosidase. *Bioorg. Med. Chem.* **2022**, *68*, 116849. [[CrossRef](#)]
117. Jaiswal, M.K.; Sharma, A.; Tiwari, V.K.; Schmidt, R.R. Recent advances in stereoselective intramolecular *O*-glycosylation. *Synth. Strateg. Carbohydr. Chem.* **2024**, *2*, 53–94. [[CrossRef](#)]
118. Sano, K.; Ishiwata, A.; Kikuma, T.; Takamori, H.; Tanaka, K.; Ito, Y.; Takeda, Y. Synthesis of sucrose-mimicking disaccharide by intramolecular aglycone delivery. *Molecules* **2024**, *29*, 1771. [[CrossRef](#)]
119. Pellissier, H. Recent developments in enantioselective zinc-catalyzed transformations. *Coord. Chem. Rev.* **2021**, *439*, 213926. [[CrossRef](#)]
120. Denmark, S.E.; O'Connor, S.P. Catalytic, enantioselective cyclopropanation of allylic alcohols. Substrate generality. *J. Org. Chem.* **1997**, *62*, 584–594. [[CrossRef](#)]

121. Hanessian, S.; Guindon, Y. Cleavage of methyl and benzyl ethers with thiotrimethylsilanes. *Tetrahedron Lett.* **1980**, *21*, 2305–2308. [[CrossRef](#)]
122. Kaufmann, E.; Hattori, H.; Miyatake-Ondoab, H.; Gademann, K. Total synthesis of the glycosylated macrolide antibiotic fidaxomicin. *Org. Lett.* **2015**, *17*, 3514–3517. [[CrossRef](#)] [[PubMed](#)]
123. Zhu, Y.-H.; Vogel, P. Synthesis of a C-disaccharide analog of the Thomsen-Friedenreich (T) epitope. *Synlett* **2001**, *2001*, 79–81. [[CrossRef](#)]
124. Berry, J.; Despras, G.; Lindhorst, T.K. A compatibility study on the glycosylation of 4,4'-dihydroxyazobenzene. *RSC Adv.* **2020**, *10*, 17432. [[CrossRef](#)]
125. Murakami, T.; Sato, Y.; Shibakami, M. Stereoselective glycosylations using benzoylated glucosyl halides with inexpensive promoters. *Carbohydr. Res.* **2008**, *343*, 1297–1308. [[CrossRef](#)]
126. Lanz, G.; Madsen, R. Glycosylation with disarmed glycosyl bromides promoted by iodonium ions. *Eur. J. Org. Chem.* **2016**, *2016*, 3119–3125. [[CrossRef](#)]
127. Baldoni, L.; Marino, C. Synthetic tools for the characterization of galactofuranosyl transferases: Glycosylations via acylated glycosyl iodides. *Carbohydr. Res.* **2013**, *374*, 75–81. [[CrossRef](#)]
128. Plante, O.J.; Palmacci, E.R.; Andrade, R.B.; Seeberger, P.H. Oligosaccharide synthesis with glycosyl phosphate and dithiophosphate triesters as glycosylating agents. *J. Am. Chem. Soc.* **2001**, *123*, 9545–9554. [[CrossRef](#)]
129. Meloncelli, P.J.; Martin, A.D.; Lowary, T.L. Glycosyl iodides. History and recent advances. *Carbohydr. Res.* **2009**, *344*, 1110–1122. [[CrossRef](#)]
130. Schmidt, R.R.; Kinzy, W. Anomeric-oxygen activation for glycoside synthesis. *Adv. Carbohydr. Chem. Biochem.* **1994**, *50*, 21–123. [[CrossRef](#)] [[PubMed](#)]
131. Schmidt, R.R.; Michel, J. Facile Synthesis of  $\alpha$ - and  $\beta$ -O-glycosyl imidates; preparation of glycosides and disaccharides. *Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 731–732. [[CrossRef](#)]
132. Pougny, J.-R.; Sinaÿ, P. Reaction d'imidates de glucopyranosyle avec l'acetonitrile. Applications synthétiques. *Tetrahedron Lett.* **1976**, *17*, 4073–4076. [[CrossRef](#)]
133. Pougny, J.-R.; Jacquinet, J.-C.; Nassr, M.; Duchet, D.; Milat, M.-L.; Sinaÿ, P. A novel synthesis of 1,2-*cis*-disaccharides. *J. Am. Chem. Soc.* **1977**, *99*, 6762–6763. [[CrossRef](#)] [[PubMed](#)]
134. Ding, F.; Ishiwata, A.; Ito, Y. Recent advances of the stereoselective bimodal glycosylations for the synthesis of various glucans. *Stud. Nat. Prod. Chem. (Bioact. Nat. Prod.)* **2022**, *74*, 1–40. [[CrossRef](#)]
135. Ishiwata, A.; Tanaka, K.; Ito, Y.; Cai, H.; Ding, F. Recent progress in 1,2-*cis* glycosylation for glucan synthesis. *Molecules* **2023**, *28*, 5644. [[CrossRef](#)]
136. Mishra, K.B.; Singh, A.K.; Kandasamy, J. Tris(pentafluorophenyl)borane-promoted stereoselective glycosylation with glycosyl trichloroacetimidates under mild conditions. *J. Org. Chem.* **2018**, *83*, 4204–4212. [[CrossRef](#)]
137. Nielsen, M.M.; Holmstrøm, T.; Pedersen, C.M. Stereoselective O-glycosylations by pyrylium salt organocatalysis. *Angew. Chem. Int. Ed.* **2022**, *61*, e202115394. [[CrossRef](#)]
138. Warne, M.E.; Fascione, M.A. Bimodal Glycosyl Donors as an Emerging Approach Towards a General Glycosylation Strategy. *Chem. Eur. J.* **2024**, *30*, e202400399. [[CrossRef](#)]
139. Aubry, S.; Sasaki, K.; Sharma, I.; Crich, D. Influence of Protecting Groups on the Reactivity and Selectivity of Glycosylation: Chemistry of the 4,6-O-Benzylidene Protected Mannopyranosyl Donors and Related Species. In *Topics in Current Chemistry*; Springer: Berlin/Heidelberg, Germany, 2011. [[CrossRef](#)]
140. Ding, F.; Ishiwata, A.; Ito, Y. Bimodal Glycosyl Donors Protected by 2-O-(*ortho*-Tosylamido)benzyl Group. *Org. Lett.* **2018**, *20*, 4384–4388. [[CrossRef](#)] [[PubMed](#)]
141. Ding, F.; Ishiwata, A.; Zhou, S.; Zhong, X.; Ito, Y. Unified Strategy toward Stereocontrolled Assembly of Various Glucans Based on Bimodal Glycosyl Donors. *J. Org. Chem.* **2020**, *85*, 5536–5558. [[CrossRef](#)] [[PubMed](#)]
142. Cai, J.; Yuan, X.; Kong, Y.; Hu, Y.; Li, J.; Jiang, S.; Dong, C.; Ding, K. Chemical approaches for the stereocontrolled synthesis of 1,2-*cis*- $\beta$ -D-rhamnosides. *Chin. J. Nat. Med.* **2023**, *21*, 886–901. [[CrossRef](#)] [[PubMed](#)]
143. Ueki, A.; Hirota, M.; Kobayashi, Y.; Komatsu, K.; Takano, Y.; Iwaoka, M.; Nakahara, Y.; Hojo, H.; Nakahara, Y. Stereoselective synthesis of benzyl-protected  $\beta$ -galactosides by propionitrile-mediated glycosylation. *Tetrahedron* **2008**, *64*, 2611–2618. [[CrossRef](#)]
144. Franconetti, A.; Ardá, A.; Asensio, J.L.; Blériot, Y.; Thibaudeau, S.; Jiménez-Barbero, J. Glycosyl oxocarbenium ions: Structure, conformation, reactivity, and interactions. *Acc. Chem. Res.* **2021**, *54*, 2552–2564. [[CrossRef](#)]
145. Xiao, Q.; Fang, S.; Ao, J.; Zhao, X.; Huang, C.; Liu, Y.; Nie, Y.; Ishiwata, A.; Tanaka, K.; Deng, W.; et al. B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub>-catalyzed stereoselective 1,2-*cis* arabinofuranosylation with a conformationally constrained donor. *ACS Omega* **2024**, *9*, 11969–11975. [[CrossRef](#)]
146. Imamura, A.; Lowary, T.L.  $\beta$ -Selective arabinofuranosylation using a 2,3-O-xylylene-protected donor. *Org. Lett.* **2010**, *12*, 3686–3689. [[CrossRef](#)]
147. Wang, Y.; Maguire-Boyle, S.; Dere, R.T.; Zhu, X. Synthesis of  $\beta$ -D-arabinofuranosides: Stereochemical differentiation between D- and L-enantiomers. *Carbohydr. Res.* **2008**, *343*, 3100–3106. [[CrossRef](#)]
148. Zhang, L.; Shen, K.; Taha, H.A.; Lowary, T.L. Stereocontrolled synthesis of  $\alpha$ -xylofuranosides using a conformationally restricted donor. *J. Org. Chem.* **2018**, *83*, 7659–7671. [[CrossRef](#)]

149. Ishiwata, A.; Akao, H.; Ito, Y. Stereoselective Synthesis of a fragment of mycobacterial arabinan. *Org. Lett.* **2006**, *8*, 5525–5528. [CrossRef]
150. Zhu, X.; Kawatkar, S.; Rao, Y.; Boons, G.J. Practical approach for the stereoselective introduction of  $\beta$ -arabinofuranosides. *J. Am. Chem. Soc.* **2006**, *128*, 11948–11957. [CrossRef] [PubMed]
151. Crich, D.; Pedersen, C.M.; Bowers, A.A.; Wink, D.J. On the use of 3,5-O-benzylidene and 3,5-O-(di-*tert*-butylsilylene)-2-O-benzylarabinothiofuranosides and their sulfoxides as glycosyl donors for the synthesis of  $\beta$ -arabinofuranosides: Importance of the activation method. *J. Org. Chem.* **2007**, *72*, 1553–1565. [CrossRef] [PubMed]
152. Sau, A.; Palo-Nieto, C.; Galan, M.C. Substrate-controlled direct  $\alpha$ -stereoselective synthesis of deoxyglycosides from glycals using  $B(C_6F_5)_3$  as catalyst. *J. Org. Chem.* **2019**, *84*, 2415–2424. [CrossRef] [PubMed]
153. Hou, M.; Xiang, Y.; Gao, J.; Zhang, J.; Wang, N.; Shi, H.; Huang, N.; Yao, H. Stereoselective synthesis of 2-deoxy glycosides via iron catalysis. *Org. Lett.* **2023**, *25*, 832–837. [CrossRef]
154. Dubey, A.; Tiwari, A.; Mandal, P.K. Tris (pentafluorophenyl) borane-catalyzed stereoselective C-glycosylation of indoles with glycosyl trichloroacetimidates: Access to 3-indolyl-C-glycosides. *J. Org. Chem.* **2021**, *86*, 8516–8526. [CrossRef]
155. Xu, Y.; Montgomery, J. Synthesis of 2-amino-2-deoxy sugars via boron-catalyzed coupling of glycosyl fluorides and silyl ether acceptors. *Org. Lett.* **2024**, *26*, 7474–7478. [CrossRef]
156. Fang, S.; Huang, C.; Ao, J.; Xiao, Q.; Zhou, S.; Deng, W.; Cai, H.; Ding, F. Total synthesis of the hexasaccharide arabinan domain of mycobacterial arabinogalactan. *Carbohydr. Res.* **2024**, *542*, 109204. [CrossRef]
157. Frisch, M.J.; Trucks, G.W.; Schlegel, H.B.; Scuseria, G.E.; Robb, M.A.; Cheeseman, J.R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G.A.; et al. *Gaussian 09*; Gaussian, Inc.: Wallingford, CT, USA, 2009.
158. Minenkov, Y.; Sharapa, D.I.; Cavallo, L. Application of semiempirical methods to transition metal complexes: Fast results but hard-to-predict accuracy. *J. Chem. Theory Comput.* **2018**, *14*, 3428–3439. [CrossRef]
159. Grimme, S.; Antony, J.; Ehrlich, S.; Krieg, H. A Consistent and Accurate Ab initio parametrization of density functional dispersion correction (DFT-D) for the 94 elements H-Pu. *J. Chem. Phys.* **2010**, *132*, 154104. [CrossRef]
160. Tekarli, S.M.; Drummond, M.L.; Williams, T.G.; Cundari, T.R.; Wilson, A.K. Performance of density functional theory for 3d transition metal-containing complexes: Utilization of the correlation consistent basis sets. *J. Phys. Chem. A* **2009**, *113*, 8607–8614. [CrossRef]
161. Sun, Y.-L.; Li, T.-H.; Chen, J.-L.; Wu, K.-J.; Hu, W.-P. Accurate multi-level electronic structure methods (MLSE-DFT) for atomization energies and reaction energy barriers. *Chem. Phys. Lett.* **2007**, *442*, 220–223. [CrossRef]
162. Schultz, N.E.; Zhao, Y.; Truhlar, D.G. Density functionals for inorganometallic and organometallic chemistry. *J. Phys. Chem. A* **2005**, *109*, 11127–11143. [CrossRef] [PubMed]
163. Goerigk, L.; Grimme, S. Efficient and accurate double-hybrid-meta-GGA density functionals—evaluation with the extended GMTKN30 database for general main group thermochemistry, kinetics, and noncovalent interactions. *J. Chem. Theory Comput.* **2011**, *7*, 291–309. [CrossRef] [PubMed]
164. Marenich, A.V.; Cramer, C.J.; Truhlar, D.G. Universal solvation model based on solute electron density and a continuum model of the solvent defined by the bulk dielectric constant and atomic surface tensions. *J. Phys. Chem. B* **2009**, *113*, 6378–6396. [CrossRef] [PubMed]
165. Ischtwan, J.; Collins, M.A. Determination of the intrinsic reaction coordinate: Comparison of gradient and local quadratic approximation methods. *J. Chem. Phys.* **1988**, *89*, 2881–2885. [CrossRef]
166. Mardirossian, N.; Head-Gordon, M.  $\Omega$ B97M-V: A combinatorially optimized, range-separated hybrid, meta-GGA density functional with VV10 nonlocal correlation. *J. Chem. Phys.* **2016**, *144*, 214110. [CrossRef]
167. Papajak, E.; Zheng, J.; Xu, X.; Leverentz, H.R.; Truhlar, D.G. Perspectives on basis sets beautiful: Seasonal plantings of diffuse basis functions. *J. Chem. Theory Comput.* **2011**, *7*, 3027–3034. [CrossRef]
168. Zheng, J.; Xu, X.; Truhlar, D.G. Minimally Augmented karlsruhe basis sets. *Theor. Chem. Acc.* **2011**, *128*, 295–305. [CrossRef]
169. Lu, T.; Chen, Q. Shermo: A general code for calculating molecular thermochemistry properties. *Comput. Theor. Chem.* **2020**, *1200*, 113249. [CrossRef]
170. Database of Frequency Scale Factors for Electronic Model Chemistries. Available online: <https://comp.chem.umn.edu/freqscale/version3b2.htm> (accessed on 15 September 2021).
171. Lee, C.; Yang, W.; Parr, R.G. Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density. *Phys. Rev. B* **1988**, *37*, 785–789. [CrossRef]
172. Becke, A.D. Density-functional thermochemistry. III. The role of exact exchange. *J. Chem. Phys.* **1993**, *98*, 5648–5652. [CrossRef]
173. Hariharan, P.C.; Pople, J.A. The influence of polarization functions on molecular orbital hydrogenation energies. *Theor. Chem. Acc.* **1973**, *28*, 213–222. [CrossRef]
174. Frisch, M.J.; Pople, J.A.; Binkley, J.S. Self-consistent molecular orbital methods 25. *J. Chem. Phys.* **1984**, *80*, 3265–3269. [CrossRef]
175. Dolg, M.; Wedig, U.; Stoll, H.; Preuss, H. Energy-adjusted ab initio pseudopotentials for the first row transition elements. *J. Chem. Phys.* **1987**, *86*, 866–872. [CrossRef]
176. Chai, J.-D.; Head-Gordon, M. Long-range corrected hybrid density functionals with damped atom–atom dispersion corrections. *Phys. Chem. Chem. Phys.* **2008**, *10*, 6615–6620. [CrossRef] [PubMed]



177. Zhao, Y.; Truhlar, D.G. The M06 suite of density functionals for main group thermochemistry, thermochemical kinetics, noncovalent interactions, excited states, and transition elements: Two new functionals and systematic testing of four M06-class functionals and 12 other functionals. *Theor. Chem. Acc.* **2008**, *120*, 215–241. [[CrossRef](#)]
178. Fuentealba, P.; Preuss, H.; Stoll, H.; Szentpaly, L.V. A proper account of core-polarization with pseudopotentials: Single valence-electron alkali compounds. *Chem. Phys. Lett.* **1982**, *89*, 418–422. [[CrossRef](#)]
179. Wu, P.; Xiao, X.; Zhou, S.; Meng, L.; Zeng, J.; Wan, Q. Glycosylation of 2-(2-propylsulfinyl)benzyl 1,2-orthoester glycosides initiated by sulfoxide activation. *Org. Lett.* **2024**, *26*, 6053–6058. [[CrossRef](#)]
180. Gurung, P.B.; Thapa, P.; Hettiarachchi, I.L.; Zhu, J. Cationic Gold(I)-Catalyzed Glycosylation with Glycosyl *N*-1,1-Dimethylpropargyl Carbamate donors. *Org. Biomol. Chem.* **2022**, *20*, 7006–7010. [[CrossRef](#)]
181. Gurung, P.B.; Shine, G.; Zhu, J. Synthesis of *Salmonella enteritidis* antigenic tetrasaccharide repeating unit by employing cationic Gold(I)-catalyzed glycosylation involving glycosyl *N*-1,1-dimethylpropargyl carbamate donors. *J. Org. Chem.* **2024**, *89*, 12547–12558. [[CrossRef](#)]
182. Shinde, G.P.; Sutar, Y.; Kasdekar, N.; Joshi, P.; Rasool, O.; Ignatowicz, L.; Hamasur, B.; Hotha, S. Synthesis of an immunologically active heptamannoside of *Mycobacterium tuberculosis* by the [Au]/[Ag]-catalyzed activation of ethynylcyclohexyl glycosyl carbonate donor. *Org. Lett.* **2024**, *26*, 2034–2038. [[CrossRef](#)] [[PubMed](#)]
183. Li, Q.; Levi, S.M.; Wagen, C.C.; Wendlandt, A.E.; Jacobsen, E.N. Site-selective, stereocontrolled glycosylation of minimally protected sugars. *Nature* **2022**, *608*, 74–79. [[CrossRef](#)] [[PubMed](#)]
184. Wang, S.; Yang, Y.; Zhu, Q.; Lin, G.Q.; Yu, B. Chemical synthesis of polysaccharides. *Curr. Opin. Chem. Biol.* **2022**, *69*, 102154. [[CrossRef](#)] [[PubMed](#)]
185. Matsuzaki, Y.; Ito, Y.; Nakahara, Y.; Ogawa, T. Synthesis of branched poly-*N*-acetyl-lactosamine type pentaantennary pentacosasaccharide: Glycan part of a glycosyl ceramide from rabbit erythrocyte membrane. *Tetrahedron Lett.* **1993**, *34*, 1061–1064. [[CrossRef](#)]
186. Pozsgay, V. A new strategy in oligosaccharide synthesis using lipophilic protecting groups: Synthesis of a tetracosasaccharide. *Tetrahedron Asymmetry* **2000**, *11*, 151–172. [[CrossRef](#)]
187. Fraser-Reid, B.; Lu, J.; Jayaprakash, K.; López, J.C. Synthesis of a 28-mer oligosaccharide core of mycobacterial lipoarabinomannan (LAM) requires only two *n*-pentenyl orthoester progenitors. *Tetrahedron Asymmetry* **2006**, *17*, 2449–2463. [[CrossRef](#)]
188. Joseph, A.A.; Pardo-Vargas, A.; Seeberger, P.H. Total synthesis of polysaccharides by automated glycan assembly. *J. Am. Chem. Soc.* **2020**, *142*, 8561–8564. [[CrossRef](#)]
189. Zhu, Q.; Shen, Z.; Chiodo, F.; Nicolardi, S.; Molinaro, A.; Silipo, A.; Yu, B. Chemical synthesis of glycans up to a 128-mer relevant to the *O*-antigen of *Bacteroides vulgatus*. *Nat. Commun.* **2020**, *11*, 4142. [[CrossRef](#)]
190. Zhang, Y.; He, H.; Chen, Z.; Huang, Y.; Xiang, G.; Li, P.; Yang, X.; Lu, G.; Xiao, G. Merging reagent modulation and remote anchimeric assistance for glycosylation: Highly stereoselective synthesis of  $\alpha$ -glycans up to a 30-mer. *Angew. Chem. Int. Ed.* **2021**, *60*, 12597–12606. [[CrossRef](#)]
191. Wang, L.; Lowary, T.L. Synthesis of structurally-defined polymeric glycosylated phosphoprenols as potential lipopolysaccharide biosynthetic probes. *Chem. Sci.* **2021**, *12*, 12192–12200. [[CrossRef](#)]
192. Zhu, Y.; Delbianco, M.; Seeberger, P.H. Automated assembly of starch and glycogen polysaccharides. *J. Am. Chem. Soc.* **2021**, *143*, 9758–9768. [[CrossRef](#)] [[PubMed](#)]
193. Joe, M.; Bai, Y.; Nacario, R.C.; Lowary, T.L. Synthesis of the docosanasaccharide arabinan domain of mycobacterial arabinogalactan and a proposed octadecasaccharide biosynthetic precursor. *J. Am. Chem. Soc.* **2007**, *129*, 9885–9901. [[CrossRef](#)] [[PubMed](#)]
194. Ishiwata, A.; Ito, Y. Synthesis of docosasaccharide arabinan motif of mycobacterial cell wall. *J. Am. Chem. Soc.* **2011**, *133*, 2275–2291. [[CrossRef](#)] [[PubMed](#)]
195. Wu, Y.; Xiong, D.; Chen, S.; Wang, Y.; Ye, X. Total synthesis of mycobacterial arabinogalactan containing 92 mono-saccharide units. *Nat. Commun.* **2017**, *8*, 14851. [[CrossRef](#)]
196. Yao, W.; Xiong, D.-C.; Yang, Y.; Geng, C.; Cong, Z.; Li, F.; Li, B.-H.; Qin, X.; Wang, L.-N.; Xue, W.-Y.; et al. Automated solution-phase multiplicative synthesis of complex glycans up to a 1,080-mer. *Nat. Synth.* **2022**, *1*, 854–863. [[CrossRef](#)]
197. Qin, X.; Xu, C.; Liu, M.; Zeng, F.; Yao, W.; Deng, Y.; Xu, T.; Sun, S.; Sun, D.; Mo, J.; et al. Synthesis of branched arabinogalactans up to a 140-mer from *Panax notoginseng* and their anti-pancreatic-cancer activity. *Nat. Synth.* **2024**, *3*, 245–255. [[CrossRef](#)]
198. Islam, M.; Shinde, G.P.; Hotha, S. Expedient synthesis of the heneicosasaccharyl mannose capped arabinomannan of the *Mycobacterium tuberculosis* cellular envelope by glycosyl carbonate donors. *Chem. Sci.* **2017**, *8*, 2033–2038. [[CrossRef](#)]
199. Marando, V.M.; Kim, D.E.; Calabretta, P.J.; Kraft, M.B.; Bryson, B.D.; Kiessling, L.L. Biosynthetic glycan labeling. *J. Am. Chem. Soc.* **2021**, *143*, 16337–16342. [[CrossRef](#)]
200. Marando, V.M.; Kim, D.E.; Kiessling, L.L. Biosynthetic incorporation for visualizing bacterial glycans. *Methods Enzymol.* **2022**, *665*, 135–151. [[CrossRef](#)]
201. Lee, S.Y.; Marando, V.M.; Smelyansky, S.R.; Kim, D.E.; Calabretta, P.J.; Warner, T.C.; Bryson, B.D.; Kiessling, L.L. Selective glycan labeling of mannose-containing glycolipids in mycobacteria. *J. Am. Chem. Soc.* **2024**, *146*, 377–385. [[CrossRef](#)]
202. Zhou, K.L.; Li, X.; Zhang, X.L.; Pan, Q. Mycobacterial Mannose-capped lipoarabinomannan: A modulator bridging innate and adaptive immunity. *Emerg. Microbes Infect.* **2019**, *8*, 1168–1177. [[CrossRef](#)] [[PubMed](#)]
203. Torrelles, J.B.; Chatterjee, D. Collected thoughts on mycobacterial lipoarabinomannan, a cell envelope lipoglycan. *Pathogens* **2023**, *12*, 1281. [[CrossRef](#)] [[PubMed](#)]

204. Ding, C.; Hu, M.; Guo, W.; Hu, W.; Li, X.; Wang, S.; Shangguan, Y.; Zhang, Y.; Yang, S.; Xu, K. Prevalence trends of latent tuberculosis infection at the global, regional, and country levels from 1990–2019. *Int. J. Infect. Dis.* **2022**, *122*, 46–62. [[CrossRef](#)] [[PubMed](#)]
205. Chakaya, J.; Petersen, E.; Nantanda, R.; Mungai, B.N.; Migliori, G.B.; Amanullah, F.; Lungu, P.; Ntoumi, F.; Kumarasamy, N.; Maeurer, M. The WHO global tuberculosis 2021 report-not so good news and turning the tide back to end TB. *Int. J. Infect. Dis.* **2022**, *124*, S26–S29. [[CrossRef](#)]

**Disclaimer/Publisher’s Note:** The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.