

Review

Advancements in Carbohydrate Scaffold Synthesis: Exploring Prins Cyclization Methodology

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Abstract: The synthesis of natural and unconventional compounds with carbohydrate structures is of great interest to glycochemists due to their vital biological roles. In recent years, there has been significant progress in developing direct and indirect synthetic strategies for constructing sugar moieties. Among these methods, the Prins reaction, employing homoallylic alcohols and carbonyl compounds, has proven invaluable for directly creating sugar skeletons. This review discusses approaches for crafting carbohydrate frameworks using the Prins reaction, utilizing both carbohydrate and non-carbohydrate starting materials.

Keywords: carbohydrates; Prins reaction; 2-deoxysugars; homoallylic alcohols; rare sugars

1. Introduction

Carbohydrates are fundamental biomolecules that play a multitude of vital roles in living systems, including cell growth, proliferation, immune responses, cell adhesion, and cell–cell communication [1–7]. Their diverse functions make them crucial for maintaining the structural and functional integrity of biological processes. In biological systems, carbohydrates exist in various forms, with many found as oligosaccharides bound to lipids or proteins. These complexes, collectively termed glycoconjugates, are essential for mediating biological recognition events such as immune signaling and pathogen–host interactions. Glycoconjugates are classified based on the nature of their glycosidic linkages, which can be N-, O-, C-, or S-linked glycosides [8–12]. The synthesis and modification of these carbohydrate structures remain a cornerstone of chemical biology and medicinal chemistry, as their applications span pharmaceuticals, materials science, and biotechnology.

Designing novel synthetic strategies for carbohydrates is an active area of research due to their immense structural complexity and the challenges of achieving stereoselectivity during synthesis. One of the most critical challenges in carbohydrate chemistry is the construction of pyran (six-membered) and furan (five-membered) rings, which are common structural motifs in natural products, glycoconjugates, and various biologically active compounds [13–18]. Achieving the stereoselective synthesis of these rings under mild conditions is a central goal in organic synthesis. Among the various approaches developed to address this challenge, the Prins reaction stands out as a highly efficient and versatile method.

The Prins reaction [19–27] has emerged as a key tool for the stereoselective formation of tetrahydropyran (THP) and tetrahydrofuran (THF) rings. This reaction involves the condensation of homoallylic alcohols with carbonyl compounds in the presence of a Brønsted or Lewis acid catalyst. Over the last few decades, the Prins reaction has gained considerable attention due to its ability to provide access to a wide variety of functionalized



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cyclic compounds. Numerous natural products and bioactive molecules containing THP rings have been synthesized using Prins methodology (Figure 1) such as Clavosolide A **1**, Cryptophycin-24 **2**, and (-)-Plyocavernoside A **3** [28–30].

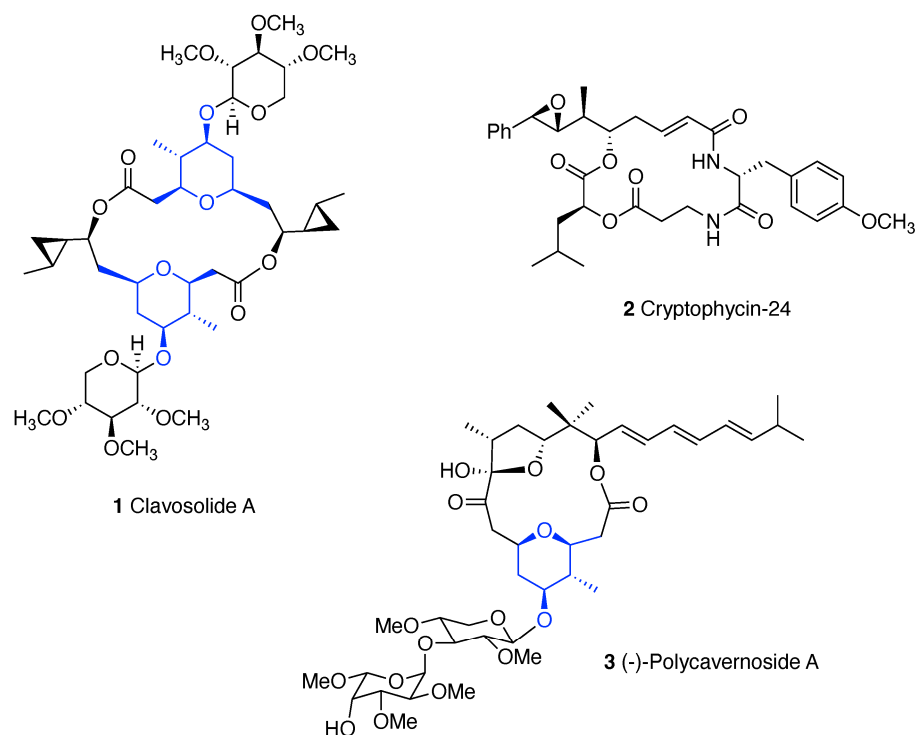


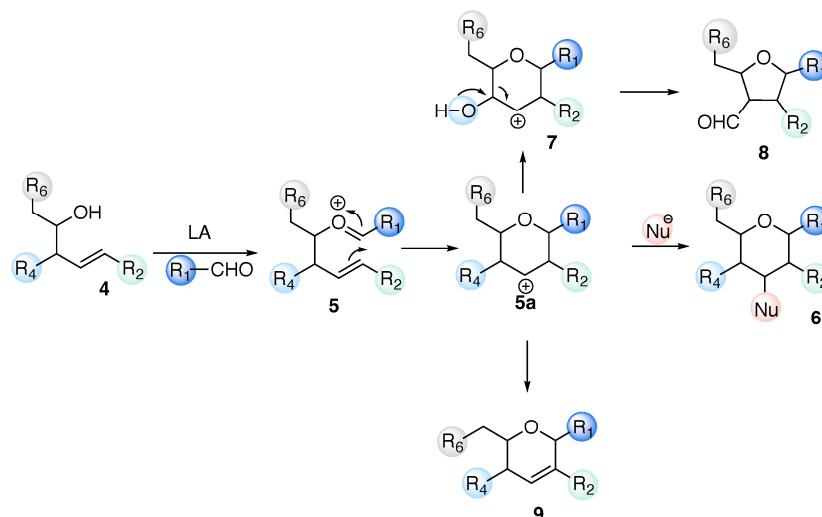
Figure 1. Synthesis of natural products by using Prins reaction.

The renewed interest in the Prins reaction stems from its ability to generate multi-functionalized carbohydrate scaffolds with diverse applications. A typical (Scheme 1) reaction pathway [31,32] involves the interaction of homoallylic alcohols **4** and carbonyl compounds in the presence of an acid catalyst, leading to the formation of an oxocarbenium ion intermediate **5**. This intermediate undergoes π -cation cyclization, resulting in the formation of a tetrahydropyran intermediate **5a**; then, through a nucleophilic attack, either the reaction proceeds intramolecularly or intermolecularly, which subsequently produces a highly functionalized and more complex molecular architecture **6**. On the other hand, this intermediate **5a** may undergo a pinacol-type rearrangement through **7**, yielding tetrahydrofuran derivatives **8**. Alternatively, the tetrahydropyran intermediate **5a** C2-H elimination yields cycloalkene products or Ferrier products **9**. This versatility makes the Prins reaction a valuable tool in synthetic organic chemistry.

Developing efficient methods for synthesizing rare sugars is another crucial aspect of carbohydrate chemistry [33–35]. Rare sugars such as altrose and allose, while less abundant in nature, exhibit unique biological properties that make them attractive for therapeutic and industrial applications. The Prins reaction has proven to be a versatile method for accessing these rare sugar scaffolds, enabling chemists to explore their potential in drug discovery and other fields [36].

Although various reviews have covered synthetic transformations of unique carbohydrate-based scaffolds, such as the carbohydrate dienes [37], 1,2- and 1,6-anhydrosugars [38,39], glycol functionalization [40–42] and C-H activations [43,44], hypervalent iodine in glycochemistry [45], and functionalization of 3-oxo-glycals [46], to the best of our knowledge, the chemistry of the Prins reaction in carbohydrate chemistry has not been reviewed recently. Given the progress made over the past several decades, and the great utility of the Prins reaction in carbohydrate chemistry as important building blocks, this review highlights the

strategic importance of the Prins reaction in the synthesis of carbohydrate moieties. The discussion is structured around the methods used to construct the extended carbohydrate core, with a focus on the number and type of bonds formed during the critical synthetic step. By providing an overview of the main strategies, this work underscores the utility of the Prins reaction as a cornerstone for advancing carbohydrate chemistry.

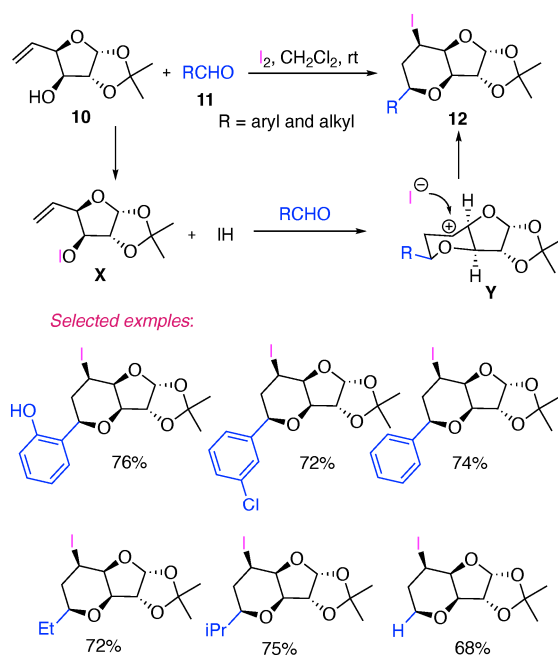


Scheme 1. General mechanism for the synthesis of carbohydrate skeleton through Prins reaction.

There is currently a wealth of inter and intramolecular Prins reactions available within the modern synthetic chemist's "toolbox." However, among the most prevalent Prins reaction types is the addition of a nucleophiles to a secondary carbocation (typically alkenes or alkynes), pinacol-type rearrangement, Sakurai–Prins reaction, and Ritter–Prins reaction. Within the context of sugar moiety synthesis via Prins cyclization and based on the origin synthon of homoallylic alcohols, these reactions are divided into two distinct subclasses: those in which a synthesis of carbohydrate scaffolds from carbohydrate synthons (2) and those in which a carbohydrate scaffolds from non-carbohydrate synthons (3).

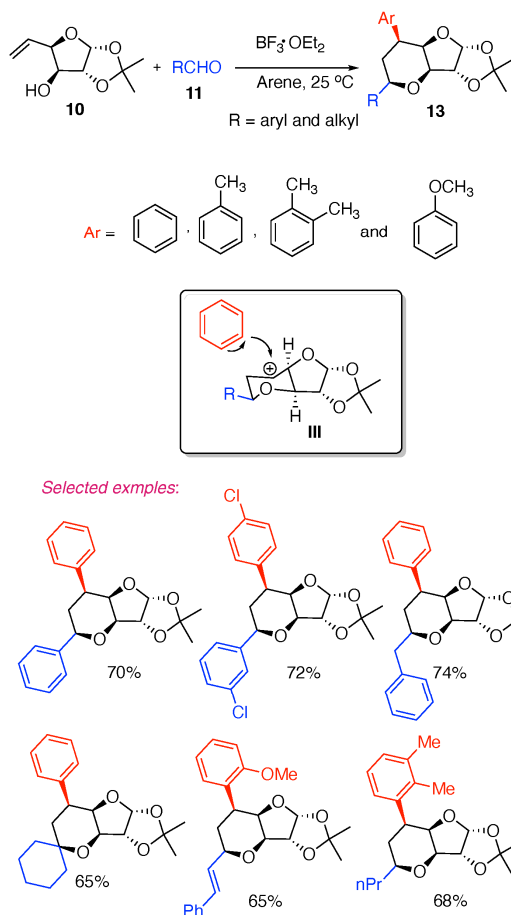
2. Carbohydrate Synthons to Carbohydrate Scaffolds

This section summarizes research that focuses on generating valuable carbohydrate scaffolds or structural units using carbohydrate-derived starting materials, particularly carbohydrate-derived homoallylic alcohols, through a process called Prins cyclization. In this specific study conducted by Yadav and colleagues, they reported [47] the synthesis of a sugar-annulated iodotetrahydropyran compound **12** by employing Prins cyclization. They combined a D-glucose-derived homoallylic alcohol **10** with an aldehyde **11** in their synthetic approach (Scheme 2). The researchers explored the use of a variety of aromatic and aliphatic aldehydes as reactants in their experiments. Importantly, they successfully obtained the desired products in moderate to good yields, indicating the effectiveness of their synthesis method. The authors of this study proposed a reaction mechanism that involves an intermediate **X** and a highly reactive carbocation **Y**. This carbocation **Y** is subsequently captured by an iodide ion, resulting in the formation of the sugar-annulated iodotetrahydropyran compound **12**.



Scheme 2. Synthesis of sugar annulated iodotetrahydropyrans.

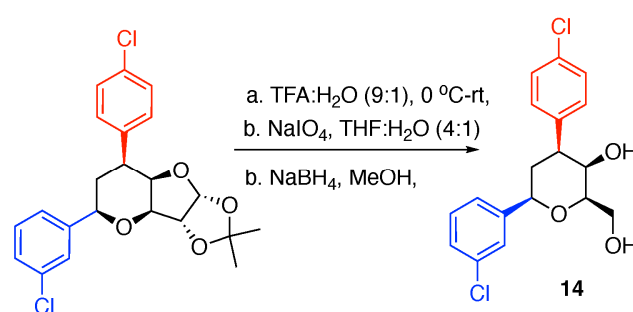
In a subsequent study, the same research group delved deeper into the Prins reaction of homoallylic alcohol **10**, as shown in Scheme 3. They investigated this reaction with various carbonyl compounds **11**, employing $\text{BF}_3 \cdot \text{OEt}_2$ as a catalyst and various arene (Scheme 3).



Scheme 3. Synthesis of sugar-fused diaryl hexahydro-2H-furo [3,2-b]pyran.

In a subsequent study, the same research group [48] conducted an in-depth investigation of the Prins/Friedel–Crafts cyclization of homoallylic alcohol **10**, as illustrated in Scheme 3. They explored the reaction of a homoallylic alcohol **10** derived from D-glucose with various carbonyl compounds **11**, using benzene as the solvent and a catalytic amount of $\text{BF}_3 \cdot \text{OEt}_2$ (0.1 equiv). The reaction proceeded efficiently at 25 °C, yielding the corresponding sugar-fused diaryl hexahydro-2H-furo [3,2-*b*]pyran **13** via intermediate III in good to excellent yields, with complete *cis*-selectivity (Scheme 3).

The authors specifically aimed to trap the tetrahydropyranyl carbocation using benzene as the C-nucleophile. Notably, they also investigated the reaction in other arene solvents, including benzene, toluene, *o*-xylene, and anisole. The reaction demonstrated compatibility with a wide range of aryl and alkyl aldehydes as well as cyclohexanone. Interestingly, one of the products was further converted into diaryl dihydroxytetrahydropyran **14**, a C-aryl glycoside (Scheme 4).

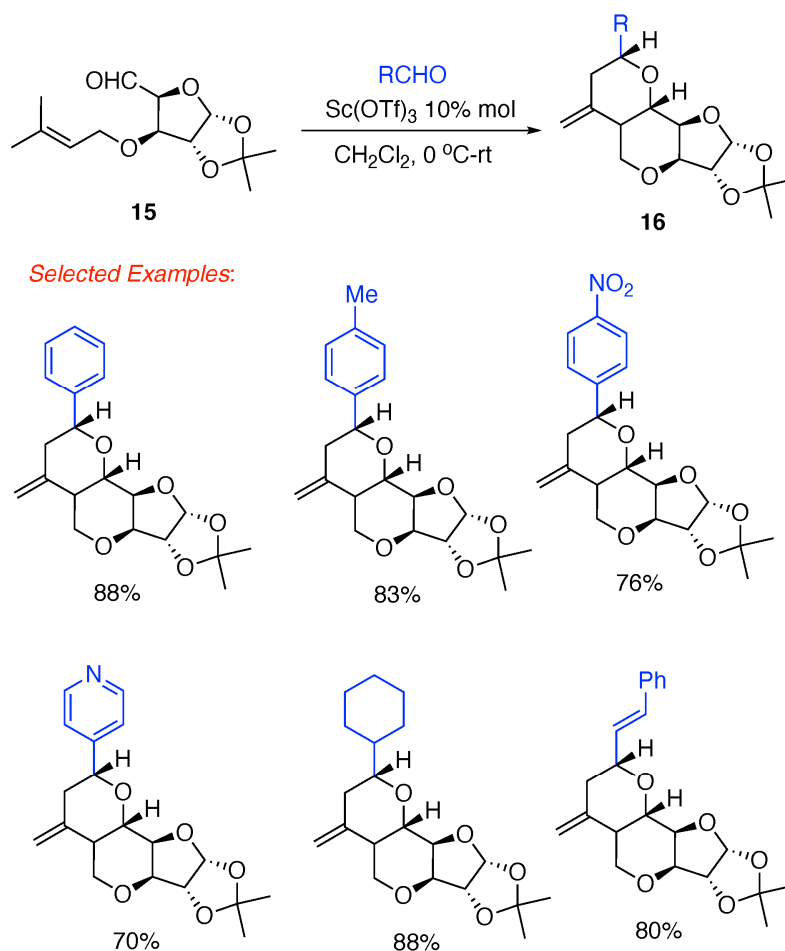


Scheme 4. Synthesis of sugar-fused diaryl hexahydro-2H-furo [3,2-*b*]pyran **14**.

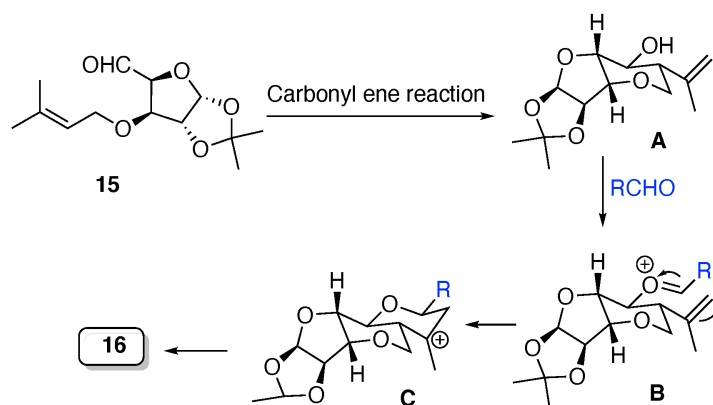
Reddy et al. reported [49] the synthesis of the hexahydro-2H-furo [3,2-*b*]pyranopyran scaffold **16** from *O*-prenyl tethered carbohydrate-derived aldehyde **15** with various aldehydes in the presence of 10 mol% $\text{Sc}(\text{OTf})_3$ in dichloromethane at 0 °C to room temperature (Scheme 5). Further, this reaction was studied with a variety of aryl and alkyl aldehydes. Eventually, this reaction was quite successful with *p*-bromobenzaldehyde and cyclohexylidene protected *O*-prenyl tethered carbohydrate-derived aldehyde to furnish the product tricyclic sugar derivative **16** (Scheme 5).

First, cyclization of *O*-prenyl tethered carbohydrate-derived aldehyde **15** is proposed, facilitated by carbonyl ene reaction and led to homoallylic alcohol **A**, with this being the Prins reaction defining step. Then **A** condenses with aldehyde in presence of $\text{Sc}(\text{OTf})_3$ could give tertiary carbocation **C** via oxocarbenium ion **B**. Further **C** could eliminate proton from methyl group and led to product **16** (Scheme 6).

In 2014, Lumba and Mukherjee [50] developed a practical protocol for the conversion of tri-*O*-acetyl-D-glucal-derived 2-C-branched sugars **17** to the corresponding *cis*-1-oxadecalines **18**. By using FeCl_3 as a catalyst system at room temperature, the target molecules could be afforded (Scheme 7). The advantages of this protocol are the use of a variety of 2-C-branched sugars.

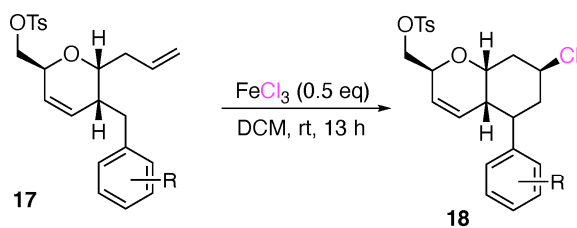


Scheme 5. Synthesis of hexahydro-2H-furo [3,2-*b*]pyranopyran scaffold.

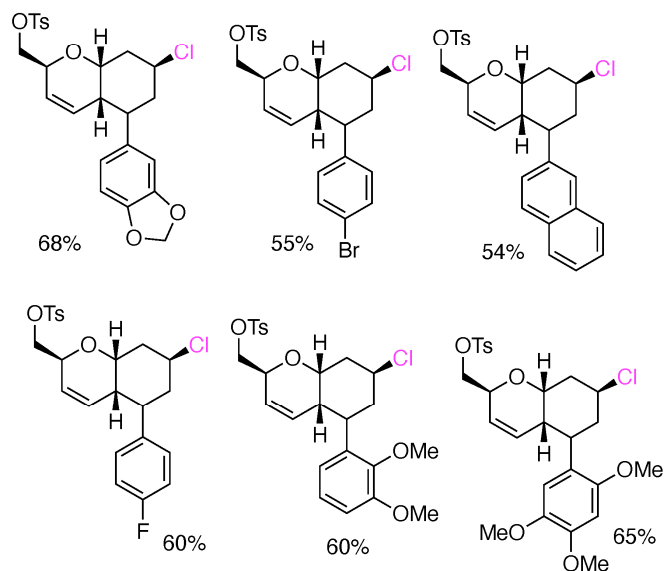


Scheme 6. Mechanism for the formation of hexahydro-2H-furo [3,2-*b*]pyranopyran.

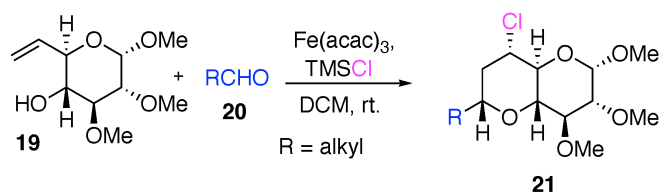
Padrón and co-workers [51] reported a simple preparation method for *trans*-fused bicyclic tetrahydropyran **21** by iron(III) catalyzed tandem reaction using tri-*O*-acetyl-D-glucal-derived homoallylic alcohol **16** and iso-valeraldehyde (Scheme 8). This reaction was further studied with more complex molecule **19**, which is derived from a-methyl-D-glucopyranoside with aldehydes and led to the *trans*-fused bicyclic tetrahydropyrans **20**. Here, the features are the good substrate generality and the mild reaction conditions.



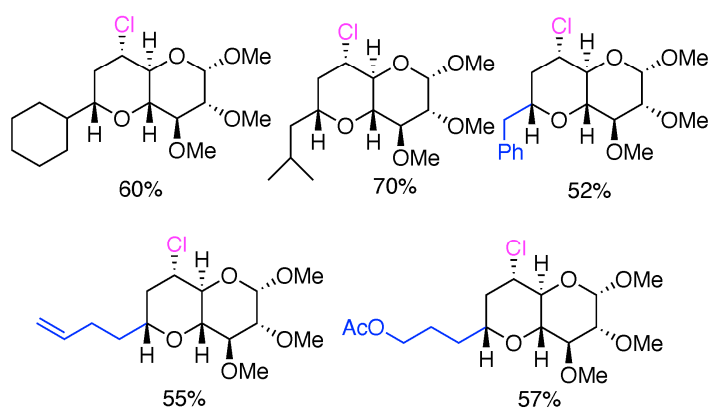
Selected examples:



Scheme 7. Synthesis of *cis*-1-oxadecalines **17** from 2-C-branched sugar **18**.



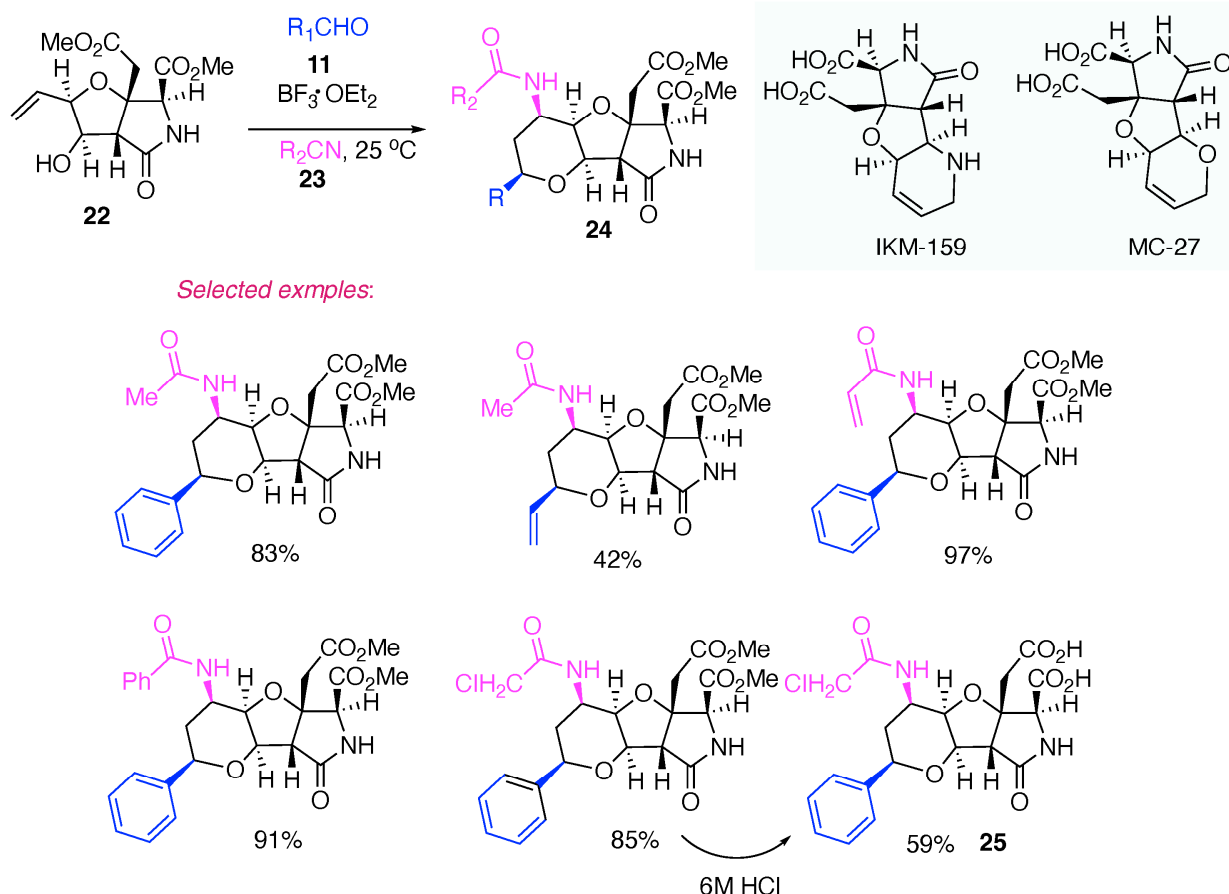
Selected examples:



Scheme 8. Synthesis of *trans*-fused bicyclic tetrahydropyrans **21** from tri-*O*-acetyl-D-glucal and α -methyl-D-glucopyranoside.

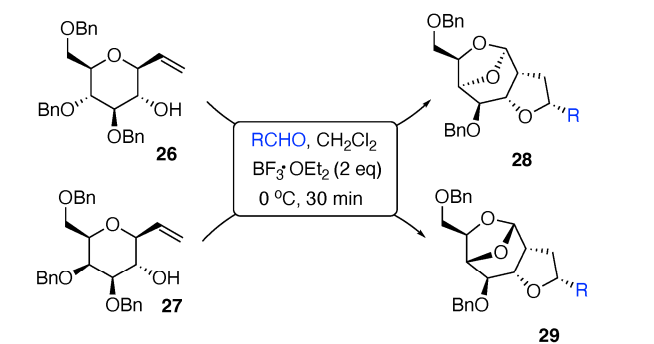
Cis-fused heterobicyclic systems are very important substrates in neuronally active agents such as marine-derived dysiherbaine and their analogues IKM-159 and MC-27.

Oikawa and co-workers [52] reported a $\text{BF}_3 \cdot \text{OEt}_2$ catalyzed condensation reaction between glucose-derived enantiomerically pure homoallylic alcohol **22** with aldehydes **11** and nitrile solvent **23**; the intended cis-fused 4-amidotetrahydropyrans **24** were obtained in a one-pot manner under relatively mild conditions (Scheme 9). Based on these results and the scope was extended to substrate **24** with variety of aldehydes and nitrile solvent via Prins-Ritter reaction to obtained cis-fused heterobicyclics **24** which were further subjected to acid hydrolysis led to the formation for novel glutamates **25**.

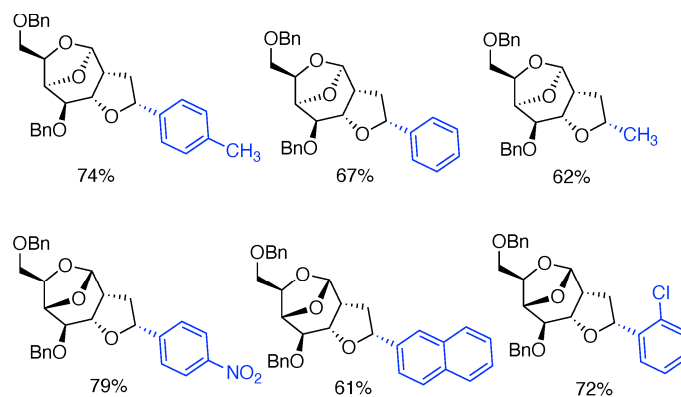


Scheme 9. Cis-fused 4-amidotetrahydropyrans towards a precursor for possible neuronal receptor ligands via Prins-Ritter reaction.

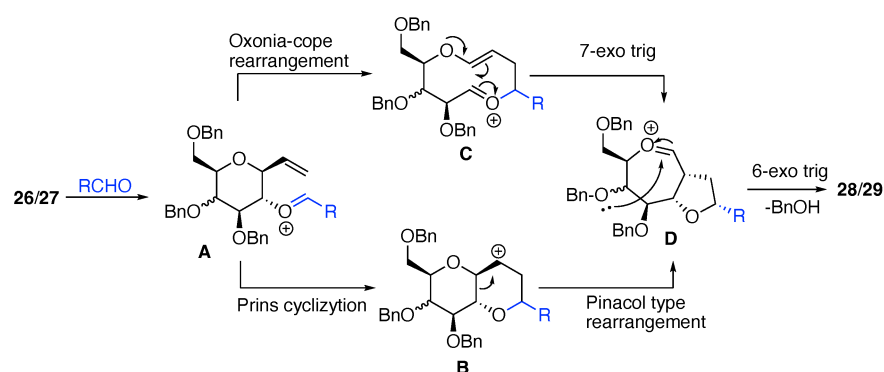
Vankar and co-workers [53] developed an efficient synthesis of bridged tricyclic ketals **28/29** with good substrate generality starting from homoallylic alcohols **26/27** derived from 1,2-anhydro and aldehydes; they used $\text{BF}_3 \cdot \text{OEt}_2$ as the catalyst (Scheme 10). Here, the main advantages include the stereoselectivity and good yields. They proposed the plausible mechanism for the formation of bridged tricyclic ketals **28/29**. It is presumed (Scheme 11) that after initial formation of the oxocarbenium ion **A**, it can either undergo Oxonia-Cope rearrangement to form **B** or simply a π -cation cyclization to form **C**. Both of these intermediates will then undergo 7-exo trig cyclization or pinacol-type rearrangement via the transition state **D**, followed by cleavage of the C4-OBn participation resulting in the form of bridged tricyclic ketals **28/29**. Later, these bridged tricyclic ketals were converted to (Scheme 12) tetrahydrofuran ring-fused heptose **31** and 2C-branched heptose **32**.



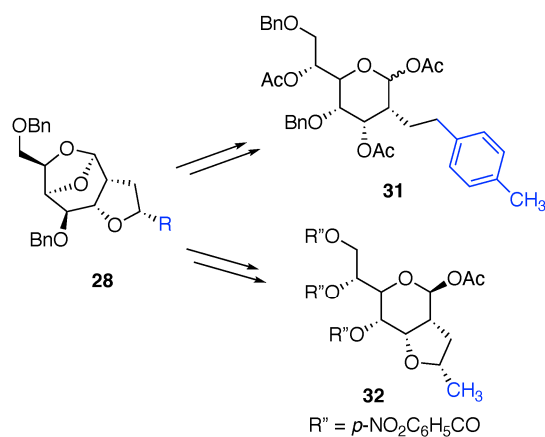
Selected examples:



Scheme 10. Synthesis of bridged tricyclic ketals **28/29** through Prins-pinacol-type rearrangement and C4-OBn participation.

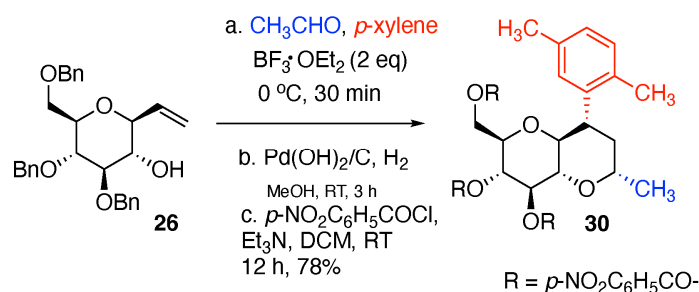


Scheme 11. Mechanism for the formation of bridged tricyclic ketals **30/31**.



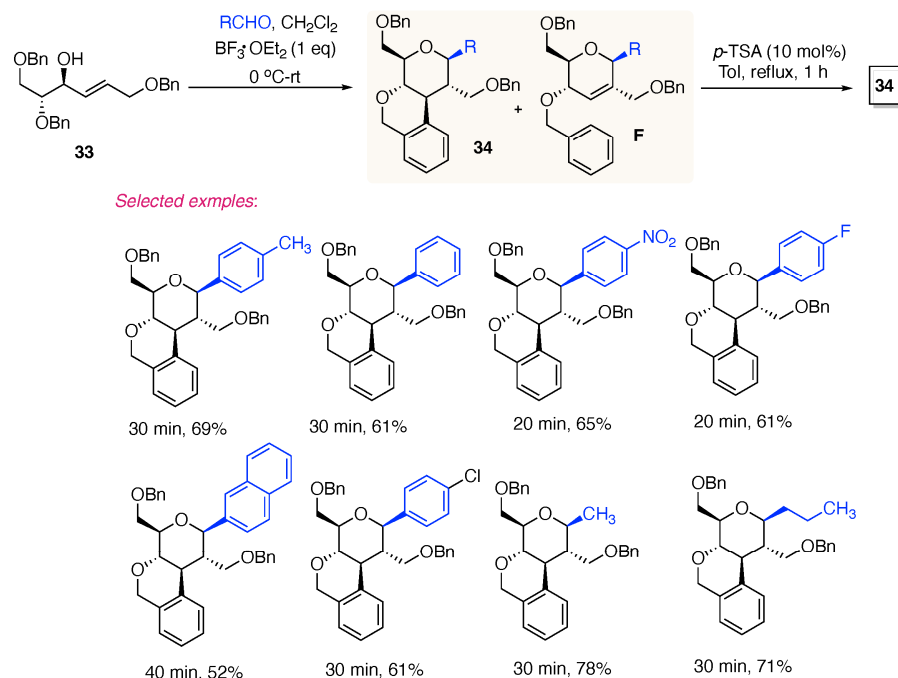
Scheme 12. Derivatization of bridged tricyclic ketal.

To gain further insights into the proposed mechanism, homoallylic alcohol **26** was treated with acetaldehyde using *p*-xylene as a solvent and two equivalents of $\text{BF}_3 \cdot \text{OEt}_2$ at 0°C . After 30 min, the *p*-xylene-trapped product was observed (Scheme 13). This intermediate was then subjected to hydrogenolysis using $\text{Pd}(\text{OH})_2/\text{C}$, followed by benzoylation of the resulting alcohol with *p*-nitrobenzoyl chloride in the presence of Et_3N , yielding the corresponding annulated sugar **30**.



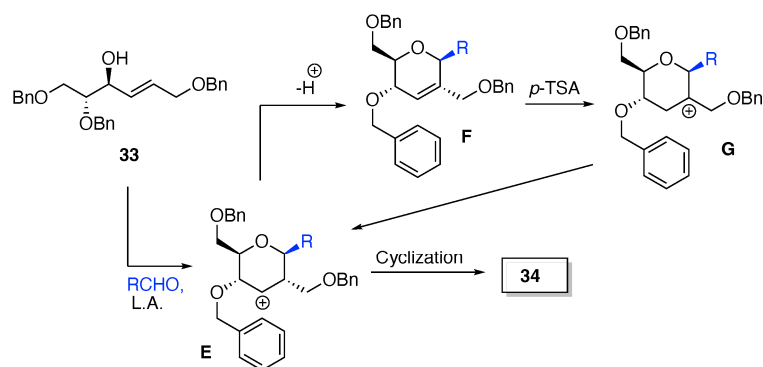
Scheme 13. Trapping with *p*-xylene.

In 2017, Vankar et al. [54] reported an efficient synthetic route for the preparation of 1C-aryl/alkyl 2C-branched sugar-fused isochroman derivatives **34**. The method involved the reaction of homoallylic alcohol **33** and various aldehydes in the presence of $\text{BF}_3 \cdot \text{OEt}_2$ in DCM, leading to the formation of 1C-aryl/alkyl 2C-branched sugar-fused isochroman derivatives **34** and intermediate **F**. Then, the crude reaction mixture was further treated with *p*-TSA in toluene, yielding exclusively the desired derivative **34**. This process achieved moderate reaction times (1 h) with yields ranging from 60–70% (Scheme 14).



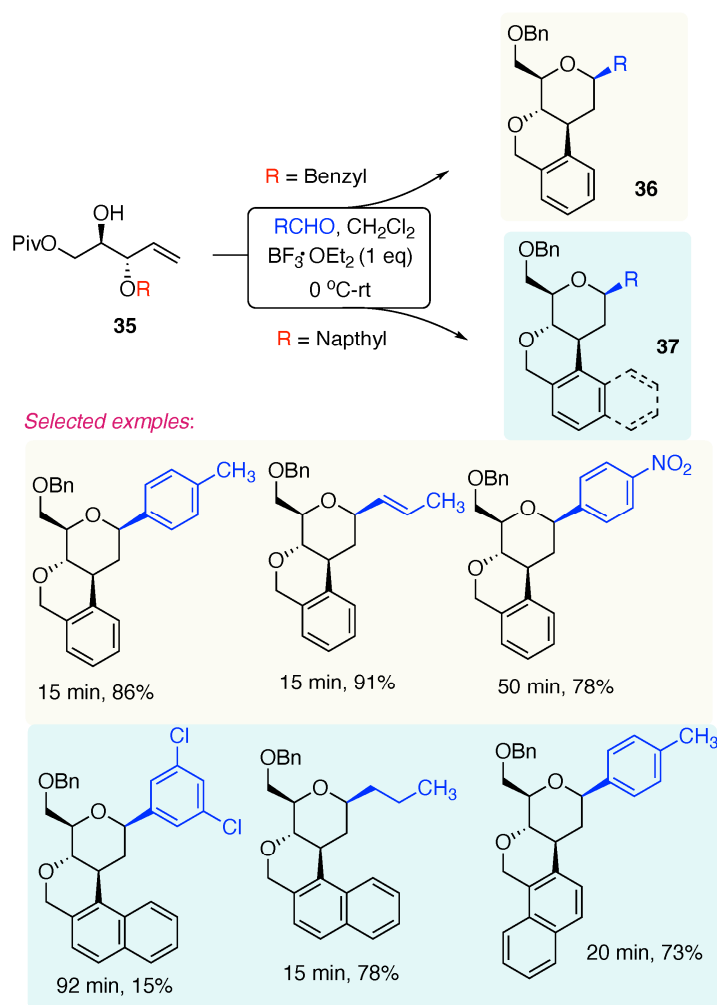
Scheme 14. Synthesis of 1C-aryl/alkyl 2C-branched sugar-fused isochroman derivatives.

In the presence of the $\text{BF}_3 \cdot \text{OEt}_2$, substrate **33** and aldehyde were condensed to produce intermediate **E**, which would undergo elimination of adjacent proton and generate dihydropyran **F**. This dihydropyran **F** treated with PTSA gives tertiary carbocation **G**, which is in equilibrium with intermediate **E**. Then, intermediate **E** may directly give the product **34** (Scheme 15).

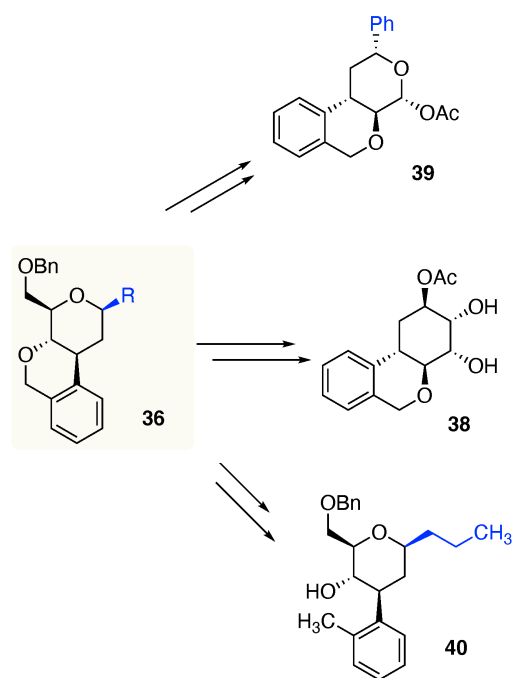


Scheme 15. Mechanism for the formation of 1C-aryl/alkyl 2C-branched sugar-fused isochroman derivatives.

Later, Dubbu and Vankar strategically synthesized [55] a series of 2-deoxy-3,4-fused-C-aryl/alkylglycosides through a cascade Prins cyclization of a D-mannitol-derived homoallylic alcohol, using $\text{BF}_3 \cdot \text{OEt}_2$ as a catalyst. Initially, (Scheme 16) D-mannitol-derived homoallylic alcohol **35** was treated with various carbonyl compounds in the presence of $\text{BF}_3 \cdot \text{OEt}_2$ in DCM, yielding 2-deoxy-3,4-fused isochroman derivatives **36/37** in good to excellent yields. The authors further modified these products to obtain potentially bioactive scaffolds **38**, **39**, and **40** (Scheme 17).

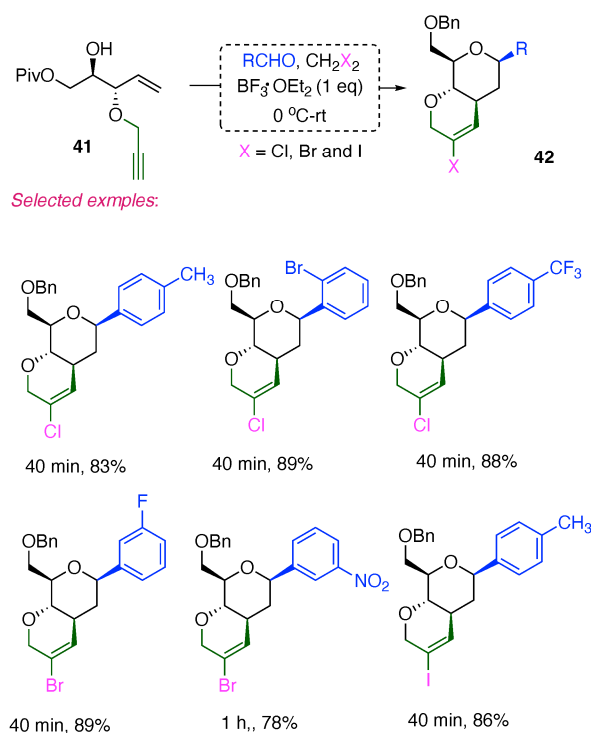


Scheme 16. Synthesis of 1C-aryl/alkyl-fused isochroman derivatives.



Scheme 17. Derivatization of sugar-fused isochroman derivatives.

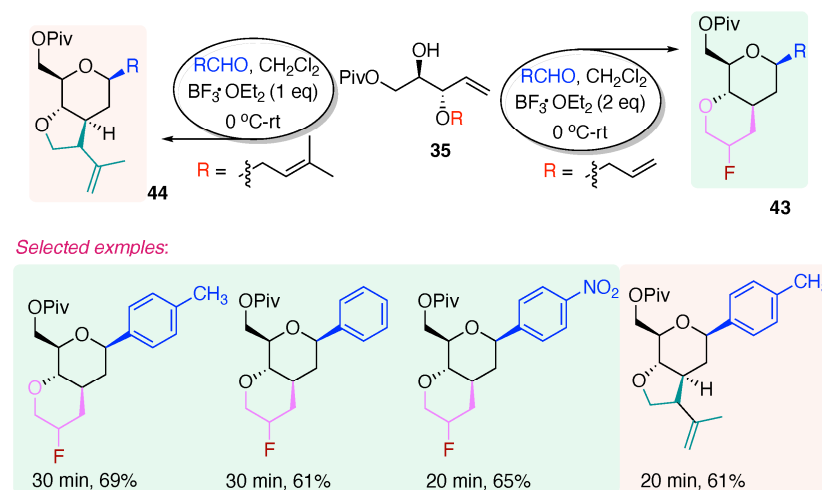
Using similar reaction conditions, but with a D-mannitol-derived homoallylic alcohol protected with a propargyl group, Dubbu and Vankar obtained [55] 1C-aryl/alkyl-fused bicyclic vinyl halide derivatives **42** in good to excellent yields. The halogen abstraction was achieved through the use of halogenated solvents. Depending on the solvent used— CH_2Cl_2 , CH_2Br_2 , CH_3I , etc.—the products obtained were 1C-aryl/alkyl-fused bicyclic vinyl chloride, vinyl bromide, or vinyl iodide derivatives, respectively (Scheme 18).



Scheme 18. Synthesis of 1C-aryl/alkyl-fused bicyclic vinyl halide derivatives.

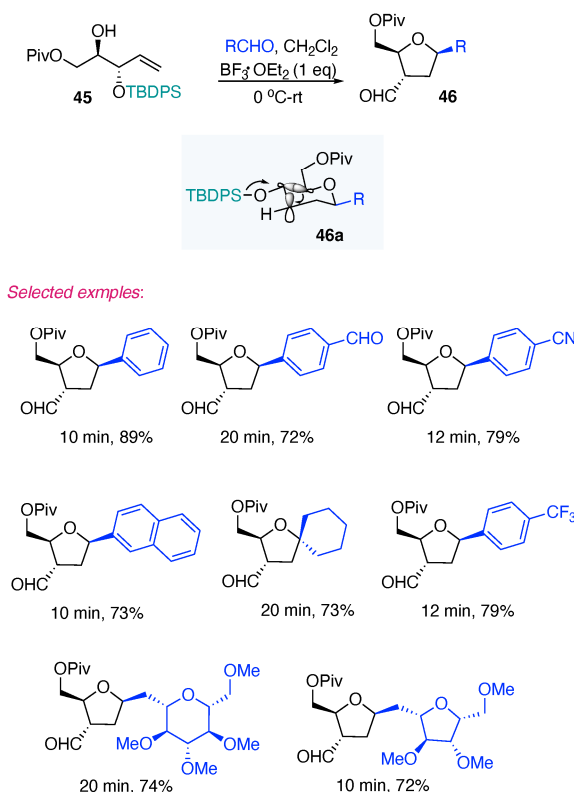
By applying similar reaction conditions, Dubbu and Vankar further transformed [55] the D-mannitol-derived homoallylic alcohol **35**, protected with allyl and substituted allyl

groups, to synthesize 1C-aryl/alkyl-fused bicyclic fluorine-substituted tetrahydropyran and furan derivatives 43/44, achieving good to excellent yields (Scheme 19).



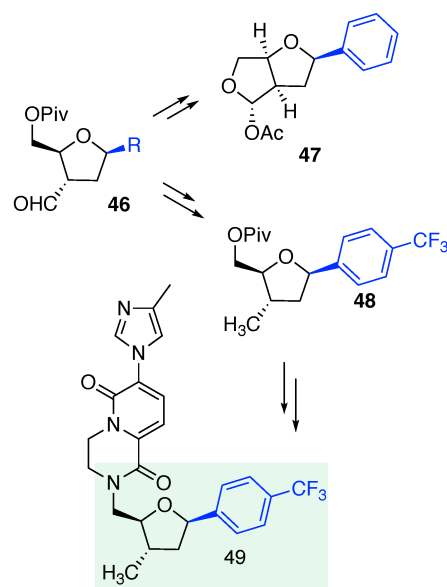
Scheme 19. Synthesis of 1C-aryl/alkyl-fused bicyclic fluorine substituted tetrahydropyrans and furan derivatives.

In 2019, Vankar reported the stereoselective synthesis of 3-deoxy-3C-formyl β -C-aryl/alkyl furanosides **46** (Scheme 20) through a cascade Prins reaction followed by a pinacol-type rearrangement [56]. This transformation involved an –OTBDPS-protected homoallylic alcohol **45**, derived from D-mannitol, reacting with various carbonyl compounds in the presence of $\text{BF}_3 \cdot \text{OEt}_2$ in DCM. The reaction provided excellent yields and high selectivity. The author proposed that this reaction proceeds via a cyclic transition state, **46a**.



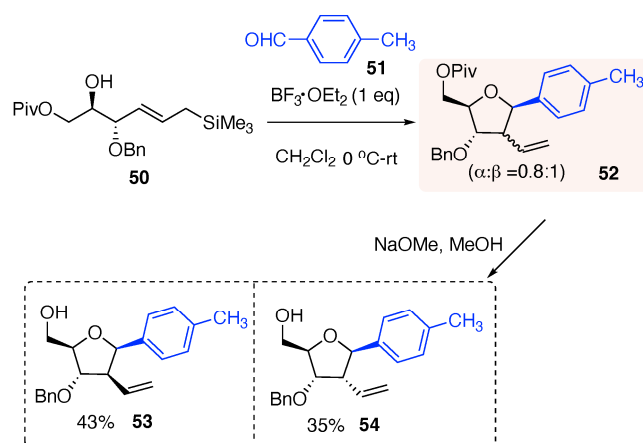
Scheme 20. Synthesis of 2,3-dideoxy-3C-formyl β -C-aryl/alkyl furanosides **48**.

Furthermore, (Scheme 21) this method was effectively applied to synthesize a fused-bicyclic β -C-aryl furanoside moiety **47** and a 2,3-dideoxy-3C-methyl β -C-aryl furanoside **48**, both of which are found in the core structures of bioactive molecules.



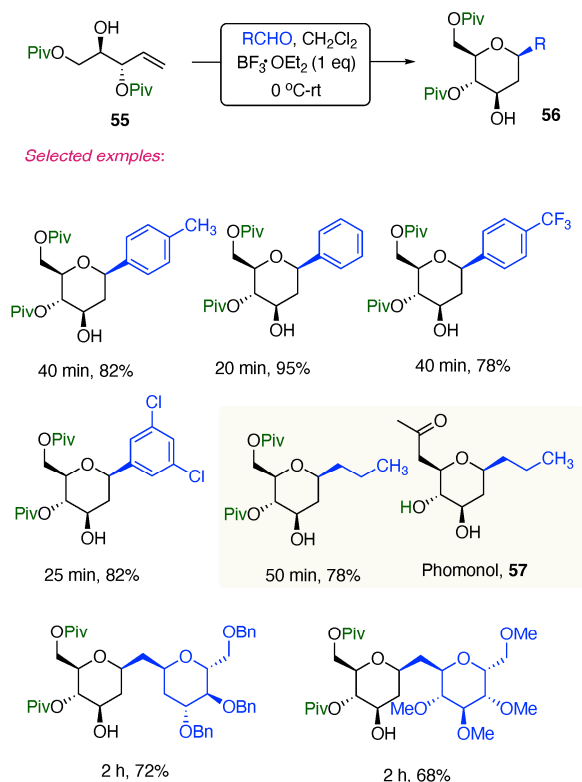
Scheme 21. Derivatization of 2,3-dideoxy-3C-formyl β -C-aryl/alkyl furanosides.

Later, Vankar and co-workers optimized (Scheme 22) the Sakurai–Prins reaction of a D-mannitol-derived homologated allylsilane homoallylic alcohol **48** with *p*-tolualdehyde **51** in the presence of $\text{BF}_3 \cdot \text{OEt}_2$ [56]. This reaction yielded 2-deoxy-2C-branched β -C-aryl furanosides in good yield (84%) as an inseparable diastereomeric mixture ($\alpha:\beta = 0.8:1$ ratio) (Scheme 22). To separate the stereoisomers, compound **48** was subsequently deprotected at the $-\text{OPiv}$ group using NaOMe/MeOH , resulting in diastereomers **53** and **54**, which were then separated by column chromatography with yields of 43% and 35%, respectively.

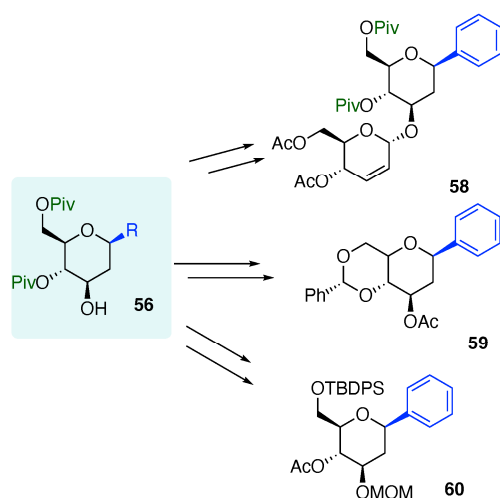


Scheme 22. Synthesis of 2-deoxy-2C-branched β -C-aryl furanosides **53** and **54**.

Vankar and co-workers further synthesized [57] a non-participating protecting group at allylic position of D-mannitol-derived homoallylic alcohol **55** and which was subjected to the Prins reaction with a variety of aldehydes in the presence of $\text{BF}_3 \cdot \text{OEt}_2$ as a catalyst and led to stereoselective 2-deoxy-C-aryl/alkyl glycosides **56** (Scheme 23). The synthetic versatility of this approach has been demonstrated in the synthesis of C-disaccharide and O-linked disaccharides **58**, and differently protected 2-deoxy- β -C-aryl glycosides **59**, **60** (Scheme 24).

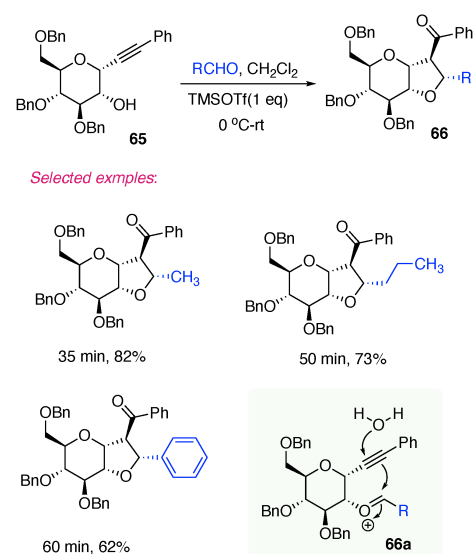
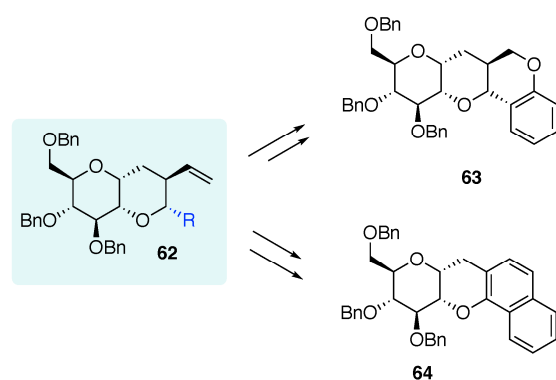
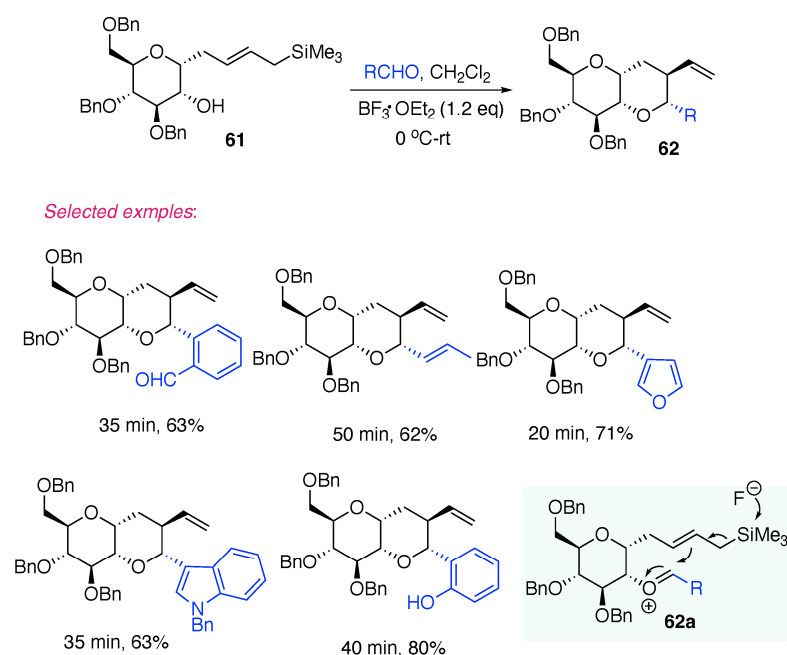


Scheme 23. Synthesis of 2-deoxy- β -C-aryl glycosides **52** from D-mannitol-derived homoallylic alcohol **51**.

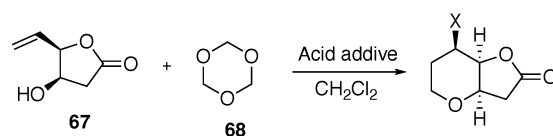


Scheme 24. Derivatization of 2-deoxy- β -C-aryl glycosides **56**.

Furthermore, Vankar and co-workers reported [58] (Scheme 25) the synthesis of 1,2-annulated tetrahydropyran-fused sugar derivatives **62** via intermediate **62a** by the reaction of a D-glucose-derived alcohol **61** with various carbonyl compounds in the presence of $\text{BF}_3 \cdot \text{Et}_2\text{O}$, via Prins cyclization. The obtained products were converted to more useful scaffolds *cis*-sugar-fused pyrano [3,2-*c*][1]benzopyran **63** and *cis*-sugar-fused 4*H*-naphtho [1,2-*b*]pyran **64** (Scheme 26). Furthermore, they investigated the reaction in the presence of TMSOTf , where 1,2-annulated tetrahydrofuran-fused sugar derivatives **66** were obtained via intermediate **66a** in moderate to excellent yields. This transformation occurred from D-glucose-derived homopropargyl alcohol **65** and several aldehydes (Scheme 27).



In 2008, Oikawa and co-workers reported [59] the Prins reaction of glucose-derived enantiomerically pure homoallylic alcohol **67** with unreactive formaldehyde equivalent, i.e., 1,3,5-trioxane **68** to trisubstituted *cis*-fused hexahydro-2H-furo[3,2-b]pyran derivatives **69–71** (Scheme 28).



Acid additive = AlX_3 (X = Cl, Br, I) **69**

TsOH (X = OTs) **70**

MsOH (X = OMs) **71**

Scheme 28. Synthesis of trisubstituted *cis*-fused hexahydro-2H-furo [3,2-b]pyran derivatives **69–71**.

3. Non-Carbohydrate Synthons to Carbohydrate Scaffolds

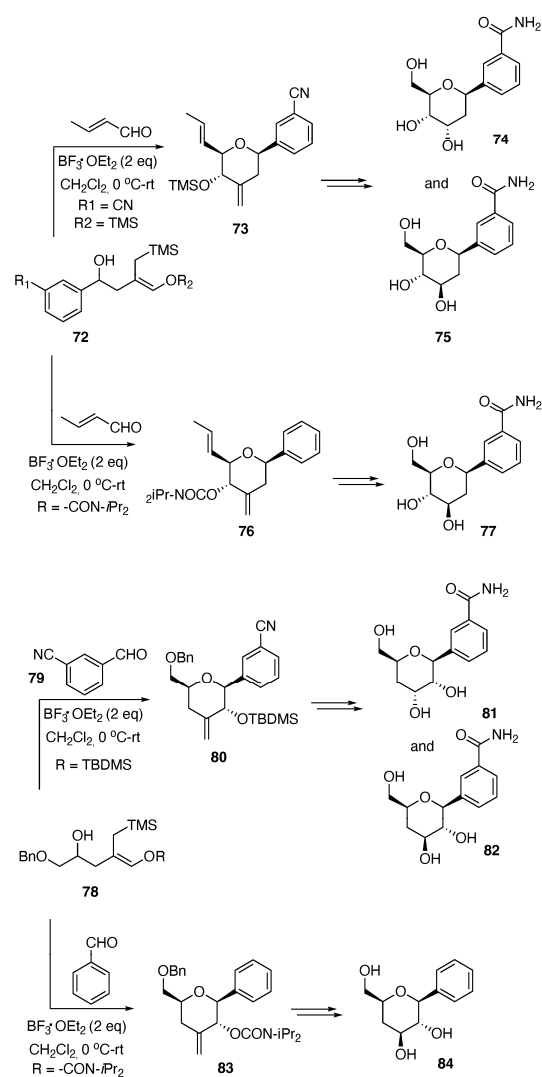
Besides exhibiting excellent biological activities, the carbohydrate-derived deoxy-C-aryl glycosides were found to be versatile substrates for the synthesis of various skeletal frameworks. Deoxy-C-aryl glycoside is a common structural motif found in a number of biologically relevant compounds, such as aquayamycin, Adriamycin, pluramycin A, and kidamycin [60]. An efficiently non-carbohydrate synthons source to sugar skeletons by applying the Prins reaction is a topic which has seen extensive study since the mid-twentieth century [60]. Within this reaction manifold, Migaud and co-workers reported [61] stereoselective synthesis of a non-carbohydrate-based core sugar skeleton **73** via Sakurai–Prins cyclization of alcohol **72** with crotonaldehyde. Further, the core sugar skeleton **73** hydroxyl groups at C-6 and C-3 were introduced by oxidative cleavage of the alkenes in **73** followed by reduction of the dicarbonyl intermediate. Subsequent acetylation of these hydroxyls, purification, and acetyl removal then yielded the final C-nucleosides **74** and **75**. Following the same reaction sequences and protocols, the synthesis of deoxy-C-aryl glycosides **77**, **81**, **82** and **84** was achieved using alcohol **72**, **78** as a building blocks, respectively (Scheme 29).

In 2016, Galan and co-workers reported [36] a de novo approach for the rapid construction of orthogonally protected L- and D-deoxysugars and analogues via Prins cyclization. In this approach, homoallylic alcohol **85** was treated with aldehyde **86** in the presence of TMSOTf and TMSOAc/AcOH, resulting in the formation of silyltetrahydropyran **87** in good to excellent yield. This compound was subsequently subjected to Tamao–Fleming oxidation, leading to the formation of 2,4-dideoxysugar **88**. By applying a similar reaction, compound **89** was converted into the 2,6-dideoxysugar **91** (Scheme 30).

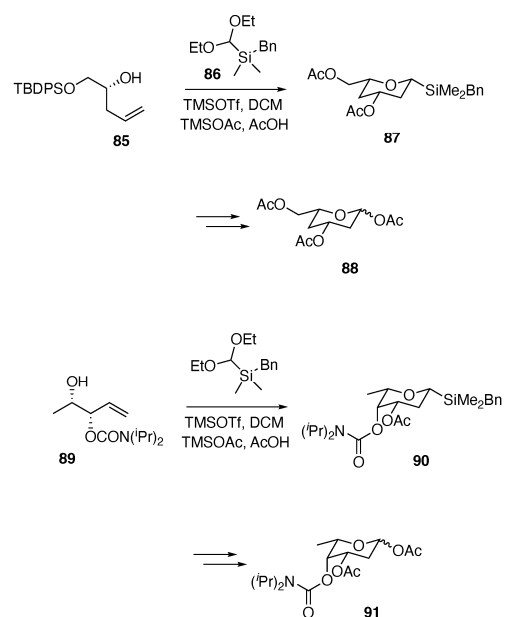
In 2016, Yadav and co-workers [29] demonstrated a diastereoselective formal synthesis of cryptophycin-24. The key step for constructing the core center involved a Prins cyclization of homoallylic alcohol **92** with aldehyde **93** in the presence of TFA in DCM, yielding core sugar skeleton **94**. Furthermore, this methodology was extended for the total synthesis of the natural product cryptophycin-24 (Scheme 31).

In 2012, Floreancig and Peh reported [28] a DDQ-mediated oxidative intramolecular Prins cyclization of compound **95**, yielding sugar core **96** in moderate yield (Scheme 32). This reaction proceeds via a diene-type intermediate.

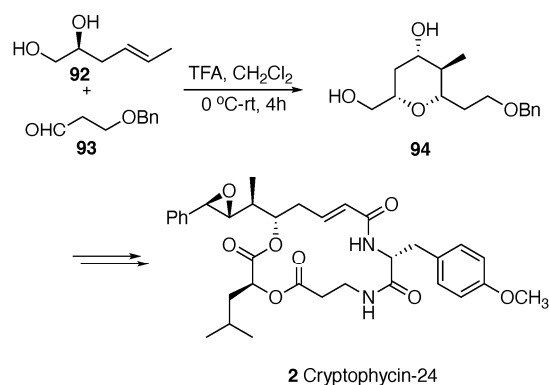
In 2010, Lee and Woo reported [30] an intramolecular Prins reaction of **97** in the presence of TMSOTf and TMSOAc/AcOH, resulting in the formation of sugar core **98** in good yield. This compound was further subsequently used for the total synthesis of (–)-Polycavernoside A **7** (Scheme 33).



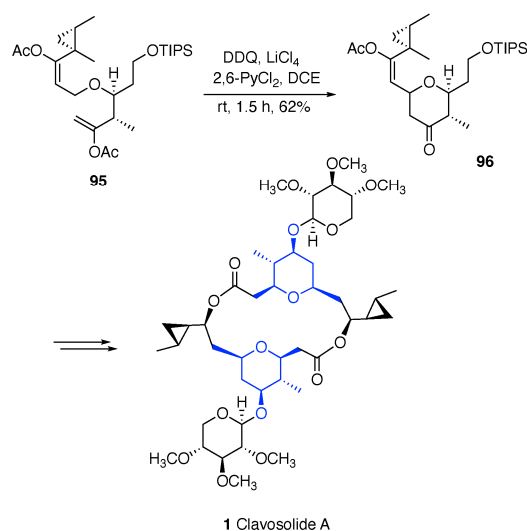
Scheme 29. Synthesis of deoxy-C-aryl glycosides from non-carbohydrate-based starting materials.



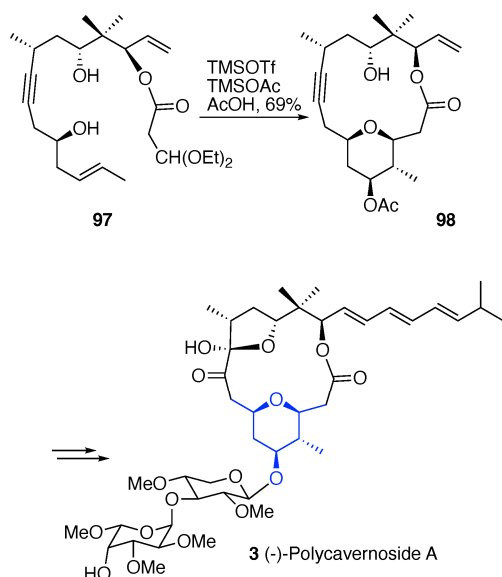
Scheme 30. Synthesis of dideoxysugars from silyltetrahydropyrans and non-carbohydrate-based starting materials via Prins reaction.



Scheme 31. Synthesis of cryptophycin-24 **2** from non-carbohydrate-based starting materials via Prins reaction.



Scheme 32. Total synthesis of Clavosolide A **7** via Prins reaction.



Scheme 33. Total synthesis of (-)-Polycavernoside A **9** via Prins reaction.

4. Conclusions

Carbohydrate-based structures are of high interest in glycochemistry due to their crucial roles in biological systems. Recent innovations have introduced both direct and

indirect methods to synthesize sugar moieties effectively. Notably, the Prins reaction—a process involving homoallylic alcohols and carbonyl compounds—has become a valuable approach for constructing sugar backbones. This review delves into various Prins reaction techniques for assembling carbohydrate frameworks, highlighting the use of both traditional carbohydrate precursors and alternative non-carbohydrate starting materials.

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