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Halogenation-induced C–N bond activation enables the synthesis of 1,2-*cis* *C*-aryl furanosides *via* deaminative cyclization†

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1,2-*cis* *C*-Aryl furanosides are prevalent in nature and exhibit significant biological activities. The 1,2-*cis* configuration is less favorable in terms of stereoelectronic and steric effects, making the synthesis of this type of skeleton highly challenging. Traditional methods for the synthesis of 1,2-*cis* *C*-aryl furanosides usually require complicated protection manipulations, resulting in lengthy synthetic routes and low overall efficiency. Here, we report a simple and highly applicable procedure for the synthesis of 1,2-*cis* *C*-aryl furanosides from unprotected aldoses *via* Petasis reaction and subsequent deaminative cyclization. Unprotected aldose mediated Petasis reactions yield linear 1,2-*trans* 1-aryl polyhydroxy amines. Halogenation of the amine motif activates the conventionally inert C–N bond and triggers the key stereoinvertive intramolecular substitution process, affording 1,2-*cis* *C*-aryl furanosides with excellent chemo- and diastereoselectivity. This procedure does not require the use of any sensitive reagents, and can be conducted in one-pot without precautions against oxygen or moisture, offering a streamlined approach to 1,2-*cis* *C*-aryl furanoside natural products and bioactive agents.

Introduction

1,2-*cis* *C*-Aryl furanosides represent a unique class of carbohydrates in which aromatic aglycons are linked to the anomeric position of furanoses *via* C–C glycosidic bonds from the same side as the C2 hydroxy group (C2-OH). This type of structure has been found in natural products isolated from traditional oriental herbs, the metabolites of bacteria or fungi, and has shown significant biological activity (Scheme 1A).[1–5] Notably, gilvocarcin V produced by the genus *Streptomyces* has shown remarkable antitumor activity and exceptionally low toxicity.[6–9] Due to their potent bioactivities, 1,2-*cis* *C*-aryl furanosides are attractive targets for total synthesis and medicinal chemistry.[10–16] However, the C–C bond linkage and 1,2-*cis* configuration pose great obstacles for the synthesis of these types of skeletons.

Naturally available unprotected hexoses and pentoses exist in solution as equilibrium mixtures of cyclic hemiacetals and linear glycosyl aldehydes, in which the pyranose forms predominate and the furanose forms are less abundant at equilibrium (Scheme 1B). To achieve the synthesis of 1,2-*cis* *C*-aryl furanosides from readily available aldoses, strategies with high selectivity are needed to ensure the construction of the furan skeleton, the C–C bond linkage, and most importantly, the 1,2-*cis* configuration. Traditional methods for the synthesis of 1,2-*cis* *C*-aryl furanosides usually first convert pyranose hemiacetals into highly protected furanosyl donors, and then construct C–C bonds *via* Lewis-acid-promoted glycosylation reactions, such as the Friedel–Crafts reaction with electron-rich arenes,[17] O-to-C rearrangement of O-aryl glycosides[18] and C2-OH-directed intramolecular aglycone delivery.[19–21] Alternatively, nucleophilic addition to linear glycosyl aldehydes with aryl reagents yields 1-aryl alditol intermediates, and cyclization through an intramolecular substitution can also afford *C*-aryl furanosides.[22–25] However, anionic aryl nucleophiles with high basicity, such as aryl lithium reagents and Grignard reagents, are needed. The addition reactions suffer from low diastereoselectivity. Inevitably, complicated protection manipulations are indispensable in the aforementioned methods, resulting in lengthy synthetic routes and low overall efficiency. Recently, List reported a concise procedure for the synthesis of the *C*-nucleoside of remdesivir from the reaction of unprotected D-ribose with electron-rich arenes.[26] Cyclization of the temporarily protected linear 1,2-*trans* alditol intermediate gave 1,2-*cis* *C*-aryl furanoside as the major product (dr up to 9 : 1) under acidic conditions. Despite these achievements, the synthesis of 1,2-*cis* *C*-aryl furanosides has lagged far behind the synthesis of *C*-glycosides.[27–37] Methods that enable the stereoselective synthesis of 1,2-*cis* *C*-aryl furanosides directly from unprotected aldoses are still greatly needed.

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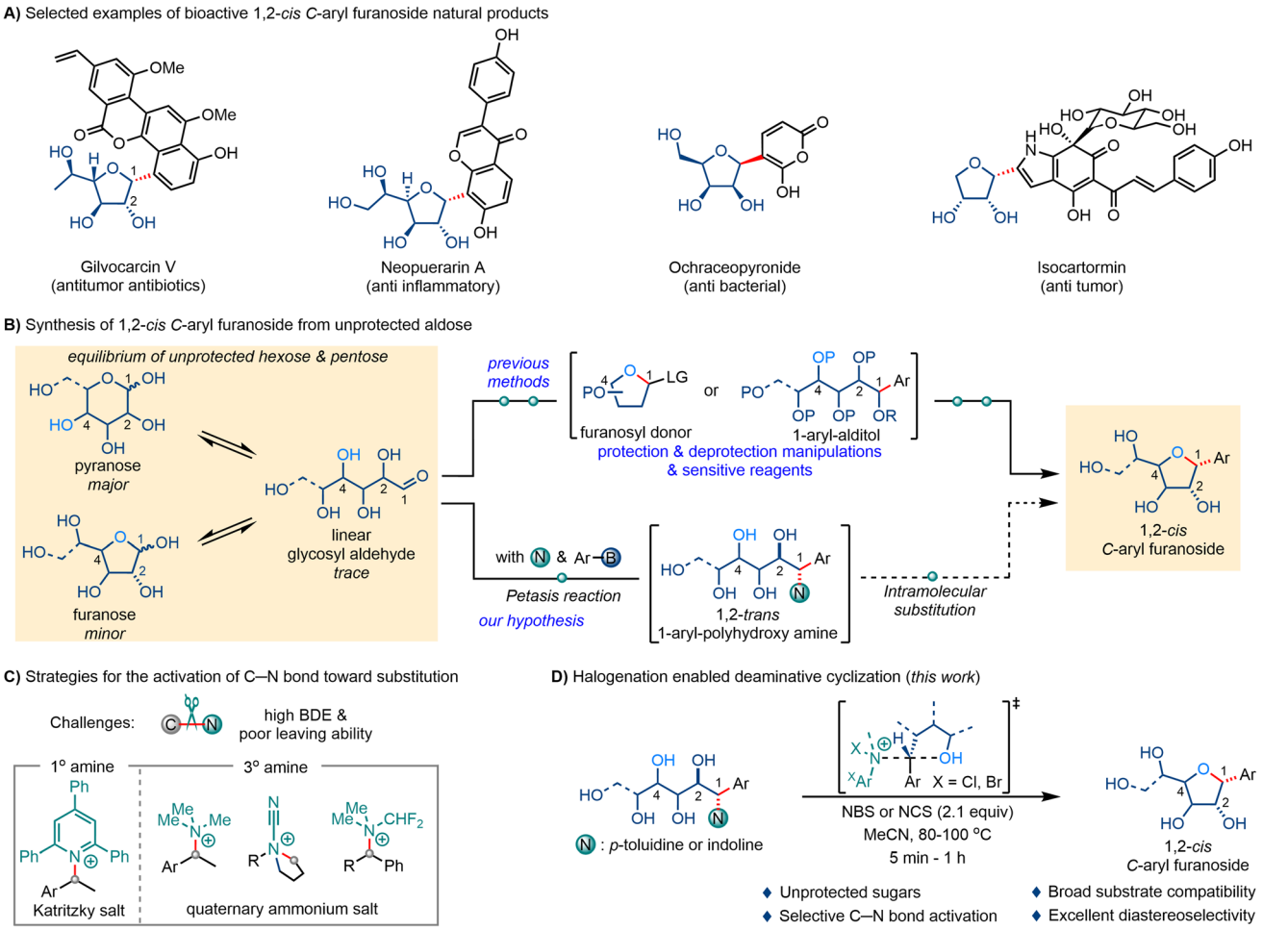


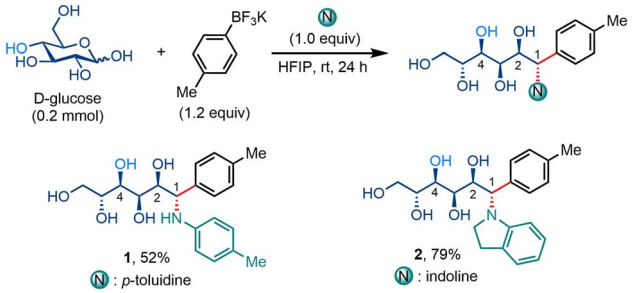
Scheme 1 Occurrence and synthetic strategies for 1,2-*cis* *C*-aryl furanosides. PO: protected hydroxy groups; LG: leaving group; BDE: bond dissociation energy; NBS: *N*-bromosuccinimide; NCS: *N*-chlorosuccinimide.

We envision that the C–C bond linkage between unprotected aldoses and aryl motifs can be constructed *via* a three-component Petasis reaction, wherein aryl-boronic acids or boronates are used as nucleophiles to attack the imines generated *in situ* from the condensation of aldehydes and amines.[38–44] The presence of a hydroxy group at the α position of the aldehyde can accelerate the nucleophilic addition process and control the diastereoselectivity, producing 1,2-*trans* hydroxy amines.[45–51] Then deaminative cyclization of the 1,2-*trans* 1-aryl-polyhydroxy amines *via* intramolecular S_N2 substitution provides a concise procedure for the synthesis of 1,2-*cis* *C*-aryl furanosides (Scheme 1B). However, organic amines are unarguably weak acids and poor leaving groups in the S_N2 reaction.[52] To increase their nucleofugality (leaving ability), primary amines must be converted to bis-sulfonimides,[53] diazo ions[54] or pyridinium cations (Katritzky salt),[55,56] and the C–N bond of tertiary amines can be activated in the form of quaternary ammonium salts by treatment with stoichiometric amounts of electrophiles, such as methyl iodide, cyanogen bromide (von Braun reaction) or difluorocarbenes (Scheme 1C).[57–74] For 1,2-*trans* 1-aryl-polyhydroxy amines, the inherent multiple free hydroxy groups may also interfere with these electrophiles, making the selective cleavage of C–N bonds a challenging transformation.[75–78] Herein, we report an efficient approach for the activation of the C–N bond and triggering of the key stereoinvertive intramolecular substitution process *via* halogenation of the amine moiety with *N*-bromosuccinimide or *N*-chlorosuccinimide (Scheme 1D). Combined with *p*-toluidine- or indoline-mediated Petasis reactions of unprotected aldoses with aryl trifluoroborates, this procedure provides a general route for the synthesis of 1,2-*cis* *C*-aryl furanoside natural products and their analogs from unprotected aldoses in two steps.

Results and discussion

Optimization of the reaction conditions

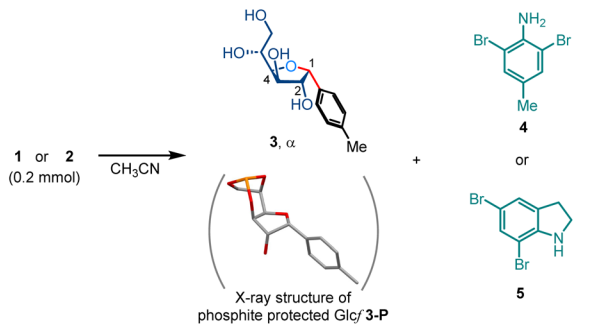
As shown in Scheme 2, *p*-toluidine and indoline were found to be the optimal amine sources in the Petasis reaction of unprotected glucose with potassium(4-methylphenyl)-trifluoroborate, affording the linear 1-aryl polyhydroxy amines **1** and **2** with excellent 1,2-*trans* selectivity (see the ESI for the



Scheme 2 Synthesis of 1,2-*trans* 1-aryl-polyhydroxy amine *via* Petasis reaction. Isolated yield on a scale of 0.2 mmol.

optimization of the Petasis reaction†). Treatment of **1** or **2** with NBS (2.1 equiv.) at elevated temperature in acetonitrile gave 1,2-*cis* *C*-aryl furanoside **3** in 85% or 76% isolated yield, respectively, with inversion of the stereochemistry at the C1 position (Table 1, entries 1 & 5). The structure of **3** was confirmed by X-ray crystallographic analysis of its phosphite derivative **3-P**.[79] In addition to succinimide, 2,6-dibromo-4-methylaniline **4** (91%) and 5,7-dibromoindoline **5** (79%) were identified as byproducts. The deaminative cyclization reaction proceeded smoothly at 60 °C (entries 2 & 6) and even at room temperature (entry 7) with decent yields. The addition of aq. HBr (1.0 equiv.) accelerated the cyclization of **1** at room temperature, giving **3** in 97% NMR yield (entry 3). NCS afforded yields comparable to those of NBS, but required slightly longer reaction times (entries 4 & 8). Notably, the Petasis reaction and deaminative cyclization reactions were conducted under an air atmosphere, and did not require any precautions against moisture.

Table 1 Reaction development[a]



Entry	Reagents and conditions	[b]Yield of **3**
1	**1**, NBS, 80 °C, 5 min	97% (85% + **4**, 91%)[c]
2	**1**, NBS, 60 °C, 6 h	70%
3	**1**, NBS, aq. HBr, rt, 6 h	97%
4	**1**, NCS, 100 °C, 30 min	95%
5	**2**, NBS, 100 °C, 5 min	89% (76% + **5**, 79%)[c]
6	**2**, NBS, 60 °C, 8 h	75%
7	**2**, NBS, rt, 24 h	61% (20%)[d]
8	**2**, NCS, 100 °C, 1 h	85%

[a] All screening reactions were carried out in an 8 mL glass vial on a scale of 0.2 mmol. [b] Yields were based on ^{1}H NMR analysis of the reaction mixture with 1,1,2,2-tetrachloroethane as internal standard. [c] Isolated yield. [d] The amount of **2** remaining.

Mechanistic studies

The inverted configuration and brominated arylamine byproducts strongly indicate that the cyclization reaction may have occurred in an intramolecular S_N2 substitution fashion. To verify the mechanism of this deaminative cyclization reaction, enantioenriched substrate (*R*)-**6** was prepared and subjected to the halogenation conditions. As the deaminative cyclization proceeded more slowly when NCS was used as the halogenation agent (Table 1, entry 1 *vs.* entry 4), (*R*)-**6** (85% ee) was treated with NCS to obtain some intermediates that participated in the cyclization reaction.

As shown in Scheme 3A, cyclized product (*S*)-**7** was isolated in 28% yield with slightly eroded enantiopurity (78% ee), along with 59% *ortho* dichlorinated intermediate (*R*)-**8** (84% ee) and 31% 2,6-dichloro-4-methylaniline **9**. Reheating (*R*)-**8** in the absence of any additive delivered (*S*)-**7** in only 12% NMR yield, and the addition of succinimide inhibited the cyclization reaction (Scheme 3B). Gratifyingly, the addition of a catalytic amount of NCS (0.1 equiv.) restored the reactivity, affording (*S*)-**7** in 91% yield, albeit with diminished enantiopurity (75% ee). The partial racemization may arise from interference by the S_N1 reaction pathway at elevated temperatures. Lowering the reaction temperature to 60 °C led to low conversion and also reduced the likelihood of racemization, giving (*S*)-**7** in 9% yield with 83% ee. These results support the presence of the *ortho* dichlorinated intermediate during the cyclization reaction, and suggest that NCS plays essential roles beyond halogenating the phenyl skeleton. NCS can transfer the chloronium ion to the nitrogen atom of aromatic amines, generating quaternary ammonium salts,[80,81] thus increasing their nucleofugality. To verify this quaternization effect, Brønsted acids that can protonize the amine motif were tested. As shown in Scheme 3B, aqueous hydrobromide (aq. HBr) can promote the cyclization of (*R*)-**8**, affording results comparable to those of NCS.

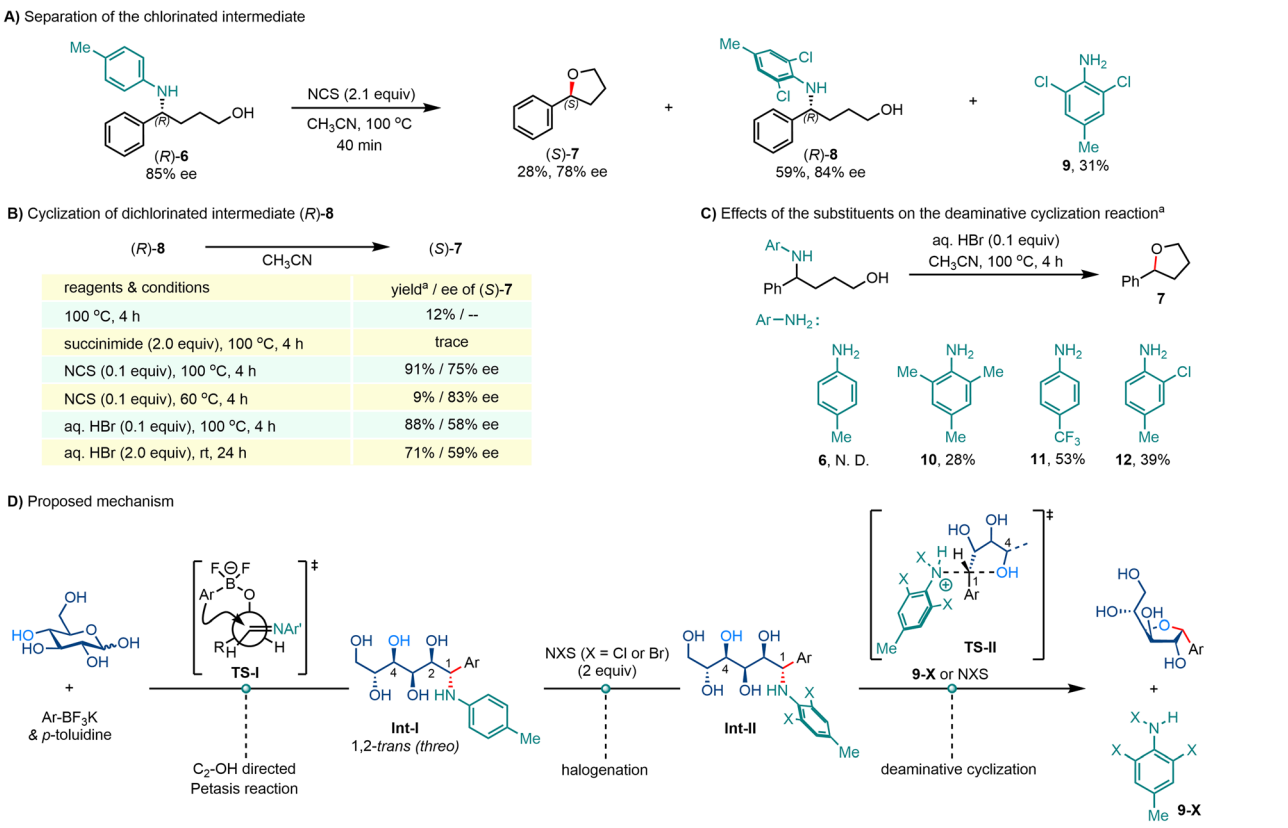
It is evident that quaternization at the nitrogen atom is crucial for inducing selective C–N bond cleavage. Quaternization enhances the acidity of the aryl-amine motif, making it a better leaving group than the neutral form. In addition, chlorination at the *ortho* position of the amine group may also facilitate C–N bond cleavage by exerting both steric effects and electronic effects. As shown in Scheme 3C, unchlorinated **6** failed to give any cyclized product with a catalytic amount (0.1 equiv.) or excess (2.0 equiv.) of aq. HBr even at 100 °C. By contrast, increasing the steric hindrance by introducing two *ortho*-methyl groups (**10**), or increasing the electron deficiency by replacing the *para*-methyl group with the CF_3 strong electron-withdrawing group (**11**), afforded much improved yields. Cyclization of mono-chlorinated amino-alcohol (**12**) also afforded 7 in 39% yield. This type of substituent induced weakening of σ bonds was also observed in the C(Me)–O bond cleavage of anisoles and was supported by DFT calculations.[82] Although amines **10–12** were amenable for the deaminative cyclization reaction, these types of anilines were unable to participate in

the Petasis reaction with unprotected aldoses. Overall, to realize this two-step protocol, arylamines with good nucleophilicity, such as *p*-toluidine or indoline, are required in the first-step Petasis reaction; then, halogenation converts them to better leaving groups, making the deaminative cyclization reaction feasible.

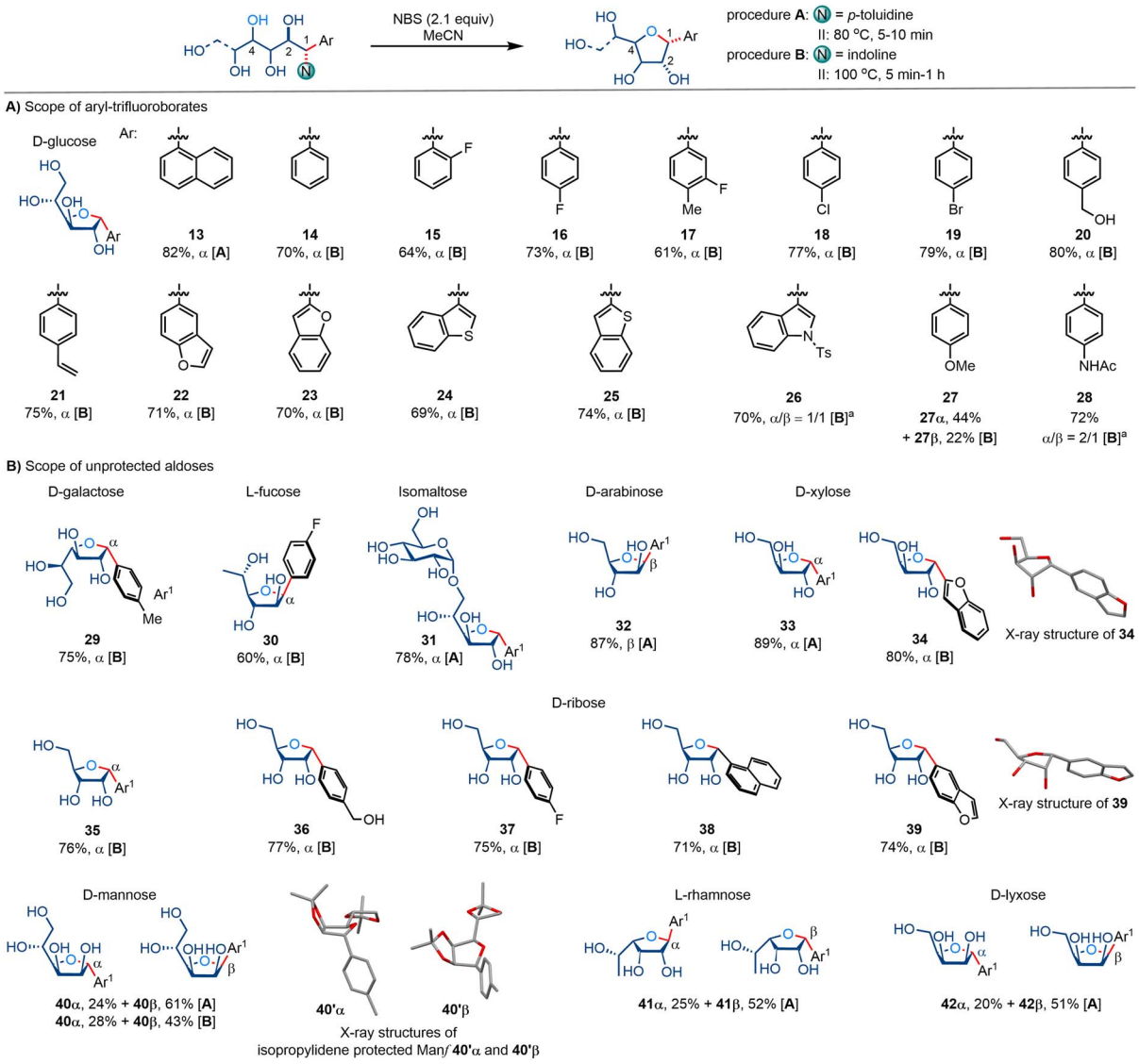
One the basis of the above results and previous reports, a possible mechanism for this two-step procedure is proposed in Scheme 3D. In the Petasis reaction, *p*-toluidine reacts with the linear aldehyde to form imine, and at the same time, C2-OH captures the arylborate to give a boronate complex.[50,51] Then, intramolecular transfer of the aryl group proceeds through transition state **TS-I** to minimize the 1,3-allylic strain, giving 1-aryl polyhydroxy amine **Int-I** with excellent trans selectivity. Halogenation at the aromatic amine skeleton affords **Int-II**, and quaternization at the nitrogen atom activates the C–N bond and then triggers the intramolecular S_N2 reaction with the C4-OH group (**TS-II**), affording 1,2-*cis* *C*-aryl furanoside. *N*-Halogenated byproduct **9-X** (X = Cl or Br) can serve as a halogenation reagent that transfers the halogen cation to succinimide, regenerating NXS, or halogenates **Int-II** directly to initiate the next round of the deaminative cyclization reaction. The *N*-chloroaniline intermediates are highly labile and generally not isolated.[83,84] Our efforts toward the isolation of **9-Cl** also failed. The formation of furanosides has been proven to be kinetically favored over the formation of pyranosides,[85,86] which is further verified here, as the presence of C5-OH or C6-OH does not affect the reaction, and no pyranoside or seven-membered product was detected.

Substrate scope. We next examined the generality of the established procedure with a variety of aryl-trifluoroborates and aldoses. As shown in Scheme 4A, a broad range of substituents on the aromatic ring were well tolerated, including halogen (**15**–**19**) and free hydroxymethyl (**20**) groups. Notably, the vinyl group, the key core pharmacophore of gilvocarcin V, was not affected under halogenation conditions, and **21** was obtained in good yield with exclusively 1,2-*cis* configuration.[87] Heteroarene-derived trifluoroborates were compatible with this two-step procedure, affording 1,2-*cis* *C*-heteroaryl furanosides in good overall yields (**22**–**25**). The deaminative cyclization of 1-aryl polyhydroxy amines carrying electron-rich arenes gave *C*-aryl furanosides as mixtures of anomers (**26**–**28**). This may be ascribed to the superior stability of the corresponding benzylic carbocations, that some *trans* anomers were generated *via* the competitive S_N1 pathway.

This two-step procedure is compatible with a broad range of unprotected aldoses (Scheme 4B). Free D-galactose (**29**), L-fucose (**30**), and even isomaltose (**31**) with seven unprotected hydroxy groups, reacted smoothly to give 1,2-*cis* *C*-aryl furanosides in good yields. In addition to hexoses, unprotected pentoses were competent substrates in this procedure. As exemplified by compounds **32**–**39**, *C*-aryl furanosides were obtained from



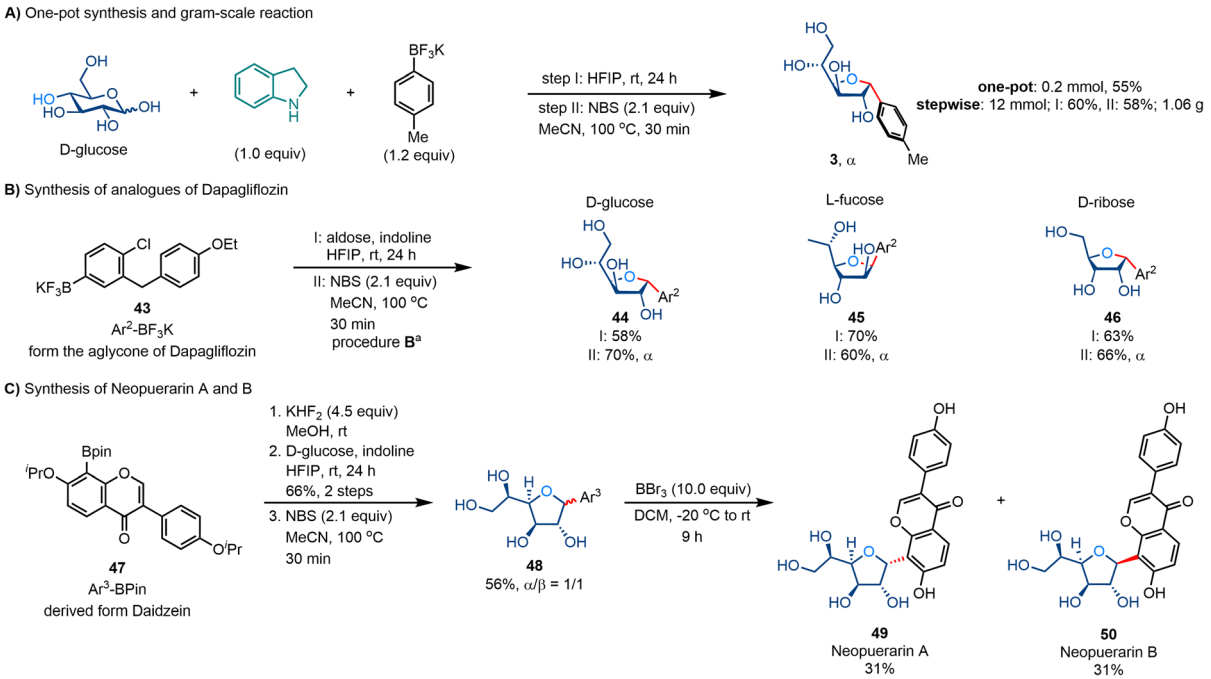
Scheme 3 Mechanistic studies. All reactions were carried out in an 8 mL glass vial on a scale of 0.2 mmol. [a]Yields were based on ^{1}H NMR analysis of the reaction mixture with 1,1,2,2-tetrachloroethane as internal standard. N. D.: not detected.



Scheme 4 Substrate scope. Isolated yields on a 0.2 mmol scale. [a]Inseparable anomers.

reactions of D-arabinose (**32**), D-xylose (**33**, **34**) and D-ribose (**35**–**39**) with an exclusively 1,2-*cis* configuration.[88] This provides a potential method for the preparation of α-*C*-nucleosides. The Petasis reaction of D-mannose, L-rhamnose and D-lyxose afforded 1-aryl polyhydroxy amines with exclusively 1,2-*trans* selectivity (see the ESI for details†).[89] The subsequent deaminative cyclization reaction delivered the products as mixtures of separable anomers (**40**–**42**). The structures of **40α** and **40β** were confirmed by X-ray crystallographic analysis after being protected with isopropylidene groups (**40′α** & **40′β**).[90] Among the expected products (**40β**, **41β** and **42β**) generated *via* the S_N2 pathway, all of the substituents on the furannosyl skeleton are located on the same side. This crowded all-*cis* configuration would cause severe steric repulsion in the transition states of the S_N2 pathway, that some α anomers were generated *via* the S_N1 pathway. Nevertheless, β anomers were still obtained as the major products, underscoring the power of the developed synthetic procedure in the synthesis of challenging all-*cis* *C*-aryl furanosides.

Synthetic utility. As depicted in Scheme 5A, the Petasis reaction and deaminative cyclization can be conducted in a one-pot manner without isolating intermediate **2** to give *C*-aryl furanoside **3** in 55% yield. The stepwise procedure can be scaled up to 12 mmol scale, yielding 1.06 g of **3** as a single anomer. This procedure is also amenable for the synthesis of *C*-aryl furanoside natural products and analogs of bioactive reagents (Scheme 5B). Using aryl-trifluoroborate **43** derived from the aglycone of the antidiabetic agent dapagliflozin,[91] a series of 1,2-*cis* *C*-aryl furanoside-type analogs of dapagliflozin were obtained from reactions with D-glucose (**44**), L-fucose (**45**) and D-ribose (**46**). The reaction of the daidzein derivative **47** with D-glucose under procedure B afforded **48** as a mixture of anomers in 56% yield ($\alpha/\beta = 1:1$). After the removal of the isopropyl group with BBr_3, natural products neopuerarin A (**49**) and neopuerarin B (**50**) were



Scheme 5 Synthetic utility. [a]Isolated yields on a 0.2 mmol scale.

obtained in 31% and 31% yields, respectively (Scheme 5C). The structures of **49** and **50** were confirmed by comparison with data reported in the literature[1,2] and X-ray crystallographic analysis of the sodium salt of **49**.[92]

Conclusions

In summary, we have developed an efficient two-step method for the synthesis of 1,2-*cis* *C*-aryl furanosides from unprotected aldoses. *p*-Toluidine- or indoline-mediated Petasis reactions with aldoses and potassium aryl-trifluoroborates enable the key C1–C(Ar) bond coupling and covert cyclic pyranoses to linear 1-aryl polyhydroxy amines with excellent 1,2-*trans* selectivity; subsequent selective halogenation at the aryl-amine motif activates the C–N bond and triggers intramolecular S_N2 substitution, furnishing 1,2-*cis* *C*-aryl furanosides. This "open-and-close" procedure is compatible with a broad range of free aldoses and aryl-trifluoroborates. The use of readily available reagents, mild reaction conditions and simple operation make this procedure highly practical for accessing 1,2-*cis* *C*-aryl furanoside natural products. This halogenation-enabled C–N bond cleavage can inspire additional strategies for the selective transformation of amine-containing substrates.

Data availability

Detailed synthetic procedures, compound characterization, NMR spectra, and X-ray crystallographic data are provided in the ESI.† Crystallographic data for **3-P**, **34**, **39**, **40-S**, **40′α**, **40′β** and **49-Na** have been deposited at the Cambridge Crystallographic Data Centre.

Author contributions

W. W. made the initial discovery of the project, finished most of the experiments and prepared the ESI.† J. W. helped with the structural identification of the products and prepared some starting material. K. J. helped with the mechanistic studies. M. Z. helped with the separation of neopuerarins. G. H. formulated the initial ideas of this work, supervised the project and prepared the manuscript.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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Notes and references

1 H.-J. Zhang, X.-P. Yang and K.-W. Wang, *J. Asian Nat. Prod. Res.*, 2010, **12**, 293–299.
2 Q.-W. Hu, H.-Y. Xiang, J.-M. Shan, Q.-Y. Jiao, S. Lv, L.-Y. Li, F. Li, D.-M. Ren and H.-X. Lou, *Fitoterapia*, 2020, **144**, 104594–104599.

3 M. A. Asmaey, D. Abatis, A. S. Abdel-Razek, G. Lambrinidis, I. Chinou, N. Fokialakis, N. Tsafantakis, M. Shaaban and N. Aligiannis, *Molecules*, 2021, **26**, 3976–3988.
4 F. Li, Z.-S. He and Y. Ye, *Acta Pharm. Sin. B*, 2017, **7**, 527–531.
5 R. Ma, S. Cheng, J.-W. Sun, W.-M. Zhu and P. Fu, *J. Nat. Prod.*, 2022, **85**, 2282–2289.
6 H. Nakano, Y. Matsuda, K. Ito, S. Ohkubo, M. Morimoto and F. Tomita, *J. Antibiot.*, 1981, **34**, 266–270.
7 K. Takahashi, M. Yoshida, F. Tomita and K. Shirahata, *J. Antibiot.*, 1981, **34**, 271–275.
8 R. K. Elespuru and S. K. Gonda, *Science*, 1984, **223**, 69–71.
9 L. R. McGee and R. Misra, *J. Am. Chem. Soc.*, 1990, **112**, 2386–2389.
10 Y. Yang and B. Yu, *Chem. Rev.*, 2017, **117**, 12281–12356.
11 K. Kitamura, Y. Ando, T. Matsumoto and K. Suzuki, *Chem. Rev.*, 2018, **118**, 1495–1598.
12 T. Matsumoto, T. Hosoya and K. Suzuki, *J. Am. Chem. Soc.*, 1992, **114**, 3568–3570.
13 T. Hosoya, E. Takashiro, T. Matsumoto and K. Suzuki, *J. Am. Chem. Soc.*, 1994, **116**, 1004–1015.
14 M. Morales-Chamorro, O. Cortezano-Arellano and A. Cordero-Vargas, *Synthesis*, 2016, **48**, 4555–4563.
15 F. Wu, J. Zhang, F.-H. Song, S.-S. Wang, H. Guo, Q. Wie, H.-Q. Dai, X.-Y. Chen, X.-K. Xia, X.-T. Liu, L.-X. Zhang, J.-Q. Yu and X.-G. Lei, *ACS Cent. Sci.*, 2020, **6**, 928–938.
16 A. Cordero-Vargas, B. Quiclet-Sire and S. Z. Zard, *Org. Biomol. Chem.*, 2005, **3**, 4432–4443.
17 R. N. Farr, D.-I. Kwok and G. D. Daves, *J. Org. Chem.*, 1992, **57**, 2093–2100.
18 T. Matsumoto, M. Katsuki and K. Suzuki, *Tetrahedron Lett.*, 1988, **29**, 6935–6938.
19 I. Singh and O. Seitz, *Org. Lett.*, 2006, **8**, 4319–4322.
20 A. Nakazaki, J. Usuki and K. Tomooka, *Synlett*, 2008, **13**, 2064–2068.
21 O. R. Martin, S. P. Rao, K. G. Kurz and H. A. El-Shenawy, *J. Am. Chem. Soc.*, 1988, **110**, 8698–8700.
22 W. Frick and R. R. Schmidt, *Liebigs Ann. Chem.*, 1989, 565–570.
23 E. Ravarino, S. K. Jana, R. Frohlich and R. Holl, *Carbohydr. Res.*, 2012, **361**, 162–169.
24 R. Cribiù, K. Eszter Borbas and I. Cumpstey, *Tetrahedron*, 2009, **65**, 2022–2031.
25 For an efficient method for the synthesis of both 1,2-*cis* and 1,2-*trans C*-aryl furanosides *via* reduction, see: M. Peifer, R. Berger, V. W. Shurtleff, J. C. Conrad and D. W. C. Macmillan, *J. Am. Chem. Soc.*, 2014, **136**, 5900–5903.
26 C. Obradors, B. Mitschke, M. H. Aukland, M. Leutzsch, O. Grossmann, S. Brunen, S. A. Schwengers and B. List, *Angew. Chem., Int. Ed.*, 2022, **61**, e202114619.
27 F. Zhu, S. O'Neill, J. Rodriguez and M. A. Walczak, *Chem.–Eur. J.*, 2019, **25**, 3147–3155.
28 F. Li and J. Qu, *Chin. J. Org. Chem.*, 2021, **41**, 3949–3964.
29 J. Ghouilem, M. de Robichon, F. Le Bideau, A. Ferry and S. Messaoudi, *Chem.–Eur. J.*, 2021, **27**, 491–511.
30 H. Gong and M. R. Gagné, *J. Am. Chem. Soc.*, 2008, **130**, 12177–12183.
31 Q.-Q. Wang, B. C. Lee, N.-X. Song and M. J. Koh, *Angew. Chem., Int. Ed.*, 2023, **62**, e202301081.
32 Y. Jiang, Y. Wei, Q.-Y. Zhou, G.-Q. Sun, X.-P. Fu, N. Levin, Y. Zhang, W.-Q. Liu, N. Song, S. Mohammed, B. G. Davis and M. J. Koh, *Nature*, 2024, **631**, 319–327.
33 C. Zhang, S.-Y. Xu, H. Zuo, X. Zhang, Q.-D. Dang and D.-W. Niu, *Nat. Synth.*, 2023, **2**, 251–260.
34 A.-R. Chen, B. Yang, Z.-H. Zhou and F. Zhu, *Chem Catal.*, 2022, **2**, 3430–3470.
35 M.-L. Liu, Y.-H. Niu, Y.-F. Wu and X.-S. Ye, *Org. Lett.*, 2016, **18**, 1836–1839.
36 Q.-Q. Wang, S. An, Z.-Q. Deng, W.-J. Zhu, Z.-Y. Huang, G. He and G. Chen, *Nat. Catal.*, 2019, **2**, 793–800.
37 Q.-Q. Wang, Y. Fu, W. Zhu, S. An, Q. Zhou, S.-F. Zhu, G. He, P. Liu and G. Chen, *CCS Chem.*, 2020, **2**, 1729–1736.
38 N. A. Petasis and I. Akrltopoulou, *Tetrahedron Lett.*, 1993, **34**, 583–586.
39 N. R. Candeias, F. Montalbano, P. M. S. D. Cal and P. M. P. Gois, *Chem. Rev.*, 2010, **110**, 6169–6193.
40 P. Wu, M. Givskov and T. E. Nielsen, *Chem. Rev.*, 2019, **119**, 11245–11290.
41 M. G. Ricardo, D. Llanes, L. A. Wessjohann and D. G. Rivera, *Angew. Chem., Int. Ed.*, 2019, **58**, 2700–2704.
42 S. Krajcovicova and D. R. Spring, *Angew. Chem., Int. Ed.*, 2023, **62**, e202307782.
43 N. A. Petasis and I. Zavialov, *J. Am. Chem. Soc.*, 1998, **120**, 11798–11799.
44 N. Kumagai, G. Muncipinto and S. L. Schreiber, *Angew. Chem., Int. Ed.*, 2006, **45**, 3635–3638.
45 N. A. Petasis, Multicomponent Reactions with Organoboron Compounds in *Multicomponent Reactions*, Wiley, Weinheim, 2005, pp. 199–223.
46 A. S. Davis, S. G. Pyne, B. W. Skelton and A. H. White, *J. Org. Chem.*, 2004, **69**, 3139–3143.
47 S. G. Pyne and C. Wentrup, *Aust. J. Chem.*, 2022, **75**, 923–944.
48 Z.-Y. Hong, L. Liu, C.-C. Hsu and C.-H. Wong, *Angew. Chem., Int. Ed.*, 2006, **45**, 7417–7421.
49 Z.-Y. Hong, L. Liu, M. Sugiyama, Y. Fu and C.-H. Wong, *J. Am. Chem. Soc.*, 2009, **131**, 8352–8353.
50 J. Tao and S. Li, *Chin. J. Chem.*, 2010, **28**, 41–49.
51 R. Y. Souza, G. A. Bataglion, D. A. C. Ferreira, C. C. Gatto, M. N. Eberlin and B. A. D. Neto, *RSC Adv.*, 2015, **5**, 76337–76341.
52 M. B. Smith, *March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, Wiley, 8th edn, 2020, p. 466.
53 P. J. DeChristopher, J. P. Adamek, G. D. Lyon, J. J. Galante, H. E. Haffner, R. J. Boggio and R. J. Baumgarten, *J. Am. Chem. Soc.*, 1969, **91**, 2384–2385.
54 W. Kirmse, *Angew. Chem., Int. Ed.*, 1976, **15**, 251–261.
55 A. R. Katritzky, *Tetrahedron*, 1980, **36**, 679–699.
56 A. R. Katritzky and C. M. Marson, *Angew. Chem., Int. Ed.*, 1984, **23**, 420–429.
57 D.-W. Yue and R. C. Larock, *Org. Lett.*, 2004, **6**, 1037–1040.
58 B. Yao, Q. Wang and J.-P. Zhu, *Angew. Chem., Int. Ed.*, 2012, **51**, 5170–5174.
59 Y. Gui and S.-K. Tian, *Org. Lett.*, 2017, **19**, 1554–1557.

60 Q.-M. Zhu, Q.-H. Yuan, M.-W. Chen, M.-P. Guo and H.-M. Huang, *Angew. Chem., Int. Ed.*, 2017, **56**, 5101–5105.
61 D. I. Bugaenko, M. A. Yurovskaya and A. V. Karchava, *Org. Lett.*, 2018, **20**, 6389–6393.
62 C.-X. Cui, H. Li, X.-J. Yang, J. Yang and X.-Q. Li, *Org. Lett.*, 2013, **15**, 5944–5947.
63 C. Yu, M. A. Shoaib, N. Iqbal, J. S. Kim, H.-J. Ha and E. J. Cho, *J. Org. Chem.*, 2017, **82**, 6615–6620.
64 Y. Kim, J. Heo, D. Kim, S. Chang and S. Seo, *Nat. Commun.*, 2020, **11**, 4761–4771.
65 J. Scharfbier, B. M. Gross and M. Oestreich, *Angew. Chem., Int. Ed.*, 2020, **59**, 1577–1580.
66 H.-Q. Fang, K.-X. Xie, S. Kemper and M. Oestreich, *Angew. Chem., Int. Ed.*, 2021, **60**, 8542–8546.
67 J.-K. Su, X.-X. Ma, Z.-L. Ou and Q.-L. Song, *ACS Cent. Sci.*, 2020, **6**, 1819–1826.
68 J.-K. Su, C.-B. Li, X.-Y. Hu, Y. Guo and Q.-L. Song, *Angew. Chem., Int. Ed.*, 2022, **61**, e202212740.
69 A. Liu, C.-F. Ni, Q.-Q. Xie and J.-B. Hu, *Angew. Chem., Int. Ed.*, 2022, **61**, e202115467.
70 H. Lim, S. Seong, Y. Kim, S. Seo and S. Han, *J. Am. Chem. Soc.*, 2021, **143**, 19966–19974.
71 Q.-Q. Tang, F.-H. Li, H.-Y. Chen, X.-J. Yin, Y. Tang and Q.-L. Zeng, *Asian J. Org. Chem.*, 2021, **10**, 1687–1690.
72 A. B. Turner, B. I. McBain, R. A. Howie and P. J. Cox, *J. Chem. Soc., Perkin Trans. 1*, 1986, 1151–1155.
73 A. B. Turner, *Chem. Commun.*, 1968, 1659–1660.
74 W.-Z. Geng, W.-X. Zhang, W. Hao and Z.-F. Xi, *J. Am. Chem. Soc.*, 2012, **134**, 20230–20233.
75 K.-B. Ouyang, W. Hao, W.-X. Zhang and Z.-F. Xi, *Chem. Rev.*, 2015, **115**, 12045–12090.
76 S. M. Pound and M. P. Watson, *Chem. Commun.*, 2018, **54**, 12286–12301.
77 J.-Y. Xu, O. P. Bercher, M. R. Talley and M. P. Watson, *ACS Catal.*, 2021, **11**, 1604–1612.
78 K. J. Berger and M. D. Levin, *Org. Biomol. Chem.*, 2021, **19**, 11–36.
79 The X-ray data of **3-P** has been deposited at the Cambridge Crystallographic Data Centre with a number of CCDC 2297443, DOI: **https://doi.org/10.5517/ccdc.csd.cc2h3p2d**.
80 R. C. Samanta and H. Yamamoto, *Chem.–Eur. J.*, 2015, **21**, 11976–11979.
81 X.-D. Xiong and Y.-Y. Yeung, *Angew. Chem., Int. Ed.*, 2016, **55**, 16101–16105.
82 M. M. Suryan, S. A. Kafafi and S. E. Stein, *J. Am. Chem. Soc.*, 1989, **111**, 4594–4600.
83 R. S. Neale, R. G. Schepers and M. R. Walsh, *J. Org. Chem.*, 1964, **29**, 3390–3393.
84 P. G. Gassman and G. A. Campbell, *J. Am. Chem. Soc.*, 1971, **93**, 2567–2569.
85 Y. Seo and M. R. Gagné, *ACS Catal.*, 2018, **8**, 6993–6999.
86 A. Yamaguchi, N. Hiyoshi, O. Sato, K. K. Bando and M. Shirai, *Green Chem.*, 2009, **11**, 48–52.
87 Alkenyl boronic acids participated Petasis reaction gave the 1,2-*trans* products in good yields, however, no desired *C*-alkenyl furanoside was obtained under the halogenation conditions.
88 The X-ray data of **34** has been deposited at the Cambridge Crystallographic Data Centre with a number of CCDC 2387663, DOI: **https://doi.org/10.5517/ccdc.csd.cc2l4kdq**; the X-ray data of **39** has been deposited at the Cambridge Crystallographic Data Centre with a number of CCDC 2297325, DOI: **https://doi.org/10.5517/ccdc.csd.cc2h3k8g**.
89 The X-ray data has been deposited at the Cambridge Crystallographic Data Centre with a number of CCDC 2297387, DOI: **https://doi.org/10.5517/ccdc.csd.cc2h3m8j**.
90 The X-ray data of **40′α** has been deposited at the Cambridge Crystallographic Data Centre with a number of CCDC 2297359, DOI: **https://doi.org/10.5517/ccdc.csd.cc2h3lcl**; the X-ray data of **40′β** has been deposited at the Cambridge Crystallographic Data Centre with a number of CCDC 2297392, DOI: **https://doi.org/10.5517/ccdc.csd.cc2h3mfp**.
91 W. Meng, B. A. Ellsworth, A. A. Nirschl, P. J. McCann, M. Patel, R. N. Girotra, G. Wu, P. M. Sher, E. P. Morrison, S. A. Biller, R. Zahler, P. P. Deshpande, A. Pullockaran, D. L. Hagan, N. Morgan, J. R. Taylor, M. T. Obermeier, W. G. Humphreys, A. Khanna, L. Discenza, J. G. Robertson, A.-Y. Wang, S.-P. Han, J. R. Wetterau, E. B. Janovitz, O. P. Flint, J. M. Whaley and W. N. Washburn, *J. Med. Chem.*, 2008, **51**, 1145–1149.
92 The X-ray data has been deposited at the Cambridge Crystallographic Data Centre with a number of CCDC 2337769, DOI: **https://doi.org/10.5517/ccdc.csd.cc2jgmxk**.