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Carbonylative Suzuki–Miyaura Coupling of 1-Iodoglycals Mediated by the *N*-Heterocyclic Carbene Catalyst PEPPSI: Preparation of *C*-Acyl Glycosides

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ABSTRACT

Suzuki–Miyaura coupling has been widely explored, particularly in the development of pharmaceutically relevant structures. Its carbonylative variant enables the insertion of a CO bridge, granting access to a variety of bioactive biaryl ketone scaffolds. Herein, we describe a carbonylative Suzuki–Miyaura strategy for the preparation of a series of *C*-acyl glycosides, thereby expanding the chemical space for the development of new derivatives in glycochemistry. The reaction proceeds under Pyridine-Enhanced Precatalyst Preparation, Stabilization, and Initiation (PEPPSI-IPr) ([1,3-Bis(2,6-Diisopropylphenyl)imidazol-2-ylidene](3-chloropyridyl)palladium(II) dichloride) catalysis, employing $Mo(CO)_6$ as a solid CO source for the in situ generation of CO, which enables the selective formation of the carbonylated products. The desired compounds were obtained in synthetically useful yields (up to 84%).

1 | Introduction

Over the years, the ability to introduce new modes of reactivity has made transition-metal catalysis an indispensable tool in organic synthesis [1]. This strategy enables the exploration of novel pathways for bond formation and cleavage, and it also provides efficient methods for constructing complex organic molecules of synthetic significance [2, 3]. The vast applications of transition-metal catalysts in organic synthesis encompass strategies such as asymmetric catalysis, C–H functionalization, and C–C activation, among others [4–6]. Metals such as palladium, platinum, nickel, copper, ruthenium, rhodium, and molybdenum play crucial roles in facilitating these chemical transformations [7].

Among these, the Suzuki–Miyaura reaction stands out as a powerful method for forging C—C bonds [8]. Its importance has been particularly highlighted in the synthesis of pharmaceutically relevant molecules, as it provides straightforward access to new chemical space and thereby facilitates structure–activity relationship studies through the diversification of key scaffolds [9]. Due to its robustness and feasibility, this transformation has become a cornerstone in drug discovery; however, it is often overemphasized, leading to an overrepresentation of biaryl motifs in libraries of biologically relevant compounds [10].

Approaches to diversifying suitable scaffolds for the Suzuki–Miyaura reaction have been investigated for the functionalization of sugar moieties. Mukherjee and Hussain explored the functionalization at the C2 position of unsaturated sugars such as glycals, performing a Suzuki coupling of a benzyl-protected 2-chloro glycal with phenylboronic acid, albeit in low yield (30%) under Pd(II) catalysis [11]. Rainier and Jana carried out the cross-coupling of benzylated 2-iodo-D-glucal with 2-aminophenylpinacolborane using a Pd(0) catalyst, achieving the arylated product in 70% isolated yield, which was subsequently employed in the synthesis of fused indolines [12]. The Suzuki–Miyaura reaction has also been

explored in aqueous media. Davis et al. developed a phosphine-free method for the synthesis of 2-aryl glycals using a Pd(II) catalyst; a limited scope of boronic acids was examined, and the corresponding arylated products were obtained in high yields [13]. Later, Juhász et al. investigated the arylation at C2 of glucals bearing electron-withdrawing groups, such as nitrile and ester, at C1. They successfully coupled these glucal derivatives with boronic acids using a Pd(0) source [14]. Malinowski explored the functionalization of boronic acid-decorated porphyrins with 2-iodoglucal through a direct C—C bond-forming protocol; the reaction was further evaluated with a diverse array of boronic acids, including substituted aryl and heterocyclic systems [15]. In a different approach, Zhu and collaborators studied the cross-electrophile coupling of 2-iodo-D-glucal with aryl iodides under Ni(II) catalysis. This method enabled access to a wide variety of arylated glycal derivatives in high yields, including bioactive molecules [16]. More recently, Zhun and collaborators employed boronic derivatives of C1-glycals, preparing stable boronic acids and thoroughly exploring their arylation using a Pd(II) catalyst. The developed protocol also enabled bioconjugation with peptide derivatives, and applications in DNA-encoded libraries as well as coupling with bioactive molecules were demonstrated [17]. Wang et al. further demonstrated the use of aryl thianthrenium salts as suitable coupling partners for boronate glycals. Notably, the reaction proceeded at room temperature; a series of arylations were performed with different boronate glycals, and the synthetic utility of the methodology for medicinal chemistry was exemplified through the late-stage functionalization of biologically active molecules [18].

A multicomponent variation of this transformation is carbonylative Suzuki–Miyaura coupling [19]. This reaction introduces a carbonyl group into the product, thereby enabling the synthesis of ketone-containing scaffolds. The three-component process is typically performed using palladium catalysts, organoboron nucleophiles as coupling partners, and aryl halides (Scheme 1A) [20–22]. This approach provides access to a wide range of symmetrical and unsymmetrical ketones, which are commonly present in pharmaceutically relevant scaffolds [23]. Representative examples of molecules containing biaryl ketone motifs include ketoprofen (I, Scheme 1B), a nonsteroidal anti-inflammatory drug; tolcapone (II, Scheme 1B), used to treat Parkinson's disease; and cariphenone A (III, Scheme 1B), a naturally occurring biaryl ketone that exhibits antioxidant activity [24, 25].

C-acyl glycosides are privileged scaffolds: They serve as analogues of *O*- and *N*-glycosides while exhibiting enhanced hydrolytic stability *in vivo* [26]. These compounds occur naturally; for example, the authors of one study isolated an unprecedented family of *C*-acyl glycosides from *Scleropyrum pentandrum*, an evergreen tree from Thailand, including scleropentacide A, which exhibits radical scavenging activity (IV, Scheme 1B) [27].

As privileged structures, the synthesis of *C*-acyl glycosides has been widely targeted. The traditional synthetic pathway involves the use of C1-aldehydes to access C1-formylated glycosides. Ozonolysis of allene glycosides is a well-established method, followed by trapping with a Grignard reagent and subsequent oxidation [28, 29]. However, such approaches suffer from the need for excess organometallic reagents and competitive elimination reactions [30, 31]. Alternatively, the use of 2-nitroglucal as a Michael-type glycosyl donor has been explored under *N*-heterocyclic carbenes (NHC) catalysis in basic medium. In this approach, aldehydes were linked to the glycoside moiety, representing the first example of catalytic acylation at the anomeric position of glycals [32].

Recently, the synthesis of *C*-acyl glycosides has been targeted through strategies involving more direct approaches to the carbonyl insertion, without the need of several steps, including SN_2-like reactions with glycosyl sulfonates [33], the preparation of nonanomeric derivatives via electron donor acceptor complex–mediated Ni(II)-catalyzed cross-coupling [34], and a three-component reaction applying Ni(II) catalysis and isobutyl chloroformate as CO source [35].

Regarding palladium-catalyzed methods, Walczak et al. [36] reported stereoretentive *C*-acylation of anomeric stannanes with thioesters as the carbonyl source. This reaction is useful for aryl, heteroaryl, vinyl, and bioactive coupling partners, as well as diverse saccharides (Scheme 1C). Shinozuka [37] investigated the palladium-catalyzed aroylation of 1-tributylstannyl glycals with aryl chlorides. By carefully controlling the palladium source, the authors achieved selective access to *C*-aroylated glycals: $Pd(OAc)_2$ promoted the aroylated product, while $Pd(PPh_3)_4$ favored the arylated product, both in synthetically useful yields.

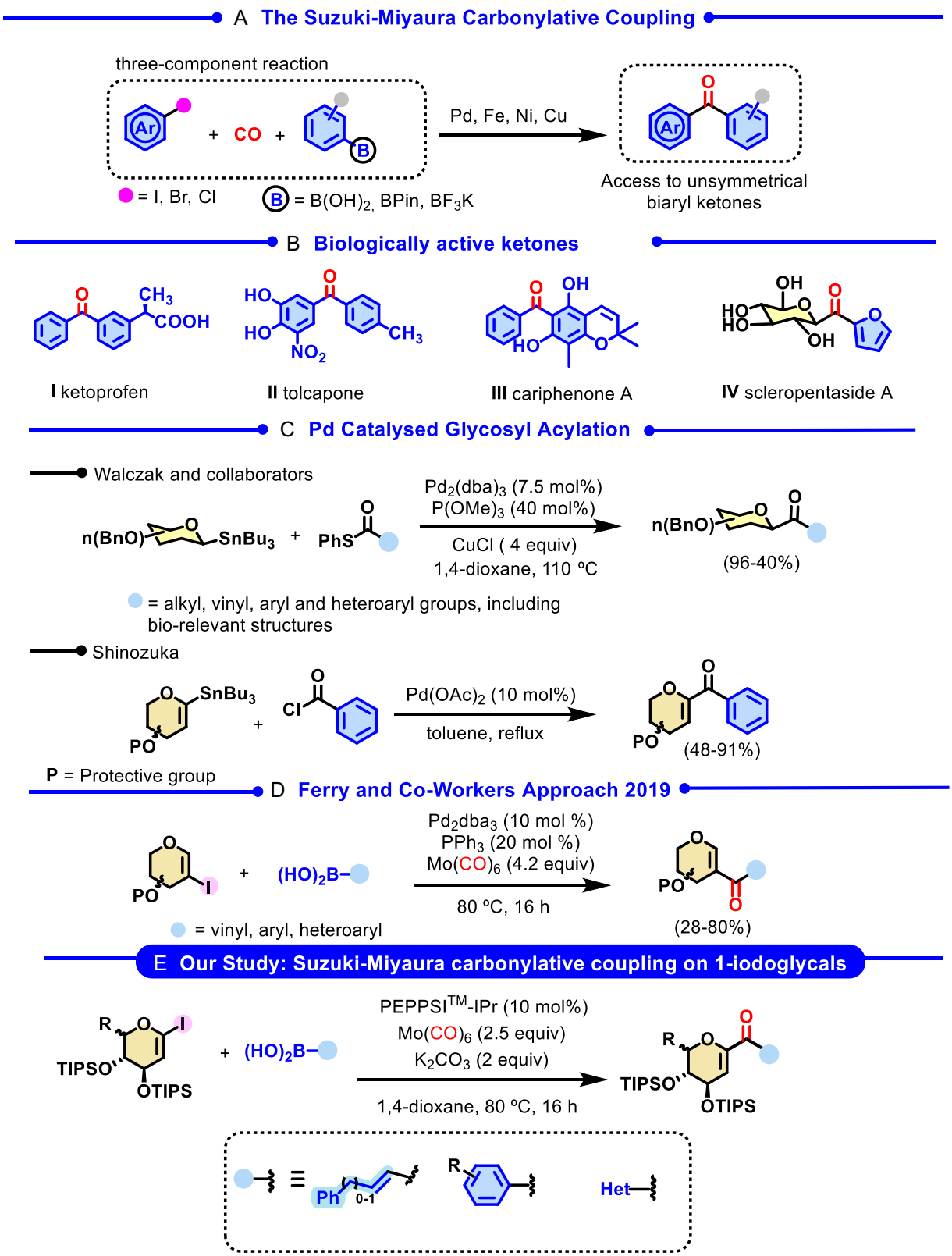
To date, the three-component carbonylative Suzuki–Miyaura reaction has primarily been applied to sugar-halide derivatives such as glycals. Ferry et al. [38] studied the carbonylative coupling of 2-iodoglycals to access *C*-2-branched glycals (Scheme 1D), evaluating a variety of aromatic and heteroaromatic boronic acids as well as the scope of glycals. In this work, we describe the carbonylative coupling of 1-iodoglycal employing in situ CO generation (Scheme 1D). By using minimal equivalents of $Mo(CO)_6$, the carbonylated products can be selectively obtained, demonstrating a more efficient and controlled approach to the synthesis of *C*-acyl glycosides.

2 | Results and Discussion

We focused on carbonylative coupling using 1-iodo-D-glucal as the sugar donor and systematically evaluated the reactivity of various boron nucleophiles (Scheme 2) under the conditions described by Ferry et al. [38]. The trifluoroborate salt did not afford the desired product in Dimethylformamide (DMF), so in an attempt to increase solubility, we tested different solvent mixtures, including 1,4-dioxane:MeOH (1:10) and the addition of water (1:99); however, we did not observe a reaction. After column chromatography, we isolated a dehalogenation byproduct in low yields, along with unreacted starting material. The use of the corresponding boronic acid led to product formation, with an isolated yield of 15%. Finally, we evaluated the pinacol ester, but there was no reaction under the tested conditions.

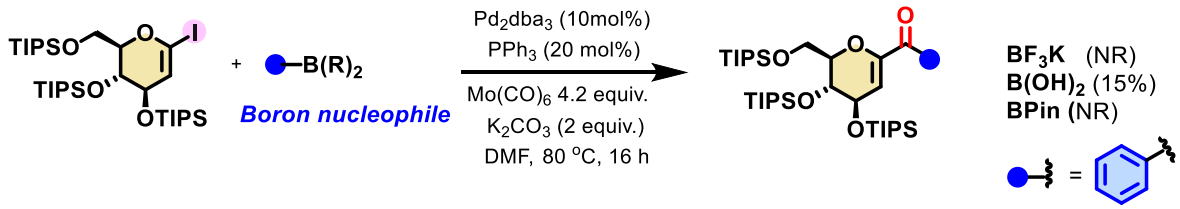
After identifying a suitable boron cross-coupling partner, we focused on optimizing the carbonylative coupling conditions. A common challenge in carbonylative Suzuki–Miyaura coupling is the occurrence of direct coupling without CO insertion [19]. We observed the formation of the direct coupling product when we used just only 1 equivalent of $Mo(CO)_6$ as the CO source. However, this side reaction was completely suppressed when we employed 2.5 equivalents of $Mo(CO)_6$. All reactions were conducted in a *one-pot* procedure.

We initiated optimization studies using 1-iodo-D-glucal (**1a**) and boronic acid (**2a**) as standard coupling partners. The solvent



SCHEME 1 | (A) Suzuki–Miyaura carbonylative coupling, (B) relevant bioactive examples, (C) Pd-catalyzed glycosyl acylation, (D) Ferry carbonylative coupling with 2-iodoglycals, and (E) our study.

chosen to commence this investigation was 1,4-dioxane, as it is well suited for carbonylative couplings [39, 40]. A systematic evaluation of the reaction parameters revealed that Pyridine-Enhanced Precatalyst Preparation, Stabilization, and Initiation (PEPPSI-IPr) is a suitable NHC catalyst. It performed efficiently with the sterically demanding glucal substrate. For further details of the conditions explored, see the Supporting Information (Table S1).



SCHEME 2 | Suzuki–Miyaura carbonylative coupling reaction of C-1 iodo glucal.

NHCs exhibit several advantageous features upon coordination, including enhanced stability toward air, moisture, heat, and oxidative conditions, as well as superior electronic properties, particularly their strong σ-donor ability [41].

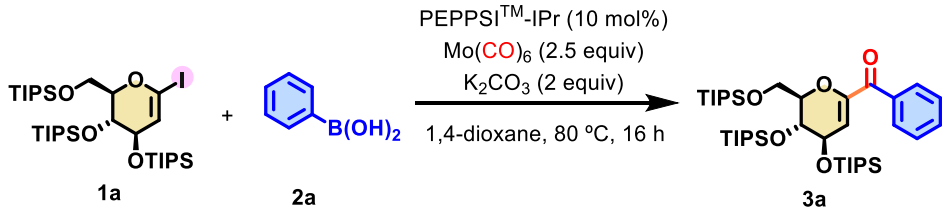
The combination of an inorganic base such as K_2CO_3, $Mo(CO)_6$ as a CO surrogate, and 1,4-dioxane as the solvent at 80°C for 16 h promoted efficient formation of the carbonylated product (Table 1, entry 1). Other palladium catalysts such as $Pd(PPh_3)_4$ also performed well (see Supporting Information, Table S1), while the use of phosphine-based catalysts, such as $Pd(PPh_3)_2Cl_2$, led to decreased yields (Table 1, entry 2).

The use of additional ligands such as RuPhos also resulted in decreased yields (Table 1, entry 3). Likewise, the combination of phosphine ligands with Pd-PEPPSI-IPr failed to improve the outcome and instead reduced the efficiency (see Supporting Information, Table S1). Regarding the base, inorganic bases such as Cs_2CO_3 and K_2CO_3 gave satisfactory results; we selected the latter due to its lower cost. Conversely, organic bases proved ineffective (Table 1, entry 4).

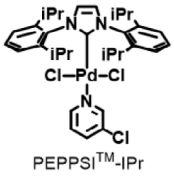
We also evaluated a range of solvents. The use of acetonitrile in combination with water completely suppressed the reaction (see Supporting Information, Table S1). Other polar aprotic solvents, such as DMF, also reduced yields (Table 1, entry 5). Aromatic polar solvents such as anisole were compatible with the transformation and are commonly used in palladium-catalyzed carbonylative couplings [11], although they afforded slightly lower yields (see Supporting Information, Table S1).

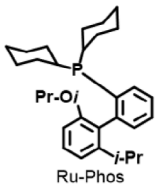
We next examined different metal carbonyls as surrogates for $Mo(CO)_6$. The use of diiron nonacarbonyl ($Fe_2(CO)_9$) completely shut down the reaction (Table 1, entry 6), while dicobalt octacarbonyl ($Co_2(CO)_8$) afforded the desired product in poor yield (see Supporting Information, Table S1). These results are consistent with the lower efficiency of iron and cobalt carbonyls previously reported by Beller et al. [42], even under elevated temperatures.

TABLE 1 | Optimization of the carbonylative Suzuki–Miyaura reaction.[a]



Entry	Variation From Standard Conditions	Yield (%)[a]
1	None	65(62)
2	$PdCl_2(PPh_3)_2Cl_2$ as catalyst	35
3	RuPhos as ligand	30
4	DBU as base	22
5	DMF as solvent	15
6	$Fe_2(CO)_9$ as CO source	NR
7	24 hours reaction	20





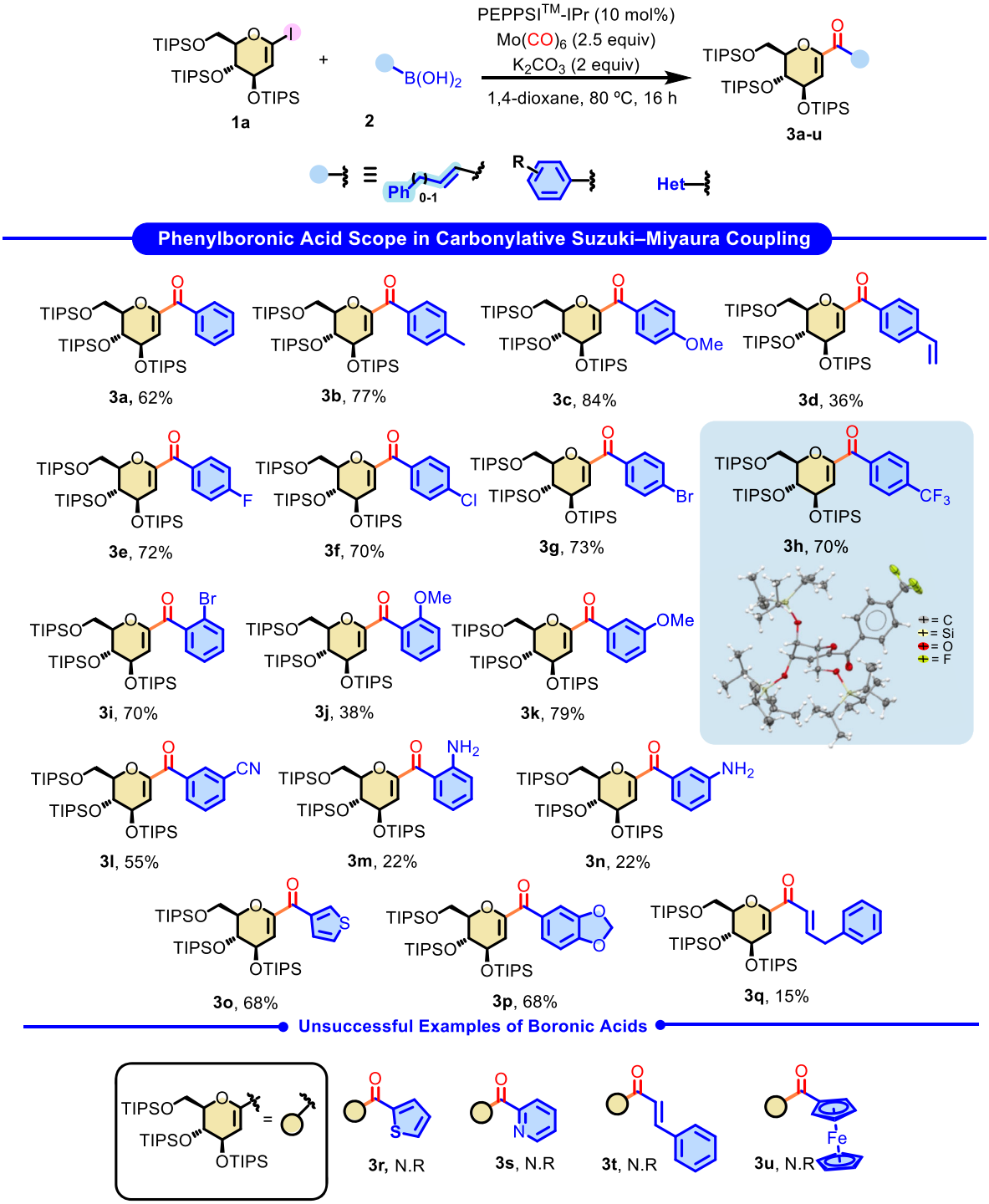
[a]The yield was determined using trichloroethene as an internal standard (IS).

Finally, extending the reaction time to 24 h (Table 1, entry 7) did not improve yields.

With the optimized reaction conditions—phenyl boronic acid (2.0 equiv), PEPPSI-IPr as the catalyst, K_2CO_3 (2.0 equiv), $Mo(CO)_6$ (2.5 equiv), in 1,4-dioxane (0.1 M)—a series of boronic acids could be subjected successfully to carbonylative coupling (Scheme 3). Under these conditions, standard phenyl boronic acid provided the corresponding product **3a** in good yield.

Next, we explored a range of electronically diverse aryl boronic acids. Electron-donating groups at the 4-position, such as methyl and methoxy, led to the isolation of products **3b** and **3c** in good to excellent yields. The use of (4-vinylphenyl) boronic acid resulted in a considerably lower yield of **3d**, likely due to the reduced stability of the vinyl derivative. Halogen substituents at the 4-position, including 4-F, 4-Cl, and 4-Br, furnished the corresponding products **3e**–**3g** in good yields. Interestingly, a strongly electron-withdrawing 4-CF_3 group also provided **3h** in good yield.

We also examined substitution at the 2-position. The 2-Br derivative gave **3i** in good yield, whereas a 2-OMe substituent led to a lower yield of **3j**, suggesting that a combination of



SCHEME 3 | The scope of boronic acid substrates.

electron-donating and electron-withdrawing effects contributes to the favourable outcomes observed for halogen-substituted derivatives. The 3-OMe group performed well, affording **3k** in good yield, while the strongly electron-withdrawing 3-CN group gave a moderate yield of **3l**.

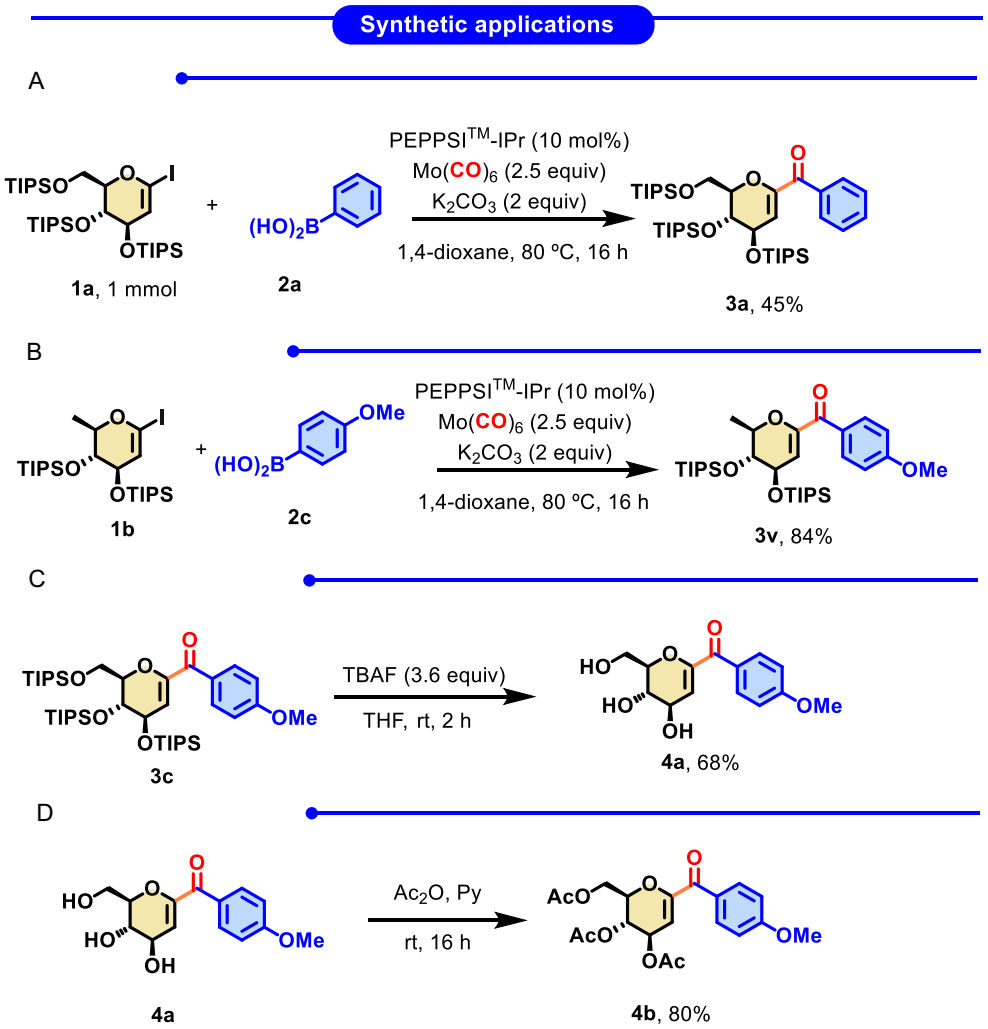
A 2-NH_2 and 3-NH_2-substituted boronic acid, a potential coordinating group, resulted in a poor yield of **3m** and **3n**. This result can be rationalized in terms of aminocarbonylation reaction between free amino group with 1-iodoglycal.

With the aim of expanding the scope, heterocyclic moieties were also investigated: 2-thiophenyl boronic acid afforded **3o** in good yield, and benzodioxole derivative (**3p**) was produced in good yield, but the use of a vinylic boronic acid afforded the coupled product in low yield (**3q**). Some boronic acid coupling partners, including 2-thienyl, 2-pyridyl, trans-(2-phenylethenyl), and ferrocenyl boronic acids, were unsuccessful under the applied conditions.

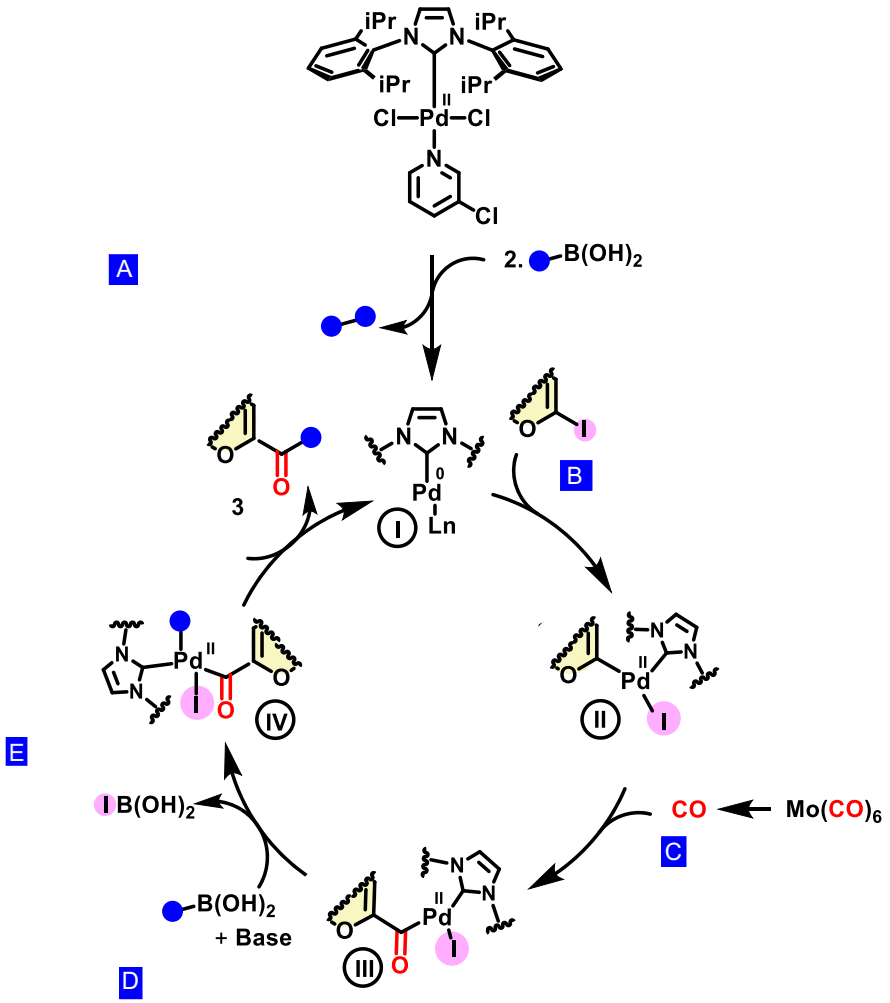
We determined the X-ray crystal structure of compound **3h** (CCDC 2 488 408). It crystallizes in the orthorhombic space group $P2_12_12_1$, with two crystallographically independent molecules in the asymmetric unit ($Z' = 2$). Both molecules are structurally equivalent, exhibiting nearly identical conformations and comparable geometric parameters. The supramolecular architecture is dominated by C—H···F hydrogen bonds and pervasive van der Waals contacts, which collectively stabilize the packing arrangement and dictate the overall organization of the crystal lattice.

Finally, we evaluated the synthetic applications of the developed methodology (Scheme 4). We assessed the robustness and versatility of the reaction at a larger scale of 1 mmol. The use of phenyl boronic acid as a coupling partner afforded **3a** in modest yield (45%, Scheme 4A). When using L-rhamnal derivative **1b**, the reaction proceeded smoothly and the coupling product **3v** was produced in 84% yield. The triisopropylsilyl (TIPS) group was deprotected with TBAF and reprotected with an acetyl group after stirring overnight in the presence of pyridine and acetic anhydride. After 16 h, the reaction gave acetylated glucal **4b** in 80% yield.

Regarding the chemistry of the functionalization of 1-iodoglycals, we would like to address some limitations in accessing a broader range of derivatives. For example, the method for generating the organolithium intermediate at position 1 of the glucal requires the use of *t*-BuLi, a strong and highly reactive base that is only



SCHEME 4 | Synthetic applications. [a] Reaction conditions for sugar deprotection: **3c** (0.2 mmol, 1 equiv), TBAF (0.72 mmol, 3.6 equiv), and THF (1.3 mL). [b] Reaction conditions for acetyl protection: **4a** (0.18 mmol, 1 equiv), acetic anhydride (0.25 mL), and pyridine (0.5 mL). (A) Scale-up. (B) Rhamnal derivative. (C) TIPS deprotection. (D) Acetyl deprotection.



SCHEME 5 | Proposed mechanism. (A) Precatalyst activation. (B) Oxidation addition. (C) CO Insertion. (D) Transmetalation. (E) Reductive elimination.

compatible with silylated protecting groups. Another limitation is that, to date; only the TIPS group has proven suitable for the preparation of 1-iodoglycals. When attempting to use other bulky groups, such as *tert*-butyldimethylsilyl (TBDMS), we observed competitive iodination on the alkyl substituents of the protecting group. This provides a plausible explanation for the absence of such derivatives in previous literature reports. A prior study by Friesen demonstrated iodination at the methyl groups of TBDMS [43], and we recovered the same undesired product under identical conditions.

Another challenge we encountered was expanding the scope of sugar derivatives. Although the preparation of 1-iodogalactal has been reported using TIPSCl as the protecting agent [44], its reproduction proved difficult, particularly under prolonged reaction times and elevated temperatures. These difficulties arise from bis-protection of the 3- and 5-hydroxyl groups of the glycal and the pronounced steric shielding of the hydroxyl at C-4. An alternative protocol using TIPSOTf as the protecting reagent is also known; however, in our hands, it was not reproducible in synthetically useful yields [45].

A plausible mechanism is depicted in Scheme 5. To catalyze the reaction, palladium must be in its active form, namely a Pd(0) complex [46]. In the literature, a sequential double transmetalation of an organoboron reagent with the palladium(II) precatalyst has been proposed, followed by reductive elimination to furnish the catalytically active NHC–Pd^0 $(L)_n$ intermediate I (activation step) [47, 48]. During this activation step, the dissociation of the throw-away ligand pyridine occurs prior to the oxidative addition of 1-iodoglycal, leading to the formation of the Pd(II)–glycal iodide intermediate II. CO, generated in situ from the release of $Mo(CO)_6$, is generally accepted to coordinate with intermediate II, yielding the acyl–palladium complex III [19]. This is followed by transmetalation with the boronic acid in a base-mediated step, affording intermediate IV. Finally, reductive elimination furnishes the desired product **3** and regenerates the NHC–Pd^0catalyst.

3 | Conclusion

In summary, we have developed a palladium-catalyzed carbonylative Suzuki–Miyaura C(sp^2)-C-(sp^2) coupling reaction that proceeds through in situ generation of CO. The use of $Mo(CO)_6$, as a solid CO surrogate, enables selective formation of carbonylated product, and mitigates directing coupling with the boronic acid. The methodology enables the production of C-1 functionalized glycals. We employed a series of aromatic, heteroaromatic, and vinylic boronic acids, which underwent smooth carbonylative coupling. The coupling products were recovered in high yields and represent novel derivatives of *C*-acyl glycosides, which are found in nature and are biologically active.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Supporting Fig. S1:** Representation of the crystal structure is illustrated with thermal ellipsoids at the 20% probability level. Atoms are distinguished by color according to their element: C (grey), O (red), H (white), F (green), and Si (light yellow). **Supporting Fig. S2:** ^{1}H NMR spectra (300 MHz, $CDCl_3$) of **1a.** **Supporting Fig. S3:** $^{13}C\{^{1}H\}$ NMR spectra (75 MHz, $CDCl_3$) of **1a.** **Supporting Fig. S4:** ^{1}H NMR spectra (300 MHz, $CDCl_3$) of **1b. Supporting Fig. S5.:** $^{13}C\{^{1}H\}$ NMR spectra (75 MHz, $CDCl_3$) of **1b. Supporting Fig. S6:** ^{1}H NMR spectra (300 MHz, $CDCl_3$) of **3a**. **Supporting Fig. S7:** $^{13}C\{^{1}H\}$ NMR spectra (75 MHz, $CDCl_3$) of **3a**. **Supporting Fig. S8:** ^{1}H NMR spectra (300 MHz, $CDCl_3$) of **3b**. **Supporting Fig. S9:** $^{13}C\{^{1}H\}$ NMR spectra (75 MHz, $CDCl_3$) of **3b**. **Supporting Fig. S10:** ^{1}H NMR spectra (300 MHz, $CDCl_3$) of **3c**. **Supporting Fig. S11:** $^{13}C\{^{1}H\}$ NMR spectra (75 MHz, $CDCl_3$) of **3c**. **Supporting Fig. S12:** ^{1}H NMR spectra (300 MHz, $CDCl_3$) of **3d**. **Supporting Fig. S13:** $^{13}C\{^{1}H\}$ NMR spectra (75 MHz, $CDCl_3$) of **3d**. **Supporting Fig. S14:** ^{1}H NMR spectra (300 MHz, $CDCl_3$) of **3e**. **Supporting Fig. S15:** $^{13}C\{^{1}H\}$ NMR spectra (75 MHz, $CDCl_3$) of **3e**. **Supporting Fig. S16:** ^{1}H NMR spectra (300 MHz, $CDCl_3$) of **3f**. **Supporting Fig. S17:** $^{13}C\{^{1}H\}$ NMR spectra (75 MHz, $CDCl_3$) of **3f**. **Supporting Fig. S18:** ^{1}H NMR spectra (300 MHz, $CDCl_3$) of **3g**. **Supporting Fig. S19:** $^{13}C\{^{1}H\}$ NMR spectra (75 MHz, $CDCl_3$) of **3g**. **Supporting Fig. S20:** ^{1}H NMR spectra (300 MHz, $CDCl_3$) of **3h**. **Supporting Fig. S21:** $^{13}C\{^{1}H\}$ NMR spectra (75 MHz, $CDCl_3$) of **3h**. **Supporting Fig. S22:** ^{1}H NMR spectra (300 MHz, $CDCl_3$) of **3i**. **Supporting Fig. S23:** $^{13}C\{^{1}H\}$ NMR spectra (75 MHz, $CDCl_3$) of **3i**. **Supporting Fig. S24:** ^{1}H NMR spectra (300 MHz, $CDCl_3$) of **3j**. **Supporting Fig. S25:** $^{13}C\{^{1}H\}$ NMR spectra (75 MHz, $CDCl_3$) of **3j**. **Supporting Fig. S26:** ^{1}H NMR spectra (300 MHz, $CDCl_3$) of **3k**. **Supporting Fig. S27:** $^{13}C\{^{1}H\}$ NMR spectra (75 MHz, $CDCl_3$) of **3k**. **Supporting Fig. S28:** ^{1}H NMR spectra (300 MHz, $CDCl_3$) of **3l**. **Supporting Fig. S29:** $^{13}C\{^{1}H\}$ NMR spectra (75 MHz, $CDCl_3$) of **3l**. **Supporting Fig. S30:** ^{1}H NMR spectra (300 MHz, $CDCl_3$) of **3m**. **Supporting Fig. S31:** $^{13}C\{^{1}H\}$ NMR spectra (75 MHz, $CDCl_3$) of **3m**. **Supporting Fig. S32:** ^{1}H NMR spectra (300 MHz, $CDCl_3$) of **3n**. **Supporting Fig. S33:** $^{13}C\{^{1}H\}$ NMR spectra (75 MHz, $CDCl_3$) of **3n**. **Supporting Fig. S34:** ^{1}H NMR spectra (300 MHz, $CDCl_3$) of **3o**. **Supporting Fig. S35:** $^{13}C\{^{1}H\}$ NMR spectra (75 MHz, $CDCl_3$) of **3o**. **Supporting Fig. S36:** ^{1}H NMR spectra (300 MHz, $CDCl_3$) of **3p**. **Supporting Fig. S37:** $^{13}C\{^{1}H\}$ NMR spectra (75 MHz, $CDCl_3$) of **3p**. **Supporting Fig. S38:** ^{1}H NMR spectra (300 MHz, $CDCl_3$) of **3q**. **Supporting Fig. S39:** $^{13}C\{^{1}H\}$ NMR spectra (75 MHz, $CDCl_3$) of **3q**. **Supporting Fig. S40:** ^{1}H NMR spectra (300 MHz, $CDCl_3$) of **3v**. **Supporting Fig. S41:** $^{13}C\{^{1}H\}$ NMR spectra (75 MHz, $CDCl_3$) of **3v**. **Supporting Fig. S42:** ^{1}H NMR spectra (300 MHz, CD_3OD) of **4a**. **Supporting Fig. S43:** $^{13}C\{^{1}H\}$ NMR spectra (75 MHz, CD_3OD) of **4a**. **Supporting Fig. S44:** ^{1}H NMR spectra (300 MHz, CD_3OD) of **4b**. **Supporting Fig. S45:** $^{13}C\{^{1}H\}$ NMR spectra (75 MHz, CD_3OD) of **4b.** **Supporting Table S1:** Optimization of the reactions conditions. **Supporting Table S2:** Crystal data and structure refinement for CCDC 2488408.