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Exploring benzylic *gem*-C(sp^3)–boron–silicon and boron–tin centers as a synthetic platform†

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A stepwise build-up of multi-substituted C_{sp^3} carbon centers is an attractive, conceptually simple, but often synthetically challenging type of disconnection. To this end, this report describes how *gem*-α,α-dimetalloid-substituted benzylic reagents bearing boron/silicon or boron/tin substituent sets are an excellent stepping stone towards diverse substitution patterns. These *gem*-dimetalloids were readily accessed, either by known carbenoid insertion into C–B bonds or by the newly developed scalable deprotonation/metallation approach. Highly chemoselective transformations of either the C–Si (or C–Sn) or the C–B bonds in the newly formed *gem*-C_{sp^3} centers have been achieved through a set of approaches, with a particular focus on exploiting the synthetically versatile polarity reversal in organometalloids by λ^3-aryliodanes. Of particular note is the metal-free arylation of the C–Si (or C–Sn) bonds in such *gem*-dimetalloids *via* the iodane-guided C–H coupling approach. DFT calculations show that this transfer of the (α-Bpin)benzyl group proceeds *via* unusual [5,5]-sigmatropic rearrangement and is driven by the high-energy iodine(III) center. As a complementary tool, the *gem*-dimetalloid C–B bond is shown to undergo a potent and chemoselective Suzuki–Miyaura arylation with diverse Ar–Cl, thanks to the development of the reactive *gem*-α,α-silyl/BF_3K building blocks.

Background and motivation

In the context of diversity-oriented synthesis, reagents bearing geminally disposed bis-metalloid units represent an attractive class of building blocks. Expected to act as bis-nucleophilic components in a variety of reactivity patterns, such molecules may set the stage for densely 1,1-disubstituted carbon centers through sequential reactions with two electrophilic partners, including *via* catalytic cross-coupling. A potentially rewarding aim is the use of the C_{sp^3}-*gem*-dimetalloid group as a platform for straightforward access to multi-substituted methanes.[1] This basic unit received a renewed spotlight as part of medicinal chemistry's "escape from the flatland" endeavor,[2] and has been the subject of important recent methodological breakthroughs.[3] In terms of the substitution pattern, compounds featuring a carbon center anchoring a *gem*-boron/boron pair have been particularly popular, whereby a variety of methods have been developed to form such C_{sp^3}-*gem*-diboronates and to selectively transform one or both of their C–B sites.[4]

Along these lines, the prospect of selective introduction of two different substituents has also prompted interest in derivatives bearing mutually distinct metalloids, either as chemically differentiated boryl fragments[5] or as a hetero-metalloid pair. Inherent reactivity differences between the two carbon–metalloid bonds can then be leveraged to gain chemo-control in modular C–C and/or C–heteroatom bond-forming sequences, with 1,1-silyl-boranes constituting an obvious paradigm for such a hetero-*gem*-dimetalloid platform.[6] As part of our interest in this area, some of us recently showed that 1,1-$SiMe_3$/$B(OR)_2$ disubstituted alkenes could be obtained by a novel boron-Wittig-type olefination using the 1,1,1-B,B,Si-trimetalloid methane species,[7] and that the newly formed olefinic C_{sp^2}-*gem*-Si,B group could be engaged in stereoselective access to tetra-substituted olefins. Encouraged by these earlier advances, we set our sight on the *gem*-B/Si-benzylic scaffold of type **1** (Scheme 1). Creative recent approaches to **1** include a Suzuki–Miyaura mono-arylation of the aforementioned 1,1,1-bis-(Bpin)-trialkylsilyl methane **2**,[8] including its enantioselective desymmetrization variant,[8b] or a homologation of an Ar–B bond using the diazo-reagent Me_3SiCHN_2, **3** (Scheme 1A and B).[9] However, these advances in the preparation of **1** contrast with the scarcity of methods that employ such *gem*-dimetalloids in the modular build-up of poly-substituted C_{sp^3} centers. For example, while the C–Bpin bond in such species was recently shown to undergo a Pd-catalyzed coupling with iodoarenes (Scheme 1C),[9b] the

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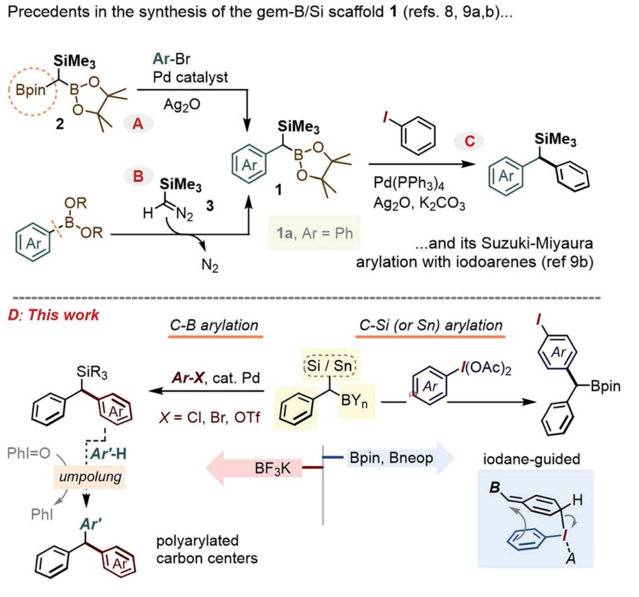
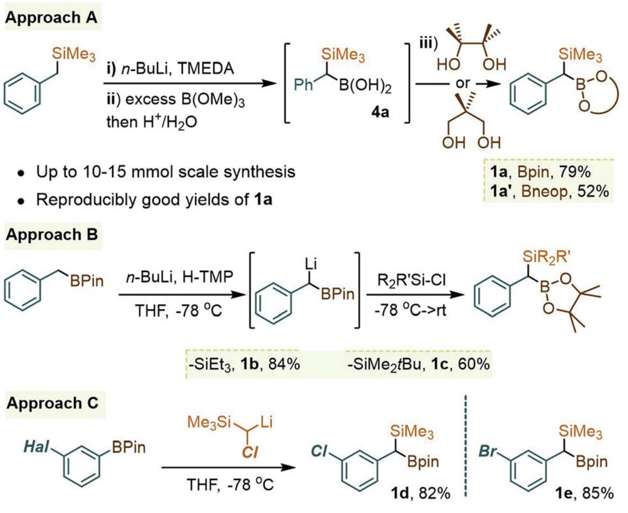


Scheme 1 (A and B) Recent approaches to the *gem*-Si/B compound class **1**, and (C) an example of Pd-catalyzed arylation of **1** with Ar–I; (D) the outline of the *gem*-dimetalloid diversification strategy described herein.



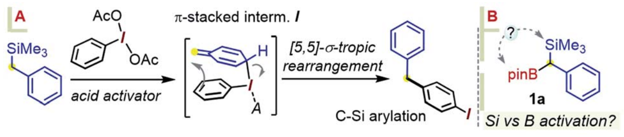
Scheme 2 Complementary deprotonation/quench approaches to the benzylic *gem*-Si/B core **1a**. Approach A: (i) in hexane using 1.0 equiv. of *n*-BuLi at rt; (ii): with 3 equiv. of $B(OMe)_3$, −78 °C to rt. Approach B: Li-TMP generated at −40 °C prior to addition of BnBpin at −78 °C. Approach C: lithiation of Me_3SiCH_2Cl with *sec*-BuLi/TMEDA followed by addition of Ar–Bpin.

chemistry at the C–Si bond has been largely limited to the more established desilylative S_N2 alkylations.[9b] In this report, we describe a series of approaches to expand the arsenal of chemoselective transformations of the *gem*-B/Si-benzylic scaffold **1**. In particular, our prior experience in polarity reversal and rearrangement reactions of organosilanes induced by hypervalent iodine compounds has now been leveraged to achieve a metal-free selective C–Si and C–Sn arylation, along with a series of umpolung reactions (Scheme 1D). Among interesting *gem*-dimetalloid targets, we also show that the trifluoroborate analogue of **1** can be prepared, allowing for the Suzuki–Miyaura arylation (see Scheme 1D left) using bromo- and chloro-arenes.

Results and discussion

As was readily appreciated from the outset, the successful usage of the *gem*-Si/B molecular platform such as **1** would be contingent upon more ready access to this compound class. Our initial approach to **1a** involved the insertion of the carbenoid-type fragment "$SiMe_3(H)C$:" of the diazo species Me_3SiCHN_2, **3**, into the B–C bond of arylboroxines, as reported recently by Ley and co-workers.[9a] Following this route (as in Scheme 1B), the phenyl derivative **1a** was obtained in good yields by heating phenylboroxine, $(PhBO)_3$, with **3** in toluene. Despite the success of this approach on small scales (1–2 mmol), we continued our search for a complementary method to access gram quantities of the reagent. After some trials, it was found that **1a** could be conveniently prepared from commercial benzyl(trimethyl)silane by deprotonation at the benzylic position, followed by quenching the resulting benzyllithium species with an electrophilic $B(OR)_3$ reagent (Scheme 2, approach A). In our hands, treating the α-$B(OH)_2$ intermediate **4a** with pinacol provided **1a** in reproducibly good yields on scales of up to 10–15 mmol. Similarly, capping the C_{sp^3}–B unit with dimethylpropane-1,3-diol could be used to obtain the Bneop derivative **1a′** in 52%; the diminished yield in the latter case is likely due to the instability of the Bneop derivatives under column chromatography on SiO_2. A second approach was also developed starting with a commercial benzylboronate core *via* deprotonation using a hindered lithium 2,2,6,6-tetramethylpiperidide base (Li-TMP), followed by the addition of a chlorosilane.[10] This route was convenient for producing derivatives with silyl groups other than $SiMe_3$, such as the *gem*-$SiEt_3$ species **1b** (84%, Scheme 2, approach B) or the Si(*t*Bu)Me_2 analogue **1c** (60%). Finally, when a suitable B- or Si-benzylic precursor was not readily available, a Matteson-type homologation[9c] of several Ar–Bpin species with an *in situ* generated $Me_3Si(Cl)CH$–Li reagent was found to proceed smoothly. Following this route, the *meta*-halo *gem* derivatives **1d** and **1e** were obtained in 82% and 85% yields, respectively (Scheme 2, approach C).

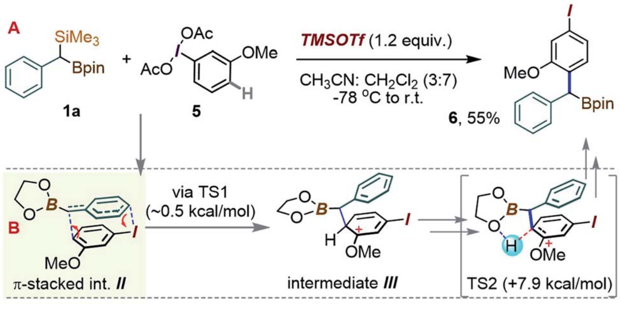
With gram quantities of the model *gem*-hetero-dimetalloid **1a** now accessible, we turned our attention to a selective transformation of its C–Si moiety. Although a Hiyama-type metal-catalyzed C–Si arylation coupling would be a valuable tool in this system, the applications of this reaction even to simple benzylsilanes are scarce, and generally require an activated silicon group.[11] As an alternative, we sought to engage **1a** in metal-free C–Si arylation with λ^3-$ArI(OAc)_2$ species. This possibility was based on our recent experience in the iodane-guided C–H benzylation of iodoarene cores, a process reported independently by the Hyatt and our laboratories.[12] As depicted in Scheme 3A for a benzylsilane model, this unusual manifold would begin with the benzyl group transfer to the iodine(III) center. While related to the iodane-guided *ortho*-C–H coupling processes,[13,14] the benzyl group in such case gave rise



Scheme 3 (A) A precedent in the iodane-guided C–Si arylation of benzylsilanes with λ^3-iodanes (Hyatt *et al.* and Shafir *et al.*), 2018–19. (B) Potential selectivity dilemma in the analogous arylation of **1a**.

to a cationic head-to-tail π-stacked intermediate **I**, which evolves *via* the C–C bond formation at the ArI *para*-C–H position.[12b] We note that the Hyatt lab also showed the possibility of similarly engaging benzylic trifluoroborate nucleophiles.[12a]

Considering an application of such a manifold to **1a**, an interesting question arises as to which of the substrate's two metalloid groups, *i.e.* Si or B, would be retained in the product (Scheme 3B). Thus, the reactivity of **1a** with the iodoanisole-based λ^3-ArI(OAc)$_2$ reagent **5** was probed at −78 °C. While no reaction took place between **1a** and **5** in a CH_3CN/CH_2Cl_2 mixture without an acid additive, enhancing the reactivity of the λ^3-iodane with an acidic activator, either $BF_3\cdot Et_2O$ or TMSOTf,[15] led to the new benzylated species **6** in 55% yield, with the new C–C created *para* to the iodine (Scheme 4). The product retains the Bpin group, suggesting a more reactive nature of the C–Si bond during the putative transmetallation step, a feature that contrasts with C–B-specific Pd-catalyzed coupling reactions (as in Scheme 1C). A DFT analysis was used to understand how the process could play out for a *gem*-B/Si-dimetalloid substrate. Calculations on the –B-glycolate analogue of **1a** (–Bgly, Scheme 4B) point to a cationic π-stacked intermediate **II** with a head-to-tail alignment of the two aromatic fragments. This species is analogous to the adduct **I**, previously identified in a *para*-CH–benzylation (Scheme 3), and similarly evolves *via* a low-lying (∼0.5 kcal mol^{-1}) transition state to form a new carbon–carbon bond *para* to iodine (Scheme 4B). The rearrangement is expected to initially provide the ring protonated intermediate **III.** Although the final aromatization may then take place through proton transfer to an external base, the presence of the boronate group in **III** may also enable an interesting low-barrier internal proton transfer from the acidic C–H site to one of the boronate O atoms (see TS2 in Scheme 4B).

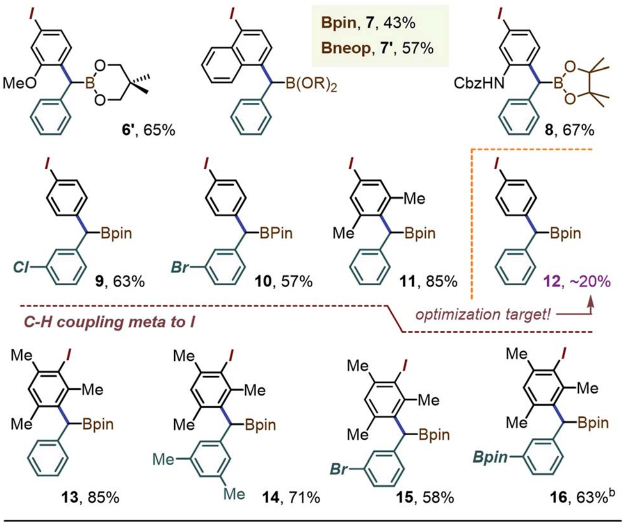


Scheme 4 (A) *Para*-selective C–H-(α-borylbenzylation) of the iodoanisole core. (B) DFT proposal for the C–C bond forming step.

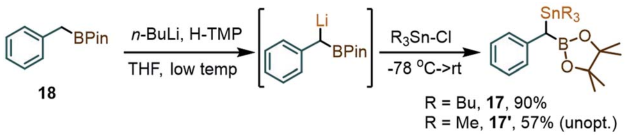
A brief scope survey showed that the coupling efficiency may benefit from the presumably less encumbered Bneop substituent, as seen in the formation of the Bneop analogue **6′** in 65% yield starting from **1a′** (Table 1). A similar moderate improvement was also seen for the C–H benzylation at the 4-position of λ^3-1-(diacetoxyiodo)-naphthalene, with a 43% yield obtained for the α-Bpin derivative **7** and a 57% yield (NMR) for the Bneop analogue **7′**. The reaction was also successful in providing the *para*-(α-boryl)benzylated derivative of the protected 3-iodoaniline (prod. **8**, 67%), the *meta*-halo derivatives **9** and **10** (63% and 57%), and the iodoxylene coupling product **11** (85%). The success of these reaction may partly be due to the presence of electron-releasing substituents in most of the iodoarene cores.[16] Indeed, the use of the non-activated simple PhI(OAc)$_2$ initially led to the target arylated species **12** in yields of ∼20%. Finally, as we previously observed for λ^3-iodoanes blocked at the *para* position,[12b] exposing **1a** to the λ^3-iodane derived from iodomesitylene led to an efficient formation of the *meta*-CH–benzylated species **13.**[17] The scope of this *meta*-substitution was then extended to the *m*-xylyl derivative **14** and the bromo-target **15.** The method was also tolerant of a *gem*-Si/B reagent bearing a second BPin substituent on the aromatic ring (Table 1, prod. **16**).

In view of the initially low yields in the coupling between **1a** and PhI(OAc)$_2$, due to the formation of benzaldehyde and other benzylic oxidation side products, we considered replacing the $SiMe_3$ fragment with a potentially more reactive $SnBu_3$ group. With that in mind, two new *gem*-Sn/B-dimetalloids **17** and **17′** were synthesized from the benzylboronate **18** *via* benzylic deprotonation followed by quenching with R_3SnCl (Scheme 5).

Table 1 Chemoselective C–Si bond transformation in **1a** and **1a′** *via* iodane-guided *para* C–H coupling[a]

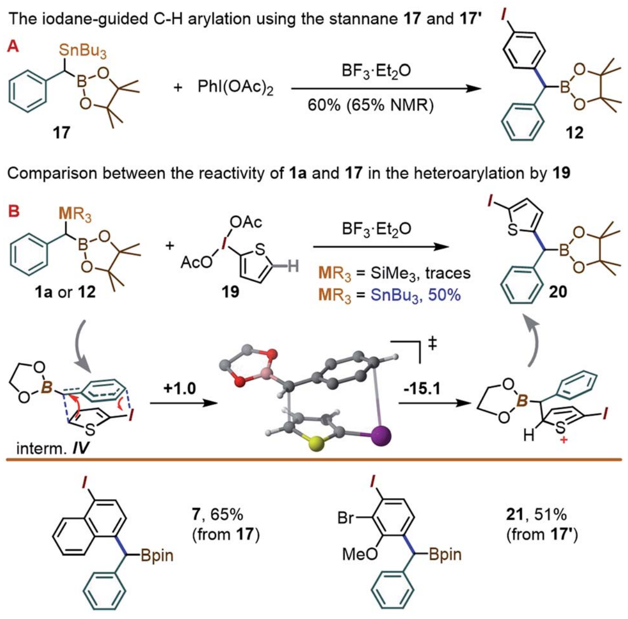


[a] Conditions analogous to those in Scheme 4A; ESI. [b] Using a *gem*-Si/B precursor obtained by Suzuki–Miyaura borylation of the Ar–Cl **1d**.



Scheme 5 Formation of the *gem*-stannyl-boryl precursors **17** and **17′**.

To our delight, a reaction between **17** and the λ^3-iodane PhI(OAc)$_2$ led to the *para*-benzylated target **12** in 60% yield (65% by NMR), *i.e.* is ∼3 times higher than for the silyl analogue **1a** (Scheme 6A). This improvement may be tentatively explained by the enhanced ability of organo-stannanes to undergo transmetallation in iodane-guided C–H coupling reactions, a feature illustrated in the 1990's by the Ochiai group,[13] and recently leveraged by Peng and co-workers in *ortho*-directed C–H cyanoalkylation.[18] Similarly, while barely a trace amount of coupling took place between **1a** and the 2-iodothiophene-derived λ^3-iodane **19**, switching to **17** led to the thienyl product **20** in 50% yield (Scheme 6B). We note that although the 2-iodothiophene core does not possess a *para* position per se with respect to **I**, the substrate's C(5)–H unit does correspond to a C–C coupling site predicted for a putative [5,5]-sigmatropic rearrangement path (see ESI†). Indeed, a DFT optimization of the expected π-stacked intermediate **IV** (analogous to **III** in Scheme 4) converges to a conformation with the benzylic CH(BPin) group placed directly above the thiophene C(5)–H site (Scheme 6 bottom). Finally, the use of the Bu$_3$Sn species **17** allowed for the synthesis of the naphthyl-derived **7** to be improved from the 43% reported in Table 1 using **1a** to 65%. The use of **17′** also allowed for the C–H coupling of an *o*-Br, *m*-OMe iodane precursor to give **21** in 51% yield.

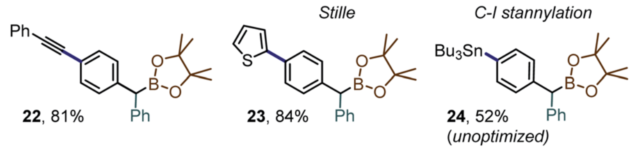


Scheme 6 The C–H coupling reaction of the new *gem*-Sn–B benzylic derivatives **17** and **17′**. The free energies in the mechanistic scheme are in kcal mol^{-1}.

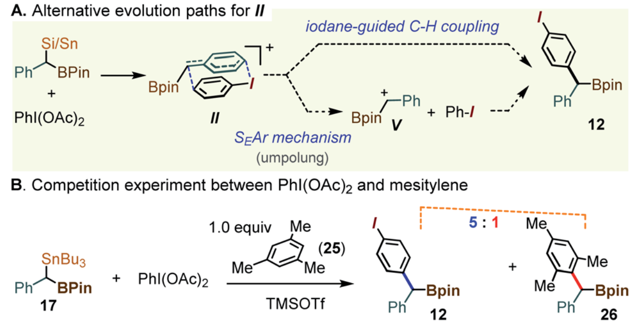
Along with the transfer of an intact boryl substituent, an important feature of the iodane-guided arylation reactions is the retention of the synthetically versatile iodine handle. A variety of downstream diversification routes could thus be assayed, including Pd-catalyzed cross-coupling reactions, *e.g.* Sonogashira alkynylation, Stille coupling or stanylation reactions (Scheme 7, prods. **22–24**).

While the pronounced *para*-C–H selectivity in the arylation of **1a** and **17** is consistent with the iodane-guided rearrangement mechanism outlined in Scheme 4, the outcome could in principle be rationalized through a particularly selective Friedel–Crafts type benzylation mechanism. Indeed, organosilanes can undergo the umpolung of the C–Si unit in the presence of simple λ^3-iodane oxidants. In the case of the *gem*-dimetalloids **1** or **17**, such a process might involve the benzyl iodonium intermediate such as **II**, which would evolve by a dissociation into the parent iodoarene and the α-boryl benzyl cation **V**. In such a sequence, the product would arise through an electrophilic attack at the ArI *para* position (see Scheme 8A). To test for the presence of free carbocationic species **V**, **17** was allowed to react with PhI(OAc)$_2$ in the presence of 1 equiv. of mesitylene, **25**. A concerted iodane-guided path would still favor the iodobenzene-derived **12**, while any free **V** would be expected to cause the functionalization of mesitylene. Here, the highly nucleophilic mesitylene was chosen so as to stack the odds in favor of such a hypothetical Friedel–Crafts process. Although the mesitylene-derived diarylmethane **26** was observed, this compound was present as a minor component, in a 1 : 5 ratio with **12** (Scheme 8B, also see the ESI for Fig. S2†). This result indicates that while the electrophilic aromatic substitution is possible, such a route does not represent the major path in the formation of **12**.

While these studies were underway, a parallel effort was directed towards securing a complementary method for the

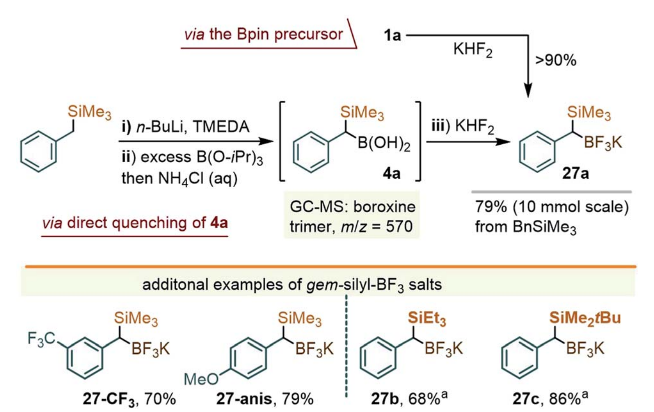


Scheme 7 Examples of downstream C–I diversification of **12**.



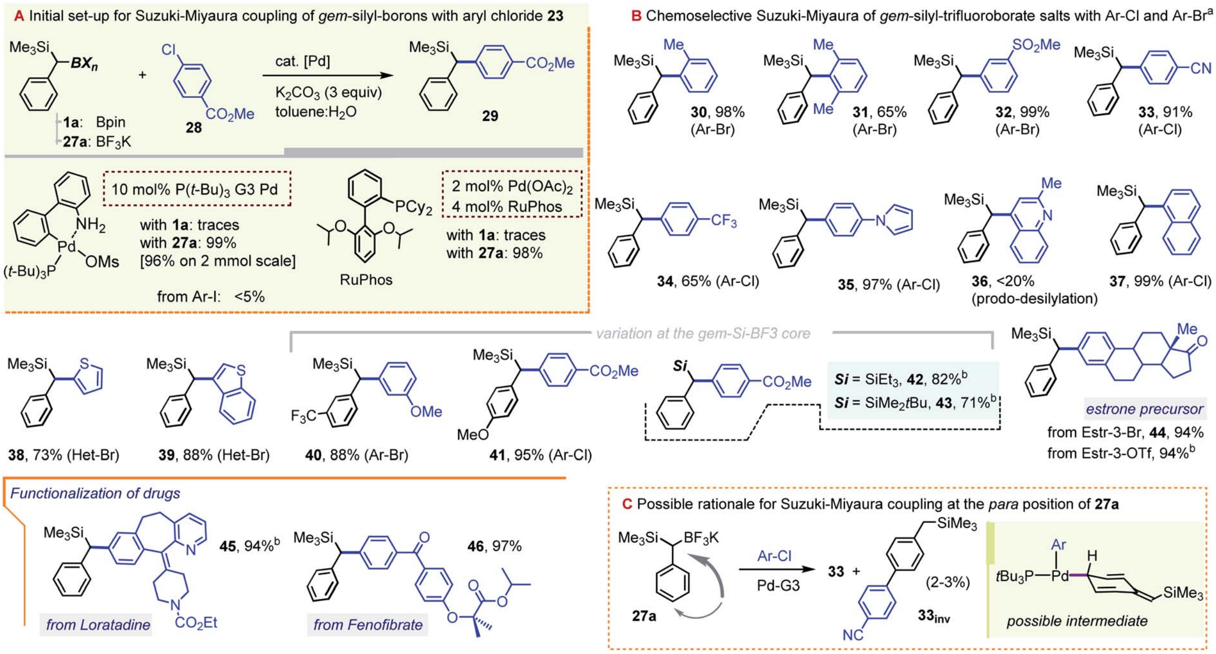
Scheme 8 Mechanistic assessment of the umpolung manifold in the oxidative coupling of **17** promoted by λ^3-iodanes.

arylation of the C–B bond in *gem*-Si/B precursors, which we thought to be possible through a metal-catalyzed coupling approach. In fact, at the time when our early efforts were getting underway (late 2018), there existed no literature reports on the coupling of α-silylated benzylboranes such as **1a**. More recently, however, Wang and co-workers described the arylation of **1** with iodoarenes using a Pd-catalyzed Ag-promoted coupling.[9b,19] In our case, the study centered on solving a more difficult coupling of *gem*-silylborylated cores with bromo- and chloro-arenes, which we hoped could be achieved using a series of newer Pd catalysts. Initial attempts to engage the Bpin precursor **1a** in the coupling with chloroarenes under a variety of catalytic conditions led to unsatisfactory results. Reasoning that a more reactive boryl substituent might prove beneficial, we sought to access the trifluoroborate derivative of **1a**. Borrowing a page from the Molander group's synthesis of the methylene reagent $Me_3Si–CH_2BF_3K$,[20] a treatment of **1a** with KHF_2 in an Et_2O/H_2O mixture led to the precipitation of a white solid identified as the *gem*-silyl potassium trifluoroborate **27a** (Scheme 9, top path). The NMR spectra of this species presented the benzylic ^1H C*H* signal at 1.26 ppm (broadened quartet, $J_{H–F} = 7.1$ Hz), and showed a displacement of the ^{11}B-NMR resonance from ~33 ppm for the –Bpin group in **1a** to ~1 ppm for **27a**. Noteworthily, no fluoro-desilylation of **27a** was observed at this stage. It was subsequently found that the lithiation/borylation approach, used earlier for the synthesis of **1a** (*i.e.* as in Scheme 2), may be redirected toward **27a** by intercepting the crude intermediate **4a** (identified by GC-MS as two diastereomeric boroxine trimers, $m/z = 570$, see the ESI†), with KHF_2 (Scheme 9). This method circumvents the need for the isolation of **1a** and allows for the ready synthesis of **27a** on a gram scale. A small family of additional trifluoroborate salts were also prepared, including **27-CF$_3$** and **27-anis**, as well the species **27b** and **27c**, the latter with variations at the silyl group (Scheme 9), either from the corresponding –Bpin precursor or *via* deprotonation/silylation sequences. All were isolated as white or off-white powders.



Scheme 9 A telescope synthesis of **27a** from benzyl(trimethyl)silane. (i) In hexane using 1.0 equiv. of *n*-BuLi at rt; (ii) with 3 equiv. of B(O-iPr)$_3$, −78 °C to rt, and overnight; (iii) in Et_2O/H_2O 4 : 1. [a]Prepared from the corresponding –Bpin precursors.

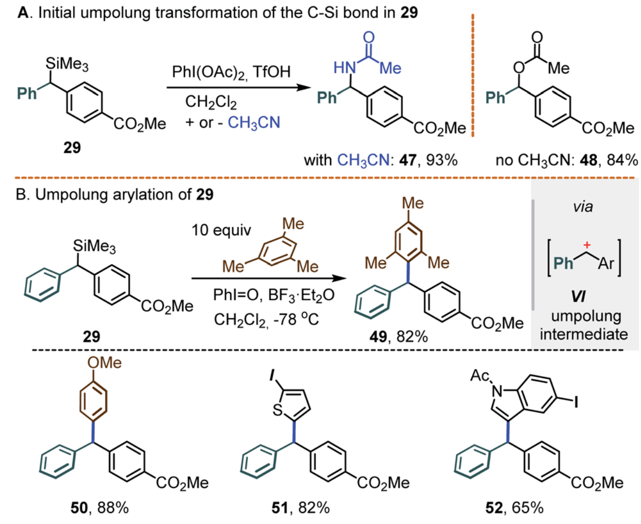
As we hoped for, a switch from a Bpin to a BF_3K *gem*-dimetalloid proved highly beneficial for the Suzuki–Miyaura coupling with chloroarenes. While in our hands **1a** failed to undergo a C–B arylation with the *p*-Cl–methylbenzoate **28**, the use of **27a** led to very promising yields of the target diarylmethane **29** using a number of modern catalytic systems. In particular, virtually quantitative conversions were achieved by using the RuPhos/Pd(OAc)$_2$ combination,[21] or by applying the 3rd generation *t*Bu$_3$P–Pd palladacycle precatalyst (*t*Bu$_3$P–Pd G3), the latter as used by Biscoe and co-workers for the aliphatic secondary trifluoroborate species (Scheme 10, gray inset).[22] The system was also suitable for bromoarenes, but gave unsatisfactory results with iodoarenes. This coupling efficiency is remarkable, given that the challenging Ar–Cl electrophile is joined with the bulky α-SiMe$_3$-substituted C(sp^3) nucleophile without the loss of the potentially sensitive α-silyl substituent. While the two catalyst systems showed similar performances, the scope of the arylation of **27a** (Scheme 10) is mainly illustrated using the Pd-G3 metallacycle. Hence, steric hindrance at the Ar–X partner was found to be well tolerated, with nearly quantitative yields obtained with the *ortho*-bromotoluene (prod. **30**, 98%), and a somewhat diminished yield for *o*,*o*-dimethyl bromoarene (**31**, 65%). Efficient coupling was also observed for a series of substituted haloarenes to give diarylmethanes **32–35** in generally excellent yields. As a limitation, the coupling of the strongly π-deficient chloroquinoline was inefficient due to rampant product desilylation (prod. **36**, <20%, observed by GC-MS). Nevertheless, the C–C coupling was also well-suited for naphthalene and thiophene-based haloarenes (see prods. **37–39**), with a somewhat lower yield in the isolation of **38** possibly due to mechanical losses during purification. The method is also suited for structure variations on the *gem*-Si-BF$_3$K component, including the successful formation of trifluorotolyl and anisyl derivatives **40** and **41**. Additionally, the method allowed for the ready formation of SiEt$_3$ and *t*BuMe$_2$Si analogues **42** and **43**, albeit with a somewhat lower yield for the latter. Our initial venture into bio-active core functionalization involved the coupling of the estrone moiety, which was possible starting with the corresponding 3-Br derivative. Interestingly, the RuPhos-based catalyst (but not the Pd-G3 system) also allowed for the direct coupling of the more readily available 3-OTf form of the precursor (prod. **44**, 94%). The method was also applied to the C–Cl moiety of the antihistaminic drug Loratadine, a polycyclic *N*-containing bioactive chloroarene, providing the α-silylbenzylated core **45** in an excellent 94% yield. Likewise, the reaction proved almost quantitative for the PPARα activator Fenofibrate as the Ar–Cl partner. Incidentally, the latter hyperlipidemic prodrug was recently considered for repurposing as a SARS-CoV-2 infection inhibitor.[23] Only mono-arylation was observed in all cases, confirming the expected resistance of the C_{sp^3}–SiMe$_3$ group towards conventional cross-coupling. Interestingly, although the two pre-catalysts were largely interchangeable, reactions conducted with the *t*Bu$_3$P–Pd G3 system frequently showed a minor GC-MS peak with the same *m*/*z* value as the target product (typically in a ~25–30 : 1 area ratio). For the –CN derivative **33**, this minor isomer, **33$_{inv}$**, was isolated and shown by NMR to correspond to the arylation at the *para* C–H



Scheme 10 Pd-catalyzed Suzuki–Miyaura coupling between benzyl-*gem*-silyl-trifluoroborates and chloro- or bromo-arenes. [a]Most examples were carried out using the tBu_3P–Pd G3 catalyst system: aryl halide (1 equiv.), *gem*-Si-BF_3K precursor (2.0 equiv.), 2–10 mol% of Pd-G3 catalyst, and K_2CO_3 (3.0 equiv.), in a toluene : H_2O mixture; see the ESI† for details in each case. [b]Employing a system composed of $Pd(OAc)_2$ (2–3%) and RuPhos (4–6%) and using the *gem*-Si-BF_3K precursor (1.1–1.3 equiv.) and K_2CO_3 (3.0 equiv.).

position of the benzylic precursor (Scheme 10C). We note that while related Pd-catalyzed *para*-selective coupling in benzylic systems is known, it typically relies on the use of benzylic electrophiles (*e.g.* benzyl chlorides), and not nucleophiles, as is the case in our system.[24] While a number of mechanistic manifolds can be envisioned leading to such side-products, one possibility is illustrated in the beige inset in Scheme 10C. Assuming a canonical oxidative addition/transmetallation path, species $\mathbf{33_{inv}}$ could arise from the isomerization of the Pd(II)-benzyl fragment to one of its *para*-palladated forms prior to reductive elimination. The bulky α-$SiMe_3$ group appears to influence the process, as no such product was observed in the control coupling using the simple benzyltrifluoroborate precursor (see the ESI†). In a few cases, *e.g.* for the Loratadine-derived **46**, the *para*-coupled species were formed in yields of up to 10%. Gratifyingly, this side reaction is fully suppressed by switching to the RuPhos-based catalyst system (*i.e.* the system used to obtain the 94% yield of **46** as shown).

As a final note, we envision that the retention of the C–Si bond under Pd catalysis opens the door for the introduction of a 3rd substituent at the central carbon. While this task was not extensively pursued, some preliminary results shown below attest to its viability. Specifically, our experience with hypervalent iodine chemistry[14a,b] led us to seek the introduction of a 3rd substituent *via* an umpolung transformation. It was found that exposing the silylated diarylmethane **29** to $PhI(OAc)_2$ and $BF_3 \cdot Et_2O$ in the standard CH_2Cl_2/CH_3CN medium led to the acetamide **47** as the main product (93%); in the absence of acetonitrile, the *O*-acetate **48** was obtained instead (84%, Scheme 11A). Seeking to suppress this C–O/N bond formation, further tests were conducted in CH_2Cl_2 using iodosobenzene, PhI=O, as an "acetate-free" λ^3-iodane oxidant. Under such conditions, a reaction between **29** and mesitylene (10 equiv.) afforded the differentially substituted triarylmethane **49** in an 82% yield, presumably *via* the intermediacy of the corresponding doubly benzylic carbocation **VI** (Scheme 11B). In a similar manner, a family of π-excessive arenes were also engaged, including anisole, 2-iodothiophene and *N*-tosyl-5-iodoindole (see triarylmethanes **50–52**, Scheme 11B, bottom).



Scheme 11 Iodane-promoted umpolung transformations of the *gem*-diaryl-α-silyl substrate **29**.

Conclusions

In summary, this work expands the synthetic landscape of versatile benzylic *gem*-boron–silicon and *gem*-boron–tin molecules, going from the generation of these species to their C–M reactivity applications. A new approach has been developed, which complements prior routes and by which gram quantities of benzylic *gem*-boron–silicon and *gem*-boron–tin reagents are obtained *via* the straightforward electrophilic α-borylation of the benzylsilane core. The products were isolated either as –Bpin or novel *gem*-silylated trifluoroborate salt derivatives. The C–Si or C–Sn sites in these species undergo metal-free oxidative arylation employing λ^3-bis(acetoxy)iodoarenes. The "iodane-guided" mechanism leads to selective coupling at the Ar–I *para* C–H site, with the molecule thus retaining both the C–I and the C–B functional groups. In addition, a protocol was identified for the Pd-catalyzed C–B arylation of hindered *gem*-$SiMe_3$–BF_3K substrates with chloro- and bromo-arenes. We envisage that these advances provide a strong foothold for further method development directed towards the modular iterative construction of multi-substituted carbon centers, a task of great importance in modern synthetic chemistry.

Data availability

Details of the experimental procedures, spectroscopic data and the results of the DFT calculations are available in the ESI file.

Author contributions

W. W. C., N. P. F., M. D. B., A. C. and L. G. R. contributed to the experimental work; A. B. C. and A. S. contributed to ideation and writing of the paper.

Conflicts of interest

There are no conflicts to declare.

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