Transition Metal Catalyst-Free, Base-Promoted 1,2-Additions of Polyfluorophenylboronates to Aldehydes and Ketones

Zhiqiang Liu, Goutam Kumar Kole, Yudha P. Budiman, Ya-Ming Tian, Alexandra Friedrich, Xiaoling Luo,* Stephen A. Westcott, Udo Radius,* and Todd B. Marder*

Abstract: A novel protocol for the transition-metal-free 1,2-addition of polyfluoroaryl boronate esters to aldehydes and ketones is reported, which provides secondary alcohols, tertiary alcohols, and ketones. Control experiments and DFT calculations indicate that both the ortho- and para-substituents on the polyfluorophenyl boronate and the counterion K+ in the carbonate base are critical. The distinguishing features of this procedure include the employment of commercially available starting materials and the broad scope of the reaction with a wide variety of carbonyl compounds giving moderate to excellent yields. Intriguing structural features involving O–H···O and O–H···N hydrogen bonding, as well as arene-perfluoroarene interactions, in this series of racemic polyfluoroaryl carbinols have also been addressed.

Introduction

Over the past few decades, the transition-metal-catalyzed 1,2-addition of organometallic reagents to the C=O functionality of aldehydes and ketones has developed as a useful method for the synthesis of substituted secondary and tertiary alcohols.[1] Numerous reagents have been used for these reactions, including organomagnesium,[2] organozinc,[1,3] organolithium,[4] organosilane,[5] organostannane,[6] organocerium,[7] and organoboron compounds.[8] In particular, organoboron reagents offer significant advantages such as air and moisture stability, low toxicity, good functional group tolerance, and availability.[8] In 1998, Miyaura and co-workers reported the addition of arylboronic acids to aldehydes and ketones, which provides secondary alcohols, tertiary alcohols, and ketones. Control experiments and DFT calculations indicate that both the ortho- and para-substituents on the polyfluorophenyl boronate and the counterion K+ in the carbonate base are critical. The distinguishing features of this procedure include the employment of commercially available starting materials and the broad scope of the reaction with a wide variety of carbonyl compounds giving moderate to excellent yields. Intriguing structural features involving O–H···O and O–H···N hydrogen bonding, as well as arene-perfluoroarene interactions, in this series of racemic polyfluoroaryl carbinols have also been addressed.

precatals for such reactions. However, transition metals can be expensive, toxic, and difficult to remove completely from the corresponding product. A transition metal-free strategy would be highly desirable for these useful transformations. The reaction products for the addition of aryloboronic acids to ketones, after hydrolysis, are tertiary alcohols, which are important building blocks for the synthesis of pharmaceuticals, agrochemical compounds, and natural products.[18] However, the nucleophilic addition of organometallic reagents to ketones can be challenging due to the inherent steric congestion around the carbonyl group, frequently resulting in the generation of products arising from side reactions such as reduction and aldol condensation.[19] Therefore, the development of an efficient, general, and convenient protocol for the synthesis of tertiary alcohols is of considerable interest.

Moreover, an ideal strategy to synthesize ketones, important and ubiquitous structural motifs,[20] lies in the transition metal-catalyzed replacement of an aldehyde’s C(O)-H group with a carbon electrophile.[21] Recently, Zheng and co-workers demonstrated the direct functionalization of aldehyde C–H bonds with aryl halides, using a precious metal palladium catalyst, which has proven to be a viable method to generate the corresponding ketone products.[22]

Polyfluoroarenes have gained extensive attention due to their important role in pharmaceutical, agrochemical, and advanced materials.[23] Thus, identifying practical and efficient concepts for the introduction of fluorine or fluorinated building blocks is highly desirable. Several studies have been reported regarding the polyfluorophenylation of aldehydes. For example, in 1999, Knochel and co-workers[24] used fluorinated aryl bromides to perform pentafluorophenylation
of aldehydes (Scheme 1a). More recently, Lam and co-workers[25] used a copper catalyst (Scheme 1b) and Gu and co-workers[26] (Scheme 1b) used an N-heterocyclic carbene (NHC) organocatalyst to obtain fluorinated aryl carbinols using polyfluorophenyl trimethylsilane as a nucleophile for the addition to aldehydes. In 2015, Huang and co-workers[27] (Scheme 1c) reported a Mg-mediated polyfluororaryl addition to aldehydes. Although some advancements in this field have been reported, these methods suffer from the requirement for highly flammable Grignard reagents, transition metals or NHC catalysts. Moreover, methods reported by Lam and co-workers and Gu and co-workers are limited to pentafluorophenyl trimethylsilane or 1,4-bis (trimethylsilyl) tetrafluorobenzene as substrates.

Recently, we reported efficient methods to generate fluorinated arylboronic acid pinacol esters (ArF-Bpin) via C-F borylation of fluoroarenes using NHC-ligated Ni complex[28a,b] and C-Cl borylation of ArF-Cl using Pd catalyst under base free condition.[28c] Likewise, we reported optimized conditions for the Suzuki-Miyaura cross-coupling reaction of ArF-Bpin compounds with ArX (X = Br, I) using a combination of CuI and 1,10-phenanthroline as a catalyst precursor.[28d] Furthermore, we reported the palladium-catalyzed homocoupling of fluorinated arylboronates,[28e] and the copper-catalyzed oxidative cross-coupling of electron-deficient polyfluorophenyl boronate esters with terminal alkynes.[28f] We report herein the transition metal-free polyfluorophenylation of ketones and aldehydes with fluorinated aryl boronates, which provides a convenient and novel strategy for the synthesis of alcohols and ketones.

Results and Discussion

Addition of arylboronic acids to aldehydes using transition metal catalysts has been well developed. We expected that the use of more Lewis acidic pentafluorophenyl-Bpin with a base would generate a nucleophilic intermediate in the absence of a transition metal. To verify our hypothesis, we initially examined the reaction of pentafluorophenyl-Bpin (1a) and benzaldehyde (2a) as a model reaction. As shown in Table 1, secondary alcohol 3a was observed as the addition product after hydrolysis when the mixture of 1a and 2a was heated in the presence of KOMe as the base (Table 1, entry 1). Encouraged by this first result, we screened the reaction parameters, including the base and the solvent, to improve the performance of the reaction. The employment of K$_2$CO$_3$ as the base dramatically increased the yield to 92% (Table 1, entry 6). The experimental results revealed that heating is required as the room temperature reaction only afforded 3a in trace amounts (Table 1, entry 7). Lower conversions were observed when reactions were conducted in coordinating solvents such as DMF, THF, and 1,4-dioxiane (Table 1, entries 8, 10, 11), and the lowest yield was obtained when CH$_3$CN was used as the solvent (Table 1, entry 9). In addition, the reaction exhibited very poor performance under aerobic conditions (Table 1, entry 12). Interestingly, increasing the amount of K$_2$CO$_3$ to 3 equiv was not helpful (Table 1, entry 13). Decreasing the amount of K$_2$CO$_3$ (0.8 equiv) did not impact the performance of the reaction (Table 1, entry 14). No reaction took place when K$_2$CO$_3$ was absent (Table 1, entry 15), indicating that K$_2$CO$_3$ as the base is important for this reaction. Not surprisingly, adventitious water quenched the reaction (Table 1, entries 16, 17). However, under anhydrous conditions, the transition metal-free

| Entry | Base   | Solvent    | Yield [%][c] |
|-------|--------|------------|--------------|
| 1     | KOH    | toluene    | 20           |
| 2     | KF     | toluene    | 25           |
| 3     | BuOLi  | toluene    | 52           |
| 4     | Cs$_2$CO$_3$ | toluene | 60          |
| 5     | Na$_2$CO$_3$ | toluene | 78          |
| 6     | K$_2$CO$_3$ | toluene | 92          |
| 7     | KO$_2$CO$_3$ | DMF    | 50           |
| 8     | K$_2$CO$_3$ | CH$_3$CN | 15           |
| 9     | K$_2$CO$_3$ | THF      | 88           |
| 10    | K$_2$CO$_3$ | 1,4-dioxiane | 79           |
| 11    | K$_2$CO$_3$ | toluene  | 35           |
| 12    | K$_2$CO$_3$ | toluene  | 83           |
| 13    | K$_2$CO$_3$ | toluene  | 92           |
| 14    | K$_2$CO$_3$ | toluene  | 66           |
| 15    | K$_2$CO$_3$ | toluene  | 25           |
| 16    | K$_2$CO$_3$ | toluene  | 0            |
| 17    | K$_2$CO$_3$ | toluene  | 25           |

[a] Conditions: 1a (0.44 mmol), 2a (0.4 mmol), base (1.0 equiv), degassed and dried solvent (3 mL), 60°C, 36 h, under argon. [b] Yields were determined by GC-MS analysis vs. a calibrated internal standard and are averages of two runs. [c] Room temperature. [d] Under air. [e] K$_2$CO$_3$ (3 equiv). [f] K$_2$CO$_3$ (0.8 equiv). [g] K$_2$CO$_3$ (0.8 equiv), degassed wet toluene. [h] K$_2$CO$_3$ (0.8 equiv), wet toluene. Moisture and air are detrimental to the yield due to the instability of the fluorinated aryl boronate[28a,b].
polyfluorophenylation of benzaldehyde with pentafluorophenyl-Bpin is feasible and leads to high yields of the desired product.

Using these optimized conditions, we evaluated the scope and the limitations of this reaction. As shown in Table 2, a series of aldehydes bearing electron-withdrawing or donating substituents at the para-, meta-, or ortho-position all worked well with pentafluorophenyl-Bpin to give the desired products (3b–3k). Notably, for reactions employing aldehydes bearing electron-donating groups, increasing the reaction temperature to 80°C for 48 hours was required to generate the corresponding products in acceptable yields. It should be noted that reactions using 4-(diethoxymethyl)benzaldehyde resulted in cleavage of the diethoxymethyl group yielding 3l. Furthermore, this methodology could be successfully extended to more complex aldehydes, such as those incorporating naphthyl and pyridyl groups (3m and 3n). The structures of compounds 3f, 3l, 3m, and 3n were unambiguously confirmed via single crystal X-ray analysis (vide infra).

After a broad range of aromatic aldehydes were examined, reactions with aliphatic aldehydes were investigated using the optimized conditions. Gratifyingly, all reactions proceeded smoothly to afford the corresponding products (3o–3q). Importantly, aldehydes containing ester groups, which are well-known to be sensitive towards Grignard reagents, also afforded the desired alcohols in excellent yield (3r).

We then briefly investigated the scope using simple ketones (Table 3). When reactions were performed at 120°C and for prolonged reaction times, the corresponding products were provided in moderate yields (3s–3u). Modest reaction yields were obtained when sterically hindered benzophenone and 2-(fluorophenyl)(phenyl)methanone were used (3v–3w). Importantly, cyclohexanone proceeded to give the desired products in good yield (3x).

To explore further the utility of this reaction, we then examined the scope using other less substituted polyfluorophenyl boronate esters with benzaldehyde (Table 4). The compounds 2,3,5,6-tetrafluorophenyl-Bpin, 2,3,4,6-tetrafluorophenyl-Bpin, and 2,4,6-trifluorophenyl-Bpin also proved to be effective in these reactions and afforded the products in excellent yields (4a–4c). Furthermore, the reaction with 2,6-difluorophenyl-Bpin proceeded to give the desired product in 80% yield (4d). However, these reaction conditions were not suitable for the reaction of 2,5-difluorophenyl-Bpin and 2-fluorophenyl-Bpin with benzaldehyde. Surprisingly, reactions with these substrates resulted in the formation of ketones (4e and 4f) when a strong base was used. Tetrafluorophenyl-Bpin reacted readily with acetophenone to yield product 4g. Unfortunately, no reaction occurred when the aryl-Bpin compound did not have an ortho-fluorine substituent (4h and 4i), as 3-fluorophenyl-Bpin, phenyl-Bpin, 4-CH3-phenyl-Bpin and 4-CN-phenyl-Bpin all failed to provide any product. These results demonstrate that the ortho-fluorine group plays a key role in related conversions.

To gain further insight into the aforementioned reactions, several mechanistic studies were conducted. The reaction of 2a with pentafluorobenzene 5 under standard conditions was

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**Table 2:** Scope of the reaction with respect to the different aldehyde substrates 2[a,b]

| R | Compound 3 | Yield (%) |
|---|------------|-----------|
| H | 3a | 92% |
| Cl | 3b | 93% |
| Br | 3c | 90% |
| OMe | 3d | 88% |
| OCH3 | 3e | 87% |
| OMe | 3f | 89% |
| H | 3g | 79% |
| Cl | 3h | 81% |
| Br | 3i | 85% |
| OMe | 3j | 85% |
| OCH3 | 3k | 80% |
| Ph | 3l | 81% |

[a] Conditions: 1a (0.44 mmol), 2 (0.4 mmol), K2CO3 (0.32 mmol), toluene (3 mL), 60°C, 36 h, Ar. [b] Isolated yields are reported.

**Table 3:** Scope of the reaction with respect to the different ketone substrates 2[a,b]

| R | Compound 3 | Yield (%) |
|---|------------|-----------|
| H | 3a | 68% |
| Cl | 3b | 65% |
| Br | 3c | 67% |
| OMe | 3d | 58% |
| OCH3 | 3e | 59% |
| Ph | 3f | 45% |
| Me | 3g | 50% |
| Me | 3h | 71% |

[a] Conditions: 1a (0.44 mmol), 2 (0.4 mmol), K2CO3 (0.32 mmol), toluene (3 mL), 120°C, 96 h, Ar. [b] Isolated yields are reported.
examined, yet 3a was not formed in any detectable amounts (Scheme 2a), indicating that the C-Bpin moiety is essential and deprotonation of the fluoroarene or nucleophilic attack at the fluoroarene by the base is not a plausible pathway. Interestingly, for the standard reaction between 1a and 2a, the yield dropped dramatically if 18-crown-6 ether and K$_2$CO$_3$ were added (Scheme 2b). This experimental result indicates that the presence of the potassium ion plays a crucial role for the outcome of the reaction. Furthermore, if the reaction of 1a and 2a was performed in the presence of only a catalytic amount of K$_2$CO$_3$ (20 mol%) (Scheme 2c), reaction rates were reduced, and a week was required to produce 3a in good, isolated yield. This finding again indicates that the potassium ion (or the base) plays an important role in the reaction. Substituting ortho-fluorines by ortho-chlorines, using either C$_6$Cl$_5$Bpin or 2,6-dichlorophenyl-1-Bpin as substrates, did not yield any product as shown by in situ GCMS studies. Likewise, 2,3,4-trifluorophenylBpin and 3,4,5-trifluorophenylBpin substrates with only one or no ortho-fluorine substituent also led to no detectable product formation. The presence of an ortho-methoxy group on the aldehyde, however, did not inhibit the reaction.

Based on previous studies$^{[28,29]}$ and experimental observations, a mechanism for the 1,2-addition of polyfluorophenylboronates to aryl aldehydes in the presence of K$_2$CO$_3$ as base is proposed, as shown in Scheme 3. K$_2$CO$_3$ interacts with the Lewis-acidic Bpin moiety of substrate 1 to generate base adduct A, which weakens the carbon-boron bond and ultimately leaves the B–C bond along with attachment of a potassium cation to the aryl group. The resulting A$_{TF}$ anion adduct B undergoes nucleophilic attack at the aldehyde carbon atom of substrate 2 to generate methanolate C. The methanolate oxygen atom then attacks the electrophilic Bpin group to obtain compound D. Transfer of K$_2$CO$_3$ from intermediate D to the boron atom of the more Lewis-acidic polyfluorophenyl-Bpin 1 finally closes the cycle and regenerates complex A. Thus, the primary reaction product is the O-borylated addition product E, which was detected by HRMS and NMR spectroscopy for the perfluorinated derivative (Supporting Information, section VIII).

To corroborate this mechanism, a detailed DFT study was performed on the model 1,2-addition of 1a to 2a, the results

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**Table 4:** Scope of the reaction with respect to different polyfluorophenyl boronate substrates 1.$^{[a,b,c]}$

| Substrate | Yield |
|-----------|-------|
| 4a: 82%  |       |
| 4b: 84%  |       |
| 4c: 80%  |       |
| 4d: 80%  |       |
| 4e: 79%  |       |
| 4f: 75%  |       |
| 4g: 68%  |       |
| 4h: ND   |       |
| 4i: ND   |       |

[a] Reaction conditions: 1a (0.44 mmol), 2 (0.4 mmol), K$_2$CO$_3$ (0.32 mmol), toluene (3 mL), 80°C, 48 h, Ar. [b] Isolated yields are reported. [c] t-BuOLi (0.32 mmol). [d] 120°C, 96 h.

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**Scheme 2:** Preliminary mechanistic studies.

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**Scheme 3:** Proposed mechanism of the 1,2-addition of polyfluorophenylboronates to aldehyde derivatives in the presence of K$_2$CO$_3$ as base.
of which are shown in Figure 1. In the initial step, \( \text{K}_2\text{CO}_3 \) coordinates to the Bpin moiety of \( 1a \) and gives rise to the pentafluorophenyl-Bpin-base complex \( 6 \) with free energy decreasing by 27.2 kcal mol\(^{-1}\). The energy of compound \( 6 \) is set as the zero point of the energy profile. The pentafluorobenzene anion (\( \text{ArF}^- \)) adduct \( 8 \) is formed endothermically by cleavage of the B-C(\( \text{ArF}^- \)) bond via transition state \( 7\text{-ts} \) with an energy barrier of 26.4 kcal mol\(^{-1}\). In the optimized structures of \( 7\text{-ts} \), K\(^+\) cations coordinate to C, O and F atoms, whereas there is only K-O coordination in compound \( 6 \). Subsequent cleavage of the B-C(\( \text{ArF}^- \)) bond can be facilitated by this pathway. The separated carbonate adduct and \( \text{ArF}^- \) group in adduct \( 8 \) are connected and stabilized by K\(^+\) cations.

Nucleophilic attack of \( \text{ArF}^- \) at the aldehyde carbon atom via transition state \( 10\text{-ts} \) occurs to achieve the coupling intermediate \( 11 \) with an energy of 17.6 kcal mol\(^{-1}\). This low activation energy barrier can be attributed to the coordination of K\(^+\) to the oxygen atom of the aldehyde, thus enhancing the electrophilicity of the aldehyde carbon atom. Subsequently, the methanolate oxygen atom attacks the Lewis-acidic boron atom to give the corresponding compound \( 13 \) irreversibly via transition state \( 12\text{-ts} \). The energy barrier for this step is 16.2 kcal mol\(^{-1}\). Finally, \( \text{K}_2\text{CO}_3 \) in compound \( 13 \) coordinates to the boron of substrate \( 1a \) via transition state \( 14\text{-ts} \), followed by cleavage of a B-O bond to give \( 16\text{-ts} \) and eventually \( 17 \), regenerating the active species \( 6 \). As shown in Figure 1, the energy barriers for these two steps are very low, indicating that intermediate \( 13 \) transforms to product \( 17 \) swiftly. The step from pentafluorophenyl-Bpin-base compound \( 6 \) to product \( 17 \) is calculated to be exergonic by 14.3 kcal mol\(^{-1}\). The base-assisted cleavage of Bpin and pentafluorophenyl (\( \text{ArF}^- \)) is calculated to be the rate determining step (RDS) with a free energy of activation of 26.4 kcal mol\(^{-1}\).

As shown in Figure 1, the cation K\(^+\) bonds with one or two F atoms in these intermediates and transition states, suggesting that the fluoride substituents possibly play an important role in the 1,2-addition of polyfluorophenylboronates to aryl aldehydes. Therefore, we calculated the activation free energies of the RDS using polyfluorophenylboronates with different numbers and positions of fluorine substituents as the substrate. The results given in Figure 2 clearly show that the energy barrier rises with a reduction in the number of F substituents. The position of the fluoride atoms also affects the energy barrier, and ortho fluorine has a stronger effect on the barrier than F substituents at other positions. The barrier for \( 24 \), with an ortho-F substituent, is higher than that of \( 22 \) by 2.6 kcal mol\(^{-1}\), whereas that of \( 26 \) with a para-F substituent rises to 39.0 kcal mol\(^{-1}\). In fact, no reaction was observed under these conditions when \( 26 \) was used as the substrate, which is consistent with our calculated results. We conclude that the ortho-F substituent is vital in this reaction for interaction with K\(^+\) along the reaction pathway, and that other F substituents also influence the reactivity for the 1,2-addition of polyfluorophenylboronates to aryl aldehydes via their electron-withdrawing effect. Thus, stronger electron-withdrawing groups located at the para or meta carbons of polyfluorophenylboronates may promote this reaction.

To ascertain the role of the K\(^+\) cation in these reactions, part of the free energy profile without the cation was also
calculated at the same level of theory, and the results are given in Figure 3. Compared with the energy profile in Figure 1, in the absence of K⁺, the process of the methanolate oxygen anion 33 attack at the Lewis-acidic boron in 30 becomes improbable, with an activation barrier of 41.4 kcal mol⁻¹, although the initial cleavage of Bpin and pentafluorophenyl (ArF) step has a lower free energy of activation. Upon addition of 18-crown-6 to the reaction, the yields drop dramatically. As a counterion, K⁺ clearly regulates the nucleophilicity of CO₃²⁻, and promotes the reactivity by interaction with oxygen or fluorine atoms. Our DFT calculations indicate that both the ortho-F substituents on the polyfluorophenylboronates and the counterion K⁺ are essential for the 1,2-addition of polyfluorophenylboronates to aryl aldehydes.

The structures of 3f, 3l, 3m, 3n, and 4d were unambiguously confirmed by single crystal X-ray diffraction. While the molecular structures are chiral (Figure 4), all the compounds represent racemic mixtures. Due to the presence of OH groups, the arrangement of the molecules in the crystal structures of all compounds is primarily determined by O–H···O or O–H···N hydrogen bonding (Supporting Information, Table S2). The presence of π···π stacking interactions between pentafluorophenyl and bromophenyl or naphthyl moieties (3f and 3m), respectively, is also observed in these examples (Figure 5, Table S3). Such an attractive interaction...
between arenes and perfluorinated arenes results from the different electronegativities of the hydrogen and fluorine atoms with respect to the carbon atoms of the aromatic rings and, hence, from opposite multipole moments of the aromatic groups. It is called the arene-perfluoroarene interaction and can be applied as a supramolecular synthon in crystal engineering. This was previously confirmed by Marder and co-workers, who have shown that this type of interaction leads to the formation of highly ordered π-stacks of alternating arene and perfluoroarene molecules in co-crystals of arenes and perfluoroarenes.

In the crystal structures of compounds 3f and 3m, the combination of both O–H···O hydrogen bonding and arene-perfluoroarene interaction leads to the intriguing formation of [O–H···I], hydrogen-bonded cyclic tetramers with graph set R_4^4(8) (Figure 5, Table S2). The molecules of the tetramer interact via arene-perfluoroarene π···π stacking between the bromophenyl or naphthyl and pentafluorophenyl moieties on the outside of the cyclic [O–H···I] ring. The interplanar separations (3.281(7)–3.687(14) Å) are typical for π···π stacking interactions[30,31] and the angles between the interacting planes are 4.96(19)–16.8(3)° (Table S3). In the higher symmetry compound 3m (space group P2_1/c with Z′ = 2, where Z′ denotes the number of molecules in the asymmetric unit), arene-perfluoroarene interactions are also present between the tetramers, in addition to C–H···π, C–H···F, and F···F interactions (Figure S6). Each tetramer of 3m is centrosymmetric and, hence, contains molecules of opposite chirality (RRSS), leading to a racemic mixture (Figure 5b). Tetramers are arranged in sheets parallel to the b,c-plane (Figure S6). In contrast, compound 3f crystallizes in the non-centrosymmetric space group P1. There are 16 symmetry-independent molecules in the asymmetric unit (Z′ = 16) of 3f, which build up four symmetry-independent hydrogen-bonded cyclic tetramers (Figure S1). Each tetramer is constituted by molecules of the same chirality (RRRR or SSRR) (Figure 5a). Thus, the chirality of the four tetramers in the asymmetric unit, i.e., (RRRR)(SSRR)(RRRR)(SSRR), leads to a racemic mixture, as shown in Figures 5a, S1 and S3. Tetramers of mixed chirality are arranged in sheets parallel to the b,c-plane with bromine atoms all pointing up or down within the sheet (Figures S2 and S3). Parallel sheets face each other either with the bromine atoms or without. In fact, crystals of 3f represent one of the rare class of crystals for which Z′ > 1 [33,34] While searching for a structure of higher symmetry, the cell parameters of 3f were also determined at 200 K. As this resulted in a similar triclinic unit-cell metric as was observed...
at 100 K, the occurrence of a phase transition at temperatures between 100 K and 200 K is unlikely.

Contrary to 3f and 3m, the dominance of hydrogen bonding and absence of arene-perfluoroarene interactions in compounds 31 (space group P1), 3n and 4d (both space group C2/c) resulted in the formation of one-dimensional hydrogen-bonded chains (Figure 6). In 31 and 3n, the intermolecular O–H···O and O–H···N hydrogen bonding interaction takes place between the alcohol (O–H, donor) and the carboxaldehyde (O, acceptor) and pyridyl (N, acceptor) groups, respectively, the latter having a stronger hydrogen bond acceptor ability compared to the alcohol group (Table S2). Depending on the position of the acceptor atom in the molecule, hydrogen-bonded chains are straight (31, Figure 6a) or zig-zag-like (3n, Figure 6b). In 31, each one-dimensional chain contains molecules of one particular chirality (either R or S), and chains of opposite chirality exhibit extensive π-stacking interaction between the phenyl groups. In this way, double-stranded linear chains projecting the C3F3 groups on both sides are formed, as shown in Figure 6a. The C3F3 groups from neighboring strands undergo interdigitation and exhibit partial offset π···π interactions between fluorinated moieties and C–F···π interactions between phenyl and perfluoroaryl groups (Figures S4 and S5, Table S3). In 3n, one-dimensional zig-zag chains are formed by molecules of alternating chirality (RSRS...) (Figure 6b). The pyridyl rings lie coplanar and the perfluoroaryl groups interdigitate via partial offset π···π interactions to form a parallel ribbon-like arrangement (Figure S7, Table S3). This structure exhibits a bilayer architecture as there are alternating hydrophobic and hydrophilic regions (Figures S7 and S8).[39] In 4d, corrugated one-dimensional chains are observed by the intermolecular O–H···O–H– hydrogen bonding interactions between the alcohol groups (Table S2), and molecules constituted of alternating pairs of same chirality (RRSSRRSS... as shown in Figure 6c and Figure S9). Other intermolecular interactions observed in 4d include C–H···F, C–H···π, and very weak, strongly offset π···π interactions (Table S3).

Conclusion

We have demonstrated here the simple conditions for the 1,2-addition of aldehydes and ketones with polyfluoroarylboronate compounds. This strategy has the following advantages: 1) transition metal-free catalyst system; 2) a variety of aromatic and aliphatic aldehydes were found to be suitable substrates for this reaction using perfluoroarylboronate-Bpin in moderate to excellent yields; and 3) sterically hindered ketones also worked well to furnish the corresponding products. This method also introduces the use of polyfluoroarylboronate-Bpin compounds instead of Grignard reagents for polyfluorophenylation of arylaldehyde and ketone substrates. Further studies of the synthesis and applications of polyfluorophenyl boronates are underway in our laboratory and will be reported in due course.

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Conflict of interest

The authors declare no conflict of interest.
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