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Synthesis of Chemically and Configurationally Stable Monofluoro Acylboronates: Effect of Ligand Structure on their Formation, Properties, and Reactivities

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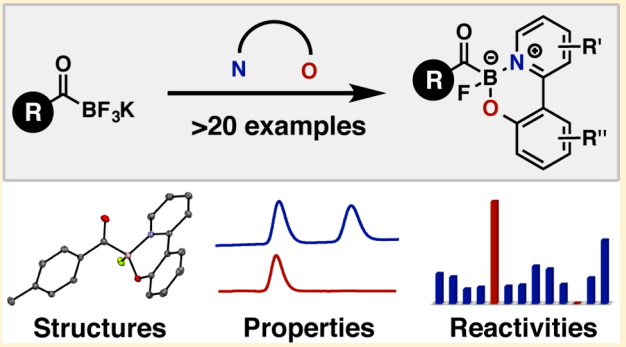
Supporting Information

ABSTRACT: The recent disclosures of two classes of acylborons, potassium acyltrifluoroborates (KATs) and *N*-methyliminodiacetyl (MIDA) acylboronates, demonstrated that certain acylboron species can be both remarkably stable and uniquely reactive. Here we report new classes of ligands for acylboronates that have a significant influence on the formation, properties, and reactivities of acylboronates. Our systematic investigations identified a class of neutral, monofluoroboronates that can be prepared in a one step, gram-scale fashion from readily accessible KATs. These monofluoroboronates are stable to air, moisture, and silica gel chromatography and can be easily handled without any special precautions. X-ray crystallography, NMR spectroscopy, and HPLC studies showed that they are tetravalent, configurationally stable *B*-chiral acylboronates. Significantly, the ligands on the boronate allow for fine-tuning of the properties and reactivity of acylboronates. In amide-forming ligation with hydroxylamines under aqueous conditions, a considerable difference in reactivity was observed as a function of ligand structure. The solid-state structures suggested that subtle steric and conformational factors modulate the reactivities of the acylboronates.



INTRODUCTION

Acylboranes and acylboronates are an intriguing class of compounds whose remarkable properties and reactivity have only recently been recognized. This stands in contrast to the substantial body of literature on alkyl, aryl, alkenyl, and alkynyl boron compounds, for which extensive synthetic studies and important reactions have long been recognized.[1] Acylborons have been proposed as intermediates in some transformations,[2] but the assumed instability of acylborons[3] prevented organic chemists from isolating and characterizing these molecules.[4,5] Indeed, in 2005 Stevenson noted that "no verified examples of acylboron derivatives had ever been isolated, and theoretical calculations suggested that acylboranes were highly reactive species and prone to rearrangement."[6,7]

In 2007 Yamashita, Nozaki, and their colleagues reported the first fully characterized acylboron **1** using a carefully designed nucleophilic boryl anion (Figure 1a).[8] In 2010, a collaborative team consisting of Curran, Lacôte, and co-workers also reported acylborane **2** from an N-heterocyclic carbene stabilized nucleophilic borane (Figure 1b).[9] The syntheses of these ligand-stabilized acylborons were landmark achievements in this area, but these studies did not explore their synthetic potential. Recently, insertion of carbon monoxide into Piers' borane[10] was realized by the aid of a frustrated Lewis pair, and formylborane **3** was isolated as a pyridine-coordinated adduct, although its synthetic utility was not well studied (Figure 1c).[11]

In 2010, Molander et al. synthesized a single example of a potassium acyltrifluoroborate (KAT, **4**) from an acyl anion equivalent and an electrophilic boron source, followed by treatment with aqueous KHF_2 (Figure 1d).[12] Yudin documented a multi step synthesis of *N*-methyliminodiacetyl (MIDA) acylboronates **5** and demonstrated their downstream transformations (Figure 1e).[13] These reports established that tetrasubstituted acylboronates are bench-stable and readily handled materials, making them suitable for further transformations.

Our interests in acylborons arose from our recent disclosure that KATs undergo extremely fast amide-forming ligations with hydroxylamines in water.[14,15] Following this discovery, we reported the syntheses of a variety of KATs on gram scale either from aldehydes[16] or aryl halides.[17] We also devised a convenient route to MIDA acylboronates from their corresponding KATs in one step and found that they possess even higher reactivity toward hydroxylamines than KATs. Unfortunately MIDA acylboronates were found to be less stable in water, limiting their application in bioconjugation reactions.[18]

The successful amide-forming reactions of MIDA acylboronate clearly demonstrated that a suitable ligand on the boron atom could alter the stability and reactivity of acylborons by modulating their physical and chemical properties. These

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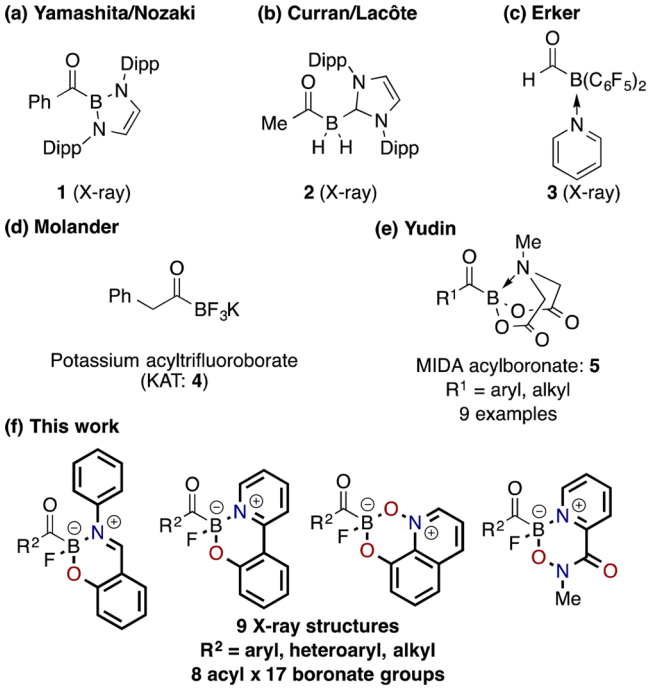


Figure 1. Reported fully characterized acylborons. Dipp = 2,6-$(i\mathrm{Pr})_2C_6H_4$.

findings encouraged us to explore further ligands on the acylborons in hopes of realizing the kind of ligand-modulated reactivity commonly observed in metal-promoted reaction.[19] We hypothesized that other new acylboron species could be generated from KATs by following a similar protocol to the one we identified for the facile formation of MIDA acylboronates.

Here we report our studies towards expanding the chemical space of acylboronates,[20] including the first systematic studies on the role of the boron ligands on the formation, properties, and reactivities of acylboronates. The acylboronates prepared during the course of these studies are tetravalent, monofluoro, configurationally stable *B*-chiral boron species; all are stable under air, in water and on silica gel. They react smoothly with hydroxylamines under aqueous conditions to give amides. A notable difference of reactivity was observed between structurally similar boronates, shedding light on the mechanism of the amide formation with hydroxylamines.

RESULTS AND DISCUSSION

Boron Ligands. At the outset of our investigations, we established strict criteria for properties of our desired acylboronates. They must be stable to air, water, and silica gel chromatography. Most reported acylborons required a glovebox for their preparation. KATs are not amenable to purification by normal phase silica gel chromatography, and MIDA acylboronates gradually decompose in water. Our efforts to find a suitable ligand on the boron began with tridentate MIDA analogs. As in our reported synthesis of MIDA acylboronates from KATs, $BF_3{\cdot}Et_2O$ was slowly added to a suspension of KAT and TMS-activated ligand in dry acetonitrile under a nitrogen atmosphere. Many possible permutations of MIDA ligand were screened, including its elongated variants and different substituents on the nitrogen atom (Figure 2).[21] Surprisingly, this procedure was successful only for the formation of the parent MIDA acylboronate **5**; any

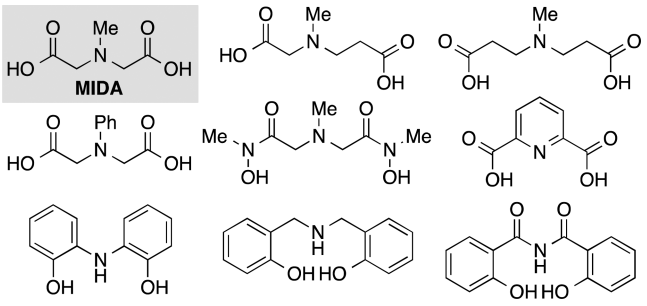
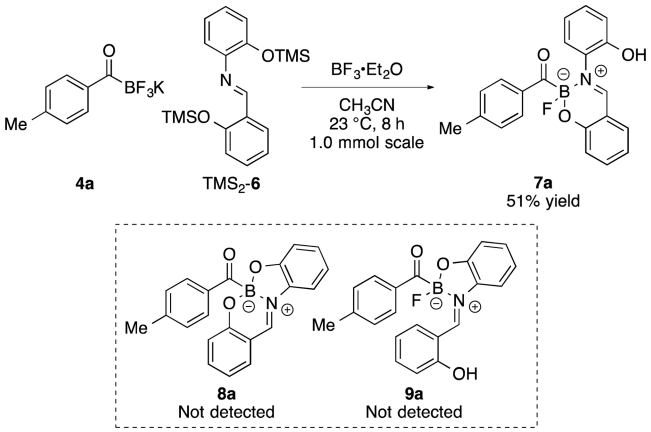


Figure 2. Selected MIDA derivatives that did not form a stable complex.

deviation from this structure resulted in the formation of unstable adducts that could not be isolated or characterized.

The first successful formation of a new acylboronate came with tridentate Schiff base ligand **6**. The obtained adduct was neither the expected bicyclic boronate **8a** nor the five-membered ring boronate **9a**, but rather the six-membered acylboronate **7a** that retained one of the fluoride ligands (Scheme 1).[22,23] The structure of **7a** was assigned based on a control experiment (see the Supporting Information, Scheme S1), and further supported by the X-ray structure of **10a** (*vide infra*).

Scheme 1. Formation of Six-Membered Acylboronate 7a from Schiff Base Ligand 6[a]



[a]Reaction conditions: **4a** (1.0 equiv), TMS_2-**6** (1.0 equiv), $BF_3{\cdot}Et_2O$ (1.0 equiv), CH_3CN (0.1 M), 23 °C.

This result led us to investigate bidentate ligands that could form a six-membered ring. We were pleased to find that many of them formed stable acylboronates that satisfied the desired criteria. Selected examples are shown in Scheme 2. As expected, acylboronate **10a** was obtained from the Schiff base ligand derived from 2-hydroxy-1-naphthaldehyde. This boronate possessed a six-membered ring containing the phenol oxygen and the imine sp^2-nitrogen. Another sp^2-nitrogen donor can be used to obtain a stable acylboronate; 2-(2′-pyridyl)phenol **14** also formed six-membered acylboronate **11a** with the phenol oxygen and the pyridine nitrogen. In addition, a nitrogen atom is not essential to construct a six-membered boronate; 8-hydroxyquinolin-*N*-oxide also gave the acylboronate **12a** through the *N*-oxide and the phenol, although the complexation was not as clean, and unidentified products were formed along with **12a**. Furthermore, other classes of oxygen donors

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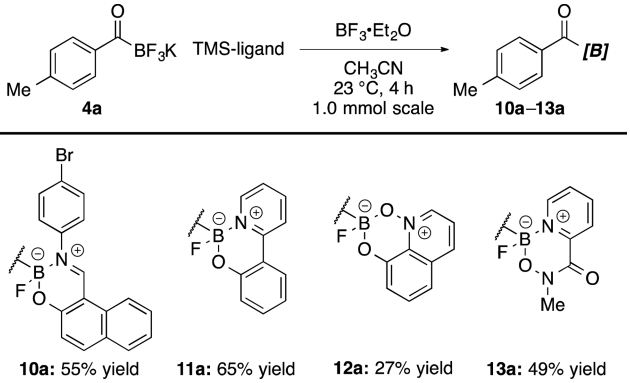
Scheme 2. Selected Examples of Acylboronates from Bidentate Ligands[a]

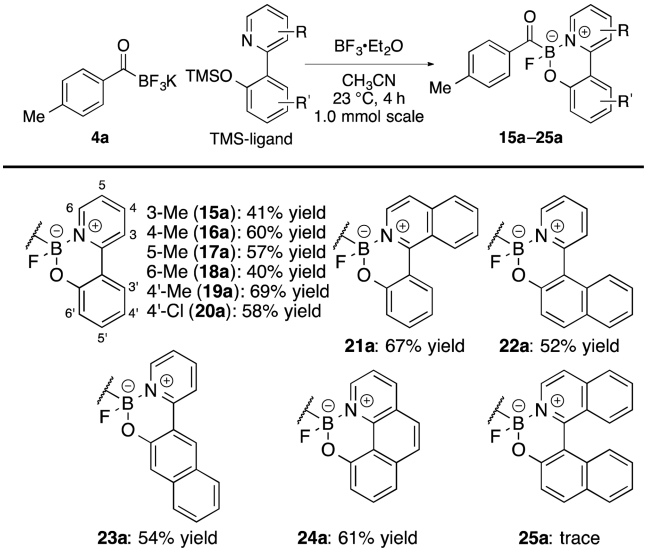


[a]Reaction conditions: **4a** (1.0 equiv), TMS-ligand (1.0 equiv), BF_3·Et_2O (1.0 equiv), CH_3CN (0.1 M), 23 °C.

are compatible with the acylboronate formation. Picolinic acid derived hydroxamic acid was a suitable ligand to form the stable acylboronate **13a**. The structures of **10a**, **11a**, **13a** and the *p*-Cl analog **12d**, all were unambiguously established by X-ray crystallography (Figure 3). These acylboronates were easily converted back to the corresponding KATs in excellent yields by treatment with aqueous KHF_2 at slightly elevated temperatures.[24,25]

In analogy to transition-metal catalysis, we anticipated that subtle changes to the ligand on boron could modulate the properties and reactivities of the acylboronates. To investigate this hypothesis, we prepared a number of derivatives of **11a** by similar procedures.[26] The complexation proved remarkably general with respect to the boronate moiety, and a wide range of acylboronates was obtained from various substituted ligands (Scheme 3). An array of methyl-substituted regioisomers **15a**–**19a** were obtained in moderate to good yield. Variation of the

Scheme 3. Boronate Group Scope with Substituted Ligands[a]



[a]Reaction conditions: **4a** (1.0 equiv), TMS-ligand (1.0 equiv), BF_3·Et_2O (1.0 equiv), CH_3CN (0.1 M), 23 °C.

electronic nature of the substituent had little influence on the reaction outcome, and **20a** was formed equally well. Extended aromatic systems on the ligand were also tolerated, delivering the desired acylboronates **21a**–**24a** with the same level of reaction efficiency. In contrast, the acylboronate **25a** derived from (±)-1-(2′-hydroxy-1′-naphthyl)isoquinoline failed to be isolated; **25a** was observed by NMR and high-resolution mass

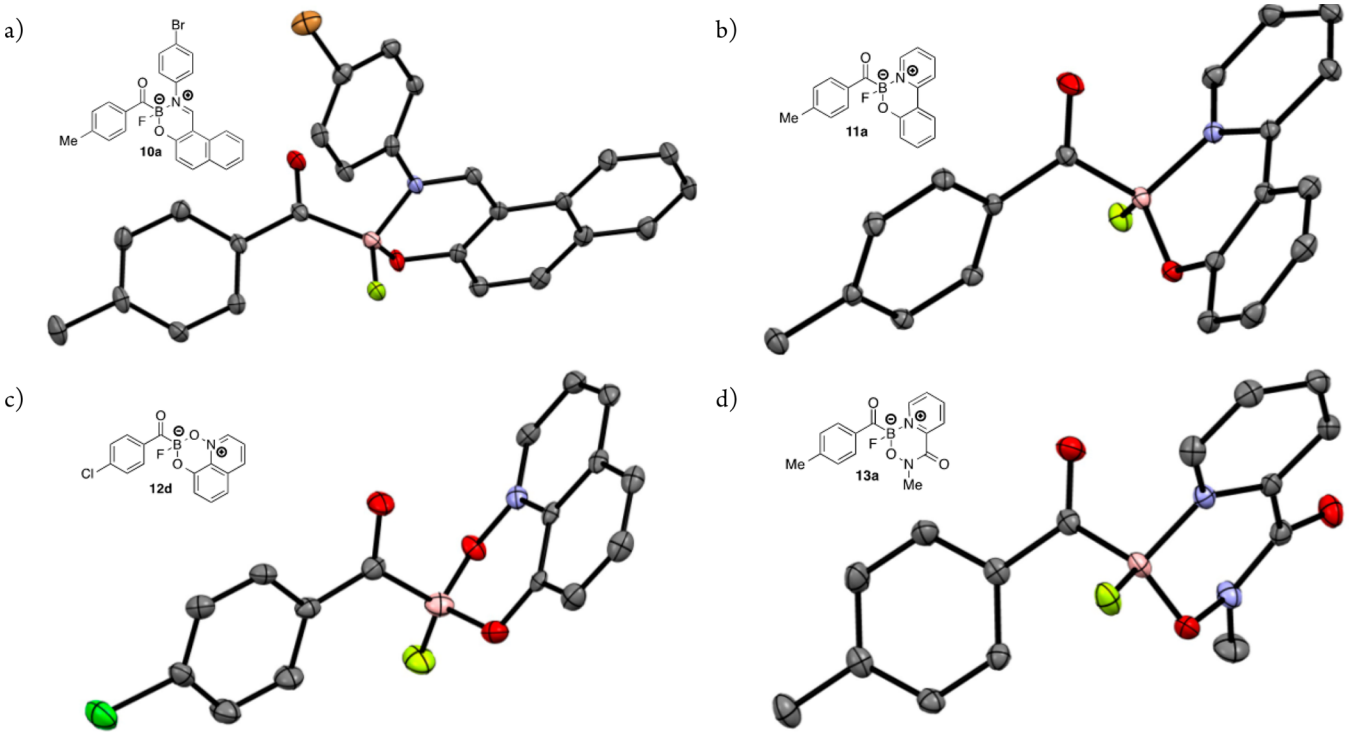


Figure 3. Solid-state structures of **10a**, **11a**, **12d**, and **13a**. ORTEP, ellipsoids are set at a 50% probability. All hydrogen atoms have been removed for clarity.

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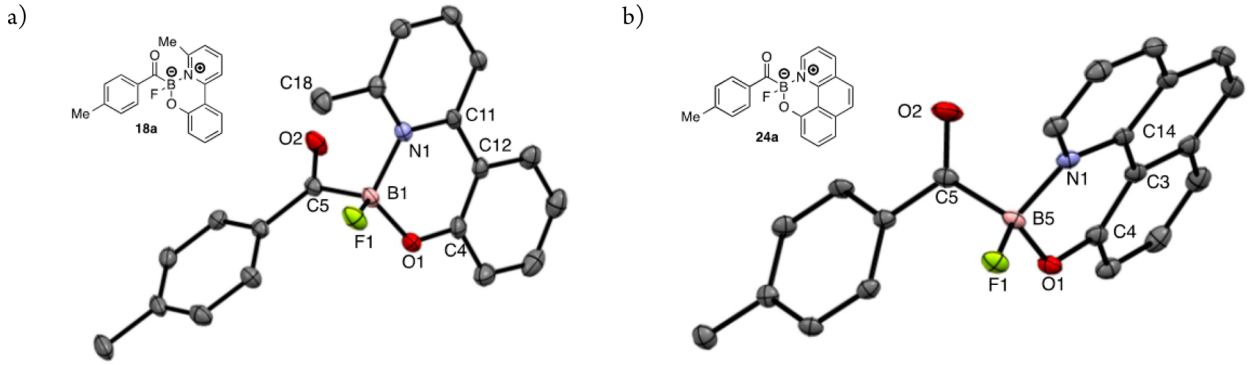
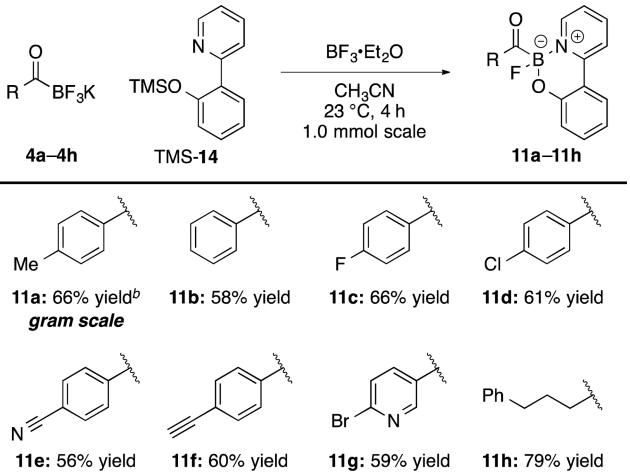


Figure 4. Solid-state structures of **18a** and **24a**. ORTEP, ellipsoids are set at a 50% probability. All hydrogen atoms have been removed for clarity. Selected bond lengths (Å) and angles (deg). (a) **18a**: O2−C5 1.239(3), N1−B1 1.615(3), B1−C5 1.642(3), O2−C5−B1 118.4(2), O1−B1−N1 110.8(2), N1−C11−C12−C4 5.1(3), O2−C5−B1−N1 23.1(2). (b) **24a**: O2−C5 1.229(2), N1−B5 1.593(2), B5−C5 1.639(3), O2−C5−B5 120.6(2), O1−B5−N1 109.4(1), N1−B5−C5−C6 6.62(2), N1−C14−C3−C4 7.3(2).

spectrometry experiments on the unpurified reaction mixtures, but was rather unstable toward silica gel.[27] In general, the substituent at 3- or 3′-position rendered acylboronates less stable than **11a** (e.g., **15a**, **21a**, and **22a**). Nevertheless, all compounds except **25a** were purified by silica gel column chromatography and analyzed in pure form. In all cases, the major byproducts were the difluoroboronates derived from BF_3·Et_2O and TMS-activated ligands without involving an acyl moiety, decreasing the product yield. We expect that substrate specific optimizations or alternative fluorophiles will avoid the formation of the undesired adducts and increase the product yield. Acylboronates **15a**, **16a**, **17a**, **18a**, and **24a** also provided a crystal suitable for X-ray diffraction (Figure 4 and the Supporting Information Figure S5).

Scope of Acylboronate Synthesis. The scope of the acyl group was also investigated (Scheme 4). Aromatic KATs were

Scheme 4. Acyl Group Scope with Ligand 14[a]



[a]Reaction conditions: **4** (1.0 equiv), TMS-**14** (1.0 equiv), BF_3·Et_2O (1.0 equiv), CH_3CN (0.1 M), 23 °C. [b]5.0 mmol scale.

smoothly converted into the corresponding acylboronates regardless of the nature of substituents. Aromatic halides, nitriles, and terminal alkynes were tolerated. Heteroaromatic KATs can also participate in this transformation, and **11g** was formed equally well. Aliphatic monofluoroacylboronate **11h** was isolated in 79% yield after silica gel column purification. The higher yield for the aliphatic substrate was attributed to a more stable acyldifluoroborane intermediate, generated from the KAT and BF_3·Et_2O, than that of the aromatic counterparts, leading to less decomposition.[28] For **11a**, the isolated yield was comparable when performed on a gram scale (5.0 mmol scale, 1.05 g of **11a**), confirming the robustness of this complexation.

Properties of Acylboronates. A summary of structural data from NMR spectroscopy and X-ray analysis is presented in Table 1, in comparison with known acylborons. For all acylboronates, the peaks for the carbonyl group in the ^{13}C NMR spectra appeared around 220−250 ppm as a broad peak due to the quadrupolar relaxation of ^{11}B. These low-field shifts are in good agreement with reported acylboranes and acylboronates.[8,11,14,18] The peaks of aliphatic carbonyls were shifted even lower than their aromatic counterparts by greater than 10 ppm (**4d** vs **4i**, **5a** vs **5h** and **11a** vs **11h**). The newly synthesized acylboronates all display signals between +0.2 and +2.9 ppm in the ^{11}B-NMR spectra, indicating a tetravalent boron species.[29]

In the solid state, C═O bond lengths of **10a** (1.226 Å), **11a** (1.235 Å), **12d** (1.234 Å), and **13a** (1.229 Å) are closer to that of benzophenone (1.223 Å)[30] rather than phenyl benzoate (1.194 Å).[31] In contrast to trisubstituted acylboron **1**, C−B, B−O, and B−N bond lengths of these are in the range of typical tetra-substituted boron species.[32] Figure 5 presents a side view of **11a** from the biaryl plane, which clearly shows a pyramidal structure of the boron. In order to coordinate to the tetrahedral boron, the biaryl moiety in the ligand is slightly twisted, with an angle of 13.17°. The O1−B1−N1 angle is 107.9°, close to the optimal 109.5°. Indeed, in all monofluoroacylboronates in Table 1, the corresponding angles formed by the boron atom and two coordinating groups in the ligand, either O−B−N or O−B−O, are between 105.1° in **13a** and 110.8° in **18a**. A tetrasubstituted boron and a suitably arranged ligand to coordinate to the boron center are presumably important for their stability. Since the conformation of ligands is restricted to tightly bind to the boron center in a bidentate fashion, only the fluorine atom and the acyl group are flexible to minimize unfavorable structural effects caused by ligands in the boronate moiety. This fact is clearly reflected by a wide span of torsion angles O−C(sp^2)−B−F in these monofluoroacylboronates. Among acylboronates that contain a different class of ligands (**10a**, **11a**, **12d**, and **13a**), the angles are in the range between 113.23° in **11a** and 166.90° in **10a**. More strikingly, even among structurally similar acylboronates, the angles cover a relatively broad range from 112.90° in **16a** to 143.87° in **18a**.

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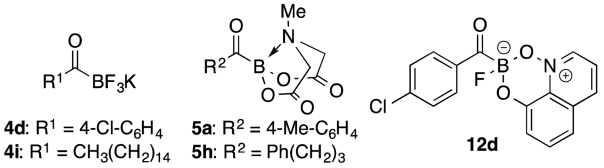
Table 1. Summary of NMR Chemical Shifts and Bond Lengths/Torsion Angles of Acylborons in Solid State

Acyl–[B]	NMR [ppm]			X-ray [Å] or [°]	
	Solvent	$^{13}C^a$	^{11}B	C=O	O–C–B–F
1[b]	C_6D_6	218	+21.8	1.241	—
4d[c]	d_6-acetone	234	–0.8	1.240	9.65
					110.06
					130.51
4i[c]	d_6-DMSO	246	–1.9	—	—
5a[d]	CD_3CN	226	+5.4	—	—
5h[d]	CD_3CN	239	+4.2	—	—
10a	$CDCl_3$	227	+1.7	1.226	166.90
11a	$CDCl_3$	229	+2.1	1.235	113.23
11h	$CDCl_3$	243	+0.6	—	—
12d	$CDCl_3$	227	+0.2	1.234	149.81
13a	$CDCl_3$	227	+2.2	1.229	120.58
15a	$CDCl_3$	229	+2.0	1.235	113.45
16a	$CDCl_3$	229	+2.0	1.234	112.90
17a	$CDCl_3$	229	+2.2	1.238	133.34
18a	$CDCl_3$	229	+2.6	1.239	143.87
24a	$CDCl_3$	228	+2.9	1.229	125.35



[a]Peak for the carbonyl group. [b]Ref 8. [c]Ref 14. [d]Ref 18.

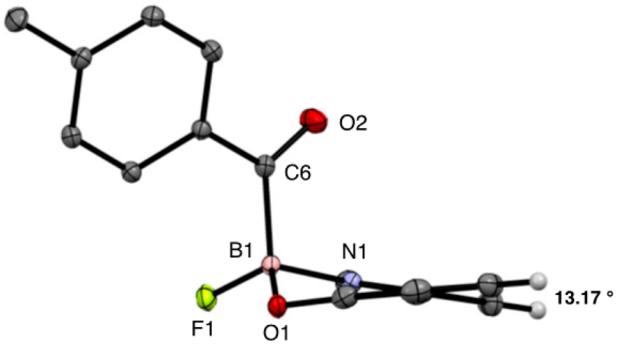


Figure 5. Side view of **11a**. ORTEP, ellipsoids are set at a 50% probability. Most hydrogen atoms have been removed for clarity.

This angle difference must result from a function of ligand structures but is not obviously correlated with the different reactivity of acylboronates observed in the amide-forming ligation with hydroxylamines (*vide infra*).

As indicated from the X-ray structures, these acylboronates are the first examples of *B*-chiral acylborons; stable *B*-chiral boronates themselves have not been widely explored.[33] In order to determine if they are configurationally stable, enantiomers of the boronate **11a** were separated on a reverse phase chiral HPLC column, and the collected peaks were reinjected. Neither racemization nor decomposition was observed even after incubating at 50 °C in MeOH (Figure 6).[34] The robustness of the boron chiral center encourages the use of

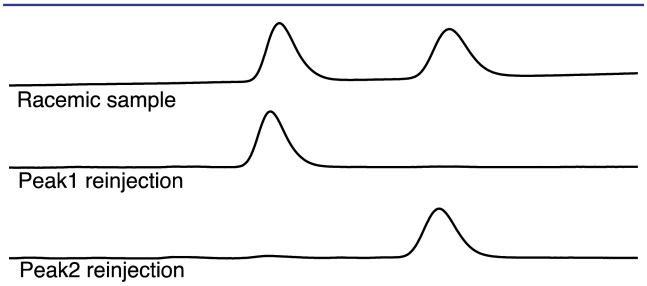


Figure 6. Chiral reverse phase HPLC spectra of **11a**. Daicel Chiralpak AD-RH, 20–95% CH_3CN in 20 min.

this class of *B*-chiral acylboronates for asymmetric synthesis in future applications.[35,36] As a solid, **11a** can be stored on the bench without special precautions for at least 6 months.

The stability of the acylboronates under the KAT ligation conditions was examined more closely by exposing **11a** and its derivatives to a 9:1 d_6-DMSO/D_2O solution. The mixtures were analyzed by ^1H NMR using Bn_2O as an internal standard, and the decomposition rate of the acylboronates was processed by pseudo-first-order kinetics. Table 2 shows the $t_{1/2}$ of various

Table 2. Half-Life of Acylboronates under Aqueous Conditions[a]

Entry	Acyl-[B]	Temp (°C)	$t_{1/2}$
1	**4a** (KAT)	23	Not observed[b]
2	**5a** (MIDA)	23	12 min
3	**11a**	23	24 h
4	**11a**	50	3.3 h
5	**15a**	23	1.0 h
6	**16a**	23	18 h
7	**17a**	23	17 h
8	**18a**	23	4.8 h
9	**19a**	23	20 h
10	**20a**	23	10 h
11	**21a**	23	1.5 h
12	**22a**	23	4.3 h
13	**23a**	23	12 h
14	**24a**	23	15 h

[a]Determined by ^1H NMR, 0.042 M, 9:1 d_6-DMSO/D_2O. Bn_2O was used as an internal standard. [b]Even after 3 days, <5% decomposition was observed.

acylboronates from the fitted curves. KAT **4a** was completely stable under the conditions, and it was difficult to determine its half-life (entry 1).[37] On the other hand, MIDA acylboronate **5a** was found to be the least stable acylboronates in Table 2 and quickly decomposed upon exposure to water (entry 2). At room temperature, monofluoroboronate **11a** slowly underwent hydrolysis (entry 3); a faster rate of decomposition was observed at 50 °C (entry 4). As we noticed during its preparation, the substituent at 3-position made the complex significantly less stable (entries 5 and 11). The difference in the

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stability between **21a** and **22a** suggests that sterics is not the sole factor behind their instability (entries 11 and 12). This was also suggested by the results from Me-substituted **19a** and Cl-substituted **20a** at the same position. Me-substituent at less crowded position had little influence on the stability (entries 6, 7, and 9). In all cases, the bidentate, monofluoroacylboronates were much more stable than the MIDA variants and should be sufficiently stable for most applications.

Reactivity of Acylboronates in Amide-Forming Ligations. We evaluated the reactivity of the newly prepared acylboronates in amide-forming ligations with hydroxylamines. In spite of the stability observed above, all acylboronates smoothly formed amides with *O*-carbamoylhydroxylamine **26**, but their reactivity varied depending on the ligand structure. The modularity of the ligand structures in acylboronates such as **10a** and **11a** presents an opportunity to obtain information about a structure−reactivity relationship; KAT has little chance for a systematic modification, and it was difficult to prepare acylboronates from MIDA analogs.

In the course of the investigation, we found that slight modifications of the ligand structure in **11a** can have a dramatic effect on their reaction rate in amide-forming ligation. The relative reactivity of various 4-methylbenzoylboronates in comparison to **11a** is illustrated in Scheme 5c; KAT **4a** and MIDA acylboronate **5a** are also included for reference. An equimolar ratio of **11b** and 4-methylbenzoylboronate was combined with 1.0 equiv hydroxylamine **26** in aqueous DMSO at 23 °C, and the product ratio was determined by HPLC analysis.

The acylboronate **24a** derived from 10-hydroxybenzo[*h*]-quinoline showed significantly lower reactivity than any other compounds evaluated. On the other hand, the introduction of a substituent at the 6-position on the pyridine ring enhanced its reactivity, making **18a** even superior to the MIDA acylboronate under these conditions, albeit being slightly less stable than **11a**.

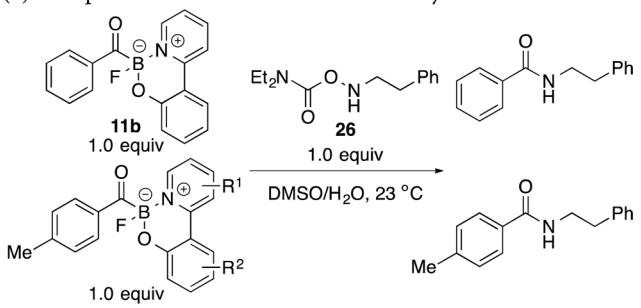
Mechanism of the Amide Formation. In addition to the hydrolytic stability in Table 2, the ground-state energies were calculated by DFT method. The calculations of a series of acylboronates at the B3LYP/6-31+G(d, p) level of theory indicated that the instability of **18a** was not the sole factor for its higher reactivity; less stable **15a** showed lower reactivity than **18a**.[38,39] This indication opposes the involvement of a decomposed but reactive intermediate, such as an acyl boronic acid, and favors a mechanism employing intact monofluoroboronates. This is also consistent with the mechanistic studies previously conducted with MIDA acylboronates.

Based on our previous studies with MIDA acylboronates, a plausible mechanistic pathway is depicted in Scheme 6. The initial addition of the hydroxylamine to the carbonyl group forms tetrahedral intermediate **27**, which is in equilibrium with iminium species **28**. The hemiaminal **27** can undergo a concerted elimination, followed by a tautomerization to form the amide. We previously postulated that a higher concentration of the productive, tetrahedral intermediate in equilibrium was key for the higher reactivity of MIDA acylboronates than KATs; the stability of the iminium intermediate derived from either MIDA acylboronates or KATs determined the position of equilibrium and regulated the overall kinetics of the amide formation.

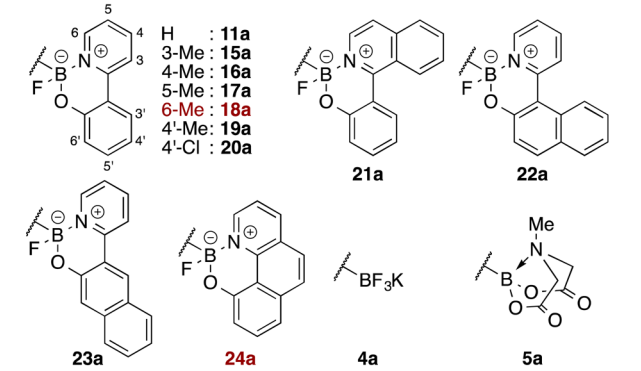
The reactivity difference between **18a** and **24a** can also be explained by different concentrations of the tetrahedral intermediates. Higher reactivity of **18a** arises from the less stable nature of the iminium species due to the steric hindrance

Scheme 5. Reactivity of Acylboronates in Amide Formation with Hydroxylamine 26[a]

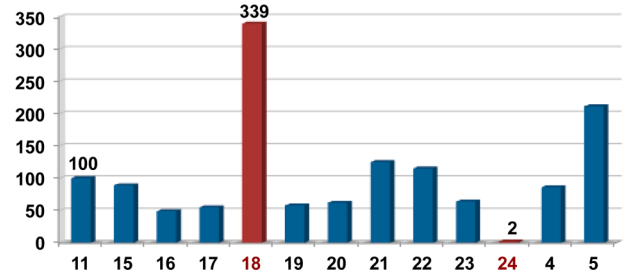
(a) Competitive amide formation between acylboronates



(b) List of evaluated acylboronates

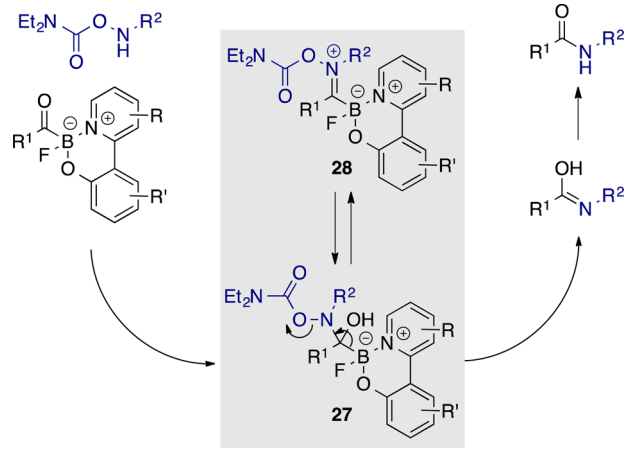


(c) Relative reactivity to **11a**[b]



[a]Reaction conditions: **11b** (1.0 equiv), 4-methylbenzoylboronate (1.0 equiv), **26** (1.0 equiv), 8:1 DMSO/H_2O, 23 °C. [b]Determined by HPLC. In the reactivity chart, **11a** was set to 100 as a standard substrate.

Scheme 6. Possible Mechanistic Pathway for the Amide Formation of Acylboronate and Hydroxylamine



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of the methyl group on the ligand. This is similar to ground-state destabilization found in enzyme catalysis.[40]

X-ray crystallography supports this conjecture. The solid-state structures of **24a**, **11a**, and **18a** notably differ in B−N bond lengths, 1.593, 1.602, and 1.615 Å, respectively (Figures 3 and 4). A longer B−N bond makes the boron atom more sp^2-like[41] and presumably leads to a less stable acylboronate. The observed tendency can be understood by the following: (1) the B−N bond in **18a** is longer so as to minimize steric repulsions between the carbonyl and the methyl group at the 6-position, and (2) the B−N bond in **24a** is shorter because linking the biaryl backbone makes the complex sterically more compact, causing less steric repulsions.[42] Since both *E* and *Z* isomers of **28** are more susceptible to steric hindrance than the parent acylboronates,[43] we conclude that a subtle steric factor on the ligand leads to notable differences in the reactivity for the amide formation.

CONCLUSIONS

In summary, we have prepared a series of new acylboronates and identified a novel class of ligands suitable for fine-tuning of the properties and reactivities of acylboronates.[44] The one step synthesis from KATs is robust and scalable, making it possible to prepare a wide range of acylboronates derived from either aromatic or aliphatic precursors and a variety of bidentate ligands. These monofluoroacylboronates are stable to air, water, and chromatography on normal phase silica gel. The stable acylborons possess a tetravalent boron and a suitably structured ligand that can coordinate tightly to the sp^3-boron center, both of which are likely key for their high stability. Many acylboronates afforded a crystal suitable for X-ray diffraction.[45] Solid-state structures and NMR analysis showed they are the first *B*-chiral acylboronates reported in the literature. Their configurational stability in protic solvents was confirmed, suggesting a possibility for asymmetric synthesis. All acylboronates prepared in this study reacted with hydroxylamines to form amides, but substantial differences in reactivities were observed as a function of ligand structures. X-ray crystallography suggested that the ligand modulates the B−N bond length, which is associated with steric factors in the complex. The difference in the reactivity is likely to arise from ground-state destabilization of the unfavorable intermediate, leading to a higher concentration of the productive intermediate. This gives useful insights into the reaction mechanism of this amide formation.

A deeper understanding of the effects of the ligand on the formation, properties, and reactivities of acylboronates is essential for further improvement of acylboron−hydroxylamine amide formation. Current efforts in our group are following this line of investigation, particularly with regard to the conditions for amide-forming ligations. The stable nature of acylboronates will enable further applications such as traceless modulation of chemoselective amide-forming ligations and bioconjugations.[46] This study also establishes acylboronates as rich and so far underexplored class of organoborons ripe for further development and exploration.

ASSOCIATED CONTENT

Supporting Information

Experimental procedures, supplementary results, CIF files for all X-ray structures, and spectroscopic data for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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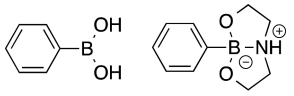

29 **30**

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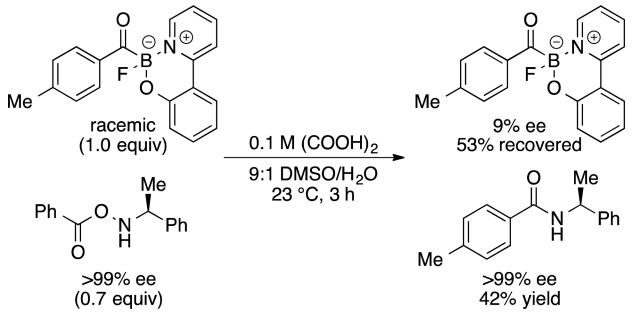

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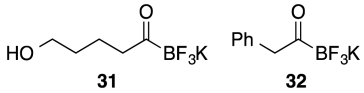

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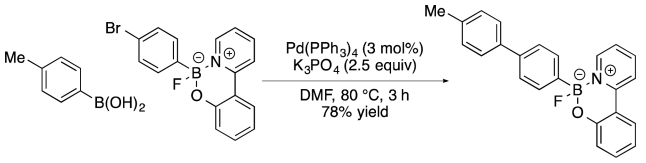
(43) A substituent also makes the tetrahedral intermediate **27** less stable, but one of the diastereomers of **27** should be less sensitive towards sterics and likely more favorably formed.

(44) Preliminary results suggest that these ligands can also modulate properties and reactivities of nonacyl boronates. The selective Suzuki−Miyaura cross coupling between an aryl boronic acid and a monofluoroboronate was easily achieved under anhydrous basic conditions.



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