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JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

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Electrophilic Aromatic Substitutions of Aryltrifluoroborates with Retention of the BF_3^- Group: Quantification of the Activating and Directing Effects of the Trifluoroborate Group

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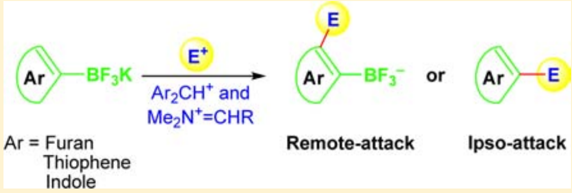
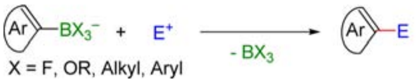
Supporting Information

ABSTRACT: Kinetics and mechanisms of transition-metal free reactions of furyl, thienyl and indolyl trifluoroborates with benzhydrylium (Ar_2CH^+) and iminium ($Me_2N^+{=}CHR$) ions have been investigated. In contrast to common belief, substitutions at CH positions are often faster than ipso-substitutions of the BF_3K group, because BF_3K activates the position attached to boron by a factor of 10^3−10^4 while adjacent CH positions are activated by factors of 10^5−10^6. Several reactions that have previously been interpreted as ipso-substitutions actually proceed via initial substitution at a vicinal or remote CH position, followed by protodeborylation. If the proton released during electrophilic substitution at a CH position is trapped by a base, the BF_3^- group can be preserved. Remote reactions of heteroaryl trifluoroborates with iminium ions provide straightforward access to novel zwitterionic ammonium or iminium trifluoroborates, which have been characterized by single-crystal X-ray analyses.



INTRODUCTION

Palladium- and rhodium-catalyzed couplings of arylborates with electrophiles belong to the most important family of CC-bond-forming reactions.[1] Transition-metal free reactions of aryl and heteroaryl-borates with electrophiles (E^+), for example, halogenations,[2] Michael additions,[3] borono Mannich,[4] and Friedel−Crafts reactions[5] are also known, and most of them have been reported to proceed via substitution of the BX_3^- group (eq 1).



(1)

However, several examples of such reactions have recently been found which do not regioselectively proceed at the ipso-position.[6] Ortho and more remote (e.g., para) electrophilic substitution reactions of arylborates have been observed,[7] but seldom with retention of the boron group.[8] Although organotrifluoroborates have been gaining increasing importance in recent years because of their compatibility with a variety of reaction conditions,[1,9] electrophilic aromatic substitution reactions of aryl and heteroaryl trifluoroborates with retention of the BF_3K substituent have to our knowledge not been reported so far.

In recent work, we have quantified the ipso-activating effect of several boron substituents and found that the trifluoroborate substituent is a strong ipso-activating group that increases the nucleophilic reactivity of the furan ring (eq 1, Ar = furan) by a factor of 10^4.[10]

We have now quantified the activating effects of the BF_3K group on vicinal and more remote positions in indoles, furans, benzofurans and thiophenes and report that it is even possible to preserve the BF_3^- group when the proton released during an electrophilic substitution at a CH position is trapped by a Brønsted base.

We will show how these data can be used for predicting scope and limitations of uncatalyzed electrophilic aromatic substitutions of aryltrifluoroborates with a variety of electrophiles including iminium ions ($Me_2N^+{=}CHR$).

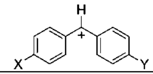
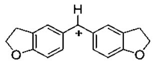
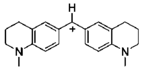
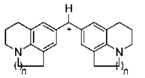
RESULTS AND DISCUSSION

Reactions of Benzhydrylium Ions 1 with Indolyl Trifluoroborates 2a−e. NMR and X-ray analyses of the products obtained from the reactions of the *p*-dimethylamino substituted benzhydrylium tetrafluoroborate **1f**-BF_4^- (Table 1) with the indolyl trifluoroborates **2a** or **2b** revealed that the electrophilic attack did not occur at the ipso-position. Scheme 1 shows that the C3 substituted indole **4** was formed in high yield when **2a** or **2b** were combined with the benzhydrylium salt **1f**-BF_4^- in acetonitrile in the absence of base (Scheme 1, middle).

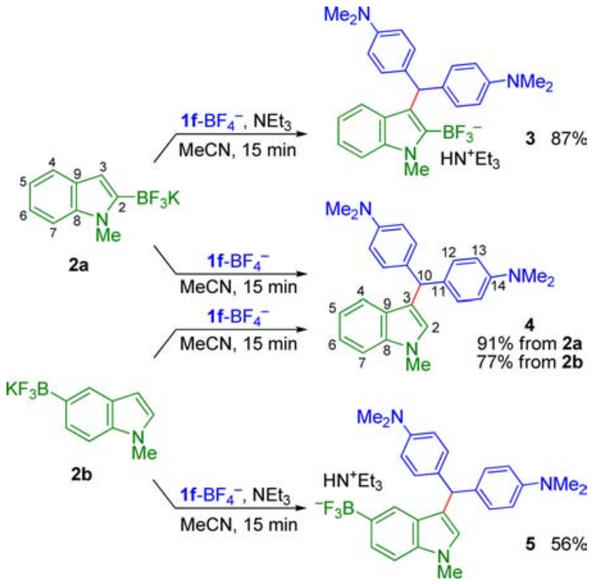
The assumption that these reactions proceed via initial attack of the benzhydrylium salt **1f**-BF_4^- at the 3-position of the indoles **2a** and **2b**, followed by protodeborylation, was confirmed by the exclusive formation of the triethylammonium salts **3** and **5** (Scheme 1) when the reactions were performed in the presence of triethylamine, which scavenges the protons released during the electrophilic attack at C-3. The X-ray structure of the ammonium indol-2-yl trifluoroborate **3** depicted in Figure 1 shows an

Received: February 18, 2013
Published: March 27, 2013

Table 1. Structures, λ_{max} in CH_3CN, and Electrophilicity Parameters *E* for the Benzhydrylium Ions 1a–j ($Ar_2CH^+X^-$) Used as Reference Electrophiles in This Work[11a–c,12]

		λ_{max} / nm	*E*
X = OMe, Y = Me	1a	478	1.48
X = Y = OMe	1b	500	0.00
	1c	524	-1.36
X = Y = N(Me)CH_2CF_3	1d	586	-3.85
X = Y = N$(CH_2CH_2)_2$O	1e	611	-5.53
X = Y = NMe_2	1f	605	-7.02
X = Y = N$(CH_2)_4$	1g	612	-7.69
	1h	620	-8.22
	1i (n = 2)	642	-9.45
	1j (n = 1)	632	-10.04

Scheme 1. Friedel–Crafts Reactions of the Benzhydrylium Salt 1f-BF_4^- with Potassium Indol-2-yl Trifluoroborate 2a and Indol-5-yl Trifluoroborate 2b in the Absence and Presence of NEt_3 at 20 °C



intermolecular N4–H···F3 hydrogen bond (2.488 Å) between the ammonium hydrogen and one of the fluorine atoms of the BF_3^- substituent, as well as an intramolecular C10–H···F1 interaction (2.272 Å, not shown in Figure 1) that may stabilize the compound.[13,14] The triethylammonium trifluoroborate **5** was less stable than **3** and undergoes a slow retro Friedel–Crafts reaction with formation of **2b** within several days in CD_3CN.[14]

In the absence of base, the benzhydrylium salt **1f**-BF_4^- reacted with *N*-Boc protected indol-2-yl trifluoroborates **2c** and **2d** at their 3-position to yield the zwitterionic ammonium difluoroborates **6** and **7**, respectively (Scheme 2), indicating that the electrophilic attack occurred exclusively in vicinal position to the BF_3^- group. Interestingly, the released proton led to cleavage of the *t*-butyl group and formation of an unprecedented 1,4,2-oxazaborolidine ring as shown in the X-ray structure of **7** (Figure 2), rather than to the cleavage of the BF_3K group as in **4**.[7a,13] In the presence of NEt_3, the indoles **2c,d** reacted in the same way as **2a,b** and gave the ammonium trifluoroborates **8** and **9** in good yields (Scheme 2).

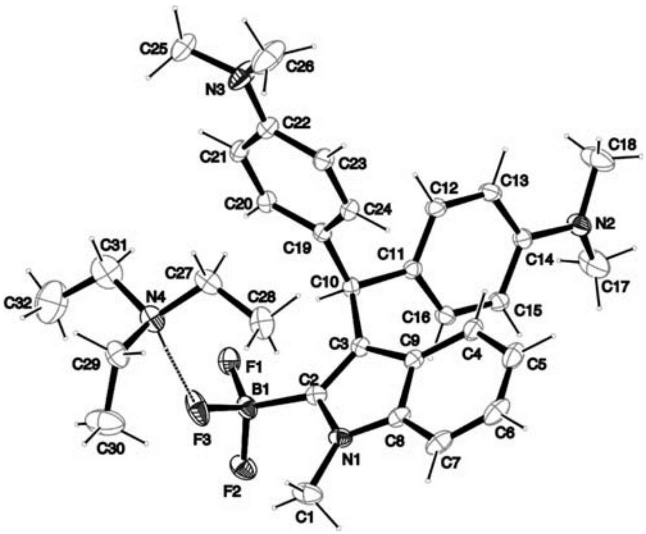
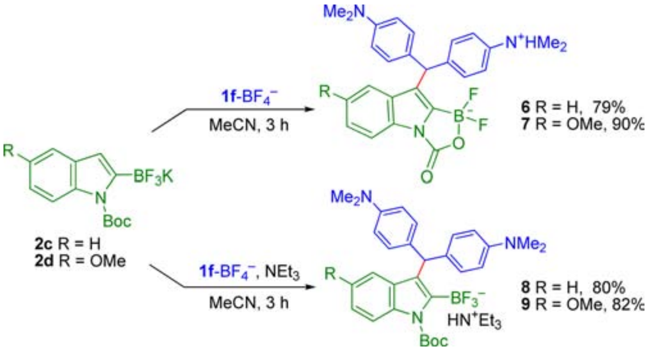


Figure 1. ORTEP drawing (50% probability ellipsoids) of **3**. Selected interatomic distances (Å) and angles (deg): C2–B1 = 1.611, C2–N1 = 1.402, C2–C3 = 1.378 and C10–H···F1 = 131.40.[13]

Scheme 2. Reactions of *N*-Boc-indol-2-yl Trifluoroborates 2c and 2d with 1f-BF_4^- in the Absence and Presence of NEt_3 at 20 °C



As summarized in Scheme 3, the initially formed Wheland intermediate of these reactions can rapidly be deprotonated by a Brønsted base to yield the C3-substituted indol-2-yl trifluoroborates; when no base is available, the protons released from the Wheland intermediate led to a fast protodeborylation reaction if R = Me or removal of the tert-butyl group and subsequent cyclization to give an oxazaborolidine ring if R = Boc (Scheme 3, bottom).

In contrast to **2c** and **2d**, neither the *N*-Boc protected indol-3-yl trifluoroborate **2e** nor the parent *N-tert*-butoxycarbonyl indole **2f** (not shown in Scheme 4) reacted with **1f**-BF_4^- under these conditions (MeCN, 20 °C, 3 h). However, **2e** reacted smoothly with the more electrophilic *p*-methoxy-substituted benzhydrylium tetrafluoroborate **1b**-BF_4^- to yield the ipso-substitution product **10** quantitatively. The benzofuran-2-yl trifluoroborate **2g**, a structural analogue of **2c**, also reacted with **1b**-BF_4^- to yield the C3-substituted product **11** and traces of the disubstituted benzofuran **12**. As in the reactions of the indoles **2a-d**, also in **2g** the BF_3K group fails to direct benzhydrylium salts **1** to the borylated position.

Reactions of Benzhydrylium Ions 1 with Furyl and Thienyl Trifluoroborates 2h–j. The potassium fur-2-yl trifluoroborate **2h** reacted with **1f**-BF_4^- in the absence of base to give a 1:7 mixture of the mono- and di-substituted products **13**

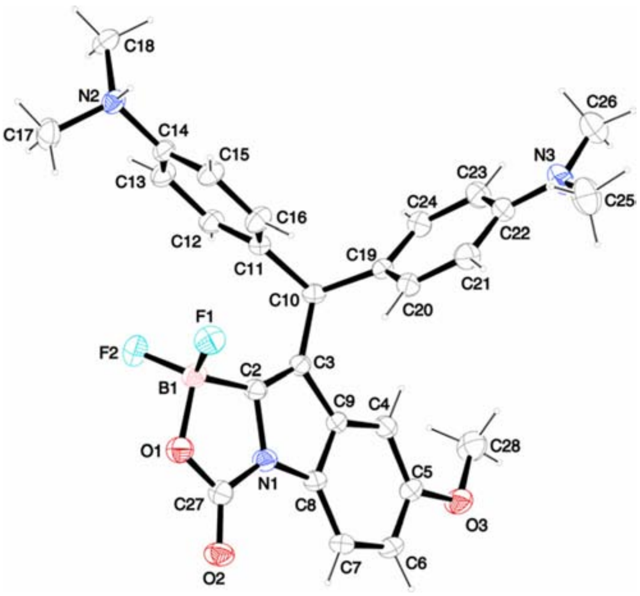
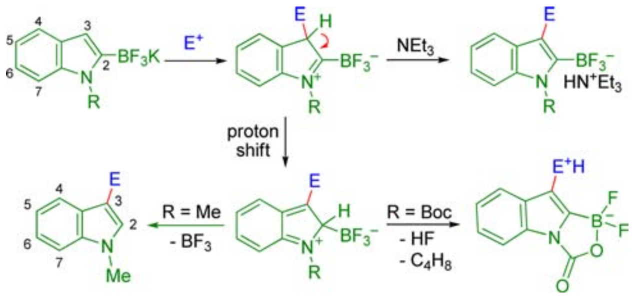
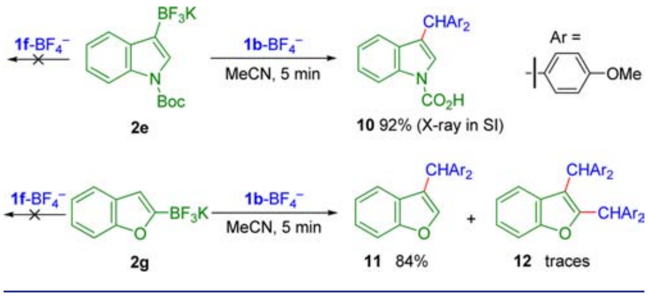


Figure 2. ORTEP drawing (50% probability ellipsoids) of the zwitterion 7. Selected interatomic distances (Å) and angles (deg) C2−B1 = 1.605, B1−O1 = 1.564, O1−C27 = 1.317, C27−N1 = 1.365, N1−C2 = 1.415, C22−N3 = 1.382, C14−N2 = 1.480 and N1−C2−B1 = 103.84, C2−B1−O1 = 99.32, B1−O1−C27 = 111.69, O1−C27−N1 = 110.52, C27−N1−C2 = 114.58.[13,14]

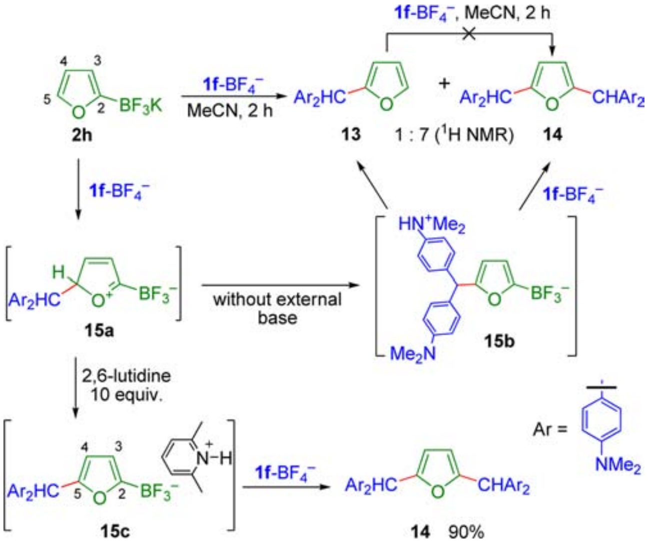
Scheme 3. Mechanistic Proposal for the Reactions of Indolyl Trifluoroborates with Electrophiles E^+



Scheme 4. Reactions of Potassium *N*-Boc-indol-3-yl Trifluoroborate 2e and Benzofuran-2-yl Trifluoroborate 2g with 1b-BF_4^- at 20 °C in MeCN



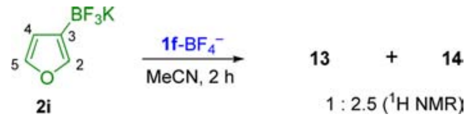
Scheme 5. Reactions of the Fur-2-yl Trifluoroborate 2h with the Benzhydrylium Salt 1f-BF_4^- at 20 °C in MeCN



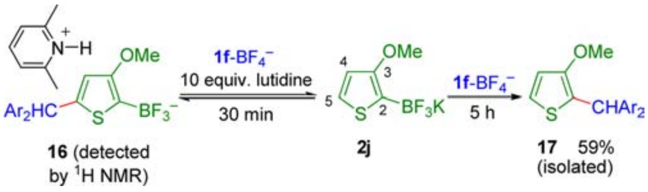
and **14**, respectively (Scheme 5). Since treatment of the monoalkylated furan **13** with the benzhydrylium salt **1f**-BF_4^- did not yield **14** under the same conditions, one can conclude that the disubstituted furan **14** is not generated via **13** as an intermediate. We, therefore, suggest that **2h** is attacked at C5 by the benzhydrylium ion **1f** to give the *σ*-adduct **15a** which tautomerizes with formation of **15b**. The dimethylanilinium fragment in **15b** is sufficiently acidic to affect protodeborylation with formation of **13**. Alternatively **15b** reacts with further **1f**-BF_4^- to give the 1,5-disubstituted furan **14**. This mechanistic proposal is supported by the observation that protodeborylation, that is, the formation of **13**, is fully suppressed when the reaction is carried out in the presence of 10 equiv of 2,6-lutidine, and **14** is thus produced in 90% yield.

The formation of **13** and **14** from fur-3-yl trifluoroborate **2i** and **1f**-BF_4^- can be explained analogously (Scheme 6).

Scheme 6. Reactions of the Fur-3-yl Trifluoroborate 2i with the Benzhydrylium Salt 1f-BF_4^- at 20 °C in MeCN



Scheme 7. Reactions of the Potassium Thien-2-yl Trifluoroborate 2j with the Benzhydrylium Salt 1f-BF_4^- at 20 °C in CD_3CN in the Absence and Presence of 2,6-Lutidine



Treatment of the thiophene **2j** with 1 equiv of the benzhydrylium salt **1f**-BF_4^- in acetonitrile at ambient temperature gave 59% of the 2,3-disubstituted thiophene **17** (Scheme 7). We have to assume that **17** is not generated directly, however, because it was not observable after 30 min, when **2j** and **1f**-BF_4^- were combined in the presence of 10 equivalents of 2,6-lutidine. Instead, the formation of the trisubstituted thiophene **16** was derived from the ^{1}H NMR spectrum with a singlet absorption at δ 6.80 ppm for the thiophene ring (see SI, p. S19), which was observed after 30 min.

After evaporation of the excess of 2,6-lutidine and redissolution of **16** in CD_3CN, a slow and quantitative conversion of **16** into **17** was observed, most probably via retro Friedel–Crafts reaction followed by irreversible ipso attack of the released benzhydrylium ion **1f**-BF_4^- at the C2 position of **2j**.

As shown in the above examples, external bases are needed to trap the products resulting from the initial attack of electrophiles at unsubstituted positions of aryltrifluoroborates. Therefore, in earlier investigations, which have been carried out in the absence of base, remote substitution might have been elusive because the initially generated products have either undergone retro Friedel–Crafts reactions or protodeborylation yielding products which do not show the site of initial attack.[1,3,4] A similar behavior has previously been reported for silylated and stannylated furans and thiophenes.[15] A rationalization for this behavior can be derived from the following kinetic data.

Kinetic Investigations. In order to quantify the activating effect of the BF_3K substituent on different positions of a π-system, we measured the kinetics of the reactions of the benzhydrylium ions **1a–j** with the heteroarenes **2a–k** spectrophotometrically (UV–vis), by following the disappearance of **1** at their maximum wavelengths λ_{max} (Table 1). As discussed previously, benzhydrylium ions **1** are suitable electrophiles for comparing nucleophiles of widely differing reactivities, because variation of the substitution of **1** in *m*- and *p*-positions allows large variations in electrophilicity while keeping the steric surroundings of the reaction centers constant.[11a–c]

By using an excess of the nucleophiles **2a–k** (10–200 equivalents), pseudo first-order conditions were achieved, as indicated by the monoexponential decays of the absorbances of the benzhydrylium ions **1** (Figure 3). The monoexponential decays showed that the protons or BF_3 released during the kinetics did not have an effect on the kinetics. In all cases, the benzhydrylium ions **1** were consumed completely, and plots of k_{obs} (s^{-1}) against the concentrations of the heteroarenes **2** were linear with negligible intercepts, as exemplified in the insert of Figure 3 for the reaction of the indole **2a** with **1g** and shown in the SI for all other reactions.

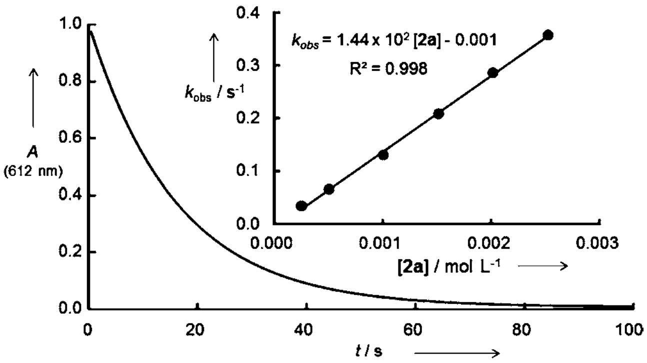
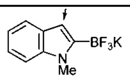
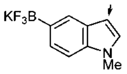
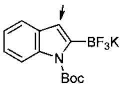
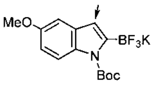
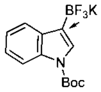
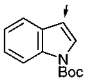
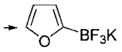
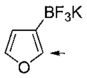
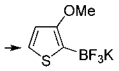
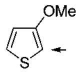


Figure 3. Exponential decay of the absorbance of cation **1g** (7.2×10^{-6} M) during the reaction with indole **2a** (5.04×10^{-4} M) in CH_3CN at 20 °C in the presence of 1.0 equiv of 2,6-lutidine ($k_{obs} = 6.43 \times 10^{-2}$ s^{-1}). (Inset) Determination of the second-order rate constant k_2 from the dependence of k_{obs} on the concentration of **2a** ($k_2 = 1.44 \times 10^2$ M^{-1} s^{-1}).

The slopes of these plots gave the second-order rate constants k_2 listed in Table 2. As the addition of a large excess of 2,6-lutidine has no or only a minor effect on the second-order rate constants k_2 reported in Table 2 (examined for **2a**, **2c**, **2h**, **2i**, and **2j**) and as the change of the counteranions of the benzhydrylium ions **1** only slightly affected the k_2 values (examined for **2i** and **2k**), we conclude that the formation of the Wheland intermediates is generally rate-determining. As the presence of 18-crown-6 ether affected the rate constants of the reaction of the *N*-Boc indole **2d** with **1e** by less than factor of 2 (Table 2), we conclude that also the coordination of the potassium counterion to the oxygen of the *N*-Boc group, which was observed in the solid state of indole **2e**,[13a] does not significantly influence the reactivities of the *N*-Boc protected indolyl-trifluoroborates in dilute acetonitrile solution.

Table 2. Second-order Rate Constants k_2 for the Reactions of the Benzhydrylium Salts 1a–j ($Ar_2CH^+X^-$, Concentration ≈ 10^{-5} M) with the Heteroarenes 2a–k (Concentration Range: 10^{-4}–10^{-3} M) in CH_3CN at 20 °C and the Resulting Reactivity Parameters *N* and s_N of 2a–k (Arrows Indicate the Site of Attack of $Ar_2CH^+X^-$)

π-nucleophiles 2		$Ar_2CH^+X^-$	k_2 / M^{-1} s^{-1}	*N*, s_N[a]
2a		**1f**-BF_4^-	$9.23 \times 10^{2\,b}$	9.55, 1.16
		1g-BF_4^-	1.02×10^2	
			$1.44 \times 10^{2\,b}$	
			$1.65 \times 10^{2\,c}$	
		1h-BF_4^-	1.35×10^1	
			$2.92 \times 10^{1\,b}$	
		1i-BF_4^-	1.31	
		1j-BF_4^-	2.81×10^{-1}	
2b		**1e**-BF_4^-	3.47×10^3	8.77, 1.09
		1f-BF_4^-	7.46×10^1	
		1g-BF_4^-	1.74×10^1	
		1h-BF_4^-	3.70	
2c		**1c**-PF_6^-	5.56×10^4	6.46, 0.96
		1d-BF_4^-	1.40×10^2	
			$2.09 \times 10^{2\,b}$	
		1e-BF_4^-	8.24	
			$1.08 \times 10^{1\,b}$	
2d		**1d**-BF_4^-	6.86×10^3	7.10, 1.18
		1e-BF_4^-	4.18×10^1	
			$6.82 \times 10^{1\,d}$	
		1f-BF_4^-	1.25	
2e		**1c**-PF_6^-	2.13×10^3	4.06, 0.79
		1d-BF_4^-	1.79	
2f		**1a**-TfO^-	1.09×10^4	1.68, 1.26
		1b-TfO^-	1.03×10^2	
		1c-TfO^-	2.87	
2h		**1d**-BF_4^-	4.95×10^1	5.99, 0.79
		1e-BF_4^-	2.32^{c}	
2i		**1d**-BF_4^-	5.11×10^2	6.83, 0.93
		1e-BF_4^-	2.19×10^1	
		1f-BF_4^-	$5.62 \times 10^{-1\,c}$	
		1f-TfO^-	3.13×10^{-1}	
		1f-BPh_4^-	3.85×10^{-1}	
2j		**1d**-BF_4^-	1.12×10^3	7.32, 0.90
		1e-BF_4^-	5.53×10^1	
		1f-BF_4^-	1.56^{e}	
2k		**1b**-TfO^-	4.33×10^3	3.06, 1.19
		1c-TfO^-	1.05×10^2	
		1c-PF_6^-	1.27×10^2	

[a] *N* and s_N parameters of **2a–k** derived from the linear plots of lg k_2 vs. *E* as shown in Figure 4, see the SI (p S39) for details; [b] With 1.0 equiv. of 2,6-lutidine/**2a**; [c] With 5.0 equiv. of 2,6-lutidine/**2a**; [d] With 1.0 equiv. of 18-crown-6 ether/**2d**. [e] No base effect was observed when performing the reaction with 1 to 10 equiv. of 2,6-lutidine/(**2h-j**).

In Figure 4, the k_2 values reported in Table 2 are plotted against the *E* values of the benzhydrylium ions **1** reported in Table 1 according to the linear free-energy relationship 2.[11]

$$\lg k_2(20\ °\mathrm{C}) = s_N(N + E) \qquad (2)$$

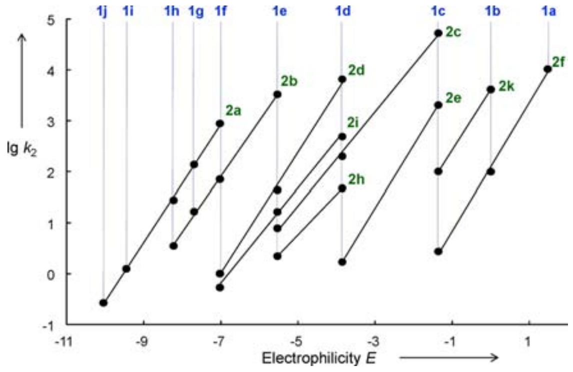
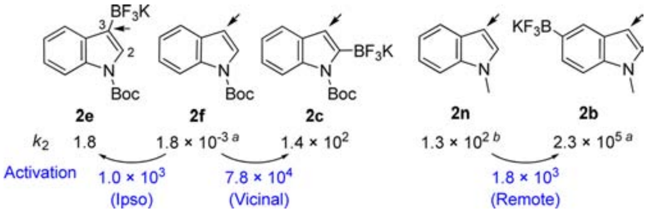


Figure 4. Plots of the logarithms of the second-order rate constants lg k_2 for the reactions of nucleophiles **2a**–**k** with the benzhydrylium ions **1a**–**j** versus their electrophilicity parameters E (see eq 2 and Tables 1 and 2). The correlation line for **2j** is not shown for the sake of clarity (see the SI, p S39 for details).

In this correlation, k_2 is the second-order rate constant (in M^{-1} s^{-1}), E (electrophilicity parameter) measures the strengths of the electrophiles, and N (nucleophilicity parameter) and s_N (sensitivity) are solvent-dependent nucleophile-specific reactivity parameters.[11]

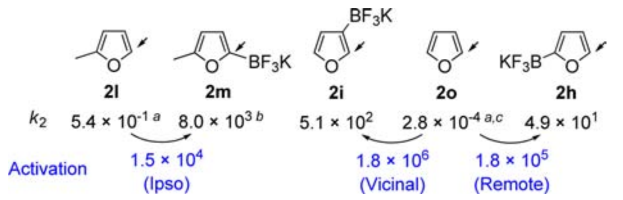
As the correlation lines for the indoles **2a**–**f**, the furans **2h**–**i** and the thiophenes **2j**–**k** in Figure 4 are not strictly parallel, the relative reactivities of the nucleophiles **2a**–**k** depend slightly on the electrophile. We, therefore, selected the cation **1d** as reference electrophile for the quantitative structure-reactivity analysis in Schemes 8 and 9. The k_2 ratios **2e**/**2f**, **2c**/**2f** and **2b**/**2n** show that BF_3K enhances the nucleophilic reactivity of the C3 position of indoles less when located in C3 (ipso) than when located in vicinal (C2) or remote (C5) positions (Scheme 8).

Scheme 8. Second-order Rate Constants k_2 (M^{-1} s^{-1}, from Table 2) for the Reactions of Indoles with the Cation 1d (E = −3.85) and Resulting Activation of the C3 Position by the BF_3K Group



[a]Calculated with eq 2 and N, s_N values from Table 2. [b]From ref 11d.

Scheme 9. Activation of Different Positions of Furan by the BF_3K Group Derived from the Second-order Rate Constants k_2 (M^{-1} s^{-1}, from Table 2) for the Reactions of Furans with the Cation 1d (E = −3.85)



[a]Calculated with eq 2 and the N and s_N values from ref 11b. [b]From ref 10. [c]k_2 is statistically corrected by a factor 2 for the furan **2o**.

The relative reactivities of the furans **2m**/**2l**, **2i**/**2o** and **2h**/**2o** (Scheme 9) also show that BF_3K enhances the nucleophilic reactivity of furans much more when located in remote positions (activation $>10^5$) than when located in the attacking (ipso) position ($\sim10^4$) as in **2m**.

The comparisons in Schemes 8 and 9 show that the ipso-activation by the BF_3K substituent is smaller than its vicinal or remote activation. As the nucleophilicity N is defined as the intercept on the abscissa of lg k_2 vs E correlations (Figure 4), and the sensitivity parameters s_N can be neglected in qualitative analyses of structure-reactivity relationships, the scale depicted in Figure 5 renders a rough comparison of the reactivities of borylated and nonborylated heteroarenes.[12]

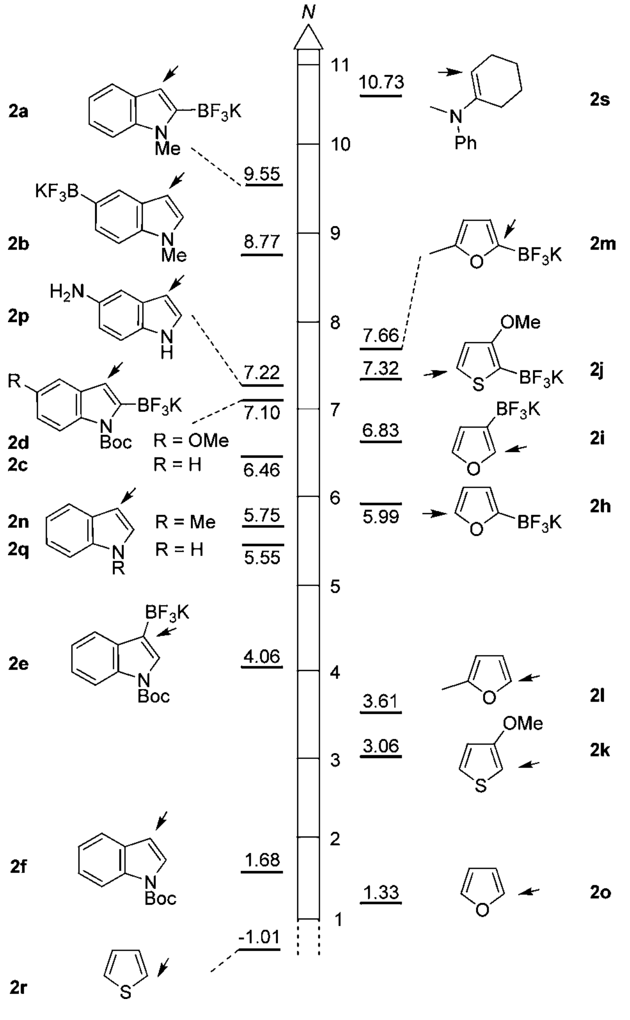


Figure 5. Comparison of the nucleophilicities of heteroaryl trifluoroborates and of related heteroarenes.[12] For N parameters of indoles **2n**–**q**, see ref 11d; for the N-Boc indole **2f**, see Table 2.

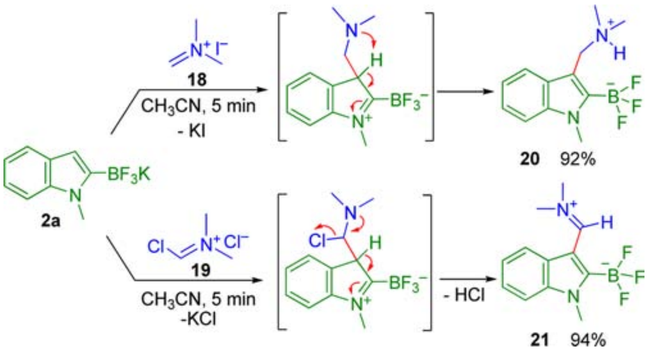
Figure 5 shows that the N-Boc group reduces the nucleophilic reactivity of the C-3 position of indole by roughly 4 orders of magnitude (from N = 5.55 for **2q** to N = 1.68 for **2f**), whereas the N-methyl group induces only a slight activation of the C-3 position (N = 5.75 for **2n**). The 10^4-fold activation of the 3-position of indoles by a 2-BF_3K group, which was derived in Scheme 8, is responsible for the fact that **2a** (N = 9.55) has a similar nucleophilicity as moderately active enamines (e.g., **2s** in

Figure 5).[12] From the N parameter of the indole **2b** ($N = 8.77$) one can further derive that a 5-BF_3K substituent activates the 3-position of indole even more than a 5-NH_2 group ($N = 7.22$ for **2p**) as replacement of NH by NCH_3 has little influence on reactivity (see above).

Figure 5 shows that the strong vicinal-activation of BF_3K raises the nucleophilic reactivities of the furans **2h** and **2i** above those of the indoles **2n** and **2q**, which open new possibilities of transition metal-free reactions of such organotrifluoroborates with a variety of electrophiles, some of which shall be discussed below.

Reactions of Heteroaryltrifluoroborates with Iminium Ions. As expected from its high N parameter, indolyl trifluoroborate **2a** reacts promptly with the Eschenmoser salt **18** ($E = -6.69$)[11b,e] and with the Vilsmeier salt **19** ($E = -5.77$)[11b,e] at the C3 position (Scheme 10). No external base was needed to preserve the trifluoroborate group since intramolecular deprotonation of the Wheland intermediate by the dimethylaminomethyl group is fast during the formation of **20**, and since fast elimination of HCl from the Wheland intermediate generated from **2a** and **19** yields the stable zwitterion **21**.

Scheme 10. Reactions of the Potassium Indol-2-yl Trifluoroborate 2a with Eschenmoser Salt 18 and Vilsmeier Salt 19 in MeCN for 5 min at 20 °C



Both, the ansa-ammonium borate **20** and the iminium borate **21** were characterized by single-crystal X-ray crystallography (Figure 6). Intra- and intermolecular N−H···F hydrogen bonding interactions between the fluorine atoms of the BF_3^- group and the ammonium hydrogen led to the formation of dimers with an intermolecular 4-membered ring in the case of **20** (Figure 6a).[16] An intramolecular C10−H···F3 hydrogen bond between a fluorine atom of the BF_3^- group and the proton of the iminium moiety and a strong electronic delocalization stabilize the hemicyanine **21** (Figure 6b).[16]

The trifluoroborates **20** and **21** are colorless, crystalline, air- and water-stable compounds, which are highly soluble in polar solvents and moderately soluble in nonpolar organic solvents as previously reported for related compounds.[16−18]

Analogous reactions were observed when 5-membered ring heteroaryl-trifluoroborates **2h−j** were treated with the iminium salts **18** and **19** (Table 3). Like benzhydrylium ions, the iminium salts **18** and **19** attacked the potassium furyl and thienyl trifluoroborates **2h−j** at remote positions of the BF_3K group to yield the zwitterionic ammonium trifluoroborates **23** and **25** and the iminium trifluoroborates **22**, **24** and **26** (Table 3).

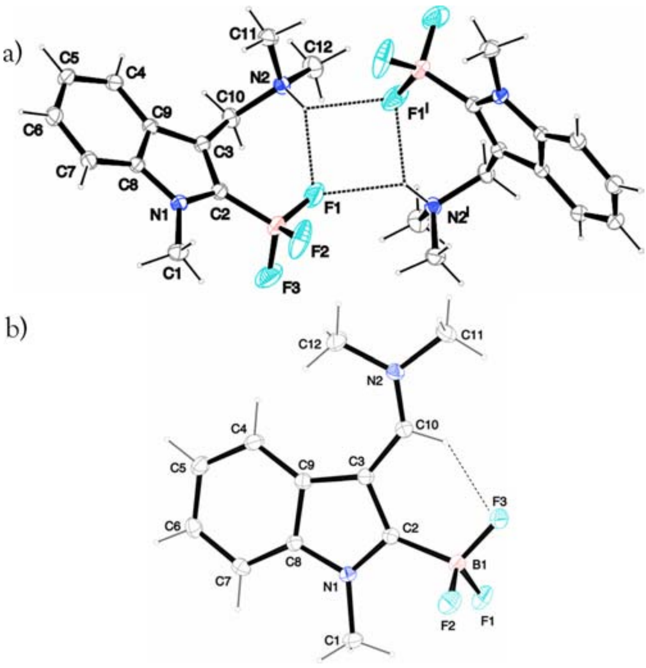
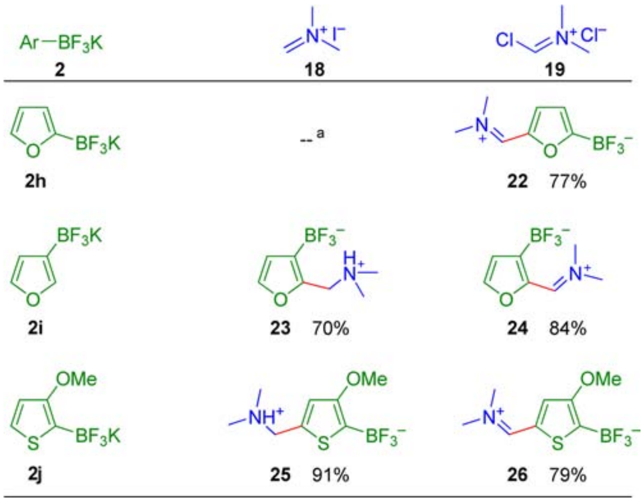


Figure 6. a) ORTEP view of the ammonium-trifluoroborate **20** (symmetry code $i = -x, y, 0.5-z$) and, b) ORTEP view of the iminium-trifluoroborate **21**; ellipsoids at the 50% probability level.[13] Selected interatomic distances (Å) and angles (deg) for **20**: C2−B1 = 1.621, N1−C2 = 1.383, C2−C3 = 1.388, C3−C10 = 1.487, C10−N2 = 1.514, N2···F1 = 2.811, N2···F1^i = 2.878, C3−C10−N2 = 113.38, C3−C2−B1 = 129.21. For **21**: C2−B1 = 1.645, N1−C2 = 1.352, C2−C3 = 1.421, C3−C10 = 1.416, C10−N2 = 1.304, C3−C10−N2 = 133.19, C3−C2−B1 = 132.92.

Table 3. Products and Yields of the Reactions of Furyl- and Thienyl-trifluoroborates 2h−j with 18 and 19 at 20 °C in MeCN for 1 h



[a] Fast decomposition prevented the characterization of this product.

CONCLUSION

Although the trifluoroborate group raises the nucleophilicity of the carbon directly attached to the boron atom (ipso-activation) by a factor of approximately 10^3−10^4, the activation of the vicinal or more remote positions of a π-system is even greater. Hence in noncatalyzed reactions of aryl and heteroaryl trifluoroborates, the BF_3K group often directs electrophiles to adjacent or remote

CH positions and because the proton released during electrophilic substitution at a CH position usually causes a subsequent protodeborylation, the entering electrophile is often found at a position different from that of the departing BF_3K group.

When bases are present to trap the released protons, it is even possible to isolate boron containing substitution products. In reactions with iminium ions, the protons are trapped intramolecularly, opening a new straightforward access to bifunctional ammonium and iminium borates, with potential applications in catalysis and molecular recognition.[16,17] Further synthetic transformations, for example, cross-coupling reactions, with the borate substituent remaining in these products are also feasible.[19] Recent examples of unselective and of remote substitutions of aryl and heteroaryl trifluoroborates and trialkylborates[6−8] can thus be rationalized.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental procedures, product characterizations, kinetic experiments, copies of all NMR spectra and crystallographic data. 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.

■ ACKNOWLEDGMENTS

Support of this work has been provided by the Alexander von Humboldt Foundation (grant for G. B.), the Deutsche Forschungsgemeinschaft (SFB 749) and the Fonds der Chemischen Industrie. We thank Dr. A. R. Ofial and Dr. B. Maji (Munich) for their help during the preparation of the manuscript. Prof. F. Terrier (Versailles, France) and Dr. S. Lakhdar (Caen, France) are acknowledged for helpful discussions.

■ ABBREVIATIONS

Boc, *t*-butoxycarbonyl; MeCN, acetonitrile

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(13) CCDC numbers for compound **3**: 874120, for **7**: 881210 (only one of the two symmetrically independent molecules is depicted in Figure 2), for **20**: 874121 and for **21**: 912272. These supplementary crystallographic data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. For the indole 2e see: (a) Berionni, G.; Mayer, P.; Mayr, H. *Acta Crystallogr., Sect. E: Struct. Rep. Online* **2012**, *68*, m551.

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