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Electrophilic Aromatic Substitutions of Aryltrifluoroborates with Retention of the BF₃⁻ Group: Quantification of the Activating and Directing Effects of the Trifluoroborate Group

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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 BF₃K group, because BF₃K 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 which 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 BF₃⁻ 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⁺), *e.g.*, halogenations,² Michael additions,³ borono Mannich,⁴ and Friedel-Crafts reactions⁵ are also known, and most of them have been reported to proceed via substitution of the BX₃⁻ group (Eq 1).

$$\begin{array}{ccc} & & & \\ & & & \\ & & & \\ & &$$

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 salts with retention of the BF₃K 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 BF₃K group on vicinal and more remote positions in indoles, furans, benzofurans and thiophenes and report that it is even possible to preserve the BF₃⁻ 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-BF₄⁻ (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-BF₄⁻ in acetonitrile in the absence of base (Scheme 1, middle).

Table 1. Structures, λ_{max} in CH₃CN, and electrophilicity parameters *E* for the benzhydrylium ions **1a-j** (Ar₂CH⁺X⁻) used as reference electrophiles in this work.^{11a-c, 12}

H	,	$\lambda_{\text{max}}/\text{ nm}$	Е
x	L _Y		
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
$X = Y = N(CH_2CH_2)_2O$	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
H	1i (n = 2)	642	-9.45
	1j (n = 1)	632	-10.04

Scheme 1. Friedel-Crafts reactions of the benzhydrylium salt 1f-BF₄⁻ with potassium indol-2-yl trifluoroborate 2a and indol-5-yl trifluoroborate 2b in the absence and presence of NEt₃ at 20 °C.



The assumption that these reactions proceed via initial attack of the benzhydrylium salt 1f-BF₄⁻ 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 intermolecular N4-H-F3 hydrogen bond (2.488 Å) between the ammonium hydrogen and one of the fluorine atoms of the BF₃⁻ substituent, as well as an intramolecular C10-H-F1 interaction (2.272 Å, not shown in Figure 1) which 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 CD₃CN.¹⁴



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

In the absence of base, the benzhydrylium salt 1f-BF₄⁻ 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 BF₃⁻ group. Interestingly, the released proton led to cleavage of the *t*-butyl group and formation of an unprecedent 1,4,2-oxazaborolidine ring as shown in the X-ray structure of 7 (Figure 2), rather than to the cleavage of the BF₃K group as in 4.^{7a,13} In the presence of NEt₃, 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).

Scheme 2. Reactions of N-Boc-indol-2-yl trifluoroborates 2c and 2d with 1f-BF₄⁻ in the absence and presence of NEt₃ at 20 °C.



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}

 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).

Scheme 3. Mechanistic proposal for the reactions of indolyl trifluoroborates with electrophiles E^* .



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-BF₄⁻ under these conditions (MeCN, 20 °C, 3 h). However, 2e reacted smoothly with the more electrophilic *p*-methoxy-substituted benzhydrylium tetrafluoroborate 1b-BF₄⁻ to yield the ipso-substitution product 10 quantitatively. The benzofuran-2-yl trifluoroborate 2g, a structural analogue of 2c, also reacted with 1b-BF₄⁻ 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 BF₃K group fails to direct benzhydrylium salts 1 to the borylated position.

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.



Reactions of benzhydrylium ions 1 with furyl and thienyl trifluoroborates 2h-j. The potassium fur-2-yl trifluoroborate 2h reacted with 1f-BF₄⁻ in the absence of base to give a 1:7 mixture of the mono- and di-substituted products 13 and 14, respectively (Scheme 5). Since treatment of the monoalkylated furan 13 with the benzhydrylium salt 1f-BF₄⁻ 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-BF₄⁻ to give the 1,5-disubstituted furan 14. This

mechanistic proposal is supported by the observation that protodeborylation, *i.e.* the formation of **13**, is fully suppressed when the reaction is carried out in the presence of 10 equivalents of 2,6-lutidine, and **14** is thus produced in 90% yield.

Scheme 5. Reactions of the fur-2-yl trifluoroborate 2h with the benzhydrylium salt 1f-BF₄⁻ at 20 °C in MeCN.



The formation of 13 and 14 from fur-3-yl trifluoroborate 2i and 1f-BF₄⁻ 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.

Treatment of the thiophene **2j** with one equivalent of the benzhydrylium salt **1f**-BF₄⁻ 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**-BF₄⁻ were combined in the presence of 10 equivalents of 2,6-lutidine. Instead, the formation of the trisubstituted thiophene **16** was derived from the ¹H 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.

Scheme 7. Reactions of the potassium thien-2-yl trifluoroborate 2j with the benzhydrylium salt 1f-BF₄⁻ at 20 °C in CD₃CN in the absence and presence of 2,6-lutidine.



After evaporation of the excess of 2,6-lutidine and redissolution of 16 in CD₃CN, 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-BF₄⁻ 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 BF₃K 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 mono-exponential decays of the absorbances of the benzhydrylium ions 1 (Figure 3). The mono-exponential decays showed that the protons or BF3 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 CH₃CN at 20 °C in the presence of 1.0 equiv. of 2,6-lutidine ($k_{obs} = 6.43 \times 10^{-2} \text{ s}^{-1}$). Insert: Determination of the second-order rate constant k_2 from the dependence of k_{obs} on the concentration of **2a** ($k_2 = 1.44 \times 10^2 \text{ M}^{-1} \text{ s}^{-1}$).

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** (Ar₂CH⁺X⁻, concentration $\approx 10^{-5}$ M) with the heteroarenes **2a-k** (concentration range: $10^{-4} - 10^{-3}$ M) in CH₃CN at 20 °C and the resulting reactivity parameters N and s_N of **2a-k**. The arrows indicate the site of attack of Ar₂CH⁺X⁻.

$\begin{array}{cccccccccccccccccccccccccccccccccccc$		π -nucleophiles 2	$Ar_2CH^*X^-$	$k_2 / M^{-1} s^{-1}$	N, s_N^{a}
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	2a		$1f-BF_4^-$	9.23 × 10 ^{2 b}	9.55, 1.16
$ \begin{array}{c} & 1.44 \times 10^{2b} \\ 1.65 \times 10^{2c} \\ 1h-BF_4^{-1} \\ 2.92 \times 10^{1b} \\ 1.35 \times 10^1 \\ 2.92 \times 10^{1b} \\ 1.31 \\ 1j-BF_4^{-1} \\ 2.81 \times 10^{-1} \\ 1.31 \\ 1j-BF_4^{-1} \\ 2.81 \times 10^{-1} \\ 1.40 \times 10^2 \\ 2.09 \times 10^{2b} \\ 1.40 \times 10^{1b} \\ 1.40 \times 10^2 \\ 2.09 \times 10^{2b} \\ 1.40 \times 10^{1b} \\ 1.40 \times 10^2 \\ 2.09 \times 10^{2b} \\ 1.40 \times 10^{1b} \\ 1.40 \times 10^2 \\ 2.09 \times 10^{2b} \\ 1.40 \times 10^{1b} \\ 1.40 \times 10^{1b} \\ 1.40 \times 10^{2} \\ 1.40 \times 10^{1b} \\ 1.40$		Γ F ₃ K	1g-BF ₄ -	1.02×10^{2}	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$		N Me		1.44 × 10 ^{2 b}	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$				1.65 × 10 ^{2 c}	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$			1h-BF₄⁻	1.35×10^{1}	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$				2.92 × 10 ^{1 b}	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$			$1i-BF_4^-$	1.31	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$			1j −BF ₄ ⁻	2.81×10^{-1}	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	2b	KF ₃ B	$1e-BF_4^-$	3.47×10^{3}	8.77, 1.09
$\begin{array}{cccccccccccccccccccccccccccccccccccc$			$1f-BF_4^-$	7.46×10^{1}	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$		N Me	$1g-BF_4^-$	1.74×10^{1}	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$			$1h-BF_4^-$	3.70	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	2c	· +	$1c-PF_6^-$	5.56 × 10 ⁴	6.46, 0.96
$\begin{array}{cccccccccccccccccccccccccccccccccccc$		BF₂K	$1d-BF_4^-$	1.40×10^{2}	- /
$\begin{array}{cccccccccccccccccccccccccccccccccccc$		N N	,	2.09 × 10 ^{2 b}	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		Boc	$1e-BF_4^-$	8.24	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$				1.08 × 10 ^{1 b}	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	2d		1d-BE. ⁻	6.86×10^{3}	7.10.1.18
$\begin{array}{cccccccccccccccccccccccccccccccccccc$		MeU BF ₂ K	$1e-BF_4^-$	4.18×10^{1}	,
$\begin{array}{cccccccccccccccccccccccccccccccccccc$		N N	···· +	6.82×10^{1} d	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$		Boc	1f-BF ₄ -	1.25	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	2e	BF₃K			
$\begin{array}{cccccccccccccccccccccccccccccccccccc$			$1c-PF_6^-$	2.13×10^{3}	4.0(0.70
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		N N	$1d-BF_4^-$	1.79	4.00, 0.79
2f Ia-TfO ⁻ 1.09×10^4 $1.68, 1.26$ Ib-TfO ⁻ 1.03×10^2 2h BF ₃ K Id-BF ₄ ⁻ 4.95×10^1 $5.99, 0.79$ 2i BF ₃ K Id-BF ₄ ⁻ 2.32° 2i BF ₃ K Id-BF ₄ ⁻ 2.19×10^1 If-BF ₄ ⁻ $5.62 \times 10^{-1} \circ 11 \times 10^2$ If-BF ₄ ⁻ $5.62 \times 10^{-1} \circ 11 \times 10^2$ If-BF ₄ ⁻ 3.13×10^{-1} If-BF ₄ ⁻ 3.85×10^{-1} 2j OMe Id-BF ₄ ⁻ 1.12×10^3 $7.32, 0.90$ Ie-BF ₄ ⁻ 1.56° 2k OMe Ib-TfO ⁻ 4.33×10^3 0.6, 1.19 Ic-TfO ⁻ 1.05×10^2		Boc			
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	2f		1a-TfO⁻	1.09×10^{4}	1.68, 1.26
$\begin{array}{cccccccccccccccccccccccccccccccccccc$			1b-TfO⁻	1.03×10^{2}	
$2h + 6 = BF_{3}K = 1d - BF_{4}^{-} = 4.95 \times 10^{1} = 5.99, 0.79$ $2i = BF_{3}K = 1d - BF_{4}^{-} = 2.32^{\circ}$ $2i = BF_{3}K = 1d - BF_{4}^{-} = 2.19 \times 10^{1} = 16^{1} - 16^{1} + 16^{1} - 16^{1} + 16^{1} - 16^{1} - 16^{1} + 16^{1} - 16^{1} - 16^{1} + 16^{1} - 16^{1} - 16^{1} + 16^{1} - 16^{1} - 16^{1} + 16^{1} - 16^{1} - 16^{1} - 16^{1} + 16^{1} - 16^{$		N	1c-TfO⁻	2.87	
2i $BF_{3}K$ $1d-BF_{4}^{-}$ 2.32° 2i $BF_{3}K$ $1d-BF_{4}^{-}$ 2.32° 2i $BF_{3}K$ $1d-BF_{4}^{-}$ 2.32° 2i $1e-BF_{4}^{-}$ 2.19×10^{1} $1f-BF_{4}^{-}$ $5.62 \times 10^{-1}^{\circ}$ $1f-TfO^{-}$ 3.13×10^{-1} $1f-BPh_{4}^{-}$ 3.85×10^{-1} 2j OMe $1d-BF_{4}^{-}$ 1.12×10^{3} $7.32, 0.90$ $1e-BF_{4}^{-}$ 1.56° 2k OMe $1b-TfO^{-}$ 4.33×10^{3} $3.06, 1.19$ $1c-TfO^{-}$ 1.05×10^{2}	21		1J DE -	4.05×10^{1}	5 00 0 70
2i $BF_{3}K$ $1d-BF_{4}^{-}$ 5.11×10^{2} $6.83, 0.93$ $1e-BF_{4}^{-}$ 2.19×10^{1} $1f-BF_{4}^{-}$ $5.62 \times 10^{-1}e$ $1f-TfO^{-}$ 3.13×10^{-1} $1f-BPh_{4}^{-}$ 3.85×10^{-1} 2j OMe $1d-BF_{4}^{-}$ 1.12×10^{3} $7.32, 0.90$ $1e-BF_{4}^{-}$ $1.56 e$ 2k OMe $1b-TfO^{-}$ 4.33×10^{3} $3.06, 1.19$ $1c-TfO^{-}$ 1.05×10^{2}	2n	→ <	1_{0} BF ⁻	4.93 × 10	5.99, 0.79
2i BF ₃ K $Id-BF_4^-$ $Ie-BF_4^-$ $1f-BF_4^-$ $1f-BF_4^-$ $1f-BF_4^-$ $1f-FO^-$ $1f-BPh_4^-$ 3.13×10^{-1} $1f-BPh_4^-$ 3.85×10^{-1} 2j OMe $Id-BF_4^-$ 1.12×10^3 7.32, 0.90 $1e-BF_4^-$ 1.56 ° 2k OMe $1b-TfO^-$ 1.05×10^2 3.06, 1.19		0 5131	re-Dr ₄	2.92	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	21	BF₂K	1d-BE-	5.11×10^{2}	683 093
$\begin{array}{c} \textbf{i} \textbf{f} - \textbf{BF}_4^- & 5.62 \times 10^{-1} \text{ e} \\ \textbf{i} \textbf{f} - \textbf{BF}_4^- & 5.62 \times 10^{-1} \text{ e} \\ \textbf{i} \textbf{f} - \textbf{TfO}^- & 3.13 \times 10^{-1} \\ \textbf{i} \textbf{f} - \textbf{BPh}_4^- & 3.85 \times 10^{-1} \end{array}$ $\begin{array}{c} \textbf{2j} \qquad \textbf{OMe} & \textbf{i} \textbf{d} - \textbf{BF}_4^- & 1.12 \times 10^3 & 7.32, 0.90 \\ \textbf{i} \textbf{e} - \textbf{BF}_4^- & 5.53 \times 10^1 \\ \textbf{i} \textbf{f} - \textbf{BF}_4^- & 1.56 \text{ e} \end{array}$ $\begin{array}{c} \textbf{2k} \qquad \textbf{OMe} & \textbf{i} \textbf{b} - \textbf{TfO}^- & 4.33 \times 10^3 & 3.06, 1.19 \\ \textbf{i} \textbf{c} - \textbf{TfO}^- & 1.05 \times 10^2 \end{array}$	<i>4</i> 1		le-BF.	2.19×10^{1}	5.65, 0.75
$\begin{array}{cccccccccccccccccccccccccccccccccccc$		<_>+	1f-BF ⁺	5.62×10^{-1} e	
$1f-BPh_{4}^{-} 3.85 \times 10^{-1}$ 2j OMe $1d-BF_{4}^{-} 1.12 \times 10^{3} 7.32, 0.90$ $1e-BF_{4}^{-} 5.53 \times 10^{1}$ $1f-BF_{4}^{-} 1.56^{\circ}$ 2k OMe $1b-TfO^{-} 4.33 \times 10^{3} 3.06, 1.19$ $1c-TfO^{-} 1.05 \times 10^{2}$		0	1f-TfO ⁻	3.13×10^{-1}	
2j OMe $1d-BF_4^ 1.12 \times 10^3$ 7.32, 0.90 $1e-BF_4^ 5.53 \times 10^1$ $1f-BF_4^ 1.56^{\circ}$ 2k OMe $1b-TfO^ 4.33 \times 10^3$ $3.06, 1.19$ $1c-TfO^ 1.05 \times 10^2$			1f-BPh₄ ⁻	3.85×10^{-1}	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	2;	OMe	1d_BE -	1.12×10^{3}	7 32 0 00
$\begin{array}{c} \bullet \\ S \\ BF_{3}K \\ If-BF_{4} \\ If-BF_{4} \\ Ic-TfO^{-} \\ 1.05 \times 10^{2} \\ Ic-TfO^{-} \\ Ic-Tf$	~J		$1e_BE^-$	5.53×10^{1}	1.52, 0.70
$2k \qquad OMe \qquad 1b-TfO^{-} \qquad 4.33 \times 10^{3} \qquad 3.06, 1.19 \\ 1c-TfO^{-} \qquad 1.05 \times 10^{2} \\ \hline$		→	1f-BE-	1.56 °	
2κ 16-110 4.33 × 10 ² 5.06, 1.19 1c-TfO ⁻ 1.05 × 10 ²	21	OMo	11. TIO-	1.30	2 06 1 10
$() = 10^{-10} - 10^{-10}$	2K		10 - 110 $1a TfO^{-}$	4.33×10^{2}	5.00, 1.19
$1c-PE^{-1} = 1.27 \times 10^{2}$		<_>> ←	1c-PE	1.03×10^{2} 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

$$\lg k_2 (20 \ ^{\circ}\text{C}) = s_N(N + E)$$
(2)

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



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).

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 BF₃K 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 BF₃K group.



^a Calculated with Eq (2) and N, s_N values from Table 2; ^b From Ref. 11d.

The relative reactivities of the furans 2m/2l, 2i/2o and 2h/2o (Scheme 9) also show that BF₃K enhances the nucleophilic reactivity of furans much more when located in remote positions (activation > 10^5) than when located in the attacking (ipso) position ($\approx 10^4$) as in 2m.

Scheme 9. Activation of different positions of furan by the BF₃K 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 20.

The comparisons in Schemes 8 and 9 show that the ipso-activation by the BF₃K substituent is smaller than its vicinal or remote activation. As the nucleophilicity N is defined as the intercept on the abscissa of log 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 non-borylated 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 and 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 10⁴-fold activation of the 3-position of indoles by a 2-BF₃K 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-BF₃K substituent activates the 3-position of indole even more than a 5-NH₂ group (N = 7.22 for 2p) as replacement of NH by NCH₃ has little influence on reactivity (see above).

Figure 5 shows that the strong vicinal-activation of BF₃K 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 BF₃⁻ 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 BF₃⁻ 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



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(4), N1–C2 = 1.383, C2–C3 = 1.388, C3–C10 = 1.487, C10–N2 = 1.514, N2⁻⁻⁻F1 = 2.811(3), N2⁻⁻⁻F1ⁱ = 2.878(3), 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.

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 BF₃K group to yield the zwitterionic ammonium trifluoroborates 23 and 25 and the iminium trifluoroborates 22, 24 and 26 (Table 3).

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 BF₃K 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 BF₃K group.

When bases are present to trap the released protons, it is even possible to isolate boron containing substitution products. 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, *e.g.* 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

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.

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ABBREVIATIONS

Boc, t-butoxycarbonyl MeCN, acetonitrile

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REFERENCES

(1) For recent reviews on organotrifluoroborates, see: (a) Darses, S.; Genet, J.-P. Chem. Rev. 2008, 108, 288. (b) Molander, G. A.; Ellis, N. Acc. Chem. Res. 2007, 40, 275. (c) Stefani, H. A.; Cella, R.; Vieira, A. S. Tetrahedron 2007, 63, 3623. (d) Darses, S.; Genet, J.-P. Eur. J. Org. Chem. 2003, 4313. For books and general reviews on organoborates, see: (e) Hall, D. G. in Boronic Acids: Preparation and Applications in Organic Synthesis, Medicine and Materials, 2nd ed., Wiley-VCH, Weinheim, Germany, 2011. (f) Yamamoto, Y. Heterocycles, 2012, 85, 799. (g) Bonin, H.; Delacroix, T.; Gras, E. Org. Biomol. Chem. 2011, 9, 4714. (h) Ishikura, M. Heterocycles, 2011, 83, 247. (i) Lennox, A. J. J.; Lloyd-Jones, G. C. Isr. J. Chem. 2010, 50, 664. (j) Gillis, E. P.; Burke, M. D. Aldrichimica Acta, 2009, 42, 17. (k) Hayashi, T.; Yamasaki, K. Chem. Rev. 2003, 103, 2829. (l) Fagnou, K.; Lautens, M. Chem. Rev. 2003, 103, 169.

(2) (a) Molander, G. A.; Cavalcanti, L. N. J. Org. Chem. 2011, 76, 7195. (b) Akula, M. R.; Yao, M.-L.; Kabalka, G. W. Tetrahedron Lett. 2010, 51, 1170. (c) Yao, M.-L.; Reddy, M. S.; Yong, L.; Walfish, I.; Blevins, D. W.; Kabalka, G. W. Org. Lett. 2010, 12, 700. (d) Cazorla, C.; Métay, E.; Andrioletti, B.; Lemaire, M. Tetrahedron Lett. 2009, 50, 3936. (e) Kabalka, G. W.; Mereddy, A. R. Tetrahedron Lett. 2004, 45, 343. For other types of uncatalyzed S_EAr reactions of organoborates with electrophiles, e.g. ipsonitration and ispo-sulfuration, see: (f) Molander, G. A.; Cavalcanti, L. N. J. Org. Chem. 2012, 77, 4402. (g) Prakash, G. K. S.; Panja, C.; Mathew, T.; Surampudi, V.; Petasis, N. A.; Olah, G. A. Org. Lett, 2004, 6, 2205. (h) Kerverdo, S.; Gingras, M. Tetrahedron Lett. 2000, 41, 6053.

(3) Selected recent examples: (a) Wu, H.; Radomkit, S.; O'Brien, J. M.; Hoveyda; A. H. J. Am. Chem. Soc., 2012, 134, 8277. (b) Pubill-Ulldemolins, C., Bonet, A., Bo, C., Gulyás, H.; Fernández, E. Chem. Eur. J. 2012, 18, 1121. (c) Lee, K.-S.; Zhugralin, A. R.; Hoveyda, A. H. J. Am. Chem. Soc. 2009, 131, 7253.

(4) (a) Candeias, N. R.; Montalbano, F.; Cal, P. M. S. D.; Gois, P. M. P. Chem. Rev. 2010, 110, 6169. (b) Vieira, A. S.; Ferreira F. P.; Fiorante, P. F.; Guadagnin, R. C.; Stefani, H. A. Tetrahedron 2008, 64, 3306. (c) Chiu, C.-W.; Gabbaï, F. P. J. Am. Chem. Soc. 2006, 128, 14248. (d) Tremblay-Morin, J.-P.; Raeppel, S.; Gaudette, F. Tetrahedron Lett. 2004, 45, 3471. (e) Harwood, L. M.; Currie, G. S.; Drew, M. G. B.; Luke, R. W. A. Chem. Commun. 1996, 1953. For transition-metal free reactions of organoborates with oxonium ions and other cationic electrophiles, see also: (f) Clausen, D. J.; Floreancig, P. E.; J. Org. Chem., 2012, 77, 6574. (g) Vo, C.-V. T.; Mitchell, T. A.; Bode, J. W. J. Am. Chem. Soc. 2011, 133, 14082. (h) Larouche-Gauthier, R.; Elford, T. G.; Aggarwal, V. K. J. Am. Chem. Soc. 2011, 133, 16794. (i) Mitchell, T. A.; Bode, J. W. J. Am. Chem. Soc. 2009, 131, 18057.

(5) (a) Kim, J.; Movassaghi, M. J. Am. Chem. Soc. 2011, 133, 14940.
(b) Lee, S.; MacMillan, D. W. C. J. Am. Chem. Soc. 2007, 129, 15438.
(c) Negishi, E.-i.; Abramovitch, A.; Merrill, R. E. J. Chem. Soc. Chem. Comm. 1975, 138.

(6) Examples of not fully ipso-regioselective reactions of arylborates with electrophiles are reported ref. 2a, 5a, 7a-c and 7e-g.

(7) (a) Ishikura, M.; Kato, H. Tetrahedron, 2002, 58, 9827. (b) Ishikura, M.; Agata, I.; Katagiri, N. J. Heterocycl. Chem. 1999, 36, 873. (c) Ishikura, M.; Terashima, M. J. Heterocycl. Chem. 1994, 31, 977. (d) Ishikura, M.; Kamada, M.; Oda, I.; Ohta, T.; Terashima, M. J. Heterocycl. Chem. 1987, 24, 377. (e) Negishi, E.-i.; Merrill, R. E.; Abramovitch, A.; Campbell, D. P. Bull. Korean Chem. Soc. 1987, 8, 424. (f) Levy, A. B. Tetrahedron Lett. 1979, 20, 4021. (g) Marinelli, E. R.; Levy, A. B. Tetrahedron Lett. 1979, 20, 2313. (h) Utimoto, K.; Okada, K.-I.; Nozaki, H. Tetrahedron Lett. 1975, 16, 4239. (i) Negishi, E.-i.; Merrill, R. E. J. Chem. Soc. Chem. Comm. 1974, 860. (j) Example of remote chlorination reactions of heteroaryl trifluoroborates are also reported in ref. 2a.

(8) For electrophilic aromatic substitutions of aryl borates and boronates with retention of the boron group, see: (a) Bartolucci, S.; Bartoccini, F.; Righi, M.; Piersanti, G. Org. Lett. **2012**, *14*, 600 (b) Appukkuttan, P.; Dehaen, W.; Van der Eycken, E. Chem. Eur. J. **2007**, *13*, 6452. (c) Isaad, J.; El Achari, A. *Tetrahedron* **2011**, 67, 4939. (d) Olah, G. A.; Piteau, M.; Laali, K.; Rao, C. B.; Farooq, O. J. Org. Chem. **1990**, *55*, 46. See also ref. 7a-d and f-i.

(9) For transition-metal-free reactions of aryltrifluoroborates with retention of the BF₃K group, see: (a) Molander, G. A.; Ajayi, K. Org. Lett. 2012, 14, 4242. (b) Molander, G. A.; Febo-Ayala, W.; Jean-Gérard, L. Org. Lett. 2009, 11, 3830. (c) Molander, G. A.; Cooper, D. J. J. Org. Chem. 2008, 73, 3885. (d) Molander, G. A.; Ham, J.; Canturk, B. Org. Lett. 2007, 9, 821. (e) Molander, G. A.; Cooper, D. J. J. Org. Chem. 2007, 72, 3558. (f) Molander, G. A.; Ellis, N. M. J. Org. Chem. 2006, 71, 7491. (g) Molander, G. A.; Ham, J. Org. Lett. 2006, 8, 2767. (h) Molander, G. A.; Petrillo, D. E. J. Am. Chem. Soc. 2006, 128, 9634. For a recent synthesis of

organotrifluoroborates under non-etching conditions, see: (i) Lennox, A. J. J.; Lloyd-Jones, G. C. Angew. Chem., Int. Ed. 2012, 51, 9385.

(10) Berionni, G.; Maji, B.; Knochel, P.; Mayr, H. Chem. Sci. 2012, 3, 878.

(11) (a) Mayr, H.; Ofial, A. R. Pure Appl. Chem. 2005, 77, 1807. (b) Mayr, H.; Kempf, B.; Ofial, A. R. Acc. Chem. Res. 2003, 36, 66. (c) Mayr, H.; Bug, T.; Gotta, M. F.; Hering, N.; Irrgang, B.; Janker, B.; Kempf, B.; Loos, R.; Ofial, A. R.; Remennikov, G.; Schimmel, H. J. Am. Chem. Soc. 2001, 123, 9500. (d) Lakhdar, S.; Westermaier, M.; Terrier, F.; Goumont, R.; Boubaker, T.; Ofial, A. R.; Mayr, H. J. Org. Chem. 2006, 71, 9088. (e) Mayr, H.; Ofial, A. R. Tetrahedron Lett. 1997, 38, 3503.

(12) Database for *N*, *s*_N and *E* parameters and references to original literature: www.cup.uni-muenchen.de/oc/mayr/DBintro.html.

(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.

(14) The intramolecular C10-H10⁻⁻F1-B1 interaction in zwitterions 3, 8, 9 and 21 also exists in CD₃CN solution as illustrated by the deshielding of the benzhydryl proton H10 ($\delta > 6.20$ ppm) as compared to the non-borylated compound 4 ($\delta = 5.44$ ppm) and 10 ($\delta = 5.46$ ppm) or to the compound 5 where there is no H10⁻⁻F interaction ($\delta = 5.47$ ppm). See also: (a) Desiraju, G. R. Angew. Chem., Int. Ed. 2011, 50, 52. (b) Mayr, H.; Ofial, A. R.; Würthwein, E.-U.; Aust, N. C. J. Am. Chem. Soc. 1997, 119, 12727.

(15) (a) Herrlich, M.; Hampel, N.; Mayr, H. Org. Lett. 2001, 3, 1629. (b) Herrlich, M.; Mayr, H.; Faust, R. Org. Lett. 2001, 3, 1633.

(16) For related zwitterionic ammonium trifluoroborates, see: (a) Batsanov, A. S.; Hérault, D.; Howard, J. A. K.; Patrick, L. G. F.; Probert, M. R.; Whiting, A. Organometallics 2007, 26, 2414. (b) Coghlan, S. W.; Giles, R. L.; Howard, J. A. K.; Patrick, L. G. F.; Probert, M. R.; Smith, G.



E.; Whiting, A. J. Organomet. Chem. 2005, 690, 4784. (c) Bresner, C.; Aldridge, S.; Fallis, I. A.; Jones, C.; Ooi, L.-L. Angew. Chem., Int. Ed. 2005, 44, 3606. Also see ref. 18.

(17) For potential applications of ammonium and iminium borates in molecular recognition and in catalysis, see: (a) Oishi, S.; Saito, S. Angew. Chem., Int. Ed. 2012, 51, 5395. (b) Gott, A. L.; Piers, W. E.; Dutton, J. L.; McDonald, R.; Parvez, M. Organometallics, 2011, 30, 4236. (c) Georgiou, I.; Ilyashenko, G.; Whiting, A. Acc. Chem. Res. 2009, 42, 756. (d) Restorp, P.; Berryman, O.B.; Sather, A. C.; Ajami, D.; Rebek, J. Chem. Commun. 2009, 5692. (e) Sumerin, V.; Schulz, F.; Atsumi, M.; Wang, C.; Nieger, M.; Leskelä, M.; Repo, T.; Pyykkö, P.; Rieger, B. J. Am. Chem. Soc. 2008, 130, 14117. (f) Zhu, L.; Shabbir S. H.; Gray, M.; Lynch, V. M.; Sorey, S.; Anslyn, E. V. J. Am. Chem. Soc. 2006, 128, 1222.

(18) The hydrolyses and stabilities of organotrifluoroborates have recently been studied : (a) Lennox, A. J. J.; Llyod-Jones G. C. J. Am. Chem. Soc. 2012, 134, 7431. (b) Ting, R.; Harwig, C. W.; Lo, J.; Li, Y.; Adam, M. J.; Ruth, T. J.; Perrin, D. M. J. Org. Chem. 2008, 73, 4662.

(19) For recent examples of cross-coupling reactions of alkylammonium trifluoroborates, including their internal salts, see: (a) Colombel, V.; Presset, M.; Oehlrich, D.; Rombouts, F.; Molander, G. A. Org. Lett. 2012, 14, 1680. (b) Fleury-Brégeot, N.; Raushel, J.; Sandrock, D. L.; Dreher, S. D.; Molander, G. A. Chem. Eur. J. 2012, 18, 9564. (c) Molander, G. A.; Beaumard, F. Org. Lett. 2011, 13, 1242. (d) Raushel, J.; Sandrock, D. L.; Josyula, K. V.; Pakyz, D.; Molander, G. A. J. Org. Chem. 2011, 76, 2762. (e) Luisi, R.; Giovine, A.; Florio, S. Chem. Eur. J. 2010, 16, 2683. (f) Molander, G. A.; Cooper, D. J. J. Org. Chem. 2008, 73, 3885. (g) Batey, R. A., Quach, T. D. Tetrahedron Lett. 2001, 42, 9099.