Angewandte
International Edition Chemie

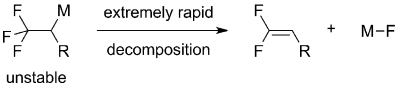
DOI: 10.1002/anie.201308036

Synthesis and Applications of α-Trifluoromethylated Alkylboron Compounds**

O. Andreea Argintaru, DaWeon Ryu, Ioana Aron, and Gary A. Molander*

The importance of incorporating fluorinated subunits into organic molecules is well established in the pharmaceutical, agrochemical, and materials industries.[1,2] Developing methods of incorporating such fluorinated moieties into organic substrates in a safe, selective, and facile manner, therefore, has been an area of great interest.[3] Among the various fluorinated moieties, the strongly electron-withdrawing trifluoromethyl group (CF_3) has garnered much attention because of the profound properties it can effect upon being implanted within a molecule.[4] However, most of the synthetic efforts have been focused on introducing CF_3 into functionalized arenes.[5]

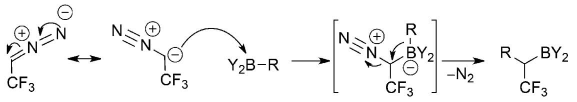
By contrast, general methods for the incorporation of CF_3 into alkyl systems are less well developed,[6–8] yet increasingly more important in terms of structural diversity and expanding chemical space.[9] β-Trifluoroethyl carbanion synthons represent an attractive set of reagents for the installation of fluorinated substructures within the realm of alkyl building blocks. However, owing to a strong driving force for the formation of metal–fluorine (M−F) bonds, the propensity for β-fluoride elimination of M−F moieties is high [Eq. (1)], and thus the chemistry of β-trifluoroethyl carbanion synthons is astonishingly limited and underdeveloped.[10]



(1)

Although Brown, Ramachandran, and co-workers have previously generated α-trifluoromethylated organoboranes through a hydroboration route,[11] these intermediates were never isolated but rather simply oxidized in situ.[12] With the boron oxidized to the corresponding alcohol, the considerable synthetic value of the trifluoroethyl subunit in subsequent transformations is diminished. Unlike the organoborons, the alcohol cannot function as a bench-stable trifluoroethyl anion or trifluoroethyl radical precursor, and the versatility of the organoboron compounds in further functionalization (e.g., C−C bond formation by metal-catalyzed cross-coupling[13] or radical reactions,[14] rhodium-catalyzed 1,2-additions,[15] amination,[16] etc.) is lost.

Herein, we report the synthesis of diverse libraries of indefinitely bench-stable trifluoromethylated building blocks, which can be further diversified through versatile organoboron transformations. This chemistry has the potential to improve the existing paradigm for the introduction of CF_3 at sp^3 centers, a reaction which is limited mostly to CF_3-based reagents such as Me_3SiCF_3 that minimally enhance molecular complexity. Our strategy was to utilize trifluoroethylidene in conjunction with tricoordinate organoborons to generate unprecedented α-trifluoromethylated organoborons through an established α-transfer mechanism (Scheme 1).



Scheme 1. α-Transfer mechanism.

The synthesis of 2,2,2-trifluorodiazoethane (CF_3CHN_2) from the corresponding ammonium salt was first described in the 1940s and was reported on a scale as large as 100–200 mmol.[17] However, CF_3CHN_2 was not used extensively in organic synthesis until the Carreira's group developed a method to generate the material and react it in situ with other organic compounds. As demonstrated by Carreira, CF_3CHN_2 has a similar reactivity profile to that of ethyl diazoacetate.[18] The reactivity of CF_3CHN_2 toward organoboron compounds, however, has never been explored, although several organoborons have been shown to react with ethyl diazoacetate and other α-diazocarbonyl compounds to give α-arylated, α-vinylated, or α-alkylated carbonyl compounds after protodeboronation.[19] Unlike the reactions of organoborons with diazocompounds such as ethyl diazoacetate, where an enol boronate is formed,[19] the B−C bond in the present process was expected to remain intact after reaction with CF_3CHN_2, thus giving rise to unprecedented organoboron compounds bearing an α-trifluoromethyl substituent.

By using the method reported by Carreira and coworkers,[18] stock solutions of CF_3CHN_2 in several organic solvents (heptanes, toluene, dichloromethane, and chlorobenzene) at varying concentrations (0.1–1 M) were prepared in 75–90% yield. With these stock solutions of CF_3CHN_2 in

---

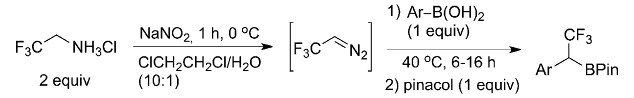
[*] O. A. Argintaru, D. Ryu, I. Aron, Prof. G. A. Molander
Roy and Diana Vagelos Laboratories, Department of Chemistry
University of Pennsylvania
231 South 34th Street, Philadelphia, PA 19104-6323 (USA)
E-mail: gmolandr@sas.upenn.edu

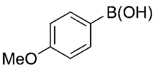
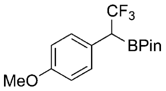
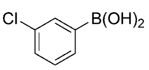
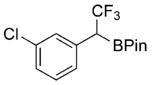
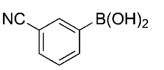
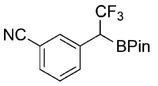
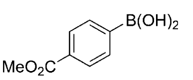
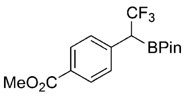
[**] We thank Frontier Scientific for boronic acids and potassium organotrifluoroborates. Financial support has been provided by the NIH (NIGMS R01 GM035249). Dr. Rakesh Kohli (University of Pennsylvania) is acknowledged for obtaining HRMS data. J.-B. Coty (University of Pennsylvania) is acknowledged for repeating the experiment using p-methoxyphenyltrifluoroborate (**2f**) and running the experiment using p-trifluoromethylphenyltrifluoroborate (**2h**).

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201308036.

hand, their reactivity with various boron species was investigated. Initial attempts were made with commercially available aryl pinacol boronates. No reactivity was observed with these substrates, and the starting materials were fully recovered. The lack of reactivity may be explained by the low Lewis acidity of boronate esters.[20] With boronic acids, reactivity was observed in various solvents and at different temperatures. After optimization of the reaction conditions, the desired α-trifluoromethylated organoborons were detected in good yields by ^{1}H NMR spectroscopy after quenching the reaction mixtures with pinacol (Table 1).

Table 1: Reactions of 2,2,2-trifluorodiazoethane with boronic acids.



Substrate	Product		Yield [%][a]
		**1a**	73 (38)[b]
			81
			85
			73

[a] Yields determined by ^{1}H NMR analysis of the crude reaction mixture. [b] Yield of isolated product. Pin = pinacol.

Although the yields of the desired products in the crude reaction mixtures were good, in most cases (especially when using electron-poor boronic acids) the α-trifluoromethylated pinacol boronates were prone to oxidation during purification using silica gel chromatography. In certain cases, simple exposure to air at room temperature led to the corresponding alcohols, and the yields of the isolated products suffered drastically. Conversion of the α-trifluoromethylated, tricoordinate boronic acids to the more stable tetracoordinate potassium organotrifluoroborates by quenching the crude reaction mixture with KHF_2 led to mixtures, and the desired products could not be isolated in high yields after successive recrystallizations.

In addition to the aforementioned purification problems, the use of boronic acids as limiting reagents in the reaction with 2,2,2-trifluorodiazoethane became rapidly unappealing for other reasons. Along with the well-known instability of some classes of boronic acids when exposed to air even at low temperatures,[21] their equilibrium with cyclic boroxines also leads to an uncertain stoichiometry. Furthermore, boronic acids and boroxines were reported to have different Lewis acidities and consequently different reactivity rates toward the diazo compounds.[19b]

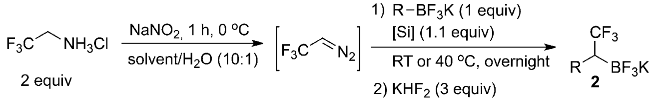
The use of potassium organotrifluoroborates (RBF_3K) as starting materials was envisioned as a more favorable alternative to boronic acids because of their precise stoichiometry and excellent stability across all classes of substrates (alkyl, alkenyl, alkynyl, aryl, and heteroaryls). Vedejs et al.[22a] and Kim and Matteson[22b] have shown that potassium organotrifluoroborates can be converted into dihaloboranes (RBX_2, X = F or Cl) upon treatment with TMSCl or $SiCl_4$. After screening a variety of silicon sources, solvents, and temperatures, the use of CH_2Cl_2 at room temperature or toluene at 40 °C, with TMSCl or *p*-tolyl$SiCl_3$ as a fluorophile proved optimal (Table 2). CH_2Cl_2 and toluene often provided similar results, but the conversion in toluene was slower than that in CH_2Cl_2 at room temperature. Therefore, a slight increase in temperature for the toluene reactions (40 °C) was necessary to achieve high conversions. During the optimization, it was observed that all reagents could be added at once, which obviated the step of preforming RBX_2 prior to the addition of the diazo solutions and facilitated the experimental setup.

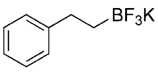
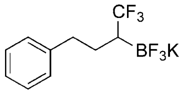
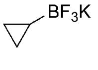
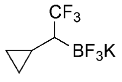
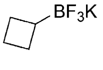
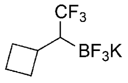
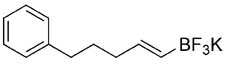
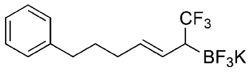
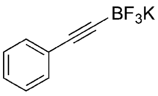
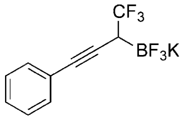
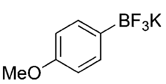
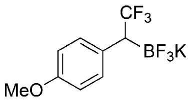
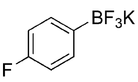
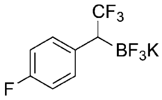
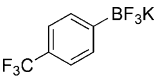
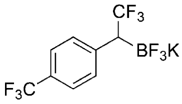
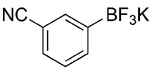
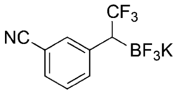
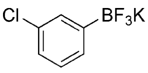
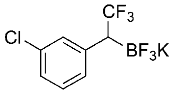
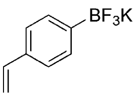
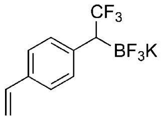
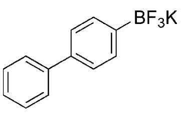
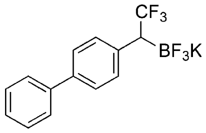
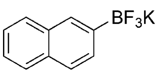
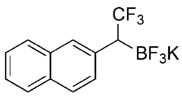
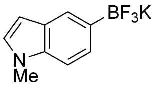
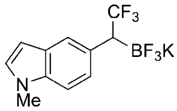
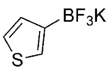
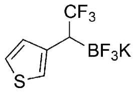
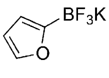
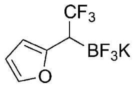
To avoid the oxidation problem mentioned in reference to Table 1, the crude reaction mixture was quenched with KHF_2, and the desired products were purified in good to excellent yields as tetracoordinate potassium trifluoroborates. The substrate scope of the transformation is extremely broad, and the purification only requires hot acetone extraction and recrystallization, thus avoiding the use of column chromatography. Primary and secondary alkyl trifluoroborates reacted in high yields (**2a**–**c**). Because of the importance of allylic and propargylic organoborons in organic synthesis,[23] our attention was then focused toward alkenyl and alkynyl potassium trifluoroborates as starting materials. These two classes of substrates smoothly underwent the reaction with 2,2,2-trifluorodiazoethane, thus leading to novel allylic and propargylic α-trifluoromethylated trifluoroborates which are indefinitely stable on the bench top (**2d**,**e**). No borotropic shift was observed when an alkenyltrifluoroborate was used, and no allenylboron was detected when starting with alkynyltrifluoroborate. The reaction of various aryltrifluoroborates was then investigated, and the desired α-trifluoromethylated benzylic products were obtained in good to excellent yields in all cases. Various functional groups such as ethers (**2f**), nitriles (**2i**), halides (**2j**), and olefins (**2k**) were tolerated under the reaction conditions, and both electron-donating and -withdrawing groups could be present on the aryltrifluoroborates without affecting the yields. Important heterocyclic systems such as indole (**2n**), thiophene (**2o**), and furan (**2p**) were also successfully converted.

All these classes of α-trifluoromethylated products isolated as trifluoroborates have been kept on the bench for over six months without any sign of decomposition. These trifluoroborates represent the first indefinitely stable α-trifluoromethylated alkylborons.

To demonstrate the potential value of the α-trifluoromethylated organoborons in synthesis, preliminary studies for the functionalization of the carbon–boron bond were performed. Reactions were carried out in situ on the α-trifluoromethylated, tricoordinate organoboron species. Oxidation was performed by quenching the crude reaction mixture with pinacol, and subsequent treatment with $NaOH/H_2O_2$ [Eq. (2)]. This method is complementary to

Table 2: Substrate scope of potassium organotrifluoroborates.



Substrate	Product		Solvent	[Si]	Yield [%][a]
		**2a**	CH_2Cl_2	TMSCl	71
		**2b**	toluene	TMSCl	80
		**2c**	toluene	TMSCl	78
		**2d**	CH_2Cl_2	*p*-tolyl-$SiCl_3$	78
		**2e**	CH_2Cl_2	TMSCl	92
		**2f**	CH_2Cl_2	*p*-tolyl-$SiCl_3$	71 (67)[b]
		**2g**	CH_2Cl_2	TMSCl	72
		**2h**	toluene	*p*-tolyl-$SiCl_3$	83
		**2i**	CH_2Cl_2	TMSCl	70
		**2j**	CH_2Cl_2	*p*-tolyl-$SiCl_3$	71
		**2k**	CH_2Cl_2	TMSCl	89
		**2l**	CH_2Cl_2	*p*-tolyl-$SiCl_3$	65
		**2m**	CH_2Cl_2	TMSCl	88
		**2n**	CH_2Cl_2	TMSCl	90
		**2o**	CH_2Cl_2	TMSCl	72
		**2p**	toluene	TMSCl	86

[a] Yield of the isolated product. [b] Reaction performed on a 10 mmol scale. TMS = trimethylsilyl.

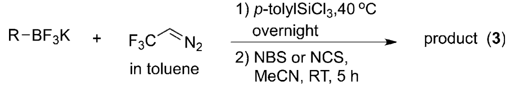
the synthesis of α-trifluoromethyl alcohols from aldehydes and the expensive Ruppert–Prakash reagent[24] or the reduction of trifluoromethyl ketones, which have limited commercial availability.[25]

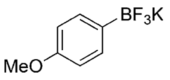
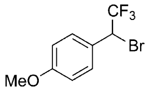
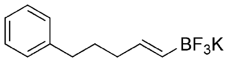
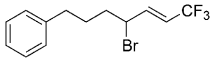
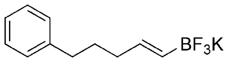
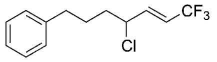
Methods to prepare benzylic α-trifluoromethyl bromides involve multistep syntheses, and require the isolation of the α-trifluoromethylated alcohol intermediates and subsequent treatment with stoichiometric amounts of NBS and triphenylphosphite, thus leading to low to moderate overall yields.[25a,26] In a one pot procedure, starting from the commercially available potassium *p*-methoxyphenyltrifluoroborate, the α-trifluoromethyl benzyl bromide **3b** was prepared in 51% yield without any further optimization (Table 3). Interestingly, when alkenyltrifluoroborates were used as starting materials, rearrangement occurred to provide the secondary allylic bromide and chloride in a regio- and stereodefined manner (**3c** and **3d**). To our best knowledge, this class of trifluoromethylated secondary allyl halides has never been reported. Previous literature reports only describe isolated multistep syntheses of a few primary trifluoromethylated allyl bromides and chlorides, along with their potential applications in organic transformations (S_N2, addition to carbonyls).[27]

Protodeboronation of the crude α-trifluoromethylated pinacol boronate was smoothly achieved using the reaction conditions reported by Aggarwal and co-workers [Eq. (3)].[28] Unlike any existing procedures,[29] this transformation provides an approach to metal-free trifluoroethylation of a variety of organic substructures. Thus, in addition to avoiding the transition-metal waste, the substrate scope of the trifluoroborate starting materials is very broad (as shown in Table 2), thus potentially allowing the introduction of CF_3CH_2 on primary and secondary alkyls, alkenyls, alkynyls, aryls, and heteroaryls by the same general experimental procedure.

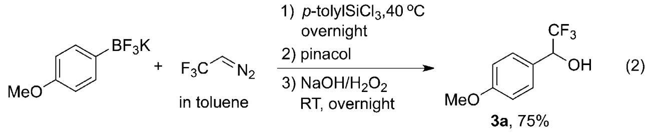
β-Fluoride elimination is a major unresolved problem when a trifluoromethyl group and a metal are situated on the same C(sp^3). For an α-trifluoromethylated organolithium or Grignard reagent, β-fluoride elimination occurs instantaneously unless strongly electron-withdrawing groups are introduced to stabilize the trifluoroethyl anions at very low temperatures.[10] The α-trifluoromethylated dihaloboranes reported herein could be heated to 40 °C under Ar without any sign of β-fluoride elimination. However, it was observed that a controlled elimination could be induced by increasing the temperature to 75 °C, wherein β-fluoride elimination occurred to form substituted 1,1-

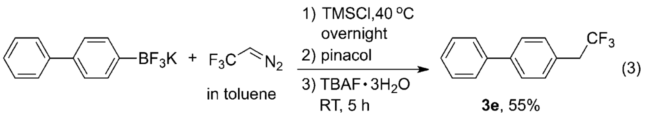
Table 3: Halogenation of α-trifluoromethyl organoborons.



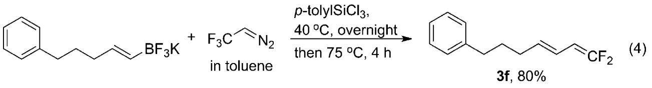
Substrate	Product		Yield [%][a]
		**3b**	51
		**3c**	60
		**3d**	61

[a] Yield of the isolated product. NBS = *N*-bromosuccinimide, NCS = *N*-chlorosuccinimide.



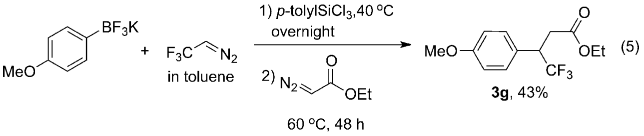


difluoro-1,3-butadienes[30] (**3f**). Although this transformation can be applied to aryl trifluoroborates to synthesize difluorostyrenes, higher yield and selectivity were obtained with an alkenyl trifluoroborate under these conditions [Eq. (4)].



Finally, to highlight another advantage of retaining the boron intact after the trifluorodiazoethane insertion, a reaction with a second diazo compound was performed. When ethyl diazoacetate (EDA) was added in situ to the α-trifluoromethylated dihaloborane, the double diazo insertion product was obtained in an overall (unoptimized) yield of 43%. After the insertion of EDA, the resulting boron enolate is rapidly protonated, thus leading directly to the observed ester.[19] It is important to note that this approach represents a complementary method to access the same class of molecules that are obtained by the addition of the Ruppert–Prakash reagent to α,β-unsaturated esters [Eq. (5)],[31] with the potential to provide access to greater structural diversity as well: the range of organoboron precursors available far exceeds that of the requisite α,β-unsaturated carbonyl substrates required for the conjugate addition reaction of the Ruppert reagent.

In conclusion, a family of shelf-stable α-trifluoromethylated organoborons has been generated for the first time. Not only is the method for generating these materials operationally simple and effective, but it can also be carried out without resorting to metal mediation. Numerous carbon–carbon and carbon–heteroatom bond-forming transformations appear to be feasible with these reagents, employing well-known reactivity patterns of organoborons. These reagents thus represent potentially powerful building blocks for selective incorporation of the CF_3 unit at sp^3-carbon centers in complex molecules.



Experimental Section

Potassium organotrifluoroborate (1 mmol) was added to a 20 mL Biotage microwave vial equipped with a stir bar. The vial was sealed and purged with argon three times. The solution of 2,2,2-trifluorodiazoethane in CH_2Cl_2 (ca. 0.5 M, 4 mL) or toluene (ca. 0.5 M, 4 mL) was added under Ar, then freshly distilled Me_3SiCl (120 mg, 1.1 mmol) or *p*-tolyl$SiCl_3$ (248 mg, 1.1 mmol) was added, and the reaction was stirred at room temperature (in CH_2Cl_2) or 40 °C (in toluene) overnight. The pressure was vented under Ar pressure. The reaction was cooled to 0 °C, then a saturated solution of KHF_2 (1 mL, 4.5 M in H_2O) was added dropwise under Ar. Acetone (3 mL) was added to increase the solubility and improve the stirring of the reaction. The reaction was allowed to warm to RT and stirred for an additional 30 min under argon. The solvent was evaporated from the crude reaction mixture, and the product was extracted into dry acetone to eliminate the inorganic salts. The acetone was evaporated and the desired product was recrystallized from the crude mixture.

Received: September 12, 2013
Published online: ■■ ■■, ■■■■

Keywords: boron · diazo compounds · silanes · synthetic methods · trifluoromethylation

[1] a) S. Purser, P. R. Moore, S. Swallow, V. Gouverneur, *Chem. Soc. Rev.* **2008**, *37*, 320–330; b) 30–40% of agrochemicals and 20–25% of pharmaceuticals on the market are estimated to contain fluorine: A. M. Thayer, *Chem. Eng. News* **2006**, *84* (33), 15–24.
[2] J. Scheirs, *Modern Fluoropolymers: High Performance Polymers for Diverse Applications*, Wiley, Chichester, **1997**.
[3] V. Gouverneur, O. Lozano in *Science of Synthesis Stereoselective Syntheses, Vol. 3* (Eds.: J. G. De Vries, G. A. Molander; P. A. Evans), Thieme, Stuttgart, **2011**, pp. 851–930.
[4] T. Yamazaki, T. Taguchi, I. Ojima in *Fluorine in Medicinal Chemistry and Chemical Biology* (Ed.: I. Ojima), Wiley-Blackwell, Chichester, **2009**, pp. 1–46.
[5] a) O. A. Tomashenko, V. Grushin, *Chem. Rev.* **2011**, *111*, 4475–4521; b) Y. Ye, M. Sanford, *Synlett* **2012**, 2005–2013; c) T. Besset, C. Schneider, D. Cahard, *Angew. Chem.* **2012**, *124*, 5134–5136; *Angew. Chem. Int. Ed.* **2012**, *51*, 5048–5050.
[6] Allylic and benzylic trifluoromethylations to afford C(sp^3)-CF_3 bonds: a) A. T. Parsons, S. L. Buchwald, *Angew. Chem.* **2011**, *123*, 9286–9289; *Angew. Chem. Int. Ed.* **2011**, *50*, 9120–9123; b) J. Xu, Y. Fu, D.-F. Luo, Y.-Y. Jiang, B. Xiao, Z.-J. Liu, T.-J. Gong, L. Liu, *J. Am. Chem. Soc.* **2011**, *133*, 15300–15303; c) X. Wang, Y. Ye, S. Zhang, J. Feng, Y. Xu, Y. Zhang, J. Wang, *J. Am.*

Chem. Soc. **2011**, *133*, 16410 – 16413; d) H. Kawai, T. Furukawa, Y. Nomura, E. Tokunga, N. Shibata, *Org. Lett.* **2011**, *13*, 3596 – 3599; e) R. Shimizu, H. Egami, Y. Hamashima, M. Sodeoka, *Angew. Chem.* **2012**, *124*, 4655 – 4658; *Angew. Chem. Int. Ed.* **2012**, *51*, 4577 – 4580; f) S. Mizuta, O. Galicia-Lopez, K. M. Engle, S. Verhoog, K. Wheelhouse, G. Rassias, V. Gouverneur, *Chem. Eur. J.* **2012**, *18*, 8583 – 8587; g) L. Zhu, S. Liu, J. T. Douglas, R. A. Altman, *Chem. Eur. J.* **2013**, DOI: 10.1002/chem.201302328; h) L. Chu, F.-L. Qing, *Org. Lett.* **2012**, *14*, 2106 – 2109.

[7] α- or β-Trifluoromethylated carbonyl compounds containing $C(sp^3){-}CF_3$ bonds: a) P. V. Pham, D. A. Nagib, D. W. C. MacMillan, *Angew. Chem.* **2011**, *123*, 6243 – 6246; *Angew. Chem. Int. Ed.* **2011**, *50*, 6119 – 6122; b) A. T. Herrmann, L. L. Smith, A. Zakarian, *J. Am. Chem. Soc.* **2012**, *134*, 6976 – 6979; c) Q.-H. Deng, H. Wadepohl, L. H. Gade, *J. Am. Chem. Soc.* **2012**, *134*, 10769 – 10772; d) V. Matoušek, A. Togni, V. Bizet, D. Cahard, *Org. Lett.* **2011**, *13*, 5762 – 5765; e) X. Liu, F. Xiong, X. Huang, L. Xu, P. Li, X. Wu, *Angew. Chem.* **2013**, *125*, 7100 – 7104; *Angew. Chem. Int. Ed.* **2013**, *52*, 6962 – 6966; f) Z.-M. Chen, W. Bai, S.-H. Wang, B.-M. Yang, Y.-Q. Tu, F.-M. Zhang, *Angew. Chem.* **2013**, *125*, 9963 – 9967; *Angew. Chem. Int. Ed.* **2013**, *52*, 9781 – 9785.

[8] General methods for the formation of $C(sp^3){-}CF_3$ bonds: a) J. Xu, B. Xiao, C.-Q. Xie, D.-F. Luo, L. Liu, Y. Fu, *Angew. Chem.* **2012**, *124*, 12719 – 12722; *Angew. Chem. Int. Ed.* **2012**, *51*, 12551 – 12554; b) S. Mizuta, S. Verhoog, K. M. Engle, T. Khotavivattana, M. O'Duill, K. Wheelhouse, G. Rassias, M. Medebielle, V. Gouverneur, *J. Am. Chem. Soc.* **2013**, *135*, 2505 – 2508; c) D. J. Wilger, N. J. Gesmundo, D. A. Nicewicz, *Chem. Sci.* **2013**, *4*, 3160 – 3165; X. Wu, L. Chu, F.-L. Qing, *Angew. Chem.* **2013**, *125*, 2254 – 2258; *Angew. Chem. Int. Ed.* **2013**, *52*, 2198 – 2202.

[9] F. Lovering, J. Bikker, C. Humblet, *J. Med. Chem.* **2009**, *52*, 6752 – 6756.

[10] K. Uneyama, T. Katagiri, H. Amii, *Acc. Chem. Res.* **2008**, *41*, 817 – 829.

[11] a) H. C. Brown, G. M. Chen, M. P. Jenning, P. V. Ramachandran, *Angew. Chem.* **1999**, *111*, 2088 – 2090; *Angew. Chem. Int. Ed.* **1999**, *38*, 2052 – 2054; b) P. V. Ramachandran, M. P. Jenning, *Org. Lett.* **2001**, *3*, 3789 – 3790.

[12] To our best knowledge, 1-methyl-2,2,2-trifluoroethyl pinacolborane is the only α-CF_3 alkylboron reported and fully characterized. However, the compound was obtained in low yeids (4 – 11 %), in an inseparable mixture with other products: T. Braun, M. A. Solomon, K. Altenhöner, M. Teltevskoi, S. Hinze, *Angew. Chem.* **2009**, *121*, 1850 – 1854; *Angew. Chem. Int. Ed.* **2009**, *48*, 1818 – 1822.

[13] a) D. L. Sandrock in *Science of Synthesis Cross Coupling and Heck-Type Reactions*, *Vol. 1* (Eds.: G. A. Molander, J. P. Wolfe, M. Larhed), Thieme, Stuttgart, **2013**, pp. 323 – 358; b) D. Imao, B. W. Glasspoole, V. S. Laberge, C. M. Crudden, *J. Am. Chem. Soc.* **2009**, *131*, 5024 – 5025; c) C.-T. Yang, Z.-Q. Zhang, H. Tajuddin, C.-C. Wu, J. Liang, J.-H. Liu, Y. Fu, M. Czyzewska, P. G. Steel, T. B. Marder, L. Liu, *Angew. Chem.* **2012**, *124*, 543 – 547; *Angew. Chem. Int. Ed.* **2012**, *51*, 528 – 532.

[14] a) G. A. Molander, V. Colombel, V. Braz, *Org. Lett.* **2011**, *13*, 1852 – 1855; b) G. Sorin, R. M. Mallorquin, Y. Contie, A. Baralle, M. Malacria, J.-P. Goddard, L. Fensterbank, *Angew. Chem.* **2010**, *122*, 8903 – 8905; *Angew. Chem. Int. Ed.* **2010**, *49*, 8721 – 8723.

[15] a) A. Ros, V. K. Aggarwal, *Angew. Chem.* **2009**, *121*, 6407 – 6410; *Angew. Chem. Int. Ed.* **2009**, *48*, 6289 – 6292; b) C. Zhang, J. Yun, *Org. Lett.* **2013**, *15*, 3416 – 3419.

[16] a) S. N. Mlynarski, A. S. Karns, J. P. Morken, *J. Am. Chem. Soc.* **2012**, *134*, 16449 – 16451; b) D. S. Matteson, G. Y. Kim, *Org. Lett.* **2002**, *4*, 2153 – 2155; c) V. Bagutski, T. G. Elford, V. K. Aggarwal, *Angew. Chem.* **2011**, *123*, 1112 – 1115; *Angew. Chem. Int. Ed.* **2011**, *50*, 1080 – 1083; d) H. C. Brown, K.-W. Kim, T. E. Cole, B. Singaram, *J. Am. Chem. Soc.* **1986**, *108*, 6761 – 6764.

[17] H. Gilman, R. G. Jones, *J. Am. Chem. Soc.* **1943**, *65*, 1458 – 1460.

[18] a) B. Morandi, E. M. Carreira, *Angew. Chem.* **2010**, *122*, 950 – 953; *Angew. Chem. Int. Ed.* **2010**, *49*, 938 – 941; b) B. Morandi, E. M. Carreira, *Angew. Chem.* **2010**, *122*, 4390 – 4392; *Angew. Chem. Int. Ed.* **2010**, *49*, 4294 – 4296; c) B. Morandi, E. M. Carreira, *Angew. Chem.* **2011**, *123*, 9251 – 9254; *Angew. Chem. Int. Ed.* **2011**, *50*, 9085 – 9088; d) B. Morandi, B. Mariampillai, E. M. Carreira, *Angew. Chem.* **2011**, *123*, 1133 – 1136; *Angew. Chem. Int. Ed.* **2011**, *50*, 1101 – 1104.

[19] a) J. Hooz, J. N. Bridson, J. G. Calzada, H. C. Brown, M. M. Midland, A. B. Levy, *J. Org. Chem.* **1973**, *38*, 2574 – 2576; b) C. Peng, W. Zhang, G. Yan, J. Wang, *Org. Lett.* **2009**, *11*, 1667 – 1670.

[20] C. E. H. Bawn, A. Ledwith, P. Matthies, *J. Polym. Sci.* **1959**, *34*, 93 – 106.

[21] D. M. Knapp, E. P. Gillis, M. D. Burke, *J. Am. Chem. Soc.* **2009**, *131*, 6961 – 6963.

[22] a) E. Vedejs, R. W. Chapman, S. C. Fields, S. Lin, M. R. Schrimpf, *J. Org. Chem.* **1995**, *60*, 3020 – 3027; b) B. J. Kim, D. S. Matteson, *Angew. Chem.* **2004**, *116*, 3118 – 3120; *Angew. Chem. Int. Ed.* **2004**, *43*, 3056 – 3058.

[23] a) H. Lachance, D. G. Hall in *Organic Reactions*, *Vol. 73* (Ed.: S. E. Denmark), Wiley, Hoboken, **2008**; b) M. J. Hesse, C. P. Butts, C. L. Willis, V. K. Aggarwal, *Angew. Chem.* **2012**, *124*, 12612 – 12616; *Angew. Chem. Int. Ed.* **2012**, *51*, 12444 – 12448; c) B. M. Partridge, L. Chausset-Boissarie, M. Burns, A. P. Pulis, V. K. Aggarwal, *Angew. Chem.* **2012**, *124*, 11965 – 11969; *Angew. Chem. Int. Ed.* **2012**, *51*, 11795 – 11799.

[24] G. K. S. Prakash, R. Krishnamurti, G. A. Olah, *J. Am. Chem. Soc.* **1989**, *111*, 393 – 395.

[25] a) Y. Yamauchi, S. Hara, H. Senboku, *Tetrahedron* **2010**, *66*, 473 – 479; b) D. M. Rudzinski, C. B. Kelly, N. E. Leadbeater, *Chem. Commun.* **2012**, *48*, 9610 – 9612.

[26] T. Okano, H. Sugiura, M. Fumoto, H. Matsubara, T. Kusukawa, M. Fujita, *J. Fluorine Chem.* **2002**, *114*, 91 – 98.

[27] a) V. Martin, H. Molines, C. Wekselman, *J. Fluorine Chem.* **1993**, *62*, 63 – 68; b) T.-P. Loh, X.-R. Li, *Eur. J. Org. Chem.* **1999**, 1893 – 1899; c) Q. Chen, X.-L. Qiu, F.-L. Qing, *J. Org. Chem.* **2006**, *71*, 3762 – 3777; d) G. A. Pinna, G. Cignarella, S. Ruiu, G. Loriga, G. Murineddu, S. Villa, G. E. Grella, G. Cossu, W. Fratta, *Bioorg. Med. Chem.* **2003**, *11*, 4015 – 4026.

[28] S. Nave, R. P. Sonawane, T. G. Elford, V. K. Aggarwal, *J. Am. Chem. Soc.* **2010**, *132*, 17096 – 17098.

[29] a) Y. Zhao, J. Hu, *Angew. Chem.* **2012**, *124*, 1057 – 1060; *Angew. Chem. Int. Ed.* **2012**, *51*, 1033 – 1036; b) A. Liang, X. Li, D. Liu, J. Li, D. Zou, Y. Wu, Y. Wu, *Chem. Commun.* **2012**, *48*, 8273 – 8275; c) S. Matsubara, M. Mitani, K. Utimoto, *Tetrahedron Lett.* **1987**, *28*, 5857 – 5860; d) Y.-S. Feng, C.-Q. Xie, W.-L. Qiao, H.-J. Xu, *Org. Lett.* **2013**, *15*, 936 – 939; e) L. M. Kreis, S. Krautwald, N. Pfeiffer, R. E. Martin, E. M. Carreira, *Org. Lett.* **2013**, *15*, 1634 – 1637.

[30] a) J. Ichikawa, C. Ikeura, T. Minami, *Synlett* **1992**, 739 – 740; b) J. Ichikawa, *J. Fluorine Chem.* **2000**, *105*, 257 – 263.

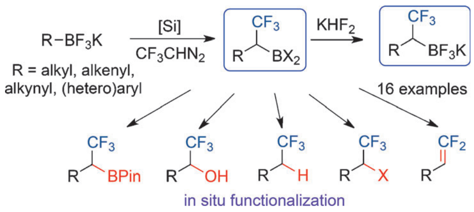
[31] A. A. Zemtsov, V. V. Levin, A. D. Dilman, M. I. Struchkova, P. A. Belyakov, V. A. Tartakovsky, *Tetrahedron Lett.* **2009**, *50*, 2998 – 3000.

Communications

Synthetic Methods

O. A. Argintaru, D. Ryu, I. Aron,
G. A. Molander* ________ ■■■■–■■■■

Synthesis and Applications of α-Trifluoromethylated Alkylboron Compounds



RBF_3K is a chemist's BFF: A metal-free synthetic route to unprecedented organoboron compounds bearing an α-trifluoromethyl substituent, employing a variety of trifluoroborate (RBF_3K) starting materials, is reported. These substrates represent the first isolated α-trifluoromethylated alkylboron building blocks, and these reagents lead to a variety of useful bench-stable, synthetic intermediates. Pin = pinacol.